

Live Complexity Training

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LCT Resources: Transdiagnostics

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Theory: There exists a complexity-based transdiagnostic biomarker of sickness behavior and its remediation.

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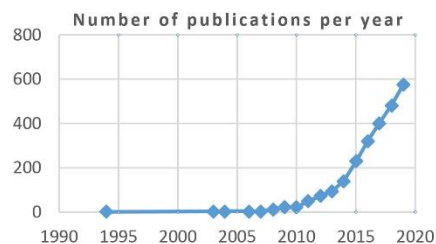
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Introduction ▲

For a decade or more the National Institute of Mental Health – NIMH – has encouraged an important [Research Domain Criteria \(RDoC\)](#) model. The significance to clinicians and patients is clear. The uncertainty of diagnoses, the abundance of comorbidities, the elusiveness of epigenetic, environmental, social and habitual trauma factors, the cost of a sickening planet all beg for a simpler and more practical alternative to a stastical manual of industry-supported existing conditions.

To this end the RDoC authors urge utilization and exploration of “transdiagnostic” markers of sickness behavior that can be monitored in anyone, in order to judge clinical progression. This applies whether the diagnosis is known, comorbid, unknown or unknowable. A transdiagnostic biomarker (TDBM) can indicate whether an intervention is moving a client toward or away from sickness behavior. The actual value of a measurement along a transdiagnostic dimension such as heart rate variability (HRV) or EEG complexity is usually not what is important. What is most important is the ability to respond to an adaptogenic intervention or challenge by moving toward even more adaptive complexification and the development of skillful means.

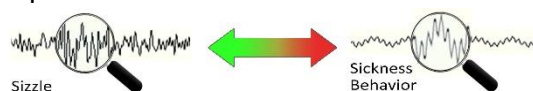


The chart to the left shows the increasing number of pubmed.gov articles that discuss [transdiagnostics](#). The document you are reading below discusses transdiagnostic biomarkers as they apply to clinicians and patients. Of special interest is the nature of the transdiagnostic biomarkers that we can observe in physiological signals such as EEG, HRV, GSR, etc. These markers are usually described as movement of a measurement along a single dimension (e.g., to the right or left).

Such biomarkers may improve through training as well as other adaptogens and clinical interventions.

Real clinical movement towards or away from sickness behavior should be detectable by any and all imaging modalities. These are called **transmodal transdiagnostic** biomarkers. [Live Complexity Training](#) (LCT) is a form of Technology-Assisted Self-Regulation / Self-Realization (TASR) that aims to teach the user how to recognize and regulate these transdiagnostic state changes especially in the electroencephalogram (EEG).

Since the movement along a transdiagnostic biomarker after intervention may be the most important indicator available it becomes important to evaluate the balance between



adaptogens (movement to left) versus anti-adaptogens (movement to right). Movement to the right in this figure leads to increased presence of

fast waves riding on slow waves. In its most classic form this EEG pattern is called a “delta brush” pattern. It is characteristic of premature birth as well as autoimmune and other

encephalopathies. Such “sickness in the signals” is characteristic of all programmed apoptosis of the cell and apoptosis of the self.

Movement to the left is characteristic of 1) normal growth, maturation and evolution; 2) recovery from sleep deprivation; 3) recovery from all forms of sickness behavior. Movement to the right is characteristic of 1) developmental delay and cognitive deterioration; 2) loss of restorative sleep; 3) all forms of sickness behavior.

Interventions that reduce the redundant fast waves and slow waves and that lead to more complexity are called adaptogens. Those that reduce the complexity of the information in the signal (i.e., move our signal to the right toward sickness behavior) are called anti-adaptogens. In this simple model what is important is the balance between adaptogenic and anti-adaptogenic influences. These influences are usually easy to see in the raw EEG.

Live Complexity Training (LCT) is a type of neurofeedback that uses digital signal processing (quantified qEEG) to confirm or extend the visual findings (movement along the transdiagnostic continuum).

Anhedonia ▲

Ducasse D, et al (2020) - **Association between anhedonia and suicidal events in patients with mood disorders: A 3-year prospective study.** *Depress Anxiety*. 2020 Jul 11. [\[ABS\]](#)

As almost all mental disorders are associated with increased suicidal-related behavior, anhedonia might be a ***trans-diagnostic*** dimension to target for suicide prevention. ...significant association between anhedonia and suicide ideation in patients with mood disorders stresses the need of targeting hedonia in mood disorders, and of research focusing on the position to pleasure in life through eudaimonia.

Mumper E, et al (2020) - **Developmental antecedents of social anhedonia: The roles of early temperament and sex.** *Dev Psychopathol*. 2020 May 7:1-9. [\[ABS\]](#)

Social anhedonia is well established as a ***transdiagnostic*** factor, but little is known about its development. This study examined whether temperament and parenting in early childhood predict social anhedonia in early adolescence. ...Our results indicated that, at age 3, lower observed sociability predicted higher levels of social anhedonia at age 12. These associations were moderated by child sex, such that males with diminished sociability reported greater social anhedonia. These findings indicate that predictors of early adolescent social anhedonia are evident as early as 3 years of age. However, these effects were evident only for males, suggesting that the pathways to social anhedonia in early adolescence differ as a function of sex.

Levchuk LA, et al (2020) - **Exploring Brain Derived Neurotrophic Factor and Cell Adhesion Molecules as Biomarkers for the Transdiagnostic Symptom Anhedonia in Alcohol Use Disorder and Comorbid Depression.** . Front Psychiatry. 2020 Apr 20;11:296. [[FULL TEXT](#)]

Alcohol Use Disorder (AUD) and depressive disorder often co-exist and have a shared heritability. ...This pilot study suggests that peripheral levels of BDNF and neuronal cell adhesion molecules (NCAM) might be reduced in AUD with and without comorbid mood disorder. Since low BDNF levels were associated with self-reported anhedonia across these conditions, BDNF and anhedonia might reflect *transdiagnostic* aspects involved in AUD and depression.

Liang YS, et al (2020) - **Social anhedonia across mental disorders: A validation study of the Anticipatory and Consummatory Interpersonal Pleasure Scale.** Psych J. 2020 Apr;9(2):160-162. [[ABS](#)]

The present study validated the Chinese version of the Anticipatory and Consummatory Interpersonal Pleasure Scale (ACIPS) in a group of patients with mental disorders. The results replicated the four-factor structure of the ACIPS in a Chinese setting and showed good discrimination validity.

Watson R, et al (2020) - **Understanding anhedonia: a qualitative study exploring loss of interest and pleasure in adolescent depression.** Eur Child Adolesc Psychiatry. 2020 Apr;29(4):489-499. [[FULL TEXT](#)]

Anhedonia (or loss of interest and pleasure) is a core symptom of depression and may predict poor treatment outcome. However, little is known about the subjective experience of anhedonia, and it is rarely targeted in psychological treatment for depression. ...

Thematic analysis was used to identify important aspects of adolescents' experiences. Four main themes were identified: (1) experiencing a loss of joy and a flattening of emotion; (2) struggling with motivation and active engagement; (3) losing a sense of connection and belonging; and (4) questioning sense of self, purpose, and the bigger picture.

The results challenge the framing of anhedonia as simply the loss of interest and pleasure. Adolescents reported a range of experiences that mapped closely onto the cluster of negative symptoms associated with schizophrenia and were similar to the sense of 'apathy' characteristic in Parkinson's disease. This highlights the potential benefit of taking a trans-diagnostic approach to understanding and treating reward deficits associated with mental health problems.

Gadow KD, et al (2020) - **Social Anhedonia in Children and Adolescents with Autism Spectrum Disorder and Psychiatry Referrals**. J Clin Child Adolesc Psychol. 2020 Mar-Apr;49(2):239-250. [\[ABS\]](#)

Lack of syndrome specificity supports the notion that SA is a useful **transdiagnostic** symptom phenotype in referred youth and challenges traditional conceptualizations of ASD as a categorical clinical phenotype.

Naguy A, et al (2020) - **Anhedonia as a transdiagnostic construct**. Asian J Psychiatr. 2020 Feb;48:101604. [\[REF\]](#)

Spano MC, et al (2019) - **Anhedonia across borders: Transdiagnostic relevance of reward dysfunction for noninvasive brain stimulation endophenotypes**. CNS Neurosci Ther. 2019 Nov;25(11):1229-1236. [\[FULL TEXT\]](#)

Anhedonia is a transdiagnostic psychopathological dimension, consisting in the impaired ability to experience pleasure. ...Anhedonia is an underexplored condition in neuromodulation trials. It may represent a valuable transdiagnostic dimension that requires further examination in order to discover new clinical predictors for treatment response.

Barkus E, et al (2019) - **A Transdiagnostic Perspective on Social Anhedonia**. Front Psychiatry. 2019 Apr 24;10:216. [\[Full Text\]](#)

...psychosis continuum, depressive disorder, posttraumatic stress disorder, eating disorders, and autism spectrum disorders, along with developmental and neurobiological factors. ...Consistent across disorders is diminished pleasure from social situations, subsequent withdrawal, and poorer social functioning in those who express social anhedonia. Nonetheless, feelings of loneliness often remain, which suggests the need for social connection is not entirely absent. Adolescence is a particularly important period of social and neural development and may provide a valuable window on the developmental origins of social anhedonia. ...Adaptive social functioning is key to recovery from mental health disorders; therefore, understanding the intricacies of social anhedonia will help to inform treatment and prevention strategies for a range of diagnostic categories.

Pushkarskaya H, et al (2019) - **Contrasting contributions of anhedonia to obsessive-compulsive, hoarding, and post-traumatic stress disorders**. J Psychiatr Res. 2019 Feb;109:202-213. [\[ABS\]](#)

Anhedonia is a **transdiagnostic** construct that can occur independent of other symptoms of depression; ... Response time during a gambling task, an index of difficulty of making value-based choices, significantly correlated with anhedonia in individuals with OCD and individuals with HD, even after controlling for general depression, but not in

individuals with PTSD. The results suggest a unique contribution of one aspect of anhedonia in obsessive-compulsive disorder and confirm the importance of investigating the role of anhedonia **transdiagnostically** beyond affective and psychotic disorders.

Szczypiński JJ, et al (2018) - **Dopamine dysregulation hypothesis: the common basis for motivational anhedonia in major depressive disorder and schizophrenia?** Rev Neurosci. 2018 Sep 25;29(7):727-744 [[ABS](#)]

...we investigated whether motivational anhedonia is the common symptom across MDD and SCH. With regard to the similarities and differences between the neural mechanisms of MDD and SCH, here we expand the current knowledge of motivation deficits and present the common underlying mechanism of motivational anhedonia - the dopamine dysregulation hypothesis - stating that any prolonged dysregulation in tonic dopamine signaling that exceeds the given equilibrium can lead to striatal dysfunction and motivational anhedonia. The implications for further research and treatment of MDD and SCH are also discussed.

Lambert C, et al (2018) - **Anhedonia in depression and schizophrenia: A transdiagnostic challenge.** CNS Neurosci Ther. 2018 Jul;24(7) [[FULL TEXT](#)]

Anhedonia as a clinical presentation of reward circuit dysregulation is an important and relatively undertreated symptom of both SZ and MDD. In order to improve patient outcomes and quality of life, it is important to consider how anhedonia fits into both diagnoses.

Swardfager W, et al (2016) - **Mapping inflammation onto mood: Inflammatory mediators of anhedonia.** Neurosci Biobehav Rev. 2016 May;64:148-66. [[ABS](#)]

Evidence supports inflammatory involvement in mood and cognitive symptoms across psychiatric, neurological and medical disorders; however, inflammation is not a sensitive or specific characteristic of these diagnoses. The National Institute of Mental Health Research Domain Criteria (RDoC) ask for a shift away from symptom-based diagnoses toward a transdiagnostic neurobiological focus in the study of brain illnesses. The RDoC matrix may provide a useful framework for integrating the effects of inflammation on brain function. Based on preclinical and clinical findings, relevant relationships span negative and positive valence systems, cognitive systems, systems for social processes and arousal/regulatory systems. As an exemplar, we consider the psychopathological domain of anhedonia, conceptualizing the relevance of inflammation (e.g., cellular immunity) and downstream processes ... We discuss implications across illnesses affecting the brain, including infection, major depressive disorder, stroke, Alzheimer's disease and type 2 diabetes.

Barkus E, et al (2019) - **A Transdiagnostic Perspective on Social Anhedonia.** Front Psychiatry. 2019 Apr 24;10:216. [[FULL TEXT](#)]

Consistent across disorders is diminished pleasure from social situations, subsequent withdrawal, and poorer social functioning in those who express social anhedonia. Nonetheless, feelings of loneliness often remain, which suggests the need for social connection is not entirely absent. Adolescence is a particularly important period of social and neural development and may provide a valuable window on the developmental origins of social anhedonia. Adaptive social functioning is key to recovery from mental health disorders; therefore, understanding the intricacies of social anhedonia will help to inform treatment and prevention strategies for a range of diagnostic categories.

Whitton AE, et al (2015) - **Reward processing dysfunction in major depression, bipolar disorder and schizophrenia.** Curr Opin Psychiatry. 2015 Jan;28(1):7-12. [\[FULL TEXT\]](#)

Emerging evidence indicates the presence of reward processing abnormalities across all three disorders, supporting a transdiagnostic approach. ...New evidence of reward processing abnormalities in MDD, bipolar disorder and schizophrenia has led to a greater understanding of the neural processes associated with symptomatology common across these conditions (e.g., anhedonia).

Zhang B, et al (2016) - **Mapping anhedonia-specific dysfunction in a transdiagnostic approach - an ALE meta-analysis.** Brain Imaging Behav. 2016 Sep;10(3):920-39. [\[FULL TEXT\]](#)

Anxiety / Depression ▲

Surova G, et al (2021) - **Fatigue and brain arousal in patients with major depressive disorder.** Eur Arch Psychiatry Clin Neurosci. 2021 Apr;271(3):527-536. [\[FULL TEXT\]](#)

Barrio-Martínez S, et al (2021) - **Factors differentiating panic disorder with and without comorbid symptoms of depression.** Psychol Psychother. 2021 May 16. [\[ABS\]](#)

These findings appear to support a transdiagnostic treatment approach for PD, which may be useful regardless of whether comorbid depression is present or not. ... Somatic symptoms were associated with a higher probability of being in the PD + MDD group.

Hijne K, et al (2020) - **The association of changes in repetitive negative thinking with changes in depression and anxiety.** J Affect Disord. 2020 Oct 1;275:157-164. [\[ABS\]](#)

Repetitive negative thinking (RNT) is a common feature of different mental disorders in the affective spectrum. Most measures of RNT are disorder-specific and measure e.g. rumination in depression or worry in anxiety. ...The findings suggest that RNT is not primarily an index of disorder status or epiphenomenon of symptom severity and may

constitute a relatively stable transdiagnostic person characteristic.

Duyser FA, et al (2020) - **Negative memory bias as a transdiagnostic cognitive marker for depression symptom severity.** J Affect Disord. 2020 Sep 1;274:1165-1172. [\[ABS\]](#)

Negative memory bias is a strong risk factor for the development and maintenance of depression. Recent evidence also found negative memory bias in other mental disorders. ...Negative memory bias is characteristic of a depressotypic processing style and present in different mental disorders. It might play a mechanistic role in the development of (subclinical) co-occurrence between mental disorders.

Choi KW, et al (2020) - **Comorbid Anxiety and Depression: Clinical and Conceptual Consideration and Transdiagnostic Treatment.** Adv Exp Med Biol. 2020;1191:219-235. [\[ABS\]](#)

Although anxiety and depression have been considered as two distinct entities according to the diagnostic criteria, anxious depression (comorbid anxiety and depression) is relatively a common syndrome. According to the DSM-5 criteria, it uses "with anxious distress specifier" to define anxious depression in its MDD section. Anxious depression is known to have different neurobiological profiles compared to non-anxious depression. Several studies have revealed significant differences between anxious depression and non-anxious depression regarding the hypothalamic-pituitary-adrenal (HPA) axis function, structural and functional brain imaging findings, inflammation markers, etc. Patients with anxious depression were significantly more likely to be found in primary care setting and more likely to be associated with female gender, non-single, unemployed, less educated, and more severe depression. Previous reports also showed that patients with anxious depression had more frequent episodes of major depression and a higher risk of suicidal ideation and previous suicide attempts than those with non-anxious depression. Although anxious depression is known to be associated with poor treatment outcomes in several studies, recent researches have sought to find better treatment strategy to improve patients with anxious depression.

Çakici N, et al (2020) - **Altered peripheral blood compounds in drug-naïve first-episode patients with either schizophrenia or major depressive disorder: a meta-analysis.** Brain Behav Immun. 2020 Aug;88:547-558. [\[ABS\]](#)

Schizophrenia and major depressive disorder (MDD) are associated with increased risks of immunologic disease and metabolic syndrome. ...Both schizophrenia and MDD show alterations in growth and immune factors from disease onset. An altered glucose metabolism seems to be present from onset in schizophrenia. These findings support efforts for further research into transdiagnostic preventive strategies and augmentation therapy for those with immune or metabolic dysfunctions.

Bredemeier K, et al (2020) - **Pretreatment levels of rumination predict cognitive-behavioral therapy outcomes in a transdiagnostic sample of adults with anxiety-related disorders.** J

Anxiety Disord. 2020 Jul 30;75:102277. [\[ABS\]](#)

Increasing research has implicated rumination in the development and maintenance of many types of psychopathology, including anxiety-related disorders. ...Results revealed that pretreatment levels of rumination significantly predicted (lower) quality of life at the end of treatment, after accounting for baseline variance in quality of life. This finding remained robust when also accounting for demographics, depression, general anxiety, and diagnosis.

Lapidus RC, et al (2020) - **Heightened affective response to perturbation of respiratory but not pain signals in eating, mood, and anxiety disorders.** PLoS One. 2020 Jul 15;15(7):e0235346. [\[FULL TEXT\]](#)

Several studies have recently suggested that an abnormal processing of respiratory interoceptive and nociceptive (painful) stimuli may contribute to eating disorder (ED) pathophysiology. Mood and anxiety disorders (MA) are also characterized by abnormal respiratory symptoms, and show substantial comorbidity with ED. ...During breath-holding, both the ED and MA groups reported significantly more stress, feelings of suffocation, and suffocation fear than HC, with the ED group reporting the most severe symptoms. Moreover, anxiety sensitivity was related to suffocation fear only in the ED group. ...These findings underscore the presence of abnormal respiratory interoception in MA and suggest that hyperreactivity to respiratory signals may be a potentially overlooked clinical feature of ED.

Banica I, et al (2020) - **The error-related negativity (ERN) moderates the association between interpersonal stress and anxiety symptoms six months later.** . Int J Psychophysiol. 2020 Jul;153:27-36. [\[FULL TEXT\]](#)

One proposed trans-diagnostic neural risk marker for anxiety is the error-related negativity (ERN), a negative deflection in the event-related potential waveform occurring within 100 ms of error commission. ...Stress interacted with ERN magnitude to predict anxiety symptoms, whereby, for individuals with an enhanced ERN at time one, greater interpersonal stress over the course of a year was significantly associated with increased anxiety symptoms at time two, even controlling for anxiety symptoms at time one. These findings suggest that enhanced performance monitoring may render individuals more susceptible to the adverse effects of interpersonal stress, thereby increasing risk for heightened anxiety.

Roque AD, et al (2020) - **Stress-induced cortisol reactivity as a predictor of success in treatment for affective dimensions.** Psychoneuroendocrinology. 2020 Jun;116:104646. [\[ABS\]](#)

Response rates to first-line treatments for depression and anxiety remain unsatisfactory. Identification of predictors or moderators that can optimize treatment matching is of scientific and clinical interest. ...Cortisol reactivity was related to treatment outcome,

with average and higher levels of stress-induced cortisol response predicting greater decreases in symptoms throughout treatment and 6-month follow-up. ...Future studies should investigate how to enhance this therapeutic benefit through capitalizing on endogenous diurnal fluctuations or exogenous cortisol manipulation.

Wilner JG, et al (2020) - **Quality of Life in Heterogeneous Anxiety Disorders: Changes across Cognitive-Behavioral Treatments.** Behav Modif. 2020 May;44(3):343-364. [\[ABS\]](#)

Quality of life is lower among individuals with anxiety disorders; however, this construct is rarely a focus in treatment research. This study explores changes in quality of life in a randomized, controlled trial of several cognitive-behavioral treatments (CBTs) for anxiety disorders. Adults with heterogeneous anxiety disorders (N = 223) were randomly assigned to (a) **unified protocol** for **transdiagnostic** treatment of emotional disorders, (b) a single-disorder protocol targeting their principal diagnosis, or (c) a waitlist control condition, and assessed at baseline, posttreatment, and 6-month follow-up. At baseline, the sample evidenced deficits in quality of life, with no significant differences in quality of life across diagnoses or condition. Results suggest improved quality of life among participants in treatment, at similar rates across treatment condition and diagnostic category, and at levels significantly higher than the waitlist. Improvements were maintained through 6-month follow-up. This study supports CBT as effective in promoting quality of life.

Huang CC, et al (2020) - **Transdiagnostic and Illness-Specific Functional Dysconnectivity Across Schizophrenia, Bipolar Disorder, and Major Depressive Disorder.** Biol Psychiatry Cogn Neurosci Neuroimaging. 2020 May;5(5):542-553. [\[ABS\]](#)

Mental disorders are typically defined as distinct diagnostic entities, but similar patterns of clinical and cognitive impairments are frequently found across diagnostic groups. We investigated whether these transdiagnostic deficits result from common neural substrates across disorders or various illness-specific mechanisms, or a combination of both. ...Disconnectivity in the somatomotor network was a common transdiagnostic profile, while there were illness-specific patterns in different parts of the prefrontal cortex for different disorders. These findings suggest that prominent psychiatric disorders share common impairments, possibly linked to perception and motor output, as well as unique dysconnectivity profiles that hypothetically mediate the more distinctive features of the disorder-specific psychopathology.

Howlett JR, et al (2020) - **Where perception meets belief updating: Computational evidence for slower updating of visual expectations in anxious individuals.** J Affect Disord. 2020 Apr 1;266:633-638. [\[FULL TEXT\]](#)

Anxious individuals display slower updating of internal models used in perceptual processing, but not those used in decision-making. This deficit could contribute to exaggerated salience of harmless stimuli in anxiety. The results have implications for the

assessment and treatment of basic processing dysfunctions in anxiety.

Swales DA, et al (2020) - **Maternal Depressive Symptoms Predict General Liability in Child Psychopathology**. J Clin Child Adolesc Psychol. 2020 Mar 27:1-12. [[ABS](#)]

The current study examines how maternal depressive symptoms relate to child psychopathology when structured via the latent bifactor model of psychopathology, a new organizational structure of psychopathological symptoms consisting of a general common psychopathology factor (p-factor) and internalizing- and externalizing-specific risk. ...Findings suggest that maternal depressive symptoms are associated with transdiagnostic risk for broad child psychopathology (p-factor).

Yao N, et al (2020) - **The Influence of Intolerance of Uncertainty on Anxiety and Depression Symptoms in Chinese-speaking Samples: Structure and Validity of The Chinese Translation of The Intolerance of Uncertainty Scale**. J Pers Assess. 2020 Mar 27:1-10. [[ABS](#)]

..., contemporary theory of intolerance of uncertainty (IU) has emphasized the role of IU as the basic transdiagnostic mechanism underlying emotional disorders, and further empirical support is awaited. ... Using the bifactor model of the IUS-12 (Chinese translation), the hierarchical model of IU affecting anxiety and depression via neuroticism was supported.

Sauer-Zavala S, et al (2020) - **Treating depressive disorders with the Unified Protocol: A preliminary randomized evaluation**. J Affect Disord. 2020 Mar 1;264:438-445. [[FULL TEXT](#)]

This study aims to examine the efficacy of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP) for individuals diagnosed with a depressive disorder. ...In this exploratory set of analyses, the UP evidenced efficacy for reduction of depressive symptoms, adding to the growing support for its utility in treating depression.

Nasiri F, et al (2020) - **Augmenting the unified protocol for transdiagnostic treatment of emotional disorders with transcranial direct current stimulation in individuals with generalized anxiety disorder and comorbid depression: A randomized controlled trial**. J Affect Disord. 2020 Feb 1;262:405-413. [[ABS](#)]

The aim of the current study was to compare the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP) with and without transcranial direct current stimulation (tDCS) in individuals suffering from generalized anxiety disorder (GAD) and comorbid depression. ... UP+tDCS showed significantly greater reductions in post-treatment anxiety..., worry..., and anxiety sensitivity...relative to UP alone. ... These results suggest augmenting UP treatment with tDCS may be an efficacious strategy to improve treatment outcomes in GAD with comorbid depression

Silveira ÉM Júnior, et al (2020) - **Decoding rumination: A machine learning approach to a**

transdiagnostic sample of outpatients with anxiety, mood and psychotic disorders. J Psychiatr Res. 2020 Feb;121:207-213. [\[ABS\]](#)

Rumination is known to be associated with poor prognosis in mental health. This study suggests that rumination is a maladaptive coping style associated not only with worry, distress and illness severity, but also with socioeconomic status. Also, rumination demonstrated a specific association with panic disorder.

Moreton SG, et al (2020) - **Embedding existential psychology within psychedelic science: reduced death anxiety as a mediator of the therapeutic effects of psychedelics.** Psychopharmacology (Berl). 2020 Jan;237(1):21-32. [\[ABS\]](#)

Psychedelic therapies can engender enduring improvements in psychological well-being. ...we present a novel hypothesis that reduced death anxiety may be a key mechanism underpinning the therapeutic effects of psychedelics. ... We conclude that an awareness of the role of death anxiety in psychopathology has the potential to guide future research into psychedelic therapies.

Sambuco N, et al (2020) - **Transdiagnostic trauma severity in anxiety and mood disorders: Functional brain activity during emotional scene processing.** Psychophysiology. 2020 Jan;57(1):e13349. [\[ABS\]](#)

Experiencing a life-threatening event (to self or other) that prompts high fear, distress, and functional impairment was associated with reduced functional limbic-visual activity, independent of a PTSD diagnosis. The findings suggest that experienced trauma may be a **transdiagnostic** vulnerability factor contributing significantly to psychopathology in many patients with anxiety and mood disorders.

Seidl E, et al (2020) - **Response to ostracism in patients with chronic depression, episodic depression and borderline personality disorder a study using Cyberball.** J Affect Disord. 2020 Jan 1;260:254-262. [\[ABS\]](#)

Social exclusion (ostracism) can lead to interactional frustration and may play an important role as trigger and symptom amplifier in affective disorders. ... The present cross-diagnostic study compares the responses to social exclusion in patients with chronic depression (CD), episodic depression (ED) and borderline personality disorder (BPD) in comparison to a healthy control group.

Patients with CD showed a higher intensity of ostracism and aversive impact, as well as the wish to escape the situation (behavioral intention) compared to ED. In most categories, CD and ED had scores between BPD and healthy controls (with this sequence) and with BPD patients showing the largest difference to healthy controls. ... Moreover, psychotherapy in CD should focus on specific needs of CD patients for developing a functional coping in threatening interpersonal situations.

Schanche E, et al (2020) - **Participant experiences of change in mindfulness-based stress reduction for anxiety disorders.** *Int J Qual Stud Health Well-being*. 2020 Jan 1;15(1):1776094. [\[ABS\]](#)

Participants of mindfulness-based stress reduction (MBSR) both describe mindfulness as a tool to "fix" anxiety and as bringing about more fundamental change towards acceptance of their anxiety. The complexity of reported change corresponds with better handling of areas representing known transdiagnostic features of anxiety disorder, such as dysfunctional cognitive processes (including attentional biases), emotional dysregulation, avoidance behaviors, and maladaptive self-relatedness. This supports MBSR as a transdiagnostic approach to the treatment of anxiety disorders.

Robinson OJ, et al (2019) - **The translational neural circuitry of anxiety.** *J Neurol Neurosurg Psychiatry*. 2019 Dec;90(12):1353-1360. [\[ABS\]](#)

Anxiety is an adaptive response that promotes harm avoidance, but at the same time excessive anxiety constitutes the most common psychiatric complaint. Moreover, current treatments for anxiety—both psychological and pharmacological—hover at around 50% recovery rates. Improving treatment outcomes is nevertheless difficult, in part because contemporary interventions were developed without an understanding of the underlying neurobiological mechanisms that they modulate. ...We highlight the roles of subcortical regions (and their subunits) such as the bed nucleus of the stria terminalis, the amygdala, and the hippocampus, as well as their connectivity to cortical regions such as dorsal medial and lateral prefrontal/cingulate cortex and insula in maintaining anxiety responding. We discuss how this circuitry might be modulated by current treatments before finally highlighting areas for future research that might ultimately improve treatment outcomes for this common and debilitating *transdiagnostic* symptom.

Menzies RE, et al (2019) - **The relationship between death anxiety and severity of mental illnesses.** *Br J Clin Psychol*. 2019 Nov;58(4):452-467. [\[ABS\]](#)

Death anxiety has been implicated theoretically and empirically in mental health and has been proposed to be a *transdiagnostic* construct. ...Across the sample, death anxiety was a strong predictor of psychopathology, including the number of lifetime diagnoses, medications, hospitalizations, distress/impairment, depression, anxiety, and stress ... Large to very large correlations were also consistently found between a measure of death anxiety and the symptom severity of 12 disorders. Neither meaning in life nor attachment style moderated the associations between death fears and psychopathology. ..., death anxiety significantly predicted symptom severity. Results may suggest the need for novel treatments which specifically target fears of death

Janiri D, et al (2019) - **Shared Neural Phenotypes for Mood and Anxiety Disorders: A Meta-analysis of 226 Task-Related Functional Imaging Studies.** *JAMA Psychiatry*. 2019 Oct 30;77(2):1-

8. [\[FULL TEXT\]](#)

Major depressive disorder, bipolar disorder, posttraumatic stress disorder, and anxiety disorders are highly comorbid and have shared clinical features. It is not yet known whether their clinical overlap is reflected at the neurobiological level. OBJECTIVE: To detect **transdiagnostic** convergence in abnormalities in task-related brain activation. In mood disorders, posttraumatic stress disorder, and anxiety disorders, the most consistent **transdiagnostic** abnormalities in task-related brain activity converge in regions that are primarily associated with inhibitory control and salience processing. Targeting these shared neural phenotypes could potentially mitigate the risk of affective morbidity in the general population and improve outcomes in clinical populations.

Mellick WH, et al (2019) - **Experiential Avoidance Predicts Persistence of Major Depressive Disorder and Generalized Anxiety Disorder in Late Adolescence.** J Clin Psychiatry. 2019 Oct 22;80(6):18m12265. [\[FULL TEXT\]](#)

Experiential avoidance (EA) is a transdiagnostic construct that may underlie the high comorbidity between major depressive disorder (MDD) and generalized anxiety disorder (GAD). ...EA appears to be an important predictor of MDD and GAD symptomatology in older adolescents, potentially serving as a treatment target.

El Bouhaddani S, et al (2019) - **Transdiagnostic school-based intervention for adolescents with early persistent psychiatric symptoms: An initial single-group effect study.** Early Interv Psychiatry. 2019 Oct;13(5):1199-1207. [\[ABS\]](#)

Mental health intervention programs for adolescents generally focus on specific symptoms, such as anxiety or depression. Psychiatric symptoms in adolescence are often heterogeneous, transient and shift over time. These characteristics require a **transdiagnostic** approach with emphasis on positive psychological development. This study aimed to examine the feasibility and effectiveness of Mastermind, a novel **transdiagnostic** intervention targeting general underlying mechanisms of psychiatric symptoms in adolescents.

A simple two-step school-based screening can identify adolescents with persistent psychiatric symptoms. The Mastermind **transdiagnostic** group intervention may be effective to reduce psychiatric symptoms, enhance self-esteem and lower the risk for developing psychiatric disorders.

Anderson R, et al (2019) - **Testing relationships between metacognitive beliefs, anxiety and depression in cardiac and cancer patients: Are they transdiagnostic?** J Psychosom Res. 2019 Sep;124:109738. [\[ABS\]](#)

Findings support the metacognitive model, suggesting that a common set of metacognitive factors contribute to psychological distress, particularly anxiety. Uncontrollability

and danger metacognitions and positive beliefs about worry appear to make independent contributions to anxiety irrespective of type of physical illness. While metacognitive beliefs were not reliably associated with depressive symptoms this may be because the current sample exhibited low depression scores.

Park SC, et al (2019) - **Diagnostic Issues of Depressive Disorders from Kraepelinian Dualism to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.** Psychiatry Investig. 2019 Sep;16(9):636-644. [\[FULL TEXT\]](#)

Staples LG, et al (2019) - **Internet-delivered treatment for young adults with anxiety and depression: Evaluation in routine clinical care and comparison with research trial outcomes.** J Affect Disord. 2019 Sep 1;256:103-109. [\[ABS\]](#)

Mood and anxiety disorders typically emerge in adolescence and early adult life, but young adults are often reluctant to seek treatment. The Mood Mechanic course is a **transdiagnostic** internet-delivered psychological intervention for symptoms of depression and anxiety, targeted at people aged 18-24 years. ...The results show that the Mood Mechanic course is effective and acceptable in routine clinical care, and that online psychological interventions designed for young adults are an effective treatment option for this hard-to-reach group.

Berking M, et al (2019) - **Affect regulation training reduces symptom severity in depression - A randomized controlled trial.** PLoS One. 2019 Aug 29;14(8):e0220436. [\[FULL TEXT\]](#)

Deficits in general emotion regulation skills have been shown to be associated with various mental disorders. Thus, general affect-regulation training has been proposed as promising **transdiagnostic** approach to the treatment of psychopathology. ...the findings provide evidence for enhancing emotion regulation skills as a common mechanism of change in psychological treatments for depression.

Sambataro F, et al (2019) - **Transdiagnostic modulation of brain networks by electroconvulsive therapy in schizophrenia and major depression.** Eur Neuropsychopharmacol. 2019 Aug;29(8):925-935. [\[ABS\]](#)

Patients had reduced connectivity within a striato-thalamic network in the thalamus as well as increased low frequency oscillations in a striatal network. ECT reduced low frequency oscillations (LFOs) on a striatal network along with increasing functional connectivity in the medial prefrontal cortex within the DMN. Following ECT treatment, the FNC of the executive network was reduced with the DMN and increased with the salience network, respectively. Our findings suggest **transnosological** effects of ECT on the connectivity of large-scale networks as well as at the level of their interplay. Furthermore, they support a transnosological approach for the investigation not only of the neural correlates of the disease but also of the brain mechanism of treatment of mental disorders.

Manning K, et al (2019) - **Recent advances in the use of imaging in psychiatry: functional magnetic resonance imaging of large-scale brain networks in late-life depression.** F1000Res. 2019 Aug 6;8:F1000 Faculty Rev-1366. [[FULL TEXT](#)]

We discuss how neural functioning of three networks is linked to symptom presentation, illness course, and cognitive decline in LLD. These networks are (1) an executive control network responsible for complex cognitive processing, (2) a default mode network normally deactivated during cognitive demanding when individuals are at rest, and a (3) salience network relevant to attending to internal and external emotional and physiological sensations. We discuss how dysfunction in multiple networks contributes to common behavioral syndromes, and we present an overview of the cognitive control, default mode, and salience networks observed in LLD.

Boersma K, et al (2019) - **Efficacy of a Transdiagnostic Emotion-Focused Exposure Treatment for Chronic Pain Patients with Comorbid Anxiety and Depression.** Pain. 2019 Aug;160(8):1708-1718. [[FULL TEXT](#)]

The comorbidity between chronic pain and emotional problems has proven difficult to address with current treatment options. This study addresses the efficacy of a transdiagnostic emotion-focused exposure treatment ("hybrid") for chronic pain patients with comorbid emotional problems. Adults ($n = 115$) with chronic musculoskeletal pain and functional and emotional problems were included in a 2-centre, parallel randomized controlled, open-label trial comparing this treatment to an active control condition receiving a guided Internet-delivered pain management treatment based on CBT principles (iCBT). The hybrid treatment ($n = 58$, 10-16 sessions) integrates exposure in vivo for chronic pain based on the fear-avoidance model with an emotion-regulation approach informed by procedures in Dialectical Behavior Therapy. The iCBT ($n = 57$; 8 treatment modules) addresses topics such as pain education, coping strategies, relaxation, problem solving, stress, and sleep management using standard CBT techniques. Patient-reported outcomes were assessed before and after treatment as well as at a 9-month primary end point. Across conditions, 78% participants completed post-treatment and 81% follow-up assessment. Intent-to-treat analyses showed that the hybrid had a significantly better post-treatment outcome on pain catastrophizing ($d = 0.39$) and pain interference ($d = 0.63$) and significantly better follow-up outcomes on depression ($d = 0.43$) and pain interference ($d = 0.51$). There were no differences on anxiety and pain intensity. Observed proportions of clinically significant improvement favoured the hybrid on all but one comparison, but no statistically significant differences were observed. We conclude that the hybrid emotion-focused treatment may be considered an acceptable, credible, and efficacious treatment option for chronic pain patients with comorbid emotional problems.

McMahon K, et al (2019) - **A Path from Childhood Sensory Processing Disorder to Anxiety Disorders: The Mediating Role of Emotion Dysregulation and Adult Sensory Processing Disorder Symptoms.** Front Integr Neurosci. 2019 Jul 9;13:22. [[FULL TEXT](#)]

... our data indicated that high symptoms of SPD (sensory processing disorder) in childhood may lead to high SPD symptoms in adulthood, which then lead to high emotion dysregulation, ultimately conferring vulnerability for an anxiety disorder diagnosis.

Arditte Hall KA, et al (2019) - **Comparing cognitive styles in social anxiety and major depressive disorders: An examination of rumination, worry, and reappraisal.** Br J Clin Psychol. 2019 Jun;58(2):231-244. [[FULL TEXT](#)]

Social anxiety disorder (SAD) and major depressive disorder (MDD) are commonly occurring and frequently comorbid disorders. ...Individuals with SAD or MDD report more rumination and worry than healthy controls, but do not differ from each other in their reliance on these cognitive styles. Individuals with comorbid SAD/MDD endorse more rumination than individuals with SAD or MDD alone, even after adjusting for differences in symptom severity. ...high reappraisal may be associated with reduced risk of psychiatric disorder, but only when rumination and worry are also high.

Golombek K, et al (2019) - **The role of emotion regulation in socially anxious children and adolescents: a systematic review.** Eur Child Adolesc Psychiatry. 2019 Jun 14. [[ABS](#)]

Study results indicate that children and adolescents with social anxiety disorder or high social anxiety show emotion dysregulation across all five domains of emotion regulation, such as enhanced social avoidance, more safety behaviors, repetitive negative thinking, biased attention and interpretation of social information, and reduced emotional expression. While enhanced social avoidance seems to be specific to childhood social anxiety, other maladaptive emotion regulation strategies, such as repetitive negative thinking, seem to occur **transdiagnostically** across different childhood anxiety disorders. Implications for current theory, interventions and future research are discussed.

Spinhoven P, et al (2019) - **Repetitive negative thinking as a mediator in prospective cross-disorder associations between anxiety and depression disorders and their symptoms.** J Behav Ther Exp Psychiatry. 2019 Jun;63:6-11. [[ABS](#)]

Comorbidity among anxiety and depression disorders and their symptoms is high. Rumination and worry have been found to mediate prospective cross-disorder relations between anxiety and depression disorders and their symptoms in adolescents and adults. We examined whether generic repetitive negative thinking (RNT), that is content- and disorder-independent, also mediates prospective cross-disorder associations between anxiety and depression disorders and their symptoms. ... The significant and rather large mediation effects seemed mainly due to the mental capacity captured by RNT, es-

pecially in the prospective relation of anxiety with future depression. ...From these results it can be concluded that repetitive negative thinking could be an important **transdiagnostic** factor, that may constitute a suitable target for treatment.

Reinholdt-Dunne ML, et al (2019) - **Modeling the Relationships between Metacognitive Beliefs, Attention Control and Symptoms in Children With and Without Anxiety Disorders: A Test of the S-REF Model.** Front Psychol. 2019 Jun 7;10:1205. [\[FULL TEXT\]](#)

In the metacognitive model, attentional control and metacognitive beliefs are key **transdiagnostic** mechanisms contributing to psychological disorder. ... Across groups, lower attention control and higher levels of maladaptive metacognitive beliefs were associated with stronger symptoms, and metacognitions were negatively associated with attention control.

Fitzgerald JM, et al (2019) - **Transdiagnostic neural correlates of volitional emotion regulation in anxiety and depression. Depress Anxiety.** 2019 May;36(5):453-464. [\[FULL TEXT\]](#)

Individuals who suffer from anxiety and/or depression face difficulty in adaptively managing emotional responses, while accumulating evidence suggests impaired emotion regulation is a **transdiagnostic** feature of psychopathology. Effectual regulation in the context of negative stimuli is characterized by engagement of the prefrontal cortex (PFC) coupled with reduced amygdala reactivity. In anxiety disorders and major depression, PFC underengagement and atypical PFC-amygdala connectivity has been observed, although patient findings based on case-control studies have been mixed with regard to magnitude, locality, and extent of dysfunction. ...Across participants, whole-brain results showed that (1) greater anxiety and depression symptom severity was related to less engagement of the dorsal anterior cingulate cortex (ACC) and (2) less FC between the amygdala and ventrolateral PFC. Results were driven by anxiety, while depression symptoms were not significant. ...These findings demonstrate that individual differences in anxiety and depression may help explain ACC and PFC dysfunction during emotion regulation observed across anxiety and depressive disorders.

Lebois LAM, et al (2019) - **Augmentation of Extinction and Inhibitory Learning in Anxiety and Trauma-Related Disorders.** Annu Rev Clin Psychol. 2019 May 7;15:257-284. [\[FULL TEXT\]](#)

This growing body of research may offer promising novel techniques to address debilitating **transdiagnostic** fear-related symptoms.

Riesel A, et al (2019) - **Error-related brain activity as a transdiagnostic endophenotype for obsessive-compulsive disorder, anxiety and substance use disorder.** Psychol Med. 2019 May;49(7):1207-1217. [\[FULL TEXT\]](#)

Alterations in neural error-signals in unaffected first-degree relatives with a family history of OCD, anxiety, or SUD support the utility of the ERN as a **transdiagnostic** endophenotype. Reduced neural error-signals may indicate vulnerability for under-controlled behavior and risk for substance use, whereas a harm- or error-avoidant response style and vulnerability for OCD and anxiety appears to be associated with increased ERN. This adds to findings suggesting a common neurobiological substrate across psychiatric disorders involving the anterior cingulate cortex and deficits in cognitive control.

Blum H, et al (2019) - **Mindfulness Meditation and Anxiety in Adolescents on an Inpatient Psychiatric Unit.** J Health Care Chaplain. 2019 Apr 25:1-19. [[ABS](#)]

This study presents the impact of chaplain-provided mindfulness meditation (MM) groups on state-anxiety in adolescent inpatients on an acute psychiatric unit, ... State-anxiety was found to decrease significantly between pre- and post-MM upon first exposure regardless of patient age, sex, and prior experience with MM. Findings also suggest the possibility that patients experiencing symptoms of psychosis may benefit more from MM as compared to other patients. Admission symptom severity was not found to be an indicator of MM attendance. These findings suggest the possibility that MM could be an effective and relatively immediate **transdiagnostic** intervention to lower state anxiety in adolescents on an inpatient psychiatric unit and invite further implementation and research by staff chaplains on such units.

Hsu KJ, et al (2019) - **Examining differential relationships among self-reported attentional control, depression, and anxiety in a transdiagnostic clinical sample.** J Affect Disord. 2019 Apr 1;248:29-33. [[ABS](#)]

Poor attentional control, defined as difficulty focusing attention on a task or shifting attention flexibly between tasks, is a **transdiagnostic** construct theorized to confer risk for, and maintain, depression and anxiety. ... with depression being associated with difficulties shifting and anxiety being associated with focusing. ... In contrast to studies conducted in non-clinical samples, attentional focusing appears to be more relevant than attentional shifting in a clinical sample for both depression and anxiety symptoms. These findings lend support to efforts to develop neurocognitive interventions that improve focusing.

Woody ML, et al (2019) - **Protracted amygdalar response predicts efficacy of a computer-based intervention targeting attentional patterns in transdiagnostic clinical anxiety.** Transl Psychiatry. 2019 Mar 28;9(1):121. [[FULL TEXT](#)]

Individuals with clinical anxiety demonstrate an attention bias toward threatening information, which is thought to be partially driven by heightened amygdala activity to perceived threat. Attention Bias Modification (ABM) is a computer-based treatment that trains attention toward neutral stimuli and away from threatening stimuli. ... ABM patients who displayed greater sustained bilateral amygdalar response in the aftermath of

neutral stimuli displayed the least improvement in self-reported (but not clinician-rated) vigilance symptoms.

McEvoy PM, et al (2019) - **Repetitive Negative Thinking as a Transdiagnostic Predictor of Depression and Anxiety Symptoms in Adolescents**. *Assessment*. 2019 Mar;26(2):324-335.

[\[ABS\]](#)

Repetitive negative thinking (RNT) is a transdiagnostic process associated with numerous emotional disorders. Most measures of RNT are disorder-specific, limiting utility in comorbid populations. Transdiagnostic measures of RNT have been developed in adults and are associated with anxiety and depression. However, a transdiagnostic measure is needed to assess RNT in adolescents as a potential vulnerability factor for emotional disorders. This study validates a transdiagnostic measure of RNT-Repetitive Thinking Questionnaire-10 (RTQ-10)-in adolescents (N = 840, Mage = 15.7 years). Exploratory and confirmatory factor analyses supported a unidimensional structure. The RTQ-10 manifested good internal consistency and measurement invariance across genders and age. RNT was equally associated with anxiety and depression symptoms irrespective of gender or age. Convergent validity was demonstrated by correlations with disorder-specific measures of RNT. These findings support the RTQ-10 as a reliable and valid transdiagnostic measure of RNT in adolescents.

Weisz JR, et al (2019) - **Are Psychotherapies for Young People Growing Stronger? Tracking Trends over Time for Youth Anxiety, Depression, Attention-Deficit/Hyperactivity Disorder, and Conduct Problems**. *Perspect Psychol Sci*. 2019 Mar;14(2):216-237. [\[ABS\]](#)

The findings suggest that new approaches to treatment design and intervention science may be needed, especially for depression and conduct problems. We suggest intensifying the search for mechanisms of change, making treatments more *transdiagnostic* and personalizable, embedding treatments within youth ecosystems, adapting treatments to the social and technological changes that alter youth dysfunction and treatment needs, and resisting old habits that can make treatments unduly skeuomorphic.

Nordahl H, et al (2019) - **What Lies beneath Trait-Anxiety? Testing the Self-Regulatory Executive Function Model of Vulnerability**. *Front Psychol*. 2019 Jan 30;10:122. [\[FULL TEXT\]](#)

Vulnerability to psychological disorder can be assessed with constructs such as trait anxiety and neuroticism which among others are *transdiagnostic* risk factors. ... These findings suggests that metacognitive beliefs may be an underlying mechanism of vulnerability attributed to trait-anxiety with the implication that the metacognitive (S-REF) model informs conceptualization of psychological vulnerability, and that metacognitive therapy applications might be employed to enhance psychological resilience.

Owens VAM, et al (2019) - **Transdiagnostic, internet-delivered cognitive behavior therapy for depression and anxiety: Exploring impact on health anxiety.** Internet Interv. 2019 Jan 18;15:60-66. [[FULL TEXT](#)]

Health anxiety is associated with significant personal distress and economic cost; as such, widely available and effective treatment options are crucial. Several studies suggest that Internet-delivered cognitive behavior therapy (ICBT) programs that specifically target health anxiety are efficacious for this condition.

... Following treatment, large reductions in health anxiety symptoms ..., depression, generalized anxiety, and disability ...were reported. Furthermore, results showed that **transdiagnostic** ICBT was rated as acceptable to people with high health anxiety symptoms. Despite elevated pre-treatment health anxiety scores, email correspondence between clients and their therapist revealed very few mentions of health anxiety. These findings provide preliminary evidence for **transdiagnostic** ICBT for symptoms of health anxiety and suggest further research is warranted.

Zhao Z, et al (2019) - **Real-Time Functional Connectivity-Informed Neurofeedback of Amygdala-Frontal Pathways Reduces Anxiety.** Psychother Psychosom. 2019;88(1):5-15. [[ABS](#)]

Deficient *emotion regulation* and exaggerated anxiety represent a major **transdiagnostic** psychopathological marker. On the neural level these deficits have been closely linked to impaired, yet treatment-sensitive, prefrontal regulatory control over the amygdala. Gaining direct control over these pathways could therefore provide an innovative and promising intervention to regulate exaggerated anxiety.

To this end the current proof-of-concept study evaluated the feasibility, functional relevance and maintenance of a novel connectivity-informed real-time fMRI neurofeedback training. **METHODS:** In a randomized crossover sham-controlled design, 26 healthy subjects with high anxiety underwent real-time fMRI-guided neurofeedback training to enhance connectivity between the ventrolateral prefrontal cortex (vLPFC) and the amygdala (target pathway) during threat exposure. Maintenance of regulatory control was assessed after 3 days and in the absence of feedback. Training-induced changes in functional connectivity of the target pathway and anxiety ratings served as primary outcomes.

Training of the target, yet not the sham control, pathway significantly increased amygdala-vLPFC connectivity and decreased levels of anxiety. Stronger connectivity increases were significantly associated with higher anxiety reduction on the group level. At the follow-up, volitional control over the target pathway was maintained in the absence of feedback.

The present results demonstrate for the first time that successful self-regulation of amygdala-prefrontal top-down regulatory circuits may represent a novel intervention to control anxiety. As such, the present findings underscore both the critical contribution

of amygdala-prefrontal circuits to emotion regulation and the therapeutic potential of connectivity-informed real-time neurofeedback.

Walther S, et al (2019) - **The utility of an RDoC motor domain to understand psychomotor symptoms in depression.** Psychol Med. 2019 Jan;49(2):212-216. [\[ABS\]](#)

Despite the clinical impact of motor symptoms such as agitation or retardation on the course of depression, these symptoms are poorly understood. Novel developments in the field of instrumentation and mobile devices allow for dimensional and continuous recording of motor behavior in various settings, particularly outside the laboratory. Likewise, the use of novel assessments enables to combine multimodal neuroimaging with behavioral measures in order to investigate the neural correlates of motor dysfunction in depression. The research domain criteria (RDoC) framework will soon include a motor domain that will provide a framework for studying motor dysfunction in mood disorders. In addition, new studies within this framework will allow investigators to study motor symptoms across different stages of depression as well as other psychiatric diagnoses. Finally, the introduction of the RDoC motor domain will help test how motor symptoms integrate with the original five RDoC domains (negative valence, positive valence, cognitive, social processes, and arousal/regulation).

Price RB, et al (2018) - **Towards personalized, brain-based behavioral intervention for transdiagnostic anxiety: Transient neural responses to negative images predict outcomes following a targeted computer-based intervention.** J Consult Clin Psychol. 2018 Dec;86(12):1031-1045. [\[FULL TEXT\]](#)

Excessive attentional deployment toward threat is a **transdiagnostic** dimension of anxiety seen at both initial and sustained stages of threat processing. However, group-level observations of these phenomena mask considerable within-group heterogeneity that has been linked to treatment outcomes, suggesting that a **transdiagnostic**, individual differences approach may capture critical, clinically relevant information.

Seventy clinically anxious individuals were randomized to receive 8 sessions of **attention bias modification** (ABM) ; ... a computer-based mechanistic intervention that specifically targets initial stages of threat processing, or a sham control ... fMRI ...Larger transient responses across a wide range of cognitive-affective regions (e.g., ventrolateral prefrontal cortex, anterior cingulate cortex, amygdala) predicted better clinical outcomes following ABM, in both a priori anatomical regions and whole-brain analyses; sustained responses did not.

Neural alterations occurring on the relatively transient timescale that is specifically targeted by ABM predict favorable clinical outcomes. Results inform how to *expand on the initial promise of neurocognitive treatments* like ABM by fine-tuning their clinical indications (e.g., *through personalized mechanistic intervention relevant across diagnoses*) and *by increasing the range of mechanisms that can be targeted* (e.g., through synergistic

treatment combinations and/or novel neurocognitive training protocols designed to tackle identified predictors of nonresponse).

Yang Z, et al (2018) - **Network changes associated with transdiagnostic depressive symptom improvement following cognitive behavioral therapy in MDD and PTSD**. Mol Psychiatry. 2018 Dec;23(12):2314-2323. [[ABS](#)]

Despite widespread use of cognitive behavioral therapy (CBT) in clinical practice, its mechanisms with respect to brain networks remain sparsely described. In this study, we applied tools from graph theory and network science to better understand the transdiagnostic neural mechanisms of this treatment for depression. A sample of 64 subjects was included in a study of network dynamics: 33 patients (15 MDD, 18 PTSD) received longitudinal fMRI resting state scans before and after 12 weeks of CBT. Depression severity was rated on the Montgomery-Asberg Depression Rating Scale (MADRS). Thirty-one healthy controls were included to determine baseline network roles. Univariate and multivariate regression analyses were conducted on the normalized change scores of within- and between-system connectivity and normalized change score of the MADRS. Penalized regression was used to select a sparse set of predictors in a data-driven manner. Univariate analyses showed greater symptom reduction was associated with an increased functional role of the Ventral Attention (VA) system as an incohesive provincial system (decreased between- and decreased within-system connectivity). Multivariate analyses selected between-system connectivity of the VA system as the most prominent feature associated with depression improvement. Observed VA system changes are interesting in light of brain controllability descriptions: attentional control systems, including the VA system, fall on the boundary between-network communities, and facilitate integration or segregation of diverse cognitive systems. Thus, increasing segregation of the VA system following CBT (decreased between-network connectivity) may result in less contribution of emotional attention to cognitive processes, thereby potentially improving cognitive control.

Li BJ, et al (2018) - **A brain network model for depression: From symptom understanding to disease intervention**. CNS Neurosci Ther. 2018 Nov;24(11):1004-1019. [[FULL TEXT](#)]

Understanding the neural substrates of depression is crucial for diagnosis and treatment. Here, we review recent studies of functional and effective connectivity in depression, in terms of functional integration in the brain. Findings from these studies, including our own, point to the involvement of at least four networks in patients with depression. Elevated connectivity of a ventral limbic affective network appears to be associated with excessive negative mood (dysphoria) in the patients; decreased connectivity of a frontal-striatal reward network has been suggested to account for loss of interest, motivation, and pleasure (anhedonia); enhanced default mode network connectivity seems to be associated with depressive rumination; and diminished connectivity of a dorsal cognitive control network is thought to underlie cognitive deficits especially ineffective top-down control of negative thoughts and emotions in depressed patients. Moreover, the

restoration of connectivity of these networks-and corresponding symptom improvement-following antidepressant treatment (including medication, psychotherapy, and brain stimulation techniques) serves as evidence for the crucial role of these networks in the pathophysiology of depression.

Mehta ND, et al (2018) - **Inflammation negatively correlates with amygdala-ventromedial prefrontal functional connectivity in association with anxiety in patients with depression: Preliminary results.** Brain Behav Immun. 2018 Oct;73:725-730. [[FULL TEXT](#)]

Biomarkers of inflammation, including inflammatory cytokines and the acute-phase reactant C-reactive protein (CRP), are reliably increased in a subset of patients with depression, anxiety disorders and post-traumatic stress disorder (PTSD). Administration of innate immune stimuli to laboratory subjects and the associated release of inflammatory cytokines has been shown to affect brain regions involved in fear, anxiety and emotional processing such as the amygdala. However, the role of inflammation in altered circuitry involving amygdala and other brain regions and its subsequent contribution to symptom severity in depression, anxiety disorders and PTSD is only beginning to be explored. Herein, medically-stable, currently unmedicated outpatients with a primary diagnosis of major depressive disorder (MDD; n = 48) underwent resting-state functional MRI (rfMRI) to determine whether altered connectivity between the amygdala and whole brain was observed in a subset of patients with high inflammation and symptoms of anxiety. Whole-brain, voxel-wise functional connectivity analysis of the right and left amygdala as a function of inflammation (plasma CRP concentrations) revealed that increased CRP predicted decreased functional connectivity between right amygdala and left ventromedial prefrontal cortex (vmPFC) (corrected $p < 0.05$). Amygdala-vmPFC connectivity was, in turn, negatively correlated with symptoms of anxiety In exploratory analyses, relationships between low amygdala-vmPFC connectivity and high anxiety were only observed in patients with a secondary diagnosis of an anxiety disorder or PTSD.

Szczypiński JJ, et al (2018) - **Dopamine dysregulation hypothesis: the common basis for motivational anhedonia in major depressive disorder and schizophrenia?** Rev Neurosci. 2018 Sep 25;29(7):727-744 [[ABS](#)]

...we investigated whether motivational anhedonia is the common symptom across MDD and SCH. With regard to the similarities and differences between the neural mechanisms of MDD and SCH, here we expand the current knowledge of motivation deficits and present the common underlying mechanism of motivational anhedonia - the dopamine dysregulation hypothesis - stating that any prolonged dysregulation in tonic dopamine signaling that exceeds the given equilibrium can lead to striatal dysfunction and motivational anhedonia. The implications for further research and treatment of MDD and SCH are also discussed.

Demetriou EA, et al (2018) - **Autism, Early Psychosis, and Social Anxiety Disorder: a**

transdiagnostic examination of executive function cognitive circuitry and contribution to disability. Transl Psychiatry. 2018 Sep 24;8(1):200. [[Full Text](#)]

This is the first study to compare EF measures across clinical groups of social impairment and suggests unique cognitive-circuitry that underpins disability within groups. Impairments in EF were broad in ASD and predicted disability, EP impairments were specific to attentional processes and SAD impairments likely relate to negative self-monitoring. Self-report, as opposed to performance-based EF, provided best capacity to predict disability. These findings contribute to transdiagnostic circuitry models and intervention strategies.

Ólafsdóttir KB, et al (2018) - **Effects of Exercise on Depression and Anxiety. A Comparison to Transdiagnostic Cognitive Behavioral Therapy.** Community Ment Health J. 2018 Aug;54(6):855-859. [[ABS](#)]

The aims of this study were (i) to know the effects of an exercise program on a group of people with depression and anxiety and (ii) to compare these effects with a transdiagnostic cognitive behavioral group therapy (TCBGT). The participants were 15 people with depression and/or anxiety symptoms. The participants followed an exercise program. Depression and anxiety symptoms were assessed with validated questionnaires. An exercise program can be used as a treatment option for people with depression and/or anxiety with good results in comparison with TCBGT.

Lambert C, et al (2018) - **Anhedonia in depression and schizophrenia: A transdiagnostic challenge.** CNS Neurosci Ther. 2018 Jul;24(7) [[FULL TEXT](#)]

Anhedonia as a clinical presentation of reward circuit dysregulation is an important and relatively undertreated symptom of both SZ and MDD. In order to improve patient outcomes and quality of life, it is important to consider how anhedonia fits into both diagnoses.

Yang Z, et al (2018) - **Cognitive Behavioral Therapy Is Associated with Enhanced Cognitive Control Network Activity in Major Depression and Posttraumatic Stress Disorder.** Biol Psychiatry Cogn Neurosci Neuroimaging. 2018 Apr;3(4):311-319 [[FULL TEXT](#)]

BACKGROUND: Both major depressive disorder (MDD) and posttraumatic stress disorder (PTSD) are characterized by depressive symptoms, abnormalities in brain regions important for cognitive control, and response to cognitive behavioral therapy (CBT). However, whether a common neural mechanism underlies CBT response across diagnoses is unknown. **METHODS:** Brain activity during a cognitive control task was measured using functional magnetic resonance imaging in 104 participants: 28 patients with MDD, 53 patients with PTSD, and 23 healthy control subjects; depression and anxiety symptoms were determined on the same day. A patient subset (n = 31) entered manualized CBT and, along with controls (n = 19), was rescanned at 12 weeks. Linear

mixed effects models assessed the relationship between depression and anxiety symptoms and brain activity before and after CBT. **RESULTS:** At baseline, activation of the left dorsolateral prefrontal cortex was negatively correlated with Montgomery-Åsberg Depression Rating Scale scores across all participants; this brain-symptom association did not differ between MDD and PTSD. Following CBT treatment of patients, regions within the cognitive control network, including ventrolateral prefrontal cortex and dorsolateral prefrontal cortex, showed a significant increase in activity. **CONCLUSIONS:** Our results suggest that dimensional abnormalities in the activation of cognitive control regions were associated primarily with symptoms of depression (with or without controlling for anxious arousal). Furthermore, following treatment with CBT, activation of cognitive control regions was similarly increased in both MDD and PTSD. These results accord with the Research Domain Criteria conceptualization of mental disorders and implicate improved cognitive control activation as a transdiagnostic mechanism for CBT treatment outcome.

Grisanzio KA, et al (2018) - **Transdiagnostic Symptom Clusters and Associations With Brain, Behavior, and Daily Function in Mood, Anxiety, and Trauma Disorders.** JAMA Psychiatry. 2018 Feb 1;75(2):201-209. [[FULL TEXT](#)]

IMPORTANCE: The symptoms that define mood, anxiety, and trauma disorders are highly overlapping across disorders and heterogeneous within disorders. ... These findings offer a data-driven framework for identifying robust subtypes that signify specific, coherent, meaningful associations between symptoms, behavior, brain function, and observable real-world function, and that cut across DSM-IV-defined diagnoses of major depressive disorder, panic disorder, and posttraumatic stress disorder.

Gustavson DE, et al (2018) - **Evidence for Transdiagnostic Repetitive Negative Thinking and Its Association with Rumination, Worry, and Depression and Anxiety Symptoms: A Commonality Analysis.** Collabra Psychol. 2018;4(1):13. [[FULL TEXT](#)]

... repetitive negative thinking may indeed lie at the core of the comorbidity between depression and anxiety symptoms, but that it is also a broader construct that encompasses intrusive thoughts and low levels of mindfulness.

Sambataro F, et al (2018) - **Anterior cingulate volume predicts response to psychotherapy and functional connectivity with the inferior parietal cortex in major depressive disorder.** Eur Neuropsychopharmacol. 2018 Jan;28(1):138-148. [[ABS](#)]

In major depressive disorder (MDD), the anterior cingulate cortex (ACC) has been associated with clinical outcome as well as with antidepressant treatment response. Nonetheless, the association between individual differences in ACC structure and function and the response to cognitive behavioral therapy (CBT) is still unexplored. For this aim, twenty-five unmedicated patients with MDD were scanned with structural and resting state functional magnetic resonance imaging before the beginning of CBT

treatment. ACC morphometry was correlated with clinical changes following psychotherapy. Furthermore, whole-brain resting state functional connectivity with the ACC was correlated with clinical measures. Greater volume in the left subgenual (subACC), the right pregenual (preACC), and the bilateral supragenual (supACC) predicted depressive symptoms improvement after CBT. Greater subACC volume was related to stronger functional connectivity with the inferior parietal cortex and dorsolateral prefrontal cortex. Stronger subACC-inferior parietal cortex connectivity correlated with greater adaptive rumination. Greater preACC volume was associated with stronger functional connectivity with the inferior parietal cortex and ventrolateral prefrontal cortex. In contrast, greater right supACC volume was related to lower functional connectivity with the inferior parietal cortex. These results suggest that ACC volume and its functional connectivity with the fronto-parietal cortex are associated with CBT response in MDD, and this may be mediated by adaptive forms of rumination. Our findings support the role of the subACC as a potential predictor for CBT response.

Sloan E, et al (2017) - **Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: A systematic review.** Clin Psychol Rev. 2017 Nov;57:141-163. [\[ABS\]](#)

A large body of research has implicated difficulties in emotion regulation as central to the development and maintenance of psychopathology. Emotion regulation has therefore been proposed as a transdiagnostic construct or an underlying mechanism in psychopathology. The transdiagnostic role of emotion regulation has yet to be systematically examined within the psychological treatment outcome literature. It can be proposed that if emotion regulation is indeed a transdiagnostic construct central to the maintenance of psychopathology, then changes in emotion regulation difficulties will occur after effective treatment and this will occur for different disorders. We conducted a systematic review, identifying 67 studies that measured changes in both emotion regulation and symptoms of psychopathology following a psychological intervention for anxiety, depression, substance use, eating pathology or borderline personality disorder. Results demonstrated that regardless of the intervention or disorder, both maladaptive emotion regulation strategy use and overall emotion dysregulation were found to significantly decrease following treatment in all but two studies. Parallel decreases were also found in symptoms of anxiety, depression, substance use, eating pathology and borderline personality disorder. These results contribute to the growing body of evidence supporting the conceptualization of emotion regulation as a transdiagnostic construct. The present study discusses the important implications of these findings for the development of unified treatments that target emotion regulation for individuals who present with multiple disorders.

Shou H, et al (2017) - **Cognitive behavioral therapy increases amygdala connectivity with the cognitive control network in both MDD and PTSD.** Neuroimage Clin. 2017 Jan 27;14:464-470. [\[FULL TEXT\]](#)

BACKGROUND: Both major depressive disorder (MDD) and post-traumatic stress disorder (PTSD) are characterized by alterations in intrinsic functional connectivity. Here we investigated changes in intrinsic functional connectivity across these disorders as a function of cognitive behavioral therapy (CBT), an effective treatment in both disorders. **METHODS:** 53 unmedicated right-handed participants were included in a longitudinal study. Patients were diagnosed with PTSD (n = 18) and MDD (n = 17) with a structured diagnostic interview and treated with 12 sessions of manualized CBT over a 12-week period. Patients received an MRI scan (Siemens 3 T Trio) before and after treatment. Longitudinal functional principal components analysis (LFPCA) was performed on functional connectivity of the bilateral amygdala with the fronto-parietal network. A matched healthy control group (n = 18) was also scanned twice for comparison. **RESULTS:** LFPCA identified four eigenimages or principal components (PCs) that contributed significantly to the longitudinal change in connectivity. The second PC differentiated CBT-treated patients from controls in having significantly increased connectivity of the amygdala with the fronto-parietal network following CBT. **LIMITATIONS:** Analysis of CBT-induced amygdala connectivity changes was restricted to the a priori determined fronto-parietal network. Future studies are needed to determine the generalizability of these findings, given the small and predominantly female sample. **CONCLUSION:** We found evidence for the hypothesis that CBT treatment is associated with changes in connectivity between the amygdala and the fronto-parietal network. CBT may work by strengthening connections between the amygdala and brain regions that are involved in cognitive control, potentially providing enhanced top-down control of affective processes that are dysregulated in both MDD and PTSD.

Upthegrove R, et al (2017) - **Depression and Schizophrenia: Cause, Consequence, or Trans-diagnostic Issue?** Schizophr Bull. 2017 Mar 1;43(2):240-244. [[FULL TEXT](#)]

The presence of depression in schizophrenia has been a challenge to the Kraepelinian dichotomy, with various attempts to save the fundamental distinction including evoking and refining diagnoses such as schizoaffective disorder. But the tectonic plates are shifting. Here we put forward a summary of recent evidence regarding the prevalence, importance, possible aetiological pathways and treatment challenges that recognizing depression in schizophrenia bring. Taken together we propose that depression is more than comorbidity and that increased effective therapeutic attention to mood symptoms will be needed to improve outcomes and to support prevention.

Mansell W, et al (2017) - **A test of the core process account of psychopathology in a heterogenous clinical sample of anxiety and depression: A case of the blind men and the elephant?** J Anxiety Disord. 2017 Mar;46:4-10. [[ABS](#)]

Many cognitive and behavioral processes, such as selective attention to threat, self-focused attention, safety-seeking behaviors, worry and thought suppression, have their foundations in research on anxiety disorders. Yet, they are now known to be transdiagnostic, i.e. shared across a wide range of psychological disorders. A more

pertinent clinical and theoretical question is whether these processes are themselves distinct, or whether they reflect a shared 'core' process that maintains psychopathology. The current study utilized a treatment-seeking clinical adult sample of 313 individuals with a range of anxiety disorders and/or depression who had completed self-report measures of widely ranging processes: affect control, rumination, worry, escape/avoidance, and safety-seeking behaviors. We found that only the first factor extracted from a principal components analysis of the items of these measures was associated with symptoms of anxiety and depression. Our findings supported the 'core process' account that had its origins in the field of anxiety disorders, and we discuss the implications for theory, clinical practice and future research across psychological disorders.

Feldker K, et al (2017) - **Transdiagnostic brain responses to disorder-related threat across four psychiatric disorders**. Psychol Med. 2017 Mar;47(4):730-743. [\[ABS\]](#)

The results suggest that pathologically heightened lateral amygdala activation is linked to experienced anxiety across anxiety disorders and trauma- and stressor-related disorders. Furthermore, the transdiagnostically shared activation network points to a common neural basis of abnormal responses to disorder-related threat stimuli across the four investigated disorders.

MacNamara A, et al (2017) - **Transdiagnostic neural correlates of affective face processing in anxiety and depression**. Depress Anxiety. 2017 Jul;34(7):621-631. [\[ABS\]](#)

RESULTS: Across the three primary diagnoses, anxiety symptom scores were associated with increased Angry > Shapes activation in the bilateral insula, anterior/midcingulate, and dorsolateral prefrontal cortex (dlPFC), while depressive symptoms were associated with reduced dlPFC activation for Angry > Shapes. Patient > HC differences were limited to non a priori regions, and no differences in BOLD activation were observed between diagnostic groups.

CONCLUSIONS: (1) Activation in paralimbic, cingulate, and lateral prefrontal regions in response to angry faces is associated with transdiagnostic anxiety and depressive symptomatology. (2) Anxiety and depressive symptoms may exert opposing influences on lateral prefrontal activation. (3) Abnormal threat processing in GAD, SAD, and MDD may reflect shared neural dysfunction that varies with symptom load.

Reinholt N, et al (2017) - **Transdiagnostic group CBT for anxiety disorders: the unified protocol in mental health services**. Cogn Behav Ther. 2017 Jan;46(1):29-43. [\[ABS\]](#)

Strange JP, et al (2017) - **Neural markers of attention to aversive pictures predict response to cognitive behavioral therapy in anxiety and depression**. Biol Psychol. 2017 Feb;123:269-277. [\[ABS\]](#)

Taylor CT, et al (2017) - **Upregulating the positive affect system in anxiety and depression: Outcomes of a positive activity intervention.** *Depress Anxiety*. 2017 Mar;34(3):267-280. [[FULL TEXT](#)]

Merino H, et al (2016) - **Are Worry and Rumination Specific Pathways Linking Neuroticism and Symptoms of Anxiety and Depression in Patients with Generalized Anxiety Disorder, Major Depressive Disorder and Mixed Anxiety-Depressive Disorder?** *PLoS One*. 2016 May 31;11(5):e0156169. [[FULL TEXT](#)]

Overall, our findings suggest that neuroticism may increase the risk of anxious and depressive symptoms via specific links involving either worry or brooding, respectively, and that both worry and brooding may operate in the three groups examined, irrespectively of whether anxiety or depression are the main emotions or whether they coexist without any clear predominance; consequently, we hypothesize the existence of "specific transdiagnostic" mechanisms.

Lang PJ, et al (2016) - **RDoC, DSM, and the reflex physiology of fear: A biodimensional analysis of the anxiety disorders spectrum.** *Psychophysiology*. 2016 Mar;53(3):336-47. [[FULL TEXT](#)]

Subsequent analyses showed significant, parallel trends of diminishing reactivity in both electrodermal and facial EMG reactions across this defensive dimension. ...In concluding, we describe our new RDoC research project, focusing on the assessment of brain circuit function as it determines hypo/hyper reactivity to challenge—somatic and autonomic—and may relate to patients' stress history and genetic inheritance.

Nusslock R, et al (2015) - **Asymmetrical frontal cortical activity associated with differential risk for mood and anxiety disorder symptoms: An RDoC perspective.** *Int J Psychophysiol*. 2015 Nov;98(2 Pt 2):249-261. [[ABS](#)]

The recently launched NIMH Research Domain Criteria (RDoC) initiative aims to examine the relationship between core biobehavioral dimensions and symptom profiles that either cut across traditional disorder categories or that are unique to specific clinical phenomenon. A biobehavioral construct that has received considerable attention and that is directly relevant to the Positive Valence Systems domain of the RDoC initiative is approach motivation. One way approach motivation is frequently operationalized is left versus right frontal electroencephalographic (EEG) activity, with greater relative left frontal EEG activity reflecting increased approach motivation and decreased relative left frontal EEG activity reflecting decreased approach motivation or increased withdrawal tendencies. The objective of the present review paper is to examine the relationship between relative left frontal EEG activity and mood and anxiety related symptoms from an RDoC perspective. We first provide an overview of the approach-withdrawal motivational model of frontal EEG asymmetry. Second, we review evidence that relative left frontal EEG activity is associated with a differential risk for unipolar depression versus bipolar disorder. Third, and in line with the mission statement of the RDoC, we

move beyond considering mood and anxiety disorders as unitary constructs or homogenous disorders and instead propose that individual differences in relative left frontal EEG activity may be uniquely associated with specific symptom clusters of depression (i.e., anhedonia), hypomania/mania (i.e., symptoms characterized by excessive approach motivation), and anxiety (i.e., anxious apprehension versus anxious arousal). Identifying the relationship between relative left frontal EEG activity and specific mood and anxiety-related symptom clusters has important implications for clinical science, assessment, and treatment.

Sharp PB, et al (2015) - **Transdiagnostic dimensions of anxiety: Neural mechanisms, executive functions, and new directions**. Int J Psychophysiol. 2015 Nov;98(2 Pt 2):365-377. [\[ABS\]](#)

Shenk CE, et al (2015) - **Symptoms of major depressive disorder subsequent to child maltreatment - Examining change across multiple levels of analysis to identify transdiagnostic risk pathways**. Dev Psychopathol. 2015 Nov;27(4 Pt 2):1503-14. [\[FULL TEXT\]](#)

Furtado M, et al (2015) - **Neuroinflammatory pathways in anxiety, posttraumatic stress, and obsessive compulsive disorders**. Psychiatry Research September 30, 2015 Volume 229, Issues 1-2, Pages 37–48. [\[ABS\]](#)

As prevalence of anxiety, posttraumatic stress, and obsessive compulsive disorders continue to rise worldwide, increasing focus has been placed on immune mediated theories in understanding the underlying mechanisms of these disorders. Associations between the dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis and these disorders have been recognized in the scientific literature, specifically in regard to cortisol levels, as well as changes in pro- and anti-inflammatory cytokines. The present commentary will systematically assess the scientific literature within the past decade in regard to the psychoneuroimmunology of anxiety, posttraumatic stress, and obsessive compulsive disorders. Understanding the mechanisms of these disorders is essential in order to determine efficacious and targeted treatment strategies, which may lead to substantial improvements in overall functioning, as well as significant decreases in societal and economic burden.

Newby JM, et al (2015) - **Systematic review and meta-analysis of transdiagnostic psychological treatments for anxiety and depressive disorders in adulthood**. Clin Psychol Rev. 2015 Aug;40:91-110. [\[FULL TEXT\]](#)

"The move away from the single-diagnosis approach towards a transdiagnostic conceptualisation and treatment of depressive and anxiety disorders represents a significant paradigm shift (Craske, 2012), mirroring a similar shift in EBTs for eating disorders (Fairburn, Cooper, & Shafran, 2003). al., 2004). 'Transdiagnostic or 'unified' treatments apply the same underlying treatment principals across mental disorders, without tailoring the protocol to specific diagnoses' (p21, McEvoy, Nathan, & Norton, 2009), and as such

operate outside the traditional diagnostic boundaries of DSM (American Psychiatric Association, 2013) or ICD (World Health Organization, 1992)."

"...The transdiagnostic approach is also compatible with the Research Domain Criteria (RDoC), put forth by the U.S. National Institute for Mental Health as an alternative to DSM or ICD, that focuses on the underlying mechanisms (e.g., cognition, negative affect, arousal) that cut across multiple disorders."

Woody ML, et al (2015) - **Integrating NIMH Research Domain Criteria (RDoC) into Depression Research.** Curr Opin Psychol. 2015 Aug;4:6-12. [\[FULL TEXT\]](#)

Akbari M, et al (2015) - **Transdiagnostic Treatment of Co-occurrence of Anxiety and Depressive Disorders based on Repetitive Negative Thinking - A Case Series.** Iran J Psychiatry. 2015 Jun;10(3):200-11. [\[FULL TEXT\]](#)

"... Barlow et al made a considerable improvement in designing theoretical-practical transdiagnostic protocols through several studies with emphasis on the **role of ‘emotion regulation’ as the main cognitive-behavioral mechanism in emotional disorders.**"

"Recent studies have shown that **repetitive negative thinking is the most important common cognitive behavioral process in formation and continuation of emotional disorders. Repetitive negative thinking includes** worry, rumination, treatment monitoring, obsessions and any other kind of repetitive negative thoughts which is the core of depression and anxiety disorders. Surveying more than 50 studies in cognitive pathology of emotional disorders shows that repetitive negative thinking is the main transdiagnostic factor in more than 13 diagnostic classes, including depression disorders, anxiety disorders, sleep disorder, eating disorder, substance abuse disorder and schizophrenic disorder (17-32)."

"Transdiagnostic treatments targeting core “higher-order” factors offer a more parsimonious approach to treatment planning that eliminates the need for multiple diagnosis-specific manuals".

Whitton AE, et al (2015) - **Reward processing dysfunction in major depression, bipolar disorder and schizophrenia.** Curr Opin Psychiatry. 2015 Jan;28(1):7-12. [\[FULL TEXT\]](#)

Emerging evidence indicates the presence of reward processing abnormalities across all three disorders, supporting a transdiagnostic approach. ...New evidence of reward processing abnormalities in MDD, bipolar disorder and schizophrenia has led to a greater understanding of the neural processes associated with symptomatology common across these conditions (e.g., anhedonia).

Leventhal AM, et al (2015) - **Anxiety, depression, and cigarette smoking - a transdiagnostic vulnerability framework to understanding emotion-smoking comorbidity.** Psychol Bull. 2015

Jan;141(1):176-212. [\[FULL TEXT\]](#)

"This approach integrates well with the National Institute on Mental Health's Research Domain Criteria, which proposes that common cross-cutting dimensions, traits, neural circuits, and biological pathways underpin and account for the presentation of various mental disorder diagnoses (Cuthbert and Insel, 2013)."

Iverach L, et al (2014) - **Death anxiety and its role in psychopathology - Reviewing the status of a transdiagnostic construct.** Clin Psychol Rev. 2014 Nov;34(7):580-93. [\[FULL TEXT\]](#)

"... research has provided compelling evidence that death anxiety is a significant issue, both theoretically and clinically. In particular, death anxiety appears to be a basic fear at the core of a range of mental disorders, including hypochondriasis, panic disorder, and anxiety and depressive disorders."

Johnson PL, et al (2014) - **Etiology, triggers and neurochemical circuits associated with unexpected, expected, and laboratory-induced panic attacks.** Neurosci Biobehav Rev. 2014 Oct;46 Pt 3:429-54. [\[FULL TEXT\]](#)

Spielberg JM, et al (2014) - **Transdiagnostic dimensions of anxiety and depression moderate motivation-related brain networks during goal maintenance.** Depress Anxiety. 2014 Oct;31(10):805-13. [\[FULL TEXT\]](#)

Woody ML, et al (2014) - **Brooding rumination and heart rate variability in women at high and low risk for depression: group differences and moderation by COMT genotype.** J Abnorm Psychol. 2014 Feb;123(1):61-7. [\[FULL TEXT\]](#)

We predicted that COMT Val158Met genotype, which has been linked to heightened amygdala reactivity and deficits in prefrontal functioning, would be associated with HRV and brooding rumination, particularly among women with a history of MDD.

McLaughlin KA, et al (2011) - **Rumination as a transdiagnostic factor in depression and anxiety.** Behav Res Ther. 2011 Mar;49(3):186-93. [\[FULL TEXT\]](#)

These findings highlight the importance of targeting rumination in transdiagnostic treatment approaches for emotional disorders.

Maia AC, et al (2013) - **Transdiagnostic treatment using a unified protocol - application for patients with a range of comorbid mood and anxiety disorders.** Trends Psychiatry Psychother. 2013;35(2):134-40. [\[FULL TEXT\]](#)

An effort to establish **one unified treatment protocol for a whole family of emotional disorders (primarily mood and anxiety disorders)** showed benefits in the field of clinical psychology and for the treatment of patients. No other data were found in the literature

describing the implementation of the unified protocol in a transdiagnostic group. Our results revealed statistically significant improvement in all variables, suggesting that the protocol proposed can become an important tool to improve quality of life, sexuality, and anxiety/depression symptoms in patients with different diagnoses.

Autism / Developmental Disorders ▲

Frazier TW, et al (2021) - **Social attention as a cross-cultural transdiagnostic neurodevelopmental risk marker**. Autism Res. 2021 May 15. [[ABS](#)]

A social attention dimension that represents an early-life preference for socially salient information was identified. This preference was cross-culturally consistent and stable across development but stronger in females and weaker in DD, especially ASD. ... Children with developmental disabilities had lower levels of social attention than neurotypical children and children with autism spectrum disorder had the lowest levels of social attention.

Kuo SS, et al (2020) - **Transdiagnostic validity of the MATRICS Consensus Cognitive Battery across the autism-schizophrenia spectrum**. Psychol Med. 2020 Jul;50(10):1623-1632. [[ABS](#)]

BACKGROUND: Autism Spectrum Disorder (ASD) and schizophrenia are neurodevelopmental disorders which share substantial overlap in cognitive deficits during adulthood. However, treatment evaluation in ASD and treatment comparisons across ASD and schizophrenia are limited by a dearth of empirical work establishing the validity of a standard cognitive battery across ASD and schizophrenia. Promisingly, the MATRICS Consensus Cognitive Battery (MCCB) has been validated in schizophrenia and encompasses cognitive domains that are impacted in ASD. ... These findings highlight MCCB's applicability to ASD and support its utility for standardizing treatment evaluation of cognitive outcomes across the autism-schizophrenia spectrum.

Dell'Osso L, et al (2020) - **Camouflaging: psychopathological meanings and clinical relevance in autism spectrum conditions**. CNS Spectr. 2020 May 26:1-3. [[ABS](#)]

Camouflaging behaviors might be considered as a transdiagnostic element, closely associated with the continuous distribution of the autism spectrum among the general and the clinical population.

Rodriguez-Seijas C, et al (2020) - **A transdiagnostic model of psychiatric symptom co-occurrence and autism spectrum disorder**. Autism Res. 2020 Apr;13(4):579-590. [[Abs](#)]

Understanding whether the co-occurrence of psychiatric symptoms within autism

spectrum disorder (ASD) are specific to the ASD diagnosis or reflect similar higher-order patterns observed in both ASD and non-ASD samples, or a confluence of the two, is of critical importance. If similar, it would suggest that comorbid psychiatric conditions among individuals with ASD are not symptoms of specific, non-ASD psychiatric disorders per se, but reflect a general liability to psychopathology associated with ASD. ... for ADHD and social anxiety, there appears to be some specific associations with the ASD diagnosis. ...underlying transdiagnostic dimensions are similar in both ASD and non-ASD children. However, there appear to be ASD-specific differences when it comes to social anxiety and attention deficit hyperactivity disorder.

Gadow KD, et al (2020) - **Social Anhedonia in Children and Adolescents with Autism Spectrum Disorder and Psychiatry Referrals**. J Clin Child Adolesc Psychol. 2020 Mar-Apr;49(2):239-250.

[\[ABS\]](#)

Lack of syndrome specificity supports the notion that SA is a useful *transdiagnostic* symptom phenotype in referred youth and challenges traditional conceptualizations of ASD as a categorical clinical phenotype.

MacDuffie KE, et al (2020) - **Sleep Problems and Trajectories of Restricted and Repetitive Behaviors in Children with Neurodevelopmental Disabilities**. J Autism Dev Disord. 2020 Mar 5.

[\[ABS\]](#)

Sleep problems are prevalent in children with neurodevelopmental disabilities and are associated with the expression of restricted and repetitive behaviors (RRBs). ... Sleep problems were associated with trajectories of higher-order (but not lower-order) RRBs in a transdiagnostic sample.

Vaidya CJ, et al (2020) - **Data-driven identification of subtypes of executive function across typical development, attention deficit hyperactivity disorder, and autism spectrum disorders**. J Child Psychol Psychiatry. 2020 Jan;61(1):51-61. [\[FULL TEXT\]](#)

Impairment of executive function (EF), the goal-directed regulation of thoughts, actions, and emotions, drives negative outcomes and is common across neurodevelopmental disorders including attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). A primary challenge to its amelioration is heterogeneity in symptom expression within and across disorders. Parsing this heterogeneity is necessary to attain diagnostic precision, a goal of the NIMH Research Domain Criteria Initiative.

We aimed to identify transdiagnostic subtypes of EF that span the normal to impaired spectrum and establish their predictive and neurobiological validity. ...We observed three transdiagnostic EF subtypes characterized by behavioral profiles that were defined by relative weakness in: (a) flexibility and emotion regulation; (b) inhibition; and (c) working memory, organization, and planning. The same tripartite structure was also present in the typically developing children. ... As hypothesized, frontal-parietal

engagement was better distinguished by EF subtype than DSM diagnosis and the subgroup characterized with inflexibility failed to modulate right IPL activation in response to increased executive demands. **CONCLUSIONS:** The observed transdiagnostic subtypes refine current diagnostic nosology and augment clinical decision-making for personalizing treatment of executive dysfunction in children.

Condy EE, et al (2019) - **Restricted repetitive behaviors in autism spectrum disorder: A systematic review from the neurovisceral integration perspective.** Biol Psychol. 2019 Nov;148:107739. [\[ABS\]](#)

The neurovisceral integration model posits that cognitive-behavioral inflexibility arises from biological inflexibility of feedback loops within the central autonomic network. The parasympathetic nervous system (PNS) is integral in this network. Activity of the PNS, which is normally tonically inhibited, can be indexed through respiratory sinus arrhythmia (RSA). When the PNS becomes disinhibited, indicating decreased flexibility within the network, RSA is reduced and cognitive-behavioral flexibility is impaired. Using this theoretical framework, cognitive-behavioral inflexibility is discussed from the Research Domain Criteria (RDoC) perspective. Restricted repetitive behaviors in autism spectrum disorder (ASD) are proposed as exemplars of cognitive-behavioral inflexibility, and behavioral and RSA literature in ASD are reviewed. RSA differences and their relation to inflexibility in ASD are discussed to support the model and to propose RSA as a biomarker for cognitive-behavioral inflexibility. Considerations for future research are discussed, in addition to implications the model might have on assessment and **transdiagnostic** treatment practices.

Mareva S, et al (2019) - **Transdiagnostic associations across communication, cognitive, and behavioural problems in a developmentally at-risk population: a network approach.** BMC Pediatr. 2019 Nov 21;19(1):452. [\[FULL TEXT\]](#)

Communication, behavioral, and executive function problems often co-occur in childhood. It is possible that bridging symptoms may be the origins of comorbidities observed on a dimensional level; problems in these areas may cascade and activate problems in other areas of the network. The potential value of applying a dynamic systems network approach to symptoms of developmental disorders is discussed.

Akkermans SEA, et al (2019) - **Frontostriatal functional connectivity correlates with repetitive behaviour across autism spectrum disorder and obsessive-compulsive disorder.** Psychol Med. 2019 Oct;49(13):2247-2255. [\[ABS\]](#)

Autism spectrum disorder (ASD) and obsessive-compulsive disorder (OCD) are neurodevelopmental disorders with considerable overlap in terms of their defining symptoms of compulsivity/repetitive behaviour. ... No diagnosis-specific differences were detected. The cross-disorder analysis, on the other hand, showed that increased functional connectivity between the left nucleus accumbens (NAcc) and a cluster in the right premotor

cortex/middle frontal gyrus was related to more severe symptoms of repetitive behaviour. ... We demonstrate the fruitfulness of applying a cross-disorder (**transdiagnostic**) approach to investigate the neural underpinnings of compulsivity/repetitive behaviour, by revealing a shared alteration in functional connectivity in ASD and OCD. We argue that this alteration might reflect aberrant reward or motivational processing of the NAcc with excessive connectivity to the premotor cortex implementing learned action patterns.

Lake EMR, et al (2019) - **The Functional Brain Organization of an Individual Allows Prediction of Measures of Social Abilities Transdiagnostically in Autism and Attention-Deficit/Hyperactivity Disorder.** Biol Psychiatry. 2019 Aug 15;86(4):315-326. [[Full Text](#)]

Predictive connections and high-hubness regions are found within a wide range of brain areas and across conventional networks. ...An individual's functional connectivity profile contains information that supports dimensional, nonbinary classification in autism spectrum disorder and ADHD.

Burton AL, et al (2019) - **Processes and pathways to binge eating: development of an integrated cognitive and behavioural model of binge eating.** J Eat Disord. 2019 Jun 7;7:18. [[FULL TEXT](#)]

The dual-pathway to binge eating identified in the new model provides a different way to understand **transdiagnostic** binge eating.

Díaz-Caneja CM, et al (2019) - **Neuroanatomical deficits shared by youth with autism spectrum disorders and psychotic disorders.** Hum Brain Mapp. 2019 Apr 1;40(5):1643-1653. [[FULL TEXT](#)]

Autism spectrum disorders (ASD) and early-onset psychosis (EOP) are neurodevelopmental disorders that share genetic, clinical and cognitive facets; it is unclear if these disorders also share spatially overlapping cortical thickness (CT) and surface area (SA) abnormalities. ...Autism spectrum disorders and early onset psychosis ... had spatially overlapping areas of cortical thinning and reduced surface area in the bilateral insula... The insula appears to be a region with **transdiagnostic** vulnerability for deficits in cortical thickness and surface area.

Mikami AY, et al (2019) - **Social functioning in youth with attention-deficit/hyperactivity disorder and autism spectrum disorder: transdiagnostic commonalities and differences.** Clin Psychol Rev. 2019 Mar;68:54-70. [[ABS](#)]

Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) are both neurodevelopmental disorders originating in childhood with high associated impairments and public health significance. There has been growing recognition of the frequent co-occurrence, and potential interrelatedness, between ADHD and ASD without intellectual disability. In fact, the most recent (5th) edition of the DSM is the first to

allow ADHD and ASD to be diagnosed in the same individual. The study of **transdiagnostic** features in ADHD and ASD is important for understanding, and treating, these commonly co-occurring disorders. Social impairment is central to the description and prognosis of both disorders, and many youth with some combination of ADHD and ASD present to clinics for social skills training interventions.

Demetriou EA, et al (2018) - **Autism, Early Psychosis, and Social Anxiety Disorder: a transdiagnostic examination of executive function cognitive circuitry and contribution to disability**. Transl Psychiatry. 2018 Sep 24;8(1):200. [[Full Text](#)]

This is the first study to compare EF measures across clinical groups of social impairment and suggests unique cognitive-circuitry that underpins disability within groups. Impairments in EF were broad in ASD and predicted disability, EP impairments were specific to attentional processes and SAD impairments likely relate to negative self-monitoring. Self-report, as opposed to performance-based EF, provided best capacity to predict disability. These findings contribute to transdiagnostic circuitry models and intervention strategies.

Rosen TE, et al (2018) - **Co-occurring psychiatric conditions in autism spectrum disorder**. Int Rev Psychiatry. 2018 Feb;30(1):40-61. [[Abst](#)]

Individuals with autism spectrum disorder (ASD) are at increased risk for experiencing one or more co-occurring psychiatric conditions. ... The utility of a transdiagnostic framework for conceptualizing co-occurring disorders in ASD is discussed, and the state of treatment research for co-occurring disorders is summarized.

Ciaramidaro A, et al (2018) - **Transdiagnostic deviant facial recognition for implicit negative emotion in autism and schizophrenia**. Eur Neuropsychopharmacol. 2018 Feb;28(2):264-275. [[Abs](#)]

Impaired facial affect recognition (FAR) is observed in schizophrenia and autism spectrum disorder (ASD) and has been linked to amygdala and fusiform gyrus dysfunction. ...In addition, the ASD group additionally showed reduced activations in medial prefrontal cortex (PFC), bilateral dorso-lateral PFC, ventro-lateral PFC, posterior-superior temporal sulcus and left temporo-parietal junction. ...our findings are consistent with a common neural deficit during implicit negative facial affect recognition in schizophrenia and autism spectrum disorders.

Aoki Y, et al (2017) - **Association of White Matter Structure with Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder**. JAMA Psychiatry. 2017 Nov 1;74(11):1120-1128. [[Full Text](#)]

Dimensional analyses provided a more complete picture of associations between ASD traits and inattention and indexes of white matter organization, particularly in the

corpus callosum. This transdiagnostic approach can reveal dimensional relationships linking white matter structure to neurodevelopmental symptoms.

Aggernaes B (2017) - **Autism: a transdiagnostic, dimensional, construct of reasoning?** Eur J Neurosci. 2018 Mar;47(6):515-533. [\[Full Text\]](#)

A possible redefinition of the concept of autism may be a condition in which the rationale of an individual's behaviour differs qualitatively from that of the social environment due to characteristic cognitive impairments affecting reasoning. ...A future challenge of autism research may be to develop theoretical models that can account for the impact of complex processes acting at the social level in addition to complex neurobiological and psychological processes. Such models could profit from a distinction among processes related to (i) basic susceptibility, (ii) adaptive processes and (iii) decompensating factors involved in the development of manifest illness.

Lu C, et al (2017) - **Shared neuroanatomical substrates of impaired phonological working memory across reading disability and autism.** Biol Psychiatry Cogn Neurosci Neuroimaging. 2016 Mar 1; 1(2): 169–177. [\[FULL TEXT\]](#)

These findings suggest that impaired PWM is transdiagnostically associated with shared neuroanatomical abnormalities in ASD and reading disability. Microstructural characteristics in left AF and right ILF may play important roles in the development of PWM. The right ILF may support a compensatory mechanism for children with impaired PWM.

Rodgers J, et al (2016) - **Towards a Treatment for Intolerance of Uncertainty in Young People with Autism Spectrum Disorder: Development of the Coping with Uncertainty in Everyday Situations (CUES©) Programme.** J Autism Dev Disord. 2016 Oct 28. [\[ABS\]](#)

Intolerance of uncertainty (IU) is indicated as an important transdiagnostic process variable in a range of anxiety disorders. Anxiety is very common in children with autism spectrum disorders (ASD). This study aimed to develop a parent group based manualized treatment programme for young people with ASD, which focused on IU.

Dougherty CC, et al (2016) - **A Comparison of Structural Brain Imaging Findings in Autism Spectrum Disorder and Attention-Deficit Hyperactivity Disorder.** Neuropsychol Rev. 2016 Mar;26(1):25-43. [\[ABS\]](#)

Distinct expressions were in total brain volume (ASD: increased volume, ADHD: decreased volume), amygdala (ASD: overgrowth, ADHD: normal), and internal capsule (ASD: unclear, ADHD: reduced FA in DTI). Considerable overlap was noted in the corpus callosum and cerebellum (lower volume in structural MRI and decreased FA in DTI), and superior longitudinal fasciculus (reduced FA in DTI). In addition, we identify brain regions which have not been studied in depth and require more research.

Foss-Feig JH, et al (2016) - **Re-conceptualizing ASD within a Dimensional Framework: Positive, Negative, and Cognitive Feature Clusters**. J Autism Dev Disord. 2016 Jan;46(1):342-51. [\[FULL TEXT\]](#)

Kulsek J, et al (2015) - **Cardiac autonomic regulation in autism and Fragile X syndrome: a review**. Psychol Bull. 2015 Jan;141(1):141-75. [\[FULL TEXT\]](#)

Evidence reviewed here supports physiological dysregulation in a subset of individuals with autism, as evidenced by patterns of hyperarousal and dampened parasympathetic vagal tone, which overlap with the well-documented physiological profile of FXS. Moreover, there is growing support for a link between aberrant cardiac activity and core deficits associated with autism, such as communication and social impairment. The delineation of physiological mechanisms common to autism and FXS could lend insight into relationships between genetic etiology and behavioral endstates, highlighting FMR1 as a potential candidate gene.

Weiss JA (2014) - **Transdiagnostic Case Conceptualization of Emotional Problems in Youth with ASD - An Emotion Regulation Approach**. Clin Psychol (New York). 2014 Dec;21(4):331-350. [\[FULL TEXT\]](#)

Guy L, et al (2014) - **Brief report: emotion regulation and respiratory sinus arrhythmia in autism spectrum disorder**. J Autism Dev Disord. 2014 Oct;44(10):2614-20. [\[ABS\]](#)

Emotion regulation (ER) may be an important transdiagnostic factor for understanding mental and behavioral health given its association with several psychiatric disorders, including autism spectrum disorder (ASD). However, there is limited research on ER in ASD, particularly using biomarkers such as respiratory sinus arrhythmia (RSA). The aim of the current study was to examine RSA among school-aged children with ASD in relation to symptoms of anxiety, executive functioning, and adaptive socialization skills. Results showed decreased RSA in children with ASD (relative to typically developing controls), reflecting decreased parasympathetic nervous system activity. In addition, decreased RSA was associated with increased symptoms of anxiety and lower socialization skills. These findings emphasize the need for interventions targeting emotional and arousal regulation in ASD.

Attention / ADD / ADHD ▲

Moukhtarian TR, et al (2020) - **Wandering minds in attention-deficit/hyperactivity disorder and borderline personality disorder**. Eur Neuropsychopharmacol. 2020 Jul 20:S0924-977X(20)30216-9. [\[ABS\]](#)

Spontaneous mind-wandering is a trans-diagnostic process present in both ADHD and BPD. Yet, the underlying mechanisms of this experience may be driven by anxiety/depression in BPD but reflect a core process in ADHD.

Vogel SC, et al (2020) - **Childhood Adversity and Dimensional Variations in Adult Sustained Attention**. Front Psychol. 2020 Apr 16;11:691. [[FULL TEXT](#)]

Sustained attention is a transdiagnostic phenotype linked with most forms of psychopathology. ...Our results demonstrate that attention differences related to childhood adversity exposure can (1) be measured using brief, performance-based measures of sustained attention, (2) persist into adulthood, and (3) be detected at the population level. These results, paired with the well-documented associations between sustained attention and psychopathology, indicate that sustained attention may be an important mechanism for understanding early influences on mental health.

Vaidya CJ, et al (2020) - **Data-driven identification of subtypes of executive function across typical development, attention deficit hyperactivity disorder, and autism spectrum disorders**. J Child Psychol Psychiatry. 2020 Jan;61(1):51-61. [[FULL TEXT](#)]

Impairment of executive function (EF), the goal-directed regulation of thoughts, actions, and emotions, drives negative outcomes and is common across neurodevelopmental disorders including attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). A primary challenge to its amelioration is heterogeneity in symptom expression within and across disorders. Parsing this heterogeneity is necessary to attain diagnostic precision, a goal of the NIMH Research Domain Criteria Initiative.

We aimed to identify transdiagnostic subtypes of EF that span the normal to impaired spectrum and establish their predictive and neurobiological validity. ...We observed three transdiagnostic EF subtypes characterized by behavioral profiles that were defined by relative weakness in: (a) flexibility and emotion regulation; (b) inhibition; and (c) working memory, organization, and planning. The same tripartite structure was also present in the typically developing children. ... As hypothesized, frontal-parietal engagement was better distinguished by EF subtype than DSM diagnosis and the subgroup characterized with inflexibility failed to modulate right IPL activation in response to increased executive demands. CONCLUSIONS: The observed transdiagnostic subtypes refine current diagnostic nosology and augment clinical decision-making for personalizing treatment of executive dysfunction in children.

Lake EMR, et al (2019) - **The Functional Brain Organization of an Individual Allows Prediction of Measures of Social Abilities Transdiagnostically in Autism and Attention-Deficit/Hyperactivity Disorder**. Biol Psychiatry. 2019 Aug 15;86(4):315-326. [[Full Text](#)]

Predictive connections and high-hubness regions are found within a wide range of brain

areas and across conventional networks. ...An individual's functional connectivity profile contains information that supports dimensional, nonbinary classification in autism spectrum disorder and ADHD.

McMahon K, et al (2019) - **A Path from Childhood Sensory Processing Disorder to Anxiety Disorders: The Mediating Role of Emotion Dysregulation and Adult Sensory Processing Disorder Symptoms.** Front Integr Neurosci. 2019 Jul 9;13:22. [[FULL TEXT](#)]

... our data indicated that high symptoms of SPD (sensory processing disorder) in childhood may lead to high SPD symptoms in adulthood, which then lead to high emotion dysregulation, ultimately conferring vulnerability for an anxiety disorder diagnosis.

Gisbert L, et al (2019) - **Genome-wide analysis of emotional lability in adult attention deficit hyperactivity disorder (ADHD).** Eur Neuropsychopharmacol. 2019 Jun;29(6):795-802. [[ABS](#)]

Emotional lability is strongly associated with Attention Deficit Hyperactivity Disorder (ADHD), represents a major source of impairment and predicts poor clinical outcome in ADHD..., these tentative results are in agreement with previous studies that suggest emotion dysregulation as a **transdiagnostic** construct and highlight the need for further investigation to disentangle the genetic basis of mood instability in ADHD and co-occurring psychiatric disorders.

Hsu KJ, et al (2019) - **Examining differential relationships among self-reported attentional control, depression, and anxiety in a transdiagnostic clinical sample.** J Affect Disord. 2019 Apr 1;248:29-33. [[ABS](#)]

Poor attentional control, defined as difficulty focusing attention on a task or shifting attention flexibly between tasks, is a **transdiagnostic** construct theorized to confer risk for, and maintain, depression and anxiety. ... with depression being associated with difficulties shifting and anxiety being associated with focusing. ... In contrast to studies conducted in non-clinical samples, attentional focusing appears to be more relevant than attentional shifting in a clinical sample for both depression and anxiety symptoms. These findings lend support to efforts to develop neurocognitive interventions that improve focusing.

Weisz JR, et al (2019) - **Are Psychotherapies for Young People Growing Stronger? Tracking Trends over Time for Youth Anxiety, Depression, Attention-Deficit/Hyperactivity Disorder, and Conduct Problems.** Perspect Psychol Sci. 2019 Mar;14(2):216-237. [[ABS](#)]

The findings suggest that new approaches to treatment design and intervention science may be needed, especially for depression and conduct problems. We suggest intensifying the search for mechanisms of change, making treatments more **transdiagnostic** and personalizable, embedding treatments within youth ecosystems, adapting treatments to

the social and technological changes that alter youth dysfunction and treatment needs, and resisting old habits that can make treatments unduly skeuomorphic.

Mikami AY, et al (2019) - **Social functioning in youth with attention-deficit/hyperactivity disorder and autism spectrum disorder: transdiagnostic commonalities and differences.** Clin Psychol Rev. 2019 Mar;68:54-70. [\[ABS\]](#)

Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) are both neurodevelopmental disorders originating in childhood with high associated impairments and public health significance. There has been growing recognition of the frequent co-occurrence, and potential interrelatedness, between ADHD and ASD without intellectual disability. In fact, the most recent (5th) edition of the DSM is the first to allow ADHD and ASD to be diagnosed in the same individual. The study of *transdiagnostic* features in ADHD and ASD is important for understanding, and treating, these commonly co-occurring disorders. Social impairment is central to the description and prognosis of both disorders, and many youth with some combination of ADHD and ASD present to clinics for social skills training interventions.

Aoki Y, et al (2017) - **Association of White Matter Structure with Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder.** JAMA Psychiatry. 2017 Nov 1;74(11):1120-1128. [\[Full Text\]](#)

Dimensional analyses provided a more complete picture of associations between ASD traits and inattention and indexes of white matter organization, particularly in the corpus callosum. This transdiagnostic approach can reveal dimensional relationships linking white matter structure to neurodevelopmental symptoms.

Arns M, et al (2014) - **Neurofeedback in ADHD and insomnia: Vigilance stabilization through sleep spindles and circadian networks.** Neurosci Biobehav Rev. 2014; 44: 183-194. [\[ABS\]](#)

Arns M, et al (2014) - **Differential effects of theta/beta and SMR neurofeedback in ADHD on sleep onset latency.** Front Hum Neurosci. 2014; 8 (1019. 9). [\[FULL TEXT\]](#)

Borderline Personality Disorder ▲

Bertsch K, et al (2021) - **Neurobiological principles of borderline personality disorder: integration into the ICD-11 model of personality disorders.** Nervenarzt. 2021 May 21. [\[ABS\]](#)

Alterations in the medial prefrontal cortex, temporoparietal junction and precuneus mediate deficits in self-referential thought processes and the mentalization of emotions and intentions of others. Enhanced connectivity between the amygdala and midline

structures is associated with hypermentalization. At the same time, elevated insula activation seems to underlie the strengthened nonreflective parts of feelings of other people. Frontolimbic alterations are transdiagnostically associated with deficient emotional regulation and negative affectivity and alterations in reward and cognitive control regions are related to impulsivity.

Moukhtarian TR, et al (2020) - **Wandering minds in attention-deficit/hyperactivity disorder and borderline personality disorder.** Eur Neuropsychopharmacol. 2020 Jul 20:S0924-977X(20)30216-9. [\[ABS\]](#)

Spontaneous mind-wandering is a trans-diagnostic process present in both ADHD and BPD. Yet, the underlying mechanisms of this experience may be driven by anxiety/depression in BPD but reflect a core process in ADHD.

Kockler TD, et al (2020) - **Specific or transdiagnostic? The occurrence of emotions and their association with distress in the daily life of patients with borderline personality disorder compared to clinical and healthy controls.** Psychiatry Res. 2020 Feb;284:112692. [\[ABS\]](#)

Patients with BPD exhibited anger more frequently than any of the clinical or healthy control groups, demonstrating specificity. The quality of anger accounted for additional distress beyond the pure emotional intensity. In patients with BPD, joy was associated with reduced distress, which was not the case in HC or PTSD. However, the majority of the comparisons (anxiety, sadness, shame, disgust, jealousy, guilt, interest) revealed transdiagnostic patterns. The distress-enhancing or distress-reducing effects of anger and joy might represent an important part of affective dysregulation in BPD.

Bayes AJ, et al (2020) - **Differentiating borderline personality disorder (BPD) from bipolar disorder: diagnostic efficiency of DSM BPD criteria.** Acta Psychiatr Scand. 2020 Feb;141(2):142-148. [\[ABS\]](#)

The transdiagnostic nature of 'affective instability' means it is less useful for diagnostic decisions, whereas 'abandonment fears' and 'identity disturbance' offer superior diagnostic efficiency in distinguishing BPD from BP.

Seidl E, et al (2020) - **Response to ostracism in patients with chronic depression, episodic depression and borderline personality disorder a study using Cyberball.** J Affect Disord. 2020 Jan 1;260:254-262. [\[ABS\]](#)

Social exclusion (ostracism) can lead to interactional frustration and may play an important role as trigger and symptom amplifier in affective disorders. ... The present cross-diagnostic study compares the responses to social exclusion in patients with chronic depression (CD), episodic depression (ED) and borderline personality disorder (BPD) in comparison to a healthy control group.

Patients with CD showed a higher intensity of ostracism and aversive impact, as well as the wish to escape the situation (behavioral intention) compared to ED. In most categories, CD and ED had scores between BPD and healthy controls (with this sequence) and with BPD patients showing the largest difference to healthy controls. ... Moreover, psychotherapy in CD should focus on specific needs of CD patients for developing a functional coping in threatening interpersonal situations.

Newton JR (2019) - **Borderline personality disorder and eating disorders: a trans-diagnostic approach to unravelling diagnostic complexity**. *Australas Psychiatry*. 2019 Dec;27(6):556-558. [\[ABS\]](#)

Trans-diagnostic elements appear to include some shared aetiological factors as well as some shared syndromal components. The shared syndromal components include problems with affect, interpersonal problems, problems with self-concept and impulsivity. The pathoplastic effects of culture, attitudes to fatness and the neurobiology of starvation and/or restriction of intake are crucial to integrate into the understanding of comorbidity of these two disorders. Transdiagnostic approaches to treatment lead to transdiagnostic improvements across the two disorders.

Donald F, et al (2019) - **Substance use and borderline personality disorder: fostering hope in the face of complexity**. *Australas Psychiatry*. 2019 Dec;27(6):569-572. [\[ABS\]](#)

Impulsivity and emotional dysregulation are common characteristics of patients presenting with co-occurring borderline personality disorder (BPD) and substance use disorder (SUD). ... Co-occurring BPD and SUD can be effectively treated within a staged, **transdiagnostic** approach with an emphasis on the therapeutic alliance.

Keng SL, et al (2019) - **Effects of brief daily mindfulness practice on affective outcomes and correlates in a high BPD trait sample**. *Psychiatry Res*. 2019 Oct;280:112485. [\[ABS\]](#)

Compared to the no-practice control condition, mindfulness practice resulted in significant improvements in trait mindfulness and self-compassion, whereas relaxation practice led to reductions in emotion regulation difficulties.

Bayes AJ, et al (2019) - **Cognitive and Behavioral Differentiation of Those with Borderline Personality Disorder and Bipolar Disorder**. *J Nerv Ment Dis*. 2019 Aug;207(8):620-625. [\[ABS\]](#)

The study findings indicate that the **transdiagnostic** nature of ED (a feature of both conditions) means it is less useful for diagnostic decisions, whereas identity disturbance is both intrinsic to BPD and offers specificity in differentiation from BP.

Sloan E, et al (2017) - **Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: A systematic review**. *Clin Psychol Rev*. 2017 Nov;57:141-163. [\[ABS\]](#)

A large body of research has implicated difficulties in emotion regulation as central to the development and maintenance of psychopathology. Emotion regulation has therefore been proposed as a transdiagnostic construct or an underlying mechanism in psychopathology. The transdiagnostic role of emotion regulation has yet to be systematically examined within the psychological treatment outcome literature. It can be proposed that if emotion regulation is indeed a transdiagnostic construct central to the maintenance of psychopathology, then changes in emotion regulation difficulties will occur after effective treatment and this will occur for different disorders. We conducted a systematic review, identifying 67 studies that measured changes in both emotion regulation and symptoms of psychopathology following a psychological intervention for anxiety, depression, substance use, eating pathology or borderline personality disorder. Results demonstrated that regardless of the intervention or disorder, both maladaptive emotion regulation strategy use and overall emotion dysregulation were found to significantly decrease following treatment in all but two studies. Parallel decreases were also found in symptoms of anxiety, depression, substance use, eating pathology and borderline personality disorder. These results contribute to the growing body of evidence supporting the conceptualization of emotion regulation as a transdiagnostic construct. The present study discusses the important implications of these findings for the development of unified treatments that target emotion regulation for individuals who present with multiple disorders.

Gibson LE, et al (2017) - **The association between traumatic life events and psychological symptoms from a conservative, transdiagnostic perspective.** Psychiatry Res. 2017 Jun;252:70-74. [\[ABS\]](#)

Findings underscore the critical role that TLE histories play in posttraumatic stress, borderline personality, and attenuated psychotic symptom expression. The relationship between TLEs and depression, cannabis and other drug use, generalized anxiety, and social anxiety disappeared after adjusting for comorbid symptoms.

Brain-derived Neurotrophic Factor ▲

Levchuk LA, et al (2020) - **Exploring Brain Derived Neurotrophic Factor and Cell Adhesion Molecules as Biomarkers for the Transdiagnostic Symptom Anhedonia in Alcohol Use Disorder and Comorbid Depression.** . Front Psychiatry. 2020 Apr 20;11:296. [\[FULL TEXT\]](#)

Alcohol Use Disorder (AUD) and depressive disorder often co-exist and have a shared heritability. ...This pilot study suggests that peripheral levels of BDNF and neuronal cell adhesion molecules (NCAM) might be reduced in AUD with and without comorbid mood disorder. Since low BDNF levels were associated with self-reported anhedonia across

these conditions, BDNF and anhedonia might reflect transdiagnostic aspects involved in AUD and depression.

Nuernberg GL, et al (2016) - **Brain-derived neurotrophic factor increase during treatment in severe mental illness inpatients.** Transl Psychiatry. 2016 Dec 13;6(12):e985. [\[FULL TEXT\]](#)

BDNF levels increased significantly between admission and discharge in SMI patients. BDNF levels showed significant reductions compared with controls both at admission and upon discharge. In addition, BDNF levels showed no difference among SMI patient diagnostic subgroups (unipolar depression, bipolar depression, schizophrenia and manic episode). The increase but non-restoration of BDNF levels, even with the general acute improvement of clinical scores, may reflect the progression of the disorder characteristically seen in these patients. BDNF levels could be considered as a marker for the presence of a nonspecific psychiatric disorder and possibly a transdiagnostic and nonspecific marker of disease activity.

Child Adversity / Trauma / Stress ▲

Krakau L, et al (2021) - **Personality functioning as a mediator of adult mental health following child maltreatment.** J Affect Disord. 2021 May 14;291:126-134. [\[ABS\]](#)

BACKGROUND: The broad range of adverse health outcomes following child maltreatment (child maltreatment) underscores the need to investigate shared trajectories that contribute to associated physical and mental health problems. ... Personality functioning may represent a transdiagnostic link to different somatic and psychological symptoms in the aftermath of child maltreatment.

Wade M, et al (2020) - **Global deficits in executive functioning are transdiagnostic mediators between severe childhood neglect and psychopathology in adolescence.** Psychol Med. 2020 Jul;50(10):1687-1694. [\[ABS\]](#)

Children reared in institutions experience profound deprivation that is associated with both heightened levels of psychopathology and deficits in executive functioning (EF). It is unclear whether deficits in EF among institutionally-reared children serve as a vulnerability factor that increases risk for later psychopathology. ... We conclude that stable, global deficits in EF serve as a cognitive endophenotype that increases transdiagnostic vulnerability to psychopathology in adolescence among those who have experienced profound early neglect.

Buzzell GA, et al (2020) - **Adolescent cognitive control and mediofrontal theta oscillations are disrupted by neglect: Associations with transdiagnostic risk for psychopathology in a**

randomized controlled trial. Dev Cogn Neurosci. 2020 Jun;43:100777. [[FULL TEXT](#)]

Children that have experienced psychosocial neglect display impairments in self-monitoring and controlling their behavior (cognitive control) and are at broad, transdiagnostic risk for psychopathology. ...Institutional rearing (neglect) predicted reduced mediofrontal theta by age 16, which was linked to heightened transdiagnostic risk for psychopathology... Earlier placement into foster care yielded greater mediofrontal activity by age 16. Moreover, foster care placement was associated with the developmental trajectory of mediofrontal theta across the adolescent period (ages 12-16), which was, in turn, associated with greater reductions in transdiagnostic risk across this same period.

Simpson J, et al (2020) - **Self-disgust mediates the relationship between childhood adversities and psychosis.** Br J Clin Psychol. 2020 Jun;59(2):260-275. [[ABS](#)]

Traumatic events in childhood have been implicated in the development of psychosis, but given that trauma is not in itself sufficient to cause psychosis, researchers have started to investigate other psychological constructs potentially involved in explaining this relationship. Given that self-disgust as a transdiagnostic construct plays a role in the development/maintenance of a range of mental health difficulties, the objective of this study was to investigate whether self-disgust mediates the relationship between childhood trauma and psychosis.

...When assessing individuals with psychosis, especially those with a trauma history explore experiences and feelings related to the construct of self-disgust. Such experiences are likely to center on feelings of repulsion towards the self / need for distance and might also manifest in the content of their psychotic experiences. Individuals with significant levels or experiences of self-disgust are likely to need specific interventions to address these; while interventions seeking to improve positive aspects of their identity might well be useful, they are unlikely to address the specific maladaptive elements of self-disgust.

Colich NL, et al (2020) - **Earlier age at menarche as a transdiagnostic mechanism linking childhood trauma with multiple forms of psychopathology in adolescent girls.** Psychol Med. 2020 May;50(7):1090-1098. [[FULL TEXT](#)]

Accelerated pubertal development in girls may be one **transdiagnostic** pathway through which threat-related experiences confer risk for the adolescent onset of mental disorders. Early pubertal maturation is a marker that could be used in both medical and mental health settings to identify trauma-exposed youth that are at risk for developing a mental disorder during adolescence in order to better target early interventions.

Vogel SC, et al (2020) - **Childhood Adversity and Dimensional Variations in Adult Sustained Attention.** Front Psychol. 2020 Apr 16;11:691. [[FULL TEXT](#)]

Sustained attention is a transdiagnostic phenotype linked with most forms of psychopathology. ...

Our results demonstrate that attention differences related to childhood adversity exposure can (1) be measured using brief, performance-based measures of sustained attention, (2) persist into adulthood, and (3) be detected at the population level. These results, paired with the well-documented associations between sustained attention and psychopathology, indicate that sustained attention may be an important mechanism for understanding early influences on mental health.

McLaughlin KA, et al (2020) - **Mechanisms linking childhood trauma exposure and psychopathology: a transdiagnostic model of risk and resilience.** BMC Med. 2020 Apr 1;18(1):96. [[FULL TEXT](#)]

Children with higher levels of social support, particularly from caregivers, are less likely to develop psychopathology following trauma exposure. ... Childhood trauma exposure is a powerful transdiagnostic risk factor associated with elevated risk for multiple forms of psychopathology across development. Changes in threat-related social and emotional processing and accelerated biological aging serve as transdiagnostic mechanisms linking childhood trauma with psychopathology. These transdiagnostic mechanisms represent critical targets for early interventions aimed at preventing the emergence of psychopathology in children who have experienced trauma.

Forbes MK, et al (2020) - **Evidence that Different Types of Peer Victimization have Equivalent Associations with Transdiagnostic Psychopathology in Adolescence.** J Youth Adolesc. 2020 Mar;49(3):590-604. [[ABS](#)]

Experiences of peer victimization are common in adolescence and have been associated with a broad variety of psychopathology in adolescence. ...The associations between peer victimization and psychopathology were not unique to specific symptom domains, but rather showed broadband associations with all symptom domains via a transdiagnostic association with general psychopathology. ... peer victimization might present a useful target for the prevention of general psychopathology.

Stowkowy J, et al (2020) - **Trauma in Youth At-Risk for Serious Mental Illness.** J Nerv Ment Dis. 2020 Jan;208(1):70-76. [[ABS](#)]

There were high frequencies of reported trauma across all stages. Symptomatic individuals experienced more trauma and bullying. Stage 1b individuals reported more physical abuse. Stage 1b also indicated psychological bullying to have a longer duration and impact on their lives. Future work should aim to clarify the complex interrelations between trauma and risk of SMI.

Sill J, et al (2020) - **Rapid brain responses to affective pictures indicate dimensions of trauma-related psychopathology in adolescents.** Psychophysiology. 2020 Jan;57(1):e13353. [[FULL TEXT](#)]

A variety of mental disorders are related to deviant brain activity, but these neural alterations do not validate psychiatric diagnostic categories. High symptom overlap and variable symptom patterns encourage a dimensional approach. Following the logic of the Research Domain Criteria (RDoC), we investigated trauma survivors for symptom clusters that might be associated with characteristics of ERPs, in particular with the early posterior negativity (EPN) elicited during affective picture processing. ...The result suggests that problems concentrating, sleeping difficulties, and mistrust seem to be **transdiagnostic** elements related to diminished early emotional discrimination represented by the EPN. Furthermore, our findings indicate that the EPN in response to emotional processing is modulated by sex.

Carbone EA, et al (2019) - **Adverse childhood experiences and clinical severity in bipolar disorder and schizophrenia: A transdiagnostic two-step cluster analysis.** J Affect Disord. 2019 Dec 1;259:104-111. [[ABS](#)]

Specific adverse childhood experiences (ACEs) are related to clinical severity among BD and SSD patients. Early life adversities related to abuse and neglect are associated to greater symptomatic severity than those related to lack of support/isolation. Our findings suggest that a history of ACEs could be used to identify patients at higher risk of unfavorable clinical features.

Peters AT, et al (2019) - **The roles of early-life adversity and rumination in neural response to emotional faces amongst anxious and depressed adults.** Psychol Med. 2019 Oct;49(13):2267-2278. [[FULL TEXT](#)]

Early-life adversity (ELA) is a risk factor for internalizing psychopathology (IP). ELA is also linked to alterations in neural phenotypes of emotion processing and maladaptive emotion regulatory strategies, such as ruminative brooding, in adulthood. We therefore expected that ELA would predict cortical brain activation to emotional faces in **transdiagnostic** IP and in turn, mediate the extent of rumination amongst patients with IPs and ELA (IP + ELA).

IP + ELA demonstrated increased activation in the superior frontal gyrus and anterior cingulate cortex (fear), superior parietal lobule, precuneus, posterior cingulate, and inferior temporal gyrus (fear only), and cuneus (fear and angry). These regions were preferentially correlated with ruminative brooding in IP + ELA, many of which mediated the link between IP + ELA and ruminative brooding. ...alterations in the neural correlates of maladaptive processing of socio-emotional information may be a common pathway by which ELA poses risk for psychopathology.

Schalinski I, et al (2019) - **Early neglect is a key determinant of adult hair cortisol concentration and is associated with increased vulnerability to trauma in a transdiagnostic sample.** *Psychoneuroendocrinology*. 2019 Oct;108:35-42. [[ABS](#)]

BACKGROUND: Childhood adversities and traumatic events have each been associated with hypothalamus-pituitary-adrenal (HPA) axis dysregulation and trauma-related symptoms in adulthood. Hair cortisol concentration (HCC) reflects cumulative cortisol levels over the course of months and is discussed as a potential marker between trauma-induced neuroendocrine dysfunction and trauma-related symptoms. ... Results strengthen evidence that inadequate care and neglect during critical periods alter HPA axis biology towards enduring reduction in cortisol, the latter being associated with augmented trauma-related symptoms upon trauma exposure. If validated by longitudinal assessments these cross-sectional findings suggest biological mechanisms of childhood adversities into psychopathology in adulthood.

Clausen AN, et al (2019) - **Machine Learning Analysis of the Relationships Between Gray Matter Volume and Childhood Trauma in a Transdiagnostic Community-Based Sample.** *Biol Psychiatry Cogn Neurosci Neuroimaging*. 2019 Aug;4(8):734-742. [[FULL TEXT](#)]

Results from this large, *transdiagnostic* sample implicate GM volume in regions central to current neurobiological theories of trauma (e.g., prefrontal cortex) as well as additional regions involved in reward, interoceptive, attentional, and sensory processing (e.g., striatal, insula, cingulate sulcus, and parietal/occipital cortices).

Weissman DG, et al (2019) - **Difficulties with emotion regulation as a transdiagnostic mechanism linking child maltreatment with the emergence of psychopathology.** *Dev Psychopathol*. 2019 Aug;31(3):899-915. [[FULL TEXT](#)]

Greater emotional reactivity and engagement in rumination mediated the longitudinal association between maltreatment and increased general psychopathology over time. Emotion dysregulation following childhood maltreatment occurs at multiple stages of the emotion generation process, in some cases varies across development, and serves as a *transdiagnostic* mechanism linking child maltreatment with general psychopathology.

Wang J, et al (2019) - **Transdiagnostic Dimensions towards Personality Pathology and Childhood Traumatic Experience in a Clinical Sample: Subtype Classification by a Cross-sectional Analysis.** *Sci Rep*. 2019 Aug 2;9(1):11248. [[FULL TEXT](#)]

Verhees MWFT, et al (2019) - **Strengthening Attachment-Based Therapies: A Case for Cognitive Bias Modification?** *J Am Acad Child Adolesc Psychiatry*. 2019 Jul;58(7):732-733. [[ABS](#)]

A recent article published in the Journal describes the effectiveness of attachment-based family therapy in decreasing suicidal ideation and depressive symptoms in adolescents. Because insecure attachment is a **transdiagnostic** risk factor in the development of psychological problems in children and adolescents, improving attachment relationships is an important therapeutic endeavor. In their article, Diamond et al. suggest that programs such as attachment-based family therapy might become more effective or "fortified by integrating more specific cognitive and emotional skills training." In the current letter, we want to argue that such a claim is theoretically meaningful, how such fortification might be achieved, and which training components might be added. Most importantly, we want to plea for clinical research that puts this claim to a test.

Maunder RG, et al (2019) - **The Relationship between Childhood Adversity and Other Aspects of Clinical Complexity in Psychiatric Outpatients.** J Interpers Violence. 2019 Jul 24;886260519865968. [[ABS](#)]

Childhood abuse and neglect were associated with many characteristics that contribute to clinical complexity, and thus to suboptimal outcomes to standard, guideline-based care. Screening may alert psychiatrists to the need for intensive, patient-centered, and trauma-informed treatments. Identifying childhood adversity as a common antecedent of clinical complexity may facilitate developing **transdiagnostic** programs that specifically target sources of complexity.

Eszlari N, et al (2019) - **Childhood Adversity Moderates the Effects of HTR2A Epigenetic Regulatory Polymorphisms on Rumination.** Front Psychiatry. 2019 Jun 14;10:394. [[FULL TEXT](#)]

These findings indicate the crucial importance of involving stress factors when considering endophenotypes and suggest that brooding is a more promising endophenotype than a broader measure of rumination. **Transdiagnostic** relevance of the brooding endophenotype and the potential of targeting epigenetic regulatory polymorphisms of HTR2A in primary and secondary prevention of depression and possibly of other disorders are also discussed.

Lange I, et al (2019) - **Neurobehavioural mechanisms of threat generalization moderate the link between childhood maltreatment and psychopathology in emerging adulthood.** J Psychiatry Neurosci. 2019 May 1;44(3):185-194. [[FULL TEXT](#)]

Childhood maltreatment is a **transdiagnostic** risk factor for later psychopathology and has been associated with altered brain circuitry involved in the processing of threat and safety.

In individuals reporting high levels of childhood maltreatment, enhanced generalization in self-reported fear and unconditioned stimulus (US) expectancy was related to higher levels of psychopathology. Imaging results revealed that in the group with high levels of

childhood maltreatment, lower activation in the left hippocampus during threat generalization was associated with a higher symptom load. Associations between threat generalization and psychopathology were nonsignificant overall in the group with no or low levels of childhood maltreatment. ... Our results suggest that threat generalization mechanisms may moderate the link between childhood maltreatment and subclinical psychopathology during emerging adulthood. Threat generalization could represent a vulnerability factor for developing later psychopathology in individuals being exposed to childhood maltreatment.

van Hoof MJ, et al (2019) - **Unresolved-disorganized attachment adjusted for a general psychopathology factor associated with atypical amygdala resting-state functional connectivity.** Eur J Psychotraumatol. 2019 Mar 14;10(1):1583525. [[FULL TEXT](#)]

Unresolved disorganized attachment (UDA) was positively associated with greater functional connectivity between the left amygdala and the left lateral occipital cortex, precuneus, and superior parietal lobule. Furthermore, UDA was negatively associated with left amygdala-medial frontal cortex connectivity. General psychopathology factor (GPF) was not significantly associated with dACC or amygdala connectivity. Conclusions: Atypical amygdala connectivity may reflect a vulnerability factor rather than a biomarker of psychopathology. The unique association of Ud and amygdala RSFC, adjusted for a GPF, across participants with and without various classifications of psychopathology illustrates that dimensional approaches based on the Adult Attachment Interview may complement psychiatric classifications in clinical research and practice.

Richmond-Rakerd LS, et al (2019) - **Adolescents Who Self-Harm and Commit Violent Crime: Testing Early-Life Predictors of Dual Harm in a Longitudinal Cohort Study.** Am J Psychiatry. 2019 Mar 1;176(3):186-195. [[FULL TEXT](#)]

Dual harmers have self-control difficulties and are immersed in violence from a young age. A treatment- rather than punishment-oriented approach is indicated to meet these individuals' needs. Connecting self-harming adolescents with delinquency-reduction programs and **transdiagnostic** approaches that target self-regulation may reduce harmful behaviors. Preventing childhood maltreatment and implementing strategies to reduce victimization exposure could mitigate risk for both internalized and externalized violence.

Riem MME, et al (2019) - **General psychopathology factor and unresolved-disorganized attachment uniquely correlated to white matter integrity using diffusion tensor imaging.** Behav Brain Res. 2019 Feb 1;359:1-8. [[ABS](#)]

Decreasing WMI (white matter integrity) in the genu and body with increasing psychopathology across diagnoses suggests demyelination in these areas and may underlie comorbidity and presence of symptoms that transcend psychopathological diagnoses. In

contrast, trauma-related WMI reductions in the splenium and IFOF (inferior fronto-occipital fasciculus) may account for heterogeneity within diagnostic categories as a function of childhood trauma.

Lincoln SH, et al (2019) - **Altered reward processing following an acute social stressor in adolescents.** PLoS One. 2019 Jan 4;14(1):e0209361. [[FULL TEXT](#)]

Altered reward processing is a *transdiagnostic* factor implicated in a wide range of psychiatric disorders. ...Two main findings emerged. First, reward-related neural activation (i.e., striatum) was blunted in the stress relative to the no-stress condition. Second, the stress condition also contributed to blunted neural response following reward in loss-related regions (i.e., dACC, anterior insula); however, there were no changes in loss sensitivity. These results highlight the importance of conceptualizing neural vulnerability within the presence of stress, as this may clarify risk for mental disorders during a critical period of development.

Albott CS, et al (2018) - **Association of Childhood Adversity with Differential Susceptibility of Transdiagnostic Psychopathology to Environmental Stress in Adulthood.** JAMA Netw Open. 2018 Nov 2;1(7):e185354. [[FULL TEXT](#)]

Multivariable comorbidity research indicates that childhood adversity increases the risk for the development of common mental disorders. This risk is explained by underlying internalizing and externalizing *transdiagnostic* constructs that are amplified by environmental stressors. ... Results provide empirical support for childhood adversity as a differential susceptibility factor engendering heightened functional and dysfunctional reactivity to later stress.

Halldorsdottir T, et al (2017) - **FKBP5 moderation of the relationship between childhood trauma and maladaptive emotion regulation strategies in adolescents.** Psychoneuroendocrinology. 2017 Jun 17;84:61-65. [[ABS](#)]

Van Tieghem MR, et al (2017) - **Neurobiological Programming of Early Life Stress: Functional Development of Amygdala-Prefrontal Circuitry and Vulnerability for Stress-Related Psychopathology.** Curr Top Behav Neurosci. 2017 Apr 25. [[ABS](#)]

Early adverse experiences are associated with heightened vulnerability for stress-related psychopathology across the lifespan. While extensive work has investigated the effects of early adversity on neurobiology in adulthood, developmental approaches can provide further insight on the neurobiological mechanisms that link early experiences and long-term mental health outcomes. In the current review, we discuss the role of emotion regulation circuitry implicated in stress-related psychopathology from a developmental and transdiagnostic perspective. We highlight converging evidence suggesting that multiple forms of early adverse experiences impact the functional development of amygdala-prefrontal circuitry. Next, we discuss how adversity-induced alterations in

amygdala-prefrontal development are associated with symptoms of emotion dysregulation and psychopathology. Additionally, we discuss potential mechanisms through which protective factors may buffer the effects of early adversity on amygdala-prefrontal development to confer more adaptive long-term outcomes. Finally, we consider limitations of the existing literature and make suggestions for future longitudinal and translational research that can better elucidate the mechanisms linking early adversity, neurobiology, and emotional phenotypes. Together, these findings may provide further insight into the neuro-developmental mechanisms underlying the emergence of adversity-related emotional disorders and facilitate the development of targeted interventions that can ameliorate risk for psychopathology in youth exposed to early life stress.

Danese A, et al (2017) - **Psychoneuroimmunology of Early-Life Stress: The Hidden Wounds of Childhood Trauma?** *Neuropsychopharmacology*. 2017 Jan;42(1):99-114. [\[ABS\]](#)

The brain and the immune system are not fully formed at birth, but rather continue to mature in response to the postnatal environment. The two-way interaction between the brain and the immune system makes it possible for childhood psychosocial stressors to affect immune system development, which in turn can affect brain development and its long-term functioning. Drawing from experimental animal models and observational human studies, we propose that the psychoneuroimmunology of early-life stress can offer an innovative framework to understand and treat psychopathology linked to childhood trauma. Early-life stress predicts later inflammation, and there are striking analogies between the neurobiological correlates of early-life stress and of inflammation. Furthermore, there are overlapping trans-diagnostic patterns of association of childhood trauma and inflammation with clinical outcomes. These findings suggest new strategies to remediate the effect of childhood trauma before the onset of clinical symptoms, such as anti-inflammatory interventions and potentiation of adaptive immunity. Similar strategies might be used to ameliorate the unfavorable treatment response described in psychiatric patients with a history of childhood trauma.

Childhood trauma is a key risk factor for psychopathology. However, little is known about how exposure to childhood trauma is translated into biological risk for psychopathology. Observational human studies and experimental animal models suggest that childhood exposure to stress can trigger an enduring systemic inflammatory response not unlike the bodily response to physical injury. In turn, these "hidden wounds" of childhood trauma can affect brain development, key behavioral domains (e.g., cognition, positive valence systems, negative valence systems), reactivity to subsequent stressors, and, ultimately, risk for psychopathology. Further research is needed to better characterize the inflammatory links between childhood trauma and psychopathology. Detecting and healing these hidden wounds may help prevent and treat psychopathology emerging after childhood trauma.

Danese A, et al (2017) - **Hidden Wounds? Inflammatory Links between Childhood Trauma and**

Psychopathology. Annu Rev Psychol. 2017 Jan 3;68:517-544. [\[ABS\]](#)

Childhood trauma is a key risk factor for psychopathology. However, little is known about how exposure to childhood trauma is translated into biological risk for psychopathology. Observational human studies and experimental animal models suggest that childhood exposure to stress can trigger an enduring systemic inflammatory response not unlike the bodily response to physical injury. In turn, these "hidden wounds" of childhood trauma can affect brain development, key behavioral domains (e.g., cognition, positive valence systems, negative valence systems), reactivity to subsequent stressors, and, ultimately, risk for psychopathology. Further research is needed to better characterize the inflammatory links between childhood trauma and psychopathology. Detecting and healing these hidden wounds may help prevent and treat psychopathology emerging after childhood trauma.

Isvoranu A-M, et al (2017) - **A Network Approach to Psychosis - Pathways between Childhood Trauma and Psychotic Symptoms.** Schizophr Bull. 2017 Jan;43(1):187-196. [\[ABS\]](#)

McLaughlin KA (2016) - **Future Directions in Childhood Adversity and Youth Psychopathology.** J Clin Child Adolesc Psychol. 2016;45(3):361-82. [\[FULL TEXT\]](#)

Teicher MH, et al (2016) - **The effects of childhood maltreatment on brain structure, function and connectivity.** Nat Rev Neurosci. 2016 Sep 19;17(10):652-66. [\[ABS\]](#)

Maltreatment-related childhood adversity is the leading preventable risk factor for mental illness and substance abuse. Although the association between maltreatment and psychopathology is compelling, there is a pressing need to understand how maltreatment increases the risk of psychiatric disorders. Emerging evidence suggests that maltreatment alters trajectories of brain development to affect sensory systems, network architecture and circuits involved in threat detection, emotional regulation and reward anticipation. This Review explores whether these alterations reflect toxic effects of early-life stress or potentially adaptive modifications, the relationship between psychopathology and brain changes, and the distinction between resilience, susceptibility and compensation

Heleniak C, et al (2016) - **Childhood Maltreatment Exposure and Disruptions in Emotion Regulation - A Transdiagnostic Pathway to Adolescent Internalizing and Externalizing Psychopathology.** Cognit Ther Res. 2016 Jun;40(3):394-415. [\[FULL TEXT\]](#)

These findings provide converging evidence for the role of emotion regulation deficits as a transdiagnostic developmental pathway linking child maltreatment with multiple forms of psychopathology.

Philip NS, et al (2016) - **Early life stress predicts thalamic hyperconnectivity: A transdiagnostic study of global connectivity.** J Psychiatr Res. 2016 Aug;79:93-100. [\[ABS\]](#)

Early life stress (ELS) is an established risk factor for psychiatric illness and is associated with altered functional connectivity within- and between intrinsic neural networks. The widespread nature of these disruptions suggests that broad imaging measures of neural connectivity, such as global based connectivity (GBC), may be particularly appropriate for studies of this population. GBC is designed to identify brain regions having maximal functional connectedness with the rest of the brain, and alterations in GBC may reflect a restriction or broadening of network synchronization. We evaluated whether ELS severity predicted GBC in a sample (N = 46) with a spectrum of ELS exposure. Participants included healthy controls without ELS, those with at least moderate ELS but without psychiatric disorders, and a group of patients with ELS- related psychiatric disorders. The spatial distribution of GBC peaked in regions of the salience and default mode networks, and ELS severity predicted increased GBC of the left thalamus (corrected $p < 0.005$, $r = 0.498$). Thalamic connectivity was subsequently evaluated and revealed reduced connectivity with the salience network, particularly the dorsal anterior cingulate cortex (corrected $p < 0.005$), only in the patient group. These findings support a model of disrupted thalamic connectivity in ELS and trauma-related negative affect states, and underscore the importance of a transdiagnostic, dimensional neuroimaging approach to understanding the sequelae of trauma exposure.

Shenk CE, et al (2015) - **Symptoms of major depressive disorder subsequent to child maltreatment - Examining change across multiple levels of analysis to identify transdiagnostic risk pathways.** Dev Psychopathol. 2015 Nov;27(4 Pt 2):1503-14. [\[FULL TEXT\]](#)

Kaufman J, et al (2015) - **The Research Domain Criteria (RDoC) Project and Studies of Risk and Resilience in Maltreated Children.** J Am Acad Child Adolesc Psychiatry. 2015 Aug;54(8):617-25. [\[FULL TEXT\]](#)

Chaney A, et al (2014) - **Effect of childhood maltreatment on brain structure in adult patients with major depressive disorder and healthy participants.** J Psychiatry Neurosci 2014;39(1):50-59. [\[FULL TEXT\]](#)

We studied 37 patients with MDD and 46 controls. Grey matter volume was significantly decreased in the hippocampus and significantly increased in the dorsomedial prefrontal cortex (DMPFC) and the orbitofrontal cortex (OFC) in participants who had experienced childhood maltreatment compared with those who had not. Patients displayed smaller left OFC and left DMPFC volumes than controls. No significant difference in hippocampal volume was evident between patients with MDD and healthy controls. In regression analyses, despite effects from depression, age and sex on the DMPFC, OFC and hippocampus, childhood maltreatment was found to independently affect these regions.

Owens M, et al (2012) - **5-HTTLPR and early childhood adversities moderate cognitive and emotional processing in adolescence.** PLoS One. 2012;7(11):e48482. [\[FULL TEXT\]](#)

Hart H, et al (2012) - **Neuroimaging of child abuse: a critical review.** Front. Hum. Neurosci., 19 March 2012. [[FULL TEXT](#)]

...the most prominent deficits associated with early childhood abuse are in the function and structure of lateral and ventromedial fronto-limbic brain areas and networks that mediate behavioral and affect control. Future, large scale multimodal neuroimaging studies in medication-naïve subjects, however, are needed that control for psychiatric co-morbidities in order to elucidate the structural and functional brain sequelae that are associated with early environmental adversity, independently of secondary co-morbid conditions.

Faravelli C, et al (2010) - **Childhood traumata, Dexamethasone Suppression Test and psychiatric symptoms: a trans-diagnostic approach.** Psychol Med. 2010 Dec;40(12):2037-48. [[ABS](#)]

RESULTS: In total, 33.5% of patients were Dexamethasone Suppression Test (DST) non-suppressors, compared with 6.1% of controls ($p=0.001$). Among patients, non-suppression was associated with particular symptoms (i.e. depressive and psychotic), but not to any specific diagnosis. Early stressful life events were significantly associated with higher salivary cortisol levels, with DST non-suppression and with approximately the same subset of symptoms. A recent stressful event seemed to be associated to the HPA response only in those subjects who were exposed to early traumata. ...CONCLUSIONS: Our report suggests a relationship between life stress, HPA axis and psychopathology. A cluster of specific psychiatric symptoms seems to be stress related. Moreover, it seems that an abnormal HPA response is possibly triggered by an excessive pressure in vulnerable individuals.

Cognitive Control / Enhancement ▲

Lerman-Sinkoff DB, et al (2019) - **Transdiagnostic Multimodal Neuroimaging in Psychosis: Structural, Resting-State, and Task Magnetic Resonance Imaging Correlates of Cognitive Control.** Biol Psychiatry Cogn Neurosci Neuroimaging. 2019 Oct;4(10):870-880. [[FULL TEXT](#)]

A priori and de novo imaging replicably identified a set of interrelated patterns across modalities and the healthy-to-psychosis spectrum, suggesting robustness of these features. Relationships between imaging and cognitive control performance suggest that shared symptomatology may be key to identifying **transdiagnostic** relationships in psychosis.

Peyrovian B, et al (2019) - **The glycine site of NMDA receptors: A target for cognitive enhancement in psychiatric disorders.** Prog Neuropsychopharmacol Biol Psychiatry. 2019 Jun 8;92:387-404. [\[ABS\]](#)

Cognitive dysfunction is a principal determinant of functional impairment in major depressive disorder (MDD) and often persists during periods of euthymia. Abnormalities in the glutamate system, particularly in N-methyl-d-aspartate receptors (NMDARs) activity, have been shown to contribute to both mood and cognitive symptoms in MDD. ... Six glycine site modulators with pro-cognitive and antidepressant properties were identified... Numerous proof-of-concept clinical trials demonstrated pro-cognitive and antidepressant effects **transdiagnostically** (e.g., in healthy participants, MDD, schizophrenia, anxiety disorders, major neurocognitive disorders). ... preliminary results suggest that the glycine site of NMDARs is a promising target to ameliorate symptoms of depression and cognitive dysfunction. Additional rigorously designed clinical studies are required to determine the cognitive effects of these agents in MDD.

Ramey T, et al (2018) - **Cognitive impairment in substance use disorders.** CNS Spectr. 2018 Dec 28;1-12. [\[FULL TEXT\]](#)

As addressed in this special issue, cognitive impairment is a **transdiagnostic** domain; thus, advances in the characterization and treatment of cognitive dysfunction in substance use disorders could have benefit across multiple psychiatric disorders

McTeague LM, et al (2017) - **Identification of Common Neural Circuit Disruptions in Cognitive Control across Psychiatric Disorders.** Am J Psychiatry. 2017 Jul 1;174(7):676-685. [\[ABS\]](#)

These findings demonstrate a common pattern of disruption across major psychiatric disorders that parallels the "multiple-demand network" observed in intact cognition. This network interfaces with the anterior-cingulo-insular or "salience network" demonstrated to be transdiagnostically vulnerable to gray matter reduction. Thus, networks intrinsic to adaptive, flexible cognition are vulnerable to broad-spectrum psychopathology. Dysfunction in these networks may reflect an intermediate transdiagnostic phenotype, which could be leveraged to advance therapeutics

Sun X, et al (2017) - **Dysfunctional metacognition across psychopathologies: A meta-analytic review.** Eur Psychiatry. 2017 Jun 7;45:139-153. [\[ABS\]](#)

McTeague LM, et al (2016) - **Transdiagnostic impairment of cognitive control in mental illness.** J Psychiatr Res. 2016 Dec;83:37-46. [\[ABS\]](#)

Accumulating findings have revealed that phenotypically diverse psychiatric disorders share a common factor or vulnerability to dysfunction that is in turn related to broad neurocognitive deficits. Furthermore, we have observed that regions of the multiple demand network, which overlap with the salience network (dorsal anterior cingulate and

bilateral anterior insula) are characterized by reduced gray matter transdiagnostically and predict weaker neurocognitive performance. In summary, transdiagnostic (as opposed to disorder-specific) patterns of symptomatic distress and neurocognitive performance deficits, concurrent with parallel anomalies of brain structure and function may largely contribute to the real-world socio-occupational impairment common across disorders.

Snyder HR, et al (2016) - **Spiraling out of control: Stress generation and subsequent rumination mediate the link between poorer cognitive control and internalizing psychopathology.** Clin Psychol Sci. 2016 Nov;4(6):1047-1064. [\[ABS\]](#)

Poor cognitive control is associated with nearly every mental disorder and has been proposed as a transdiagnostic risk factor for psychopathology, including depression and anxiety. What specific mechanisms might cause individuals with poor cognitive control to experience higher levels of psychopathology? The current research tests a new process model linking poor cognitive control to depression and anxiety symptoms via increased dependent stress (i.e., self-generated stressors) and subsequent rumination. This model was supported across two studies in youth during the key period for emergence of internalizing psychopathology. Study 1 provides longitudinal evidence for prospective prediction of change in symptoms. Study 2 confirms this model using well-established executive function tasks in a cross-sectional study. These findings have potential implications for understanding why cognitive control impairments may be broadly associated with psychopathology, and suggest that interventions to prevent stress generation might be effective in preventing negative consequences of poor cognitive control.

Cyberchondria ▲

Vismara M, et al (2021) - **A preliminary investigation of Cyberchondria and its correlates in a clinical sample of patients with obsessive-compulsive disorder, anxiety and depressive disorders attending a tertiary psychiatric clinic.** Int J Psychiatry Clin Pract. 2021 May 25:1-12. [\[ABS\]](#)

Cyberchondria (CYB) represents a common transdiagnostic syndrome in patients with obsessive-compulsive disorder, anxiety, and depressive disorders. ...Health anxiety/hypochondriasis showed a strong correlation with CYB. Patients with a positive family history of psychiatric disorders and those prescribed benzodiazepines or mood-stabilisers showed higher CYB symptom severity. Considering the spread of Internet use for health-related information, additional studies investigating CYB in clinical samples are encouraged.

Dementia / Neurodegeneration ▲

Cornblath EJ, et al (2020) - **Defining and predicting transdiagnostic categories of neurodegenerative disease.** Nat Biomed Eng. 2020 Aug 3. [[ABS](#)]

...we show that six non-overlapping disease clusters can simultaneously account for tau neurofibrillary tangles, α -synuclein inclusions, neuritic plaques, inclusions of the transcriptional repressor TDP-43, angiopathy, neuron loss and gliosis. We also show that membership to the six transdiagnostic disease clusters, which explains more variance in cognitive phenotypes than can be explained by individual diagnoses, can be accurately predicted from scores of the Mini-Mental Status Exam, protein levels in cerebrospinal fluid, and genotype at the APOE and MAPT loci, via cross-validated multiple logistic regression.

Murley AG, et al (2020) - **Redefining the multidimensional clinical phenotypes of frontotemporal lobar degeneration syndromes.** Brain. 2020 May 1;143(5):1555-1571. [[FULL TEXT](#)]

The syndromes caused by frontotemporal lobar degeneration have highly heterogeneous and overlapping clinical features. ... we examined 310 patients with a syndrome likely to be caused by frontotemporal lobar degeneration, including behavioural variant frontotemporal dementia, non-fluent, and semantic variants of primary progressive aphasia (PPA), progressive supranuclear palsy and corticobasal syndrome. ... Sixty-two per cent of participants had phenotypic features that met the diagnostic criteria for more than one syndrome. Behavioural disturbance was prevalent in all groups.

Together, these results show that syndromes associated with frontotemporal lobar degeneration do not form discrete mutually exclusive categories from their clinical features or structural brain changes, but instead exist in a multidimensional spectrum. Patients often manifest diagnostic features of multiple disorders while deficits in behaviour, movement and language domains are not confined to specific diagnostic groups. It is important to recognize individual differences in clinical phenotype, both for clinical management and to understand pathogenic mechanisms. We suggest that a transdiagnostic approach to the spectrum of frontotemporal lobar degeneration syndromes provides a useful framework with which to understand disease aetiology, progression, and heterogeneity and to target future treatments to a higher proportion of patients.

Creese B, et al (2019) - **Examining the association between genetic liability for schizophrenia and psychotic symptoms in Alzheimer's disease.** Transl Psychiatry. 2019 Oct 22;9(1):273. [[FULL TEXT](#)]

Gilmour G, et al (2019) - **Relating constructs of attention and working memory to social withdrawal in Alzheimer's disease and schizophrenia: issues regarding paradigm selection.** *Neurosci Biobehav Rev.* 2019 Feb;97:47-69. [[ABS](#)]

Central nervous system diseases are not currently diagnosed based on knowledge of biological mechanisms underlying their symptoms. Greater understanding may be offered through an agnostic approach to traditional disease categories, where learning more about shared biological mechanisms across conditions could potentially reclassify subgroups of patients to allow realisation of more effective treatments. This review represents the output of the collaborative group "PRISM", tasked with considering assay choices for assessment of attention and working memory in a **transdiagnostic** cohort of Alzheimer's disease and schizophrenia patients exhibiting symptomatic spectra of social withdrawal.

Strikwerda-Brown C, et al (2019) - **Neurocognitive mechanisms of theory of mind impairment in neurodegeneration: a transdiagnostic approach.** *Neuropsychiatr Dis Treat.* 2019 Feb 20;15:557-573. [[FULL TEXT](#)]

Much of human interaction is predicated upon our innate capacity to infer the thoughts, beliefs, emotions, and perspectives of others, in short, to possess a "theory of mind" (ToM). ... Arguing from a novel, **transdiagnostic** perspective, we consider how ToM vulnerability reflects the progressive degradation of neural circuits specialized for an array of higher-order cognitive processes. This mechanistic approach enables us to consider the common and unique neurocognitive mechanisms that underpin ToM dysfunction across neurodegenerative disorders and for the first time examine its relation to behavioral disturbances across social, intimate, legal, and criminal settings.

Husain M (2017) - **Transdiagnostic neurology: neuropsychiatric symptoms in neurodegenerative diseases.** *Brain* (2017) 140 (6): 1535-1536. [[ABS](#)]

...it is also worth considering the possibility that hyper-specialism comes at a potential cost: loss of the ability to perceive, or even care about, the significance of common symptoms that cross conventional disease boundaries.

Swardfager W, et al (2016) - **Mapping inflammation onto mood: Inflammatory mediators of anhedonia.** *Neurosci Biobehav Rev.* 2016 May;64:148-66. [[ABS](#)]

Evidence supports inflammatory involvement in mood and cognitive symptoms across psychiatric, neurological and medical disorders; however, inflammation is not a sensitive or specific characteristic of these diagnoses. The National Institute of Mental Health Research Domain Criteria (RDoC) ask for a shift away from symptom-based diagnoses toward a **transdiagnostic** neurobiological focus in the study of brain illnesses. The RDoC matrix may provide a useful framework for integrating the effects of inflammation on

brain function. Based on preclinical and clinical findings, relevant relationships span negative and positive valence systems, cognitive systems, systems for social processes and arousal/regulatory systems. As an exemplar, we consider the psychopathological domain of anhedonia, conceptualizing the relevance of inflammation (e.g., cellular immunity) and downstream processes ... We discuss implications across illnesses affecting the brain, including infection, major depressive disorder, stroke, **Alzheimer's disease** and type 2 diabetes.

Distress Tolerance ▲

Patel ZS, et al (2021) - **Parent Distress Intolerance, Repetitive Negative Thinking, and Mental Health Service Use.** Child Psychiatry Hum Dev. 2021 Jun;52(3):365-375. [\[ABS\]](#)

Burr EK, et al (2020) - **Distress Intolerance in Relation to Reliance on Cigarettes for Weight, Shape, and Appetite Control.** Int J Behav Med. 2020 Apr;27(2):247-254. [\[ABS\]](#)

Distress intolerance, one's inability to withstand distressing emotional or physical states, is a transdiagnostic vulnerability implicated in affect-based health behaviors, ...Distress intolerance may play an etiological role in maladaptive use of cigarettes to control appetite, weight, and body dissatisfaction among daily smokers, particularly those with weight- or shape-related concerns. Interventions aimed at increasing perceived ability to withstand distress could potentially reduce reliance on cigarettes for the aforementioned purposes.

Fava GA, et al (2019) - **Mental Pain as a Transdiagnostic Patient-Reported Outcome Measure.** Psychother Psychosom. 2019;88(6):341-349. [\[ABS\]](#)

Assessment of mental pain may have important clinical implications in intervention research, both in psychopharmacology and psychotherapy. The **transdiagnostic** features of mental pain are supported by its association with a number of psychiatric disorders, such as depression, anxiety, eating disorders, as well as borderline personality disorder. Further, addressing mental pain may be an important pathway to prevent and diminish the opioid epidemic.

Guidi J, et al (2019) - **Mental Pain and Euthymia as Transdiagnostic Clinimetric Indices in Primary Care.** Psychother Psychosom. 2019;88(4):252-253. [\[REF\]](#)

Crabtree MA, et al (2019) - **Factor Structure and Initial Validation of a Brief Measure of Perceived Emotional and Physical Distress Tolerance in Post-9/11 US Veterans.** Mil Psychol. 2019 Jul 17;31(5). [\[FULL TEXT\]](#)

Distress tolerance (i.e., perceived or actual capacity to tolerate aversive internal states) has received considerable research attention as a **transdiagnostic** risk-factor underlying the development and maintenance of psychopathology. Lower levels of emotional distress tolerance have been linked to psychopathology (e.g. Posttraumatic Stress Disorder) within Military populations; ...The Distress Tolerance Index reflected a longitudinally invariant two-factor structure (emotional and physical distress tolerance), with excellent internal consistency and preliminary evidence of convergent validity. Thus, the DTI represents a brief, reliable and temporally stable measure of physical and emotional distress tolerance.

Mazzer K, et al (2019) - **A longitudinal view of rumination, poor sleep and psychological distress in adolescents.** J Affect Disord. 2019 Feb 15;245:686-696. [[ABS](#)]

BACKGROUND: Given the high prevalence and negative impact of psychological problems during adolescence, examining **transdiagnostic** factors that may have scope to positively influence a variety of psychological problems is imperative. ... Reducing rumination, rather than targeting sleep patterns, may work towards preventing the development of a number of psychological problems and is a strategy anticipated to function across disorders to improve young people's mental wellbeing.

Holiday SB, et al (2016) - **Depression, posttraumatic stress, and alcohol misuse in young adult veterans - The transdiagnostic role of distress tolerance.** Drug Alcohol Depend. 2016 Apr 1;161:348-55. [[FULL TEXT](#)]

"This is the first study to examine the role of distress tolerance in the relationship between mental health and alcohol misuse in a U.S. military veteran population. These results suggest that distress tolerance plays a role in the relationship between common postdeployment mental health concerns and alcohol misuse in young adult veterans. Given the significant health and psychosocial consequences of depression, PTSD, problem drinking, and the potential for tri-morbidity of these three conditions among young veterans and other high-risk populations, additional investigation of transdiagnostic factors that underlie these comorbidities is warranted and may be essential to informing prevention and treatment efforts."

Wolitzky-Taylor K, et al (2015) - **Examination of anxiety sensitivity and distress tolerance as transdiagnostic mechanisms linking multiple anxiety pathologies to alcohol use problems in adolescents.** Alcohol Clin Exp Res. 2015 Mar;39(3):532-9. [[FULL TEXT](#)]

Feldman G, et al (2014) - **Mindfulness and rumination as predictors of persistence with a distress tolerance task.** Pers Individ Dif. 2014 Jan 1;56. [[FULL TEXT](#)]

Distress tolerance (DT) is a proposed transdiagnostic factor in psychopathology, yet sources of individual differences in DT are largely unknown. The present study examined mindfulness and rumination facets as predictors of persistence on a standardized DT task

(mirror tracing). Acting with awareness (a facet of mindfulness) and reflection (a potentially adaptive form of rumination) predicted increased DT. Increased task-induced skin conductance reactivity predicted decreased DT. These results held after controlling for task skill and subjective and heart rate reactivity. Together, these results suggest that teaching skills to promote mindful awareness and reflection hold promise as interventions to enhance DT.

Eating Disorders ▲

Lapidus RC, et al (2020) - **Heightened affective response to perturbation of respiratory but not pain signals in eating, mood, and anxiety disorders.** PLoS One. 2020 Jul 15;15(7):e0235346. [\[FULL TEXT\]](#)

Several studies have recently suggested that an abnormal processing of respiratory interoceptive and nociceptive (painful) stimuli may contribute to eating disorder (ED) pathophysiology. Mood and anxiety disorders (MA) are also characterized by abnormal respiratory symptoms, and show substantial comorbidity with ED. ...During breath-holding, both the ED and MA groups reported significantly more stress, feelings of suffocation, and suffocation fear than HC, with the ED group reporting the most severe symptoms. Moreover, anxiety sensitivity was related to suffocation fear only in the ED group. ...These findings underscore the presence of abnormal respiratory interoception in MA and suggest that hyperreactivity to respiratory signals may be a potentially overlooked clinical feature of ED.

Zelkowitz RL, et al (2020) - **Longitudinal relations of self-criticism with disordered eating behaviors and nonsuicidal self-injury.** . Int J Eat Disord. 2020 Jul;53(7):1097-1107. [\[ABS\]](#)

Self-criticism has been proposed as a transdiagnostic predictor of disordered eating and nonsuicidal self-injury (NSSI). ...NSSI showed cross-sectional associations with a range of disordered eating behaviors. Self-criticism reflects a common correlate of both disordered eating and NSSI. Evidence supported transdiagnostic longitudinal impact of self-criticism across multiple forms of disordered eating but provided more limited support for impacts on NSSI.

Askew AJ, et al (2020) - **Not all body image constructs are created equal: Predicting eating disorder outcomes from preoccupation, dissatisfaction, and overvaluation.** Int J Eat Disord. 2020 Jun;53(6):954-963. [\[ABS\]](#)

Preoccupation, overvaluation, and dissatisfaction are differentially related to eating disorder and psychiatric outcomes, indicating that no one body image construct can capture clinical risk in eating disorders. Preoccupation was the most consistent

concurrent and longitudinal predictor.

Kambanis PE, et al (2020) - **Prevalence and correlates of psychiatric comorbidities in children and adolescents with full and subthreshold avoidant/restrictive food intake disorder.** Int J Eat Disord. 2020 Feb;53(2):256-265. [[FULL TEXT](#)]

We aimed to characterize the current and lifetime prevalence of comorbid psychiatric diagnoses and suicidality in treatment- and nontreatment-seeking individuals with full and subthreshold avoidant/restrictive food intake disorder (ARFID). ...Our findings underscore the severity of psychopathology among individuals with ARFID and related presentations, and also highlight the potential that shared psychopathology between specific ARFID profiles and other psychiatric disorders represent transdiagnostic constructs (e.g., avoidant behavior) that may be relevant treatment targets.

Larsen JT, et al (2020) - **Prenatal and perinatal factors and risk of eating disorders.** Psychol Med. 2020 Jan 8;1-11. [[ABS](#)]

We found that similar to the comparison disorders, prematurity was associated with increased eating disorder risk. Conversely, patterns of increasing risks of EDs, especially in AN, with increasing parental ages differed from the more U-shaped patterns observed for depressive and anxiety disorders.

Cummings JR, et al (2020) - **Parental substance use and child reward-driven eating behaviors.** Appetite. 2020 Jan 1;144:104486. [[FULL TEXT](#)]

Family history of substance use may be an important *transdiagnostic* risk factor that identifies children at risk for obesogenic, reward-driven eating behaviors.

Smith KE, et al (2020) - **The ecological validity of trait-level rumination measures among women with binge eating symptoms.** Eat Weight Disord. 2020 Jan 1;10.1007/s40519-019-00838-x. [[FULL TEXT](#)]

Martin E, et al (2019) - **Interoception and disordered eating: A systematic review.** Neurosci Biobehav Rev. 2019 Dec;107:166-191. [[ABS](#)]

104 studies with 32883 participants were included. Deficits in interoception were observed across disordered eating types and interoceptive modalities suggesting that interoception may constitute a *transdiagnostic* feature of disordered eating.

Newton JR (2019) - **Borderline personality disorder and eating disorders: a trans-diagnostic approach to unravelling diagnostic complexity.** Australas Psychiatry. 2019 Dec;27(6):556-558. [[ABS](#)]

Trans-diagnostic elements appear to include some shared aetiological factors as well as some shared syndromal components. The shared syndromal components include problems with affect, interpersonal problems, problems with self-concept and impulsivity. The pathoplastic effects of culture, attitudes to fatness and the neurobiology of starvation and/or restriction of intake are crucial to integrate into the understanding of comorbidity of these two disorders. Transdiagnostic approaches to treatment lead to transdiagnostic improvements across the two disorders.

Kesby A, et al (2019) - **Intolerance of uncertainty and eating disorder behaviour: Piloting a consumption task in a non-clinical sample.** J Behav Ther Exp Psychiatry. 2019 Dec;65:101492. [\[ABS\]](#)

Intolerance of uncertainty (IU) is a **transdiagnostic** process contributing to the maintenance of anxiety disorders, and is a potential target for treatment. Recent literature has investigated IU as a cognitive process underpinning pathological fear and anxiety in Anorexia Nervosa (AN). ...Trait IU was correlated with cognitive rigidity, worry, global eating disorder symptoms, and, in particular, dietary restraint. Should these findings be replicated in a clinical sample, then IU might emerge as an adjunctive treatment target for AN.

Prefit AB, et al (2019) - **Emotion regulation across eating pathology: A meta-analysis.** Appetite. 2019 Dec 1;143:104438. [\[ABS\]](#)

In terms of specific emotion regulation strategies, large magnitude of associations were identified for the relations between lack of emotional awareness, clarity, acceptance, reappraisal, problem-solving, and eating disorders. Rumination, avoidance of emotions, and suppression also showed large associations with anorexia nervosa and bulimia nervosa. Overall, emotion regulation did not differ across eating disorders, a finding supporting the **transdiagnostic** character of emotion regulation problems in eating pathology. These findings have important theoretical and practical implications for prevention and intervention programs.

Davis HA, et al (2019) - **Transactions between early binge eating and personality predict transdiagnostic risk.** Eur Eat Disord Rev. 2019 Nov;27(6):614-627. [\[FULL TEXT\]](#)

Psychiatric comorbidities are prevalent in youth eating disorders. In a sample of 1,906 youth from the United States (49.2% female), followed from elementary school into high school, we found support for a model to help explain this comorbidity. Endorsement of binge eating in fifth grade (elementary school) predicted increases in negative urgency, negative affect, and lack of planning in seventh grade (middle school). In turn, seventh grade negative urgency predicted increases in 10th grade (high school) externalizing dysfunction (binge eating, alcohol use problems, and smoking) and internalizing dysfunction (depressive symptoms). Seventh grade negative affect predicted increases in 10th grade binge eating and depressive symptoms. Seventh grade lack of planning predicted increases only in 10th grade externalizing behaviours. Early engagement in

binge eating may elevate risk for multiple forms of dysfunction, at least in part due to its prediction of high-risk personality change in middle school.

Cummings JR, et al (2019) - **Maternal nicotine dependence is associated with longitudinal increases in child obesogenic eating behaviors.** *Pediatr Obes.* 2019 Nov;14(11):e12541. [[FULL TEXT](#)]

Maternal nicotine dependence may be a **transdiagnostic** risk factor that identifies children at risk for reward-driven, obesogenic eating behavior.

Wang SB, et al (2019) - **Cognitive rigidity and heightened attention to detail occur transdiagnostically in adolescents with eating disorders.** *Eat Disord.* 2019 Nov 1:1-13. [[FULL TEXT](#)]

Our findings suggest cognitive inflexibility and heightened attention to detail occur **transdiagnostically** in adolescents with eating disorders and are unlikely to be a scar of the disorder. Future prospective research is needed to determine whether these cognitive styles represent an endophenotype of eating disorders.

Voderholzer U, et al (2019) - **Comparing severity and qualitative facets of depression between eating disorders and depressive disorders: Analysis of routine data.** *J Affect Disord.* 2019 Oct 1;257:758-764. [[ABS](#)]

Qualitative differences suggested that individual additional symptoms of depression need to be differently addressed in therapy. The pronounced Negative View of Self in EDs is in line with the "core low self-esteem", a central component of the prevalent **transdiagnostic** model of EDs.

Stice E, et al (2019) - **Randomized trial of a dissonance-based transdiagnostic group treatment for eating disorders: An evaluation of target engagement.** *J Consult Clin Psychol.* 2019 Sep;87(9):772-786. [[FULL TEXT](#)]

Test whether a dissonance-based **transdiagnostic** eating disorder treatment reduces valuation of the thin beauty ideal and high-calorie binge foods, the intervention targets, and eating pathology relative to waitlist controls. ... Results provide novel evidence that Body Project Treatment (BPT) affected the hypothesized intervention targets and reduced variables that are putatively secondary to pursuit of the thin ideal, including body dissatisfaction, negative affect, and eating disorder symptoms.

Kauffman BY, et al (2019) - **Anxiety sensitivity in relation to eating expectancies among college students.** *J Am Coll Health.* 2019 Sep 9:1-5. [[FULL TEXT](#)]

Disordered eating is highly prevalent on college campuses and is associated with a host of negative outcomes. ...Results indicated that higher levels of anxiety sensitivity was associated with greater levels of expectancies of eating to help manage negative affect, expectancies of eating to alleviate boredom, and expectancies of eating to lead to feeling out of control. ... These findings suggest that college students with higher anxiety sensitivity may have a greater risk for maladaptive eating expectancies.

Weissman DG, et al (2019) - **Difficulties with emotion regulation as a transdiagnostic mechanism linking child maltreatment with the emergence of psychopathology.** Dev Psychopathol. 2019 Aug;31(3):899-915. [[FULL TEXT](#)]

Greater emotional reactivity and engagement in rumination mediated the longitudinal association between maltreatment and increased general psychopathology over time. Emotion dysregulation following childhood maltreatment occurs at multiple stages of the emotion generation process, in some cases varies across development, and serves as a **transdiagnostic** mechanism linking child maltreatment with general psychopathology.

Garke M, et al (2019) - **Symptom shifting and associations with mental illness: A transdiagnostic approach applied to eating disorders.** J Abnorm Psychol. 2019 Aug;128(6):585-595. [[ABS](#)]

As hypothesized, "symptom shifters" were more prone to engage in deliberate self-harm and shifted to both deliberate self-harm and substance use across time. They had higher reported levels of symptoms indicative of mental illness (e.g., anxiety and compulsivity) and more pronounced functional impairment (clinician rated and self-rated), compared to nonshifters. Taken together, this study demonstrates that a subgroup of individuals diagnosed with eating disorder(s) shift between distinct psychiatric symptoms across time, indicating that they may share a common vulnerability to engaging in problem behaviors and a need for a more comprehensive and individualized treatment plan.

Puttevils L, et al (2019) - **Investigating transdiagnostic factors in eating disorders: Does self-esteem moderate the relationship between perfectionism and eating disorder symptoms?** Eur Eat Disord Rev. 2019 Jul;27(4):381-390. [[ABS](#)]

According to Fairburns **transdiagnostic** model of eating disorders (EDs), high levels of perfectionism and low self-esteem are two core traits across EDs. ... This study found that the interaction between perfectionism and self-esteem on DFT can be seen as **transdiagnostic**, although this effect is not found in each ED separately.

Burton AL, et al (2019) - **Processes and pathways to binge eating: development of an integrated cognitive and behavioural model of binge eating.** J Eat Disord. 2019 Jun 7;7:18. [[FULL TEXT](#)]

The dual-pathway to binge eating identified in the new model provides a different way to understand **transdiagnostic** binge eating.

Tanck JA, et al (2019) - **Gender Differences in Affective and Evaluative Responses to Experimentally Induced Body Checking of Positively and Negatively Valenced Body Parts**. Front Psychol. 2019 May 14;10:1058. [[FULL TEXT](#)]

Body checking (BC) is defined as behavior aimed at gaining information on body shape, size, or weight. Besides its occurrence as a **transdiagnostic** symptom in eating disorders (EDs), BC is widespread in non-clinical populations. It is associated with body dissatisfaction and the development of body image disturbances and ED.... These findings suggest that BC of any body part (i.e., positively or negatively valenced) leads to increased negative affect for both genders. Eating pathology significantly influences the affective responses to BC for both genders. Changes in state body satisfaction, however, only occur in females. An explanation might be that men generally report higher body satisfaction, resulting in a more stable body image. Females and males with pathological eating behavior seem to be more vulnerable to changes in negative affect. As negative affect is equally increased after NBC and PBC for both genders, BC might play a central role in the maintenance of body image disturbances in males and females.

Foye U, et al (2019) - **'The body is a battleground for unwanted and unexpressed emotions': exploring eating disorders and the role of emotional intelligence**. Eat Disord. 2019 May-Jun;27(3):321-342. [[ABS](#)]

Emotional difficulties have been observed in individuals with eating disorders across a wide range of studies, including poor interoceptive awareness, confusion of emotional states and difficulties with emotional language.

Sala M, et al (2019) - **Repetitive negative thinking predicts eating disorder behaviors: A pilot ecological momentary assessment study in a treatment seeking eating disorder sample**. Behav Res Ther. 2019 Jan;112:12-17. [[ABS](#)]

There are short-term and long-term negative effects of repetitive negative thinking in the eating disorders. Targeting repetitive negative thinking may be important for decreasing eating disorder behaviors.

Sloan E, et al (2017) - **Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: A systematic review**. Clin Psychol Rev. 2017 Nov;57:141-163. [[ABS](#)]

A large body of research has implicated difficulties in emotion regulation as central to the development and maintenance of psychopathology. Emotion regulation has therefore been proposed as a **transdiagnostic** construct or an underlying mechanism in psychopathology. The transdiagnostic role of emotion regulation has yet to be

systematically examined within the psychological treatment outcome literature. It can be proposed that if emotion regulation is indeed a transdiagnostic construct central to the maintenance of psychopathology, then changes in emotion regulation difficulties will occur after effective treatment and this will occur for different disorders. We conducted a systematic review, identifying 67 studies that measured changes in both emotion regulation and symptoms of psychopathology following a psychological intervention for anxiety, depression, substance use, eating pathology or borderline personality disorder. Results demonstrated that regardless of the intervention or disorder, both maladaptive emotion regulation strategy use and overall emotion dysregulation were found to significantly decrease following treatment in all but two studies. Parallel decreases were also found in symptoms of anxiety, depression, substance use, eating pathology and borderline personality disorder. These results contribute to the growing body of evidence supporting the conceptualization of emotion regulation as a **transdiagnostic** construct. The present study discusses the important implications of these findings for the development of unified treatments that target emotion regulation for individuals who present with multiple disorders.

Vannucci A, et al (2015) - **Behavioral and neurodevelopmental precursors to binge-type eating disorders: support for the role of negative valence systems.** Psychol Med. 2015 Oct;45(14):2921-36. [[FULL TEXT](#)]

Vann A, et al (2014) - **The transdiagnostic nature of metacognitions in women with eating disorders.** Eat Disord. 2014;22(4):306-20. [[ABS](#)]

"There is emerging evidence for the important role of metacognitions in the presentation of eating disorders (EDs); however it is unclear to what extent these metacognitions are transdiagnostic. This study used a mixed methods convergent design to explore this question by triangulating both qualitative and quantitative data from 27 women, aged 18-55 years, with diagnoses of anorexia nervosa, bulimia nervosa, or eating disorders not otherwise specified. The results indicated that metacognitions in EDs may be transdiagnostic and may in part explain temporal migration between diagnoses and the degree of comorbidity associated with EDs."

Kelly AC, et al (2014) - **Are improvements in shame and self-compassion early in eating disorders treatment associated with better patient outcomes?** Int J Eat Disord. 2014 Jan;47(1):54-64. [[ABS](#)]

Multilevel modeling revealed that patients who experienced greater decreases in their level of shame in the first 4 weeks of treatment had faster decreases in their eating disorder symptoms over 12 weeks of treatment. In addition, patients who had greater increases in their level of self-compassion early in treatment had faster decreases in their feelings of shame over 12 weeks, even when controlling for their early change in eating disorder symptoms. These results suggest that CFT theory may help to explain the maintenance of eating disorders. Clinically, findings suggest that intervening with shame

early in treatment, perhaps by building patients' self-compassion, may promote better eating disorders treatment response.

Electromagnetic Field Exposure ▲

Smith-Roe SL, et al (2020) - **Evaluation of the genotoxicity of cell phone radiofrequency radiation in male and female rats and mice following subchronic exposure.** Environmental and Molecular Mutagenesis, Vol 61, Issue 2, Feb 2020: 276-290. [[FULL TEXT](#)]

Radio frequency radiation is associated with increased DNA damage in the frontal cortex and hippocampus of male mice and leukocytes of female mice.

Pritchard C, et al (2019) - **Are rises in Electro-Magnetic Field in the human environment, interacting with multiple environmental pollutions, the tripping point for increases in neurological deaths in the Western World?** Med Hypotheses. 2019 Jun;127:76-83. [[FULL TEXT](#)]

Misek J, et al (2018) - **Heart rate variability affected by radiofrequency electromagnetic field in adolescent students.** Bioelectromagnetics. 2018 May;39(4):277-288.

Djordjevic NZ, et al (2017) - **Anxiety-like behavioural effects of extremely low-frequency electromagnetic field in rats.** Environ Sci Pollut Res Int. 2017 Jul 29 [[ABS](#)]

Emotional Regulation ▲

Colombo D, et al (2021) - **Virtual Reality for the Enhancement of Emotion Regulation.** Clin Psychol Psychother. 2021 May 28. [[ABS](#)]

Corpas J, et al (2021) - **Cognitive processes associated with emotional disorders: implications for efficient psychological treatments.** J Ment Health. 2021 May 14:1-9. [[ABS](#)]

For "pure" disorders, targeting a concrete cognitive process might be an optimal therapeutic option. However, due to the high comorbidity among EDs, we support the dissemination of the transdiagnostic treatment approach in which all cognitive factors are taken into account.

Herpers PCM, et al (2020) - **Treatment Refractory Internalizing Behaviour across Disorders: An Aetiological Model for Severe Emotion Dysregulation in Adolescence.** Child Psychiatry Hum Dev. 2020 Aug 3. [[ABS](#)]

To optimize treatment efficacy for both internalizing and externalizing behavior, we emphasize the importance of transdiagnostic interventions, such as addressing non-compliance, restoration of trust between parents and their child, and limitation of avoidance behavior.

Byrd AL, et al (2020) - **An interaction between early threat exposure and the oxytocin receptor in females: Disorder-specific versus general risk for psychopathology and social-emotional mediators.** Dev Psychopathol. 2020 Jul 22;1-16. [[ABS](#)]

Early threat exposure is a transdiagnostic risk factor for psychopathology, and evidence suggests that genetic variation in the oxytocin receptor (OXTR) moderates this association. ...the interactive effects of early threat exposure and OXTR variation (rs53576) predicted general psychopathology, with threat-exposed women carrying at least one copy of the rs53576 A-allele at greatest risk. This interaction was mediated via emotional dysregulation in adolescence, with threat-exposed A-allele carriers demonstrating greater emotion dysregulation, and greater emotion dysregulation predicting general psychopathology in early adulthood. Findings suggest that this G×E places women at risk for a broad range of psychopathology via effects on emotion dysregulation.

Horvath SA, et al (2020) - **Emotion dysregulation as a correlate of food and alcohol disturbance in undergraduate students.** Eat Behav. 2020 Jun 20;38:101409. [[ABS](#)]

Disordered eating behaviors (e.g., binge eating, food restriction, self-induced vomiting, and laxative use) as well as alcohol use and related issues are prevalent in undergraduate students and are often comorbid with one another. Recently, the unique combination of these behaviors, termed food and alcohol disturbance (FAD), has received empirical attention. FAD involves compensatory behaviors performed in preparation for, or in response to, alcohol use in order to counteract calories consumed from alcohol and/or to increase intoxication. ...FAD was positively associated with emotion dysregulation at the bivariate level, but emotion dysregulation was not uniquely associated with FAD after accounting for disordered eating, alcohol use and problems, and body mass index.

McTeague LM, et al (2020) - **Identification of Common Neural Circuit Disruptions in Emotional Processing Across Psychiatric Disorders.** Am J Psychiatry. 2020 May 1;177(5):411-421. [[FULL TEXT](#)]

These findings demonstrate a pattern of neurocircuit disruption across major psychiatric disorders in regions and networks key to adaptive emotional reactivity and regulation. More specifically, disruption corresponded prominently to the "salience" network, the ventral striatal/ventromedial prefrontal "reward" network, and the lateral orbitofrontal "nonreward" network. Consistent with the Research Domain Criteria initiative, these findings suggest that psychiatric illness may be productively formulated as dysfunction in

transdiagnostic neurobehavioral phenotypes such as neurocircuit activation.

Fantini-Hauwel C, et al (2020) - **Emotion Regulation Difficulties Are Not Always Associated with Negative Outcomes on Women: The Buffer Effect of HRV**. Front Psychol. 2020 Apr 30;11:697. [\[FULL TEXT\]](#)

Overall, high resting HRV appears to dampen the consequences of trait emotion regulation difficulties.

Zwicker A, et al (2020) - **Affective lability in offspring of parents with major depressive disorder, bipolar disorder and schizophrenia**. Eur Child Adolesc Psychiatry. 2020 Apr;29(4):445-451. [\[ABS\]](#)

Affective lability, defined as the propensity to experience excessive and unpredictable changes in mood, has been proposed as a potential transdiagnostic predictor of major mood and psychotic disorders. A parental diagnosis of bipolar disorder has been associated with increased affective lability in offspring. ... Our results suggest that elevated affective lability during childhood is a marker of familial risk for mood disorders.

Barkus E (2020) - **Effects of working memory training on emotion regulation: Transdiagnostic review**. Psych J. 2020 Apr;9(2):258-279. [\[ABS\]](#)

Working memory training is widely used transdiagnostically to improve cognition. However, more recently, studies using working memory training packages have targeted emotion-regulation outcomes to determine whether far transfer effects can be achieved. ...Working memory training could improve cognitive efficiency, which, in turn, increases the availability of cognitive resources during times when emotion regulation is taxed. Working memory training offers a possibility for improving emotion regulation transdiagnostically.

Kostyrka-Allchorne K, et al (2020) - **Research Review: Do parent ratings of infant negative emotionality and self-regulation predict psychopathology in childhood and adolescence? A systematic review and meta-analysis of prospective longitudinal studies**. J Child Psychol Psychiatry. 2020 Apr;61(4):401-416. [\[ABS\]](#)

Identifying low-cost and easy to implement measures of infant markers of later psychopathology may improve targeting of early intervention for prevention. ...Questionnaire-based assessments of infant negative emotionality may have transdiagnostic potential to contribute to a risk index of later childhood psychopathology. Behavioral inhibition, surgency/extraversion and activity ratings may provide more specific predictive power.

Lam AHY, et al (2020) - **The Effectiveness of a Mindfulness-Based Psychoeducation Programme**

for Emotional Regulation in Individuals with Schizophrenia Spectrum Disorders: A Pilot Randomised Controlled Trial. Neuropsychiatr Dis Treat. 2020 Mar 12;16:729-747. [[FULL TEXT](#)]

Emotion dysregulation has emerged as a transdiagnostic factor that potentially exacerbates the risk of early-onset, maintenance, and relapse of psychosis. ...The MBPP appeared to be effective for improving emotion regulation, which will contribute to future large-scale RCT to confirm the treatment effects in more diverse groups of schizophrenic patients.

Koch T, et al (2020) - **Emotion regulation as a transdiagnostic factor in Afghan refugees.** Psychol Trauma. 2020 Mar;12(3):235-243. [[ABS](#)]

In response to the high rates of comorbidity as well as the severe social impairment among refugees, the examination of transdiagnostic factors such as emotion regulation appears particularly promising in this group. This study investigates the contribution of difficulties in emotion regulation to the self-reported symptom levels of posttraumatic stress disorder (PTSD), depression, and anxiety/insomnia, which are highly prevalent symptoms among refugees. In addition, the link between emotion regulation and social impairment is examined. ...The findings indicate that emotion regulation may be a transdiagnostic key factor contributing to symptoms of different mental disorders as well as social impairment in trauma-exposed refugees. It highlights the need and potential directions for transdiagnostic interventions that target these difficulties.

Weiss NH, et al (2020) - **The interplay of negative and positive emotion dysregulation on mental health outcomes among trauma-exposed community individuals.** Psychol Trauma. 2020 Mar;12(3):219-226. [[FULL TEXT](#)]

Emotion dysregulation is a transdiagnostic construct with relevance to a wide range of mental health outcomes. ...Both negative and positive emotion dysregulation were positively related to PTSD, depression, and alcohol and drug misuse. ... These findings suggest that the relation of positive emotion dysregulation to mental health outcomes may not be dependent on negative emotion dysregulation, supporting the utility of both negative and positive emotion dysregulation in identifying and treating mental health outcomes in trauma-exposed individuals.

Gaffrey MS, et al (2020) - **Amygdala Functional Connectivity Is Associated with Emotion Regulation and Amygdala Reactivity in 4- to 6-Year-Olds.** J Am Acad Child Adolesc Psychiatry. 2020 Feb 28:S0890-8567(20)30125-8. [[ABS](#)]

Emotion dysregulation has been suggested to be a potent risk factor for multiple psychiatric conditions. Altered amygdala-prefrontal cortex (PFC) connectivity has been consistently linked to emotion dysregulation. Recent data indicate that amygdala-PFC functional connectivity undergoes a prolonged period of development, with amygdala reactivity during early childhood potentially shaping this unfolding process.... Right

amygdala-medial PFC (mPFC) functional connectivity was positively associated with child emotion regulation ability and negatively associated with child negative affect and right amygdala reactivity to facial expressions of emotion.

Bridgett DJ (2020) - **Editorial: Out of Control: More Evidence That Both Family Ecology and Genetic Influences Contribute to the Origins of Poor Self-Control among Adolescents.** J Am Acad Child Adolesc Psychiatry. 2020 Feb;59(2):222-224. [\[ABS\]](#)

Poor self-control, and poor self-regulation more broadly, plays a notable role in myriad outcomes of concern to our field and to society. Poor self-control has been implicated in criminality, academic difficulties, occupational challenges, problematic interpersonal relationships, lower income, and financial problems, and has been identified as a **transdiagnostic** risk factor for psychiatric difficulties across the life span. Poor self-control also has been associated with health outcomes such as elevated risk for obesity.

Cludius B, et al (2020) - **Emotion regulation as a transdiagnostic process.** Emotion. 2020 Feb;20(1):37-42. [\[ABS\]](#)

Silton RL, et al (2020) - **Regulating positive emotions: Implications for promoting well-being in individuals with depression.** Emotion. 2020 Feb;20(1):93-97. [\[ABS\]](#)

Experiencing positive emotions is paramount to derive vitality from daily lived experiences. Positive emotions are associated with a range of beneficial outcomes, including longevity, reduced incidents of stroke, improved sleep quality, larger social networks, increased prosocial behavior, lower cortisol levels, and increased endogenous opioids and oxytocin. Despite these benefits, only limited research has focused on understanding positive emotion regulation within the context of depression. Rather, mechanisms related to the regulation of negative emotion have been the focus of research and evidence-based treatments. This interdisciplinary review article aims to advance knowledge regarding the role of positive emotion regulation in individuals with depression to inform the development of transdiagnostic evidenced-based approaches to treatment that bolster the experience of positive life events.

Sperry SH, et al (2020) - **Emotion dynamics concurrently and prospectively predict mood psychopathology.** J Affect Disord. 2020 Jan 15;261:67-75. [\[ABS\]](#)

Altered emotion dynamics may represent a transdiagnostic risk factor for mood psychopathology. ... Negative affect variability and instability predicted the development of new bipolar spectrum disorders at the follow-up.

Mazefsky CA, et al (2020) - **Psychometric Properties of the Emotion Dysregulation Inventory in a Nationally Representative Sample of Youth.** J Clin Child Adolesc Psychol. 2020 Jan 7:1-13. [\[ABS\]](#)

The Emotion Dysregulation Inventory (EDI)... Although it was developed to improve measurement of emotion dysregulation in youth with autism spectrum disorder, emotion dysregulation has transdiagnostic significance. ...Analyses supported the original two-factor structure of the EDI, reflecting factors for Reactivity and Dysphoria. ...The EDI is an efficient and precise measure of emotion dysregulation for use in general community and clinical samples as well as samples of youth with ASD.

Powers A, et al (2020) - **Intergenerational transmission of risk for PTSD symptoms in African American children: The roles of maternal and child emotion dysregulation.** Psychol Trauma. 2020 Jan 2;10.1037/tra0000543. [[FULL TEXT](#)]

Emotion dysregulation is a transdiagnostic risk factor for many mental health disorders and develops in the context of early trauma exposure. Research suggests intergenerational risk associated with trauma exposure and posttraumatic stress disorder (PTSD), such that maternal trauma experiences and related symptoms can negatively impact child outcomes across development. ...Both maternal and child emotion dysregulation could be valuable treatment targets for improving maternal mental health and parenting behaviors and bolstering child health outcomes, thus reducing intergenerational transmission of risk associated with trauma

Soehner AM, et al (2019) - **Unstable wakefulness during resting-state fMRI and its associations with network connectivity and affective psychopathology in young adults.** J Affect Disord. 2019 Nov 1;258:125-132. [[FULL TEXT](#)]

Drifts between wakefulness and sleep are common during resting state functional MRI (rsfMRI). Among healthy adults, within-scanner sleep can impact functional connectivity of default mode (DMN), task-positive (TPN), and thalamo-cortical networks. Because dysfunctional arousal states (i.e., sleepiness, sleep disturbance) are common in affective disorders, individuals with affective psychopathology may be more prone to unstable wakefulness during rsfMRI, hampering the estimation of clinically meaningful functional connectivity biomarkers.

Beauchaine TP, et al (2019) - **Emotion dysregulation and emerging psychopathology: A trans-diagnostic, transdisciplinary perspective.** Dev Psychopathol. 2019 Aug;31(3):799-804. [[REF](#)]

Lin B, et al (2019) - **Intergenerational transmission of emotion dysregulation: Part I. Psychopathology, self-injury, and parasympathetic responsivity among pregnant women.** Dev Psychopathol. 2019 Aug;31(3):817-831. [[FULL TEXT](#)]

The World Health Organization recently reported that maternal mental health is a major public health concern. As many as one in four women suffer from psychiatric disorders at some point during pregnancy or the first postpartum year. Furthermore, *self-injurious thoughts and behaviors (SITBs)* represent one of the leading causes of death among women during this time. Thus, efforts to identify women at risk for serious forms of psychopathology and especially for SITBs are of utmost importance. Despite this urgency,

current single-diagnostic approaches fail to recognize a significant subset of women who are vulnerable to perinatal stress and distress. The current study was among the first to investigate emotion dysregulation—a multilevel, **transdiagnostic** risk factor for psychopathology—and its associations with stress, distress, and SITBs in a sample of pregnant women (26–40 weeks gestation) recruited to reflect a range of emotion dysregulation. Both self-reported emotion dysregulation and respiratory sinus arrhythmia, a biomarker of emotion dysregulation, demonstrated expected associations with measures of mental health, including depression, anxiety, borderline personality pathology, and SITBs. In addition, self-reported emotion dysregulation was associated with blunted respiratory sinus arrhythmia responsivity to an ecologically valid infant cry task. Findings add to the literature considering **transdiagnostic** risk during pregnancy using a multiple-levels-of-analysis approach.

Silverman MH, et al (2019) - **Trait neuroticism and emotion neurocircuitry: Functional magnetic resonance imaging evidence for a failure in emotion regulation.** Dev Psychopathol. 2019 Aug;31(3):1085–1099. [[FULL TEXT](#)]

Although neuroticism was not significantly associated with magnitude of amygdala activation or amygdala habituation, it was associated with amygdala-ventromedial prefrontal cortex connectivity, which has been implicated in emotion regulation. Results suggest that trait neuroticism may represent a failure in top-down control and regulation of emotional reactions, rather than overactive emotion generation processes, per se. These findings suggest that neuroticism, which has been associated with increased rates of **transdiagnostic** psychopathology, may represent a failure in the inhibitory neurocircuitry associated with emotion regulation.

Weissman DG, et al (2019) - **Difficulties with emotion regulation as a transdiagnostic mechanism linking child maltreatment with the emergence of psychopathology.** Dev Psychopathol. 2019 Aug;31(3):899–915. [[FULL TEXT](#)]

Greater emotional reactivity and engagement in rumination mediated the longitudinal association between maltreatment and increased general psychopathology over time. Emotion dysregulation following childhood maltreatment occurs at multiple stages of the emotion generation process, in some cases varies across development, and serves as a **transdiagnostic** mechanism linking child maltreatment with general psychopathology.

Park J, et al (2019) - **Daily experiences of emotional clarity and their association with internalizing symptoms in naturalistic settings.** Emotion. 2019 Aug;19(5):764–775. [[ABS](#)]

Overall, the present study provides support for the **transdiagnostic** nature of emotional clarity and clarifies the mechanisms by which emotional clarity may impact symptoms over time in daily life. Theoretical and clinical implications for the role of emotional clarity in psychopathology are discussed.

Gisbert L, et al (2019) - **Genome-wide analysis of emotional lability in adult attention deficit hyperactivity disorder (ADHD)**. Eur Neuropsychopharmacol. 2019 Jun;29(6):795-802. [\[ABS\]](#)

Emotional lability is strongly associated with Attention Deficit Hyperactivity Disorder (ADHD), represents a major source of impairment and predicts poor clinical outcome in ADHD..., these tentative results are in agreement with previous studies that suggest emotion dysregulation as a **transdiagnostic** construct and highlight the need for further investigation to disentangle the genetic basis of mood instability in ADHD and co-occurring psychiatric disorders.

Gross JJ, et al (2019) - **Mental illness and well-being: an affect regulation perspective**. World Psychiatry. 2019 Jun;18(2):130-139. [\[FULL TEXT\]](#)

Golombek K, et al (2019) - **The role of emotion regulation in socially anxious children and adolescents: a systematic review**. Eur Child Adolesc Psychiatry. 2019 Jun 14. [\[ABS\]](#)

Study results indicate that children and adolescents with social anxiety disorder or high social anxiety show emotion dysregulation across all five domains of emotion regulation, such as enhanced social avoidance, more safety behaviors, repetitive negative thinking, biased attention and interpretation of social information, and reduced emotional expression. While enhanced social avoidance seems to be specific to childhood social anxiety, other maladaptive emotion regulation strategies, such as repetitive negative thinking, seem to occur **transdiagnostically** across different childhood anxiety disorders. Implications for current theory, interventions and future research are discussed.

Fitzgerald JM, et al (2019) - **Transdiagnostic neural correlates of volitional emotion regulation in anxiety and depression**. **Depress Anxiety**. 2019 May;36(5):453-464. [\[FULL TEXT\]](#)

Individuals who suffer from anxiety and/or depression face difficulty in adaptively managing emotional responses, while accumulating evidence suggests impaired emotion regulation is a **transdiagnostic** feature of psychopathology. Effectual regulation in the context of negative stimuli is characterized by engagement of the prefrontal cortex (PFC) coupled with reduced amygdala reactivity. In anxiety disorders and major depression, PFC underengagement and atypical PFC-amygdala connectivity has been observed, although patient findings based on case-control studies have been mixed with regard to magnitude, locality, and extent of dysfunction. ...Across participants, whole-brain results showed that (1) greater anxiety and depression symptom severity was related to less engagement of the dorsal anterior cingulate cortex (ACC) and (2) less FC between the amygdala and ventrolateral PFC. Results were driven by anxiety, while depression symptoms were not significant. ...These findings demonstrate that individual differences in anxiety and depression may help explain ACC and PFC dysfunction during emotion regulation observed across anxiety and depressive disorders.

Ling G, et al (2019) - **Individual variation in brain network topology is linked to emotional intelligence.** Neuroimage. 2019 Apr 1;189:214-223. [[FULL TEXT](#)]

Social cognitive ability is a significant determinant of functional outcome, and deficits in social cognition are a disabling symptom of psychotic disorders. ... We identified a region in the left superior parietal lobule (SPL) where individual network topology is linked to emotional intelligence. Specifically, in high scoring individuals, this region is a node of the Default Mode Network and in low scoring individuals, it is a node of the Dorsal Attention Network.

Panchal P, et al (2019) - **Cognitive emotional processing across mood disorders.** CNS Spectr. 2019 Feb;24(1):54-63. [[ABS](#)]

Special consideration is given to the shared phenomenon of mood instability and its role as a potential **transdiagnostic** marker across the prodrome and maintenance of mood disorders.

Mohajerin B, et al (2019) - **Application of a transdiagnostic treatment for emotional disorders to body dysmorphic disorder: A randomized controlled trial.** J Affect Disord. 2019 Feb 15;245:637-644. [[ABS](#)]

Body dysmorphic disorder (BDD) is a common disorder which is associated with a high rate of comorbidity and functional impairment. Although research shows that cognitive-behavioral therapy can be an efficacious treatment for BDD, there is growing evidence that dysregulated emotion is a core deficit. The *Unified Protocol for the Transdiagnostic Treatment of Emotional Disorders (UP)* is a transdiagnostic, emotion focused cognitive-behavioral therapy protocol that has been developed to target emotion regulation processes that play an important role in the development and maintenance of many emotional disorders

To our knowledge, this is the first examination of the **UP** for BDD, and results suggest that this disorder shares common mechanisms with other disorders of emotion, and that the UP may be an additional efficacious treatment for this condition.

Miller AB, et al (2019) - **Emotion Reactivity and Regulation in Adolescent Girls Following an Interpersonal Rejection.** J Cogn Neurosci. 2019 Feb;31(2):249-261. [[FULL TEXT](#)]

Failures in emotion regulation, especially as a result of interpersonal stress, are implicated as **transdiagnostic** risk factors for psychopathology. ... study provides evidence that a targeted rejection increases self-report and neural markers of emotion reactivity and that girls increase prefrontal activation to regulate emotions after a targeted rejection.

Um M, et al (2019) - **Shared Neural Correlates Underlying Addictive Disorders and Negative Urgency.** Brain Sci. 2019 Feb 8;9(2):36. [[FULL TEXT](#)]

Negative urgency is a personality trait reflecting the tendency to act rashly in response to extreme negative emotions and is considered a **transdiagnostic** endophenotype for problematic levels of addictive behaviors. Recent research has begun to identify the neural correlates of negative urgency, many of which appear to overlap with neural circuitry underlying addictive disorders associated with negative urgency. ... Patterns of structure and function in the ventral striatum, frontal regions, such as the prefrontal cortex (PFC) and orbitofrontal cortex (OFC), and amygdala are common across addictive disorders and are related to both real-world risky behaviors and self-report measures of negative urgency.

Guimond AJ, et al (2019) - **Is emotion regulation associated with cancer-related psychological symptoms?** Psychol Health. 2019 Jan;34(1):44-63. [[ABS](#)]

Although preliminary, these results are consistent with the hypothesis that maladaptive ER strategies, assessed subjectively, may cross-sectionally act as a **transdiagnostic** mechanism underlying several cancer-related psychological symptoms.

Rosellini AJ, et al (2019) - **The Multidimensional Emotional Disorder Inventory (MEDI): Assessing transdiagnostic dimensions to validate a profile approach to emotional disorder classification.** Psychol Assess. 2019 Jan;31(1):59-72. [[FULL TEXT](#)]

The goal of the current study was to develop and validate the Multidimensional Emotional Disorder Inventory (MEDI) to efficiently assess nine empirically supported **transdiagnostic** dimensions proposed in the Brown and Barlow (2009) profile approach to emotional disorder classification: neurotic temperament, positive temperament, depression, autonomic arousal, somatic anxiety, social anxiety, intrusive cognitions, traumatic reexperiencing, and avoidance. ... Because it provides an efficient assessment of several well-established emotional disorder traits and phenotypes, the MEDI also may have utility for general research or clinical purposes

Zhao Z, et al (2019) - **Real-Time Functional Connectivity-Informed Neurofeedback of Amygdala-Frontal Pathways Reduces Anxiety.** Psychother Psychosom. 2019;88(1):5-15. [[ABS](#)]

Deficient *emotion regulation* and exaggerated anxiety represent a major **transdiagnostic** psychopathological marker. On the neural level these deficits have been closely linked to impaired, yet treatment-sensitive, prefrontal regulatory control over the amygdala. Gaining direct control over these pathways could therefore provide an innovative and promising intervention to regulate exaggerated anxiety.

To this end the current proof-of-concept study evaluated the feasibility, functional relevance and maintenance of a novel connectivity-informed real-time fMRI neurofeedback

training. **METHODS:** In a randomized crossover sham-controlled design, 26 healthy subjects with high anxiety underwent real-time fMRI-guided neurofeedback training to enhance connectivity between the ventrolateral prefrontal cortex (vlPFC) and the amygdala (target pathway) during threat exposure. Maintenance of regulatory control was assessed after 3 days and in the absence of feedback. Training-induced changes in functional connectivity of the target pathway and anxiety ratings served as primary outcomes.

Training of the target, yet not the sham control, pathway significantly increased amygdala-vlPFC connectivity and decreased levels of anxiety. Stronger connectivity increases were significantly associated with higher anxiety reduction on the group level. At the follow-up, volitional control over the target pathway was maintained in the absence of feedback.

The present results demonstrate for the first time that successful self-regulation of amygdala-prefrontal top-down regulatory circuits may represent a novel intervention to control anxiety. As such, the present findings underscore both the critical contribution of amygdala-prefrontal circuits to emotion regulation and the therapeutic potential of connectivity-informed real-time neurofeedback.

Sloan E, et al (2017) - **Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: A systematic review.** Clin Psychol Rev. 2017 Nov;57:141-163. [[ABS](#)]

A large body of research has implicated difficulties in emotion regulation as central to the development and maintenance of psychopathology. Emotion regulation has therefore been proposed as a transdiagnostic construct or an underlying mechanism in psychopathology. The transdiagnostic role of emotion regulation has yet to be systematically examined within the psychological treatment outcome literature. It can be proposed that if emotion regulation is indeed a transdiagnostic construct central to the maintenance of psychopathology, then changes in emotion regulation difficulties will occur after effective treatment and this will occur for different disorders. We conducted a systematic review, identifying 67 studies that measured changes in both emotion regulation and symptoms of psychopathology following a psychological intervention for anxiety, depression, substance use, eating pathology or borderline personality disorder. Results demonstrated that regardless of the intervention or disorder, both maladaptive emotion regulation strategy use and overall emotion dysregulation were found to significantly decrease following treatment in all but two studies. Parallel decreases were also found in symptoms of anxiety, depression, substance use, eating pathology and borderline personality disorder. These results contribute to the growing body of evidence supporting the conceptualization of emotion regulation as a transdiagnostic construct. The present study discusses the important implications of these findings for the development of unified treatments that target emotion regulation for individuals who present with multiple disorders.

Powers A, et al (2017) - **Neural correlates and structural markers of emotion dysregulation in traumatized civilians.** Soc Cogn Affect Neurosci. 2017 May 1;12(5):823-831. [\[FULL TEXT\]](#)

Keil V, et al (2017) - **Children with social anxiety and other anxiety disorders show similar deficits in habitual emotional regulation: evidence for a transdiagnostic phenomenon.** Eur Child Adolesc Psychiatry. 2017 Jul;26(7):749-757. [\[ABS\]](#)

Malhi GS, et al (2017) - **Irritability and internalizing symptoms: Modeling the mediating role of emotion regulation.** J Affect Disord. 2017 Mar 15;211:144-149. [\[ABS\]](#)

Stanton K, et al (2016) - **A transdiagnostic approach to examining the incremental predictive power of emotion regulation and basic personality dimensions.** J Abnorm Psychol. 2016 Oct;125(7):960-975. [\[ABS\]](#)

These data provide a starting point for developing a finer-grained understanding of how emotion dysregulation and personality traits are implicated in a range of psychopathology, highlighting the value of adopting an integrative approach of examining emotion regulation and personality traits concurrently

Jenkins LM, et al (2016) – **Shared white matter alterations across emotional disorders: A voxel-based meta-analysis of fractional anisotropy.** Neuroimage Clin. 2016 Sep 28;12:1022-1034. [\[FULL TEXT\]](#)

Distinct diagnostic categories of ED show commonalities in WM tracts with reduced FA when compared to HC, which links brain networks involved in cognitive and affective processing. This meta-analysis facilitates an increased understanding of the biological markers that are shared by these ED

Fernandez KC, et al (2016) - **Emotion Regulation: A Transdiagnostic Perspective on a New RDoC Domain.** Cognit Ther Res. 2016 Jun;40(3):426-440. [\[FULL TEXT\]](#)

Kepecs A, et al (2015) - **Emotor control: computations underlying bodily resource allocation, emotions, and confidence.** Dialogues Clin Neurosci. 2015 Dec;17(4):391-401. [\[FULL TEXT\]](#)

Siegle GH, et al (2015) - **Prolonged physiological reactivity and loss: Association of pupillary reactivity with negative thinking and feelings.** Int J Psychophysiol. 2015 Nov;98(2 Pt 2):310-320. [\[FULL TEXT\]](#)

Broome MR, et al (2015) - **Mood instability: significance, definition and measurement.** Br J Psychiatry. 2015 Oct;207(4):283-5. [\[FULL TEXT\]](#)

Mood instability is common, and an important feature of several psychiatric disorders. We discuss the definition and measurement of mood instability, and review its

prevalence, characteristics, neurobiological correlates and clinical implications. We suggest that mood instability has underappreciated transdiagnostic potential as an investigational and therapeutic target.

Beauchaine TP (2015) - **Respiratory Sinus Arrhythmia: A Transdiagnostic Biomarker of Emotion Dysregulation and Psychopathology.** Curr Opin Psychol. 2015 Jun 1;3:43-47. [\[FULL TEXT\]](#)

In the past two decades, respiratory sinus arrhythmia (RSA)—an index of parasympathetic nervous system (PNS)-mediated cardiac control—has emerged as a reliable peripheral biomarker of emotion regulation (ER). Reduced RSA and excessive RSA reactivity (i.e., withdrawal) to emotional challenge are observed consistently among individuals with poor ER capabilities, including those with various forms of internalizing and externalizing psychopathology, and those with specific psychopathological syndromes, including anxiety, phobias, attention problems, autism, callousness, conduct disorder, depression, non-suicidal self-injury, panic disorder, and trait hostility. Emerging evidence suggests that low RSA and excessive RSA reactivity index poor ER because they are downstream peripheral markers of prefrontal cortex (PFC) dysfunction. Poorly modulated inhibitory efferent pathways from the medial PFC to the PNS result in reduced RSA and excessive RSA reactivity. According to this perspective, RSA is a non-invasive proxy for poor executive control over behavior, which characterizes most forms of psychopathology.

Neacsiu AD, et al (2015) - **Identity disturbance and problems with emotion regulation are related constructs across diagnoses.** Clin Psychol. 2015 Apr;71(4):346-61. [\[ABS\]](#)

Bebko G, et al (2015) - **Decreased amygdala-insula resting state connectivity in behaviorally and emotionally dysregulated youth.** Psychiatry Res. 2015 Jan 30;231(1):77-86. [\[FULL TEXT\]](#)

Resting state connectivity between amygdala and posterior insula decreased with increasing severity of behavioral and emotional dysregulation and depression; this suggests an intrinsic functional uncoupling of key neural regions supporting emotion processing and regulation. These findings support the RDoC dimensional approach for characterizing pathophysiologic processes that cut across different psychiatric disorders.

Guy L, et al (2014) - **Brief report: emotion regulation and respiratory sinus arrhythmia in autism spectrum disorder.** J Autism Dev Disord. 2014 Oct;44(10):2614-20. [\[ABS\]](#)

Emotion regulation (ER) may be an important transdiagnostic factor for understanding mental and behavioral health given its association with several psychiatric disorders, including autism spectrum disorder (ASD). However, there is limited research on ER in ASD, particularly using biomarkers such as respiratory sinus arrhythmia (RSA). The aim of the current study was to examine RSA among school-aged children with ASD in relation to symptoms of anxiety, executive functioning, and adaptive socialization skills. Results showed decreased RSA in children with ASD (relative to typically developing controls),

reflecting decreased parasympathetic nervous system activity. In addition, decreased RSA was associated with increased symptoms of anxiety and lower socialization skills. These findings emphasize the need for interventions targeting emotional and arousal regulation in ASD.

Gruber J, et al (2013) - **Reward dysregulation and mood symptoms in an adolescent outpatient sample.** J Abnorm Child Psychol. 2013 Oct;41(7):1053-65. [\[FULL TEXT\]](#)

Fairholme CP, et al (2013) - **Sleep disturbance and emotion dysregulation as transdiagnostic processes in a comorbid sample.** Behav Res Ther. 2013 Sep;51(9):540-6. [\[FULL TEXT\]](#)

Insomnia and emotion dysregulation appear to be transdiagnostic processes uniquely associated with symptom severity across a number of different domains and might be important treatment targets for individuals with PTSD and alcohol dependence.

Hechtman LA, et al (2013) - **Positive Emotion Regulation and Psychopathology - A Transdiagnostic Cultural Neuroscience Approach.** J Exp Psychopathol. 2013 May 13;4(5):502-528. [\[FULL TEXT\]](#)

Dadds MR, et al (2012) - **Outcomes, moderators, and mediators of empathic-emotion recognition training for complex conduct problems in childhood.** Psychiatry Res. 2012 Oct 30;199(3):201-7. [\[ABS\]](#)

Diagnostic status of the child did not moderate outcomes; however, levels of callous-unemotional (CU) traits moderated outcomes such that children with high CU traits responded less well to TAU, while ERT produced significant improvements in affective empathy and conduct problems in these children. Emotion recognition training has potential as an adjunctive intervention specifically for clinically referred children with high CU traits, regardless of their diagnostic status.

Error Monitoring ▲

Michael JA, et al (2021) - **EEG correlates of attentional control in anxiety disorders: A systematic review of error-related negativity and correct-response negativity findings.** J Affect Disord. 2021 May 24;291:140-153. [\[ABS\]](#)

Findings indicate the promising utility of ERN of attentional control as a robust, transdiagnostic trait marker of clinical anxiety.

Hill KE, et al (2016) - **Contextualizing individual differences in error monitoring: Links with impulsivity, negative affect, and conscientiousness.** Psychophysiology. 2016 Aug;53(8):1143-53.

[ABS]

Ladouceur CD (2016) - **The error-related negativity: A transdiagnostic marker of sustained threat.** Psychophysiology. 2016 Mar;53(3):389-92. [ABS]

The creation of the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) project has been the driving force behind the reconceptualization of the pathogenesis of psychiatric disorders. In this commentary, I explore whether the error-related negativity can be considered as a transdiagnostic marker of sustained threat based on findings from Weinberg, Meyer et al.'s (2016) study in relation to current findings in the literature.

Weinberg A, et al (2016) - **Error-related negativity (ERN) and sustained threat: Conceptual framework and empirical evaluation in an adolescent sample.** Psychophysiology. 2016 Mar;53(3):372-85. [FULL TEXT]

Executive Functioning / Pre-Frontal Cortex ▲

Polderman TJC (2020) - **Editorial: The Genetic Overlap Between Cognitive Abilities and a Transdiagnostic Vulnerability for Psychopathology.** J Am Acad Child Adolesc Psychiatry. 2020 Jun;59(6):701-702. [ABS]

Cognitive abilities, such as working memory, selective attention, inhibition, alertness, and flexibility, are collectively known as executive functioning (EF), which is essential in daily life routines. For instance, EF is important when planning a series of actions, in novel situations, or during the performance of complex tasks. General intelligence, or g, is a related construct and involves, for instance, the ability to reason, plan, solve problems, think abstractly, and learn from experience. The concept g is usually measured with a psychometric intelligence test. It has been known for more than a decade that EF and, in particular, g are negatively correlated with psychopathology

Harden KP, et al (2020) - **Genetic Associations between Executive Functions and a General Factor of Psychopathology.** J Am Acad Child Adolesc Psychiatry. 2020 Jun;59(6):749-758. [FULL TEXT]

Symptoms of psychopathology covary across diagnostic boundaries, and a family history of elevated symptoms for a single psychiatric disorder places an individual at heightened risk for a broad range of other psychiatric disorders. ...General Executive Functions and General Intelligence robustly index genetic risk for **transdiagnostic** symptoms of psychopathology in childhood. Delineating the developmental and neurobiological mechanisms underlying observed associations between cognitive abilities and psychopathology remains a priority for ongoing research.

Zelazo PD (2020) - **Executive Function and Psychopathology: A Neurodevelopmental Perspective**. Annu Rev Clin Psychol. 2020 May 7;16:431-454. [\[ABS\]](#)

Executive function (EF) skills are neurocognitive skills that support the reflective, top-down coordination and control of other brain functions, and there is neural and behavioral evidence for a continuum from more "cool" EF skills activated in emotionally neutral contexts to more "hot" EF skills needed for the reversal of motivationally significant tendencies. Difficulties in EF are transdiagnostic indicators of atypical development. A neurodevelopmental model traces the pathway from adverse childhood experiences and stress to disruption of the development of neural systems supporting reflection and EF skills to an increased risk for general features of psychopathology. Research indicates that EF skills can be cultivated through scaffolded training and are a promising target for therapeutic and preventive intervention. Intervention efficacy can be enhanced by mitigating disruptive bottom-up influences such as stress, training both hot and cool EF skills, and adding a reflective, metacognitive component to promote far transfer of trained skills.

Mullin BC, et al (2020) - **Subjective Executive Function Weaknesses Are Linked to Elevated Internalizing Symptoms among Community Adolescents**. Assessment. 2020 Apr;27(3):560-571. [\[FULL TEXT\]](#)

Analyses revealed strong associations between poorer self- and parent-reported executive function skills and the severity of anxiety and depression symptoms. Problems with executive function were also associated with externalizing symptoms. These results indicate that subjective ratings of executive function capture important aspects of cognitive problems that are highly relevant to adolescent psychopathology in a transdiagnostic fashion.

Williams PG, et al (2019) - **The association between individual differences in executive functioning and resting high-frequency heart rate variability**. Biol Psychol. 2019 Nov;148:107772. [\[ABS\]](#)

Both resting high-frequency heart rate variability (HF-HRV) and executive functioning (EF) are individual differences implicated in vulnerability to a wide range of adverse outcomes. ... Results confirmed a significant association between EF and resting HF-HRV, but no association with resting state sympathetic nervous system activation (pre-ejection period). These findings may inform future investigation of transdiagnostic mechanisms related to these two individual difference factors.

Elias R, et al (2019) - **Feasibility and Preliminary Efficacy of an Adapted Transdiagnostic Treatment for Children with Executive Function Deficits**. J Cogn Psychother. 2019 Nov 1;33(4):343-356. [\[ABS\]](#)

Few psychological interventions exist to target executive function difficulties in children and adolescents. The current study modified the Unstuck and On Target! intervention protocol for use in an outpatient clinic setting with a diagnostically diverse group of participants. ...Although preliminary, efficacy appears promising and suggests that parent-rated executive function, as well as behavioral and emotional challenges, are amenable to change as a result of intervention participation.

Snyder HR, et al (2019) - **Transdiagnostic mechanisms of psychopathology in youth: Executive functions, dependent stress, and rumination.** Cognit Ther Res. 2019 Oct;43(5):834-851. [\[FULL TEXT\]](#)

Executive function (EF) deficits have been proposed as transdiagnostic risk factors for psychopathology, and recent research suggests EF impairments are associated with what is shared across forms of psychopathology (p factor).

Rosch KS, et al (2019) - **Development of the frontal lobe.** Handb Clin Neurol. 2019;163:351-367. [\[ABS\]](#)

...disruptions in fronto-subcortical circuitry governing motivated behavior appear to contribute to a range of developmental disorders, including attention-deficit/hyperactivity disorder (ADHD), and confer vulnerability for psychopathology more broadly. The particular deficits that manifest in altered behavior depend upon the specific circuitry that is compromised due to the functional specificity of distinct regions of the frontal lobe and its interconnections with subcortical structures.

Neurobiologic models of motivated behavior provide a valuable framework for characterizing developmental disorders from a **transdiagnostic** dimensional systems perspective. Improved characterization of approach and avoidance motivation across neurodevelopmental disorders has the potential to inform the development of novel interventions and personalized medicine.

Macdonald AN, et al (2016) - **Prefrontal mechanisms of comorbidity from a transdiagnostic and ontogenic perspective.** Dev Psychopathol. 2016 Nov;28(4pt1):1147-1175. [\[ABS\]](#)

Accumulating behavioral and genetic research suggests that most forms of psychopathology share common genetic and neural vulnerabilities and are manifestations of a relatively few core underlying processes. These findings support the view that comorbidity mostly arises, not from true co-occurrence of distinct disorders, but from the behavioral expression of shared vulnerability processes across the life span. The purpose of this review is to examine the role of the prefrontal cortex (PFC) in the shared vulnerability mechanisms underlying the clinical phenomena of comorbidity from a transdiagnostic and ontogenic perspective. In adopting this perspective, we suggest complex transactions between neurobiologically rooted vulnerabilities inherent in PFC circuitry and environmental factors (e.g., parenting, peers, stress, and substance use)

across development converge on three key PFC-mediated processes: executive functioning, emotion regulation, and reward processing. We propose that individual differences and impairments in these PFC-mediated functions provide intermediate mechanisms for transdiagnostic symptoms and underlie behavioral tendencies that evoke and interact with environmental risk factors to further potentiate vulnerability.

du Pont A, et al (2019) - **Rumination and executive functions: Understanding cognitive vulnerability for psychopathology.** J Affect Disord. 2019 Sep 1;256:550-559. [[FULL TEXT](#)]

INTRODUCTION: Both rumination, a pattern of repetitive, self-focused thought in response to distress, and deficits in executive functions (EFs), a set of cognitive abilities that facilitate higher-order thinking, have **transdiagnostic** associations with psychopathology. ...Common EF abilities and rumination are correlated yet largely independent constructs that both predict psychopathology.

Exercise ▲

Dauwan M, et al (2019) - **Physical exercise improves quality of life, depressive symptoms, and cognition across chronic brain disorders: a transdiagnostic systematic review and meta-analysis of randomized controlled trials.** J Neurol. 2019 Aug 14. [[ABS](#)]

We performed a meta-analysis to synthesize evidence on the efficacy and safety of physical exercise as an add-on therapeutic intervention for quality of life (QoL), depressive symptoms and cognition across six chronic brain disorders: Alzheimer's disease, Huntington's disease, multiple sclerosis, Parkinson's disease, schizophrenia and unipolar depression. ...Exercise is an efficacious and safe add-on therapeutic intervention showing a medium-sized effect on QoL and a large effect on mood in patients with chronic brain disorders, with a positive dose-response correlation. Exercise also improved several cognitive domains with small but significant effects.

Jacquart J, et al (2019) - **The effects of exercise on transdiagnostic treatment targets: A meta-analytic review.** Behav Res Ther. 2019 Apr;115:19-37. [[ABS](#)]

The present study meta-analytically reviewed the effects of exercise on four **transdiagnostic** treatment targets: anxiety sensitivity (AS), distress tolerance (DT), stress reactivity (SR), and general self-efficacy (GSE). ...Exercise interventions had a large effect on reducing AS, a medium effect on increasing GSE ... and a small effect on reducing SR. Evidence from four studies suggested that exercise interventions had a small but non-significant effect on increasing DT. This meta-analysis provides preliminary evidence exercise can engage certain **transdiagnostic** targets.

Ólafsdóttir KB, et al (2018) - **Effects of Exercise on Depression and Anxiety. A Comparison to Transdiagnostic Cognitive Behavioral Therapy.** Community Ment Health J. 2018 Aug;54(6):855-859. [\[ABS\]](#)

The aims of this study were (i) to know the effects of an exercise program on a group of people with depression and anxiety and (ii) to compare these effects with a transdiagnostic cognitive behavioral group therapy (TCBGT). The participants were 15 people with depression and/or anxiety symptoms. The participants followed an exercise program. Depression and anxiety symptoms were assessed with validated questionnaires. An exercise program can be used as a treatment option for people with depression and/or anxiety with good results in comparison with TCBGT.

Fear ▲

Norrholm SD, et al (2015) - **Fear load: The psychophysiological over-expression of fear as an intermediate phenotype associated with trauma reactions.** Int J Psychophysiol. 2015 Nov;98(2 Pt 2):270-275. [\[FULL TEXT\]](#)

Yancey JR, et al (2015) - **Aversive startle potentiation and fear pathology: Mediating role of threat sensitivity and moderating impact of depression.** Int J Psychophysiol. 2015 Nov;98(2 Pt 2):262-269. [\[FULL TEXT\]](#)

Heart Rate Variability ▲

Fantini-Hauwel C, et al (2020) - **Emotion Regulation Difficulties Are Not Always Associated with Negative Outcomes on Women: The Buffer Effect of HRV.** Front Psychol. 2020 Apr 30;11:697. [\[FULL TEXT\]](#)

Overall, high resting HRV appears to dampen the consequences of trait emotion regulation difficulties.

Williams PG, et al (2019) - **The association between individual differences in executive functioning and resting high-frequency heart rate variability.** Biol Psychol. 2019 Nov;148:107772. [\[ABS\]](#)

Both resting high-frequency heart rate variability (HF-HRV) and executive functioning (EF) are individual differences implicated in vulnerability to a wide range of adverse outcomes. ... Results confirmed a significant association between EF and resting HF-HRV,

but no association with resting state sympathetic nervous system activation (pre-ejection period). These findings may inform future investigation of **transdiagnostic** mechanisms related to these two individual difference factors.

Condy EE, et al (2019) - **Restricted repetitive behaviors in autism spectrum disorder: A systematic review from the neurovisceral integration perspective.** Biol Psychol. 2019 Nov;148:107739. [\[ABS\]](#)

The neurovisceral integration model posits that cognitive-behavioral inflexibility arises from biological inflexibility of feedback loops within the central autonomic network. The parasympathetic nervous system (PNS) is integral in this network. Activity of the PNS, which is normally tonically inhibited, can be indexed through **respiratory sinus arrhythmia** (RSA). When the PNS becomes disinhibited, indicating decreased flexibility within the network, RSA is reduced and cognitive-behavioral flexibility is impaired. Using this theoretical framework, cognitive-behavioral inflexibility is discussed from the Research Domain Criteria (RDoC) perspective. Restricted repetitive behaviors in autism spectrum disorder (ASD) are proposed as exemplars of cognitive-behavioral inflexibility, and behavioral and RSA literature in ASD are reviewed. RSA differences and their relation to inflexibility in ASD are discussed to support the model and to propose RSA as a biomarker for cognitive-behavioral inflexibility. Considerations for future research are discussed, in addition to implications the model might have on assessment and **transdiagnostic** treatment practices.

Chalmers JA, et al (2016) - **Worry is associated with robust reductions in heart rate variability - A transdiagnostic study of anxiety psychopathology.** BMC Psychol. 2016 Jun 3;4(1):32. [\[FULL TEXT\]](#)

"The specific symptom of worry – not the diagnosis of an anxiety disorder – was associated with the most robust reductions in HRV, indicating that HRV may provide a transdiagnostic biomarker of worry. These results enhance understanding of the relationship between the cardiac autonomic nervous system and anxiety psychopathology, providing support for dimensional-trait models consistent with the Research Domain Criteria framework."

Beauchaine TP, et al (2015) - **Heart rate variability as a transdiagnostic biomarker of psychopathology.** Int J Psychophysiol. 2015 Nov;98(2 Pt 2):338-350. [\[ABS\]](#)

"The Research Domain Criteria (RDoC), developed by the National Institute of Mental Health as a neuroscience-informed alternative to traditional psychiatric nosology, is an explicitly dimensional system in which classification of psychopathology is derived inductively (i.e., from basic science), across multiple levels of analysis (e.g., genetic, neural, psychophysiological, and behavioral). Although RDoC is often presented as paradigmatically revolutionary, a review of the history of psychophysiology suggests that roots of RDoC thinking extend at least as far back as the mid-20th Century. In this paper,

we briefly and selectively review the historical emergence of neurobiologically-informed dimensional trait models of psychopathology, and we summarize our thinking regarding high frequency heart rate variability (HF-HRV) as a transdiagnostic biomarker of self-regulation and cognitive control. When functional interactions between HF-HRV and systems of behavioral approach and avoidance are considered, diverse patterns of behavioral maladjustment can be subsumed into a single model. This model accommodates the general bifactor structure of psychopathology, and suggests that HF-HRV can be viewed as an autonomic, transdiagnostic biomarker of mental illness."

Gruber J, et al (2015) - **Heart rate variability as a potential indicator of positive valence system disturbance: A proof of concept investigation.** *Int J Psychophysiol.* 2015 Nov;98(2 Pt 2):240-248. [\[ABS\]](#)

One promising avenue toward a better understanding of the pathophysiology of positive emotional disturbances is to examine high-frequency heart rate variability (HRV-HF), which has been implicated as a potential physiological index of disturbances in positive emotional functioning. To date, only a few psychopathology relevant studies have systematically quantified HRV-HF profiles using more ecologically valid methods in everyday life. Using an experience-sampling approach, the present study examined both mean levels and intra-individual variability of HRV-HF - as well as comparison measures of cardiovascular arousal, sympathetic activity, and gross somatic movement - in everyday life, using ambulatory psychophysiological measurement across a six-day consecutive period among a spectrum of community adult participants with varying degrees of positive valence system disturbance, including adults with bipolar I disorder (BD; n=21), major depressive disorder (MDD; n=17), and healthy non-psychiatric controls (CTL; n=28). Groups did not differ in mean HRV-HF, but greater HRV-HF instability (i.e., intra-individual variation in HRV-HF) was found in the BD compared to both MDD and CTL groups. Subsequent analyses suggested that group differences in HRV-HF variability were largely accounted for by variations in clinician-rated manic symptoms. However, no association was found between HRV-HF variability and dimensional measures of positive affectivity. This work provides evidence consistent with a quadratic relationship between HRV-HF and positive emotional disturbance and represents a valuable step toward developing a more ecologically valid model of positive valence system disturbances and their underlying psychophysiological mechanisms within an RDoC framework.

Beauchaine TP (2015) - **Respiratory Sinus Arrhythmia: A Transdiagnostic Biomarker of Emotion Dysregulation and Psychopathology.** *Curr Opin Psychol.* 2015 Jun 1;3:43-47. [\[FULL TEXT\]](#)

In the past two decades, respiratory sinus arrhythmia (RSA)—an index of parasympathetic nervous system (PNS)-mediated cardiac control—has emerged as a reliable peripheral biomarker of emotion regulation (ER). Reduced RSA and excessive RSA reactivity (i.e., withdrawal) to emotional challenge are observed consistently among individuals with poor ER capabilities, including those with various forms of internalizing and externalizing psychopathology, and those with specific psychopathological

syndromes, including anxiety, phobias, attention problems, autism, callousness, conduct disorder, depression, non-suicidal self-injury, panic disorder, and trait hostility. Emerging evidence suggests that low RSA and excessive RSA reactivity index poor ER because they are downstream peripheral markers of prefrontal cortex (PFC) dysfunction. Poorly modulated inhibitory efferent pathways from the medial PFC to the PNS result in reduced RSA and excessive RSA reactivity. According to this perspective, RSA is a non-invasive proxy for poor executive control over behavior, which characterizes most forms of psychopathology.

Tegeler CH, et al (2015) - **Rightward dominance in temporal high-frequency electrical asymmetry corresponds to higher resting heart rate and lower baroreflex sensitivity in a heterogeneous population.** Brain Behav. 2015 Jun;5(6):e00343. [\[FULL TEXT\]](#)

In a heterogeneous population, individuals with rightward compared to leftward temporal high-frequency electrical asymmetry had higher resting heart rate and lower BRS. Two-channel recording of brain electrical activity from bilateral temporal regions appears to hold promise for further investigation as a means to assess cortical activity associated with autonomic cardiovascular regulation.

Kulsek J, et al (2015) - **Cardiac autonomic regulation in autism and Fragile X syndrome: a review.** Psychol Bull. 2015 Jan;141(1):141-75. [\[FULL TEXT\]](#)

Evidence reviewed here supports physiological dysregulation in a subset of individuals with autism, as evidenced by patterns of hyperarousal and dampened parasympathetic vagal tone, which overlap with the well-documented physiological profile of FXS. Moreover, there is growing support for a link between aberrant cardiac activity and core deficits associated with autism, such as communication and social impairment. The delineation of physiological mechanisms common to autism and FXS could lend insight into relationships between genetic etiology and behavioral endstates, highlighting FMR1 as a potential candidate gene.

Guy L, et al (2014) - **Brief report: emotion regulation and respiratory sinus arrhythmia in autism spectrum disorder.** J Autism Dev Disord. 2014 Oct;44(10):2614-20. [\[ABS\]](#)

Emotion regulation (ER) may be an important transdiagnostic factor for understanding mental and behavioral health given its association with several psychiatric disorders, including autism spectrum disorder (ASD). However, there is limited research on ER in ASD, particularly using biomarkers such as respiratory sinus arrhythmia (RSA). The aim of the current study was to examine RSA among school-aged children with ASD in relation to symptoms of anxiety, executive functioning, and adaptive socialization skills. Results showed decreased RSA in children with ASD (relative to typically developing controls), reflecting decreased parasympathetic nervous system activity. In addition, decreased RSA was associated with increased symptoms of anxiety and lower socialization skills. These findings emphasize the need for interventions targeting emotional and arousal

regulation in ASD.

Woody ML, et al (2014) - **Brooding rumination and heart rate variability in women at high and low risk for depression: group differences and moderation by COMT genotype.** J Abnorm Psychol. 2014 Feb;123(1):61-7. [\[FULL TEXT\]](#)

We predicted that COMT Val158Met genotype, which has been linked to heightened amygdala reactivity and deficits in prefrontal functioning, would be associated with HRV and brooding rumination, particularly among women with a history of MDD.

Inflammation ▲

De Picker L, et al (2020) - **Immune and Neuroendocrine Trait and State Markers in Psychotic Illness: Decreased Kynurenines Marking Psychotic Exacerbations.** Front Immunol. 2020 Jan 17;10:2971. [\[FULL TEXT\]](#)

...The acute psychotic state is marked by state-specific increases of immune markers and decreases in peripheral IDO pathway markers. Increased CRP, CCL2, and IL1RA, and decreased KA and KA/Kyn are trait markers of psychotic illness.

Anderson G, et al (2020) - **Gut Dysbiosis Dysregulates Central and Systemic Homeostasis via Suboptimal Mitochondrial Function: Assessment, Treatment and Classification Implications.** Curr Top Med Chem. 2020;20(7):524-539. [\[ABS\]](#)

The gut and mitochondria have emerged as two important hubs at the cutting edge of research across a diverse array of medical conditions, including most psychiatric conditions. This article highlights the interaction of the gut and mitochondria over the course of development, with an emphasis on the consequences for transdiagnostic processes across psychiatry, but with relevance to wider medical conditions. As well as raised levels of circulating lipopolysaccharide (LPS) arising from increased gut permeability, the loss of the short-chain fatty acid, butyrate, is an important mediator of how gut dysbiosis modulates mitochondrial function. Reactive cells, central glia and systemic immune cells are also modulated by the gut, in part via impacts on mitochondrial function in these cells. Gut-driven alterations in the activity of reactive cells over the course of development are proposed to be an important determinant of the transdiagnostic influence of glia and the immune system. Stress, including prenatal stress, also acts via the gut. The suppression of butyrate, coupled to raised LPS, drives oxidative and nitrosative stress signalling that culminates in the activation of acidic sphingomyelinase-induced ceramide. Raised ceramide levels negatively regulate mitochondrial function, both directly and via its negative impact on daytime, arousal-promoting orexin and night-time sleep-promoting pineal gland-derived melatonin. Both

orexin and melatonin positively regulate mitochondria oxidative phosphorylation. Consequently, gut-mediated increases in ceramide have impacts on the circadian rhythm and the circadian regulation of mitochondrial function. Butyrate, orexin and melatonin can positively regulate mitochondria via the disinhibition of the pyruvate dehydrogenase complex, leading to increased conversion of pyruvate to acetyl- CoA. Acetyl-CoA is a necessary co-substrate for the initiation of the melatonergic pathway in mitochondria and therefore the beneficial effects of mitochondria melatonin synthesis on mitochondrial function. This has a number of treatment implications across psychiatric and wider medical conditions, including the utilization of sodium butyrate and melatonin. Overall, gut dysbiosis and increased gut permeability have significant impacts on central and systemic homeostasis via the regulation of mitochondrial function, especially in central glia and systemic immune cells

Morris G, et al (2020) - **The role of microglia in neuroprogressive disorders: mechanisms and possible neurotherapeutic effects of induced ketosis.** Prog Neuropsychopharmacol Biol Psychiatry. 2020 Apr 20;99:109858. [\[ABS\]](#)

A comprehensive review of molecular mechanisms involved in the promotion and maintenance of distinct microglia phenotypes is provided. The acquisition and perpetuation of predominantly pro-inflammatory microglial phenotypes have been implicated in the pathophysiology of several neuroprogressive diseases and is associated with reduced ATP production via oxidative phosphorylation, increased ATP generation by glycolysis, elevated oxidative and nitrosative stress and other metabolic, inflammatory and hormonal insults. Microglia can also adopt a predominantly anti-inflammatory phenotypes with neuroprotective properties. Strategies that promote and maintain a predominantly anti-inflammatory phenotype may hold promise as novel therapeutic opportunities for neuroprogressive illness. Induced ketosis may promote a transition towards predominantly anti-inflammatory microglial states/phenotypes by several mechanisms, including inhibition of glycolysis and increased NAD⁺ production; engagement of microglial GPR109A receptors; histone deacetylase inhibition; and elevated n-3 polyunsaturated fatty acids levels. Since microglia activation can now be assessed in vivo, these data provide a clear rationale for the design of transdiagnostic randomized controlled trials of the ketogenic diet and other ketosis-inducing strategies for neuroprogressive diseases, which may also provide mechanistic insights through the assessment of "target engagement".

Hylén U, et al (2020) - **Increased inflammasome activity in markedly ill psychiatric patients: An explorative study.** J Neuroimmunol. 2020 Feb 15;339:577119. [\[ABS\]](#)

The aim of this study was to investigate inflammatory perturbations in 40 patients with severe and complex psychiatric disorders by studying the activity of the NLRP3 inflammasome, with a trans-diagnostic approach. Gene expression of CASP1, NLRP3, PYCARD, IL1B, IL1RN, TNF showed a significant increase in the patient group compared to a matched control group. Plasma levels of IL1Ra, IL-18, TNF, IL-6 and CRP were

increased in the patient group. Within the patient group, increased gene expression of inflammatory markers correlated with increased disease severity. The findings support the inflammation hypothesis for markedly ill psychiatric patients across diagnostic groups.

Finke C (2019) - **A transdiagnostic pattern of psychiatric symptoms in autoimmune encephalitis.** *Lancet Psychiatry.* 2019 Mar;6(3):191-193. [\[REF\]](#)

Danese A, et al (2017) - **Hidden Wounds? Inflammatory Links between Childhood Trauma and Psychopathology.** *Annu Rev Psychol.* 2017 Jan 3;68:517-544. [\[ABS\]](#)

Childhood trauma is a key risk factor for psychopathology. However, little is known about how exposure to childhood trauma is translated into biological risk for psychopathology. Observational human studies and experimental animal models suggest that childhood exposure to stress can trigger an enduring systemic inflammatory response not unlike the bodily response to physical injury. In turn, these "hidden wounds" of childhood trauma can affect brain development, key behavioral domains (e.g., cognition, positive valence systems, negative valence systems), reactivity to subsequent stressors, and, ultimately, risk for psychopathology. Further research is needed to better characterize the inflammatory links between childhood trauma and psychopathology. Detecting and healing these hidden wounds may help prevent and treat psychopathology emerging after childhood trauma.

Subramaniapillai M, et al (2017) - **Inflammation: opportunities for treatment stratification among individuals diagnosed with mood disorders.** *Dialogues Clin Neurosci.* 2017 Mar;19(1):27-36. [\[FULL TEXT\]](#)

Furtado M, et al (2015) - **Neuroinflammatory pathways in anxiety, posttraumatic stress, and obsessive compulsive disorders.** *Psychiatry Research* September 30, 2015 Volume 229, Issues 1-2, Pages 37–48. [\[ABS\]](#)

As prevalence of anxiety, posttraumatic stress, and obsessive compulsive disorders continue to rise worldwide, increasing focus has been placed on immune mediated theories in understanding the underlying mechanisms of these disorders. Associations between the dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis and these disorders have been recognized in the scientific literature, specifically in regard to cortisol levels, as well as changes in pro- and anti-inflammatory cytokines. The present commentary will systematically assess the scientific literature within the past decade in regard to the psychoneuroimmunology of anxiety, posttraumatic stress, and obsessive compulsive disorders. Understanding the mechanisms of these disorders is essential in order to determine efficacious and targeted treatment strategies, which may lead to substantial improvements in overall functioning, as well as significant decreases in societal and economic burden.

McNamara RK (2015) - **Mitigation of Inflammation-Induced Mood Dysregulation by Long-Chain Omega-3 Fatty Acids.** J Am Coll Nutr. 2015;34 Suppl 1:48-55. [\[FULL TEXT\]](#)

Recent prospective longitudinal evidence suggests that elevations in the LCn-6/LCn-3 fatty acid ratio are a modifiable risk factor for the development of mood symptoms, including depression and irritability, in response to immune-inflammatory signaling. Together these data suggest that increasing LCn-3 fatty acid intake and biostatus represents a feasible strategy to mitigate the negative impact of elevated immune-inflammatory signaling on mood stability.

Turisch M, et al (2014) - **Association of trauma exposure with proinflammatory activity - a transdiagnostic meta-analysis.** Transl Psychiatry. 2014 Jul 22;4:e413. [\[FULL TEXT\]](#)

"...trauma exposure was positively associated with C-reactive protein (CRP), interleukin (IL)-1 β , IL-6, and tumor necrosis factor (TNF)- α ..."

"Positive correlations between inflammation and trauma exposure across a range of sample types and diagnoses were found. ... The results suggest that chronic inflammation likely represents one potential mechanism underlying risk of health problems in trauma survivors."

Rosenblat JD, et al (2014) - **Inflamed moods: a review of the interactions between inflammation and mood disorders.** Prog Neuropsychopharmacol Biol Psychiatry. 2014 Aug 4;53:23-34. [\[ABS\]](#)

Mood disorders have been recognized by the World Health Organization (WHO) as the leading cause of disability worldwide. Notwithstanding the established efficacy of conventional mood agents, many treated individuals continue to remain treatment refractory and/or exhibit clinically significant residual symptoms, cognitive dysfunction, and psychosocial impairment. Therefore, a priority research and clinical agenda is to identify pathophysiological mechanisms subserving mood disorders to improve therapeutic efficacy. During the past decade, inflammation has been revisited as an important etiologic factor of mood disorders. Therefore, the purpose of this synthetic review is threefold: 1) to review the evidence for an association between inflammation and mood disorders, 2) to discuss potential pathophysiologic mechanisms that may explain this association and 3) to present novel therapeutic options currently being investigated that target the inflammatory-mood pathway. Accumulating evidence implicates inflammation as a critical mediator in the pathophysiology of mood disorders. Indeed, elevated levels of pro-inflammatory cytokines have been repeatedly demonstrated in both major depressive disorder (MDD) and bipolar disorder (BD) patients. Further, the induction of a pro-inflammatory state in healthy or medically ill subjects induces 'sickness behavior' resembling depressive symptomatology. Potential mechanisms involved include, but are not limited to, direct effects of pro-inflammatory cytokines on monoamine levels, dysregulation of the hypothalamic-pituitary-adrenal

(HPA) axis, pathologic microglial cell activation, impaired neuroplasticity and structural and functional brain changes. Anti-inflammatory agents, such as acetyl-salicylic acid (ASA), celecoxib, anti-TNF- α agents, minocycline, curcumin and omega-3 fatty acids, are being investigated for use in mood disorders. Current evidence shows improved outcomes in mood disorder patients when anti-inflammatory agents are used as an adjunct to conventional therapy; however, further research is needed to establish the therapeutic benefit and appropriate dosage.

McNamara RK, et al (2012) - **Elevated immune-inflammatory signaling in mood disorders: a new therapeutic target?** Expert Rev Neurother. 2012 Sep;12(9):1143-61. [\[FULL TEXT\]](#)

Potential pathogenic mechanisms linked with elevated immune-inflammatory signaling include perturbations in central serotonin neurotransmission and progressive white matter pathology. Both heritable genetic factors and environmental factors including dietary fatty-acid composition may act in concert to sustain elevated immune-inflammatory signaling. Collectively, these data suggest that elevated immune-inflammatory signaling is a mechanism that is relevant to the pathoetiology of mood disorders, and may therefore represent a new therapeutic target for the development of more effective treatments.

Irritability ▲

Evans SC A, et al (2021) - **Modular, Transdiagnostic Approach to Treating Severe Irritability in Children and Adolescents.** Child Adolesc Psychiatr Clin N Am. 2021 Jul;30(3):623-636. [\[ABS\]](#)

Breda M, et al (2021) -**Irritability in developmental age: A narrative review of a dimension crossing paediatric psychopathology.** Aust N Z J Psychiatry. 2021 May 20:48674211011245. [\[ABS\]](#)

Investigating the presence of irritability in all children with related disorders is mandatory if we consider the risk for functional impairment and affective and behavioural disorders associated with high levels of irritability. ...a dimensional approach to irritability could allow to identify prodromal phase and prevent the evolution towards clinical pathological expressions.

Mohamed Ali O, et al (2021) - **Observational measures of early irritability predict children's psychopathology risk.** Dev Psychopathol. 2021 May 20:1-13. [\[ABS\]](#)

Irritability is a transdiagnostic feature of diverse forms of psychopathology and a rapidly growing literature implicates the construct in child maladaptation. ... Children's irritability observed during tasks that did not typically elicit anger predicted their later

depressive and hyperactivity symptoms, above and beyond parent-reported irritability and context-appropriate observed anger...

Beauchaine TP, et al (2020) - **Irritability as a Transdiagnostic Vulnerability Trait: Current Issues and Future Directions.** Behav Ther. 2020 Mar;51(2):350-364. [\[ABS\]](#)

In recent years, irritability has received increasing attention among mental health professionals given its transdiagnostic associations with diverse forms of psychopathology. ...we situate irritability in the literatures on child temperament and adult personality, and describe a model in which irritability derives from low tonic dopamine (DA) levels and low phasic DA reactivity in subcortical neural structures implicated in appetitive responding. We note that different findings often emerge in neuroimaging studies when irritability is assessed in circumscribed diagnostic groups versus representative samples.

Hawks JL, et al (2020) - **Development and Application of an Innovative Transdiagnostic Treatment Approach for Pediatric Irritability.** Behav Ther. 2020 Mar;51(2):334-349. [\[ABS\]](#)

Recent work has drawn attention to the previously underrecognized role that irritability plays in childhood psychopathology. ... In the current pilot study, we adapted the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Children (UP-C) for the treatment of pediatric irritability in a sample of 19 children (ages 8 to 12) with primary presenting concerns of irritability and/or disruptive behaviors. Results supported the feasibility and acceptability of this treatment and provided preliminary evidence that such an approach may yield improved outcomes for symptoms of pediatric irritability and disruptive behaviors.

Evans SC, et al (2020) - **Exploring Longitudinal Mechanisms of Irritability in Children: Implications for Cognitive-Behavioral Intervention.** Behav Ther. 2020 Mar;51(2):238-252. [\[ABS\]](#)

Severe irritability is a common and clinically important problem longitudinally associated with internalizing and externalizing problems in children. ...irritability predicted higher depressive symptoms, anxiety, reactive aggression, oppositionality, intolerance of uncertainty, and poor emotion coping.

Roy AK, et al (2020) - **Advances in the Conceptualization, Assessment, and Treatment of Pediatric Irritability.** Behav Ther. 2020 Mar;51(2):207-210. [\[ABS\]](#)

Pediatric irritability is a functionally impairing transdiagnostic symptom underlying a substantial proportion of child mental health referrals. ... this special series brings together the latest work from leading experts across three interrelated domains: (a) progress in understanding the phenomenology and course of pediatric irritability; (b) advances in the assessment of pediatric irritability; and (c) innovations in the treatment of pediatric irritability. The papers in this special series collectively offer critical steps

forward for better understanding pediatric irritability and improving proper assessment, classification, and clinical management.

Toohey MJ (2020) - **Irritability characteristics and parameters in an international sample.** J Affect Disord. 2020 Feb 15;263:558-567. [[ABS](#)]

Irritability is a symptom of fifteen psychiatric disorders and is widely known to scholars and the public. However, little is known about irritability as an individual construct. ...These findings support the conceptualization of irritability as a universal construct. It is recommended that future research continue to explore irritability to better help understand it as an independent construct in the context of diagnosis, assessment, research, and treatment.

Smith JD, et al (2019) - **Dysregulated Irritability as a Window on Young Children's Psychiatric Risk: Transdiagnostic Effects via the Family Check-Up.** Dev Psychopathol. 2019 Dec;31(5):1887-1899. [[FULL TEXT](#)]

Building on prior work using Tom Dishion's Family Check-Up, the current article examined intervention effects on dysregulated irritability in early childhood. Dysregulated irritability, defined as reactive and intense response to frustration, and prolonged angry mood, is an ideal marker of neurodevelopmental vulnerability to later psychopathology because it is a **transdiagnostic** indicator of decrements in self-regulation that are measurable in the first years of life that have lifelong implications for health and disease. ...Results indicate that family-based programs initiated in early childhood can reduce early childhood irritability and later risk for psychopathology. This holds promise for earlier identification and prevention approaches that target transdiagnostic pathways. Implications for future basic and prevention research are discussed.

Jirsaraie RJ, et al (2019) - **Accelerated cortical thinning within structural brain networks is associated with irritability in youth.** Neuropsychopharmacology. 2019 Dec;44(13):2254-2262. [[FULL TEXT](#)]

... irritability is associated with widespread reductions in cortical thickness and accelerated cortical thinning, particularly within the frontal and temporal cortex. Aberrant structural maturation of regions important for emotional regulation may in part underlie symptoms of irritability.

Dennis EL, et al (2019) - **Irritability and brain volume in adolescents: cross-sectional and longitudinal associations.** Soc Cogn Affect Neurosci. 2019 Jul 31;14(7):687-698. [[FULL TEXT](#)]

Irritability is garnering increasing attention in psychiatric research as a **transdiagnostic** marker of both internalizing and externalizing disorders. These disorders often emerge during adolescence, highlighting the need to examine changes in the brain and in psychological functioning during this developmental period. ...More irritable individuals had

larger hippocampi, insula, medial orbitofrontal cortex and cingulum/cingulate cortex and smaller putamen and internal capsule. Across the brain, more irritable individuals also had larger volume and less volume contraction in a number of areas that typically decrease in volume over the developmental period studied here, suggesting delayed maturation. These structural changes may increase adolescents' vulnerability for internalizing and externalizing disorders.

Tseng WL, et al (2019) - **Brain Mechanisms of Attention Orienting Following Frustration: Associations With Irritability and Age in Youths.** Am J Psychiatry. 2019 Jan 1;176(1):67-76. [[FULL TEXT](#)]

Childhood irritability is a common, impairing problem with changing age-related manifestations that predict long-term adverse outcomes. ...Following frustration, levels of irritability correlated with activity in neural systems mediating attention orienting, top-down regulation of emotions, and motor execution. Although most associations were independent of age, dysfunction in the anterior cingulate cortex and posterior regions was more pronounced in young children with irritability.

Interoception ▲

Lapidus RC, et al (2020) - **Heightened affective response to perturbation of respiratory but not pain signals in eating, mood, and anxiety disorders.** PLoS One. 2020 Jul 15;15(7):e0235346. [[FULL TEXT](#)]

Several studies have recently suggested that an abnormal processing of respiratory interoceptive and nociceptive (painful) stimuli may contribute to eating disorder (ED) pathophysiology. Mood and anxiety disorders (MA) are also characterized by abnormal respiratory symptoms, and show substantial comorbidity with ED. ...During breath-holding, both the ED and MA groups reported significantly more stress, feelings of suffocation, and suffocation fear than HC, with the ED group reporting the most severe symptoms. Moreover, anxiety sensitivity was related to suffocation fear only in the ED group. ...These findings underscore the presence of abnormal respiratory interoception in MA and suggest that hyperreactivity to respiratory signals may be a potentially overlooked clinical feature of ED.

Martin E, et al (2019) - **Interoception and disordered eating: A systematic review.** Neurosci Biobehav Rev. 2019 Dec;107:166-191. [[ABS](#)]

104 studies with 32883 participants were included. Deficits in interoception were observed across disordered eating types and interoceptive modalities suggesting that interoception may constitute a **transdiagnostic** feature of disordered eating.

Kranzler A, et al (2016) - **Emotional Awareness - A Transdiagnostic Predictor of Depression and Anxiety for Children and Adolescents.** J Clin Child Adolesc Psychol. 2016;45(3):262-9. [[FULL TEXT](#)]

Trevisan DA, et al (2019) - **A meta-analysis on the relationship between interoceptive awareness and alexithymia: Distinguishing interoceptive accuracy and sensibility.** J Abnorm Psychol. 2019 Nov;128(8):765-776. [[ABS](#)]

...alexithymia was moderately associated with interoceptive awareness in samples with psychiatric and developmental disorders, but the relationship was nonsignificant in healthy, typically developing samples. Results suggest interoception may represent a shared **transdiagnostic** vulnerability that underlies atypical emotional processing in a variety of disparate clinical populations but that current operationalization and measurement of interoceptive awareness continues to create confusion and inconsistency in the literature.

Murphy J, et al (2019) - **Classifying individual differences in interoception: Implications for the measurement of interoceptive awareness.** Psychon Bull Rev. 2019 Oct;26(5):1467-1471. [[FULL TEXT](#)]

Khalsa SS, et al (2016) - **Can Interoception Improve the Pragmatic Search for Biomarkers in Psychiatry?** Front Psychiatry. 2016 Jul 25;7:121. [[FULL TEXT](#)]

Disrupted interoception is a prominent feature of the diagnostic classification of several psychiatric disorders. However, progress in understanding the interoceptive basis of these disorders has been incremental, and the application of interoception in clinical treatment is currently limited to panic disorder. To examine the degree to which the scientific community has recognized interoception as a construct of interest, we identified and individually screened all articles published in the English language on interoception and associated root terms in Pubmed, Psychinfo, and ISI Web of Knowledge. This search revealed that interoception is a multifaceted process that is being increasingly studied within the fields of psychiatry, psychology, neuroscience, and biomedical science. To illustrate the multifaceted nature of interoception, we provide a focused review of one of the most commonly studied interoceptive channels, the cardiovascular system, and give a detailed comparison of the most popular methods used to study cardiac interoception. We subsequently review evidence of interoceptive dysfunction in panic disorder, depression, somatic symptom disorders, anorexia nervosa, and bulimia nervosa. For each disorder, we suggest how interoceptive predictions constructed by the brain may erroneously bias individuals to express key symptoms and behaviors, and outline questions that are suitable for the development of neuroscience-based mental health interventions. We conclude that interoception represents a viable avenue for clinical and translational research in psychiatry, with a well-established conceptual framework, a neural basis, measurable biomarkers, interdisciplinary appeal,

and transdiagnostic targets for understanding and improving mental health outcomes.

Yoris A, et al (2015) - **The roles of interoceptive sensitivity and metacognitive interoception in panic.** Behav Brain Funct. 2015 Apr 8;11. [\[FULL TEXT\]](#)

Patients did not differ from controls in IS. However, significant differences were found in MI measures. Patients presented increased worries in their beliefs about somatic sensations compared to controls. These results reflect a discrepancy between direct body sensing (IS) and reflexive thoughts about body states (MI).

Our findings support the idea that hypervigilance to body symptoms is not necessarily a bottom-up dispositional tendency (where patients are hypersensitive about bodily signals), but rather a metacognitive process related to threatening beliefs about body/somatic sensations.

Moeller SJ, et al (2014) - **Impaired self-awareness in human addiction: deficient attribution of personal relevance.** Trends Cogn Sci. 2014 Dec;18(12):635-41. [\[FULL TEXT\]](#)

Compromised self-awareness of illness-related deficits and behaviors in psychopathology (e.g., schizophrenia) has been associated with deficient functioning of *cortical midline regions* including the ventromedial prefrontal cortex (vmPFC), implicated in personal relevance. Here, we review and critically analyze recent evidence to suggest that vmPFC abnormalities could similarly underlie deficient tagging of personal relevance in drug addiction, evidenced by a constellation of behaviors encompassing drug-biased attention, negative outcome insensitivity, self-report/behavior dissociation, and social inappropriateness. This novel framework might clarify, for example, why drug-addicted individuals often ruin long-standing relationships or forego important job opportunities while continuing to engage in uncontrolled drug-taking. Therapeutic interventions targeting personal relevance and associated vmPFC functioning could enhance self-awareness and facilitate more adaptive behavior in this chronically relapsing psychopathology.

Boswell JF, et al (2013) - **Anxiety sensitivity and interoceptive exposure - a transdiagnostic construct and change strategy.** Behav Ther. 2013 Sep;44(3):417-31. [\[FULL TEXT\]](#)

Memory ▲

Barkus E (2020) - **Effects of working memory training on emotion regulation: Transdiagnostic review.** Psych J. 2020 Apr;9(2):258-279. [\[ABS\]](#)

Working memory training is widely used transdiagnostically to improve cognition.

However, more recently, studies using working memory training packages have targeted emotion-regulation outcomes to determine whether far transfer effects can be achieved. ...Working memory training could improve cognitive efficiency, which, in turn, increases the availability of cognitive resources during times when emotion regulation is taxed. Working memory training offers a possibility for improving emotion regulation transdiagnostically.

Reininghaus U, et al (2019) - **Reasoning bias, working memory performance and a transdiagnostic phenotype of affective disturbances and psychotic experiences in the general population.** Psychol Med. 2019 Aug;49(11):1799-1809. [[ABS](#)] 60228

The jumping to conclusions (JTC) reasoning bias and decreased working memory performance (WMP) are associated with psychosis, but associations with affective disturbances (i.e. depression, anxiety, mania) remain inconclusive. Recent findings also suggest a **transdiagnostic** phenotype of co-occurring affective disturbances and psychotic experiences (PEs). ... The findings suggest that JTC bias and decreased WMP may contribute to a **transdiagnostic** phenotype of co-occurring affective disturbances and PEs.

Gilmour G, et al (2019) - **Relating constructs of attention and working memory to social withdrawal in Alzheimer's disease and schizophrenia: issues regarding paradigm selection.** Neurosci Biobehav Rev. 2019 Feb;97:47-69. [[ABS](#)]

Central nervous system diseases are not currently diagnosed based on knowledge of biological mechanisms underlying their symptoms. Greater understanding may be offered through an agnostic approach to traditional disease categories, where learning more about shared biological mechanisms across conditions could potentially reclassify subgroups of patients to allow realisation of more effective treatments. This review represents the output of the collaborative group "PRISM", tasked with considering assay choices for assessment of attention and working memory in a **transdiagnostic** cohort of Alzheimer's disease and schizophrenia patients exhibiting symptomatic spectra of social withdrawal.

Harvey AG, et al (2016) - **Improving outcome for mental disorders by enhancing memory for treatment.** Behav Res Ther. 2016 Jun;81:35-46. [[ABS](#)]

Harvey AG, et al (2014) - **Improving Outcome of Psychosocial Treatments by Enhancing Memory and Learning.** Perspect Psychol Sci. 2014 Mar;9(2):161-79. [[FULL TEXT](#)]

Mindfulness ▲

Fortuna LR, et al (2020) - **Development of a cognitive behavioral therapy with integrated**

mindfulness for Latinx immigrants with co-occurring disorders: Analysis of intermediary outcomes. Psychol Trauma. 2020 Aug 6. [\[ABS\]](#)

Transdiagnostic interventions have been increasingly used in the management of a variety of mental health and substance use conditions, and in the context of chronic stress. We discuss the development and evaluation of the Integrated Intervention for Dual Problems and Early Action (IIDEA), a 10-session manualized intervention that includes cognitive therapy and mindfulness practice designed to improve symptoms of anxiety, depression, posttraumatic stress, and co-occurring substance use problems. ...Conclusions: Findings suggest that skills related to the studied intermediary outcomes can be helpful for Latinx immigrants experiencing circumstances of ongoing exposure to adversity and traumatic stress.

Taylor J, et al (2020) - **Mindfulness and yoga for psychological trauma: systematic review and meta-analysis.** J Trauma Dissociation. 2020 May 26:1-38. [\[ABS\]](#)

Mindfulness-based interventions (MBIs), with postures, breath, relaxation, and meditation, such as Mindfulness-based Stress Reduction (MBSR) and yoga, are complex interventions increasingly used for trauma-related psychiatric conditions. Prior reviews have adopted a disorder-specific focus. However, trauma is a risk factor for most psychiatric conditions. We adopted a **transdiagnostic** approach to evaluate the efficacy of MBIs for the consequences of trauma, agnostic to diagnosis. ... this review suggests a **transdiagnostic** approach could be adopted in the treatment of trauma sequelae with MBIs.

Schirda B, et al (2020) - **Mindfulness training for emotion dysregulation in multiple sclerosis: A pilot randomized controlled trial.** Rehabil Psychol. 2020 May 7. [\[ABS\]](#)

OBJECTIVE: People with multiple sclerosis (PwMS) report greater emotion dysregulation, which is associated with increased symptoms of depression and anxiety, and reduced quality of life. ...Our pilot study provides preliminary support for mindfulness-based training (MBT) to reduce self-reported emotion dysregulation in PwMS. Given the widespread prevalence of mental health disturbances in this population, MBT can serve as a promising rehabilitation tool for PwMS.

Craig C, et al (2020) - **Compassion focused therapy: a systematic review of its effectiveness and acceptability in clinical populations.** Expert Rev Neurother. 2020 Apr;20(4):385-400. [\[ABS\]](#)

Compassion focused therapy (CFT) is an increasingly popular therapeutic modality. Its holistic and integrative approach to universal human suffering means that it is well placed as a **transdiagnostic** therapy. ...Expert opinion: CFT shows promise for a range of mental health problems, especially when delivered in a group format over at least 12 hours.

Lam AHY, et al (2020) - **The Effectiveness of a Mindfulness-Based Psychoeducation Programme for Emotional Regulation in Individuals with Schizophrenia Spectrum Disorders: A Pilot Randomised Controlled Trial.** Neuropsychiatr Dis Treat. 2020 Mar 12;16:729-747. [\[FULL TEXT\]](#)

Emotion dysregulation has emerged as a **transdiagnostic** factor that potentially exacerbates the risk of early-onset, maintenance, and relapse of psychosis. ...The MBPP appeared to be effective for improving emotion regulation, which will contribute to future large-scale RCT to confirm the treatment effects in more diverse groups of schizophrenic patients.

Frances S, et al (2020) - **Study protocol for a randomized control trial to investigate the effectiveness of an 8-week mindfulness-integrated cognitive behavior therapy (MiCBT) transdiagnostic group intervention for primary care patients.** BMC Psychiatry. 2020 Jan 6;20(1):7. [\[FULL TEXT\]](#)

Mindfulness-integrated cognitive behavior therapy (MiCBT) is a **transdiagnostic** intervention that integrates aspects of CBT, including exposure skills targeting avoidance, with training in mindfulness meditation skills adopted from the Vipassana or insight tradition taught by the Burmese teachers U Ba Khin and Goenka. MiCBT is distinguished from both cognitive therapy and mindfulness-based cognitive therapy by the use of a theoretical framework which proposes that the locus of reinforcement of behavior is the interoceptive experience (body sensations) that co-arises with self-referential thinking. Consequently, MiCBT has a strong focus on body scanning to develop interoceptive awareness and equanimity.

Schanche E, et al (2020) - **Participant experiences of change in mindfulness-based stress reduction for anxiety disorders.** Int J Qual Stud Health Well-being. 2020 Jan 1;15(1):1776094. [\[ABS\]](#)

Participants of mindfulness-based stress reduction (MBSR) both describe mindfulness as a tool to "fix" anxiety and as bringing about more fundamental change towards acceptance of their anxiety. The complexity of reported change corresponds with better handling of areas representing known **transdiagnostic** features of anxiety disorder, such as dysfunctional cognitive processes (including attentional biases), emotional dysregulation, avoidance behaviors, and maladaptive self-relatedness. This supports MBSR as a transdiagnostic approach to the treatment of anxiety disorders.

Wupperman P, et al (2019) - **Treatment for Individuals with Severe Mental Illness Who Use Illicit Drugs While Maintained on Methadone: Mindfulness and Modification Therapy.** J Nerv Ment Dis. 2019 Dec;207(12):1005-1011. [\[ABS\]](#)

This pilot study investigated the feasibility and acceptability of a 12-week, **transdiagnostic** group therapy (mindfulness and modification therapy [MMT]) tailored for opioid-dependent individuals (N = 6) with SMI and illicit drug use. Retention was

83%. At posttreatment and 2-month follow-up, participants rated the treatment as highly helpful (9 of 10; 8.67 of 10, respectively), reported routinely practicing the guided-mindfulness exercises, and reported high confidence that they would continue to practice. Assessments revealed clinically meaningful decreases in reported days of illicit drug use at posttreatment and follow-up, with large effect sizes. Preliminary evidence suggests that MMT may be a feasible and acceptable therapy that may improve treatment engagement in this underserved population.

Keng SL, et al (2019) - **Effects of brief daily mindfulness practice on affective outcomes and correlates in a high BPD trait sample.** Psychiatry Res. 2019 Oct;280:112485. [\[ABS\]](#)

Compared to the no-practice control condition, mindfulness practice resulted in significant improvements in trait mindfulness and self-compassion, whereas relaxation practice led to reductions in emotion regulation difficulties.

Birtwell K, et al (2019) - **An Exploration of Formal and Informal Mindfulness Practice and Associations with Wellbeing.** Mindfulness (N Y). 2019;10(1):89-99. [\[FULL TEXT\]](#)

Mindfulness has *transdiagnostic* applicability, but little is known about how people first begin to practice mindfulness and what sustains practice in the long term. The aim of the present research was to explore the experiences of a large sample of people practicing mindfulness, including difficulties with practice and associations between formal and informal mindfulness practice and wellbeing. ... Mindfulness teachers will be able to use the present findings to further support their students by reminding them of the benefits as well as normalising some of the challenges of mindfulness practice including falling asleep.

Blum H, et al (2019) - **Mindfulness Meditation and Anxiety in Adolescents on an Inpatient Psychiatric Unit.** J Health Care Chaplain. 2019 Apr 25:1-19. [\[ABS\]](#)

This study presents the impact of chaplain-provided mindfulness meditation (MM) groups on state-anxiety in adolescent inpatients on an acute psychiatric unit, ... State-anxiety was found to decrease significantly between pre- and post-MM upon first exposure regardless of patient age, sex, and prior experience with MM. Findings also suggest the possibility that patients experiencing symptoms of psychosis may benefit more from MM as compared to other patients. Admission symptom severity was not found to be an indicator of MM attendance. These findings suggest the possibility that MM could be an effective and relatively immediate *transdiagnostic* intervention to lower state anxiety in adolescents on an inpatient psychiatric unit and invite further implementation and research by staff chaplains on such units.

Greeson JM, et al (2018) - **Mindfulness Meditation Targets Transdiagnostic Symptoms Implicated in Stress-Related Disorders: Understanding Relationships between Changes in Mindfulness, Sleep Quality, and Physical Symptoms.** Evid Based Complement Alternat Med.

2018; 2018: 4505191. [[FULL TEXT](#)]

Van der Gucht K, et al (2017) - **Processes of change in a school-based mindfulness programme: cognitive reactivity and self-coldness as mediators.** Cogn Emot. 2017 Mar 31:1-8. [[ABS](#)]

Garland EL, et al (2016) - **Mindfulness-Oriented Recovery Enhancement versus CBT for co-occurring substance dependence, traumatic stress, and psychiatric disorders: Proximal outcomes from a pragmatic randomized trial.** Behav Res Ther. 2016 Feb;77:7-16. [[FULL TEXT](#)]

Results suggest that MORE, as an integrative therapy designed to bolster self-regulatory capacity, may hold promise as a treatment for intersecting clinical conditions.

Kim MK, et al (2016) - **Impact of Mindfulness-Based Cognitive Therapy on Intolerance of Uncertainty in Patients with Panic Disorder.** Psychiatry Investig. 2016 Mar;13(2):196-202. [[FULL TEXT](#)]

IU may play a critical role in the diagnosis and treatment of panic disorder. MBCT is effective in lowering IU in patients with panic disorder.

Feldman G, et al (2016) - **Dispositional Mindfulness Uncouples Physiological and Emotional Reactivity to a Laboratory Stressor and Emotional Reactivity to Executive Functioning Lapses in Daily Life.** Mindfulness (N Y). 2016 Apr 1;7(2):527-541. [[FULL TEXT](#)]

Feldman G, et al (2014) - **Mindfulness and rumination as predictors of persistence with a distress tolerance task.** Pers Individ Dif. 2014 Jan 1;56. [[FULL TEXT](#)]

Distress tolerance (DT) is a proposed transdiagnostic factor in psychopathology, yet sources of individual differences in DT are largely unknown. The present study examined mindfulness and rumination facets as predictors of persistence on a standardized DT task (mirror tracing). Acting with awareness (a facet of mindfulness) and reflection (a potentially adaptive form of rumination) predicted increased DT. Increased task-induced skin conductance reactivity predicted decreased DT. These results held after controlling for task skill and subjective and heart rate reactivity. Together, these results suggest that teaching skills to promote mindful awareness and reflection hold promise as interventions to enhance DT.

Luoma JB, et al (2012) - **Mindfulness in the Treatment of Suicidal Individuals.** Cogn Behav Pract. 2012 Jan 5;19(2):265-276. [[FULL TEXT](#)]

Motion / Motor / Movement ▲

Kent JS, et al (2020) - **Exploring the Relationship of Transdiagnostic Mood and Psychosis Symptom Domains with Motor Dysfunction.** Neuropsychobiology. 2020;79(4-5):301-312. [\[ABS\]](#)

A number of motor abnormalities have been reported in psychotic disorders, including dyskinesia and psychomotor slowing. There is also evidence for many of the same motor abnormalities in biological first-degree relatives and accruing evidence for motor abnormalities in bipolar disorder. In addition to motor dysfunction, there are also shared symptom domains amongst these populations.

Walther S, et al (2019) - **The utility of an RDoC motor domain to understand psychomotor symptoms in depression.** Psychol Med. 2019 Jan;49(2):212-216. [\[ABS\]](#)

Despite the clinical impact of motor symptoms such as agitation or retardation on the course of depression, these symptoms are poorly understood. Novel developments in the field of instrumentation and mobile devices allow for dimensional and continuous recording of motor behavior in various settings, particularly outside the laboratory. Likewise, the use of novel assessments enables to combine multimodal neuroimaging with behavioral measures in order to investigate the neural correlates of motor dysfunction in depression. The research domain criteria (RDoC) framework will soon include a motor domain that will provide a framework for studying motor dysfunction in mood disorders. In addition, new studies within this framework will allow investigators to study motor symptoms across different stages of depression as well as other psychiatric diagnoses. Finally, the introduction of the RDoC motor domain will help test how motor symptoms integrate with the original five RDoC domains (negative valence, positive valence, cognitive, social processes, and arousal/regulation).

Nguyen J, et al (2016) - **Schizophrenia: The micro-movements perspective.** Neuropsychologia. 2016 May;85:310-26. [\[FULL TEXT\]](#)

Specifically, velocity-dependent signatures show that SZ patients move significantly slower than controls with more noise and randomness in their moment-by-moment hand micro-motions. Furthermore, the normative geometric-dependent signatures of deliberateness are absent from the goal-directed reaches in SZ, but present within normative ranges in their spontaneous hand retractions to rest. Given that the continuous flow of micro-motions contributes to internally sensed feedback from self-produced movements, it is highly probable that sensory-motor integration with externally perceived inputs is impaired. Such impairments in this SZ cohort seem to specifically alter the balance between deliberate and spontaneous control of actions. We interpret these results as potential indexes of avolition and lack of agency and action ownership. We frame our results in the broad context of Precision Psychiatry initiatives and discuss possible implications on the putative contributions of the peripheral nervous system to the internal models for the cognitive control of self-produced actions in the individual with a clinical diagnosis of SZ.

Bernard JA, et al (2015) - **Updating the research domain criteria: the utility of a motor dimension.** Psychol Med. 2015 Oct;45(13):2685-9. [[FULL TEXT](#)]

Within the NIMH Research Domain Criteria (RDoC) framework, dimensions of behavior are investigated across diagnoses with the goal of developing a better understanding of their underlying neural substrates. Currently, this framework includes five domains: cognitive, social, arousal/regulatory, negative, and positive valence systems. We argue that the inclusion of a motor systems domain is sorely needed as well. Independent of medication, distinct areas of motor dysfunction (e.g. motor planning/inhibition/learning/coordination, involuntary movements) commonly appear across a number of mental disorders (e.g. schizophrenia, bipolar disorder, autism, attention deficit hyperactivity disorder, Alzheimer's disease, depression) as well as neurological disorders accompanied by significant psychological symptoms (e.g. Parkinson's disease). In addition, motor systems are amenable to study across multiple levels of analysis from the cellular molecular level focusing on cytoarchitectonics and neurotransmitter systems, to networks and circuits measured using neuroimaging, and finally at the level of overt behavioral performance. Critically, the neural systems associated with motor performance have been relatively well defined, and different circuits have been linked to distinct aspects of motor behavior. As such, they may also be differentially associated with symptoms and motor dysfunction across diagnoses, and be uniquely informative about underlying etiology. Importantly, motor signs can change across stages of illness; they are also often present in the prodromal phases of disease and closely linked with course, suggesting that these behaviors represent a core feature reflective of pathogenic processes. The inclusion of a motor domain would allow researchers to better understand psychopathology more broadly, and may also reveal important contributions to disease processes across diagnoses.

Kepecs A, et al (2015) - **Emotor control: computations underlying bodily resource allocation, emotions, and confidence.** Dialogues Clin Neurosci. 2015 Dec;17(4):391-401. [[FULL TEXT](#)]

...this computational approach to emotions resonates with the emerging view that psychiatric nosology may be best parameterized in terms of disorders of the cognitive computations underlying complex behavior.

Nitric oxide and peroxynitrite ▲

Pacher P, et al (2007) - **Nitric oxide and peroxynitrite in health and disease.** Physiol Rev. 2007 Jan;87(1):315-424. [[FULL TEXT](#)]

A crucial aspect of NO signaling is to act as a shock absorber to dampen physiological responses to prevent parasitic oscillations from overwhelming complex control systems.

Its diffusive nature also allows NO to act as a retrograde neuromessenger that can transiently affect thousands of synapses within specific areas of the brain. Overwhelming evidence has established a role for NO in essentially all major pathological processes affecting humans. But NO itself is unlikely to be the proximal toxin in these processes.

Obsessive-Compulsive Disorder ▲

Den Ouden L, et al (2020) - **The role of Experiential Avoidance in transdiagnostic compulsive behavior: A structural model analysis.** Addict Behav. 2020 Sep;108:106464. [[ABS](#)]

Compulsivity is recognized as a transdiagnostic phenotype, underlying a variety of addictive and obsessive-compulsive behaviors. ...The present study investigated if there was a relationship between the affective process Experiential Avoidance (EA), an unwillingness to tolerate negative internal experiences, and the frequency and severity of transdiagnostic compulsive behaviors. ... The effect of EA on compulsivity was fully mediated by psychological distress, which in turn had a strong direct effect on compulsivity. This suggests distress is a key mechanism in explaining why people with high EA are more prone to compulsive behaviors.

Seow TXF, et al (2020) - **Transdiagnostic Phenotyping Reveals a Host of Metacognitive Deficits Implicated in Compulsivity.** Sci Rep. 2020 Feb 19;10(1):2883. [[FULL TEXT](#)]

Recent work suggests that obsessive-compulsive disorder (OCD) patients have a breakdown in the relationship between explicit beliefs (i.e. confidence about states) and updates to behavior. ...Consistent with prior case-control work, we found that decreases in action-confidence coupling were associated with OCD symptoms, but also 5/8 of the other clinical phenotypes tested (8/8 with no correction applied). This non-specific pattern was explained by a single transdiagnostic symptom dimension characterized by compulsivity that was linked to inflated confidence and several deficits in utilizing evidence to update confidence. These data highlight the importance of metacognitive deficits for our understanding of compulsivity and underscore how transdiagnostic methods may prove a more powerful alternative over studies examining single disorders.

Parkes L, et al (2019) - **Transdiagnostic variations in impulsivity and compulsivity in obsessive-compulsive disorder and gambling disorder correlate with effective connectivity in cortical-striatal-thalamic-cortical circuits.** Neuroimage. 2019 Nov 15;202:116070. [[FULL TEXT](#)]

Across all participants, higher disinhibition correlated with lower bottom-up connectivity in the dorsal circuit and greater bottom-up connectivity in the ventral circuit, and higher compulsivity correlated with lower bottom-up connectivity in the dorsal circuit. In patients, higher clinical severity was also linked to lower bottom-up connectivity in

the dorsal circuit, but these findings were independent of phenotypic variation, demonstrating convergence towards behaviourally and clinically relevant changes in brain dynamics. Effective connectivity did not differ as a function of traditional diagnostic labels and only weak associations were observed for functional connectivity measures. Together, our results demonstrate that cortical-striatal-thalamic-cortical dysfunction across obsessive-compulsive disorder and gambling disorder may be better characterized by dimensional phenotypes than diagnostic comparisons, supporting investigation of quantitative liability phenotypes.

Akkermans SEA, et al (2019) - **Frontostriatal functional connectivity correlates with repetitive behaviour across autism spectrum disorder and obsessive-compulsive disorder**. Psychol Med. 2019 Oct;49(13):2247-2255. [\[ABS\]](#)

Autism spectrum disorder (ASD) and obsessive-compulsive disorder (OCD) are neurodevelopmental disorders with considerable overlap in terms of their defining symptoms of compulsivity/repetitive behaviour. ... No diagnosis-specific differences were detected. The cross-disorder analysis, on the other hand, showed that increased functional connectivity between the left nucleus accumbens (NAcc) and a cluster in the right premotor cortex/middle frontal gyrus was related to more severe symptoms of repetitive behaviour. ... We demonstrate the fruitfulness of applying a cross-disorder (**transdiagnostic**) approach to investigate the neural underpinnings of compulsivity/repetitive behaviour, by revealing a shared alteration in functional connectivity in ASD and OCD. We argue that this alteration might reflect aberrant reward or motivational processing of the NAcc with excessive connectivity to the premotor cortex implementing learned action patterns.

Albertella L, et al (2019) - **Compulsivity is measurable across distinct psychiatric symptom domains and is associated with familial risk and reward-related attentional capture**. CNS Spectr. 2019 Oct 24:1-8. [\[ABS\]](#)

Compulsivity can be seen across various mental health conditions and refers to a tendency toward repetitive habitual acts that are persistent and functionally impairing. Compulsivity involves dysfunctional reward-related circuitry and is thought to be significantly heritable. Despite this, its measurement from a **transdiagnostic** perspective has received only scant research attention. H... These findings suggest that the Cambridge-Chicago Compulsivity Trait Scale is suitable for use in online studies and constitutes a transdiagnostic marker for a range of compulsive symptoms, their familial loading, and related cognitive markers.

Albertella L, et al (2019) - **Reward-related attentional capture is associated with severity of addictive and obsessive-compulsive behaviors**. Psychol Addict Behav. 2019 Aug;33(5):495-502. [\[FULL TEXT\]](#)

A cue that signals reward can capture attention and elicit approach behaviors in people and animals. The current study examined whether attentional capture by reward-related cues is associated with severity of addiction-related and obsessive-compulsive behaviors. ...Reward-related attentional capture was associated with severity of compulsivity, **transdiagnostically**. These findings have implications for understanding the mechanisms that underlie compulsive behaviors and suggest that reward-related attentional capture is a promising **transdiagnostic** cognitive risk marker for compulsivity.

Riesel A, et al (2019) - **Error-related brain activity as a transdiagnostic endophenotype for obsessive-compulsive disorder, anxiety and substance use disorder**. Psychol Med. 2019 May;49(7):1207-1217. [\[FULL TEXT\]](#)

Alterations in neural error-signals in unaffected first-degree relatives with a family history of OCD, anxiety, or SUD support the utility of the ERN as a **transdiagnostic** endophenotype. Reduced neural error-signals may indicate vulnerability for under-controlled behavior and risk for substance use, whereas a harm- or error-avoidant response style and vulnerability for OCD and anxiety appears to be associated with increased ERN. This adds to findings suggesting a common neurobiological substrate across psychiatric disorders involving the anterior cingulate cortex and deficits in cognitive control.

Riesel A, et al (2019) - **The erring brain: Error-related negativity as an endophenotype for OCD- A review and meta-analysis**. Psychophysiology. 2019 Apr;56(4):e13348. [\[ABS\]](#)

Obsessive-compulsive disorder (OCD) is a complex and heterogeneous disorder that is associated with high personal and societal costs. Feelings of doubt, worry, and repetitive behavior, key symptoms of OCD, have been linked to hyperactive error signals in the brain. The error-related negativity (ERN) represents a validated marker of error processing in the ERP. Increased ERN amplitudes in OCD have been reported very robustly over the last 20 years. ... Furthermore, alterations in ERN are not limited to OCD and may constitute a **transdiagnostic** endophenotype. Altered neural error signals might serve as a diagnostic or predictive marker and represent a promising target for interventions.

Castriotta N, et al (2019) - **Intolerance of uncertainty in hoarding disorder**. J Obsessive Compuls Relat Disord. 2019 Apr;21:97-101. [\[FULL TEXT\]](#)

Intolerance of uncertainty (IU) has been proposed as a **transdiagnostic** risk and maintenance factor underlying various forms of psychopathology. ... IU was positively and significantly associated with greater urges to acquire and greater difficulties discarding possessions, beyond shared variance accounted for by anxiety and depression. Higher pre-treatment IU predicted increased odds of treatment non-response. **CONCLUSIONS:** Elevated IU is associated with specific hoarding symptom clusters and may be an important target for HD treatment.

Burchi E, et al (2019) - **Compulsivity in Alcohol Use Disorder and Obsessive Compulsive Disorder: Implications for Neuromodulation**. Front Behav Neurosci. 2019 Apr 11;13:70. [[FULL TEXT](#)]

Alcohol use Disorder (AUD) is one of the leading causes of morbidity and mortality worldwide. The progression of the disorder is associated with the development of compulsive alcohol use, which in turn contributes to the high relapse rate and poor longer term functioning reported in most patients, even with treatment. While the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines AUD by a cluster of symptoms, parsing its heterogeneous phenotype by domains of behavior such as compulsivity may be a critical step to improve outcomes of this condition. Still, neurobiological underpinnings of compulsivity need to be fully elucidated in AUD in order to better design targeted treatment strategies. In this manuscript, we review and discuss findings supporting common mechanisms between AUD and OCD, dissecting the construct of compulsivity and focusing specifically on characteristic disruptions in habit learning and cognitive control in the two disorders. Finally, **neuromodulatory interventions** are proposed as a probe to test compulsivity as key pathophysiologic feature of AUD, and as a potential therapy for the subgroup of individuals with compulsive alcohol use, i.e., the more resistant stage of the disorder. This **transdiagnostic** approach may help to destigmatize the disorder, and suggest potential treatment targets across different conditions.

Miegel F, et al (2019) - **Dysfunctional beliefs in patients with obsessive-compulsive disorder and depression as assessed with the Beliefs Questionnaire (BQ)**. Psychiatry Res. 2019 Feb;272:265-274. [[ABS](#)]

Patients with OCD and depression scored higher on the Beliefs Questionnaire (BQ) compared to nonclinical controls. OCD patients displayed higher values on overestimation of threat and the fear of becoming insane. Correlation between BQ and OBQ total scores was high ($r = 0.751$), supporting the validity of the new scale. Our results show that two beliefs are OCD-specific. However, the BQ covers mainly **transdiagnostic** features and should be replicated with the inclusion of an anxiety disorder sample.

Pushkarskaya H, et al (2019) - **Contrasting contributions of anhedonia to obsessive-compulsive, hoarding, and post-traumatic stress disorders**. J Psychiatr Res. 2019 Feb;109:202-213. [[ABS](#)]

Anhedonia is a **transdiagnostic** construct that can occur independent of other symptoms of depression; ... Response time during a gambling task, an index of difficulty of making value-based choices, significantly correlated with anhedonia in individuals with OCD and individuals with HD, even after controlling for general depression, but not in individuals with PTSD. The results suggest a unique contribution of one aspect of anhedonia in obsessive-compulsive disorder and confirm the importance of investigating the role of anhedonia **transdiagnostically** beyond affective and psychotic disorders.

Furtado M, et al (2015) - **Neuroinflammatory pathways in anxiety, posttraumatic stress, and**

obsessive compulsive disorders. Psychiatry Research September 30, 2015 Volume 229, Issues 1-2, Pages 37–48. [\[ABS\]](#)

As prevalence of anxiety, posttraumatic stress, and obsessive compulsive disorders continue to rise worldwide, increasing focus has been placed on immune mediated theories in understanding the underlying mechanisms of these disorders. Associations between the dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis and these disorders have been recognized in the scientific literature, specifically in regard to cortisol levels, as well as changes in pro- and anti-inflammatory cytokines. The present commentary will systematically assess the scientific literature within the past decade in regard to the psychoneuroimmunology of anxiety, posttraumatic stress, and obsessive compulsive disorders. Understanding the mechanisms of these disorders is essential in order to determine efficacious and targeted treatment strategies, which may lead to substantial improvements in overall functioning, as well as significant decreases in societal and economic burden.

Pain ▲

Day MA, et al (2021) - **Transdiagnostic Cognitive Processes in Chronic Pain and Comorbid PTSD and Depression in Veterans.** Ann Behav Med. 2021 May 26:kaab033. [\[ABS\]](#)

Across increasing complexity of comorbidity profiles (i.e., one vs. two comorbid conditions), ruminative absorption with pain emerged as a cognitive process that transverse diagnoses and contributes to worse outcomes.

Ravn SL, et al (2020) - **There's Nothing Broken. You've Had a Whiplash, That's It: A Qualitative Study of Comorbid Posttraumatic Stress Disorder and Whiplash Associated Disorders.** Pain Med. 2020 Feb 26:pnz369. [\[ABS\]](#)

BACKGROUND: Posttraumatic stress disorder (PTSD) symptoms are common in chronic Whiplash associated disorders (WAD) and have been found to be associated with higher levels of pain and disability. Theoretical frameworks have suggested that PTSD and pain not only coexist, but also mutually maintain one another. ...These findings underlined the great complexity and variability of the comorbidity and the traumatic event, but also emphasized how experiences of psyche and soma seem closely connected in these patients. The results provide support for the importance of thorough assessment by multidisciplinary teams, minimizing distress post-injury, and a critical approach to the idea of mutual maintenance between pain and PTSD.

Fava GA, et al (2019) - **Mental Pain as a Transdiagnostic Patient-Reported Outcome Measure.** Psychother Psychosom. 2019;88(6):341-349. [\[ABS\]](#)

Assessment of mental pain may have important clinical implications in intervention research, both in psychopharmacology and psychotherapy. The **transdiagnostic** features of mental pain are supported by its association with a number of psychiatric disorders, such as depression, anxiety, eating disorders, as well as borderline personality disorder. Further, addressing mental pain may be an important pathway to prevent and diminish the opioid epidemic.

Boersma K, et al (2019) - **Efficacy of a transdiagnostic emotion-focused exposure treatment for chronic pain patients with comorbid anxiety and depression: a randomized controlled trial.** Pain. 2019 Aug;160(8):1708-1718. [\[FULL TEXT\]](#)

The comorbidity between chronic pain and emotional problems has proven difficult to address with current treatment options. This study addresses the efficacy of a **transdiagnostic** emotion-focused exposure treatment ("hybrid") for chronic pain patients with comorbid emotional problems. ... We conclude that the hybrid emotion-focused treatment may be considered an acceptable, credible, and efficacious treatment option for chronic pain patients with comorbid emotional problems.

Zale EL, et al (2019) - **Gender differences in associations between pain-related anxiety and alcohol use among adults with chronic pain.** Am J Drug Alcohol Abuse. 2019;45(5):479-487. [\[ABS\]](#)

Pain-related anxiety is a **transdiagnostic** vulnerability factor that has been implicated in both pain and substance-related ... Pain-related anxiety was positively associated with alcohol-related consequences and alcohol dependence symptoms measured by the AUDIT (Alcohol Use Disorders Identification Test) among males, but not females.

Linton SJ (2013) - **A Transdiagnostic Approach to Pain and Emotion.** J Appl Biobehav Res. 2013 Jun; 18(2): 82–103. [\[ABS\]](#)

"Avoidance, catastrophic worry, and thought suppression are put forward as three examples of potential transdiagnostic mechanisms that may underlie a co-occurring emotion and pain problem."

Parkinson's Disease ▲

Wong OWH, et al (2019) - **Characterizing the Relationship between Eye Movement Parameters and Cognitive Functions in Non-demented Parkinson's Disease Patients with Eye Tracking.** J Vis Exp. 2019 Sep 26;(151). [\[ABS\]](#)

It was found that prolonged fixation duration was associated with poorer performance in

verbal fluency, visual and verbal memory, allowing further exploration on the use of eye movement parameters as proxy markers for cognitive function in Parkinson's disease patients. ...and could be applied **transdiagnostically** to other disease entities for similar research questions.

Ramdave S, et al (2019) - **Unmasking neurobiological commonalities between addictive disorders and impulse control disorders in Parkinson's disease**. Brain Imaging Behav. 2019 Feb 1. [\[ABS\]](#)

Changes in reward circuitry have been studied extensively in substance and behavioural addictions. However, comparatively little is known about the neurobiology underlying impulse control disorders (ICDs) in Parkinson's disease, which show roughly similar risk factors and behavioural presentations to both stimulant and behavioural addictions. ICDs occur in a subset of susceptible patients with Parkinson's disease (PD) following intake of dopamine replacement therapy (DRT). These behavioural disorders often have debilitating effects on a patient's quality of life and increase caregiver burden. ...

Results revealed that strikingly similar (a) deficits in dopaminergic receptor expression, (b) connectivity changes in corticostriatal circuitry and (c) neural responses to cue exposure are observed in both ICDs (impulse control disorders) in PD and addictive disorders. These findings point to the value of adopting a **transdiagnostic** approach when studying addicted populations and pave the way for demystifying this peculiar, often-devastating phenomenon in PD that has so far proven extremely difficult to treat and predict with any precision.

Passamonti L, et al (2018) - **The neuroanatomical and neurochemical basis of apathy and impulsivity in frontotemporal lobar degeneration**. Curr Opin Behav Sci. 2018 Aug;22:14-20. [\[FULL TEXT\]](#)

Apathy and impulsivity are common and often coexistent consequences of frontotemporal lobar degeneration (FTLD). They increase patient morbidity and career distress, but remain under-estimated and poorly treated. Recent **transdiagnostic** approaches that span the spectrum of clinical presentations of FTLD and Parkinsonism, indicate that apathy and impulsivity can be fractionated into multiple neuroanatomical and pharmacological systems. These include ventral/dorsal fronto-striatal circuits for reward-sensitivity, response-inhibition, and decision-making; moderated by noradrenaline, dopamine, and serotonin.

Garafalo S, et al (2017) - **Cortical and Striatal Reward Processing in Parkinson's Disease Psychosis**. Front Neurol. 2017 Apr 24;8:156. [\[FULL TEXT\]](#)

There was reduced activation in PD patients with a history of psychosis, compared to those without, in the posterior cingulate cortex and the VS during reward anticipation ($p < 0.05$ small volume corrected). The results suggest that cortical and striatal

abnormalities in reward processing, a putative pathophysiological mechanism of psychosis in schizophrenia, may also contribute to the pathogenesis of psychotic symptoms in PD. The finding of posterior cingulate dysfunction is in keeping with prior results highlighting cortical dysfunction in the pathogenesis of PD psychosis.

Post-Traumatic Stress Disorder (PTSD) / Trauma ▲

Bernstein EE, et al (2020) - **Mnemonic discrimination in treatment-seeking adults with and without PTSD.** Behav Res Ther. 2020 Aug;131:103650. [\[ABS\]](#)

Posttraumatic stress disorder (PTSD) is characterized by overgeneralized emotional reactivity following a trauma. Similarities between current, safe contexts and past, threatening events trigger recurrent, distressing responses and can contribute to a host of symptoms, including reexperiencing and hypervigilance. Mnemonic discrimination, a component process of episodic memory, could promote overgeneralization when impaired. Mnemonic discrimination reflects the integration of old and new experiences and one's ability to differentiate them despite their similarities. ...Findings suggest that poor mnemonic discrimination is transdiagnostically associated with emotional disorders. Future work is merited to explore this as a measurable and potentially malleable, though non-specific, risk factor.

Gutner CA, et al (2020) - **Dealing with complexity and comorbidity: Opportunity for transdiagnostic treatment for PTSD.** Curr Treat Options Psychiatry. 2019 Jun;6(2):119-131. [\[FULL TEXT\]](#)

Global and domestic studies suggest that a transdiagnostic approach has the potential to address many challenges providers encounter when treating traumatized populations. Existing research shows that transdiagnostic approaches (including the Unified Protocol, Common Elements Treatment Approach, and Modular Approach to Therapy for Children) are effective across low and high resourced settings, populations, and with comorbid mental health symptoms. Moreover, transdiagnostic approaches offer flexibility in treatment delivery, adaptability across contexts, and parsimonious training to treatment providers. They also provide a standalone alternative for unable or unwilling individuals to engage in traditional single diagnosis trauma-focused treatment, or those presenting with complex presentations that might otherwise require sequential courses of targeted interventions.

Taylor J, et al (2020) - **Mindfulness and yoga for psychological trauma: systematic review and meta-analysis.** J Trauma Dissociation. 2020 May 26:1-38. [\[ABS\]](#)

Mindfulness-based interventions (MBIs), with postures, breath, relaxation, and

meditation, such as Mindfulness-based Stress Reduction (MBSR) and yoga, are complex interventions increasingly used for trauma-related psychiatric conditions. Prior reviews have adopted a disorder-specific focus. However, trauma is a risk factor for most psychiatric conditions. We adopted a transdiagnostic approach to evaluate the efficacy of MBIs for the consequences of trauma, agnostic to diagnosis. ... this review suggests a transdiagnostic approach could be adopted in the treatment of trauma sequelae with MBIs.

Weiss NH, et al (2020) - **The interplay of negative and positive emotion dysregulation on mental health outcomes among trauma-exposed community individuals.** Psychol Trauma. 2020 Mar;12(3):219-226. [[FULL TEXT](#)]

Emotion dysregulation is a transdiagnostic construct with relevance to a wide range of mental health outcomes. ...Both negative and positive emotion dysregulation were positively related to PTSD, depression, and alcohol and drug misuse. ... These findings suggest that the relation of positive emotion dysregulation to mental health outcomes may not be dependent on negative emotion dysregulation, supporting the utility of both negative and positive emotion dysregulation in identifying and treating mental health outcomes in trauma-exposed individuals.

Ravn SL, et al (2020) - **There's Nothing Broken. You've Had a Whiplash, That's It: A Qualitative Study of Comorbid Posttraumatic Stress Disorder and Whiplash Associated Disorders.** Pain Med. 2020 Feb 26;pnz369. [[ABS](#)]

BACKGROUND: Posttraumatic stress disorder (PTSD) symptoms are common in chronic Whiplash associated disorders (WAD) and have been found to be associated with higher levels of pain and disability. Theoretical frameworks have suggested that PTSD and pain not only coexist, but also mutually maintain one another. ...These findings underlined the great complexity and variability of the comorbidity and the traumatic event, but also emphasized how experiences of psyche and soma seem closely connected in these patients. The results provide support for the importance of thorough assessment by multidisciplinary teams, minimizing distress post-injury, and a critical approach to the idea of mutual maintenance between pain and PTSD.

Mekawi Y, et al (2020) - **The role of negative affect in the association between attention bias to threat and posttraumatic stress: An eye-tracking study.** Psychiatry Res. 2020 Feb;284:112674. [[FULL TEXT](#)]

Biased processing of threatening stimuli, including attention toward and away from threat, has been implicated in the development and maintenance of PTSD symptoms. ... negative affect may be an important etiological process through which attention bias patterns could impact PTSD symptom severity. Implications for psychological and pharmacological therapeutic interventions targeting threat-related attention biases and negative affect are discussed.

Frost L, et al (2020) - **What is the relationship between post-traumatic stress disorder, extreme appraisals of internal state and symptoms in bipolar disorder?** Behav Cogn Psychother. 2020 Jan;48(1):103-115. [\[ABS\]](#)

Findings provide partial support for the integrative cognitive model of bipolar disorder and highlight the need for transdiagnostic treatments in bipolar disorder due to the prevalence and impact of trauma and co-morbidity. Working on trauma experiences in therapy may impact on depressive symptoms for those with bipolar disorder and co-morbid PTSD.

Gros DF, et al (2020) - **Efficacy of transdiagnostic behavior therapy on transdiagnostic avoidance in veterans with emotional disorders.** J Clin Psychol. 2020 Jan;76(1):31-39. [\[ABS\]](#)

To date, transdiagnostic treatments have primarily investigated treatment outcomes of general psychiatric symptomatology, rather than the specific transdiagnostic symptoms implicated in their protocols. The present study sought to address this significant gap in the literature by investigating the effect of transdiagnostic behavior therapy (TBT) on transdiagnostic avoidance. ... The findings support the hypothesized effect of TBT in self-report measures of four types of transdiagnostic avoidance in participants diagnosed with various emotional disorders. These findings contribute to the growing literature on the potential benefits of the transdiagnostic approaches to address symptomatology across diagnoses.

Powers A, et al (2020) - **Intergenerational transmission of risk for PTSD symptoms in African American children: The roles of maternal and child emotion dysregulation.** Psychol Trauma. 2020 Jan 2;10.1037/tra0000543. [\[FULL TEXT\]](#)

Emotion dysregulation is a transdiagnostic risk factor for many mental health disorders and develops in the context of early trauma exposure. Research suggests intergenerational risk associated with trauma exposure and posttraumatic stress disorder (PTSD), such that maternal trauma experiences and related symptoms can negatively impact child outcomes across development. ...Both maternal and child emotion dysregulation could be valuable treatment targets for improving maternal mental health and parenting behaviors and bolstering child health outcomes, thus reducing intergenerational transmission of risk associated with trauma

van Heemstra HE, et al (2019) - **7ROSES, a transdiagnostic intervention for promoting self-efficacy in traumatized refugees: a first quantitative evaluation.** Eur J Psychotraumatol. 2019 Oct 15;10(1):1673062. [\[FULL TEXT\]](#)

Due to traumatic experiences and highly prevalent post-migration stressors, refugees are vulnerable for developing psychopathology. ...7ROSES, a **transdiagnostic** intervention that aims to increase self-efficacy among treatment-seeking refugees in dealing with

post-migration stressors. Because it can be applied by non-specialist health care workers, it can be disseminated on a large scale, thereby increasing options for psychosocial support for refugees. ...Findings provide preliminary evidence that 7ROSES could improve self-efficacy and general mental health in refugees with psychopathology.

Schalinski I, et al (2019) - **Early neglect is a key determinant of adult hair cortisol concentration and is associated with increased vulnerability to trauma in a transdiagnostic sample.** *Psycho-neuroendocrinology*. 2019 Oct;108:35-42. [\[ABS\]](#)

BACKGROUND: Childhood adversities and traumatic events have each been associated with hypothalamus-pituitary-adrenal (HPA) axis dysregulation and trauma-related symptoms in adulthood. Hair cortisol concentration (HCC) reflects cumulative cortisol levels over the course of months and is discussed as a potential marker between trauma-induced neuroendocrine dysfunction and trauma-related symptoms. ... Results strengthen evidence that inadequate care and neglect during critical periods alter HPA axis biology towards enduring reduction in cortisol, the latter being associated with augmented trauma-related symptoms upon trauma exposure. If validated by longitudinal assessments these cross-sectional findings suggest biological mechanisms of childhood adversities into psychopathology in adulthood.

Moring JC, et al (2019) - **Conceptualizing comorbid PTSD and depression among treatment-seeking, active duty military service members.** *J Affect Disord*. 2019 Sep 1;256:541-549. [\[FULL TEXT\]](#)

Results demonstrated that the relationship between PTSD and depression among active duty service members can be explained by both *transdiagnostic* factors and disorder-specific symptoms.

López CM, et al (2019) - **Residual Insomnia and Nightmares Postintervention Symptom Reduction Among Veterans Receiving Treatment for Comorbid PTSD and Depressive Symptoms.** *Behav Ther*. 2019 Sep;50(5):910-923. [\[ABS\]](#)

Consistent with previous research, greater residual insomnia symptoms were predictive of smaller treatment gains. Findings illustrate the potential significance of insomnia during the course of *transdiagnostic* treatment (e.g., PTSD and depression), leading to several important clinical assessment and treatment implications.

Crabtree MA, et al (2019) - **Factor Structure and Initial Validation of a Brief Measure of Perceived Emotional and Physical Distress Tolerance in Post-9/11 US Veterans.** *Mil Psychol*. 2019 Jul 17;31(5). [\[FULL TEXT\]](#)

Distress tolerance (i.e., perceived or actual capacity to tolerate aversive internal states) has received considerable research attention as a *transdiagnostic* risk-factor underlying the development and maintenance of psychopathology. Lower levels of emotional

distress tolerance have been linked to psychopathology (e.g. Posttraumatic Stress Disorder) within Military populations; ...The Distress Tolerance Index reflected a longitudinally invariant two-factor structure (emotional and physical distress tolerance), with excellent internal consistency and preliminary evidence of convergent validity. Thus, the DTI represents a brief, reliable and temporally stable measure of physical and emotional distress tolerance.

Pinna G (2019) - **Animal Models of PTSD: The Socially Isolated Mouse and the Biomarker Role of Allopregnanolone**. Front Behav Neurosci. 2019 Jun 11;13:114. [[FULL TEXT](#)]

Post-traumatic stress disorder (PTSD) is a debilitating undertreated condition that affects 8%-13% of the general population and 20%-30% of military personnel. Currently, there are no specific medications that reduce PTSD symptoms or biomarkers that facilitate diagnosis, inform treatment selection or allow monitoring drug efficacy. PTSD animal models rely on stress-induced behavioral deficits that only partially reproduce PTSD neurobiology. PTSD heterogeneity, including comorbidity and symptoms overlap with other mental disorders, makes this attempt even more complicated. Allopregnanolone, a neurosteroid that positively, potently and allosterically modulates GABAA receptors and, by this mechanism, regulates emotional behaviors, is mainly synthesized in brain corticolimbic glutamatergic neurons. In PTSD patients, allopregnanolone down-regulation correlates with increased PTSD re-experiencing and comorbid depressive symptoms, CAPS-IV scores and Simms dysphoria cluster scores. In PTSD rodent models, including the socially isolated mouse, decrease in corticolimbic allopregnanolone biosynthesis is associated with enhanced contextual fear memory and impaired fear extinction. Allopregnanolone, its analogs or agents that stimulate its synthesis offer treatment approaches for facilitating fear extinction and, in general, for neuropsychopathologies characterized by a neurosteroid biosynthesis downregulation. The socially isolated mouse model reproduces several other deficits previously observed in PTSD patients, including altered GABAA receptor subunit subtypes and lack of benzodiazepines pharmacological efficacy. **Transdiagnostic** behavioral features, including expression of anxiety-like behavior, increased aggression, a behavioral component to reproduce behavioral traits of suicidal behavior in humans, as well as alcohol consumption are heightened in socially isolated rodents. Potentials for assessing novel biomarkers to predict, diagnose, and treat PTSD more efficiently are discussed in view of developing a precision medicine for improved PTSD pharmacological treatments.

Lebois LAM, et al (2019) - **Augmentation of Extinction and Inhibitory Learning in Anxiety and Trauma-Related Disorders**. Annu Rev Clin Psychol. 2019 May 7;15:257-284. [[FULL TEXT](#)]

This growing body of research may offer promising novel techniques to address debilitating **transdiagnostic** fear-related symptoms.

Raines AM, et al (2019) - **Intolerance of uncertainty and DSM-5 PTSD symptoms: Associations among a treatment seeking veteran sample**. J Anxiety Disord. 2019 Mar;62:61-67. [[ABS](#)]

Results revealed that IU (Intolerance of uncertainty) was significantly associated with overall PTSD symptom severity, above and beyond relevant covariates. Further, IU was significantly associated with the PTSD avoidance and hyperarousal clusters. Prospective IU, rather than inhibitory IU, accounted for these unique associations. These findings add to a growing body of literature establishing IU as a **transdiagnostic** risk factor and point to the importance of future research on the role of IU in contributing to and/or maintaining PTSD symptoms.

Britton PC, et al (2019) - **Insomnia and risk for suicidal behavior: A test of a mechanistic trans-diagnostic model in veterans**. J Affect Disord. 2019 Feb 15;245:412-418. [[ABS](#)]

In veterans, insomnia symptoms may be associated with increased PTSD and depressive symptoms, which may be associated with increased risk for suicidal behavior directly and indirectly through relationship disruptions.

Barredo J, et al (2019) - **Neuroimaging Correlates of Suicidality in Decision-Making Circuits in Posttraumatic Stress Disorder**. Front Psychiatry. 2019 Feb 12;10:44. [[FULL TEXT](#)]

These results provide a preliminary demonstration that biomarkers of suicidality in decision-making networks observed in depression may generalize to PTSD and highlight the promise of these circuits as **transdiagnostic** biomarkers of suicidality.

Yang Z, et al (2018) - **Network changes associated with transdiagnostic depressive symptom improvement following cognitive behavioral therapy in MDD and PTSD**. Mol Psychiatry. 2018 Dec;23(12):2314-2323. [[ABS](#)]

Despite widespread use of cognitive behavioral therapy (CBT) in clinical practice, its mechanisms with respect to brain networks remain sparsely described. In this study, we applied tools from graph theory and network science to better understand the transdiagnostic neural mechanisms of this treatment for depression. A sample of 64 subjects was included in a study of network dynamics: 33 patients (15 MDD, 18 PTSD) received longitudinal fMRI resting state scans before and after 12 weeks of CBT. Depression severity was rated on the Montgomery-Asberg Depression Rating Scale (MADRS). Thirty-one healthy controls were included to determine baseline network roles. Univariate and multivariate regression analyses were conducted on the normalized change scores of within- and between-system connectivity and normalized change score of the MADRS. Penalized regression was used to select a sparse set of predictors in a data-driven manner. Univariate analyses showed greater symptom reduction was associated with an increased functional role of the Ventral Attention (VA) system as an incohesive provincial system (decreased between- and decreased within-system connectivity). Multivariate analyses selected between-system connectivity of the VA system as the most prominent feature associated with depression improvement. Observed VA system changes are interesting in light of brain controllability descriptions:

attentional control systems, including the VA system, fall on the boundary between-network communities, and facilitate integration or segregation of diverse cognitive systems. Thus, increasing segregation of the VA system following CBT (decreased between-network connectivity) may result in less contribution of emotional attention to cognitive processes, thereby potentially improving cognitive control.

Barredo J, et al (2018) - **Network Functional Architecture and Aberrant Functional Connectivity in Post-Traumatic Stress Disorder: A Clinical Application of Network Convergence**. Brain Connect. 2018 Nov;8(9):549-557. [[ABS](#)]

Posttraumatic stress disorder (PTSD) is associated with disrupted functional connectivity in multiple neural networks. Multinetwork models of PTSD hypothesize that aberrant regional connectivity emerges from broad network-level disruptions. However, few studies have tested how characteristics of network-level organization influence regional functional connectivity in PTSD. This gap in knowledge impacts both our understanding of the pathophysiology of the disorder and the development of network-targeted PTSD treatments. We acquired resting-state imaging from a naturalistic sample of patients with PTSD (n = 42) and healthy controls (n = 42). Group differences in functional connectivity were identified using region of interest analyses and estimations of within- and between neural network activity; PTSD patients demonstrated reduced amygdala-orbitofrontal connectivity and increased default mode network (DMN) connectivity compared with controls. We then used convergence-a novel measure representing the capacity for functional integration-to test whether differences in functional architecture underlie connectivity signatures of PTSD. This approach found that reduced frontoparietal network (FPN) convergence was associated with reduced amygdala-orbitofrontal connectivity. Furthermore, in controls only, increased DMN convergence was associated with reduced DMN-to-salience network connectivity, and increased FPN convergence was associated with reduced FPN-to-ventral attention network connectivity. These results suggest that FPN functional architecture may underlie insufficiencies in top-down control in PTSD, with results broadly supporting the notion that networks' functional architecture influences the breakdown of normative functional relationships in PTSD. This work also indicates the potential of convergence to be applied to clinical populations in future research studies.

Yang Z, et al (2018) - **Cognitive Behavioral Therapy Is Associated with Enhanced Cognitive Control Network Activity in Major Depression and Posttraumatic Stress Disorder**. Biol Psychiatry Cogn Neurosci Neuroimaging. 2018 Apr;3(4):311-319. [[FULL TEXT](#)]

BACKGROUND: Both major depressive disorder (MDD) and posttraumatic stress disorder (PTSD) are characterized by depressive symptoms, abnormalities in brain regions important for cognitive control, and response to cognitive behavioral therapy (CBT). However, whether a common neural mechanism underlies CBT response across diagnoses is unknown. METHODS: Brain activity during a cognitive control task was measured using functional magnetic resonance imaging in 104 participants: 28 patients

with MDD, 53 patients with PTSD, and 23 healthy control subjects; depression and anxiety symptoms were determined on the same day. A patient subset (n = 31) entered manualized CBT and, along with controls (n = 19), was rescanned at 12 weeks. Linear mixed effects models assessed the relationship between depression and anxiety symptoms and brain activity before and after CBT. RESULTS: At baseline, activation of the left dorsolateral prefrontal cortex was negatively correlated with Montgomery-Åsberg Depression Rating Scale scores across all participants; this brain-symptom association did not differ between MDD and PTSD. Following CBT treatment of patients, regions within the cognitive control network, including ventrolateral prefrontal cortex and dorsolateral prefrontal cortex, showed a significant increase in activity. CONCLUSIONS: Our results suggest that dimensional abnormalities in the activation of cognitive control regions were associated primarily with symptoms of depression (with or without controlling for anxious arousal). Furthermore, following treatment with CBT, activation of cognitive control regions was similarly increased in both MDD and PTSD. These results accord with the Research Domain Criteria conceptualization of mental disorders and implicate improved cognitive control activation as a transdiagnostic mechanism for CBT treatment outcome.

Gibson LE, et al (2017) - **The association between traumatic life events and psychological symptoms from a conservative, transdiagnostic perspective.** Psychiatry Res. 2017 Jun;252:70-74. [\[ABS\]](#)

Findings underscore the critical role that TLE histories play in posttraumatic stress, borderline personality, and attenuated psychotic symptom expression. The relationship between TLEs and depression, cannabis and other drug use, generalized anxiety, and social anxiety disappeared after adjusting for comorbid symptoms.

Schmidt U, et al (2017) - **Integrating NIMH Research Domain Criteria (RDoC) into PTSD Research.** Curr Top Behav Neurosci. 2017 Mar 25. [\[ABS\]](#)

Three and a half decades of research on posttraumatic stress disorder (PTSD) has produced substantial knowledge on the pathobiology of this frequent and debilitating disease. However, despite all research efforts, so far no drug that has specifically targeted PTSD core symptoms progressed to clinical use. Instead, although not overly efficient, serotonin re-uptake inhibitors continue to be considered the gold standard of PTSD pharmacotherapy. The psychotherapeutic treatment and symptom-oriented drug therapy options available for PTSD treatment today show some efficacy, although not in all PTSD patients, in particular not in a substantial percent of those suffering from the detrimental sequelae of repeated childhood trauma or in veterans with combat related PTSD. PTSD has this in common with other psychiatric disorders - in particular effective treatment for incapacitating conditions such as resistant major depression, chronic schizophrenia, and frequently relapsing obsessive-compulsive disorder as well as dementia has not yet been developed through modern neuropsychiatric research. In response to this conundrum, the National Institute of Mental Health launched the

Research Domain Criteria (RDoC) framework which aims to leave diagnosis-oriented psychiatric research behind and to move on to the use of research domains overarching the traditional diagnosis systems. To the best of our knowledge, the paper at hand is the first that has systematically assessed the utility of the RDoC system for PTSD research. Here, we review core findings in neurobiological PTSD research and match them to the RDoC research domains and units of analysis. Our synthesis reveals that several core findings in PTSD such as amygdala overactivity have been linked to all RDoC domains without further specification of their distinct role in the pathophysiological pathways associated with these domains. This circumstance indicates that the elucidation of the cellular and molecular processes ultimately decisive for regulation of psychic processes and for the expression of psychopathological symptoms is still grossly incomplete. All in all, we find the RDoC research domains to be useful but not sufficient for PTSD research. Hence, we suggest adding two novel domains, namely stress and emotional regulation and maintenance of consciousness. As both of these domains play a role in various if not in all psychiatric diseases, we judge them to be useful not only for PTSD research but also for psychiatric research in general.

Zambrano-Vazquez L, et al (2017) - **Using the Research Domain Criteria Framework to Track Domains of Change in Comorbid PTSD and SUD.** Psychol Trauma. 2017 Feb 6. [\[ABS\]](#)

Shou H, et al (2017) - **Cognitive behavioral therapy increases amygdala connectivity with the cognitive control network in both MDD and PTSD.** Neuroimage Clin. 2017 Jan 27;14:464-470. [\[FULL TEXT\]](#)

We found evidence for the hypothesis that CBT treatment is associated with changes in connectivity between the amygdala and the fronto-parietal network. CBT may work by strengthening connections between the amygdala and brain regions that are involved in cognitive control, potentially providing enhanced top-down control of affective processes that are dysregulated in both MDD and PTSD.

Jenness JL, et al (2016) - **Catastrophizing, rumination, and reappraisal prospectively predict adolescent PTSD symptom onset following a terrorist attack.** Depress Anxiety. 2016 Aug 24. [\[ABS\]](#)

RESULTS: Greater pre-trauma engagement in rumination predicted onset of PTSD symptoms following the attack. Adolescents who engaged in catastrophizing also had greater PTSD symptoms post-attack, but only when exposed to high levels of media coverage of the attacks; the same pattern was observed for adolescents who engaged in low levels of cognitive reappraisal.

CONCLUSIONS: Engagement in specific emotion regulation strategies prior to a traumatic event predicts the onset of PTSD symptoms among youths exposed to trauma, extending transdiagnostic models of emotion regulation to encompass trauma-related psychopathology in children and adolescents.

Holiday SB, et al (2016) - **Depression, posttraumatic stress, and alcohol misuse in young adult veterans - The transdiagnostic role of distress tolerance.** Drug Alcohol Depend. 2016 Apr 1;161:348-55. [\[FULL TEXT\]](#)

"This is the first study to examine the role of distress tolerance in the relationship between mental health and alcohol misuse in a U.S. military veteran population. These results suggest that distress tolerance plays a role in the relationship between common post-deployment mental health concerns and alcohol misuse in young adult veterans. Given the significant health and psychosocial consequences of depression, PTSD, problem drinking, and the potential for tri-morbidity of these three conditions among young veterans and other high-risk populations, additional investigation of transdiagnostic factors that underlie these comorbidities is warranted and may be essential to informing prevention and treatment efforts."

Parlar M, et al (2016) - **Dissociative symptoms are associated with reduced neuropsychological performance in patients with recurrent depression and a history of trauma exposure.** Eur J Psychotraumatol. 2016 Feb 25;7:29061. [\[FULL TEXT\]](#)

Montalvo-Ortiz JL, et al (2016) - **RDoC and translational perspectives on the genetics of trauma-related psychiatric disorders.** Am J Med Genet B Neuropsychiatr Genet. 2016 Jan;171B(1):81-91. [\[FULL TEXT\]](#)

Furtado M, et al (2015) - **Neuroinflammatory pathways in anxiety, posttraumatic stress, and obsessive compulsive disorders.** Psychiatry Research September 30, 2015 Volume 229, Issues 1-2, Pages 37–48. [\[ABS\]](#)

As prevalence of anxiety, posttraumatic stress, and obsessive compulsive disorders continue to rise worldwide, increasing focus has been placed on immune mediated theories in understanding the underlying mechanisms of these disorders. Associations between the dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis and these disorders have been recognized in the scientific literature, specifically in regard to cortisol levels, as well as changes in pro- and anti-inflammatory cytokines. The present commentary will systematically assess the scientific literature within the past decade in regard to the psychoneuroimmunology of anxiety, posttraumatic stress, and obsessive compulsive disorders. Understanding the mechanisms of these disorders is essential in order to determine efficacious and targeted treatment strategies, which may lead to substantial improvements in overall functioning, as well as significant decreases in societal and economic burden.

Lobo I, et al (2015) - **EEG correlates of the severity of posttraumatic stress symptoms: A systematic review of the dimensional PTSD literature.** J Affect Disord. 2015 Sep 1;183:210-20. [\[ABS\]](#)

BACKGROUND: Considering the Research Domain Criteria (RDoC) framework, it is crucial to investigate posttraumatic stress disorder (PTSD) as a spectrum that ranges from normal to pathological. This dimensional approach is especially important to aid early PTSD detection and to guide better treatment options. In recent years, electroencephalography (EEG) has been used to investigate PTSD; however, reviews regarding EEG data related to PTSD are lacking, especially considering the dimensional approach. This systematic review examined the literature regarding EEG alterations in trauma-exposed people with posttraumatic stress symptoms (PTSS) to identify putative EEG biomarkers of PTSS severity.

RESULTS: The literature search yielded 1178 references, of which 34 studies were eligible for inclusion. Despite variability among the reviewed studies, the PTSS severity was often associated with P2, P3-family event-related potentials (ERPs) and alpha rhythms.

CONCLUSIONS: EEG provides promising candidates to act as biomarkers, although further studies are required to confirm the findings. Thus, EEG, in addition to being cheaper and easier to implement than other central techniques, has the potential to reveal biomarkers of PTSS severity

Lanius RA (2015) - **Trauma-related dissociation and altered states of consciousness: a call for clinical, treatment, and neuroscience research.** Eur J Psychotraumatol. 2015 May 19;6:27905. [\[FULL TEXT\]](#)

Schmidt U (2015) - **A plea for symptom-based research in psychiatry (subthreshold PTSD).** Eur J Psychotraumatol. 2015 May 19;6:27660. [\[FULL TEXT\]](#)

The significant proportion of patients suffering from subthreshold diagnoses such as partial posttraumatic stress disorder (PTSD) shows that today's diagnostic entities do not fully meet the reality and needs of clinical practice. Moreover, as stated also in the recently announced concept of research domain criteria (RDoC), the use of today's traditional diagnostic systems in psychiatric research does not sufficiently promote an integrative understanding of mental disorders across multiple units of analysis from behavior to neurobiology.

Subthreshold PTSD has, like other subthreshold psychiatric diagnoses, not yet been clearly defined. Diagnostic entities such as subthreshold PTSD are subject to a certain arbitrariness as they are mainly the result of empiricism. This fact stresses the urgent need for neurobiologically-informed psychiatric diagnoses and motivated the here-presented proposal of a symptom-based research concept. As proposed here, and before by other researchers, symptom-based research in psychiatry should refrain from studying patient cohorts compiled according to diagnoses but, instead, should focus on assessing cohorts grouped according to chief complaints or predominant psychopathological symptoms.

Lee SW, et al (2014) - **A bihemispheric autonomic model for traumatic stress effects on health and behavior.** Front Psychol. 2014 Aug 1;5:843. [[FULL TEXT](#)]

A bihemispheric autonomic model (BHAM) may support advanced understanding of traumatic stress effects on physiology and behavior. The model builds on established data showing hemispheric lateralization in management of the autonomic nervous system, and proposes that traumatic stress can produce dominant asymmetry in activity of bilateral homologous brain regions responsible for autonomic management. Rightward and leftward dominant asymmetries are associated with sympathetic high arousal or parasympathetic freeze tendencies, respectively, and return to relative symmetry is associated with improved autonomic regulation. Autonomic auto-calibration for recovery (inverse of Jacksonian dissolution proposed by polyvagal theory) has implications for risk behaviors associated with traumatic life stress. Trauma-induced high arousal may be associated with risk for maladaptive behaviors to attenuate arousal (including abuse of alcohol or sedative-hypnotics). Trauma-induced freeze mode (including callous-unemotional trait) may be associated with low resting heart rate and risk for conduct disorders. The model may explain higher prevalence of leftward hemispheric abnormalities reported in studies of violence. Implications of the BHAM are illustrated through case examples of a military special operations officer with history of traumatic brain injury and post-traumatic stress disorder, and a university student with persisting post-concussion symptoms. Both undertook use of a noninvasive closed-loop neurotechnology - high-resolution, relational, resonance-based, electroencephalic mirroring - with ensuing decrease in hemispheric asymmetry, improvement in heart rate variability, and symptom reduction. Finally, the BHAM aligns with calls for researchers to use brain-behavioral constructs (research domain criteria or RDoC, proposed by the National Institutes of Mental Health) as building blocks for assessment and intervention in mental health science.

O'Donnell M (2014) - **Psychosocial recovery after serious injury.** Eur J Psychotraumatol. 2014 Dec 9;5:26516. [[FULL TEXT](#)]

Results: A wide range of psychiatric disorders developed following injury, which included posttraumatic stress disorder, agoraphobia, depression, and substance use disorders (Bryant, O'Donnell, Creamer, Silove, & McFarlane, 2010). Although prevalence rates for these disorders were generally consistent over time, examination of trajectory data showed that different people had the disorders at different times. Importantly, the data showed that early anxiety, depression, and PTSD symptoms played a significant role in the development of long term disability after injury (Carty, O'Donnell, Evans, Kazantzis, & Creamer, 2011; O'Donnell et al., 2013).

Conclusions: These data support the view that transdiagnostic models for early intervention may be required to address the complex psychiatric disorder trajectories that develop after injury.

Turisch M, et al (2014) - **Association of trauma exposure with proinflammatory activity - a transdiagnostic meta-analysis**. Transl Psychiatry. 2014 Jul 22;4:e413. [\[FULL TEXT\]](#)

"...trauma exposure was positively associated with C-reactive protein (CRP), interleukin (IL)-1 β , IL-6, and tumor necrosis factor (TNF)- α ..."

"Positive correlations between inflammation and trauma exposure across a range of sample types and diagnoses were found. ... The results suggest that chronic inflammation likely represents one potential mechanism underlying risk of health problems in trauma survivors."

Weston CS (2014) - **Posttraumatic stress disorder: a theoretical model of the hyperarousal subtype**. Front Psychiatry. 2014 Apr 4;5:37. [\[FULL TEXT\]](#)

Schmidt U, et al (2013) - **Biomarkers in Posttraumatic Stress Disorder: Overview and Implications for Future Research**. Disease Markers Volume 35 (2013), Issue 1, Pages 43–54. [\[ABS\]](#)

Sripada RK, et al (2012) - **Neural dysregulation in posttraumatic stress disorder: evidence for disrupted equilibrium between salience and default mode brain networks**. Psychosom Med. 2012 Nov-Dec;74(9):904-11. [\[FULL TEXT\]](#)

OBJECTIVE: Convergent research demonstrates disrupted attention and heightened threat sensitivity in posttraumatic stress disorder (PTSD). This might be linked to aberrations in large-scale networks subserving the detection of salient stimuli (i.e., the salience network [SN]) and stimulus-independent, internally focused thought (i.e., the default mode network [DMN]).

During resting-state scanning, participants with PTSD showed reduced coupling within the DMN, greater coupling within the SN, and increased coupling between the DMN and the SN. Our findings suggest a relative dominance of threat-sensitive circuitry in PTSD, even in task-free conditions. Disequilibrium between large-scale networks subserving salience detection versus internally focused thought may be associated with PTSD pathophysiology.

Psychosis, Schizophrenia ▲

Feola B, et al (2020) - **Evidence for inhibited temperament as a transdiagnostic factor across mood and psychotic disorders**. J Affect Disord. 2020 Sep 1;274:995-1003. [\[ABS\]](#)

The conceptualization of risk for psychiatric illness is moving from risk factors for specific psychiatric disorders to factors that confer risk for multiple disorders. One potential transdiagnostic risk factor is inhibited temperament, a trait characterized by a fearful **or avoidant response to novelty**. Inhibited temperament is an established risk factor for anxiety disorders, and evidence suggests inhibited temperament is elevated in schizophrenia, bipolar disorder, and major depressive disorder. ...Inhibited temperament was similarly elevated in all patient groups compared to controls. Inhibited temperament was similarly associated with anxiety, depression, negative affect, and quality of life across patient groups.

Donaldson KR, et al (2020) - **Associations of mismatch negativity with psychotic symptoms and functioning transdiagnostically across psychotic disorders**. J Abnorm Psychol. 2020 Aug;129(6):570-580. [[ABS](#)]

Results showed that MMN amplitude was reduced in cases overall compared to never-psychotic individuals, with no differences between psychotic disorders. Furthermore, there were transdiagnostic associations of reduced duration MMN (MMN-D) with worse auditory hallucinations ($r = .14$) and disorganization ($r = .14$), frequency MMN (MMN-F) with real-word functioning ($r = .20$) and episodic memory ($r = -.22$), and both components with executive functioning (MMN-D: $r = -.17$; MMN-F: $r = -.15$)

Çakici N, et al (2020) - **Altered peripheral blood compounds in drug-naïve first-episode patients with either schizophrenia or major depressive disorder: a meta-analysis**. Brain Behav Immun. 2020 Aug;88:547-558. [[ABS](#)]

Schizophrenia and major depressive disorder (MDD) are associated with increased risks of immunologic disease and metabolic syndrome. ...Both schizophrenia and MDD show alterations in growth and immune factors from disease onset. An altered glucose metabolism seems to be present from onset in schizophrenia. These findings support efforts for further research into transdiagnostic preventive strategies and augmentation therapy for those with immune or metabolic dysfunctions.

Kuo SS, et al (2020) - **Transdiagnostic validity of the MATRICS Consensus Cognitive Battery across the autism-schizophrenia spectrum**. Psychol Med. 2020 Jul;50(10):1623-1632. [[ABS](#)]

BACKGROUND: Autism Spectrum Disorder (ASD) and schizophrenia are neurodevelopmental disorders which share substantial overlap in cognitive deficits during adulthood. However, treatment evaluation in ASD and treatment comparisons across ASD and schizophrenia are limited by a dearth of empirical work establishing the validity of a standard cognitive battery across ASD and schizophrenia. Promisingly, the MATRICS Consensus Cognitive Battery (MCCB) has been validated in schizophrenia and encompasses cognitive domains that are impacted in ASD. ... These findings highlight MCCB's applicability to ASD and support its utility for standardizing treatment evaluation of cognitive outcomes across the autism-schizophrenia spectrum.

Cheng PWC, et al (2020) - **The role of dopamine dysregulation and evidence for the transdiagnostic nature of elevated dopamine synthesis in psychosis: a positron emission tomography (PET) study comparing schizophrenia, delusional disorder, and other psychotic disorders.** Neuropsychopharmacology. 2020 Jul 1. [\[ABS\]](#)

These data indicate that delusional disorder, schizophrenia and other psychotic disorders have similar dysregulated mechanisms of dopamine synthesis, which supports the utility of abnormal dopamine synthesis in transdiagnoses of these psychotic conditions.

Watts AL, et al (2020) - **Incipient alcohol use in childhood: Early alcohol sipping and its relations with psychopathology and personality.** Dev Psychopathol. 2020 Jun 11:1-13. [\[ABS\]](#)

Prior research has shown that sipping of alcohol begins to emerge during childhood and is potentially etiologically significant for later substance use problems. Seventeen percent of the sample reported sipping alcohol outside of a religiously sanctioned activity by age 9 or 10. ...Several aspects of psychopathology and personality emerged as small but reliable correlates of sipping. Nonreligious sipping was related to youth-reported impulsogenic traits, aspects of behavioral activation, **prodromal psychotic**-like symptoms, and mood disorder diagnoses, as well as parent-reported externalizing disorder diagnoses. Religious sipping was unexpectedly associated with certain aspects of impulsivity. Together, our findings point to the potential importance of impulsivity and other transdiagnostic indicators of psychopathology (e.g., emotion dysregulation, novelty seeking) in the earliest forms of drinking behavior.

Shah JL, et al (2020) - **Transdiagnostic clinical staging in youth mental health: a first international consensus statement.** World Psychiatry. 2020 Jun; 19(2): 233–242. [\[FULL TEXT\]](#)

Li T, et al (2020) - **Mapping common grey matter volume deviation across child and adolescent psychiatric disorders.** Neurosci Biobehav Rev. 2020 May 30;115:273-284. [\[ABS\]](#)

Childhood and adolescence represent a time notable for the emergence of many psychiatric disorders, where comorbidity and co-occurrence of symptoms are well-documented. ...Compared to healthy peers, youth psychiatric disorders are characterized by reduced grey matter volume (GMV) of amygdala and lateral orbitofrontal cortex and enhanced GMV of ventromedial prefrontal cortex and precuneus. ... These regions and their networks mapped onto systems implicated in negative valence, positive valence, as well as social and cognitive functioning. Together, our findings are consistent with transdiagnostic models of psychopathology, uncovering common structural disturbance across youth psychiatric disorders, potentially reflecting an intermediate transdiagnostic phenotype in association with broad dimensions of youth psychopathology.

Doucet GE, et al (2020) - **Transdiagnostic and disease-specific abnormalities in the default-mode network hubs in psychiatric disorders: A meta-analysis of resting-state functional**

imaging studies. Eur Psychiatry. 2020 May 29;63(1):e57. [[FULL TEXT](#)]

BACKGROUND. The default mode network (DMN) dysfunction has emerged as a consistent biological correlate of multiple psychiatric disorders. Specifically, there is evidence of alterations in DMN cohesiveness in schizophrenia, mood and anxiety disorders. The aim of this study was to synthesize at a fine spatial resolution the intra-network functional connectivity of the DMN in adults diagnosed with schizophrenia, mood and anxiety disorders, capitalizing on powerful meta-analytic tools provided by activation likelihood estimation. **METHODS.** Results from 70 whole-brain resting-state functional magnetic resonance imaging articles published during the last 15 years were included comprising observations from 2,789 patients and 3,002 healthy controls. **RESULTS.** **Specific regional changes in DMN cohesiveness located in the anteromedial and posteromedial cortex emerged as shared and trans-diagnostic brain phenotypes.** Disease-specific dysconnectivity was also identified. Unmedicated patients showed more DMN functional alterations, highlighting the importance of interventions targeting the functional integration of the DMN. **CONCLUSION.** This study highlights functional alteration in the major hubs of the DMN, suggesting common abnormalities in self-referential mental activity across psychiatric disorders.

Blanchard JJ, et al (2020) - **Sleep Problems and Social Impairment in Psychosis: A Transdiagnostic Study Examining Multiple Social Domains.** Front Psychiatry. 2020 May 28;11:486. [[FULL TEXT](#)]

Psychotic disorders are characterized by profound social impairment. An accumulation of research has explored the contribution of symptoms, cognitive functioning, and behavioral skills deficits to this social dysfunction. Recent research indicates that sleep disturbance has significant social implications in nonclinical populations - this research suggests that sleep problems may also be relevant to understanding social impairment in psychosis.

We hypothesized that greater sleep disturbance and sleep-related impairment would be associated with more negative or problematic perceptions of social relationships (i.e., less social support, less companionship, and greater distress), poorer social functioning in the community, smaller social networks, and poorer behavioral ratings of social competency. Results supported these hypotheses indicating that sleep disturbance and sleep-related impairment have widespread deleterious impacts on perceptions of social relationships, social functioning, and competence

Kent JS, et al (2020) - **Exploring the Relationship of Transdiagnostic Mood and Psychosis Symptom Domains with Motor Dysfunction.** Neuropsychobiology. 2020;79(4-5):301-312. [[ABS](#)]

A number of motor abnormalities have been reported in psychotic disorders, including dyskinesia and psychomotor slowing. There is also evidence for many of the same motor abnormalities in biological first-degree relatives and accruing evidence for motor

abnormalities in bipolar disorder. In addition to motor dysfunction, there are also shared symptom domains amongst these populations.

Qi S, et al (2020) - **The relevance of transdiagnostic shared networks to the severity of symptoms and cognitive deficits in schizophrenia: a multimodal brain imaging fusion study.** Transl Psychiatry. 2020 May 18;10(1):149. [[FULL TEXT](#)]

Schizophrenia (SZ) is frequently concurrent with substance use, depressive symptoms, social communication and attention deficits... This study reveals symptom driven transdiagnostic shared networks between SZ and other mental disorders via multi-group data mining, indicating that some potential common underlying brain networks associated with schizophrenia differently with respect to symptoms and cognition

Huang CC, et al (2020) - **Transdiagnostic and Illness-Specific Functional Dysconnectivity across Schizophrenia, Bipolar Disorder, and Major Depressive Disorder.** Biol Psychiatry Cogn Neurosci Neuroimaging. 2020 May;5(5):542-553. [[ABS](#)]

Mental disorders are typically defined as distinct diagnostic entities, but similar patterns of clinical and cognitive impairments are frequently found across diagnostic groups. We investigated whether these transdiagnostic deficits result from common neural substrates across disorders or various illness-specific mechanisms, or a combination of both. ...Disconnectivity in the somatomotor network was a common transdiagnostic profile, while there were illness-specific patterns in different parts of the prefrontal cortex for different disorders. These findings suggest that prominent psychiatric disorders share common impairments, possibly linked to perception and motor output, as well as unique dysconnectivity profiles that hypothetically mediate the more distinctive features of the disorder-specific psychopathology.

Zou YM, et al (2020) - **Effort-cost computation in a transdiagnostic psychiatric sample: Differences among patients with schizophrenia, bipolar disorder, and major depressive disorder.** Psych J. 2020 Apr;9(2):210-222. [[ABS](#)]

Amotivational symptoms are observed in schizophrenia (SCZ), bipolar disorder (BD), and major depressive disorder (MDD). ...SCZ, BD, and MDD patients made comparably fewer high-effort choices than HCs in the high-reward magnitude, high-reward probability, and high-expected-value conditions. Self-reported amotivation did not correlate with decision-making on the EEfRT. Our findings suggest that reduced effort expenditure for reward is a **transdiagnostic** phenotype in SCZ, BD, and MDD.

Sheffield JM, et al (2020) - **Thalamocortical Anatomical Connectivity in Schizophrenia and Psychotic Bipolar Disorder.** Schizophr Bull. 2020 Mar 27:sbaa022. [[ABS](#)]

Anatomical connectivity between the thalamus and cortex, including the prefrontal cortex (PFC), is abnormal in schizophrenia. ... Psychosis was associated with lower PFC-

thalamic and elevated somatosensory-thalamic anatomical connectivity. ... Altered thalamocortical anatomical connectivity, especially reduced PFC-thalamic connectivity, is a transdiagnostic feature of psychosis detectable in the early stage of illness.

Lam AHY, et al (2020) - **The Effectiveness of a Mindfulness-Based Psychoeducation Programme for Emotional Regulation in Individuals with Schizophrenia Spectrum Disorders: A Pilot Randomised Controlled Trial.** Neuropsychiatr Dis Treat. 2020 Mar 12;16:729-747. [[FULL TEXT](#)]

Emotion dysregulation has emerged as a transdiagnostic factor that potentially exacerbates the risk of early-onset, maintenance, and relapse of psychosis. ...The MBPP appeared to be effective for improving emotion regulation, which will contribute to future large-scale RCT to confirm the treatment effects in more diverse groups of schizophrenic patients.

Meyer N, et al (2020) - **Sleep and Circadian Rhythm Disturbance in Remitted Schizophrenia and Bipolar Disorder: A Systematic Review and Meta-analysis.** Schizophr Bull. 2020 Mar 10:sbaa024. [[ABS](#)]

In both disorders, longer overall sleep duration, but also disturbed initiation, continuity, and reduced motor activity were found. Common, modifiable factors may be associated with these sleep-circadian phenotypes and advocate for further development of transdiagnostic interventions that target them.

Kasanova Z, et al (2020) - **Temporal associations between sleep quality and paranoia across the paranoia continuum: An experience sampling study.** J Abnorm Psychol. 2020 Jan;129(1):122-130. [[ABS](#)]

Sleep disturbances are prevalent among individuals with a psychotic disorder and have been linked to symptoms of paranoia across the entire psychosis continuum. Emerging evidence suggests that rather than a secondary symptom, poor quality of sleep may contribute to elevated paranoid ideation. ... In the everyday lives of individuals on the paranoia continuum, low quality of sleep appears to drive paranoia through its impact on negative affect. These findings identify sleep quality as an important target of transdiagnostic interventions for psychotic and affective symptomatology.

Hazan H, et al (2020) - **The prognostic significance of attenuated psychotic symptoms in help-seeking youth.** Schizophr Res. 2020 Jan;215:277-283. [[ABS](#)]

Attenuated psychotic symptoms are a prognostic indicator of persistent transdiagnostic mental health problems and reduced response to treatment in help-seeking youth over the short term. Hence, it is critical to screen and assess attenuated psychotic symptoms at the primary and secondary mental health services level, especially given that these subclinical symptoms are rarely voluntarily reported.

Upthegrove R, et al (2020) - **Cytokines, Oxidative Stress and Cellular Markers of Inflammation in Schizophrenia.** Curr Top Behav Neurosci. 2020;44:49-66. [\[ABS\]](#)

In this article, we review current evidence linking immune dysfunction in schizophrenia and related psychotic disorders focusing particularly on circulating cytokines, oxidative stress and cellular markers of inflammation in various stages on illness from drug-naïve first episode psychosis to chronic schizophrenia. Acute psychotic episode is associated with low-grade systemic inflammation in some patients, as reflected by increased concentrations of cytokines and other inflammatory markers in peripheral blood. Evidence from general population-based longitudinal cohort studies reporting an association between elevated inflammatory markers in childhood/adolescence and risk of schizophrenia and related psychosis subsequently in adulthood suggest that inflammation could be a causal risk factor for psychosis rather than simply be a consequence of illness. Mendelian randomization studies also suggest that associations between IL-6, CRP and schizophrenia are likely to be causal. In addition, we discuss evidence for disruptions in oxidative stress markers and CSF cytokine levels in schizophrenia, and potential reasons for reported **transdiagnostic** associations for inflammatory cytokines including role of early-life adversity/maltreatment. We argue that low-grade inflammation is a clinically useful feature, because it is associated with poor response to antipsychotic medication in first episode psychosis. We discuss clinical implications for immunological understanding of schizophrenia including scope for clinical trials of anti-inflammatory agents and notable gaps in current knowledge, and offer suggestions for future research.

Van Voorhis AC, et al (2019) - **Abnormal neural functions associated with motor inhibition deficits in schizophrenia and bipolar disorder.** Hum Brain Mapp. 2019 Dec 15;40(18):5397-5411. [\[FULL TEXT\]](#)

Failed modulation of brain processes in relation to response inhibition probability and the lengthening of motor response selection appear to be **transdiagnostic** abnormalities spanning schizophrenia and bipolar disorder.

Karcher NR, et al (2019) - **Functional Connectivity of the Striatum in Schizophrenia and Psychotic Bipolar Disorder.** Biol Psychiatry Cogn Neurosci Neuroimaging. 2019 Nov;4(11):956-965. [\[FULL TEXT\]](#)

The current study found evidence of **transdiagnostic** corticostriatal dysconnectivity in both schizophrenia and psychotic bipolar disorder, including reduced salience network connectivity, as well as reduced connectivity between the putamen and the medial prefrontal cortex. Overall, the current study points to the relative importance of salience network hypoconnectivity in psychotic disorders.

Liu J, et al (2019) - **Impact of emotion dysregulation and cognitive insight on psychotic and depressive symptoms during the early course of schizophrenia spectrum disorders.** Early Interv Psychiatry. 2019 Nov 6. [\[ABS\]](#)

Our findings provide preliminary support for the associations between emotion dysregulation and psychopathology in early SSD. Further research is needed to examine the **transdiagnostic** role of emotion dysregulation in the etiology and treatment of a wider range of psychotic disorders.

Taylor SF, et al (2019) - **The Fragile Brain: Stress Vulnerability, Negative Affect and GABAergic Neurocircuits in Psychosis**. Schizophr Bull. 2019 Oct 24;45(6):1170-1183. [[FULL TEXT](#)]

Given that postmortem parvalbumin positive interneuron disruptions have been identified in other conditions, such as bipolar disorder and autism, stress vulnerability may reflect a **transdiagnostic** dimension of psychopathology.

Sandstrom A, et al (2019) - **Offspring of parents with schizophrenia, bipolar disorder, and depression: a review of familial high-risk and molecular genetics studies**. Psychiatr Genet. 2019 Oct;29(5):160-169. [[ABS](#)]

Although family history remains the single strongest predictor of illness, molecular genetic tools are becoming increasingly informative. The next decade may see family history and molecular genetics complementing each other to facilitate a **transdiagnostic** approach to early risk identification and prevention.

Fusar-Poli P, et al (2019) - **Improving the Detection of Individuals at Clinical Risk for Psychosis in the Community, Primary and Secondary Care: An Integrated Evidence-Based Approach**. Front Psychiatry. 2019 Oct 24;10:774. [[FULL TEXT](#)]

A **transdiagnostic** individualized risk calculator could be used to automatically screen secondary mental health care medical notes to detect those at risk of psychosis and refer them to standard CHR-P assessment. Similar risk estimation tools for use in primary care are under development and promise to boost the detection of patients at risk in this setting.

Stoychev KR (2019) - **Neuroimaging Studies in Patients with Mental Disorder and Co-occurring Substance Use Disorder: Summary of Findings**. Front Psychiatry. 2019 Oct 23;10:702. [[FULL TEXT](#)]

Introduction: More than half of psychiatric patients have comorbid substance use disorder (dual diagnosis) and this rate, confirmed by many epidemiological studies, is substantially higher compared to general population. Combined operation of self-medication mechanisms, common etiological factors, and mutually causative influences most likely accounts for comorbidity, which, despite its clinical prevalence, remains underrepresented in psychiatric research, especially in terms of neuroimaging.

...When analyzing neuroimaging findings in SZ and bipolar disorder subjects, dorsolateral

prefrontal, cingular, and insular cortex emerge as common affected areas in both groups which might indicate a shared endophenotypic (i.e., **transdiagnostic**) disruption of brain networks involved in executive functioning, emotional processing, and social cognition, rendering affected individuals susceptible to both mental disorder and substance misuse. In patients with anxiety disorders and substance misuse, a common neuroimaging finding is reduced volume of limbic structures (n. accumbens, hippocampus and amygdala). Whether this is a neuropathological marker of common predisposition to specific behavioral symptoms and drug addiction or a result from neuroadaptation changes secondary to substance misuse is unknown. Future neuroimaging studies with larger samples, longitudinal design, and genetic subtyping are warranted to enhance current knowledge on comorbidity.

Creese B, et al (2019) - **Examining the association between genetic liability for schizophrenia and psychotic symptoms in Alzheimer's disease.** Transl Psychiatry. 2019 Oct 22;9(1):273. [\[FULL TEXT\]](#)

Laskemoen JF, et al (2019) - **Sleep disturbances in schizophrenia spectrum and bipolar disorders - a transdiagnostic perspective.** Compr Psychiatry. 2019 May;91:6-12. [\[ABS\]](#)

Sleep disturbances, including insomnia, hypersomnia and delayed sleep phase, are frequent in SCZ and BD, and associated with more severe clinical symptomatology across diagnostic groups. This suggests that sleep disturbance is a clinically relevant transdiagnostic phenomenon.

Pennou A, et al (2019) - **Mobile Intervention for Individuals with Psychosis, Dual Disorders, and Their Common Comorbidities: A Literature Review.** Front Psychiatry. 2019 May 3;10:302. [\[FULL TEXT\]](#)

Over 50% of people diagnosed with a severe mental illness, such as schizophrenia or bipolar disorder, will meet criteria for a substance use disorder in their lifetime. This dual disorder often starts during youth and leads to significant societal costs, including lower employability rates, more hospitalizations, and higher risk of homelessness and of suicide attempts when compared to those with a serious mental illness without substance misuse. Moreover, many individuals presenting with comorbid disorders also present with other psychological difficulties as well, such as personality disorders or anxiety and depression, also known as complex comorbid disorders. **Transdiagnostic** treatments that focus on core difficulties found in people with complex dual disorders, such as emotional regulation, are direly needed. Emotional **regulation skills** can help reduce distress related to psychotic symptoms and maintain abstinence in substance use disorders. New technologies in the field of communications have developed considerably over the past decade and have the potential to improve access to such treatments, a major problem in many health care settings. As such, this paper aims at: presenting core difficulties present in many individuals with dual disorders, reviewing the scientific literature pertaining to the use of mobile applications in mental health and addictions, and presenting

the development and potential of a new application for emotional regulation for people with dual disorders.

Díaz-Caneja CM, et al (2019) - **Neuroanatomical deficits shared by youth with autism spectrum disorders and psychotic disorders**. Hum Brain Mapp. 2019 Apr 1;40(5):1643-1653. [\[FULL TEXT\]](#)

Autism spectrum disorders (ASD) and early-onset psychosis (EOP) are neurodevelopmental disorders that share genetic, clinical and cognitive facets; it is unclear if these disorders also share spatially overlapping cortical thickness (CT) and surface area (SA) abnormalities. ...Autism spectrum disorders and early onset psychosis ... had spatially overlapping areas of cortical thinning and reduced surface area in the bilateral insula... The insula appears to be a region with **transdiagnostic** vulnerability for deficits in cortical thickness and surface area.

Ospina LH, et al (2019) - **Alexithymia predicts poorer social and everyday functioning in schizophrenia and bipolar disorder**. Psychiatry Res. 2019 Mar;273:218-226. [\[FULL TEXT\]](#)

Alexithymia, or the inability to identify and describe one's emotions, is significantly higher in bipolar disorder (BD) and schizophrenia (SZ), compared to healthy controls (HC). Alexithymia has also been observed to predict psychosocial functioning in SZ. We investigated whether alexithymia predicted social and everyday functioning in BD, as well as **transdiagnostically** in HC, BD, and SZ patients. ...Results suggest that aspects of alexithymia significantly predict functioning among these psychiatric groups, above and beyond the contributions of previously identified factors such as neurocognition and social cognition.

Hart KL, et al (2019) - **Risk tolerance measured by probability discounting among individuals with primary mood and psychotic disorders**. Neuropsychology. 2019 Mar;33(3):417-424. [\[ABS\]](#)

Change in risk tolerance is a feature of multiple psychiatric disorders and may contribute to adverse outcomes. ... This study supports the **transdiagnostic** measurement of risk-taking behaviors, even when such behaviors are not the primary area of psychopathology. Quantifying risk-taking may enable targeted therapeutic strategies across disorders.

Gilmour G, et al (2019) - **Relating constructs of attention and working memory to social withdrawal in Alzheimer's disease and schizophrenia: issues regarding paradigm selection**. Neurosci Biobehav Rev. 2019 Feb;97:47-69. [\[ABS\]](#)

Central nervous system diseases are not currently diagnosed based on knowledge of biological mechanisms underlying their symptoms. Greater understanding may be offered through an agnostic approach to traditional disease categories, where learning more about shared biological mechanisms across conditions could potentially reclassify subgroups of patients to allow realisation of more effective treatments. This review represents the output of the collaborative group "PRISM", tasked with considering assay

choices for assessment of attention and working memory in a **transdiagnostic** cohort of Alzheimer's disease and schizophrenia patients exhibiting symptomatic spectra of social withdrawal.

Gong Q, et al (2019) - **Dysconnectivity of the medio-dorsal thalamic nucleus in drug-naïve first episode schizophrenia: diagnosis-specific or trans-diagnostic effect?** Transl Psychiatry. 2019 Jan 16;9(1):9. [[FULL TEXT](#)]

Converging lines of evidence implicate the thalamocortical network in schizophrenia. In particular, the onset of the illness is associated with aberrant functional integration between the medio-dorsal thalamic nucleus (MDN) and widespread prefrontal, temporal and parietal cortical regions. Because the thalamus is also implicated in other psychiatric illnesses including post-traumatic stress disorder (PTSD) and major depressive disorder (MDD), the diagnostic specificity of these alterations is unclear.

The only significant schizophrenia-specific effect was increased EC (effective connectivity) between the right MDN and the right pallidum ($p < 0.05$ corrected). In contrast, there were a number of significant trans-diagnostic alterations, with both right and left MDN displaying **transdiagnostic** increased EC with several prefrontal and parietal regions bilaterally ($p < 0.05$ corrected). EC alterations between the MDN and the cortex are not specific to schizophrenia but are a **transdiagnostic** feature of psychiatric disorders, consistent with emerging conceptualizations of mental illness based on a single general psychopathology factor. Therefore, dysconnectivity of the MDN could potentially be used to assess the presence of general psychopathology above and beyond traditional diagnostic boundaries.

Szczypiński JJ, et al (2018) - **Dopamine dysregulation hypothesis: the common basis for motivational anhedonia in major depressive disorder and schizophrenia?** Rev Neurosci. 2018 Sep 25;29(7):727-744. [[ABS](#)]

Abnormalities in reward processing are crucial symptoms of major depressive disorder (MDD) and schizophrenia (SCH). Recent neuroscientific findings regarding MDD have led to conclusions about two different symptoms related to reward processing: motivational and consummatory anhedonia, corresponding, respectively, to impaired motivation to obtain rewards ('wanting'), and diminished satisfaction from consuming them ('liking'). One can ask: which of these is common for MDD and SCH. In our review of the latest neuroscientific studies, we show that MDD and SCH do not share consummatory anhedonia, as SCH patients usually have unaltered liking. Therefore, we investigated whether motivational anhedonia is the common symptom across MDD and SCH. With regard to the similarities and differences between the neural mechanisms of MDD and SCH, here we expand the current knowledge of motivation deficits and present the common underlying mechanism of motivational anhedonia - the dopamine dysregulation hypothesis - stating that any prolonged dysregulation in tonic dopamine signaling that exceeds the given equilibrium can lead to striatal dysfunction and

motivational anhedonia. The implications for further research and treatment of MDD and SCH are also discussed.

Demetriou EA, et al (2018) - **Autism, Early Psychosis, and Social Anxiety Disorder: a transdiagnostic examination of executive function cognitive circuitry and contribution to disability.** Transl Psychiatry. 2018 Sep 24;8(1):200. [[Full Text](#)]

This is the first study to compare EF measures across clinical groups of social impairment and suggests unique cognitive-circuitry that underpins disability within groups. Impairments in EF were broad in ASD and predicted disability, EP impairments were specific to attentional processes and SAD impairments likely relate to negative self-monitoring. Self-report, as opposed to performance-based EF, provided best capacity to predict disability. These findings contribute to transdiagnostic circuitry models and intervention strategies.

Sambataro F, et al (2019) - **Transdiagnostic modulation of brain networks by electroconvulsive therapy in schizophrenia and major depression.** Eur Neuropsychopharmacol. 2019 Aug;29(8):925-935. [[ABS](#)]

Patients had reduced connectivity within a striato-thalamic network in the thalamus as well as increased low frequency oscillations in a striatal network. ECT reduced low frequency oscillations (LFOs) on a striatal network along with increasing functional connectivity in the medial prefrontal cortex within the DMN. Following ECT treatment, the FNC of the executive network was reduced with the DMN and increased with the salience network, respectively. Our findings suggest *transnosological* effects of ECT on the connectivity of large-scale networks as well as at the level of their interplay. Furthermore, they support a transnosological approach for the investigation not only of the neural correlates of the disease but also of the brain mechanism of treatment of mental disorders.

de Oliveira L, et al (2019) - **Predicting Bipolar Disorder Risk Factors in Distressed Young Adults From Patterns of Brain Activation to Reward: A Machine Learning Approach.** Biol Psychiatry Cogn Neurosci Neuroimaging. 2019 Aug;4(8):726-733. [[FULL TEXT](#)]

The severity of a specific hypo/mania-related symptom was predicted from patterns of whole-brain activation in two independent samples. Given that emerging manic symptoms predispose to bipolar disorders, these findings could provide neural biomarkers to aid early identification of individual-level bipolar disorder risk in young adults.

Malhi GS, et al (2019) - **Transdiagnostic conceptualization: Giving psychosis and mood a personality.** Schizophr Res. 2019 Aug;210:50-51. [[REF](#)]

Lambert C, et al (2018) - **Anhedonia in depression and schizophrenia: A transdiagnostic challenge.** CNS Neurosci Ther. 2018 Jul;24(7). [[FULL TEXT](#)]

Anhedonia as a clinical presentation of reward circuit dysregulation is an important and relatively undertreated symptom of both SZ and MDD. In order to improve patient outcomes and quality of life, it is important to consider how anhedonia fits into both diagnoses.

Ciaramidaro A, et al (2018) - **Transdiagnostic deviant facial recognition for implicit negative emotion in autism and schizophrenia**. Eur Neuropsychopharmacol. 2018 Feb;28(2):264-275. [\[Abstract\]](#)

Impaired facial affect recognition (FAR) is observed in schizophrenia and autism spectrum disorder (ASD) and has been linked to amygdala and fusiform gyrus dysfunction. ...In addition, the ASD group additionally showed reduced activations in medial prefrontal cortex (PFC), bilateral dorso-lateral PFC, ventro-lateral PFC, posterior-superior temporal sulcus and left temporo-parietal junction. ...our findings are consistent with a common neural deficit during implicit negative facial affect recognition in schizophrenia and autism spectrum disorders.

Gong Q, et al (2017) - **Network-Level Dysconnectivity in Drug-Naïve First-Episode Psychosis: Dissociating Transdiagnostic and Diagnosis-Specific Alterations**. Neuropsychopharmacology. 2017 Mar;42(4):933-940. [\[FULL TEXT\]](#)

The FEP, MDD, and PTSD groups showed reductions in intranetwork connectivity of the default mode network relative to the HC group ($p < 0.05$ corrected); therefore, intranetwork alterations were expressed across the three diagnostic groups. In addition, the FEP group showed heightened internetwork connectivity between the default mode network, particularly the anterior cingulate cortex, and the central executive network relative to the MDD, PTSD, and HC groups

Isvoranu A-M, et al (2017) - **A Network Approach to Psychosis - Pathways between Childhood Trauma and Psychotic Symptoms**. Schizophr Bull. 2017 Jan;43(1):187-196. [\[ABS\]](#)

Upthegrove R, et al (2017) - **Depression and Schizophrenia: Cause, Consequence, or Trans-diagnostic Issue?** Schizophr Bull. 2017 Mar 1;43(2):240-244. [\[FULL TEXT\]](#)

The presence of depression in schizophrenia has been a challenge to the Kraepelinian dichotomy, with various attempts to save the fundamental distinction including evoking and refining diagnoses such as schizoaffective disorder. But the tectonic plates are shifting. Here we put forward a summary of recent evidence regarding the prevalence, importance, possible aetiological pathways and treatment challenges that recognizing depression in schizophrenia bring. Taken together we propose that depression is more than comorbidity and that increased effective therapeutic attention to mood symptoms will be needed to improve outcomes and to support prevention.

Bak M, et al (2016) - **An n=1 Clinical Network Analysis of Symptoms and Treatment in Psychosis**. PLoS One Published: September 19, 2016. [\[FULL TEXT\]](#)

Nguyen J, et al (2016) - **Schizophrenia: The micro-movements perspective**. Neuropsychologia. 2016 May;85:310-26. [\[FULL TEXT\]](#)

Specifically, velocity-dependent signatures show that SZ patients move significantly slower than controls with more noise and randomness in their moment-by-moment hand micro-motions. Furthermore, the normative geometric-dependent signatures of deliberateness are absent from the goal-directed reaches in SZ, but present within normative ranges in their spontaneous hand retractions to rest. Given that the continuous flow of micro-motions contributes to internally sensed feedback from self-produced movements, it is highly probable that sensory-motor integration with externally perceived inputs is impaired. Such impairments in this SZ cohort seem to specifically alter the balance between deliberate and spontaneous control of actions. We interpret these results as potential indexes of avolition and lack of agency and action ownership. We frame our results in the broad context of Precision Psychiatry initiatives and discuss possible implications on the putative contributions of the peripheral nervous system to the internal models for the cognitive control of self-produced actions in the individual with a clinical diagnosis of SZ.

Ford JM (2016) - **Studying auditory verbal hallucinations using the RDoC framework**. Psychophysiology. 2016 Mar;53(3):298-304. [\[FULL TEXT\]](#)

Whitton AE, et al (2015) - **Reward processing dysfunction in major depression, bipolar disorder and schizophrenia**. Curr Opin Psychiatry. 2015 Jan;28(1):7-12. [\[FULL TEXT\]](#)

PURPOSE OF REVIEW: This article reviews the recent literature on reward processing dysfunction in major depression (MDD), bipolar disorder and schizophrenia, with a focus on approach motivation, reward learning and reward-based decision-making. **RECENT FINDINGS:** Emerging evidence indicates the presence of reward processing abnormalities across all three disorders, supporting a transdiagnostic approach. In particular, findings are consistent with a role of abnormal phasic striatal dopamine signaling, which is critical for reinforcement learning, efficient mobilization of effort to obtain reward and allocation of attention to reward-predictive cues. Specifically, reward-related striatal signaling appears blunted in MDD and the negative symptoms of schizophrenia, elevated in bipolar (hypo)mania, and contextually misallocated in the positive symptoms of psychosis. However, whether shared or distinct pathophysiological mechanisms contribute to abnormal striatal signaling across the three disorders remains unknown. **SUMMARY:** New evidence of reward processing abnormalities in MDD, bipolar disorder and schizophrenia has led to a greater understanding of the neural processes associated with symptomatology common across these conditions (e.g., anhedonia). Dissecting various subcomponents of reward processing that map onto partially different neurobiological pathways and investigating their dysregulation in different psychiatric

disorders holds promise for developing more targeted, and hopefully efficacious treatment and intervention strategies.

Fanous AH (2015) - **Can genomics help usher schizophrenia into the age of RDoC and DSM-6.** Schizophr Bull. 2015 May;41(3):535-41. [\[FULL TEXT\]](#)

Ford JM, et al (2014) - **Studying hallucinations within the NIMH RDoC framework.** Schizophr Bull. 2014 Jul;40 Suppl 4:S295-304. [\[FULL TEXT\]](#)

Reaction Time Variability ▲

Karalunas SL, et al (2014) - **Annual research review: Reaction time variability in ADHD and autism spectrum disorders: measurement and mechanisms of a proposed trans-diagnostic phenotype.** J Child Psychol Psychiatry. 2014 Jun;55(6):685-710. [\[FULL TEXT\]](#)

Repetitive Negative Thinking / Rumination / Intrusion ▲

Hijne K, et al (2020) - **The association of changes in repetitive negative thinking with changes in depression and anxiety.** J Affect Disord. 2020 Oct 1;275:157-164. [\[ABS\]](#)

Repetitive negative thinking (RNT) is a common feature of different mental disorders in the affective spectrum. Most measures of RNT are disorder-specific and measure e.g. rumination in depression or worry in anxiety. ...The findings suggest that RNT is not primarily an index of disorder status or epiphenomenon of symptom severity and may constitute a relatively stable transdiagnostic person characteristic.

Stone LB, et al (2020) - **The autonomic correlates of dysphoric rumination and post-rumination savoring.** Physiol Behav. 2020 Oct 1;224:113027. [\[FULL TEXT\]](#)

Trait dysphoric rumination is a transdiagnostic factor associated with depression and anxiety that has also been linked with blunted respiratory sinus arrhythmia (RSA), an index of reduced emotion regulation capacity... In summary, dysphoric rumination co-occurred with sympathetic activation, and subsequent savoring successfully recruited sympathetic activity (PEP) redirected on positive moods and events. Results also emphasize the utility of examining sympathetic and parasympathetic indices, and coordination among autonomic indices to delineate autonomic activity associated with emotion regulation strategies.

Bredemeier K, et al (2020) - **Pretreatment levels of rumination predict cognitive-behavioral**

therapy outcomes in a transdiagnostic sample of adults with anxiety-related disorders. J Anxiety Disord. 2020 Jul 30;75:102277. [\[ABS\]](#)

Increasing research has implicated rumination in the development and maintenance of many types of psychopathology, including anxiety-related disorders. ...Results revealed that pretreatment levels of rumination significantly predicted (lower) quality of life at the end of treatment, after accounting for baseline variance in quality of life. This finding remained robust when also accounting for demographics, depression, general anxiety, and diagnosis.

Hamonniere T, et al (2020) - Toward a better understanding of the influence of repetitive negative thinking in alcohol use disorder: An examination of moderation effect of metacognitive beliefs and gender. Addict Behav. 2020 Jul 21;111:106561. [\[ABS\]](#)

Repetitive negative thinking (RNT), the most studied forms of which are depressive ruminations and anxious worry, is a unique transdiagnostic process responsible for the development and maintenance of many mental disorders. ... Results indicated that the 'capture mental resources' factor of RNT is a significant predictor of alcohol use disorder (AUD) severity, independent from anxiety and depression, and that this effect is moderated by metacognitive beliefs and gender. RNT is a significant predictor of AUD severity only for people with high negative beliefs about thoughts regarding uncontrollability and danger. ... Treatments that reduce attentional impairments caused by RNT and modify dysfunctional metacognitive beliefs could be promising for some patients with AUD.

Stamatis CA, et al (2020) - Repetitive negative thinking following exposure to a natural stressor prospectively predicts altered stress responding and decision-making in the laboratory. Behav Res Ther. 2020 Jun;129:103609. [\[ABS\]](#)

Repetitive negative thinking (RNT) represents a transdiagnostic risk factor for affective disorders, and stress is theorized to exacerbate this vulnerability. ... Post-hurricane RNT predicted greater increases in loss averse decision-making and negative affect during the early-phase response to the laboratory stressor, as well as poorer cortisol recovery in the late-phase stress response. Results highlight the role of loss aversion and stress in understanding RNT as an affective vulnerability factor.

Huang I, et al (2020) - The roles of repetitive negative thinking and perfectionism in explaining the relationship between sleep onset difficulties and depressed mood in adolescents. Sleep Health. 2020 Apr;6(2):166-171. [\[ABS\]](#)

These findings highlight that repetitive negative thinking is significantly associated with both difficulty initiating sleep and depressed mood, supporting the conceptualization of repetitive negative thinking as a transdiagnostic process. Further, individual differences in perfectionism may amplify the relationship between repetitive negative thinking and

mood. The role of repetitive negative thinking and perfectionism in explaining the link between sleep onset problems and depressed mood has important clinical implications through providing possible treatment targets.

Watkins ER, et al (2020) - **Reflecting on rumination: Consequences, causes, mechanisms and treatment of rumination.** Behav Res Ther. 2020 Apr;127:103573. [\[ABS\]](#)

We review research showing that rumination has multiple negative consequences: (a) exacerbating psychopathology by magnifying and prolonging negative mood states, interfering with problem-solving and instrumental behaviour and reducing sensitivity to changing contingencies; (b) acting as a transdiagnostic mental health vulnerability impacting anxiety, depression, psychosis, insomnia, and impulsive behaviours; (c) interfering with therapy and limiting the efficacy of psychological interventions; (d) exacerbating and maintaining physiological stress responses.

Silveira ÉM Júnior, et al (2020) - **Decoding rumination: A machine learning approach to a transdiagnostic sample of outpatients with anxiety, mood and psychotic disorders.** J Psychiatr Res. 2020 Feb;121:207-213. [\[ABS\]](#)

Rumination is known to be associated with poor prognosis in mental health. This study suggests that rumination is a maladaptive coping style associated not only with worry, distress and illness severity, but also with socioeconomic status. Also, rumination demonstrated a specific association with panic disorder.

Makovac E, et al (2020) - **Can't get it off my brain: Meta-analysis of neuroimaging studies on perseverative cognition.** Psychiatry Res Neuroimaging. 2020 Jan 30;295:111020. [\[ABS\]](#)

Perseverative cognition (i.e. rumination and worry) describes intrusive, uncontrollable, repetitive thoughts. These negative affective experiences are accompanied by physiological arousal, as if the individual were facing an external stressor. Perseverative cognition is a transdiagnostic symptom... Perseverative cognition is accompanied by the engagement of prefrontal, insula and cingulate regions, whose interaction may support the characteristic conjunction of self-referential and affective processing with (aberrant) cognitive control and embodied (autonomic) arousal. Within this context, ACC engagement appears critical for the pathological expression of rumination and worry.

Smith KE, et al (2020) - **The ecological validity of trait-level rumination measures among women with binge eating symptoms.** Eat Weight Disord. 2020 Jan 1;10.1007/s40519-019-00838-x. [\[FULL TEXT\]](#)

Magson NR, et al (2019) - **Measuring repetitive negative thinking: Development and validation of the Persistent and Intrusive Negative Thoughts Scale (PINTS).** Psychol Assess. 2019 Nov;31(11):1329-1339. [\[ABS\]](#)

It was concluded that the Persistent and Intrusive Negative Thoughts Scale (PINTS) is a brief, valid, and useful tool for investigating repetitive negative thinking as a **transdiagnostic** process in the etiology and maintenance of psychological disorders in both children and adults

Peters AT, et al (2019) - **The roles of early-life adversity and rumination in neural response to emotional faces amongst anxious and depressed adults.** Psychol Med. 2019 Oct;49(13):2267-2278. [[FULL TEXT](#)]

Early-life adversity (ELA) is a risk factor for internalizing psychopathology (IP). ELA is also linked to alterations in neural phenotypes of emotion processing and maladaptive emotion regulatory strategies, such as ruminative brooding, in adulthood. We therefore expected that ELA would predict cortical brain activation to emotional faces in **transdiagnostic** IP and in turn, mediate the extent of rumination amongst patients with IPs and ELA (IP + ELA).

IP + ELA demonstrated increased activation in the superior frontal gyrus and anterior cingulate cortex (fear), superior parietal lobule, precuneus, posterior cingulate, and inferior temporal gyrus (fear only), and cuneus (fear and angry). These regions were preferentially correlated with ruminative brooding in IP + ELA, many of which mediated the link between IP + ELA and ruminative brooding. ...alterations in the neural correlates of maladaptive processing of socio-emotional information may be a common pathway by which ELA poses risk for psychopathology.

Snyder HR, et al (2019) - **Transdiagnostic mechanisms of psychopathology in youth: Executive functions, dependent stress, and rumination.** Cognit Ther Res. 2019 Oct;43(5):834-851. [[FULL TEXT](#)]

Executive function (EF) deficits have been proposed as transdiagnostic risk factors for psychopathology, and recent research suggests EF impairments are associated with what is shared across forms of psychopathology (p factor).

Memedovic S, et al (2019) - **Rumination and problematic substance use among individuals with a long-term history of illicit drug use.** Drug Alcohol Depend. 2019 Oct 1;203:44-50. [[ABS](#)]

Findings indicate that ruminative brooding is related to a poorer substance use profile among people with long-term illicit drug use and highlight the potential benefits of targeting brooding during substance use treatment.

Wahl K, et al (2019) - **Is repetitive negative thinking a transdiagnostic process? A comparison of key processes of RNT in depression, generalized anxiety disorder, obsessive-compulsive disorder, and community controls.** J Behav Ther Exp Psychiatry. 2019 Sep;64:45-53. [[ABS](#)]

The purpose of the study was to test whether the processes of repetitive negative thinking (RNT) differ across major depression disorder (MDD), generalized anxiety disorder (GAD), and obsessive-compulsive disorder (OCD). ... Data support the **transdiagnostic** hypothesis of RNT. **Transdiagnostic** prevention and intervention techniques seem highly recommendable given these findings.

Lydon-Staley DM, et al (2019) - **Repetitive negative thinking in daily life and functional connectivity among default mode, fronto-parietal, and salience networks**. Transl Psychiatry. 2019 Sep 18;9(1):234. [\[FULL TEXT\]](#)

Repetitive negative thinking (RNT) is a maladaptive response to sadness and a **transdiagnostic** risk-factor. ...We show that RNT increases following sadness for participants with higher than average between-network connectivity of the default mode network and the fronto-parietal network. We also show that RNT increases following increases in sadness for participants with lower than average between-network connectivity of the fronto-parietal network and the salience network. We also find that flexibility of the salience network's pattern of connections with brain regions is protective against increases in RNT following sadness. Our findings highlight the importance of functional brain networks implicated in cognitive conflict signaling, self-referential thought, and cognitive flexibility for understanding maladaptive responses to sadness in daily life and provide support for the impaired disengagement hypothesis of RNT.

du Pont A, et al (2019) - **Rumination and executive functions: Understanding cognitive vulnerability for psychopathology**. J Affect Disord. 2019 Sep 1;256:550-559. [\[FULL TEXT\]](#)

INTRODUCTION: Both rumination, a pattern of repetitive, self-focused thought in response to distress, and deficits in executive functions (EFs), a set of cognitive abilities that facilitate higher-order thinking, have **transdiagnostic** associations with psychopathology. ...Common EF abilities and rumination are correlated yet largely independent constructs that both predict psychopathology.

Heckendorff H, et al (2019) - **Efficacy of an internet and app-based gratitude intervention in reducing repetitive negative thinking and mechanisms of change in the intervention's effect on anxiety and depression: Results from a randomized controlled trial**. Behav Res Ther. 2019 Aug;119:103415. [\[ABS\]](#)

Repetitive negative thinking (RNT) has been identified as a **transdiagnostic** process that is involved in various forms of psychopathology, including anxiety and depression. This randomized controlled trial compared a 5-week internet and app-based gratitude intervention (intervention group; IG) with adherence-focused guidance against a wait list control group (WLG) in reducing RNT in a sample with elevated RNT. ... The gratitude intervention investigated in this study was found to be effective in reducing RNT. Gratitude interventions might affect mental health by two parallel pathways: increasing resources and reducing risk factors.

Gavazzeni JA, et al (2019) - **Psychometric Properties of the Swedish Version of the Brief Repetitive Thinking Questionnaire (RTQ-10): An Internet-Based Study on Degrees of Affective Symptoms and Levels of Distress.** Psychopathology. 2019;52(4):256-264. [\[ABS\]](#)

INTRODUCTION: Repetitive negative thinking (RNT) is reported in a wide variety of emotional disorders, although it is most often associated with either depression or anxiety disorders, assessed as symptoms of rumination and worry. Early detection of indicators for RNT across disorders is needed. To this end we explored the psychometric properties of a **transdiagnostic** measure, i.e., the Swedish version of the brief Repetitive Thinking Questionnaire ... These results provide additional psychometric support for the RTQ-10 as a **transdiagnostic** measure. It can be administered online to assess RNT as a risk factor for emotional disorders.

du Pont A, et al (2019) - **Are rumination and neuroticism genetically or environmentally distinct risk factors for psychopathology?** J Abnorm Psychol. 2019 Jul;128(5):385-396. [\[FULL TEXT\]](#)

These findings suggest that rumination and neuroticism share most genetic influences yet are influenced by distinct environmental influences. Furthermore, our results indicate that a comprehensive understanding of **transdiagnostic** risk factors must include an examination of both genetic and environmental influences.

Devynck F, et al (2019) - **Does Repetitive Negative Thinking Influence Alcohol Use? A Systematic Review of the Literature.** Front Psychol. 2019 Jul 3;10:1482. [\[FULL TEXT\]](#)

... a strong positive association between RNT and alcohol use or alcohol-related problems, regardless of the form of RNT. The results were more heterogeneous in the 17 studies conducted among adolescents and students, leading the authors to conclude that the results varied as a function of the severity of alcohol use. The results of this study suggest to focus on RNT from a **transdiagnostic** perspective in AUD. This processual approach may improve AUD treatment and relapse prevention.

Kornacka M, et al (2019) - **Concrete vs. Abstract Processing in Repetitive Negative Thinking: Distinct Functional Effects on Emotional Reactivity and Attentional Control.** Front Psychol. 2019 Jun 18;10:1372. [\[FULL TEXT\]](#)

Repetitive negative thinking (RNT) is a **transdiagnostic** process linked to emotional regulation impairment and involved in mood, anxiety, eating disorders and addictions. Attentional disengagement impairment is one of the factors hypothesized to be responsible for the recurrent and uncontrollable character of RNT.

... The analysis revealed that participants in abstract RNT condition presented higher emotional reactivity comparing to concrete or distraction conditions. The results indi-

cated no differences between induction conditions in attentional disengagement. However, participants after concrete RNT induction had longer mean response times in exogenous cueing task comparing to control induction suggesting that they detected presented stimuli slower than participants in control condition. The results raised an important, from clinical point of view, question of distinctive impact of two types of RNT on emotional reactivity and attentional processes.

Arditte Hall KA, et al (2019) - **Comparing cognitive styles in social anxiety and major depressive disorders: An examination of rumination, worry, and reappraisal.** Br J Clin Psychol. 2019 Jun;58(2):231-244. [[FULL TEXT](#)]

Social anxiety disorder (SAD) and major depressive disorder (MDD) are commonly occurring and frequently comorbid disorders. ...Individuals with SAD or MDD report more rumination and worry than healthy controls, but do not differ from each other in their reliance on these cognitive styles. Individuals with comorbid SAD/MDD endorse more rumination than individuals with SAD or MDD alone, even after adjusting for differences in symptom severity. ...high reappraisal may be associated with reduced risk of psychiatric disorder, but only when rumination and worry are also high.

Eszlari N, et al (2019) - **Childhood Adversity Moderates the Effects of HTR2A Epigenetic Regulatory Polymorphisms on Rumination.** Front Psychiatry. 2019 Jun 14;10:394. [[FULL TEXT](#)]

These findings indicate the crucial importance of involving stress factors when considering endophenotypes and suggest that brooding is a more promising endophenotype than a broader measure of rumination. **Transdiagnostic** relevance of the brooding endophenotype and the potential of targeting epigenetic regulatory polymorphisms of HTR2A in primary and secondary prevention of depression and possibly of other disorders are also discussed.

Pascual-Vera B, et al (2019) - **The cross-cultural and transdiagnostic nature of unwanted mental intrusions.** Int J Clin Health Psychol. 2019 May;19(2):85-96. [[FULL TEXT](#)]

Unwanted mental intrusions (UMIs), typically discussed in relation to Obsessive-Compulsive Disorder (OCD), are highly prevalent, regardless of the specific nationality, religion, and/or cultural context. Studies have also shown that UMIs related to Body Dysmorphic Disorder (BDD), Illness anxiety/Hypochondriasis (IA-H), and Eating Disorders (EDs) are commonly experienced. ...Overall, 64% of the total sample reported having experienced the four UMIs. The EDs intrusions were the most frequently experienced, whereas hypochondriacal intrusions were the least frequent but the most disturbing. All the UMIs were significantly related to each other in frequency and disturbance, and all of them were associated with clinical measures of OCD, BDD, IA-H, and EDs. **CONCLUSIONS:** UMIs are a common phenomenon across different cultural contexts and operate **transdiagnostically** across clinically different disorders.

Eszlari N, et al (2019) - **Genome-wide association analysis reveals KCTD12 and miR-383-binding genes in the background of rumination.** Transl Psychiatry. 2019 Mar 18;9(1):119. [[FULL TEXT](#)]

Results of the first genome-wide association study on rumination identified genes previously implicated in psychiatric disorders underscoring the **transdiagnostic** nature of rumination, and pointed to the possible role of the dorsolateral prefrontal cortex, hippocampus, and cerebellum in this cognitive process.

Weissman DG, et al (2019) - **Difficulties with emotion regulation as a transdiagnostic mechanism linking child maltreatment with the emergence of psychopathology.** Dev Psychopathol. 2019 Aug;31(3):899-915. [[FULL TEXT](#)]

Greater emotional reactivity and engagement in rumination mediated the longitudinal association between maltreatment and increased general psychopathology over time. Emotion dysregulation following childhood maltreatment occurs at multiple stages of the emotion generation process, in some cases varies across development, and serves as a **transdiagnostic** mechanism linking child maltreatment with general psychopathology.

McEvoy PM, et al (2019) - **Repetitive Negative Thinking as a Transdiagnostic Predictor of Depression and Anxiety Symptoms in Adolescents.** Assessment. 2019 Mar;26(2):324-335. [[ABS](#)]

Repetitive negative thinking (RNT) is a transdiagnostic process associated with numerous emotional disorders. Most measures of RNT are disorder-specific, limiting utility in comorbid populations. Transdiagnostic measures of RNT have been developed in adults and are associated with anxiety and depression. However, a transdiagnostic measure is needed to assess RNT in adolescents as a potential vulnerability factor for emotional disorders. This study validates a transdiagnostic measure of RNT-Repetitive Thinking Questionnaire-10 (RTQ-10)-in adolescents (N = 840, Mage = 15.7 years). Exploratory and confirmatory factor analyses supported a unidimensional structure. The RTQ-10 manifested good internal consistency and measurement invariance across genders and age. RNT was equally associated with anxiety and depression symptoms irrespective of gender or age. Convergent validity was demonstrated by correlations with disorder-specific measures of RNT. These findings support the RTQ-10 as a reliable and valid transdiagnostic measure of RNT in adolescents.

Luca M (2019) - **Maladaptive Rumination as a Transdiagnostic Mediator of Vulnerability and Outcome in Psychopathology.** J Clin Med. 2019 Mar 5;8(3):314. [[FULL TEXT](#)]

Mazzer K, et al (2019) - **A longitudinal view of rumination, poor sleep and psychological distress in adolescents.** J Affect Disord. 2019 Feb 15;245:686-696. [[ABS](#)]

BACKGROUND: Given the high prevalence and negative impact of psychological problems during adolescence, examining **transdiagnostic** factors that may have scope to positively influence a variety of psychological problems is imperative. ... Reducing rumination, rather than targeting sleep patterns, may work towards preventing the development of a number of psychological problems and is a strategy anticipated to function across disorders to improve young people's mental wellbeing.

Sala M, et al (2019) - **Repetitive negative thinking predicts eating disorder behaviors: A pilot ecological momentary assessment study in a treatment seeking eating disorder sample.** Behav Res Ther. 2019 Jan;112:12-17. [[ABS](#)]

There are short-term and long-term negative effects of repetitive negative thinking in the eating disorders. Targeting repetitive negative thinking may be important for decreasing eating disorder behaviors.

Gustavson DE, et al (2018) - **Evidence for Transdiagnostic Repetitive Negative Thinking and Its Association with Rumination, Worry, and Depression and Anxiety Symptoms: A Commonality Analysis.** Collabra Psychol. 2018;4(1):13. [[FULL TEXT](#)]

... repetitive negative thinking may indeed lie at the core of the comorbidity between depression and anxiety symptoms, but that it is also a broader construct that encompasses intrusive thoughts and low levels of mindfulness.

Pascual-Vera B, et al (2017) - **Are unwanted mental intrusions a transdiagnostic variable?** Psicothema. 2017 May;29(2):166-171. [[ABS](#)]

Samtani S, et al (2017) - **Assessing maladaptive repetitive thought in clinical disorders: A critical review of existing measures.** Clin Psychol Rev. 2017 Apr;53:14-28. [[ABS](#)]

Klemanski DH, et al (2017) - **Emotion Regulation and the Transdiagnostic Role of Repetitive Negative Thinking in Adolescents with Social Anxiety and Depression.** Cognit Ther Res. 2017 Apr;41(2):206-219. [[FULL TEXT](#)]

Results indicated that adolescents with high levels of social anxiety and depression symptoms reported decreased emotional awareness, dysregulated emotion expression, and reduced use of emotion management strategies. The hypothesized structural model in which RNT functions as a transdiagnostic factor exhibited a better fit than an alternative model in which worry and rumination function as separate predictors of symptomatology. Findings implicate emotion regulation deficits and RNT in the developmental psychopathology of youth anxiety and mood disorders.

Devynck F, et al (2017) - **Repetitive Thinking in Alcohol-Dependent Patients.** Subst Use Misuse. 2017 Jan 2;52(1):108-118. [[ABS](#)]

Snyder HR, et al (2016) - **Spiraling out of control: Stress generation and subsequent rumination mediate the link between poorer cognitive control and internalizing psychopathology.** Clin Psychol Sci. 2016 Nov;4(6):1047-1064. [\[ABS\]](#)

Poor cognitive control is associated with nearly every mental disorder and has been proposed as a transdiagnostic risk factor for psychopathology, including depression and anxiety. What specific mechanisms might cause individuals with poor cognitive control to experience higher levels of psychopathology? The current research tests a new process model linking poor cognitive control to depression and anxiety symptoms via increased dependent stress (i.e., self-generated stressors) and subsequent rumination. This model was supported across two studies in youth during the key period for emergence of internalizing psychopathology. Study 1 provides longitudinal evidence for prospective prediction of change in symptoms. Study 2 confirms this model using well-established executive function tasks in a cross-sectional study. These findings have potential implications for understanding why cognitive control impairments may be broadly associated with psychopathology, and suggest that interventions to prevent stress generation might be effective in preventing negative consequences of poor cognitive control.

Grierson AB, et al (2016) - **The role of rumination in illness trajectories in youth: linking trans-diagnostic processes with clinical staging models.** Psychol Med. 2016 Sep;46(12):2467-84. [\[FULL TEXT\]](#)

In summary, the normative developmental trajectory of rumination and its role in the evolution of mental disorders and physical illness demonstrates that rumination presents a detectable, modifiable trans-diagnostic risk factor in youth.

Jenness JL, et al (2016) - **Catastrophizing, rumination, and reappraisal prospectively predict adolescent PTSD symptom onset following a terrorist attack.** Depress Anxiety. 2016 Aug 24. [\[ABS\]](#)

RESULTS: Greater pretrauma engagement in rumination predicted onset of PTSD symptoms following the attack. Adolescents who engaged in catastrophizing also had greater PTSD symptoms postattack, but only when exposed to high levels of media coverage of the attacks; the same pattern was observed for adolescents who engaged in low levels of cognitive reappraisal.

CONCLUSIONS: Engagement in specific emotion regulation strategies prior to a traumatic event predicts the onset of PTSD symptoms among youths exposed to trauma, extending transdiagnostic models of emotion regulation to encompass trauma-related psychopathology in children and adolescents.

Merino H, et al (2016) - **Are Worry and Rumination Specific Pathways Linking Neuroticism and Symptoms of Anxiety and Depression in Patients with Generalized Anxiety Disorder, Major**

Depressive Disorder and Mixed Anxiety-Depressive Disorder? PLoS One. 2016 May 31;11(5):e0156169. [\[FULL TEXT\]](#)

Overall, our findings suggest that neuroticism may increase the risk of anxious and depressive symptoms via specific links involving either worry or brooding, respectively, and that both worry and brooding may operate in the three groups examined, irrespectively of whether anxiety or depression are the main emotions or whether they coexist without any clear predominance; consequently, we hypothesize the existence of "specific transdiagnostic" mechanisms.

Hilt LM, et al (2016) - **Can't Take My Eyes Off of You: Eye Tracking Reveals How Ruminating Young Adolescents Get Stuck.** J Clin Child Adolesc Psychol. 2016 Feb 24:1-10. [\[ABS\]](#)

These findings suggest that rumination is associated with increased attention to emotional information during the later stages of selective attention rather than earlier orienting to emotional cues. Implications for prevention and treatment of psychopathology are discussed.

Siegle GH, et al (2015) - **Prolonged physiological reactivity and loss: Association of pupillary reactivity with negative thinking and feelings.** Int J Psychophysiol. 2015 Nov;98(2 Pt 2):310-320. [\[FULL TEXT\]](#)

Hill LM, et al (2015) - **Rumination and Moderators of Multifinality: Predicting Internalizing Symptoms and Alcohol Use During Adolescence.** J Clin Child Adolesc Psychol. 2015 Oct 29:1-8. [\[FULL TEXT\]](#)

Akbari M, et al (2015) - **Transdiagnostic Treatment of Co-occurrence of Anxiety and Depressive Disorders based on Repetitive Negative Thinking - A Case Series.** Iran J Psychiatry. 2015 Jun;10(3):200-11. [\[FULL TEXT\]](#)

"... Barlow et al made a considerable improvement in designing theoretical-practical transdiagnostic protocols through several studies with emphasis on the **role of 'emotion regulation' as the main cognitive-behavioral mechanism in emotional disorders.**"

"Recent studies have shown that **repetitive negative thinking is the most important common cognitive behavioral process in formation and continuation of emotional disorders. Repetitive negative thinking includes** worry, rumination, treatment monitoring, obsessions and any other kind of repetitive negative thoughts which is the core of depression and anxiety disorders. Surveying more than 50 studies in cognitive pathology of emotional disorders shows that repetitive negative thinking is the main transdiagnostic factor in more than 13 diagnostic classes, including depression disorders, anxiety disorders, sleep disorder, eating disorder, substance abuse disorder and schizophrenic disorder (17-32)."

"Transdiagnostic treatments targeting core "higher-order" factors offer a more parsimonious approach to treatment planning that eliminates the need for multiple diagnosis-specific manuals".

McLaughlin KA, et al (2014) - **Rumination as a transdiagnostic factor underlying transitions between internalizing symptoms and aggressive behavior in early adolescents.** J Abnorm Psychol. 2014 Feb; 123(1). [\[FULL TEXT\]](#)

Woody ML, et al (2014) - **Brooding rumination and heart rate variability in women at high and low risk for depression: group differences and moderation by COMT genotype.** J Abnorm Psychol. 2014 Feb;123(1):61-7. [\[FULL TEXT\]](#)

We predicted that COMT Val158Met genotype, which has been linked to heightened amygdala reactivity and deficits in prefrontal functioning, would be associated with HRV and brooding rumination, particularly among women with a history of MDD.

McEvoy PM, et al (2013) - **The relationship between worry, rumination, and comorbidity: evidence for repetitive negative thinking as a transdiagnostic construct.** J Affect Disord. 2013 Oct;151(1):313-20. [\[ABS\]](#)

"Consistent with the transdiagnostic hypothesis, RNT was associated with a range of anxiety disorders and depression and with comorbidity for those with a principal depressive disorder, supporting recent evidence that RNT is a transdiagnostic process. The presence of RNT, specifically worry and rumination, should be assessed and treated regardless of diagnostic profile. Future research may show that both pure and comorbid depressed or anxious patients receive incremental benefit from transdiagnostic protocols developed to treat core pathological processes of RNT traditionally associated with separate disorders."

Mennin DS, et al (2013) - **What, Me Worry and Ruminate About DSM-5 and RDoC? The Importance of Targeting Negative Self-Referential Processing.** Clin Psychol (New York). 2013 Sep;20(3):258-267. [\[FULL TEXT\]](#)

Schanche E (2013) - **The transdiagnostic phenomenon of self-criticism.** Psychotherapy (Chic). 2013 Sep;50(3):316-21. [\[ABS\]](#)

In the past 20 years, research has established excessive self-criticism as a transdiagnostic phenomenon that plays a role in the development and maintenance of a range of psychological disorders (Gilbert & Irons, 2005). Several therapeutic approaches have consequently developed interventions targeted at helping patients cultivate a more compassionate and caretaking stance toward themselves (Gilbert & Irons, 2005; McCullough Vaillant, 1997). Various definitions of compassion all involve the qualities of kindness, gentleness, and warmth (Gilbert, McEwan, Matos, & Ravis, 2011). A more compassionate orientation toward oneself is believed to regulate difficult emotions and

reduce negative rumination and such contribute to a lessening of symptoms, interpersonal problems, and social isolation (see Gilbert et al., 2011). Empirical findings indicate that individuals who are more self-compassionate tend to have more social connectedness and less anxiety, depression, shame, fear of failure, and burnout (Barnard & Curry, 2011).

McLaughlin KA, et al (2011) - **Rumination as a transdiagnostic factor in depression and anxiety.** Behav Res Ther. 2011 Mar;49(3):186-93. [\[FULL TEXT\]](#)

These findings highlight the importance of targeting rumination in transdiagnostic treatment approaches for emotional disorders.

Sickness Behavior ▲

Andreasson A, et al (2016) - **A global measure of sickness behaviour: Development of the Sickness Questionnaire.** J Health Psychol. 2016 Jul 24. pii. [\[ABS\]](#)

Symptoms after inflammatory activation, so-called sickness behaviour, overlap with trans-diagnostic complaints.

Sleep / Insomnia ▲

Arns M, et al (2021) - Review - **Identification and Management of Circadian Rhythm Sleep Disorders as a Transdiagnostic Feature in Child and Adolescent Psychiatry.** J Am Acad Child Adolesc Psychiatry 2021 Feb 5;S0890-8567(21)00059-9. [\[FULL TEXT\]](#)

Careful clinical attention to and management of CRDs in child and adolescent psychiatry have the potential for significant benefit not only in the domain of sleep but also in a range of cognitive, affective, and behavioral outcomes.

Scholes S, et al (2020) - **Modulation of Slow-Wave Sleep: Implications for Psychiatry.** Curr Psychiatry Rep. 2020 Jul 24;22(10):52. [\[ABS\]](#)

Our review reveals partial support to the potential efficacy of SWS modulation as a transdiagnostic intervention that uses sleep to improve cognitive functions of individuals diagnosed with psychiatric disorders and cognitive deficits

McLean CP (2020) - **Introduction to the Special Issue: The Impact and Treatment of Sleep Disturbance.** Behav Ther. 2020 Jul;51(4):519-521. [\[ABS\]](#)

There is now widespread recognition that sleep disturbance is more than an epiphenomenon of psychopathology. ...Sleep disturbance overlaps and interacts with comorbid psychological disorders through a complex transdiagnostic process that impacts the development, maintenance, and treatment of psychological disorders.

Dong L, et al (2020) - **A transdiagnostic sleep and circadian intervention for adolescents: six-month follow-up of a randomized controlled trial.** J Child Psychol Psychiatry. 2020 Jun;61(6):653-661. [[FULL TEXT](#)]

BACKGROUND: This study examined the 6-month follow-up outcomes of the Transdiagnostic Sleep and Circadian Intervention (TranS-C), compared to Psychoeducation about sleep and health (PE). ... In at-risk adolescents, the evidence supports the TranS-C treatment effects over six months on improving sleep and circadian functioning on selected outcomes but not on reducing risk in five health domains.

Blanchard JJ, et al (2020) - **Sleep Problems and Social Impairment in Psychosis: A Transdiagnostic Study Examining Multiple Social Domains.** Front Psychiatry. 2020 May 28;11:486. [[FULL TEXT](#)]

Psychotic disorders are characterized by profound social impairment. An accumulation of research has explored the contribution of symptoms, cognitive functioning, and behavioral skills deficits to this social dysfunction. Recent research indicates that sleep disturbance has significant social implications in nonclinical populations - this research suggests that sleep problems may also be relevant to understanding social impairment in psychosis.

We hypothesized that greater sleep disturbance and sleep-related impairment would be associated with more negative or problematic perceptions of social relationships (i.e., less social support, less companionship, and greater distress), poorer social functioning in the community, smaller social networks, and poorer behavioral ratings of social competency. Results supported these hypotheses indicating that sleep disturbance and sleep-related impairment have widespread deleterious impacts on perceptions of social relationships, social functioning, and competence

Huang I, et al (2020) - **The roles of repetitive negative thinking and perfectionism in explaining the relationship between sleep onset difficulties and depressed mood in adolescents.** Sleep Health. 2020 Apr;6(2):166-171. [[ABS](#)]

These findings highlight that repetitive negative thinking is significantly associated with both difficulty initiating sleep and depressed mood, supporting the conceptualization of repetitive negative thinking as a transdiagnostic process. Further, individual differences in perfectionism may amplify the relationship between repetitive negative thinking and mood. The role of repetitive negative thinking and perfectionism in explaining the link

between sleep onset problems and depressed mood has important clinical implications through providing possible treatment targets.

Kearns JC, et al (2020) - **Sleep problems and suicide risk in youth: A systematic review, developmental framework, and implications for hospital treatment.** Gen Hosp Psychiatry. 2020 Mar-Apr;63:141-151. [[ABS](#)]

OBJECTIVE: Sleep problems are *transdiagnostic* symptoms that confer significant risk for suicidal thoughts and behaviors (STBs) in adults. ... Sleep problems may be particularly important intervention target because they are easily assessed across healthcare settings and are amenable to treatment.

Meyer N, et al (2020) - **Sleep and Circadian Rhythm Disturbance in Remitted Schizophrenia and Bipolar Disorder: A Systematic Review and Meta-analysis.** Schizophr Bull. 2020 Mar 10:sbaa024. [[ABS](#)]

In both disorders, longer overall sleep duration, but also disturbed initiation, continuity, and reduced motor activity were found. Common, modifiable factors may be associated with these sleep-circadian phenotypes and advocate for further development of transdiagnostic interventions that target them.

Obeysekare JL, et al (2020) - **Delayed sleep timing and circadian rhythms in pregnancy and transdiagnostic symptoms associated with postpartum depression.** Transl Psychiatry. 2020 Jan 21;10(1):14. [[FULL TEXT](#)]

Later sleep timing, circadian preference, and circadian rhythm timing predict worse outcomes across multiple domains, including mood disorders, substance use, impulse control, and cognitive function. Delayed sleep timing in this sample of at-risk women was associated with more symptoms of mania, depression, and OCD in the postpartum period. Sleep timing may be a modifiable risk factor for postpartum depression.

Kasanova Z, et al (2020) - **Temporal associations between sleep quality and paranoia across the paranoia continuum: An experience sampling study.** J Abnorm Psychol. 2020 Jan;129(1):122-130. [[ABS](#)]

Sleep disturbances are prevalent among individuals with a psychotic disorder and have been linked to symptoms of paranoia across the entire psychosis continuum. Emerging evidence suggests that rather than a secondary symptom, poor quality of sleep may contribute to elevated paranoid ideation. ... In the everyday lives of individuals on the paranoia continuum, low quality of sleep appears to drive paranoia through its impact on negative affect. These findings identify sleep quality as an important target of transdiagnostic interventions for psychotic and affective symptomatology.

Riemann D, et al (2020) - **Sleep, insomnia, and depression.** Neuropsychopharmacology. 2020 Jan;45(1):74-89. [[FULL TEXT](#)]

Since ancient times it is known that melancholia and sleep disturbances co-occur. The introduction of polysomnography into psychiatric research confirmed a disturbance of sleep continuity in patients with depression, revealing not only a decrease in Slow Wave Sleep, but also a disinhibition of REM (rapid eye movement) sleep, demonstrated as a shortening of REM latency, an increase of REM density, as well as total REM sleep time. Initial hopes that these abnormalities of REM sleep may serve as differential-diagnostic markers for subtypes of depression were not fulfilled. Almost all antidepressant agents suppress REM sleep and a time-and-dose-response relationship between total REM sleep suppression and therapeutic response to treatment seemed apparent. The so-called Cholinergic REM Induction Test revealed that REM sleep abnormalities can be mimicked by administration of cholinomimetic agents. Another important research avenue is the study of *chrono-medical timing* of sleep deprivation and light exposure for their positive effects on mood in depression. Present day research takes the view on insomnia, i.e., prolonged sleep latency, problems to maintain sleep, and early morning awakening, as a **transdiagnostic** symptom for many mental disorders, being most closely related to depression. Studying insomnia from different angles as a **transdiagnostic** phenotype has opened many new perspectives for research into mechanisms but also for clinical practice. Thus, the question is: can the early and adequate treatment of insomnia prevent depression? This article will link current understanding about sleep regulatory mechanisms with knowledge about changes in physiology due to depression.

Meers J, et al (2020) - **Sleep Spindle Density is Associated with Worry in Children with Generalized Anxiety Disorder and Healthy Controls.** J Affect Disord. 2020 Jan 1; 260: 418–425. [[FULL TEXT](#)]

Hamilton JL, et al (2020) - **Higher Rates of Sleep Disturbance among Offspring of Parents with Recurrent Depression Compared to Offspring of Nondepressed Parents.** J Pediatr Psychol. 2020 Jan 1;45(1):1-11. [[ABS](#)]

Youth who have a parent with recurrent depression are at high risk for mental health problems. ...Offspring of parents with depression exhibited more sleep disturbance (e.g., problematic nighttime behaviors and daytime sleepiness) than low-risk youth as reported by both parents and youth. For parent-reported sleep disturbance, there were also sex differences. High-risk girls had more sleep disturbance than high-risk boys or low-risk girls. Our findings highlight one potential transdiagnostic risk factor that may emerge among high-risk youth, and sex-specific differences in sleep disturbance, which have implications for prevention and intervention.

Gumport NB, et al (2019) - **Usefulness and Utilization of Treatment Elements from the Transdiagnostic Sleep and Circadian Intervention for Adolescents with an Evening Circadian Preference.** Behav Res Ther. 2019 Dec; 123: 103504. [[FULL TEXT](#)]

Soehner AM, et al (2019) - **Unstable wakefulness during resting-state fMRI and its associations with network connectivity and affective psychopathology in young adults.** J Affect Disord. 2019 Nov 1;258:125-132. [[FULL TEXT](#)]

Drifts between wakefulness and sleep are common during resting state functional MRI (rsfMRI). Among healthy adults, within-scanner sleep can impact functional connectivity of default mode (DMN), task-positive (TPN), and thalamo-cortical networks. Because dysfunctional arousal states (i.e., sleepiness, sleep disturbance) are common in affective disorders, individuals with affective psychopathology may be more prone to unstable wakefulness during rsfMRI, hampering the estimation of clinically meaningful functional connectivity biomarkers.

Dong L, et al (2019) - **Is improving sleep and circadian problems in adolescence a pathway to improved health? A mediation analysis.** J Consult Clin Psychol. 2019 Sep;87(9):757-771. [[FULL TEXT](#)]

OBJECTIVE: The present study tested whether improvements in sleep and circadian problems mediate the effect of a novel **transdiagnostic** sleep and circadian intervention (TranS-C) on improvements in 5 health domains (emotional, cognitive, behavioral, social, and physical) in community-residing, evening chronotype adolescents who were at risk for problems in these 5 health domains. ... TranS-C exerts effects on reducing risk in multiple mental and physical health domains through reducing sleep and circadian problems in evening chronotype adolescents.

López CM, et al (2019) - **Residual Insomnia and Nightmares Postintervention Symptom Reduction Among Veterans Receiving Treatment for Comorbid PTSD and Depressive Symptoms.** Behav Ther. 2019 Sep;50(5):910-923. [[ABS](#)]

Consistent with previous research, greater residual insomnia symptoms were predictive of smaller treatment gains. Findings illustrate the potential significance of insomnia during the course of **transdiagnostic** treatment (e.g., PTSD and depression), leading to several important clinical assessment and treatment implications.

Laskemoen JF, et al (2019) - **Sleep disturbances in schizophrenia spectrum and bipolar disorders - a transdiagnostic perspective.** Compr Psychiatry. 2019 May;91:6-12. [[ABS](#)]

Sleep disturbances, including insomnia, hypersomnia and delayed sleep phase, are frequent in SCZ and BD, and associated with more severe clinical symptomatology across diagnostic groups. This suggests that sleep disturbance is a clinically relevant transdiagnostic phenomenon.

McCallum SM, et al (2019) - **Associations of fatigue and sleep disturbance with nine common mental disorders.** J Psychosom Res. 2019 Aug;123:109727. [\[ABS\]](#)

Sleep disturbance and fatigue have independent associations with many mental disorders after correcting for comorbidity and known confounds. The disorders providing the greatest contribution to sleep disturbance and fatigue were GAD and MDD. Sleep disturbance and fatigue may be appropriate *transdiagnostic* targets for improving symptoms and global functioning for people with mental disorders.

Scott J, et al (2019) - **A pragmatic effectiveness randomized controlled trial of the duration of psychiatric hospitalization in a trans-diagnostic sample of patients with acute mental illness admitted to a ward with either blue-depleted evening lighting or normal lighting conditions.** Trials. 2019 Aug 1;20(1):472. [\[FULL TEXT\]](#)

There is increasing recognition of the need to stabilize sleep-wake cycles in individuals with major mental disorders. As such, clinicians and researchers advocate the use of interventions targeted at sleep and circadian dysrhythmias as an adjunct to the standard treatments offered for acute illness episodes of a broad range of diagnoses. To determine the trans-diagnostic generalizability of chronotherapy, we explore the benefits of admitting individuals with an acute illness episode to a psychiatric inpatient unit where changes in light exposure are integrated into the therapeutic environment.

Greeson JM, et al (2018) - **Mindfulness Meditation Targets Transdiagnostic Symptoms Implicated in Stress-Related Disorders: Understanding Relationships between Changes in Mindfulness, Sleep Quality, and Physical Symptoms.** Evid Based Complement Alternat Med. 2018; 2018: 4505191. [\[FULL TEXT\]](#)

Bijlenga D, Arns M, et al (2019) - **The role of the circadian system in the etiology and pathophysiology of ADHD: Time to redefine ADHD?** Atten Defic Hyperact Disord. 2019; 11: 5-19. [\[ABS\]](#)

“The treatment options discussed are focused on improvement of sleep quality, quantity, and phase-resetting, by means of improving sleep hygiene, chronotherapy, treatment of specific sleep disorders, and by strengthening certain neuronal networks involved in sleep, e.g., by sensorimotor rhythm neurofeedback. Ultimately, the main question is addressed: whether ADHD needs to be redefined. We propose a novel view on ADHD, where a part of the ADHD symptoms are the result of chronic sleep disorders, with most evidence for the delayed circadian rhythm as the underlying mechanism. This substantial subgroup should receive treatment of the sleep disorder in addition to ADHD symptom treatment.”

Britton PC, et al (2019) - **Insomnia and risk for suicidal behavior: A test of a mechanistic trans-diagnostic model in veterans.** J Affect Disord. 2019 Feb 15;245:412-418. [\[ABS\]](#)

In veterans, insomnia symptoms may be associated with increased PTSD and depressive symptoms, which may be associated with increased risk for suicidal behavior directly and indirectly through relationship disruptions.

Henderson SEM, et al (2019) - **Associations between social jetlag and mental health in young people: A systematic review.** Chronobiol Int. 2019; 36: 1316-1333. [\[ABS\]](#)

“Of interest is the impact of the natural shift in young people towards a more evening-type sleep pattern (chronotype), whilst social constraints encourage early waking to fit with school/work timings. This leads to a misalignment in sleep timing between weekdays and weekends, known as social jetlag, which may contribute to emerging mental health difficulties seen during this age group.”

Sheaves B, et al (2018) - **Adapted CBT to Stabilize Sleep on Psychiatric Wards: a Transdiagnostic Treatment Approach.** Behav Cogn Psychother. 2018 Nov; 46(6): 661–675. [\[FULL TEXT\]](#)

“Almost all patients admitted at acute crisis to a psychiatric ward experience clinically significant symptoms of insomnia. ...This therapy has proven popular with patients.”

Logan RW, et al (2017) - **Impact of sleep and circadian rhythms on addiction vulnerability in adolescents.** Biol Psychiatry. 2018 Jun 15;83(12):987-996. [\[FULL TEXT\]](#)

Drews HJ, et al (2018) - **Slow-wave sleep predicts long-term social functioning in severe mental illness.** PLoS One. 2018; 13(8): e0202198. [\[FULL TEXT\]](#)

Becker SP, et al (2018) - **Shortened sleep duration causes sleepiness, inattention, and oppositionality in adolescents with attention-deficit/hyperactivity disorder: Findings from a crossover sleep restriction/extension study.** J Am Acad Child Adolesc Psychiatry. 2018; 58: 433-442. [\[FULL TEXT\]](#)

Dolsen MR, et al (2017) - **Neurophysiological correlates of suicidal ideation in major depressive disorder: Hyperarousal during sleep.** J Affect Disord. 2017 Apr 1;212:160-166. [\[FULL TEXT\]](#)

Lunn RM, et al (2017) - **Health consequences of electric lighting practices in the modern world: A report on the National Toxicology Program’s workshop on shift work at night, artificial light at night, and circadian disruption.** Sci Total Environ. 2017; 607-608: 1073-1084. [\[FULL TEXT\]](#)

Future studies should more comprehensively characterize and measure the relevant light-related exposures and link these exposures to both time-independent biomarkers of circadian disruption and biomarkers of adverse health outcomes. This information should lead to improvements in human epidemiological and animal or in vitro models, more rigorous health hazard assessments, and intervention strategies to minimize the occurrence of adverse health outcomes due to these exposures.

Harvey AG, et al (2016) - **A transdiagnostic sleep and circadian treatment to improve severe mental illness outcomes in a community setting - study protocol for a randomized controlled trial.** Trials. 2016 Dec 20;17(1):606. [[FULL TEXT](#)]

Perlis ML, et al (2016) - **Suicide and sleep: Is it a bad thing to be awake when reason sleeps?** Sleep Med Rev. 2016 Oct;29:101-7. [[FULL TEXT](#)]

Baglioni C, et al (2016) - **Sleep and mental disorders: A meta-analysis of polysomnographic research.** Psychol Bull. 2016 Sep;142(9):969-990. [[FULL TEXT](#)]

Sleep continuity disturbances imply a transdiagnostic imbalance in the arousal system likely representing a basic dimension of mental health.

Palagini L, et al (2016) - **Transdiagnostic factors across fibromyalgia and mental disorders: sleep disturbances may play a key role. A clinical review.** Clin Exp Rheumatol. 2016 Mar-Apr;34(2 Suppl 96):S140-4. [[ABS](#)]

Harvey AG, et al (2016) - **A transdiagnostic sleep and circadian treatment to improve severe mental illness outcomes in a community setting: study protocol for a randomized controlled trial.** Trials. 2016; 17: 606. [[FULL TEXT](#)]

Dolsen MR, et al (2014) - **Insomnia as a transdiagnostic process in psychiatric disorders.** Curr Psychiatry Rep. 2014 Sep;16(9). [[FULL TEXT](#)]

"Insomnia is a major public health concern, and is highly comorbid with a broad range of psychiatric disorders. Although insomnia has historically been considered a symptom of other disorders, this perspective has shifted. Epidemiological and experimental studies suggest that insomnia is related to the onset and course of several psychiatric disorders. Furthermore, several randomized controlled trials show that cognitive behavioral therapy for insomnia delivered to individuals who meet diagnostic criteria for insomnia and another psychiatric disorder improves the insomnia as well as the symptoms of the comorbid psychiatric disorder. Taken together, these results encompassing a range of methodologies have provided encouraging evidence and point toward insomnia as a transdiagnostic process in psychiatric disorders."

Arns M, et al (2014) - **Neurofeedback in ADHD and insomnia: Vigilance stabilization through sleep spindles and circadian networks.** Neurosci Biobehav Rev. 2014; 44: 183-194. [[ABS](#)]

Arns M, et al (2014) - **Differential effects of theta/beta and SMR neurofeedback in ADHD on sleep onset latency.** Front Hum Neurosci. 2014; 8 (1019). 9). [[FULL TEXT](#)]

Fairholme CP, et al (2013) - **Sleep disturbance and emotion dysregulation as transdiagnostic processes in a comorbid sample.** Behav Res Ther. 2013 Sep;51(9):540-6. [[FULL TEXT](#)]

Insomnia and emotion dysregulation appear to be transdiagnostic processes uniquely associated with symptom severity across a number of different domains and might be important treatment targets for individuals with PTSD and AD." (alcohol dependence)

Astill RG, et al (2012) - **Sleep, cognition, and behavioral problems in school-age children: A century of research meta-analyzed.** Psychol Bull. 2012; 138: 1109-1138. [\[ABS\]](#)

Gruber R, et al (2012) - **Impact of sleep extension and restriction on children's emotional lability and impulsivity.** Pediatrics. 2012; 130: e1155-e1161. [\[ABS\]](#)

"Conclusions: A modest extension in sleep duration was associated with significant improvement in alertness and emotional regulation, whereas a modest sleep restriction had opposite effects."

Harvey AG, et al (2011) - **Sleep disturbance as transdiagnostic: Consideration of neurobiological mechanisms.** Clin Psychol Rev. 2011 Mar;31(2):225-35. [\[FULL TEXT\]](#)

"Sleep disturbance is increasingly recognized as an important, but understudied, mechanism in the complex and multi-factorial causation of the symptoms and functional disability associated with psychiatric disorders. This review proposes that it is biologically plausible for sleep disturbance to be mechanistically transdiagnostic. More specifically, we propose that sleep disturbance is aetiologically linked to various forms of psychopathology..."

"The clinical implications include potentially powerful and inexpensive interventions including interventions targeting light exposure, dark exposure, the regulation of social rhythms and the reduction of anxiety. We also consider the possibility of developing a 'transdiagnostic' treatment; one treatment that would reduce sleep disturbance across psychiatric disorders."

Social Cognition ▲

Green LM, et al (2020) - **Social Problems in Children: Exploring the Contribution of Triarchic Traits and Parenting.** Child Psychiatry Hum Dev. 2020 Feb;51(1):151-162. [\[ABS\]](#)

Social problems are **transdiagnostically** relevant in the development of various forms of psychopathology. It is thus important to consider contributing factors both at the individual and contextual level. ...Higher levels of disinhibition and meanness were associated with increased social problems in the context of higher levels of negative, or decreased levels of positive parenting; boldness acted as a protective factor in these contexts. Results suggest that the triarchic trait dimensions (1) can be studied in

children, (2) act as risk and protective factors, and (3) interact with parenting to contribute to social problems.

Wendt LP, et al (2019) - **The latent structure of interpersonal problems: Validity of dimensional, categorical, and hybrid models.** J Abnorm Psychol. 2019 Nov;128(8):823-839. [[FULL TEXT](#)]

Interpersonal problems are key *transdiagnostic* constructs in psychopathology. ... Our results indicate that the latent structure of interpersonal problems is best represented by continuous dimensions, especially when one allows for non-normal latent distributions

Porcelli S, et al (2019) - **Social brain, social dysfunction and social withdrawal.** Neurosci Biobehav Rev. 2019 Feb;97:10-33. [[ABS](#)]

Consistently, social deficits sometimes represent the first signs of a number of neuropsychiatric disorders including schizophrenia (SCZ), Alzheimer's disease (AD) and major depressive disorder (MDD) which leads to a progressive social dysfunction. ...Interestingly, AD, SCZ, and MDD affect the social brain in similar ways. Thus, social dysfunction and its most evident clinical expression (i.e., social withdrawal) may represent an innovative *transdiagnostic* domain, with the potential of being an independent entity in terms of biological roots, with the perspective of targeted interventions.

Gur RC, et al (2016) - **Social cognition as an RDoC domain.** Am J Med Genet B Neuropsychiatr Genet. 2016 Jan;171B(1):132-41. [[FULL TEXT](#)]

Substance use disorder / Addiction ▲

Hamonniere T, et al (2020) - **Toward a better understanding of the influence of repetitive negative thinking in alcohol use disorder: An examination of moderation effect of metacognitive beliefs and gender.** Addict Behav. 2020 Jul 21;111:106561. [[ABS](#)]

Repetitive negative thinking (RNT), the most studied forms of which are depressive ruminations and anxious worry, is a unique transdiagnostic process responsible for the development and maintenance of many mental disorders. ... Results indicated that the 'capture mental resources' factor of RNT is a significant predictor of alcohol use disorder (AUD) severity, independent from anxiety and depression, and that this effect is moderated by metacognitive beliefs and gender. RNT is a significant predictor of AUD severity only for people with high negative beliefs about thoughts regarding uncontrollability and danger. ... Treatments that reduce attentional impairments caused by RNT and modify dysfunctional metacognitive beliefs could be promising for some

patients with AUD.

Yoon G, et al (2020) - **Alcohol Craving and Psychiatric Disorders among Current Drinkers.** Am J Addict. 2020 Jul 15. [\[ABS\]](#)

Cravers had higher prevalence rates of current psychiatric disorders than non-cravers. Even after adjustment for other psychiatric disorders including alcohol use disorder (AUD), cravers had significantly higher odds of any substance use disorder..., any mood disorder..., any anxiety disorder..., and any personality disorder..., than non-cravers. Interestingly, cravers without AUD had even higher rates of any anxiety disorder and any personality disorder than non-cravers with AUD. ...alcohol craving may be related to transdiagnostic features that are present across various psychiatric disorders.

Penolazzi B, et al (2020) - **Testing the transdiagnostic hypothesis of inhibitory control deficits in addictions: An experimental study on gambling disorder.** J Behav Addict. 2020 Jun 16;9(2):339-346. [\[ABS\]](#)

Many psychopathologies, including addictions, are characterized by inhibitory control deficits. In this regard, recent studies on substance-related disorders (SRD) have shown an impairment in the ability to inhibit potentially interfering memories, despite preserved motor inhibition. To investigate whether the same dissociation could also characterize gambling disorder (GD) in a transdiagnostic perspective, we tested both cognitive and motor inhibitory processes through dedicated tasks, for the first time in this behavioral addiction.

Watts AL, et al (2020) - **Incipient alcohol use in childhood: Early alcohol sipping and its relations with psychopathology and personality.** Dev Psychopathol. 2020 Jun 11:1-13. [\[ABS\]](#)

Prior research has shown that sipping of alcohol begins to emerge during childhood and is potentially etiologically significant for later substance use problems. Seventeen percent of the sample reported sipping alcohol outside of a religiously sanctioned activity by age 9 or 10. ...Several aspects of psychopathology and personality emerged as small but reliable correlates of sipping. Nonreligious sipping was related to youth-reported impulsogenic traits, aspects of behavioral activation, prodromal psychotic-like symptoms, and mood disorder diagnoses, as well as parent-reported externalizing disorder diagnoses. Religious sipping was unexpectedly associated with certain aspects of impulsivity. Together, our findings point to the potential importance of impulsivity and other transdiagnostic indicators of psychopathology (e.g., emotion dysregulation, novelty seeking) in the earliest forms of drinking behavior.

Cummings JR, et al (2020) - **Prospective associations between parental substance use and youth highly processed food intake in the Fragile Families and Child Wellbeing Study.** Drug Alcohol Depend. 2020 Jun 1;211:107965. [\[FULL TEXT\]](#)

BACKGROUND: Given growing evidence of overlap in characteristics of addictive substances and highly processed foods (e.g., ice cream), transdiagnostic approaches may be appropriate. Prior work indicates youth with parents who use addictive substances are at risk for greater substance use. ...Prenatal exposure to illicit drugs may present transdiagnostic risk for greater youth highly processed food intake and substance use.

Burr EK, et al (2020) - **Distress Intolerance in Relation to Reliance on Cigarettes for Weight, Shape, and Appetite Control.** Int J Behav Med. 2020 Apr;27(2):247-254. [[ABS](#)]

Distress intolerance, one's inability to withstand distressing emotional or physical states, is a transdiagnostic vulnerability implicated in affect-based health behaviors, ...Distress intolerance may play an etiological role in maladaptive use of cigarettes to control appetite, weight, and body dissatisfaction among daily smokers, particularly those with weight- or shape-related concerns. Interventions aimed at increasing perceived ability to withstand distress could potentially reduce reliance on cigarettes for the aforementioned purposes.

Levchuk LA, et al (2020) - **Exploring Brain Derived Neurotrophic Factor and Cell Adhesion Molecules as Biomarkers for the Transdiagnostic Symptom Anhedonia in Alcohol Use Disorder and Comorbid Depression.** . Front Psychiatry. 2020 Apr 20;11:296. [[FULL TEXT](#)]

Alcohol Use Disorder (AUD) and depressive disorder often co-exist and have a shared heritability. ...This pilot study suggests that peripheral levels of BDNF and neuronal cell adhesion molecules (NCAM) might be reduced in AUD with and without comorbid mood disorder. Since low BDNF levels were associated with self-reported anhedonia across these conditions, BDNF and anhedonia might reflect transdiagnostic aspects involved in AUD and depression.

Wu LL, et al (2020) - **Impaired regulation of both addiction-related and primary rewards in individuals with internet gaming disorder.** Psychiatry Res. 2020 Feb 22;286:112892. [[ABS](#)]

Poor executive function (EF) has been implicated in addictions. Among "hot" EFs (i.e., those involving motivations and emotions), poor regulation of craving has been proposed to underlie addiction development in substance-use disorders (SUDs), making such regulation a potential treatment target. However, regulation of craving remains poorly understood in internet gaming disorder (IGD)...The findings are consistent with studies in substance use disorders (SUDs), suggesting that impaired regulation of craving may be a relevant transdiagnostic construct across SUDs and behavioral addictions. The findings suggest targeting regulation of "hot" processes should be considered in IGD treatment development.

Limbrick-Oldfield EH, et al (2020) - **Neural and neurocognitive markers of vulnerability to gambling disorder: a study of unaffected siblings.** Neuropsychopharmacology. 2020 Jan;45(2):292-300. [[FULL TEXT](#)]

Psychological and neurobiological markers in individuals with gambling disorder (GD) could reflect transdiagnostic vulnerability to addiction or neuroadaptive consequences of long-term gambling. ... Within the GD group, activity in the thalamus and caudate correlated negatively with gambling severity. Increased impulsivity and risk-taking in GD are present in biological relatives of cases with GD, suggesting these markers may represent pre-existing vulnerability to GD.

Donald F, et al (2019) - **Substance use and borderline personality disorder: fostering hope in the face of complexity**. *Australas Psychiatry*. 2019 Dec;27(6):569-572. [[ABS](#)]

Impulsivity and emotional dysregulation are common characteristics of patients presenting with co-occurring borderline personality disorder (BPD) and substance use disorder (SUD). ... Co-occurring BPD and SUD can be effectively treated within a staged, **transdiagnostic** approach with an emphasis on the therapeutic alliance.

Wupperman P, et al (2019) - **Treatment for Individuals with Severe Mental Illness Who Use Illicit Drugs While Maintained on Methadone: Mindfulness and Modification Therapy**. *J Nerv Ment Dis*. 2019 Dec;207(12):1005-1011. [[ABS](#)]

This pilot study investigated the feasibility and acceptability of a 12-week, **transdiagnostic** group therapy (mindfulness and modification therapy [MMT]) tailored for opioid-dependent individuals (N = 6) with SMI and illicit drug use. Retention was 83%. At posttreatment and 2-month follow-up, participants rated the treatment as highly helpful (9 of 10; 8.67 of 10, respectively), reported routinely practicing the guided-mindfulness exercises, and reported high confidence that they would continue to practice. Assessments revealed clinically meaningful decreases in reported days of illicit drug use at posttreatment and follow-up, with large effect sizes. Preliminary evidence suggests that MMT may be a feasible and acceptable therapy that may improve treatment engagement in this underserved population.

Cummings JR, et al (2019) - **Maternal nicotine dependence is associated with longitudinal increases in child obesogenic eating behaviors**. *Pediatr Obes*. 2019 Nov;14(11):e12541. [[FULL TEXT](#)]

Maternal nicotine dependence may be a **transdiagnostic** risk factor that identifies children at risk for reward-driven, obesogenic eating behavior.

Memedovic S, et al (2019) - **Rumination and problematic substance use among individuals with a long-term history of illicit drug use**. *Drug Alcohol Depend*. 2019 Oct 1;203:44-50. [[ABS](#)]

Findings indicate that ruminative brooding is related to a poorer substance use profile among people with long-term illicit drug use and highlight the potential benefits of targeting brooding during substance use treatment.

Albertella L, et al (2019) - **Reward-related attentional capture is associated with severity of addictive and obsessive-compulsive behaviors.** Psychol Addict Behav. 2019 Aug;33(5):495-502.

[\[FULL TEXT\]](#)

A cue that signals reward can capture attention and elicit approach behaviors in people and animals. The current study examined whether attentional capture by reward-related cues is associated with severity of addiction-related and obsessive-compulsive behaviors. ...Reward-related attentional capture was associated with severity of compulsivity, **transdiagnostically**. These findings have implications for understanding the mechanisms that underlie compulsive behaviors and suggest that reward-related attentional capture is a promising **transdiagnostic** cognitive risk marker for compulsivity.

Tiego J, et al (2019) - **Overlapping dimensional phenotypes of impulsivity and compulsivity explain co-occurrence of addictive and related behaviors.** CNS Spectr. 2019 Aug;24(4):426-440.

[\[ABS\]](#)

Impulsivity and compulsivity have been implicated as important **transdiagnostic** dimensional phenotypes with potential relevance to addiction. ...A model of impulsivity and compulsivity that represents these constructs as overlapping dimensional phenotypes has important implications for understanding addictive and related behaviors in terms of shared etiology, comorbidity, and potential **transdiagnostic** treatments.

Devynck F, et al (2019) - **Does Repetitive Negative Thinking Influence Alcohol Use? A Systematic Review of the Literature.** Front Psychol. 2019 Jul 3;10:1482. [\[FULL TEXT\]](#)

... a strong positive association between RNT and alcohol use or alcohol-related problems, regardless of the form of RNT. The results were more heterogeneous in the 17 studies conducted among adolescents and students, leading the authors to conclude that the results varied as a function of the severity of alcohol use. The results of this study suggest to focus on RNT from a **transdiagnostic** perspective in AUD. This processual approach may improve AUD treatment and relapse prevention.

Riesel A, et al (2019) - **Error-related brain activity as a transdiagnostic endophenotype for obsessive-compulsive disorder, anxiety and substance use disorder.** Psychol Med. 2019 May;49(7):1207-1217. [\[FULL TEXT\]](#)

Alterations in neural error-signals in unaffected first-degree relatives with a family history of OCD, anxiety, or SUD support the utility of the ERN as a **transdiagnostic** endophenotype. Reduced neural error-signals may indicate vulnerability for under-controlled behavior and risk for substance use, whereas a harm- or error-avoidant response style and vulnerability for OCD and anxiety appears to be associated with increased ERN. This adds to findings suggesting a common neurobiological substrate across psychiatric disorders involving the anterior cingulate cortex and deficits in cognitive control.

Pennou A, et al (2019) - **Mobile Intervention for Individuals with Psychosis, Dual Disorders, and Their Common Comorbidities: A Literature Review.** Front Psychiatry. 2019 May 3;10:302. [\[FULL TEXT\]](#)

Over 50% of people diagnosed with a severe mental illness, such as schizophrenia or bipolar disorder, will meet criteria for a substance use disorder in their lifetime. This dual disorder often starts during youth and leads to significant societal costs, including lower employability rates, more hospitalizations, and higher risk of homelessness and of suicide attempts when compared to those with a serious mental illness without substance misuse. Moreover, many individuals presenting with comorbid disorders also present with other psychological difficulties as well, such as personality disorders or anxiety and depression, also known as complex comorbid disorders. **Transdiagnostic** treatments that focus on core difficulties found in people with complex dual disorders, such as emotional regulation, are direly needed. Emotional **regulation skills** can help reduce distress related to psychotic symptoms and maintain abstinence in substance use disorders. New technologies in the field of communications have developed considerably over the past decade and have the potential to improve access to such treatments, a major problem in many health care settings. As such, this paper aims at: presenting core difficulties present in many individuals with dual disorders, reviewing the scientific literature pertaining to the use of mobile applications in mental health and addictions, and presenting the development and potential of a new application for emotional regulation for people with dual disorders.

Weissman DG, et al (2019) - **Difficulties with emotion regulation as a transdiagnostic mechanism linking child maltreatment with the emergence of psychopathology.** Dev Psychopathol. 2019 Aug;31(3):899-915. [\[FULL TEXT\]](#)

Greater emotional reactivity and engagement in rumination mediated the longitudinal association between maltreatment and increased general psychopathology over time. Emotion dysregulation following childhood maltreatment occurs at multiple stages of the emotion generation process, in some cases varies across development, and serves as a **transdiagnostic** mechanism linking child maltreatment with general psychopathology.

Burchi E, et al (2019) - **Compulsivity in Alcohol Use Disorder and Obsessive Compulsive Disorder: Implications for Neuromodulation.** Front Behav Neurosci. 2019 Apr 11;13:70. [\[FULL TEXT\]](#)

Alcohol use Disorder (AUD) is one of the leading causes of morbidity and mortality worldwide. The progression of the disorder is associated with the development of compulsive alcohol use, which in turn contributes to the high relapse rate and poor longer term functioning reported in most patients, even with treatment. While the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines AUD by a cluster of symp-

toms, parsing its heterogeneous phenotype by domains of behavior such as compulsivity may be a critical step to improve outcomes of this condition. Still, neurobiological underpinnings of compulsivity need to be fully elucidated in AUD in order to better design targeted treatment strategies. In this manuscript, we review and discuss findings supporting common mechanisms between AUD and OCD, dissecting the construct of compulsivity and focusing specifically on characteristic disruptions in habit learning and cognitive control in the two disorders. Finally, **neuromodulatory interventions** are proposed as a probe to test compulsivity as key pathophysiologic feature of AUD, and as a potential therapy for the subgroup of individuals with compulsive alcohol use, i.e., the more resistant stage of the disorder. This **transdiagnostic** approach may help to destigmatize the disorder, and suggest potential treatment targets across different conditions.

Um M, et al (2019) - **Shared Neural Correlates Underlying Addictive Disorders and Negative Urgency**. Brain Sci. 2019 Feb 8;9(2):36. [\[FULL TEXT\]](#)

Negative urgency is a personality trait reflecting the tendency to act rashly in response to extreme negative emotions and is considered a **transdiagnostic** endophenotype for problematic levels of addictive behaviors. Recent research has begun to identify the neural correlates of negative urgency, many of which appear to overlap with neural circuitry underlying addictive disorders associated with negative urgency. ... Patterns of structure and function in the ventral striatum, frontal regions, such as the prefrontal cortex (PFC) and orbitofrontal cortex (OFC), and amygdala are common across addictive disorders and are related to both real-world risky behaviors and self-report measures of negative urgency.

Ramdave S, et al (2019) - **Unmasking neurobiological commonalities between addictive disorders and impulse control disorders in Parkinson's disease**. Brain Imaging Behav. 2019 Feb 1. [\[ABS\]](#)

Changes in reward circuitry have been studied extensively in substance and behavioural addictions. However, comparatively little is known about the neurobiology underlying impulse control disorders (ICDs) in Parkinson's disease, which show roughly similar risk factors and behavioural presentations to both stimulant and behavioural addictions. ICDs occur in a subset of susceptible patients with Parkinson's disease (PD) following intake of dopamine replacement therapy (DRT). These behavioural disorders often have debilitating effects on a patient's quality of life and increase caregiver burden. ...

Results revealed that strikingly similar (a) deficits in dopaminergic receptor expression, (b) connectivity changes in corticostriatal circuitry and (c) neural responses to cue exposure are observed in both ICDs (impulse control disorders) in PD and addictive disorders. These findings point to the value of adopting a **transdiagnostic** approach when studying addicted populations and pave the way for demystifying this peculiar, often-devastating phenomenon in PD that has so far proven extremely difficult to treat and predict with any precision.

Zale EL, et al (2019) - **Gender differences in associations between pain-related anxiety and alcohol use among adults with chronic pain.** Am J Drug Alcohol Abuse. 2019;45(5):479-487.

[\[ABS\]](#)

Pain-related anxiety is a **transdiagnostic** vulnerability factor that has been implicated in both pain and substance-related ... Pain-related anxiety was positively associated with alcohol-related consequences and alcohol dependence symptoms measured by the AU-DIT (Alcohol Use Disorders Identification Test) among males, but not females.

Ramey T, et al (2018) - **Cognitive impairment in substance use disorders.** CNS Spectr. 2018 Dec 28;1-12. [\[FULL TEXT\]](#)

As addressed in this special issue, cognitive impairment is a **transdiagnostic** domain; thus, advances in the characterization and treatment of cognitive dysfunction in substance use disorders could have benefit across multiple psychiatric disorders

Sloan E, et al (2017) - **Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: A systematic review.** Clin Psychol Rev. 2017 Nov;57:141-163. [\[ABS\]](#)

A large body of research has implicated difficulties in emotion regulation as central to the development and maintenance of psychopathology. Emotion regulation has therefore been proposed as a transdiagnostic construct or an underlying mechanism in psychopathology. The transdiagnostic role of emotion regulation has yet to be systematically examined within the psychological treatment outcome literature. It can be proposed that if emotion regulation is indeed a transdiagnostic construct central to the maintenance of psychopathology, then changes in emotion regulation difficulties will occur after effective treatment and this will occur for different disorders. We conducted a systematic review, identifying 67 studies that measured changes in both emotion regulation and symptoms of psychopathology following a psychological intervention for anxiety, depression, substance use, eating pathology or borderline personality disorder. Results demonstrated that regardless of the intervention or disorder, both maladaptive emotion regulation strategy use and overall emotion dysregulation were found to significantly decrease following treatment in all but two studies. Parallel decreases were also found in symptoms of anxiety, depression, substance use, eating pathology and borderline personality disorder. These results contribute to the growing body of evidence supporting the conceptualization of emotion regulation as a transdiagnostic construct. The present study discusses the important implications of these findings for the development of unified treatments that target emotion regulation for individuals who present with multiple disorders.

Zambrano-Vazquez L, et al (2017) - **Using the Research Domain Criteria Framework to Track Domains of Change in Comorbid PTSD and SUD.** Psychol Trauma. 2017 Feb 6. [\[ABS\]](#)

Logan RW, et al (2017) - **Impact of sleep and circadian rhythms on addiction vulnerability in adolescents.** Biol Psychiatry. 2018 Jun 15;83(12):987-996. [\[FULL TEXT\]](#)

Yip SW, et al (2017) - **Gray-matter relationships to diagnostic and transdiagnostic features of drug and behavioral addictions.** Addict Biol. 2017 Feb 1. [\[ABS\]](#)

Sofuoglu M, et al (2016) - **Cognitive Function as a Transdiagnostic Treatment Target in Stimulant Use Disorders.** J Dual Diagn. 2016;12(1):90-106 [\[FULL TEXT\]](#)

Holiday SB, et al (2016) - **Depression, posttraumatic stress, and alcohol misuse in young adult veterans - The transdiagnostic role of distress tolerance.** Drug Alcohol Depend. 2016 Apr 1;161:348-55. [\[FULL TEXT\]](#)

"This is the first study to examine the role of distress tolerance in the relationship between mental health and alcohol misuse in a U.S. military veteran population. These results suggest that distress tolerance plays a role in the relationship between common post-deployment mental health concerns and alcohol misuse in young adult veterans. Given the significant health and psychosocial consequences of depression, PTSD, problem drinking, and the potential for tri-morbidity of these three conditions among young veterans and other high-risk populations, additional investigation of transdiagnostic factors that underlie these comorbidities is warranted and may be essential to informing prevention and treatment efforts."

Eaton NR, et al (2015) - **Transdiagnostic factors of psychopathology and substance use disorders: a review.** Soc Psychiatry Psychiatr Epidemiol. 2015 Feb;50(2):171-82. [\[ABS\]](#)

"... many forms of psychopathology and substance use disorders are manifestations of relatively few transdiagnostic latent factors. ...Transdiagnostic factors account for the development and continuity of disorders and comorbidity over time ...and serve as foci for efficient, broadband intervention approaches."

Leventhal AM, et al (2015) - **Anxiety, depression, and cigarette smoking - a transdiagnostic vulnerability framework to understanding emotion-smoking comorbidity.** Psychol Bull. 2015 Jan;141(1):176-212. [\[FULL TEXT\]](#)

"This approach integrates well with the National Institute on Mental Health's Research Domain Criteria, which proposes that common cross-cutting dimensions, traits, neural circuits, and biological pathways underpin and account for the presentation of various mental disorder diagnoses (Cuthbert and Insel, 2013)."

Sher KJ (2015) - **Moving the Alcohol Addiction RDoC forward.** Alcohol Clin Exp Res. 2015 Apr;39(4):591. [\[FULL TEXT\]](#)

Wolitzky-Taylor K, et al (2015) - **Examination of anxiety sensitivity and distress tolerance as transdiagnostic mechanisms linking multiple anxiety pathologies to alcohol use problems in adolescents.** Alcohol Clin Exp Res. 2015 Mar;39(3):532-9. [\[FULL TEXT\]](#)

Hill LM, et al (2015) - **Rumination and Moderators of Multifinality: Predicting Internalizing Symptoms and Alcohol Use During Adolescence.** J Clin Child Adolesc Psychol. 2015 Oct 29:1-8. [\[FULL TEXT\]](#)

Moeller SJ, et al (2014) - **Impaired self-awareness in human addiction: deficient attribution of personal relevance.** Trends Cogn Sci. 2014 Dec;18(12):635-41. [\[FULL TEXT\]](#)

Compromised self-awareness of illness-related deficits and behaviors in psychopathology (e.g., schizophrenia) has been associated with deficient functioning of *cortical midline regions* including the ventromedial prefrontal cortex (vmPFC), implicated in personal relevance. Here, we review and critically analyze recent evidence to suggest that vmPFC abnormalities could similarly underlie deficient tagging of personal relevance in drug addiction, evidenced by a constellation of behaviors encompassing drug-biased attention, negative outcome insensitivity, self-report/behavior dissociation, and social inappropriateness. This novel framework might clarify, for example, why drug-addicted individuals often ruin long-standing relationships or forego important job opportunities while continuing to engage in uncontrolled drug-taking. Therapeutic interventions targeting personal relevance and associated vmPFC functioning could enhance self-awareness and facilitate more adaptive behavior in this chronically relapsing psychopathology.

Arns M, et al (2014) - **Neurofeedback in ADHD and insomnia: Vigilance stabilization through sleep spindles and circadian networks.** Neurosci Biobehav Rev. 2014; 44: 183-194. [\[ABS\]](#)

Arns M, et al (2014) - **Differential effects of theta/beta and SMR neurofeedback in ADHD on sleep onset latency.** Front Hum Neurosci. 2014; 8 (1019. 9). [\[FULL TEXT\]](#)

Suicidality ▲

Harman G, et al (2021) - **Prediction of suicidal ideation and attempt in 9 and 10 year-old children using transdiagnostic risk features.** PLoS One. 2021 May 25;16(5):e0252114. [\[ABS\]](#)

Important features from these models included feelings of loneliness and worthlessness, impulsivity, prodromal psychosis symptoms, and behavioral problems. This investigation provided an unprecedented opportunity to identify suicide risk in youth. The use of machine learning to examine a large number of predictors spanning a variety of domains provides novel insight into transdiagnostic factors important for risk classification.

Ducasse D, et al (2020) - **Association between anhedonia and suicidal events in patients with mood disorders: A 3-year prospective study.** *Depress Anxiety*. 2020 Jul 11. [[ABS](#)]

As almost all mental disorders are associated with increased suicidal-related behavior, anhedonia might be a trans-diagnostic dimension to target for suicide prevention. ...significant association between anhedonia and suicide ideation in patients with mood disorders stresses the need of targeting hedonia in mood disorders, and of research focusing on the position to pleasure in life through eudaimonia.

Herpers PCM, et al (2020) - **Suicidality in adolescents with therapy refractory internalising behaviour.** *Tijdschr Psychiatr*. 2020;62(4):283-290. [[ABS](#)]

Suicidality in adolescence is increasingly becoming a societal problem, especially because there remains a small group of patients in which treatment effectiveness is small. ...Applying an aetiological model for therapy refractory internalising behaviour may help to increase efficacy of treatment. Thus, transdiagnostic treatment can be offered, being less dependent on specific DSM classifications. Focus of treatment is on restoration of basic trust between the youngster and his parents, and on ending avoidance behaviour that is based on social anxiety.

Kearns JC, et al (2020) - **Sleep problems and suicide risk in youth: A systematic review, developmental framework, and implications for hospital treatment.** *Gen Hosp Psychiatry*. 2020 Mar-Apr;63:141-151. [[ABS](#)]

OBJECTIVE: Sleep problems are *transdiagnostic* symptoms that confer significant risk for suicidal thoughts and behaviors (STBs) in adults. ... Sleep problems may be particularly important intervention target because they are easily assessed across healthcare settings and are amenable to treatment.

Dillon KH, et al (2020) - **Associations between anger and suicidal ideation and attempts: A prospective study using the National Epidemiologic Survey on Alcohol and Related Conditions.** *J Psychiatr Res*. 2020 Mar;122:17-21. [[FULL TEXT](#)]

Suicide is among the leading causes of death in the United States, with rates having risen substantially over the past two decades. Anger is a common symptom of several disorders associated with suicide, and the little research that has been done in the area suggests that it may be an often overlooked transdiagnostic risk factor for both suicidal ideation and behavior. ... Findings suggests the potential benefit of integrating anger assessment and treatment into research and clinical programs focused on reducing suicide.

Huber RS, et al (2019) - **A qualitative systematic review of suicide behavior using the cognitive systems domain of the research domain criteria (RDoC) framework.** *Psychiatry Res*. 2019

Dec;282:112589. [\[ABS\]](#)

Neurocognitive deficits are associated with both suicide behavior (SB) and psychiatric disorders. Application of a **transdiagnostic** framework to identify neurocognitive commonalities of SB may clarify important risk factors of SB across psychiatric disorders. ... Use of the RDoC cognitive systems framework to evaluate SB revealed that cognitive deficits may be a **transdiagnostic** risk factor for SB, especially alterations in cognitive control.

Tilton-Weaver L, et al (2019) - **Depressive symptoms and non-suicidal self-injury during adolescence: Latent patterns of short-term stability and change.** J Adolesc. 2019 Aug;75:163-174. [\[ABS\]](#) <https://pubmed.ncbi.nlm.nih.gov/31400556>

The significant unique predictors suggest that adolescents who reported being subjected to relational aggression, having negative experiences while drinking, and low self-esteem had a greater probability of moving from moderate to high levels or maintaining high levels of depressive symptoms and self-injury, compared to adolescents classified in the other statuses. ... Focusing on negative interpersonal experiences and self-esteem as **transdiagnostic** conditions may guide research and aid clinicians in supporting adolescents who feel depressed and engage in self-injury.

Peckham AD, et al (2019) - **From Urges to Action: Negative Urgency and Nonsuicidal Self-Injury in an Acute Transdiagnostic Sample.** Arch Suicide Res. 2019 Jul 1:1-17. [\[FULL TEXT\]](#)

Urgency-rash action during strong emotion-is a robust correlate of nonsuicidal self-injury (NSSI). This study tested whether urgency is associated with time between NSSI urges and NSSI, ... Negative urgency more than doubled the likelihood of NSSI history ($p < .001$, OR = 2.39).

Auerbach RP, et al (2019) - **Mental disorder comorbidity and suicidal thoughts and behaviors in the World Health Organization World Mental Health Surveys International College Student initiative.** Int J Methods Psychiatr Res. 2019 Jun;28(2):e1752. [\[FULL TEXT\]](#)

OBJECTIVES: Comorbidity is a common feature of mental disorders. However, needs assessment surveys focus largely on individual disorders rather than on comorbidity even though the latter is more important for predicting suicidal thoughts and behaviors. ... The high level of comorbidity underscores the need to develop and test **transdiagnostic** approaches for treatment in college students.

Spinhoven P, et al (2019) - **Repetitive negative thinking as a mediator in prospective cross-disorder associations between anxiety and depression disorders and their symptoms.** J Behav Ther Exp Psychiatry. 2019 Jun;63:6-11. [\[ABS\]](#)

Comorbidity among anxiety and depression disorders and their symptoms is high. Rumination and worry have been found to mediate prospective cross-disorder relations between anxiety and depression disorders and their symptoms in adolescents and adults. We examined whether generic repetitive negative thinking (RNT), that is content- and disorder-independent, also mediates prospective cross-disorder associations between anxiety and depression disorders and their symptoms. ... The significant and rather large mediation effects seemed mainly due to the mental capacity captured by RNT, especially in the prospective relation of anxiety with future depression. ... From these results it can be concluded that repetitive negative thinking could be an important **transdiagnostic** factor, that may constitute a suitable target for treatment.

Demers LA, et al (2019) - **Alexithymia is associated with neural reactivity to masked emotional faces in adolescents who self-harm.** J Affect Disord. 2019 Apr 15;249:253-261. [[FULL TEXT](#)]

Non-suicidal self-injury (NSSI) is a major, **transdiagnostic** mental health problem among adolescents. Alexithymia has been identified as a developmental risk factor for NSSI. ... Among adolescents who self-harm, those with higher levels of externally-oriented thinking may be less alert to subtle positively-valenced emotion cues. For this subset of adolescents with NSSI, interventions designed to enhance mental representation of emotional responses and attention to positive emotions may be appropriate.

Richmond-Rakerd LS, et al (2019) - **Adolescents Who Self-Harm and Commit Violent Crime: Testing Early-Life Predictors of Dual Harm in a Longitudinal Cohort Study.** Am J Psychiatry. 2019 Mar 1;176(3):186-195. [[FULL TEXT](#)]

Dual harmers have self-control difficulties and are immersed in violence from a young age. A treatment- rather than punishment-oriented approach is indicated to meet these individuals' needs. Connecting self-harming adolescents with delinquency-reduction programs and **transdiagnostic** approaches that target self-regulation may reduce harmful behaviors. Preventing childhood maltreatment and implementing strategies to reduce victimization exposure could mitigate risk for both internalized and externalized violence.

Britton PC, et al (2019) - **Insomnia and risk for suicidal behavior: A test of a mechanistic transdiagnostic model in veterans.** J Affect Disord. 2019 Feb 15;245:412-418. [[ABS](#)]

In veterans, insomnia symptoms may be associated with increased PTSD and depressive symptoms, which may be associated with increased risk for suicidal behavior directly and indirectly through relationship disruptions.

Barredo J, et al (2019) - **Neuroimaging Correlates of Suicidality in Decision-Making Circuits in Posttraumatic Stress Disorder.** Front Psychiatry. 2019 Feb 12;10:44. [[FULL TEXT](#)]

These results provide a preliminary demonstration that biomarkers of suicidality in decision-making networks observed in depression may generalize to PTSD and highlight the promise of these circuits as **transdiagnostic** biomarkers of suicidality.

Dolsen MR, et al (2017) - **Neurophysiological correlates of suicidal ideation in major depressive disorder: Hyperarousal during sleep.** J Affect Disord. 2017 Apr 1;212:160-166. [[FULL TEXT](#)]

Perlis ML, et al (2016) - **Suicide and sleep: Is it a bad thing to be awake when reason sleeps?** Sleep Med Rev. 2016 Oct;29:101-7. [[FULL TEXT](#)]

Ballard ED, et al (2016) - **Nocturnal Wakefulness Is Associated With Next-Day Suicidal Ideation in Major Depressive Disorder and Bipolar Disorder.** J Clin Psychiatry. 2016 Jun;77(6):825-31. [[FULL TEXT](#)] <https://pubmed.ncbi.nlm.nih.gov/28682534/>

Luoma JB, et al (2012) - **Mindfulness in the Treatment of Suicidal Individuals.** Cogn Behav Pract. 2012 Jan 5;19(2):265-276. [[FULL TEXT](#)]

Threat Sensitivity ▲

Byrd AL, et al (2020) - **An interaction between early threat exposure and the oxytocin receptor in females: Disorder-specific versus general risk for psychopathology and social-emotional mediators.** Dev Psychopathol. 2020 Jul 22:1-16. [[ABS](#)]

Early threat exposure is a transdiagnostic risk factor for psychopathology, and evidence suggests that genetic variation in the oxytocin receptor (OXTR) moderates this association. ...the interactive effects of early threat exposure and OXTR variation (rs53576) predicted general psychopathology, with threat-exposed women carrying at least one copy of the rs53576 A-allele at greatest risk. This interaction was mediated via emotional dysregulation in adolescence, with threat-exposed A-allele carriers demonstrating greater emotion dysregulation, and greater emotion dysregulation predicting general psychopathology in early adulthood. Findings suggest that this G×E places women at risk for a broad range of psychopathology via effects on emotion dysregulation.

Mekawi Y, et al (2020) - **The role of negative affect in the association between attention bias to threat and posttraumatic stress: An eye-tracking study.** Psychiatry Res. 2020 Feb;284:112674. [[FULL TEXT](#)]

Biased processing of threatening stimuli, including attention toward and away from threat, has been implicated in the development and maintenance of PTSD symptoms. ... negative affect may be an important etiological process through which attention bias

patterns could impact PTSD symptom severity. Implications for psychological and pharmacological therapeutic interventions targeting threat-related attention biases and negative affect are discussed.

Jirsaraie RJ, et al (2019) - **Accelerated cortical thinning within structural brain networks is associated with irritability in youth.** Neuropsychopharmacology. 2019 Dec;44(13):2254-2262.

[\[FULL TEXT\]](#)

... irritability is associated with widespread reductions in cortical thickness and accelerated cortical thinning, particularly within the frontal and temporal cortex. Aberrant structural maturation of regions important for emotional regulation may in part underlie symptoms of irritability.

Weissman DG, et al (2019) - **Altered Neural Processing of Threat-Related Information in Children and Adolescents Exposed to Violence: A Transdiagnostic Mechanism Contributing to the Emergence of Psychopathology.** J Am Acad Child Adolesc Psychiatry. 2019 Aug 29:S0890-8567(19)31928-8. [\[FULL TEXT\]](#)

Reduced recruitment of the dACC-a region involved in salience processing, conflict monitoring, and cognitive control-in response to threat-related cues may convey increased **transdiagnostic** psychopathology risk in youths exposed to violence.

Hettema JM (2016) – **Psychophysiology of threat response, paradigm shifts in psychiatry, and RDoC: Implications for genetic investigation of psychopathology.** Psychophysiology. 2016 Mar;53(3):348-50. [\[FULL TEXT\]](#)

RDoC itself does not propose an alternative nosology, but rather seeks to unfetter research from clinical definitions and provide an initial framework and set of constructs for reconceptualizing psychiatric research directions in line with basic neuroscience concepts. Basic neuroscience research has, of course, progressed along its own path just fine. However, a persisting problem has been in its general independence from conceptions of psychopathology as defined in DSM (American Psychiatric Association, 2013). The RDoC framework seeks to reorient conceptions of psychopathology by encouraging infusion of neuroscientific thinking and data into such conceptions.

Ladouceur CD (2016) – **The error-related negativity: A transdiagnostic marker of sustained threat.** Psychophysiology. 2016 Mar;53(3):389-92. [\[ABS\]](#)

The creation of the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) project has been the driving force behind the reconceptualization of the pathogenesis of psychiatric disorders. In this commentary, I explore whether the error-related negativity can be considered as a transdiagnostic marker of sustained threat based on findings from Weinberg, Meyer et al.'s (2016) study in relation to current findings in the literature.

Weinberg A, et al (2016) - **Error-related negativity (ERN) and sustained threat: Conceptual framework and empirical evaluation in an adolescent sample.** Psychophysiology. 2016 Mar;53(3):372-85. [\[FULL TEXT\]](#)

Yancey JR, et al (2016) - **Psychoneurometric operationalization of threat sensitivity: Relations with clinical symptom and physiological response criteria.** Psychophysiology. 2016 Mar;53(3):393-405. [\[FULL TEXT\]](#)

Transdiagnostic Interventions ▲

González-Blanch C, et al (2021) - **Moderators and predictors of treatment outcome in transdiagnostic group cognitive-behavioral therapy for primary care patients with emotional disorders.** Depress Anxiety. 2021 May 27. [\[ABS\]](#)

Providing transdiagnostic group cognitive-behavioral therapy before prescribing antidepressant medication and while people are still working may enhance the effects of adding this psychological treatment to treatment as usual in primary care.

Powell CLYM, et al (2021) - **A pilot trial of a transdiagnostic treatment for emotional disorders-a locally adapted variant of group Unified Protocol (UP) for Chinese adults.** Transl Behav Med. 2021 May 25;11(5):1142-1150. [\[ABS\]](#)

There has been increasing interest in transdiagnostic cognitive-behavioral therapy (CBT), which is more cost efficient yet yields similar effect sizes when compared to disorder-specific CBT. The Unified Protocol (UP) for Transdiagnostic Treatment of Emotional Disorders was adapted for Hong Kong Chinese adults with common mental disorders, such as depression and anxiety. ... It achieved comparable effect sizes to those observed in western populations.

Fortuna LR, et al (2020) - **Development of a cognitive behavioral therapy with integrated mindfulness for Latinx immigrants with co-occurring disorders: Analysis of intermediary outcomes.** Psychol Trauma. 2020 Aug 6. [\[ABS\]](#)

Objectives: Transdiagnostic interventions have been increasingly used in the management of a variety of mental health and substance use conditions, and in the context of chronic stress. We discuss the development and evaluation of the Integrated Intervention for Dual Problems and Early Action (IIDEA), a 10-session manualized intervention that includes cognitive therapy and mindfulness practice designed to improve symptoms of anxiety, depression, posttraumatic stress, and co-occurring substance use problems. ...Conclusions: Findings suggest that skills related to the studied

intermediary outcomes can be helpful for Latinx immigrants experiencing circumstances of ongoing exposure to adversity and traumatic stress.

Scholes S, et al (2020) - **Modulation of Slow-Wave Sleep: Implications for Psychiatry.** Curr Psychiatry Rep. 2020 Jul 24;22(10):52. [\[ABS\]](#)

Our review reveals partial support to the potential efficacy of SWS modulation as a transdiagnostic intervention that uses sleep to improve cognitive functions of individuals diagnosed with psychiatric disorders and cognitive deficits

Barlow DH, et al (2020) - **The unified protocol for transdiagnostic treatment of emotional disorders.** World Psychiatry. 2020 Jun;19(2):245-246. [\[FULL TEXT\]](#)

García-Escalera J, et al (2020) - **The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Adolescents (UP-A) Adapted as a School-Based Anxiety and Depression Prevention Program: An Initial Cluster Randomized Wait-List-Controlled Trial.** Behav Ther. 2020 May;51(3):461-473. [\[ABS\]](#)

Anxiety and depression are common debilitating conditions that show high comorbidity rates in adolescence. The Unified Protocol for **Transdiagnostic** Treatment of Emotional Disorders in Adolescents (UP-A; Ehrenreich-May et al., 2018) is one of the few existing resources aimed at applying transdiagnostic treatment principles across the core dysfunctions implicated in the development of both anxiety and depression using a single protocol. ...An unexpected decline in anxiety and depression levels from pre- to posttreatment and follow-up was found in both groups ($p = .009$, $d = -0.22$), and overall differences between conditions did not reach significance.

Wilner JG, et al (2020) - **Quality of Life in Heterogeneous Anxiety Disorders: Changes across Cognitive-Behavioral Treatments.** Behav Modif. 2020 May;44(3):343-364. [\[ABS\]](#)

Quality of life is lower among individuals with anxiety disorders; however, this construct is rarely a focus in treatment research. This study explores changes in quality of life in a randomized, controlled trial of several cognitive-behavioral treatments (CBTs) for anxiety disorders. Adults with heterogeneous anxiety disorders ($N = 223$) were randomly assigned to (a) **unified protocol** for **transdiagnostic** treatment of emotional disorders, (b) a single-disorder protocol targeting their principal diagnosis, or (c) a waitlist control condition, and assessed at baseline, posttreatment, and 6-month follow-up. At baseline, the sample evidenced deficits in quality of life, with no significant differences in quality of life across diagnoses or condition. Results suggest improved quality of life among participants in treatment, at similar rates across treatment condition and diagnostic category, and at levels significantly higher than the waitlist. Improvements were maintained through 6-month follow-up. This study supports CBT as effective in promoting quality of life.

Fernández-Martínez I, et al (2020) - **Effects of Super Skills for Life on the social skills of anxious children through video analysis.** Psicothema. 2020 May;32(2):229-236. [\[ABS\]](#)

Super Skills for Life (SSL) is an innovative **transdiagnostic** cognitive-behavioral prevention program that has demonstrated positive results targeting children's internalizing problems. SSL has a strong component aimed at enhancing social competence, including strategies such as video-feedback with cognitive preparation. ...This study provides initial support for the usefulness of SSL to immediately improve social skills in young children with anxiety symptoms.

Sauer-Zavala S, et al (2020) - **Does the Unified Protocol really change neuroticism? Results from a randomized trial.** Psychol Med. 2020 Apr 21:1-10. [\[ABS\]](#)

Neuroticism is associated with the onset and maintenance of a number of mental health conditions, as well as a number of deleterious outcomes (e.g. physical health problems, higher divorce rates, lost productivity, and increased treatment seeking); thus, the consideration of whether this trait can be addressed in treatment is warranted.

At week 16, participants in the UP condition exhibited significantly lower levels of neuroticism than participants in the symptom-focused CBT and Waiting List conditions, and these group differences remained after controlling for simultaneous fluctuations in depression and anxiety symptoms.

Craig C, et al (2020) - **Compassion focused therapy: a systematic review of its effectiveness and acceptability in clinical populations.** Expert Rev Neurother. 2020 Apr;20(4):385-400. [\[ABS\]](#)

Compassion focused therapy (CFT) is an increasingly popular therapeutic modality. Its holistic and integrative approach to universal human suffering means that it is well placed as a **transdiagnostic** therapy. ...Expert opinion: CFT shows promise for a range of mental health problems, especially when delivered in a group format over at least 12 hours.

Barkus E (2020) - **Effects of working memory training on emotion regulation: Transdiagnostic review.** Psych J. 2020 Apr;9(2):258-279. [\[ABS\]](#)

Working memory training is widely used transdiagnostically to improve cognition. However, more recently, studies using working memory training packages have targeted emotion-regulation outcomes to determine whether far transfer effects can be achieved. ...Working memory training could improve cognitive efficiency, which, in turn, increases the availability of cognitive resources during times when emotion regulation is taxed. Working memory training offers a possibility for improving emotion regulation transdiagnostically.

Paulus DJ, et al (2020) - **Trajectory of change in anxiety sensitivity in relation to anxiety, depression, and quality of life among persons living with HIV/AIDS following transdiagnostic cognitive-behavioral therapy.** Cogn Behav Ther. 2020 Mar;49(2):149-163. [\[FULL TEXT\]](#)

The current study sought to examine treatment-related changes in anxiety sensitivity and how the trajectory of change relates to anxiety and depressive symptoms as well as overall quality of life. Individuals (n = 35) with HIV/AIDS and elevated anxiety symptoms received CBT for anxiety. Results indicated that reductions in anxiety sensitivity were significantly related to changes in anxiety, depression, and quality of life. Together, these data suggest that changes in anxiety sensitivity are significantly related to changes in anxiety/depression and quality of life among PLHIV seeking treatment.

Howells L, et al (2020) - **Evaluation of a non-diagnostic 'Psychology of Emotions' group intervention within a UK youth IAPT service: a mixed-methods approach.** Behav Cogn Psychother. 2020 Mar;48(2):129-141. [\[ABS\]](#)

BACKGROUND: A novel CBT-based intervention, tailored for young people, was developed in response to concerns about traditional diagnostically based approaches. Psychology of Emotions workshops use a normative approach to emotional difficulty instead of a diagnostic framework. ... Psychology of Emotions is a promising treatment option, delivered outside of a diagnostic framework, for young people with mild to moderate mental health difficulties seen within IAPT services.

Clark LA, et al (2020) - **Personality profiles as potential targets for intervention: Identification and replication.** Personal Ment Health. 2020 Feb;14(1):142-163. [\[ABS\]](#)

The alternative dimensional model of personality disorder (PD) diagnosis, based on personality-functioning impairment and pathological traits, opens the door for tailoring treatments to individuals with more homogeneous personality profiles than diagnostic categories. Such a **transdiagnostic** PD treatment approach requires robust, replicable, personality-relevant dimensions, which we found using a large battery of self-report measures: Self-pathology and negative affectivity (NA) traits, interpersonal pathology and detachment traits, and interpersonal pathology and antagonism traits.

Timulak L, et al (2020) - **Emotion-focused therapy as a transdiagnostic treatment for depression, anxiety and related disorders: Protocol for an initial feasibility randomised control trial.** HRB Open Res. 2020 Feb 13;3:7. [\[FULL TEXT\]](#)

Depression, anxiety and related disorders, including obsessive-compulsive disorders and trauma/stressor related disorders, have high prevalence, chronic courses and cause significant impairment. These disorders are also highly co-morbid, and appear to share etiology and maintenance factors. Recent developments have seen the emergence of transdiagnostic approaches that systematically address the common/shared features of these disorders. A key advantage of transdiagnostic approaches is that they can reduce

the pressure on mental health professionals to be proficient in a plethora of single-disorder focused treatments.

Moreton SG, et al (2020) - **Embedding existential psychology within psychedelic science: reduced death anxiety as a mediator of the therapeutic effects of psychedelics.**

Psychopharmacology (Berl). 2020 Jan;237(1):21-32. [\[ABS\]](#)

Psychedelic therapies can engender enduring improvements in psychological well-being. ...we present a novel hypothesis that reduced death anxiety may be a key mechanism underpinning the therapeutic effects of psychedelics. ... We conclude that an awareness of the role of death anxiety in psychopathology has the potential to guide future research into psychedelic therapies.

Gilbert K, et al (2020) - **Radically Open Dialectical Behavior Therapy: Social Signaling, Transdiagnostic Utility and Current Evidence.** Psychol Res Behav Manag. 2020 Jan 8;13:19-28.

[\[FULL TEXT\]](#)

At the core of an overcontrolled personality and coping style is a tendency to have too much self-control, exhibiting as behavioral and cognitive inflexibility, high inhibition of emotion, high detail-focused processing and perfectionism, and a lack of social connectedness. Overcontrol underlies a wide variety of psychiatric illnesses and as such, an innovative transdiagnostic therapy called Radically Open Dialectical Behavior Therapy (RO DBT) has been developed to treat disorders characterized by overcontrol. ...RO DBT targets maladaptive social signaling in order to help individuals "rejoin the tribe," hypothesizing that increasing social connectedness by means of targeting social signaling is the central mechanism of change in treatment. Because RO DBT is used for individuals with an overcontrolled personality style, rather than individual disordered symptoms, it can be used transdiagnostically across a range of comorbid disorders, including treatment-resistant depression and anxiety, anorexia nervosa, and personality disorders such as obsessive-compulsive personality disorder.

Aboraya A (2019) - **A plea for a transdiagnostic tool and consistent psychiatric vocabulary is answered: The Standard for Clinicians' Interview in Psychiatry (SCIP).** Asian J Psychiatr. 2019 Dec;46:41-43. [\[REF\]](#)

Ruggero CJ, et al (2019) - **Integrating the Hierarchical Taxonomy of Psychopathology (HiTOP) into clinical practice.** J Consult Clin Psychol. 2019 Dec;87(12):1069-1084. [\[FULL TEXT\]](#)

Diagnosis is a cornerstone of clinical practice for mental health care providers, yet traditional diagnostic systems have well-known shortcomings, including inadequate reliability, high comorbidity, and marked within-diagnosis heterogeneity. The Hierarchical Taxonomy of Psychopathology (HiTOP) is a data-driven, hierarchically based alternative to traditional classifications that conceptualizes psychopathology as a set of dimensions organized into increasingly broad, *transdiagnostic* spectra. Prior work has

shown that using a dimensional approach improves reliability and validity, but translating a model like HiTOP into a workable system that is useful for health care providers remains a major challenge.

Gros DF, et al (2019) - **A randomized controlled trial comparing Transdiagnostic Behavior Therapy (TBT) and behavioral activation in veterans with affective disorders.** Psychiatry Res. 2019 Nov;281:112541. [\[ABS\]](#)

This randomized controlled trial (RCT) compared the efficacy of **Transdiagnostic** Behavior Therapy (TBT) to Behavioral Activation Treatment for Depression (BATD) in veterans diagnosed with affective disorders. ...Participants demonstrated significant treatment improvements across all assessments, including measures of depression, anxiety (general, cognitive, and somatic), stress, PTSD symptoms, and transdiagnostic impairment. Group differences with small effect sizes were observed in most of the studied measures, favoring TBT compared to BATD. Together, the findings support the growing literature on the efficacy of transdiagnostic psychotherapies, compared to disorder-specific treatments (DSTs).

Ishikawa SI. et al (2019) - **Developing the Universal Unified Prevention Program for diverse disorders for school-aged children.** Child Adolesc Psychiatry Ment Health. 2019 Nov 13;13:44. [\[FULL TEXT\]](#)

Psychological problems during childhood and adolescence are highly prevalent, frequently comorbid, and incur severe social burden. A school-based universal prevention approach is one avenue to address these issues. ...We discussed current research and practical issues of using universal prevention to address mental health problems in school, based on implementation science for user-centered design.

Chalder T, et al (2019) - **Persistent physical symptoms reduction intervention: a system change and evaluation in secondary care (PRINCE secondary) - a CBT-based transdiagnostic approach: study protocol for a randomised controlled trial.** BMC Psychiatry. 2019 Oct 22;19(1):307. [\[FULL TEXT\]](#)

This trial will provide a powered evaluation of the efficacy and cost-effectiveness of a transdiagnostic CBT approach versus standard medical care for patients with persistent physical symptoms.

Khakpoor S, et al (2019) - **Emotion regulation as the mediator of reductions in anxiety and depression in the Unified Protocol (UP) for transdiagnostic treatment of emotional disorders: double-blind randomized clinical trial.** Trends Psychiatry Psychother. 2019 Oct 17;41(3):227-236. [\[ABS\]](#)

...the current study investigates the role of emotion regulation as the mediator of the treatment outcomes of therapy using the Unified Protocol (UP) for **transdiagnostic**

treatment of emotional disorders. ...Emotion regulation can be considered as a potential mediating factor and as predictive of outcomes of **transdiagnostic** treatment based on the Unified Protocol.

van Heemstra HE, et al (2019) - **7ROSES, a transdiagnostic intervention for promoting self-efficacy in traumatized refugees: a first quantitative evaluation.** Eur J Psychotraumatol. 2019 Oct 15;10(1):1673062. [[FULL TEXT](#)]

Due to traumatic experiences and highly prevalent post-migration stressors, refugees are vulnerable for developing psychopathology. ...7ROSES, a **transdiagnostic** intervention that aims to increase self-efficacy among treatment-seeking refugees in dealing with post-migration stressors. Because it can be applied by non-specialist health care workers, it can be disseminated on a large scale, thereby increasing options for psychosocial support for refugees. ...Findings provide preliminary evidence that 7ROSES could improve self-efficacy and general mental health in refugees with psychopathology.

El Bouhaddani S, et al (2019) - **Transdiagnostic school-based intervention for adolescents with early persistent psychiatric symptoms: An initial single-group effect study.** Early Interv Psychiatry. 2019 Oct;13(5):1199-1207. [[ABS](#)]

Mental health intervention programs for adolescents generally focus on specific symptoms, such as anxiety or depression. Psychiatric symptoms in adolescence are often heterogeneous, transient and shift over time. These characteristics require a **transdiagnostic** approach with emphasis on positive psychological development. This study aimed to examine the feasibility and effectiveness of Mastermind, a novel **transdiagnostic** intervention targeting general underlying mechanisms of psychiatric symptoms in adolescents.

A simple two-step school-based screening can identify adolescents with persistent psychiatric symptoms. The Mastermind **transdiagnostic** group intervention may be effective to reduce psychiatric symptoms, enhance self-esteem and lower the risk for developing psychiatric disorders.

Staples LG, et al (2019) - **Internet-delivered treatment for young adults with anxiety and depression: Evaluation in routine clinical care and comparison with research trial outcomes.** J Affect Disord. 2019 Sep 1;256:103-109. [[ABS](#)]

Mood and anxiety disorders typically emerge in adolescence and early adult life, but young adults are often reluctant to seek treatment. The Mood Mechanic course is a **transdiagnostic** internet-delivered psychological intervention for symptoms of depression and anxiety, targeted at people aged 18-24 years. ...The results show that the Mood Mechanic course is effective and acceptable in routine clinical care, and that online psychological interventions designed for young adults are an effective treatment option for this hard-to-reach group.

Gros DF (2019) - **Efficacy of Transdiagnostic Behavior Therapy across the Affective Disorders.** Am J Psychother. 2019 Sep 1;72(3):59-66. [\[ABS\]](#)

This study supports the efficacy of transdiagnostic behavior therapy across various affective disorders, including depression and PTSD. These findings suggest a possible reduction in the number of treatment protocols providers need to learn in order to treat patients with affective disorders.

Sakiris N, et al (2019) - **A systematic review and meta-analysis of the Unified Protocol as a transdiagnostic emotion regulation based intervention.** Clin Psychol Rev. 2019 Aug;72:101751. [\[ABS\]](#)

Recent advances in clinical practice emphasise transdiagnostic interventions as an effective alternative to single disorder approaches. This current systematic review and meta-analysis evaluated the treatment efficacy of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP) across internalising disorders, as an emotion regulation (ER) based intervention program. Across 15 studies and 1244 participants, large effect size reductions were found across symptoms of anxiety, depression, generalised anxiety disorder, obsessive-compulsive disorder, panic disorder with/without agoraphobia, social anxiety disorder, and borderline personality disorder. In addition, there were moderate effect sizes indicating increased use of adaptive and decreased use of maladaptive ER strategies, highlighting the UP as an effective ER based intervention. Secondary treatment benefits in functional impairment and quality of life were also evident. Implications on future transdiagnostic ER based research are discussed.

Forbes MK, et al (2019) - **Opportunities for the prevention of mental disorders by reducing general psychopathology in early childhood.** Behav Res Ther. 2019 Aug;119:103411. [\[FULL TEXT\]](#)

This paper explores the concept that reducing general psychopathology early in the life course provides unprecedented opportunities to prevent the development of all forms of psychopathology later in life. We review empirical evidence for the existence of the general factor of psychopathology and theories regarding the psychological nature of the factor. We then highlight specific examples of environmental risk factors for general psychopathology and discuss translational implications for the **transdiagnostic** prevention of psychopathology beginning in early childhood. Ultimately, we propose a developmentally informed and **transdiagnostic** stepped care approach to intervention in which reduction of general psychopathology in early childhood represents the foundational step for prevention and intervention of subsequent psychopathology. This model heralds three key benefits over the current treatment zeitgeist: (1) Reducing the burden and confusion in healthcare and education systems by providing a coherent and systematic structure for early intervention across a child's development, (2) maximising the breadth of the impact of intervention by focusing on common shared risks across psychopathology, and (3) increasing the efficiency of intervention by corresponding with

the development of psychopathology and leveraging the emergence of general psychopathology in early childhood.

Schwartz KTG, et al (2019) - **Social and Non-Social Reward: A Preliminary Examination of Clinical Improvement and Neural Reactivity in Adolescents Treated with Behavioral Therapy for Anxiety and Depression.** Front Behav Neurosci. 2019 Aug 23;13:177. [[FULL TEXT](#)]

Pediatric anxiety and depression are highly prevalent and debilitating disorders that often co-occur. Neural circuitry of reward processing has been shown to be implicated in both, and there is an emerging evidence base linking treatment response to brain patterns of reward processing. ...a successful randomized controlled trial testing the efficacy of a **transdiagnostic**, brief behavioral treatment for youth diagnosed with anxiety or depression. ..., connectivity as a function of degree of treatment response was apparent and robust.

Heckendorf H, et al (2019) - **Efficacy of an internet and app-based gratitude intervention in reducing repetitive negative thinking and mechanisms of change in the intervention's effect on anxiety and depression: Results from a randomized controlled trial.** Behav Res Ther. 2019 Aug;119:103415. [[ABS](#)]

Repetitive negative thinking (RNT) has been identified as a **transdiagnostic** process that is involved in various forms of psychopathology, including anxiety and depression. This randomized controlled trial compared a 5-week internet and app-based gratitude intervention (intervention group; IG) with adherence-focused guidance against a wait list control group (WLG) in reducing RNT in a sample with elevated RNT. ... The gratitude intervention investigated in this study was found to be effective in reducing RNT. Gratitude interventions might affect mental health by two parallel pathways: increasing resources and reducing risk factors.

Andersson G, et al (2019) - **Internet Interventions for Adults with Anxiety and Mood Disorders: A Narrative Umbrella Review of Recent Meta-Analyses.** Can J Psychiatry. 2019 Jul;64(7):465-470. [[FULL TEXT](#)]

Internet-delivered cognitive behaviour therapy (ICBT) has existed for 20 years and there are now several controlled trials for a range of problems. In this paper, we focused on recent meta-analytic reviews of the literature and found moderate to large effects reported for panic disorder, social anxiety disorder, generalized anxiety disorder, posttraumatic stress disorder, and major depression. In total, we reviewed 9 recent meta-analytic reviews out of a total of 618 meta-analytic reviews identified using our search terms. In these selected reviews, 166 studies were included, including overlap in reviews on similar conditions. We also covered a recent review on **transdiagnostic** treatments and 2 reviews on face-to-face v. internet treatment. The growing number of meta-analytic reviews of studies now suggests that ICBT works and can be as effective as face-to-face therapy.

Callesen P, et al (2019) - **A Preliminary Evaluation of Transdiagnostic Group Metacognitive Therapy in a Mixed Psychological Disorder Sample.** Front Psychol. 2019 Jun 20;10:1341. [[FULL TEXT](#)]

Objective: Comorbidity is common among anxiety and depression. **Transdiagnostic** treatment approaches have been developed to optimize treatment and offer a more unified approach suitable for individuals with comorbidities. Metacognitive therapy (MCT) is a **transdiagnostic** therapy for psychological disorder and is based on the meta-cognitive model. ... These preliminary findings support the continued use of group MCT in the current outpatient clinic and suggest that it may be an efficacious and cost-effective treatment when delivered in "transdiagnostic" groups.

Beard C, et al (2019) - **Smartphone, Social Media, and Mental Health App Use in an Acute Transdiagnostic Psychiatric Sample.** JMIR Mhealth Uhealth. 2019 Jun 7;7(6):e13364. [[FULL TEXT](#)]

The high interest in and willingness to use mental health apps, paired with the only moderate current reported usage, indicate a potential unmet treatment opportunity in psychiatric populations. There is potential to optimize non-mental health-specific apps to better support the needs of those with mental illness and to design a new wave of mental health apps that match the needs of these populations as well as the way they use smartphones in daily life.

Burton CL, et al (2019) - **Psychotherapy for the Spectrum of Sexual Minority Stress: Application and Technique of the ESTEEM Treatment Model.** Cogn Behav Pract. 2019 May;26(2):285-299. [[FULL TEXT](#)]

Converging evidence points to minority stress as a risk factor that predisposes sexual minority individuals to a variety of negative psychosocial health outcomes, particularly depression and anxiety, substance use, and sexual risk-taking. This paper outlines the techniques and theoretical underpinnings for implementing an emerging empirically supported psychotherapy targeting the **transdiagnostic** mechanisms linking minority stress with these outcomes for sexual minority clients.

Mohajerin B, et al (2019) - **Application of a transdiagnostic treatment for emotional disorders to body dysmorphic disorder: A randomized controlled trial.** J Affect Disord. 2019 Feb 15;245:637-644. [[ABS](#)]

Body dysmorphic disorder (BDD) is a common disorder which is associated with a high rate of comorbidity and functional impairment. Although research shows that cognitive-behavioral therapy can be an efficacious treatment for BDD, there is growing evidence that dysregulated emotion is a core deficit. The *Unified Protocol for the Transdiagnostic Treatment of Emotional Disorders (UP)* is a transdiagnostic, emotion focused cognitive-

behavioral therapy protocol that has been developed to target emotion regulation processes that play an important role in the development and maintenance of many emotional disorders

To our knowledge, this is the first examination of the UP for BDD, and results suggest that this disorder shares common mechanisms with other disorders of emotion, and that the UP may be an additional efficacious treatment for this condition.

Owens VAM, et al (2019) - **Transdiagnostic, internet-delivered cognitive behavior therapy for depression and anxiety: Exploring impact on health anxiety.** Internet Interv. 2019 Jan 18;15:60-66. [[FULL TEXT](#)]

Health anxiety is associated with significant personal distress and economic cost; as such, widely available and effective treatment options are crucial. Several studies suggest that Internet-delivered cognitive behavior therapy (ICBT) programs that specifically target health anxiety are efficacious for this condition.

... Following treatment, large reductions in health anxiety symptoms ..., depression, generalized anxiety, and disability ...were reported. Furthermore, results showed that **transdiagnostic** ICBT was rated as acceptable to people with high health anxiety symptoms. Despite elevated pre-treatment health anxiety scores, email correspondence between clients and their therapist revealed very few mentions of health anxiety. These findings provide preliminary evidence for **transdiagnostic** ICBT for symptoms of health anxiety and suggest further research is warranted.

Meidlinger PC, et al (2017) - **The new transdiagnostic cognitive behavioral treatments: Commentary for clinicians and clinical researchers.** J Anxiety Disord. 2017 Mar;46:101-109. [[ABS](#)]

Recognition of the limitations of the current categorical diagnostic system and increased understanding of commonalities across clinical problems associated with negative emotion, including anxiety and depression, has led to the development of **transdiagnostic** psychological interventions. This new approach holds promise in shifting our emphasis from diagnostic categories to treating core construct that cut across disorders.

Traumatic Brain Injury

McCormick BF, et al (2020) - **Mild Traumatic Brain Injury as a Predictor of Classes of Youth Internalizing and Externalizing Psychopathology.** Child Psychiatry Hum Dev. 2020 May 5. [[ABS](#)]

Mild traumatic brain injury (mTBI), is a developing public health problem. Evidence

suggests that youth who suffer a mTBI experience worse outcomes than similar adults. ... The results of the current study suggest that mTBI may be an important transdiagnostic risk factor associated with developmental patterns of internalizing and externalizing psychopathology.

Uncertainty ▲

Yao N, et al (2020) - **The Influence of Intolerance of Uncertainty on Anxiety and Depression Symptoms in Chinese-speaking Samples: Structure and Validity of The Chinese Translation of The Intolerance of Uncertainty Scale.** J Pers Assess. 2020 Mar 27:1-10. [\[ABS\]](#)

... contemporary theory of intolerance of uncertainty (IU) has emphasized the role of IU as the basic transdiagnostic mechanism underlying emotional disorders, and further empirical support is awaited. ... Using the bifactor model of the IUS-12 (Chinese translation), the hierarchical model of IU affecting anxiety and depression via neuroticism was supported.

Wheaton MG, et al (2020) - **Intolerance of uncertainty and obsessive-compulsive personality disorder.** Personal Disord. 2020 Feb 17. doi: 10.1037/per0000396. [\[ABS\]](#)

Intolerance of uncertainty (IU) has been investigated as a transdiagnostic factor linked to many conditions, including anxiety disorders and obsessive-compulsive disorder (OCD). ...Intolerance of uncertainty (IU) significantly mediated the relationship between OCPD traits and reduced quality of life. These results highlight the importance of considering IU in the context of OCPD, with possible implications for improving treatment. Limitations and future directions for research are discussed.

Kesby A, et al (2019) - **Intolerance of uncertainty and eating disorder behaviour: Piloting a consumption task in a non-clinical sample.** J Behav Ther Exp Psychiatry. 2019 Dec;65:101492. [\[ABS\]](#)

Intolerance of uncertainty (IU) is a **transdiagnostic** process contributing to the maintenance of anxiety disorders, and is a potential target for treatment. Recent literature has investigated IU as a cognitive process underpinning pathological fear and anxiety in Anorexia Nervosa (AN). ...Trait IU was correlated with cognitive rigidity, worry, global eating disorder symptoms, and, in particular, dietary restraint. Should these findings be replicated in a clinical sample, then IU might emerge as an adjunctive treatment target for AN.

McEvoy PM, et al (2019) - **The impact of methodological and measurement factors on transdiagnostic associations with intolerance of uncertainty: A meta-analysis.** Clin Psychol Rev. 2019 Nov;73:101778. [\[ABS\]](#)

Intolerance of uncertainty is a dispositional trait associated with a range of psychological disorders, ... The first aim of this meta-analysis was to quantify the strengths of the association between IU and symptoms of generalised anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, obsessive compulsive disorder, depression, and eating disorders. ... The results indicate that IU has robust, moderate associations with a range of disorder symptoms, providing definitive evidence for the **transdiagnostic** nature of IU.

Sadeh N, et al (2019) - **Engaging in Risky and Impulsive Behaviors to Alleviate Distress Mediates Associations between Intolerance of Uncertainty and Externalizing Psychopathology.** J Pers Disord. 2019 Nov 4;1-16. [\[ABS\]](#)

Despite increasing recognition that intolerance of uncertainty is a **transdiagnostic** dimension of psychopathology, very little research has investigated its relevance for externalizing psychopathology and related risky/impulsive behavior. ...Relations between intolerance of uncertainty and externalizing symptoms/risky behaviors were mediated by a motivation to engage in these behaviors to avoid distress, but not by the motivation to experience pleasurable emotions. Findings suggest that difficulty tolerating uncertainty may confer risk for the externalizing spectrum of psychopathology by increasing the likelihood that an individual will engage in risky behaviors to alleviate distressing or unpleasant emotions.

Raines AM, et al (2019) - **Intolerance of uncertainty and DSM-5 PTSD symptoms: Associations among a treatment seeking veteran sample.** J Anxiety Disord. 2019 Mar;62:61-67. [\[ABS\]](#)

Results revealed that IU (Intolerance of uncertainty) was significantly associated with overall PTSD symptom severity, above and beyond relevant covariates. Further, IU was significantly associated with the PTSD avoidance and hyperarousal clusters. Prospective IU, rather than inhibitory IU, accounted for these unique associations. These findings add to a growing body of literature establishing IU as a **transdiagnostic** risk factor and point to the importance of future research on the role of IU in contributing to and/or maintaining PTSD symptoms.

Correa KA, et al (2019) - **The role of intolerance of uncertainty in current and remitted internalizing and externalizing psychopathology.** J Anxiety Disord. 2019 Mar;62:68-76. [\[ABS\]](#)

Intolerance of Uncertainty ...was more consistently related to fear disorders, demonstrated incremental validity over and above the effects of neuroticism/negative affectivity, and may be a key, transdiagnostic mechanism in fear disorders.

Bottesi G, et al (2019) - **Seeking certainty about Intolerance of Uncertainty: Addressing old and new issues through the Intolerance of Uncertainty Scale-Revised.** PLoS One. 2019 Feb 11;14(2):e0211929. [\[FULL TEXT\]](#)

Intolerance of Uncertainty is a **transdiagnostic** process that spans a range of emotional disorders and it is usually measured through the Intolerance of Uncertainty Scale-12. ... In light of the promising psychometric properties, the use of the Italian Intolerance of Uncertainty Scale-Revised as a univocal measure is encouraged in both research and clinical practice.

Rodgers J, et al (2016) - **Towards a Treatment for Intolerance of Uncertainty in Young People with Autism Spectrum Disorder: Development of the Coping with Uncertainty in Everyday Situations (CUES©) Programme.** J Autism Dev Disord. 2016 Oct 28. [[ABS](#)]

Intolerance of uncertainty (IU) is indicated as an important transdiagnostic process variable in a range of anxiety disorders. Anxiety is very common in children with autism spectrum disorders (ASD). This study aimed to develop a parent group based manualized treatment programme for young people with ASD, which focused on IU.

Hoven M, et al (2019) - **Abnormalities of confidence in psychiatry: an overview and future perspectives.** Transl Psychiatry. 2019 Oct 21;9(1):268. [[FULL TEXT](#)]

We hypothesize a dysfunction of confidence at the root of psychiatric symptoms either expressed subclinically in the general population or clinically in the patient population. Our review reveals a robust association between confidence abnormalities and psychiatric symptomatology. Confidence abnormalities are present in subclinical/prodromal phases of psychiatric disorders, show a positive relationship with symptom severity, and appear to normalize after recovery. In the reviewed literature, the strongest evidence was found for a decline in confidence in (sub)clinical OCD, and for a decrease in confidence discrimination in (sub)clinical schizophrenia. We found suggestive evidence for increased/decreased confidence in addiction and depression/anxiety, respectively. Confidence abnormalities may help to understand underlying psychopathological substrates across disorders, and should thus be considered transdiagnostically.

Tay AK, et al (2019) - **Theoretical background, first stage development and adaptation of a novel Integrative Adapt Therapy (IAT) for refugees.** Epidemiol Psychiatr Sci. 2019 Aug 23;29:e47. [[ABS](#)]

Refugees are confronted with the task of adapting to the long-term erosion of psychosocial systems and institutions that in stable societies support psychological well-being and mental health. We provide an overview of the theoretical principles and practical steps taken to develop a novel psychotherapeutic approach, Integrative Adapt Therapy (IAT), which aims to assist refugees to adapt to these changes

Castriotta N, et al (2019) - **Intolerance of uncertainty in hoarding disorder.** J Obsessive Compuls Relat Disord. 2019 Apr;21:97-101. [[FULL TEXT](#)]

Intolerance of uncertainty (IU) has been proposed as a **transdiagnostic** risk and maintenance factor underlying various forms of psychopathology. ... IU was positively and significantly associated with greater urges to acquire and greater difficulties discarding possessions, beyond shared variance accounted for by anxiety and depression. Higher pre-treatment IU predicted increased odds of treatment non-response. CONCLUSIONS: Elevated IU is associated with specific hoarding symptom clusters and may be an important target for HD treatment.

Price RB, et al (2018) - **Towards personalized, brain-based behavioral intervention for transdiagnostic anxiety: Transient neural responses to negative images predict outcomes following a targeted computer-based intervention.** J Consult Clin Psychol. 2018 Dec;86(12):1031-1045.

[\[FULL TEXT\]](#)

Excessive attentional deployment toward threat is a **transdiagnostic** dimension of anxiety seen at both initial and sustained stages of threat processing. However, group-level observations of these phenomena mask considerable within-group heterogeneity that has been linked to treatment outcomes, suggesting that a **transdiagnostic**, individual differences approach may capture critical, clinically relevant information.

Seventy clinically anxious individuals were randomized to receive 8 sessions of **attention bias modification** (ABM) ; ... a computer-based mechanistic intervention that specifically targets initial stages of threat processing, or a sham control ... fMRI ...Larger transient responses across a wide range of cognitive-affective regions (e.g., ventrolateral prefrontal cortex, anterior cingulate cortex, amygdala) predicted better clinical outcomes following ABM, in both a priori anatomical regions and whole-brain analyses; sustained responses did not.

Neural alterations occurring on the relatively transient timescale that is specifically targeted by ABM predict favorable clinical outcomes. Results inform how to *expand on the initial promise of neurocognitive treatments* like ABM by fine-tuning their clinical indications (e.g., *through personalized mechanistic intervention relevant across diagnoses*) and *by increasing the range of mechanisms that can be targeted* (e.g., through synergistic treatment combinations and/or novel neurocognitive training protocols designed to tackle identified predictors of nonresponse).

McEvoy PM, et al (2016) - **The search for universal transdiagnostic and trans-therapy change processes: Evidence for intolerance of uncertainty.** J Anxiety Disord. 2016 Jun;41:96-107. [\[ABS\]](#)

Carleton RN (2016) - **Fear of the unknown: One fear to rule them all?** J Anxiety Disord. 2016 Jun;41:5-21. [\[FULL TEXT\]](#)

Oglesby ME, et al (2016) - **Interpretation bias for uncertain threat: A replication and extension.** J Behav Ther Exp Psychiatry. 2016 Jun;51:35-42. [\[ABS\]](#)

These findings are the first to detect the presence of a negative interpretation bias for uncertain information among individuals high in IU utilizing a task designed to directly measure an individual's interpretation of information. Given the efficacy and low economic burden associated with interpretation bias modification protocols, and the transdiagnostic nature of IU, targeting IU within these protocols could have a tremendous public health impact.

Hulst BMV, et al (2017) - **What to expect and when to expect it: an fMRI study of expectancy in children with ADHD symptoms.** Eur Child Adolesc Psychiatry. 2017 May;26(5):583-590. [[FULL TEXT](#)]

Morriss J, et al (2016) - **What Is Going On Around Here? Intolerance of Uncertainty Predicts Threat Generalization.** PLoS One, Published: May 11, 2016. [[FULL TEXT](#)]

Kim MK, et al (2016) - **Impact of Mindfulness-Based Cognitive Therapy on Intolerance of Uncertainty in Patients with Panic Disorder.** Psychiatry Investig. 2016 Mar;13(2):196-202. [[FULL TEXT](#)]

IU may play a critical role in the diagnosis and treatment of panic disorder. MBCT is effective in lowering IU in patients with panic disorder.

Kim MK, et al (2016) - **Impact of Mindfulness-Based Cognitive Therapy on Intolerance of Uncertainty in Patients with Panic Disorder.** Psychiatry Investig. 2016 Mar;13(2):196-202. [[FULL TEXT](#)]

IU may play a critical role in the diagnosis and treatment of panic disorder. MBCT is effective in lowering IU in patients with panic disorder.

Einstein DA (2014) - **Extension of the Transdiagnostic Model to Focus on Intolerance of Uncertainty: A Review of the Literature and Implications for Treatment.** Clin Psychol (New York). 2014 Sep;21(3):280-300. [[FULL TEXT](#)]

Carleton RN (2016) - **Into the unknown: A review and synthesis of contemporary models involving uncertainty.** J Anxiety Disord. 2016 Apr;39:30-43. [[FULL TEXT](#)]

Mahoney AE, et al (2012) - **A transdiagnostic examination of intolerance of uncertainty across anxiety and depressive disorders.** Cogn Behav Ther. 2012;41(3):212-22. [[ABS](#)]

Intolerance of uncertainty (IU) has been identified as a potential maintaining factor for generalised anxiety disorder; however, there is a growing evidence to suggest that IU may contribute to other anxiety and depressive disorders. Moreover, certain components of IU (namely prospective and inhibitory IU) have been shown to be differentially associated with symptoms of emotional disorders. The aim of this study was to determine the extent to which individuals with various anxiety and depressive

disorders endorsed IU, firstly as a trait variable (with prospective and inhibitory components) and secondly in reference to regularly occurring, diagnostically relevant situations (situation-specific IU). The degree to which diagnosis predicted IU was examined in a highly comorbid clinical sample (N=218). Regardless of specific diagnoses, the degree of comorbidity emerged as a significant predictor of prospective IU and situation-specific IU. Conversely, specific diagnoses of social phobia, generalized anxiety disorder, depression, and obsessive compulsive disorder were uniquely related to inhibitory IU. These findings suggest that IU is a transdiagnostic construct and have implications for current diagnosis-specific and transdiagnostic theory and clinical practice.

Boswell JF, et al (2013) - **Intolerance of uncertainty: a common factor in the treatment of emotional disorders.** J Clin Psychol. 2013 Jun;69(6):630-45. [\[FULL TEXT\]](#)

Change in IU can be observed across problem areas in transdiagnostic treatment and such change is correlated with treatment outcome.

Appendix A – General References ▲

Keshavan MS (2021) - **Characterizing transdiagnostic premorbid biotypes can help progress in selective prevention in psychiatry.** World Psychiatry. 2021 Jun;20(2):231-232. [\[FULL TEXT\]](#)

Fusar-Poli P, et al (2021) - **Preventive psychiatry: a blueprint for improving the mental health of young people.** World Psychiatry. 2021 Jun;20(2):200-221. [\[FULL TEXT\]](#)

Geoffrion S, et al (2021) - **Psychosocial Profiles of Patients Admitted to Psychiatric Emergency Services: Results from the Signature Biobank Project** Can J Psychiatry. 2021 May 20:7067437211018793. [\[ABS\]](#)

Our results suggest that a transdiagnostic approach allows to highlight distinct clinical portraits of patients admitted to psychiatric emergency services. Importantly, developmental factors were predictive of specific profiles. Such transdiagnostic approach is a first step towards precision medicine, which could lead to develop targeted interventions.

Mauri M, et al (2020) - **The utility of NIRS technology for exploring emotional processing in children.** J Affect Disord. 2020 Sep 1;274:819-824. [\[ABS\]](#)

Deficits in emotional processing and, in particular, in emotional self-regulation represent non-specific risk factors for transdiagnostic poor outcomes. ...Researches have been

focusing on the investigation of possible emotional processing and regulation biomarkers. ...NIRS seems a reliable tool to describe brain activation during emotional processing and regulation. Moreover, it seems to be particularly useful in studies including either developmental-aged participants or clinical samples, due to its clear advantages and non-intrusiveness, offering a potential marker for deficits in emotional processing and regulation. ...All the works revised found significant associations between NIRS data and emotional indexes.

Duyser FA, et al (2020) - **Negative memory bias as a transdiagnostic cognitive marker for depression symptom severity.** J Affect Disord. 2020 Sep 1;274:1165-1172. [\[ABS\]](#)

Negative memory bias is a strong risk factor for the development and maintenance of depression. Recent evidence also found negative memory bias in other mental disorders. ...Negative memory bias is characteristic of a depressotypic processing style and present in different mental disorders. It might play a mechanistic role in the development of (subclinical) co-occurrence between mental disorders.

Feola B, et al (2020) - **Evidence for inhibited temperament as a transdiagnostic factor across mood and psychotic disorders.** J Affect Disord. 2020 Sep 1;274:995-1003. [\[ABS\]](#)

The conceptualization of risk for psychiatric illness is moving from risk factors for specific psychiatric disorders to factors that confer risk for multiple disorders. One potential transdiagnostic risk factor is inhibited temperament, a trait characterized by a fearful **or avoidant response to novelty**. Inhibited temperament is an established risk factor for anxiety disorders, and evidence suggests inhibited temperament is elevated in schizophrenia, bipolar disorder, and major depressive disorder. ...Inhibited temperament was similarly elevated in all patient groups compared to controls. Inhibited temperament was similarly associated with anxiety, depression, negative affect, and quality of life across patient groups.

Romanowska S, et al (2020) - **Social and role functioning in youth at risk of serious mental illness.** Early Interv Psychiatry. 2020 Aug;14(4):463-469. [\[ABS\]](#)

AIM: Functional impairment is common in serious mental illness (SMI). This study assessed social and role functioning in a sample of youth at risk of SMI who met different stages of risk based on a transdiagnostic clinical staging model described by McGorry and colleagues. ... This study demonstrates that mild to moderate functional impairments are present in young people experiencing subthreshold psychiatric symptoms and distress in the absence of a diagnosable mental illness. Results partially validate the model in that social although not role functioning declines across the stages.

Bernstein EE, et al (2020) - **Mnemonic discrimination in treatment-seeking adults with and without PTSD.** Behav Res Ther. 2020 Aug;131:103650. [\[ABS\]](#)

Posttraumatic stress disorder (PTSD) is characterized by overgeneralized emotional reactivity following a trauma. Similarities between current, safe contexts and past, threatening events trigger recurrent, distressing responses and can contribute to a host of symptoms, including reexperiencing and hypervigilance. Mnemonic discrimination, a component process of episodic memory, could promote overgeneralization when impaired. Mnemonic discrimination reflects the integration of old and new experiences and one's ability to differentiate them despite their similarities. ...Findings suggest that poor mnemonic discrimination is transdiagnostically associated with emotional disorders. Future work is merited to explore this as a measurable and potentially malleable, though non-specific, risk factor.

Dryburgh NSJ, et al (2020) - **Evidence Base Update for Measures of Social Skills and Social Competence in Clinical Samples of Youth.** J Clin Child Adolesc Psychol. 2020 Jul 22;1-23. [[ABS](#)]

Social skills and social competence are key transdiagnostic processes in developmental psychopathology and are the focus of an array of clinical interventions. In this Evidence Base Update, we evaluated the psychometric properties of measures of social skills and social competence used with clinical samples of children and adolescents. ...these measures had adequate to excellent norms, internal consistency, and test-retest reliability. There was at least adequate evidence of construct validity and treatment sensitivity in clinical samples for nearly all measures assessed.

Nakamura M, et al (2020) - **Orbitofrontal Sulcogyral Pattern as a Transdiagnostic Trait Marker of Early Neurodevelopment in the Social Brain.** Clin EEG Neurosci. 2020 Jul;51(4):275-284. [[FULL TEXT](#)]

Brinn A, et al (2020) - **Neutrophil-lymphocyte ratio across psychiatric diagnoses: a cross-sectional study using electronic health records.** BMJ Open. 2020 Jul 19;10(7):e036859. [[FULL TEXT](#)]

Neutrophil-lymphocyte ratio (NLR) was elevated compared with controls in patients with diagnoses including dementia, alcohol dependence, schizophrenia, bipolar affective disorder, depression, non-phobic anxiety disorders and mild mental retardation ($p < 0.05$). NLR also correlated with age, antipsychotic use and hypnotic use. NLR was found to be higher in individuals of 'white' ethnicity and lower in individuals of 'black' ethnicity. ...Elevated NLR may reflect a transdiagnostic pathological process occurring in a subpopulation of psychiatric patients. NLR may be useful to identify and stratify patients who could benefit from adjunctive anti-inflammatory treatment.

Tasa-Vinyals E, et al (2020) - **Intimate Partner Violence among Patients Diagnosed with Severe Mental Disorder.** J Nerv Ment Dis. 2020 Jul 10. [[ABS](#)]

Intimate partner violence (IPV) has a remarkable impact on mental health and is common in people diagnosed with severe mental disorders (SMDs)... Female gender and

childhood trauma significantly increased the likelihood of IPV victimization. Gender, childhood trauma, and SMD are relevant factors in IPV analysis and prevention. Diathesis of trauma, psychosocial vulnerability to revictimization and intersectional feminist theory help explain our results.

Edmiston EK, et al (2020) - **Assessing Relationships Among Impulsive Sensation Seeking, Reward Circuitry Activity, and Risk for Psychopathology: A Functional Magnetic Resonance Imaging Replication and Extension Study.** Biol Psychiatry Cogn Neurosci Neuroimaging. 2020 Jul;5(7):660-668. [\[FULL TEXT\]](#)

High trait impulsive sensation seeking (ISS), the tendency to engage in behavior without forethought and to seek out new or extreme experiences, is a transdiagnostic risk factor for externalizing and mood disorders, particularly bipolar disorder. .. We replicated findings showing that reward expectancy-related left ventro-lateral prefrontal cortex (L vLPFC) activity is a biomarker for negative urgency, the tendency to react with frustration during distressing conditions. Negative urgency also statistically mediated the relationship between L vLPFC activity and measures indicative of hypomanic symptoms.

Wolock ER, et al (2020) - **Chronic Illness and Internalizing Symptomatology in a Transdiagnostic Clinical Sample of Youth.** J Pediatr Psychol. 2020 Jul 1;45(6):633-642. [\[ABS\]](#)

Having multiple chronic illnesses may elevate children's risk of depression symptomatology, even in comparison to other children seeking mental health care. This suggests a need to identify factors that may exacerbate depression symptoms in physically ill children who are initiating therapy and to determine whether different or more intensive services may be helpful for this group.

Romer AL, et al (2020) - **Pervasively Thinner Neocortex as a Transdiagnostic Feature of General Psychopathology.** Am J Psychiatry. 2020 Jun 30:appiajp202019090934. [\[ABS\]](#)

A pattern of pervasively reduced neocortical thickness appears to be common across all forms of mental disorders and may represent a transdiagnostic feature of general psychopathology. As has been documented with regard to symptoms and diagnoses, the underlying brain structural correlates of mental disorders may not exhibit specificity, and the continued pursuit of such specific correlates may limit progress toward more effective strategies for etiological understanding, prevention, and intervention.

Balabanovic J, et al (2020) - **Engaging patients with "medically unexplained symptoms" in psychological therapy: An integrative and transdiagnostic approach.** Psychol Psychother. 2020 Jun;93(2):347-366. [\[ABS\]](#)

Kramer E, et al (2020) - **Diagnostic Associations of Processing Speed in a Transdiagnostic Pediatric Sample.** Sci Rep. 2020 Jun 22;10(1):10114. [\[FULL TEXT\]](#)

Our examination of PS in a large, transdiagnostic sample suggested more specific associations with ADHD and learning disorders than the literature currently suggests. Implications for understanding how PS interacts with a highly heterogeneous childhood sample are discussed.

Cauda F, et al (2020) - **Hubs of long-distance co-alteration characterize brain pathology.** Hum Brain Mapp. 2020 Jun 20. [[ABS](#)]

It is becoming clearer that the impact of brain diseases is more convincingly represented in terms of co-alterations rather than in terms of localization of alterations. In this context, areas characterized by a long mean distance of co-alteration may be considered as hubs with a crucial role in the pathology.

The anterodorsal prefrontal cortices appeared to be a transdiagnostic hub of long-distance co-alterations. Also, the disease-specific analyses showed that long-distance co-alterations are more able than classic meta-analyses to identify areas involved in pathology and symptomatology. Moreover, the distance maps were correlated with the normative connectivity. Our findings substantiate the network degeneration hypothesis in brain pathology. At the same time, they suggest that the concept of co-alteration might be a useful tool for clinical neuroscience.

Roque AD, et al (2020) - **Stress-induced cortisol reactivity as a predictor of success in treatment for affective dimensions.** Psychoneuroendocrinology. 2020 Jun;116:104646. [[ABS](#)]

Response rates to first-line treatments for depression and anxiety remain unsatisfactory. Identification of predictors or moderators that can optimize treatment matching is of scientific and clinical interest. ...Cortisol reactivity was related to treatment outcome, with average and higher levels of stress-induced cortisol response predicting greater decreases in symptoms throughout treatment and 6-month follow-up. ...Future studies should investigate how to enhance this therapeutic benefit through capitalizing on endogenous diurnal fluctuations or exogenous cortisol manipulation.

Harden KP, et al (2020) - **Genetic Associations between Executive Functions and a General Factor of Psychopathology.** J Am Acad Child Adolesc Psychiatry. 2020 Jun;59(6):749-758. [[FULL TEXT](#)]

Symptoms of psychopathology covary across diagnostic boundaries, and a family history of elevated symptoms for a single psychiatric disorder places an individual at heightened risk for a broad range of other psychiatric disorders. ...General Executive Functions and General Intelligence robustly index genetic risk for **transdiagnostic** symptoms of psychopathology in childhood. Delineating the developmental and neurobiological mechanisms underlying observed associations between cognitive abilities and psychopathology remains a priority for ongoing research.

Shah JL, et al (2020) - **Transdiagnostic clinical staging in youth mental health: a first international consensus statement.** World Psychiatry. 2020 Jun;19(2):233-242. [\[FULL TEXT\]](#)

Recognizing that current frameworks for classification and treatment in psychiatry are inadequate, particularly for use in young people and early intervention services, transdiagnostic clinical staging models have gained prominence. These models aim to identify where individuals lie along a continuum of illness, to improve treatment selection and to better understand patterns of illness continuity, discontinuity and aetiopathogenesis.

Melero S, et al (2020) - **How Does Perfectionism Influence the Development of Psychological Strengths and Difficulties in Children?** Int J Environ Res Public Health. 2020 Jun 8;17(11):4081. [\[FULL TEXT\]](#)

Results showed that 27.6% of the children belonged to the high perfectionism group, characterized by an elevated Socially Prescribed Perfectionism (SPP). Compared to girls, boys presented higher scores in all perfectionism measures. The younger children presented higher SPP and lower Self-oriented Perfectionism-Critical (SOP-Critical) than the older group. High perfectionism was related to psychological problems. The SOP-Critical increased the likelihood of developing emotional symptoms and total difficulties, and SPP was associated with behavioral and peer problems. In contrast, Self-oriented Perfectionism-Striving (SOP-Striving) was related to greater prosocial behavior. This research has important implications for the design of transdiagnostic strategies targeting the prevention and intervention of psychological difficulties in schoolchildren.

Thomas PJ, et al (2020) - **Graph theoretical measures of the uncinate fasciculus subnetwork as predictors and correlates of treatment response in a transdiagnostic psychiatric cohort.** Psychiatry Res Neuroimaging. 2020 May 30;299:111064. [\[FULL TEXT\]](#)

The internalizing psychopathologies (IP) are a highly prevalent group of disorders for which little data exists to guide treatment selection. We examine whether graph theoretical metrics from white matter connectomes may serve as biomarkers of disease and predictors of treatment response. We focus on the uncinate fasciculus subnetwork, which has been previously implicated in these disorders.

Of note, right amygdala betweenness centrality was increased in patients relative to controls. In addition, white matter integrity of the uncinate fasciculus was decreased at baseline in patients versus controls. The SSRI and CBT cohorts had increased left frontal superior orbital betweenness centrality and left frontal medial orbital clustering coefficient, respectively, suggesting the presence of treatment specific neural correlates of treatment response. This study provides insight on shared white matter network features of IPs and elucidates potential biomarkers of treatment response that may be

modality-specific.

Li T, et al (2020) - **Mapping common grey matter volume deviation across child and adolescent psychiatric disorders**. *Neurosci Biobehav Rev*. 2020 May 30;115:273-284. [[ABS](#)]

Childhood and adolescence represent a time notable for the emergence of many psychiatric disorders, where comorbidity and co-occurrence of symptoms are well-documented. ...Compared to healthy peers, youth psychiatric disorders are characterized by reduced grey matter volume (GMV) of amygdala and lateral orbitofrontal cortex and enhanced GMV of ventromedial prefrontal cortex and precuneus. ... These regions and their networks mapped onto systems implicated in negative valence, positive valence, as well as social and cognitive functioning. Together, our findings are consistent with transdiagnostic models of psychopathology, uncovering common structural disturbance across youth psychiatric disorders, potentially reflecting an intermediate transdiagnostic phenotype in association with broad dimensions of youth psychopathology.

Doucet GE, et al (2020) - **Transdiagnostic and disease-specific abnormalities in the default-mode network hubs in psychiatric disorders: A meta-analysis of resting-state functional imaging studies**. *Eur Psychiatry*. 2020 May 29;63(1):e57. [[FULL TEXT](#)]

BACKGROUND. The default mode network (DMN) dysfunction has emerged as a consistent biological correlate of multiple psychiatric disorders. Specifically, there is evidence of alterations in DMN cohesiveness in schizophrenia, mood and anxiety disorders. The aim of this study was to synthesize at a fine spatial resolution the intra-network functional connectivity of the DMN in adults diagnosed with schizophrenia, mood and anxiety disorders, capitalizing on powerful meta-analytic tools provided by activation likelihood estimation. **METHODS.** Results from 70 whole-brain resting-state functional magnetic resonance imaging articles published during the last 15 years were included comprising observations from 2,789 patients and 3,002 healthy controls. **RESULTS.** Specific regional changes in DMN cohesiveness located in the anteromedial and posteromedial cortex emerged as shared and trans-diagnostic brain phenotypes. Disease-specific dysconnectivity was also identified. Unmedicated patients showed more DMN functional alterations, highlighting the importance of interventions targeting the functional integration of the DMN. **CONCLUSION.** This study highlights functional alteration in the major hubs of the DMN, suggesting common abnormalities in self-referential mental activity across psychiatric disorders.

Restrepo A, et al (2020) - **Problematic internet use in children and adolescents: associations with psychiatric disorders and impairment**. *BMC Psychiatry*. 2020 May 27;20(1):252. [[FULL TEXT](#)]

BACKGROUND: Problematic internet use (PIU) is an increasingly worrisome issue, as youth population studies are establishing links with internalizing and externalizing problems. ...PIU was positively associated with depressive disorders... the combined

presentation of ADHD, Autism Spectrum Disorder, greater levels of impairment and increased sleep disturbances. ... The association between PIU and psychopathology, as well as its impact on impairment and sleep disturbances, highlight the urgent need to gain an understanding of mechanisms in order to inform public health recommendations on internet use in U.S. youth.

Vismara M, et al (2020) - **Is cyberchondria a new transdiagnostic digital compulsive syndrome? A systematic review of the evidence.** Compr Psychiatry. 2020 May;99:152167. [[ABS](#)]

BACKGROUND: Cyberchondria (CYB) has been described relatively recently as a behavior characterized by excessive online searching for medical information that is associated with increasing levels of health anxiety. ...CYB showed a self-reported association with health anxiety, hypochondriasis and obsessive-compulsive disorder (OCD) as well as other forms of problematic usage of the internet (PIU). The psychological mechanisms associated with CYB include low self-esteem, anxiety sensitivity, intolerance of uncertainty, pain catastrophizing and certain meta-cognitive beliefs. ... CYB represents a clinically relevant transdiagnostic compulsive behavioral syndrome, closely related to PIU and usually presenting in association with health anxiety, hypochondriasis and/or OCD. CYB is clearly in need of further study and we identify key areas for future research.

Haidl TK, et al (2020) - **Validation of the Bullying Scale for Adults - Results of the PRONIA-study.** J Psychiatr Res. 2020 May 11;129:88-97. [[ABS](#)]

Bullying as a specific subtype of adverse life events is a major risk factor for poor mental health. ...
Bullying experiences were significantly less frequent in healthy controls than in patient groups...
Four factors were identified: 1. Sexual harassment, 2. Emotional Abuse, 3. Physical Abuse, 4. Problems at school. ...The Bullying Scale for Adults can be used to assess bullying as a transdiagnostic risk factor of mental disorders in different mental disorders, esp. psychosis and depression.

Nogovitsyn N, et al (2020) - **Aberrant limbic brain structures in young individuals at risk for mental illness.** Psychiatry Clin Neurosci. 2020 May;74(5):294-302. [[ABS](#)]

Alterations in limbic structures may be present before the onset of serious mental illness, but whether subfield-specific limbic brain changes parallel stages in clinical risk is unknown. To address this gap, we compared the hippocampus, amygdala, and thalamus subfield-specific volumes in adolescents at various stages of risk for mental illness. ... Aberrant subfield-specific changes within the limbic system may serve as biological evidence to support transdiagnostic clinical staging in mental illness. Differential patterns of volume deficits characterize those at risk for mental illness and may be indicative of a risk-stage progression.

Opel N, et al (2020) - **Cross-Disorder Analysis of Brain Structural Abnormalities in Six Major Psychiatric Disorders: A Secondary Analysis of Mega- and Meta-analytical Findings From the ENIGMA Consortium.** Biol Psychiatry. 2020 May 11:S0006-3223(20)31585-7. [\[ABS\]](#)

Neuroimaging studies have consistently reported similar brain structural abnormalities across different psychiatric disorders. ...Brain structural abnormalities in major depressive disorder, bipolar disorder, schizophrenia, and obsessive-compulsive disorder were highly correlated ($r = .443$ to $r = .782$), and one shared latent underlying factor explained between 42.3% and 88.7% of the brain structural variance of each disorder. The observed shared morphometric signature of these disorders showed little similarity with brain structural patterns related to physiological aging. In contrast, patterns of brain structural abnormalities independent of all other disorders were observed in both attention-deficit/hyperactivity disorder and autism spectrum disorder.

Luyten P, et al (2020) - **The Mentalizing Approach to Psychopathology: State of the Art and Future Directions.** Annu Rev Clin Psychol. 2020 May 7;16:297-325. [\[ABS\]](#)

Mentalizing is the capacity to understand others and oneself in terms of internal mental states. It is assumed to be underpinned by four dimensions: automatic-controlled, internally-externally focused, self-other, and cognitive-affective. Research suggests that mental disorders are associated with different imbalances in these dimensions. Addressing the quality of mentalizing as part of psychosocial treatments may benefit individuals with various mental disorders. We suggest that mentalizing is a helpful transtheoretical and transdiagnostic concept to explain vulnerability to psychopathology and its treatment.

Taquet M, et al (2020) - **A structural brain network of genetic vulnerability to psychiatric illness.** Mol Psychiatry. 2020 May 6. [\[ABS\]](#)

Psychiatry is undergoing a paradigm shift from the acceptance of distinct diagnoses to a representation of psychiatric illness that crosses diagnostic boundaries. How this transition is supported by a shared neurobiology remains largely unknown. In this study, we first identify single nucleotide polymorphisms (SNPs) associated with psychiatric disorders based on 136 genome-wide association studies. We then conduct a joint analysis of these SNPs and brain structural connectomes in 678 healthy children in the PING study. We discovered a strong, robust, and transdiagnostic mode of genome-connectome covariation which is positively and specifically correlated with genetic risk for psychiatric illness at the level of individual SNPs. Similarly, this mode is also significantly positively correlated with polygenic risk scores for schizophrenia, alcohol use disorder, major depressive disorder, a combined bipolar disorder-schizophrenia phenotype, and a broader cross-disorder phenotype, and significantly negatively correlated with a polygenic risk score for educational attainment. The resulting "vulnerability network" is shown to mediate the influence of genetic risks onto behaviors related to psychiatric vulnerability (e.g., marijuana, alcohol, and caffeine misuse,

perceived stress, and impulsive behavior). Its anatomy overlaps with the default-mode network, with a network of cognitive control, and with the occipital cortex. These findings suggest that the brain vulnerability network represents an endophenotype funneling genetic risks for various psychiatric illnesses through a common neurobiological root. It may form part of the neural underpinning of the well-recognized but poorly explained overlap and comorbidity between psychiatric disorders.

Gillan CM, et al (2020) - **Carving Out New Transdiagnostic Dimensions for Research in Mental Health**. Biol Psychiatry Cogn Neurosci Neuroimaging. 2020 Apr 30:S2451-9022(20)30107-5. [\[ABS\]](#)

Schwarz K, et al (2020) - **Transdiagnostic Prediction of Affective, Cognitive, and Social Function Through Brain Reward Anticipation in Schizophrenia, Bipolar Disorder, Major Depression, and Autism Spectrum Diagnoses**. Schizophr Bull. 2020 Apr 10;46(3):592-602. [\[FULL TEXT\]](#)

The relationship between transdiagnostic, dimensional, and categorical approaches to psychiatric nosology is under intense debate. To inform this discussion, we studied neural systems linked to reward anticipation across a range of disorders and behavioral dimensions. ...We found that blunted ventral striatum (vST) responses were present in SZ, BP, and ASD but not in MD. Activation within the vST predicted individual differences in affective, cognitive, and social functioning across diagnostic boundaries. Network alterations extended beyond the reward network to include regions implicated in executive control. We further confirmed the robustness of our results in various control analyses. ..Our findings suggest that altered brain responses during reward anticipation show transdiagnostic alterations that can be mapped onto dimensional measures of functioning. They also highlight the role of executive control of reward and salience signaling in the disorders we study and show the power of systems-level neuroscience to account for clinically relevant behaviors.

Ma Q, et al (2020) - **Transdiagnostic Dysfunctions in Brain Modules Across Patients with Schizophrenia, Bipolar Disorder, and Major Depressive Disorder: A Connectome-Based Study**. Schizophr Bull. 2020 Apr 10;46(3):699-712. [\[FULL TEXT\]](#)

Psychiatric disorders, including schizophrenia (SCZ), bipolar disorder (BD), and major depressive disorder (MDD), share clinical and neurobiological features. ... These alterations in modular organization significantly correlate with clinical scores in patients. ...This study demonstrates common hyper-integrated modular architectures of functional brain networks among patients with SCZ, BD, and MDD. These findings reveal a transdiagnostic mechanism of network dysfunction across psychiatric disorders from a connectomic perspective.

Siugzdaite R, et al (2020) - **Transdiagnostic Brain Mapping in Developmental Disorders**. Curr Biol. 2020 Apr 6;30(7):1245-1257. [\[FULL TEXT\]](#)

A simulated attack on each child's connectome revealed that some brain networks were strongly organized around highly connected hubs. Children with these networks had only selective cognitive impairments or no cognitive impairments at all. By contrast, the same attacks had a significantly different impact on some children's networks, because their brain efficiency was less critically dependent on hubs. These children had the most widespread and severe cognitive impairments. On this basis, we propose a new framework in which the nature and mechanisms of brain-to-cognition relationships are moderated by the organizational context of the overall network.

Veldsman M (2020) - **Atrophy network mapping of transdiagnostic cognitive and neuropsychiatric symptoms**. Brain. 2020 Apr 1;143(4):1053-1056. [\[FULL TEXT\]](#)

Swales DA, et al (2020) - **Maternal Depressive Symptoms Predict General Liability in Child Psychopathology**. J Clin Child Adolesc Psychol. 2020 Mar 27:1-12. [\[ABS\]](#)

The current study examines how maternal depressive symptoms relate to child psychopathology when structured via the latent bifactor model of psychopathology, a new organizational structure of psychopathological symptoms consisting of a general common psychopathology factor (p-factor) and internalizing- and externalizing-specific risk. ...Findings suggest that maternal depressive symptoms are associated with transdiagnostic risk for broad child psychopathology (p-factor).

Collier KM, et al (2020) - **Explanatory variables for women's increased risk for mental health problems in Vietnam**. Soc Psychiatry Psychiatr Epidemiol. 2020 Mar;55(3):359-369. [\[ABS\]](#)

The United Nations Sustainable Development Goals include gender equality for women, including health, as one of seventeen targets. Within this broad domain, a wide range of research indicates that being female is associated with increased risk for mental health problems, particularly in low- and middle-income countries (LMIC). ... These results suggest that support for gender equality including in regard to economic stability and education may be critical for reducing broad gender disparities in mental health functioning.

Davidson M, et al (2020) - **Do DSM classifications help or hinder drug development?** Dialogues Clin Neurosci. 2020 Mar;22(1):73-79. [\[FULL TEXT\]](#)

...efforts should be made to explore psychotropic development transdiagnostically, free of the DSM boundaries. However, currently there exists no alternative diagnostic system that is clearly superior to the DSM in terms of communications between the stakeholders in drug development.

Crouse JJ, et al (2020) - **Transdiagnostic neurocognitive subgroups and functional course in young people with emerging mental disorders: a cohort study**. BJPsych Open. 2020 Mar 19;6(2):e31. [\[FULL TEXT\]](#)

Neurocognitive impairments robustly predict functional outcome. However, heterogeneity in neurocognition is common within diagnostic groups, and data-driven analyses reveal homogeneous neurocognitive subgroups cutting across diagnostic boundaries. ...Cluster analysis of neurocognitive test scores derived three subgroups described as 'normal range' (n = 243, 38.6%), 'intermediate impairment' (n = 252, 40.1%), and 'global impairment' (n = 134, 21.3%). The major mental disorder categories (depressive, anxiety, bipolar, psychotic and other) were represented in each neurocognitive subgroup. The global impairment subgroup had lower functioning for 3 years of follow-up ... Neurocognitive impairment may follow a continuum of severity across the major syndrome-based mental disorders, with data-driven neurocognitive subgroups predictive of functional course. Of note, the global impairment subgroup had longstanding functional impairment despite continuing engagement with clinical services.

Grabell AS, et al (2020) - **Children's Facial Muscular Movements and Risk for Early Psychopathology: Assessing Clinical Utility.** Behav Ther. 2020 Mar;51(2):253-267. [[ABS](#)]

The presence of negative expressions with eye constriction in response to a short frustration prompt may serve as an indicator of early psychopathology, raising the potential for novel assessment tools that may enhance precision of early identification.

Dagleish T, et al (2020) - **Transdiagnostic approaches to mental health problems: Current status and future directions.** J Consult Clin Psychol. 2020 Mar;88(3):179-195. [[FULL TEXT](#)]

Despite a longstanding and widespread influence of the diagnostic approach to mental ill health, there is an emerging and growing consensus that such psychiatric nosologies may no longer be fit for purpose in research and clinical practice. In their place, there is gathering support for a "transdiagnostic" approach that cuts across traditional diagnostic boundaries or, more radically, sets them aside altogether, to provide novel insights into how we might understand mental health difficulties. ... In this Introduction to a Special Section on Transdiagnostic Approaches to Psychopathology, we provide a narrative review of the transdiagnostic literature in order to situate the Special Section articles in context.

Petersen CS, et al (2020) - **Toward a transdiagnostic neurocircuitry-based biomarker model for pro-cognitive effects: challenges, opportunities, and next steps.** CNS Spectr. 2020 Mar 3:1-5. [[ABS](#)]

Cognitive impairment has emerged as a key treatment priority in neuropsychiatric disorders. However, there is a lack of treatments with solid and lasting efficacy on cognition. A neurocircuitry-based biomarker model of pro-cognitive effects is critically needed to select among new candidate treatments. ... cognitive impairments are consistently accompanied by aberrant (hypo- and hyper-) activity in the dorsal prefrontal

cortex (PFC) and the default mode network (DMN), and that activity change in these regions commonly occurs with cognitive improvements.

Eaton NR (2020) - **Measurement and mental health disparities: Psychopathology classification and identity assessment.** Personal Ment Health. 2020 Feb;14(1):76-87. [\[ABS\]](#)

...literature is based almost entirely on traditional mental disorder constructs (e.g. major depressive disorder and borderline personality disorder) as defined by official nosologies, but these disorders are associated with numerous problems of reliability and validity. Advances in psychopathology classification research have converged on an alternative conceptualization of mental disorder structure, which comprises a set of transdiagnostic dimensions that cut across traditional diagnostic boundaries and overcome the limitations of traditional diagnoses.

Gilbert K, et al (2020) - **The Overcontrol in Youth Checklist (OCYC): Behavioral and Neural Validation of a Parent-Report of Child Overcontrol in Early Childhood.** Child Psychiatry Hum Dev. 2020 Feb;51(1):27-38. [\[FULL TEXT\]](#)

Self-control is protective against psychopathology in childhood. However, too much self-control, namely overcontrol, potentiates risk. Overcontrol is a constellation of child characteristics related to high need for control, perfectionism, inflexibility, social comparison, and performance monitoring and is a transdiagnostic risk factor associated with psychiatric disorders across the lifespan.

The current study validated the Overcontrol in Youth Checklist (OCYC) in 4-7 year old children and examined relationships with cognitive, social, and psychiatric, neural and behavioral indicators. The OCYC demonstrated good psychometrics and was associated with deficits in cognitive shifting, social functioning, and preschool psychopathology. Higher OCYC scores were associated with a blunted Δ ERN, an indicator of performance monitoring in preschoolers. Findings demonstrate the OCYC to be a developmentally valid measure of overcontrol that identifies this transdiagnostic risk factor early in development.

Arenella K, et al (2020) - **Self-reassurance and self-efficacy for controlling upsetting thoughts predict depression, anxiety, and perceived stress in help-seeking female family caregivers.** Int Psychogeriatr. 2020 Feb;32(2):229-240. [\[ABS\]](#)

The results indicate that self-reassurance and self-efficacy for controlling upsetting thoughts are effective resources linked to mental health outcomes. Although results were obtained with cross-sectional data, these findings suggest the potential of targeting these resources in transdiagnostic interventions for family caregivers.

Fava GA, et al (2020) - **The pursuit of euthymia.** World Psychiatry. 2020 Feb;19(1):40-50. [\[FULL TEXT\]](#)

The pursuit of euthymia cannot be conceived as a therapeutic intervention for specific mental disorders, but as a transdiagnostic strategy to be incorporated in an individualized therapeutic plan.

Bedwell JS, et al (2020) - **Childhood Cat Bites Relate to Increased Adulthood Severity of Schizotypy, Psychotic-Like Experiences, and Social Anhedonia in a Transdiagnostic Psychiatric Sample.** Psychopathology. 2020;53(1):36-47. [[FULL TEXT](#)]

Previous research has linked childhood cat scratches and bites to an increased risk for depression, and childhood cat ownership to increased risk of schizophrenia, bipolar disorder, and social anhedonia. Our group previously reported that childhood cat bites, but not ownership, related to increased schizotypy severity in an undergraduate sample. ...Across the entire sample, self-report of cat bites prior to age 13, but not after, related to greater current severity of overall schizotypy, self-reported and clinician-rated psychotic-like symptoms, and social anhedonia, when compared to individuals who reported no lifetime cat bites.

Gallagher MW, et al (2020) - **Examining Hope as a Transdiagnostic Mechanism of Change across Anxiety Disorders and CBT Treatment Protocols.** Behav Ther. 2020 Jan;51(1):190-202. [[FULL TEXT](#)]

Hope is a trait that represents the capacity to identify strategies or pathways to achieve goals and the motivation or agency to effectively pursue those pathways. Hope has been demonstrated to be a robust source of resilience to anxiety and stress and there is limited evidence that, as has been suggested for decades, hope may function as a core process or transdiagnostic mechanism of change in psychotherapy.

van Oort J, et al (2020) - **Absence of default mode downregulation in response to a mild psychological stressor marks stress-vulnerability across diverse psychiatric disorders.** Neuroimage Clin. 2020;25:102176. [[FULL TEXT](#)]

Clinically, it is well-established that vulnerability to stress is a common feature across a broad spectrum of psychiatric disorders. However, this link has been mechanistically studied almost exclusively in patients with so-called stress-related disorders such as depression and anxiety. To probe transdiagnostic mechanisms, we set out to study the acute stress response across a broader range of psychiatric disorders taking a large-scale brain network perspective. We investigated the brain's response to a mild, experimentally well-controlled psychological stressor in the form of an aversive movie. We studied 168 patients with stress-related and/or neurodevelopmental disorders (including comorbidity) and 46 control subjects. We focused on three networks that have a central role in the brain's stress response and are affected in a wide range of psychiatric disorders: the salience network (SN), default mode network (DMN) and frontoparietal network (FPN). Our results support an increased vulnerability to stress

across all patients, indicated by a higher subjective stress level at baseline and follow-up compared to matched controls. At the brain systems level, the stress response was characterized by a relatively decreased FPN connectivity and an absence of a decrease in the within DMN connectivity across all disorders compared to controls. At the neurocognitive level, these findings may reflect a diminished top-down control and a tendency to more pronounced (negative) self-referential processing. Besides these shared aspects of the maladaptive stress response, we also discuss indications for disorder-specific aspects. Taken together, our results emphasize the importance of investigating the mechanistic underpinnings of psychiatric disorders transdiagnostically as recently done in neurogenetics.

Wilver NL (2020) - **Effects of safety behavior fading on appearance concerns and related symptoms.** J Consult Clin Psychol. 2020 Jan;88(1):65-74. [[ABS](#)]

Appearance-related safety behaviors (SBs; e.g., mirror checking, grooming) have been implicated in body dysmorphic disorder (BDD), eating disorders, and social anxiety disorder. ...This study provides strong evidence for the importance of appearance-related SBs in the maintenance of BDD and other disorders characterized by body image disturbances. Findings point to the potential utility of decreasing appearance-related SBs as a **transdiagnostic** treatment strategy

Arevian AC, et al (2020) - **Clinical state tracking in serious mental illness through computational analysis of speech.** PLoS One. 2020 Jan 15;15(1):e0225695. [[FULL TEXT](#)]

Mellem MS, et al (2020) - **Machine Learning Models Identify Multimodal Measurements Highly Predictive of Transdiagnostic Symptom Severity for Mood, Anhedonia, and Anxiety.** Biol Psychiatry Cogn Neurosci Neuroimaging. 2020 Jan;5(1):56-67. [[ABS](#)]

Insights from neuroimaging-based biomarker research have not yet translated into clinical practice. This translational gap may stem from a focus on diagnostic classification, rather than on prediction of transdiagnostic psychiatric symptom severity....Combining resting-state functional MRI with select questions from clinical scales enabled high prediction of symptom severity across diagnostically distinct patient groups and revealed that connectivity measures beyond a few intrinsic resting-state networks may carry relevant information for symptom severity.

Jacob KS (2019) - **Idioms of distress, mental symptoms, syndromes, disorders and transdiagnostic approaches.** Asian J Psychiatr. 2019 Dec;46:7-8. [[ABS](#)]

Euro-American idioms of distress and their corresponding symptom clusters have been universalised as mental disorders and are now the gold standard for psychiatric diagnosis around the globe. This paper discusses issues related to mental disorder diagnosis from a cultural perspective. It argues that psychiatric diagnoses, while having good in-

ter-rater reliability, lack external validity. It contends that psychiatric categories and labels are supported by the current political economy of health. ...The paper argues that new (psychiatric) idioms are easily adopted across regions and societies, and that they eventually change contexts and cultures.

Fusar-Poli P, et al (2019) - **European college of neuropsychopharmacology network on the prevention of mental disorders and mental health promotion (ECNP PMD-MHP)**. Eur Neuropsychopharmacol. 2019 Dec;29(12):1301-1311. [\[ABS\]](#)

Prevention is the most promising way to reduce the high personal, familial, societal, clinical and economic costs of mental disorders in Europe and worldwide. A complementary approach is to go beyond the prevention of mental ill health, to promote good mental health. This manuscript highlights the first European consortium fostering cutting-edge multidisciplinary research in these two areas.... The ECNP PMD-MHP Network adopts a **transdiagnostic**, lifespan, clinical staging model which cuts across different mental disorders and different methodologies.

Kebets V, et al (2019) - **Somatosensory-Motor Dysconnectivity Spans Multiple Transdiagnostic Dimensions of Psychopathology**. Biol Psychiatry. 2019 Nov 15;86(10):779-791. [\[ABS\]](#)

There is considerable interest in a dimensional **transdiagnostic** approach to psychiatry. ...Our analyses revealed three latent components corresponding to general psychopathology, cognitive dysfunction, and impulsivity. Each component was associated with a unique whole-brain resting-state functional connectivity signature and was shared across all participants. ... Strikingly, all three components featured connectivity alterations within the somatosensory-motor network and its connectivity with subcortical structures and cortical executive networks. CONCLUSIONS: We identified three distinct dimensions with dissociable (but overlapping) whole-brain resting-state functional connectivity signatures across healthy individuals and individuals with psychiatric illness, providing potential intermediate phenotypes that span diagnostic categories

Mansell W (2019) - **Transdiagnostic psychiatry goes above and beyond classification**. World Psychiatry. 2019 Oct;18(3):360-361. [\[FULL TEXT\]](#)

Fusar-Poli P, et al (2019) - **TRANSD recommendations: improving transdiagnostic research in psychiatry**. World Psychiatry. 2019 Oct;18(3):361-362. [\[FULL TEXT\]](#)

Zainal NH, et al (2019) - **Cross-Cultural and Gender Invariance of Transdiagnostic Processes in the United States and Singapore**. Assessment. 2019 Sep 20;1073191119869832. [\[FULL TEXT\]](#)

The Research Domain Criteria define cognitive and emotional processes (e.g., rumination, intolerance of uncertainty, anxiety sensitivity, emotion dysregulation) as key transdiagnostic elements of psychopathology. However, there is currently a dearth of construct equivalence studies on measures of these processes. We thus aimed to validate

the latent structures of five transdiagnostic constructs using established and newer measures...

Fuller T, et al (2019) - **Shared Genetics of Psychiatric Disorders**. F1000Res. 2019 Sep 12;8:F1000 Faculty Rev-1626. [\[FULL TEXT\]](#)

Increasing evidence that most mental disorders share many common genetic risk variants and environmental risk modifiers suggests that the broad spectrum of psychiatric pathology represents the pleiotropic display of a more limited series of pathologic events in neuronal development than was originally believed, regulated by many common risk variants and a smaller number of rare ones.

Forbes MK, et al (2019) - **The Great Recession and Mental Health in the United States**. Clin Psychol Sci. 2019 Sep;7(5):900-913. [\[FULL TEXT\]](#)

The full scope of the impact of The Great Recession on individuals' mental health has not been quantified to date. This study aimed to determine whether financial, job-related, and housing impacts experienced by individuals during the recession predicted changes in the occurrence of symptoms of depression, generalized anxiety, panic attacks, and problematic alcohol or other substance use. ... for individuals each recession impact experienced was associated with long-lasting and **transdiagnostic** declines in mental health. These relationships were stronger for some sociodemographic groups, suggesting the need for additional support for people who suffer marked losses during recessions and for those without a strong safety net.

Gluschkoff K, et al (2019) - **The General Psychopathology Factor: Structural Stability and Generalizability to Within-Individual Changes**. Front Psychiatry. 2019 Aug 30;10:594. [\[FULL TEXT\]](#)

The bifactor structure with a general psychopathology factor is stable over time and describes temporal changes in psychopathology. The findings support the notion that the general psychopathology factor describes a **transdiagnostic** etiology and may therefore provide a useful target for intervention and treatment.

Class QA, et al (2019) - **Socioemotional dispositions of children and adolescents predict general and specific second-order factors of psychopathology in early adulthood: A 12-year prospective study**. J Abnorm Psychol. 2019 Aug;128(6):574-584. [\[FULL TEXT\]](#)

We previously hypothesized that the ubiquitous, but patterned correlations among all dimensions of psychopathology reflect a hierarchy of progressively more nonspecific causal influences, with a general factor of psychopathology-also dubbed the p factor-reflecting the most **transdiagnostic** causal influences. We further hypothesized that the general factor is a manifestation of individual differences in 1 or more trait-like dispositions, particularly negative emotionality, that are nonspecifically associated with risk for essentially every dimension of psychopathology.

Amlung M, et al (2019) - **Delay Discounting as a Transdiagnostic Process in Psychiatric Disorders: A Meta-analysis.** JAMA Psychiatry. 2019 Aug 28;76(11):1176-86. [\[FULL TEXT\]](#)

Delay discounting is a behavioral economic index of impulsive preferences for smaller-immediate or larger-delayed rewards that is argued to be a **transdiagnostic** process across health conditions. ... Results of this study appear to provide empirical support for delay discounting as a **transdiagnostic** process across most of the psychiatric disorders examined; the literature search also revealed limited studies in some disorders, notably posttraumatic stress disorder, which is a priority area for research.

Pasion R, et al (2019) - **ERN as a transdiagnostic marker of the internalizing-externalizing spectrum: A dissociable meta-analytic effect.** Neurosci Biobehav Rev. 2019 Aug;103:133-149. [\[ABS\]](#)

... reduced ERN (Error-Related Negativity in EEG) amplitude was observed in externalizing, while increased ERN amplitude was reported in internalizing. ... Overall, our findings highlight that ERN reduction interacts with the multiple phenotypic expressions of externalizing at a general level, while more specific factors - such as differences in sensitivity and aversion to errors - may explain increased ERN amplitude in internalizing.

Blanco C, et al (2019) - **Psychiatric disorders and risk for multiple adverse outcomes: a national prospective study.** Mol Psychiatry. 2019 Jul 26;10.1038. [\[FULL TEXT\]](#)

Most psychiatric disorders, when examined individually, are associated with a broad range of adverse outcomes. However, psychiatric disorders often co-occur and their co-occurrence is well explained by a limited number of **transdiagnostic** factors. ... Our findings reveal that associations between psychiatric disorders and adverse outcomes occur through broad psychological dimensions. Understanding the biological and psychological mechanisms underlying these dimensions should yield key intervention targets to decrease the individual suffering and societal burden associated with common psychiatric disorders.

Mitelman SA (2019) - **Transdiagnostic neuroimaging in psychiatry: A review.** Psychiatry Res. 2019 Jul;277:23-38. [\[ABS\]](#)

Transdiagnostic approach has a long history in neuroimaging, predating its recent ascendance as a paradigm for new psychiatric nosology. Various psychiatric disorders have been compared for commonalities and differences in neuroanatomical features and activation patterns, with different aims and rationales. This review covers both structural and functional neuroimaging publications with direct comparison of different psychiatric disorders, including schizophrenia, bipolar disorder, major depressive disorder, autism spectrum disorder, obsessive-compulsive disorder, attention-deficit/hyperactivity disorder, conduct disorder, anorexia nervosa, and bulimia nervosa. Major findings are systematically presented along with specific rationales for each comparison.

Bakker GM (2019) - **A new conception and subsequent taxonomy of clinical psychological problems.** BMC Psychol. 2019 Jul 10;7(1):46. [[FULL TEXT](#)]

A taxonomy of the objects of study, theory, assessment, and intervention is critical to the development of all clinical sciences.

Clinical psychology has been conceptually and administratively dominated by the taxonomy of an adjacent discipline - psychiatry's Diagnostic and statistical manual of mental disorders (DSM). Many have called for a 'paradigm shift' away from a medical nosology of diseases toward clinical psychology's own taxonomy of clinical psychological problems (CPPs), without being able to specify what is to be listed and classified.

The critical psychological-level phenomenon underlying **CPPs** is the occurrence of 'problem-maintaining circles' (**PMCs**) of causally related cognitions, emotions, behaviours, and/or stimuli. *This concept provides an empirically-derived, theory-based, treatment-relevant, categorical, essentialist, parsimonious, and nonstigmatizing definition of CPPs.* It distinguishes psychological problems in which PMCs have not (yet?) formed, and which may respond to 'counseling', clinical psychological problems in which active PMCs require clinical intervention, and psychopathological problems which are unlikely to be 'cured' by PMC-breaking alone.

A subsequent classification and coding system of PMCs is proposed, and expected benefits to research, communication, and the quality of case formulation in clinical psychology are described, reliant upon a development effort of some meaningful fraction of that which has been devoted to the DSM.

Skimming KA, et al (2019) - **Transdiagnostic Approach to Olfactory Reference Syndrome: Neurobiological Considerations.** Harv Rev Psychiatry. 2019 May/Jun;27(3):193-200. [[ABS](#)]

Olfactory reference syndrome (ORS) describes a constellation of emotional and behavioral symptoms that cause clinically significant distress or impairment arising from the false belief that one is emitting an offensive odor. ...While no primary neuroscientific research has specifically investigated ORS, an overlapping circuitry has been implicated in the neurobiology of obsessive-compulsive, trauma and stressor, and psychotic spectrum disorders, suggesting that the phenomenology of ORS can best be understood through a dimensional, rather than categorical, approach.

Halcomb M, et al (2019) - **Integrating Preclinical and Clinical Models of Negative Urgency.** Front Psychiatry. 2019 May 23;10:324. [[FULL TEXT](#)]

Overwhelming evidence suggests that negative urgency is robustly associated with rash, ill-advised behavior, and this trait may hamper attempts to treat patients with substance use disorder. ... Given that negative urgency is a **transdiagnostic** risk factor that

impedes treatment success, the impact of this work could be large in reducing client suffering and societal costs.

Conway CC, et al (2019) - **A Hierarchical Taxonomy of Psychopathology Can Transform Mental Health Research**. *Perspect Psychol Sci*. 2019 May;14(3):419-436. [\[FULL TEXT\]](#)

For more than a century, research on psychopathology has focused on categorical diagnoses. Although this work has produced major discoveries, growing evidence points to the superiority of a dimensional approach to the science of mental illness.

Gong Q, et al (2019) - **A transdiagnostic neuroanatomical signature of psychiatric illness**. *Neuropsychopharmacology*. 2019 Apr;44(5):869-875. [\[FULL TEXT\]](#)

Despite an increasing focus on **transdiagnostic** approaches to mental health, it remains unclear whether different diagnostic categories share a common neuroanatomical basis. The current investigation sought to investigate whether a transdiagnostic set of structural alterations characterized schizophrenia, depression, post-traumatic stress disorder, and obsessive-compulsive disorder, and determine whether any such alterations reflected markers of psychiatric illness or pre-existing familial vulnerability. ... these findings indicate that increased putamen volume may reflect a transdiagnostic marker of familial vulnerability to psychopathology. This is consistent with emerging conceptualizations of psychiatric illness, in which each disorder is understood as a combination of diagnosis-specific features and a transdiagnostic factor reflecting general psychopathology.

Sauer-Zavala S, et al (2019) - **Evaluating transdiagnostic, evidence-based mental health care in a safety-net setting serving homeless individuals**. *Psychotherapy (Chic)*. 2019 Mar;56(1):100-114. [\[ABS\]](#)

Homeless individuals experience higher rates of mental illness than the general population, though this group is less likely to receive evidence-based psychological treatment for these difficulties. One explanation for this science-to-service gap may be that most empirically supported interventions are designed to address a single disorder, which may not map on to the substantial comorbidity present in safety-net samples, and create a high training burden for often under-resourced clinicians who must learn multiple protocols to address the needs of their patients. One solution may be to prioritize the dissemination of **transdiagnostic** interventions that *can reduce therapist burden and simultaneously address comorbid conditions*. The purpose of the present article is to describe the process of conducting a pilot study administering the **Unified Protocol (UP)**, a **transdiagnostic** treatment for the range of emotional disorders, at a community-based organization that provides health care and other services to homeless individuals and families in Boston, Massachusetts. Therapists on a specialized behavioral health unit received didactic training in the intervention, followed by weekly consultation while they provided the UP to patients on their caseload. Qualitative and quantitative data were

collected from both patients and therapists. Barriers to use of the UP by therapists, as well as to conducting research in this setting, will be discussed, along with the solutions that were used.

Patzelt EH, et al (2019) - **The transdiagnostic structure of mental effort avoidance**. Sci Rep. 2019 Feb 8;9(1):1689. [\[FULL TEXT\]](#)

Wichers M, et al (2019) - **Can we predict the direction of sudden shifts in symptoms? Transdiagnostic implications from a complex systems perspective on psychopathology**. Psychol Med. 2019 Feb;49(3):380-387. [\[FULL TEXT\]](#)

(Research) designs should be able to follow sudden transitions 'live' using frequent observations of symptoms within individuals and apply a **transdiagnostic** approach to psychopathology. If the assumptions proposed are supported by empirical studies then this will signify a large improvement in the possibility for personalized estimations of the course of psychiatric symptoms. Such information can be extremely useful for early intervention strategies aimed at preventing specific psychiatric problems.

Eisenbarth H, et al (2019) - **The influence of stressful life events, psychopathy, and their interaction on internalizing and externalizing psychopathology**. Psychiatry Res. 2019 Feb;272:438-446. [\[FULL TEXT\]](#)

We hypothesized that (1) exposure to stressful life events would be a **transdiagnostic** risk factor for psychopathology, (2) primary and secondary psychopathy would be differentially associated with internalizing psychopathology ...These findings demonstrate that deviations from normative effort expenditure are associated with a number of constructs that are common to several forms of psychiatric illness.

Hanlon CA (2019) - **Treating cue-reactivity with brain stimulation: a new (transdiagnostic) approach**. Neuropsychopharmacology. 2019 Jan;44(1):232-233. [\[FULL TEXT\]](#)

Gong Q, et al (2019) - **Dysconnectivity of the medio-dorsal thalamic nucleus in drug-naïve first episode schizophrenia: diagnosis-specific or trans-diagnostic effect?** Transl Psychiatry. 2019 Jan 16;9(1):9. [\[FULL TEXT\]](#)

Converging lines of evidence implicate the thalamocortical network in schizophrenia. In particular, the onset of the illness is associated with aberrant functional integration between the medio-dorsal thalamic nucleus (MDN) and widespread prefrontal, temporal and parietal cortical regions. Because the thalamus is also implicated in other psychiatric illnesses including post-traumatic stress disorder (PTSD) and major depressive disorder (MDD), the diagnostic specificity of these alterations is unclear.

The only significant schizophrenia-specific effect was increased EC (effective connectivity) between the right MDN and the right pallidum ($p < 0.05$ corrected). In contrast,

there were a number of significant trans-diagnostic alterations, with both right and left MDN displaying **transdiagnostic** increased EC with several prefrontal and parietal regions bilaterally ($p < 0.05$ corrected). EC alterations between the MDN and the cortex are not specific to schizophrenia but are a **transdiagnostic** feature of psychiatric disorders, consistent with emerging conceptualizations of mental illness based on a single general psychopathology factor. Therefore, dysconnectivity of the MDN could potentially be used to assess the presence of general psychopathology above and beyond traditional diagnostic boundaries.

Fettes P, et al (2017) - **Cortico-Striatal-Thalamic Loop Circuits of the Orbitofrontal Cortex: Promising Therapeutic Targets in Psychiatric Illness**. Front Syst Neurosci. 2017 Apr 27;11:25. [\[FULL TEXT\]](#)

Mayo LM, et al (2019) - **In the face of stress: Interpreting individual differences in stress-induced facial expressions**. Neurobiol Stress. 2019 Apr 20;10:100166. [\[FULL TEXT\]](#)

Here, we review the role of facial expressions according to the leading affective neuroscience theories, including constructed emotion and social-motivation accounts. We specifically highlight recent data (Mayo et al, 2018) demonstrating the way in which stress shapes facial expressions and how this is influenced by individual factors. In particular, we focus on the consequence of genetic variation within the endocannabinoid system, a neuromodulatory system implicated in stress and emotion, and its impact on stress-induced facial muscle activity. In a re-analysis of this dataset, we highlight how gender may also influence these processes, conceptualized as variation in the "fight-or-flight" or "tend-and-befriend" behavioral responses to stress. We speculate on how these interpretations may contribute to a broader understanding of facial expressions, discuss the potential use of facial expressions as a **transdiagnostic** marker of psychiatric disease, and suggest future work necessary to resolve outstanding questions.

Hoffman M, et al (2019) - **Estimating transdiagnostic symptom networks: The problem of "skips" in diagnostic interviews**. Psychol Assess. 2019 Jan;31(1):73-81. [\[FULL TEXT\]](#)

Murano T, et al (2019) - **Transcriptomic immaturity inducible by neural hyperexcitation is shared by multiple neuropsychiatric disorders**. Commun Biol. 2019 Jan 22;2:32. [\[FULL TEXT\]](#)

Biomarkers are needed to improve the diagnosis of neuropsychiatric disorders, which are often associated to excitatory/inhibitory imbalances in neural transmission and abnormal maturation. Here, we characterized different disease conditions by mapping changes in the expression patterns of maturation-related genes whose expression was altered by experimental neural hyperexcitation in published studies. This analysis revealed two gene expression patterns: decreases in maturity markers and increases in immaturity markers. These two groups of genes were characterized by the over-representation of genes related to synaptic function and chromosomal modification, respectively. Using these two groups in a **transdiagnostic** analysis of 87 disease datasets for

eight neuropsychiatric disorders and 12 datasets from corresponding animal models, we found that transcriptomic pseudoimmaturity inducible by neural hyperexcitation is shared by multiple neuropsychiatric disorders, such as schizophrenia, Alzheimer disorders, and amyotrophic lateral sclerosis. Our results indicate that this endophenotype serves as a basis for the **transdiagnostic** characterization of these disorders.

Apolinário-Hagen J (2019) - **Internet-Delivered Psychological Treatment Options for Panic Disorder: A Review on Their Efficacy and Acceptability.** Psychiatry Investig. 2019 Jan;16(1):37-49. [\[FULL TEXT\]](#)

Internet-delivered psychological treatments have been suggested as a chance to expand the access to professional help. ... Especially selfguided and **transdiagnostic** Cognitive Behavioral Therapy approaches appear being efficient options for the dissemination in routine care.

Cauda F, et al (2019) - **The alteration landscape of the cerebral cortex.** Neuroimage. 2019 Jan 1;184:359-371. [\[FULL TEXT\]](#)

... no cerebral area appears to be only altered by a specific disorder. Our study shows that the overlap of areas with high A-entropy provides support for a **transdiagnostic** approach to brain disorders but, at the same time, suggests that fruitful differences can be traced among brain diseases, as some areas can exhibit an alteration profile more specific to certain disorders than to others.

Ballespí S, et al (2018) - **Beyond diagnosis: Mentalization and mental health from a transdiagnostic point of view in adolescents from non-clinical population.** Psychiatry Res. 2018 Dec;270:755-763. [\[ABS\]](#)

An increasing volume of evidence suggests that mentalization can be an important factor in the transition from mental health to mental illness and vice versa. ...These results suggest that mentalization may contribute to mental health beyond symptoms, not so much associated with psychopathology, but rather resilience and well-being.

Carcone D, et al (2017) - **Six Years of Research on the National Institute of Mental Health's Research Domain Criteria (RDoC) Initiative: A Systematic Review.** Front Cell Neurosci. 2017 Mar 3;11:46. [\[FULL TEXT\]](#)

Maia ACC, et al (2017) - **Improvement in quality of life and sexual functioning in a comorbid sample after the unified protocol transdiagnostic group treatment.** J Psychiatr Res. 2017 Oct;93:30-36. [\[ABS\]](#)

Lupien SJ, et al (2017) - **The DSM5/RDoC debate on the future of mental health research: implication for studies on human stress and presentation of the signature bank.** Stress. 2017 Jan;20(1):95-111. [\[ABS\]](#)

Lukat J, et al (2017) - **Predictors of Incidence, Remission and Relapse of Axis I Mental Disorders in Young Women: A Transdiagnostic Approach.** Clin Psychol Psychother. 2017 Mar;24(2):322-331. [\[ABS\]](#)

Mulder R, et al (2017) - **Common versus specific factors in psychotherapy: opening the black box.** Lancet Psychiatry. 2017 Jul 5. pii: S2215-0366(17)30100-1. [\[ABS\]](#)

Rather than continuing the debate, research needs to encompass new psychotherapies such as e-therapies, transdiagnostic treatments, psychotherapy component studies, and findings from neurobiology to elucidate the effective process components of psychotherapy.

Ceusters W, et al (2017) - **Ontological Realism for the Research Domain Criteria for Mental Disorders.** Stud Health Technol Inform. 2017;235:431-435. [\[ABS\]](#)

Weisz J, et al (2017) - **Initial Test of a Principle-Guided Approach to Transdiagnostic Psychotherapy with Children and Adolescents.** J Clin Child Adolesc Psychol. 2017 Jan-Feb;46(1):44-58. [\[ABS\]](#)

Dindo L, et al (2017) - **Acceptance and Commitment Therapy: A Transdiagnostic Behavioral Intervention for Mental Health and Medical Conditions.** Neurotherapeutics. 2017 Jul;14(3):546-553. [\[ABS\]](#)

...commitment therapy (ACT) is an empirically supported psychotherapy that offers promise for patients suffering from a wide range of mental and physical conditions, while addressing these gaps and challenges in the field. ACT rests on the fundamental premise that pain, grief, disappointment, illness, and anxiety are inevitable features of human life, with the therapeutic goal of helping individuals productively adapt to these types of challenges by developing greater psychological flexibility rather than engaging in counterproductive attempts to eliminate or suppress undesirable experiences. This is achieved through committed pursuit of valued life areas and directions, even in the face of the natural desire to escape or avoid painful and troubling experiences, emotions, and thoughts. ACT is **transdiagnostic** (applies to more than one condition), process-focused, and flexibly delivered. In a relatively short period of time, ACT has been effectively implemented across a broad range of therapeutic settings, including mental health, primary care, and specialty medical clinics. ACT has also been delivered in a variety of formats...

Torous J, et al (2017) - **New dimensions and new tools to realize the potential of RDoC: digital phenotyping via smartphones and connected devices.** Transl Psychiatry. 2017 Mar 7;7(3):e1053. [\[FULL TEXT\]](#)

Garafalo S, et al (2017) - **Cortical and Striatal Reward Processing in Parkinson's Disease**

Psychosis. Front Neurol. 2017 Apr 24;8:156. [\[FULL TEXT\]](#)

There was reduced activation in PD patients with a history of psychosis, compared to those without, in the posterior cingulate cortex and the VS during reward anticipation ($p < 0.05$ small volume corrected). The results suggest that cortical and striatal abnormalities in reward processing, a putative pathophysiological mechanism of psychosis in schizophrenia, may also contribute to the pathogenesis of psychotic symptoms in PD. The finding of posterior cingulate dysfunction is in keeping with prior results highlighting cortical dysfunction in the pathogenesis of PD psychosis.

Lo MC, et al (2017) – **Closed-loop neuromodulation systems: next-generation treatments for psychiatric illness.** Int Rev Psychiatry. 2017 Apr;29(2):191-204. [\[ABS\]](#)

Despite deep brain stimulation's positive early results in psychiatric disorders, well-designed clinical trials have yielded inconsistent clinical outcomes. One path to more reliable benefit is closed-loop therapy: stimulation that is automatically adjusted by a device or algorithm in response to changes in the patient's electrical brain activity. These interventions may provide more precise and patient-specific treatments. This article first introduces the available closed-loop neuromodulation platforms, which have shown clinical efficacy in epilepsy and strong early results in movement disorders. It discusses the strengths and limitations of these devices in the context of psychiatric illness. It then describes emerging technologies to address these limitations, including pre-clinical developments such as wireless deep neurostimulation and genetically targeted neuromodulation. Finally, ongoing challenges and limitations for closed-loop psychiatric brain stimulation development, most notably the difficulty of identifying meaningful biomarkers for titration, are discussed. This is considered in the recently-released Research Domain Criteria (RDoC) framework, and how neuromodulation and RDoC are jointly very well suited to address the problem of treatment-resistant illness is described.

Meidlinger PC, et al (2017) - **The new transdiagnostic cognitive behavioral treatments: Commentary for clinicians and clinical researchers.** J Anxiety Disord. 2017 Mar;46:101-109. [\[ABS\]](#)

Recognition of the limitations of the current categorical diagnostic system and increased understanding of commonalities across clinical problems associated with negative emotion, including anxiety and depression, has led to the development of transdiagnostic psychological interventions. This new approach holds promise in shifting our emphasis from diagnostic categories to treating core construct that cut across disorders.

Holroyd CB, et al (2016) - **The research domain criteria framework: The case for anterior cingulate cortex.** Neurosci Biobehav Rev. 2016 Dec;71:418-443. [\[ABS\]](#)

We argue that ACC function contributes to individual differences in personality traits

related to reward sensitivity and persistence, and propose that the maladaptive expression of these traits contributes to multiple mental and neurological disorders. Our discussion is organized around a computational framework that relates the reward processing and control functions of ACC, as revealed by two electrophysiological phenomena called the reward positivity and frontal midline theta oscillations, to a distributed neural system underlying cognitive control.

Husain M (2017) - **Transdiagnostic neurology: neuropsychiatric symptoms in neurodegenerative diseases.** Brain (2017) 140 (6): 1535-1536. [\[ABS\]](#)

...it is also worth considering the possibility that hyper-specialism comes at a potential cost: loss of the ability to perceive, or even care about, the significance of common symptoms that cross conventional disease boundaries.

Laposa JM, et al (2017) - **Unified Protocol Transdiagnostic Treatment in Group Format.** Behav Modif. 2017 Mar;41(2):253-268. [\[ABS\]](#)

Garvey M, et al (2016) - **The National Institute of Mental Health Research Domain Criteria and Clinical Research in Child and Adolescent Psychiatry.** J Am Acad Child Adolesc Psychiatry. 2016 Feb;55(2):93-8. [\[FULL TEXT\]](#)

RDoC encourages investigators to investigate psychopathology dimensionally: greater or lesser degrees of healthy/adapted functioning of neurobiological, cognitive, and behavioral processes (constructs) that cut across current diagnostic categories.

Glatt CE, et al (2016) - **Common Polymorphisms in the Age of Research Domain Criteria (RDoC): Integration and Translation.** Biol Psychiatry. 2016 Jan 1;79(1):25-31. [\[FULL TEXT\]](#)

Halpin M (2016) - **The DSM and Professional Practice: Research, Clinical, and Institutional Perspectives.** J Health Soc Behav. 2016 Jun;57(2). [\[ABS\]](#)

In the clinic, the DSM influences how disorders are conceptualized and diagnosed. Institutionally, the DSM aligns the patient-professional encounter to insurance and pharmaceutical interests. I conclude that the DSM operates as multiple, context-specific taxonomies that pervasively influence professional practices, such that all possible actions must orient to DSM criteria, with professionals both a source and an object of institutionalized gaze.

Iacono WG (2016) - **Achieving Success with the Research Domain Criteria (RDoC): Going beyond the Matrix.** Psychophysiology. 2016 March; 53(3): 308–311. [\[FULL TEXT\]](#)

Jenkins LM, et al (2016) – **Shared white matter alterations across emotional disorders: A voxel-based meta-analysis of fractional anisotropy.** Neuroimage Clin. 2016 Sep 28;12:1022-1034. [\[FULL TEXT\]](#)

Distinct diagnostic categories of ED show commonalities in WM tracts with reduced FA when compared to HC, which links brain networks involved in cognitive and affective processing. This meta-analysis facilitates an increased understanding of the biological markers that are shared by these ED

Kozak MJ, et al (2016) - **The NIMH Research Domain Criteria Initiative: Background, Issues, and Pragmatics.** Psychophysiology. 2016 Mar;53(3):286-97. [\[ABS\]](#)

Lilienfeld SO, et al (2016) - **Clashing Diagnostic Approaches: DSM-ICD Versus RDoC.** Annu Rev Clin Psychol. 2016;12:435-63. [\[FULL TEXT\]](#)

Though more of promissory note than a formalized system at present, the RDoC aims to develop a system of psychiatric classification based not on signs, symptoms, and course, ala Kraepelin, but instead on markers of psychobiological systems linked to adaptive – and maladaptive – functioning.

MacNamara A, et al (2016) - **Psychobiological operationalization of RDoC constructs: Methodological and conceptual opportunities and challenges.** Psychophysiology. 2016 Mar;53(3):406-9. [\[FULL TEXT\]](#)

Maj M (2016) - **Narrowing the gap between ICD/DSM and RDoC constructs: possible steps and caveats.** World Psychiatry. 2016 Oct;15(3):193-194. [\[FULL TEXT\]](#)

McTeague LM, et al (2016) - **Transdiagnostic impairment of cognitive control in mental illness.** J Psychiatr Res. 2016 Dec;83:37-46. [\[ABS\]](#)

McTeague LM (2016) - **Reconciling RDoC and DSM approaches in clinical psychophysiology and neuroscience, Psychophysiology and Neuroscience.** 2016 Mar;53(3):323-7. [\[FULL TEXT\]](#)
<https://www.ncbi.nlm.nih.gov/pubmed/26877120>

Nelson LD, et al (2016) - **Neurobehavioral Traits as Transdiagnostic Predictors of Clinical Problems. Assessment.** 2016 Feb;23(1):75-85. [\[FULL TEXT\]](#)
<https://www.ncbi.nlm.nih.gov/pubmed/25657306>

van Amelsvoort T, et al (2016) - **Effect of Pharmacological Interventions on the Fronto-Cingulo-Parietal Cognitive Control Network in Psychiatric Disorders - A Transdiagnostic Systematic Review of fMRI Studies.** Front Psychiatry. 2016 May 18;7:82. [\[FULL TEXT\]](#)

Zalta AK, et al (2016) - **Conducting Psychopathology Prevention Research in the RDoC Era.** Clin Psychol (New York). 2016 Mar;23(1):94-104. [\[FULL TEXT\]](#)

Cuthbert BN (2015) - **Research Domain Criteria: toward future psychiatric nosologies.** Dialogues Clin Neurosci. 2015 Mar;17(1):89-97. [\[FULL TEXT\]](#)

The Research Domain Criteria (RDoC) project was initiated by the National Institute of Mental Health (NIMH) in early 2009 as the implementation of Goal 1.4 of its just-issued strategic plan. In keeping with the NIMH mission, to "transform the understanding and treatment of mental illnesses through basic and clinical research," RDoC was explicitly conceived as a research-related initiative. The statement of the relevant goal in the strategic plan reads: "Develop, for research purposes, new ways of classifying mental disorders based on dimensions of observable behavior and neurobiological measures." Due to the novel approach that RDoC takes to conceptualizing and studying mental disorders, it has received widespread attention, well beyond the borders of the immediate research community. This review discusses the rationale for the experimental framework that RDoC has adopted, and its implications for the nosology of mental disorders in the future.

De Los Reyes A, et al (2015) - **Introduction to the special issue: toward implementing physiological measures in in clinical child and adolescent assessments.** J Clin Child Adolesc Psychol. 2015;44(2):221-37. [[ABS](#)]

The National Institute of Mental Health recently launched the Research Domain Criteria (RDoC). The RDoC is an initiative to improve classification of mental health concerns by promoting research on the brain mechanisms underlying these concerns, with the ultimate goal of developing interventions that target these brain mechanisms. A key focus of RDoC involves opening new lines of research examining patients' responses on biological measures. The RDoC presents unique challenges to mental health professionals who work with children and adolescents. Indeed, mental health professionals rarely integrate biological measures into clinical assessments. Thus, RDoC's ability to improve patient care rests, in part, on the development of strategies for implementing biological measures within mental health assessments. Further, mental health professionals already carry out comprehensive assessments that frequently yield inconsistent findings. These inconsistencies have historically posed challenges to interpreting research findings as well as assessment outcomes in practice settings. In this introductory article, we review key issues that informed the development of a special issue of articles demonstrating methods for implementing low-cost measures of physiological functioning in clinical child and adolescent assessments. We also outline a conceptual framework, informed by theoretical work on using and interpreting multiple informants' clinical reports (De Los Reyes, Thomas, Goodman, & Kundey, 2013), to guide hypothesis testing when using physiological measures within clinical child and adolescent assessments. This special issue and the conceptual model described in this article may open up new lines of research testing paradigms for implementing clinically feasible physiological measures in clinical child and adolescent assessments.

Dias TGC, et al (2015) - **Characterizing heterogeneity in children with and without ADHD based on reward system connectivity.** Dev Cogn Neurosci. 2015 Feb;11:155-74. [[FULL TEXT](#)]

Glannon W (2015) - **Research domain criteria: a final paradigm for psychiatry.** Front Hum Neurosci. 2015 Sep 8;9:488. [\[FULL TEXT\]](#)

Biomarkers, neuromodulation and neuroimaging together may lead to more personalized diagnosis and treatment for psychiatric patients. They could contribute to “precision medicine” for psychiatry, where “treatments are targeted to the needs of individual patients on the basis of genetic, biomarker, phenotypic, or psychosocial characteristics that distinguish a given patient from other patients with similar clinical presentations” (Jameson and Longo, 2015, p. 1).

Explaining psychiatric disorders in terms of dysfunctional circuits in the brain also allows for alternative novel hypotheses that go beyond monoamines and dopamine. Some of these are based on findings of abnormalities in the brain’s resting-state activity.

....and thalamus, a distributed network that mediates conscious processing (Kubicki et al., 2005).

In schizophrenia, there is impaired functional connectivity and low- frequency fluctuations in midline regions. In depression, there is hyperactivity in the midline network and hypoactivity in the lateral network. This imbalance disrupts the connection between the brain and the environment, with a pathological increase in self-focus and a corresponding decrease in environment-focus at the phenomenal level of consciousness.

The neural circuits on which the RDoC focuses may not adequately consider the effects of neuro-immune and neuro- endocrine interactions in the pathophysiology of depression, schizophrenia and possibly other disorders. Cytokines released in response to infection may result in elevated levels of inflammatory biomarkers in the blood. These in turn may lead to inflammatory changes in the brain and alteration of neural circuits that could trigger or exacerbate mood disturbances and cognitive and volitional impairment in depression (Raison et al., 2006, 2013).

Goodkind M, et al (2015) - **Identification of a common neurobiological substrate for mental illness.** JAMA Psychiatry. 2015 Apr;72(4):305-15. [\[FULL TEXT\]](#)

Based on the voxel-based morphometry meta-analysis of 193 studies comprising 15 892 individuals across 6 diverse diagnostic groups (schizophrenia, bipolar disorder, depression, addiction, obsessive-compulsive disorder, and anxiety), we found that gray matter loss converged across diagnoses in 3 regions: the dorsal anterior cingulate, right insula, and left insula. By contrast, there were few diagnosis-specific effects, distinguishing only schizophrenia and depression from other diagnoses. In the parallel follow-up analyses of the 3 independent healthy participant data sets, we found that the common gray matter loss regions formed a tightly interconnected network during tasks and at resting and that lower gray matter in this network was associated with poor executive functioning.

CONCLUSIONS AND REVELANCE: We identified a concordance across psychiatric diagnoses in terms of integrity of an anterior insula/dorsal anterior cingulate-based network, which may relate to executive function deficits observed across diagnoses. This concordance provides an organizing model that emphasizes the importance of shared neural substrates across psychopathology, despite likely diverse etiologies, which is currently not an explicit component of psychiatric nosology.

Gros DE (2015) - **Design challenges in transdiagnostic psychotherapy research: Comparing Transdiagnostic Behavior Therapy (TBT) to existing evidence-based psychotherapy in veterans with affective disorders.** Contemp Clin Trials. 2015 Jul;43:114-9. [\[ABS\]](#)

Frohlich F, et al (2015) - **Targeting the neurophysiology of cognitive systems with transcranial alternating current stimulation.** Expert Rev Neurother. 2015 Feb;15(2):145-67. [\[FULL TEXT\]](#)

Hofmann M, et al (2015) - **The relationship between skill deficits and disability - a transdiagnostic study.** J Clin Psychol. 2015 Apr;71(4):413-21. [\[ABS\]](#)

Transdiagnostic skills (e.g., emotion regulation, stress management) and related self-concepts (e.g., self-esteem) are associated with the pathogenesis and course of different mental disorders. Evidence suggests that skill deficits coincide with not only specific psychopathology but also psychological strain and disability. ...The improvement of skills and related self-concepts during therapy contributed substantially to the improvement of disability ratings.

Krueger RF, et al (2015) - **Transdiagnostic factors of mental disorders.** World Psychiatry 14:1 - February 2015. [\[FULL TEXT\]](#)

"Research on disorder dimensionality and comorbidity suggests that many mental disorders are manifestations of relatively few core underlying dimensions."

Transdiagnostic factors are poised to play a major part in RDoC-oriented investigations of psychopathology. ...such, transdiagnostic factors appear uniquely suited to bridge psychiatric phenomena and biological substrates of behavior,"

In terms of the links between environmental exposures and disorders, studies suggest that transdiagnostic factors largely mediate these associations, meaning that an exposure (e.g., discrimination, adverse childhood experiences) likely raises transdiagnostic factor levels, which manifest as higher rates of multiple observed disorders (5). These findings clarify the diffuse impact of individual exposures on multiple disorders."

" ... disorders' associations with important outcomes are driven by transdiagnostic variance rather than disorder-specific variance."

Maj M (2015) - **The media campaign on the DSM-5: recurring comments and lessons for the future of diagnosis in psychiatric practice.** Epidemiol Psychiatr Sci. 2015 Jun;24(3):197-202. [\[ABS\]](#)

Recurring arguments in the media campaign preceding and following the publication of the DSM-5 have been that the manual, referred to as 'the bible of psychiatry', mislabels many people who are basically normal, and that the diagnostic categories it contains are invalid, not being based on laboratory tests. We present data on the use of the DSM worldwide, and discuss the need to assess systematically the pros and cons of operational and prototype approaches to psychiatric diagnosis.

McCoy TH, et al (2015) - **A clinical perspective on the relevance of research domain criteria in electronic health records.** Am J Psychiatry. 2015 Apr;172(4):316-20. [\[FULL TEXT\]](#)

Objective: The limitations of the DSM nosology for capturing dimensionality and overlap in psychiatric syndromes, and its poor correspondence to underlying neurobiology, have been well established. The Research Domain Criteria (RDoC), a proposed dimensional model of psychopathology, may offer new insights into psychiatric illness. For psychiatric clinicians, however, because tools for capturing these domains in clinical practice have not yet been established, the relevance and means of transition from the categorical system of DSM-5 to the dimensional models of RDoC remains unclear. The authors explored a method of extracting these dimensions from existing electronic health record (EHR) notes.

Method: The authors used information retrieval and natural language processing methods to extract estimates of the RDoC dimensions in the EHRs of a large health system. They parsed and scored EHR documentation for 2,484 admissions covering 2,010 patients admitted to a psychiatric inpatient unit between 2011 and 2013. These domain scores were compared with DSM-IV-based ICD-9 codes to assess face validity. As a measure of predictive validity, these scores were examined for association with two outcomes: length of hospital stay and time to all-cause hospital readmission. Together, these analyses were intended to address the extent to which RDoC symptom domains might capture clinical features already available in narrative notes but not reflected in DSM diagnoses.

Results: In mixed-effects models, loadings for the RDoC cognitive and arousal domains were associated with length of hospital stay, while the negative valence and social domains were associated with hazard of all-cause hospital readmission.

Conclusions: These findings show that a computationally derived tool based on RDoC workgroup reports identifies symptom distributions in clinician notes beyond those captured by ICD-9 codes, and these domains have significant predictive validity. More generally, they point to the possibility that clinicians already document RDoC-relevant

symptoms, albeit not in a quantified form.

Morris SE, et al (2015) - **Psychophysiological science and the research domain criteria: A commentary.** Int J Psychophysiol. 2015 Nov;98(2 Pt 2):378-380. [[FULL TEXT](#)]

...the field of psychophysiology already thinks along the lines of RDoC in terms of using biobehavioral constructs, looking for convergence amongst constructs using various methodologies, and utilizing dimensional measurements in studies. In this sense, RDoC is not novel; however, by specifying a formal research platform it provides explicit encouragement and guidance for using such principles in understanding psychiatric phenomena, rather than continuing to focus research efforts on traditional diagnostic categories alone.

Scott K, et al (2015) - **Using Measurement-Based Care to Enhance Any Treatment.** Cogn Behav Pract. 2015 Feb;22(1):49-59. [[FULL TEXT](#)]

Measurement-based care (MBC) can be defined as the practice of basing clinical care on client data collected throughout treatment. MBC is considered a core component of numerous evidence-based practices (e.g., Beck & Beck, 2011; Klerman, Weissman, Rounsaville, & Chevron, 1984) and has emerging empirical support as an evidence-based framework that can be added to any treatment (Lambert et al., 2003, Trivedi et al., 2007). The observed benefits of MBC are numerous. MBC provides insight into treatment progress, highlights ongoing treatment targets, reduces symptom deterioration, and improves client outcomes (Lambert et al., 2005). Moreover, as a framework to guide treatment, MBC has transtheoretical and transdiagnostic relevance with broad reach across clinical settings.

Shankman SA, et al (2015) - **Psychopathology research in the RDoC era: Unanswered questions and the importance of the psychophysiological unit of analysis.** Int J Psychophysiol. 2015 Nov;98(2 Pt 2):330-337. [[FULL TEXT](#)]

Tegeler CH, et al (2015) - **Rightward dominance in temporal high-frequency electrical asymmetry corresponds to higher resting heart rate and lower baroreflex sensitivity in a heterogeneous population.** Brain Behav. 2015 Jun;5(6):e00343. [[FULL TEXT](#)]

In a heterogeneous population, individuals with rightward compared to leftward temporal high-frequency electrical asymmetry had higher resting heart rate and lower BRS. Two-channel recording of brain electrical activity from bilateral temporal regions appears to hold promise for further investigation as a means to assess cortical activity associated with autonomic cardiovascular regulation.

Terbeck S, et al (2015) - **The role of metabotropic glutamate receptor 5 in the pathogenesis of mood disorders and addiction: combining preclinical evidence with human Positron Emission Tomography (PET) studies.** Front Neurosci. 2015 Mar 18;9:86. [[FULL TEXT](#)]

Glutamate was previously mostly investigated in non-human studies, however initial human clinical PET research now also supports the hypothesis that, by mediating brain excitability, neuroplasticity and social cognition, abnormal metabotropic glutamate activity might predispose individuals to a broad range of psychiatric problems.

Vaidyanathan U, et al (2015) - **The art of smart science: Weaving theory and risky study design into psychopathology research and RDoC.** Psychological Inquiry. 2015a;26:286–292. [[FULL TEXT](#)]

Vaidyanathan U, et al (2015) - **The Power of Theory, Research Design, and Transdisciplinary Integration in Moving Psychopathology Forward.** Psychol Inq. 2015;26(3):209-230. [[FULL TEXT](#)]

What is required, then, to adequately evaluate a scientific question? Simple models can help make sense of unruly data, but heavy reliance on statistics is a poor route to scientific insight. As everyone reading this knows, it takes a question, a theory, a design, an analysis, and a result.

Instead of relying on a single discipline or single methodology, a more appropriate strategy involves identifying concordance between results from different methodologies.

Verona E, et al (2015) - **Aggression proneness: Transdiagnostic processes involving negative valence and cognitive systems.** Int J Psychophysiol. 2015 Nov;98(2 Pt 2):321-329. [[ABS](#)]

Results provide evidence that tendencies toward angry and aggressive behavior relate to reduced inhibitory control processing (no-go P3) specifically during relevant threat-word blocks, suggesting deterioration of cognitive control by acute or sustained threat sensitivity. These findings highlight the value of ERP methodologies for clarifying the interplay of Negative Valence and Cognitive System processes in aggression proneness.

Wigman JT, et al (2015) - **Exploring the underlying structure of mental disorders: cross-diagnostic differences and similarities from a network perspective using both a top-down and a bottom-up approach.** Psychol Med. 2015 Aug;45(11):2375-87. [[ABS](#)]

Cuthbert BN, et al (2014) - **The RDoC framework: continuing commentary.** World Psychiatry. 2014 Jun;13(2):196-7. [[FULL TEXT](#)]

Fang A, et al (2014) - **Attachment Style Moderates the Effects of Oxytocin on Social Behaviors and Cognitions during Social Rejection: Applying an RDoC Framework to Social Anxiety.** Clin Psychol Sci. 2014 Nov 1;2(6):740-747. [[FULL TEXT](#)]

Fulford KW, et al (2014) - **Taking the long view: an emerging framework for translational psychiatric science.** World Psychiatry. 2014 Jun;13(2):110-7. [[FULL TEXT](#)]

Fulford DW (2014) - **RDoC+: taking translation seriously.** World Psychiatry. 2014 Feb;13(1):54-5. [\[FULL TEXT\]](#)

Hofmann SG (2014) - **Toward a cognitive-behavioral classification system for mental disorders.** Behav Ther. 2014 Jul;45(4):576-87. [\[FULL TEXT\]](#)

Langenecker SA, et al (2014) - **Current Neural and Behavioral Dimensional Constructs across Mood Disorders.** Curr Behav Neurosci Rep. 2014 Sep 1;1(3):144-153. [\[FULL TEXT\]](#)

Layous K, et al (2014) - **Positive activities as protective factors against mental health conditions.** J Abnorm Psychol. 2014 Feb;123(1):3-12. [\[FULL TEXT\]](#)

Miller GA, et al (2014) - **Hunting genes, hunting endophenotypes.** Psychophysiology. 2014 Dec;51(12):1329-30. [\[FULL TEXT\]](#)

Sartorius N (2014) - **The only one or one of many? A comment on the RDoC project.** World Psychiatry. 2014 Feb;13(1):50-1. [\[FULL TEXT\]](#)

Seligman ME (2014) - **The real mental illnesses: Susan Nolen-Hoeksema (1959-2013) in memoriam.** J Abnorm Psychol. 2014 Feb;123(1):1-2. [\[ABS\]](#)

Susan Nolen-Hoeksema's life work concerned rumination, gender differences in depression, and the "transdiagnostic" processes in mental illness. The articles in this special section expand on these themes. Her work on transdiagnostic processes leads us to consider that the real mental illnesses are not the congeries of symptoms in the Diagnostic and Statistical Manual of Mental Disorders, but these processes themselves.

Castellanos FX, et al (2013) - **Clinical applications of the functional connectome.** Neuroimage. 2013 Oct 15;80:527-40. [\[FULL TEXT\]](#)

Cuthbert BN, Insel TR (2013) - **Toward the future of psychiatric diagnosis: the seven pillars of RDoC.** BMC Med. 2013 May 14;11:126. [\[FULL TEXT\]](#)

Maia AC, et al (2013) - **Transdiagnostic treatment using a unified protocol - application for patients with a range of comorbid mood and anxiety disorders.** Trends Psychiatry Psychother. 2013;35(2):134-40. [\[FULL TEXT\]](#)

An effort to establish **one unified treatment protocol for a whole family of emotional disorders (primarily mood and anxiety disorders)** showed benefits in the field of clinical psychology and for the treatment of patients. No other data were found in the literature describing the implementation of the unified protocol in a transdiagnostic group. Our results revealed statistically significant improvement in all variables, suggesting that the protocol proposed can become an important tool to improve quality of life, sexuality, and anxiety/depression symptoms in patients with different diagnoses.

Walter H (2013) - **The third wave of biological psychiatry**. Front Psychol. 2013 Sep 5;4:582. [\[FULL TEXT\]](#)

In contrast to earlier biological psychiatry approaches, the mental plays a more prominent role in the third wave. This will become apparent by discussing the recent controversy evolving around the recently published DSM-5 and the competing transdiagnostic Research Domain Criteria approach of the National Institute of Mental Health that is built on concepts of cognitive neuroscience. A look at current conceptualizations in biological psychiatry as well as at some discussions in current philosophy of mind on situated cognition, reveals that the thesis, that mental brain disorders are brain disorders has to be qualified with respect to how mental states are constituted and with respect to multilevel explanations of which factors contribute to stable patterns of psychopathological signs and symptoms.

Buckholtz JW, et al (2012) - **Psychopathology and the human connectome: toward a transdiagnostic model of risk for mental illness**. Neuron. 2012 Jun 21;74(6):990-1004. [\[FULL TEXT\]](#)

The panoply of cognitive, affective, motivational, and social functions that underpin everyday human experience requires precisely choreographed patterns of interaction between networked brain regions. Perhaps not surprisingly, diverse forms of psychopathology are characterized by breakdowns in these interregional relationships. Here, we discuss how functional brain imaging has provided insights into the nature of brain dysconnectivity in mental illness. Synthesizing work to date, we propose that genetic and environmental risk factors impinge upon systems-level circuits for several core dimensions of cognition, producing transdiagnostic symptoms. We argue that risk-associated disruption of these circuits mediates susceptibility to broad domains of psychopathology rather than discrete disorders

Conway CC, et al (2012) - **Expanding stress generation theory - test of a transdiagnostic model**. J Abnorm Psychol. 2012 Aug; 121(3): 754–766.. [\[FULL TEXT\]](#)

Farchione TJ, et al (2012) - **Unified protocol for transdiagnostic treatment of emotional disorders: a randomized controlled trial**. Behav Ther. 2012 Sep;43(3):666-78. [\[FULL TEXT\]](#)

Morris SE, et al (2012) - **Research Domain Criteria: cognitive systems, neural circuits, and dimensions of behavior**. Dialogues Clin Neurosci. 2012 Mar;14(1):29-37. [\[FULL TEXT\]](#)

Insel T, et al (2010) - **Research domain criteria (RDoC) - Toward a new classification framework for research on mental disorders**. Am J Psychiatry. 2010 Jul;167(7):748-51. [\[FULL TEXT\]](#)

Appendix B – Selected Articles for Group Study

Cauda F, et al (2020) - **Hubs of long-distance co-alteration characterize brain pathology.** Hum Brain Mapp. 2020 Jun 20. [\[ABS\]](#)

It is becoming clearer that the impact of brain diseases is more convincingly represented in terms of co-alterations rather than in terms of localization of alterations. In this context, areas characterized by a long mean distance of co-alteration may be considered as hubs with a crucial role in the pathology.

The anterodorsal prefrontal cortices appeared to be a transdiagnostic hub of long-distance co-alterations. Also, the disease-specific analyses showed that long-distance co-alterations are more able than classic meta-analyses to identify areas involved in pathology and symptomatology. Moreover, the distance maps were correlated with the normative connectivity. Our findings substantiate the network degeneration hypothesis in brain pathology. At the same time, they suggest that the concept of co-alteration might be a useful tool for clinical neuroscience.

Doucet GE, et al (2020) - **Transdiagnostic and disease-specific abnormalities in the default-mode network hubs in psychiatric disorders: A meta-analysis of resting-state functional imaging studies.** Eur Psychiatry. 2020 May 29;63(1):e57. [\[FULL TEXT\]](#)

BACKGROUND. The default mode network (DMN) dysfunction has emerged as a consistent biological correlate of multiple psychiatric disorders. Specifically, there is evidence of alterations in DMN cohesiveness in schizophrenia, mood and anxiety disorders. The aim of this study was to synthesize at a fine spatial resolution the intra-network functional connectivity of the DMN in adults diagnosed with schizophrenia, mood and anxiety disorders, capitalizing on powerful meta-analytic tools provided by activation likelihood estimation. **METHODS.** Results from 70 whole-brain resting-state functional magnetic resonance imaging articles published during the last 15 years were included comprising observations from 2,789 patients and 3,002 healthy controls. **RESULTS.** **Specific regional changes in DMN cohesiveness located in the anteromedial and posteromedial cortex emerged as shared and trans-diagnostic brain phenotypes.** Disease-specific dysconnectivity was also identified. Unmedicated patients showed more DMN functional alterations, highlighting the importance of interventions targeting the functional integration of the DMN. **CONCLUSION.** This study highlights functional alteration in the major hubs of the DMN, suggesting common abnormalities in self-referential mental activity across psychiatric disorders.

Huang CC, et al (2020) - **Transdiagnostic and Illness-Specific Functional Dysconnectivity Across Schizophrenia, Bipolar Disorder, and Major Depressive Disorder.** Biol Psychiatry Cogn Neurosci Neuroimaging. 2020 May;5(5):542-553. [\[ABS\]](#)

Mental disorders are typically defined as distinct diagnostic entities, but similar patterns

of clinical and cognitive impairments are frequently found across diagnostic groups. We investigated whether these transdiagnostic deficits result from common neural substrates across disorders or various illness-specific mechanisms, or a combination of both. ...**Disconnectivity in the somatomotor network was a common transdiagnostic profile**, while there were illness-specific patterns in different parts of the prefrontal cortex for different disorders. These findings suggest that prominent psychiatric disorders share common impairments, possibly linked to perception and motor output, as well as unique dysconnectivity profiles that hypothetically mediate the more distinctive features of the disorder-specific psychopathology.

Ma Q, et al (2020) - **Transdiagnostic Dysfunctions in Brain Modules Across Patients with Schizophrenia, Bipolar Disorder, and Major Depressive Disorder: A Connectome-Based Study.** Schizophr Bull. 2020 Apr 10;46(3):699-712. [[FULL TEXT](#)]

Psychiatric disorders, including schizophrenia (SCZ), bipolar disorder (BD), and major depressive disorder (MDD), share clinical and neurobiological features. ... These alterations in modular organization significantly correlate with clinical scores in patients. ...This study demonstrates common hyper-integrated modular architectures of functional brain networks among patients with SCZ, BD, and MDD. These findings reveal a transdiagnostic mechanism of network dysfunction across psychiatric disorders from a connectomic perspective.

van Oort J, et al (2020) - **Absence of default mode downregulation in response to a mild psychological stressor marks stress-vulnerability across diverse psychiatric disorders.** Neuroimage Clin. 2020;25:102176. [[FULL TEXT](#)]

Clinically, it is well-established that vulnerability to stress is a common feature across a broad spectrum of psychiatric disorders. However, this link has been mechanistically studied almost exclusively in patients with so-called stress-related disorders such as depression and anxiety. To probe transdiagnostic mechanisms, we set out to study the acute stress response across a broader range of psychiatric disorders taking a large-scale brain network perspective. We investigated the brain's response to a mild, experimentally well-controlled psychological stressor in the form of an aversive movie. We studied 168 patients with stress-related and/or neurodevelopmental disorders (including comorbidity) and 46 control subjects. We focused on three networks that have a central role in the brain's stress response and are affected in a wide range of psychiatric disorders: the salience network (SN), default mode network (DMN) and frontoparietal network (FPN). Our results support an increased vulnerability to stress across all patients, indicated by a higher subjective stress level at baseline and follow-up compared to matched controls. At the brain systems level, the stress response was characterized by a relatively decreased FPN connectivity and an absence of a decrease in the within DMN connectivity across all disorders compared to controls. At the neurocognitive level, these findings may reflect a diminished top-down control and a tendency to more pronounced (negative) self-referential processing. Besides these

shared aspects of the maladaptive stress response, we also discuss indications for disorder-specific aspects. Taken together, our results emphasize the importance of investigating the mechanistic underpinnings of psychiatric disorders transdiagnostically as recently done in neurogenetics.

Robinson OJ, et al (2019) - **The translational neural circuitry of anxiety.** J Neurol Neurosurg Psychiatry. 2019 Dec;90(12):1353-1360. [\[ABS\]](#)

Anxiety is an adaptive response that promotes harm avoidance, but at the same time excessive anxiety constitutes the most common psychiatric complaint. Moreover, current treatments for anxiety-both psychological and pharmacological-hover at around 50% recovery rates. Improving treatment outcomes is nevertheless difficult, in part because contemporary interventions were developed without an understanding of the underlying neurobiological mechanisms that they modulate. ...We highlight the roles of subcortical regions (and their subunits) such as the bed nucleus of the stria terminalis, the amygdala, and the hippocampus, as well as their connectivity to cortical regions such as dorsal medial and lateral prefrontal/cingulate cortex and insula in maintaining anxiety responding. We discuss how this circuitry might be modulated by current treatments before finally highlighting areas for future research that might ultimately improve treatment outcomes for this common and debilitating **transdiagnostic** symptom.

Menzies RE, et al (2019) - **The relationship between death anxiety and severity of mental illnesses.** Br J Clin Psychol. 2019 Nov;58(4):452-467. [\[ABS\]](#)

Death anxiety has been implicated theoretically and empirically in mental health and has been proposed to be a **transdiagnostic** construct. ...Across the sample, death anxiety was a strong predictor of psychopathology, including the number of lifetime diagnoses, medications, hospitalizations, distress/impairment, depression, anxiety, and stress ... Large to very large correlations were also consistently found between a measure of death anxiety and the symptom severity of 12 disorders. Neither meaning in life nor attachment style moderated the associations between death fears and psychopathology. ..., death anxiety significantly predicted symptom severity. Results may suggest the need for novel treatments which specifically target fears of death

Parkes L, et al (2019) - **Transdiagnostic variations in impulsivity and compulsivity in obsessive-compulsive disorder and gambling disorder correlate with effective connectivity in cortical-striatal-thalamic-cortical circuits.** Neuroimage. 2019 Nov 15;202:116070. [\[FULL TEXT\]](#)

Across all participants, higher disinhibition correlated with lower bottom-up connectivity in the dorsal circuit and greater bottom-up connectivity in the ventral circuit, and higher compulsivity correlated with lower bottom-up connectivity in the dorsal circuit. In patients, higher clinical severity was also linked to lower bottom-up connectivity in the dorsal circuit, but these findings were independent of phenotypic variation, demon-

strating convergence towards behaviourally and clinically relevant changes in brain dynamics. Effective connectivity did not differ as a function of traditional diagnostic labels and only weak associations were observed for functional connectivity measures. Together, our results demonstrate that cortical-striatal-thalamic-cortical dysfunction across obsessive-compulsive disorder and gambling disorder may be better characterized by dimensional phenotypes than diagnostic comparisons, supporting investigation of quantitative liability phenotypes.

Lydon-Staley DM, et al (2019) - **Repetitive negative thinking in daily life and functional connectivity among default mode, fronto-parietal, and salience networks**. Transl Psychiatry. 2019 Sep 18;9(1):234. [[FULL TEXT](#)]

Repetitive negative thinking (RNT) is a maladaptive response to sadness and a **transdiagnostic** risk-factor. ...We show that RNT increases following sadness for participants with higher than average between-network connectivity of the default mode network and the fronto-parietal network. We also show that RNT increases following increases in sadness for participants with lower than average between-network connectivity of the fronto-parietal network and the salience network. We also find that flexibility of the salience network's pattern of connections with brain regions is protective against increases in RNT following sadness. Our findings highlight the importance of functional brain networks implicated in cognitive conflict signaling, self-referential thought, and cognitive flexibility for understanding maladaptive responses to sadness in daily life and provide support for the impaired disengagement hypothesis of RNT.

Manning K, et al (2019) - **Recent advances in the use of imaging in psychiatry: functional magnetic resonance imaging of large-scale brain networks in late-life depression**. F1000Res. 2019 Aug 6;8:F1000 Faculty Rev-1366. [[FULL TEXT](#)]

We discuss how neural functioning of three networks is linked to symptom presentation, illness course, and cognitive decline in LLD. These networks are (1) an executive control network responsible for complex cognitive processing, (2) a default mode network normally deactivated during cognitive demanding when individuals are at rest, and a (3) salience network relevant to attending to internal and external emotional and physiological sensations. We discuss how dysfunction in multiple networks contributes to common behavioral syndromes, and we present an overview of the cognitive control, default mode, and salience networks observed in LLD.

Bakker GM (2019) - **A new conception and subsequent taxonomy of clinical psychological problems**. BMC Psychol. 2019 Jul 10;7(1):46. [[FULL TEXT](#)]

A taxonomy of the objects of study, theory, assessment, and intervention is critical to the development of all clinical sciences.

Clinical psychology has been conceptually and administratively dominated by the taxonomy of an adjacent discipline - psychiatry's Diagnostic and statistical manual of mental disorders (DSM). Many have called for a 'paradigm shift' away from a medical nosology of diseases toward clinical psychology's own taxonomy of clinical psychological problems (CPPs), without being able to specify what is to be listed and classified.

The critical psychological-level phenomenon underlying **CPPs** is the occurrence of 'problem-maintaining circles' (**PMCs**) of causally related cognitions, emotions, behaviours, and/or stimuli. *This concept provides an empirically-derived, theory-based, treatment-relevant, categorical, essentialist, parsimonious, and nonstigmatizing definition of CPPs.* It distinguishes psychological problems in which PMCs have not (yet?) formed, and which may respond to 'counseling', clinical psychological problems in which active PMCs require clinical intervention, and psychopathological problems which are unlikely to be 'cured' by PMC-breaking alone.

A subsequent classification and coding system of PMCs is proposed, and expected benefits to research, communication, and the quality of case formulation in clinical psychology are described, reliant upon a development effort of some meaningful fraction of that which has been devoted to the DSM.

Wichers M, et al (2019) - **Can we predict the direction of sudden shifts in symptoms? Transdiagnostic implications from a complex systems perspective on psychopathology.** Psychol Med. 2019 Feb;49(3):380-387. [[FULL TEXT](#)]

(Research) designs should be able to follow sudden transitions 'live' using frequent observations of symptoms within individuals and apply a **transdiagnostic** approach to psychopathology. If the assumptions proposed are supported by empirical studies then this will signify a large improvement in the possibility for personalized estimations of the course of psychiatric symptoms. Such information can be extremely useful for early intervention strategies aimed at preventing specific psychiatric problems.

Murano T, et al (2019) - **Transcriptomic immaturity inducible by neural hyperexcitation is shared by multiple neuropsychiatric disorders.** Commun Biol. 2019 Jan 22;2:32. [[FULL TEXT](#)]

Biomarkers are needed to improve the diagnosis of neuropsychiatric disorders, which are often associated to excitatory/inhibitory imbalances in neural transmission and abnormal maturation. Here, we characterized different disease conditions by mapping changes in the expression patterns of maturation-related genes whose expression was altered by experimental neural hyperexcitation in published studies. This analysis revealed two gene expression patterns: decreases in maturity markers and increases in immaturity markers. These two groups of genes were characterized by the over-representation of genes related to synaptic function and chromosomal modification, respectively. Using these two groups in a **transdiagnostic** analysis of 87 disease datasets for eight neuropsychiatric disorders and 12 datasets from corresponding animal models, we

found that transcriptomic pseudoimmaturity inducible by neural hyperexcitation is shared by multiple neuropsychiatric disorders, such as schizophrenia, Alzheimer disorders, and amyotrophic lateral sclerosis. Our results indicate that this endophenotype serves as a basis for the **transdiagnostic** characterization of these disorders.

Zhao Z, et al (2019) - **Real-Time Functional Connectivity-Informed Neurofeedback of Amygdala-Frontal Pathways Reduces Anxiety**. Psychother Psychosom. 2019;88(1):5-15. [\[ABS\]](#)

Deficient *emotion regulation* and exaggerated anxiety represent a major **transdiagnostic** psychopathological marker. On the neural level these deficits have been closely linked to impaired, yet treatment-sensitive, prefrontal regulatory control over the amygdala. Gaining direct control over these pathways could therefore provide an innovative and promising intervention to regulate exaggerated anxiety.

To this end the current proof-of-concept study evaluated the feasibility, functional relevance and maintenance of a novel connectivity-informed real-time fMRI neurofeedback training. **METHODS:** In a randomized crossover sham-controlled design, 26 healthy subjects with high anxiety underwent real-time fMRI-guided neurofeedback training to enhance connectivity between the ventrolateral prefrontal cortex (vlPFC) and the amygdala (target pathway) during threat exposure. Maintenance of regulatory control was assessed after 3 days and in the absence of feedback. Training-induced changes in functional connectivity of the target pathway and anxiety ratings served as primary outcomes.

Training of the target, yet not the sham control, pathway significantly increased amygdala-vlPFC connectivity and decreased levels of anxiety. Stronger connectivity increases were significantly associated with higher anxiety reduction on the group level. At the follow-up, volitional control over the target pathway was maintained in the absence of feedback.

The present results demonstrate for the first time that successful self-regulation of amygdala-prefrontal top-down regulatory circuits may represent a novel intervention to control anxiety. As such, the present findings underscore both the critical contribution of amygdala-prefrontal circuits to emotion regulation and the therapeutic potential of connectivity-informed real-time neurofeedback.

Price RB, et al (2018) - **Towards personalized, brain-based behavioral intervention for transdiagnostic anxiety: Transient neural responses to negative images predict outcomes following a targeted computer-based intervention**. J Consult Clin Psychol. 2018 Dec;86(12):1031-1045. [\[FULL TEXT\]](#)

Excessive attentional deployment toward threat is a **transdiagnostic** dimension of anxiety seen at both initial and sustained stages of threat processing. However, group-level observations of these phenomena mask considerable within-group heterogeneity that

has been linked to treatment outcomes, suggesting that a **transdiagnostic**, individual differences approach may capture critical, clinically relevant information.

Seventy clinically anxious individuals were randomized to receive 8 sessions of **attention bias modification** (ABM) ; ... a computer-based mechanistic intervention that specifically targets initial stages of threat processing, or a sham control ... fMRI ...Larger transient responses across a wide range of cognitive-affective regions (e.g., ventrolateral prefrontal cortex, anterior cingulate cortex, amygdala) predicted better clinical outcomes following ABM, in both a priori anatomical regions and whole-brain analyses; sustained responses did not.

Neural alterations occurring on the relatively transient timescale that is specifically targeted by ABM predict favorable clinical outcomes. Results inform how to *expand on the initial promise of neurocognitive treatments* like ABM by fine-tuning their clinical indications (e.g., *through personalized mechanistic intervention relevant across diagnoses*) and *by increasing the range of mechanisms that can be targeted* (e.g., through synergistic treatment combinations and/or novel neurocognitive training protocols designed to tackle identified predictors of nonresponse).

END