

Clinical Implications in PTSD

Allbaugh, L. J., George, G., Klengel, T., Profetto, A., Marinack, L., O'Malley, F., & Ressler, K. J. (2024). Children of trauma survivors: Influences of parental posttraumatic stress and child-perceived parenting. *Journal of Affective Disorders*, 354, 224–231. <https://doi.org/10.1016/j.jad.2024.03.067>

Children whose parents have PTSD are at an increased risk for both internalizing and externalizing disorders. This risk transmission may operate through multiple mechanisms, such as an increased risk for trauma exposure, genetic/epigenetic changes, and changes in parenting style that promote psychopathology. This study aimed to both replicate the interaction between parental PTSD symptoms (PTSS) and parenting behaviors (both positive, adaptive parenting behaviors and more maladaptive, harmful parenting behaviors) on child PTSS, and extend these findings by investigating this association based on child-report. Ninety-three mother-child dyads (62 no parent PTSS; 31 parent PTSS) were recruited and assessed virtually using measures of PTSS and parenting styles. Consistent with previous research, results confirmed a positive association between parental and child PTSS (child reported). Results also identified an interaction between PTSS and parenting behaviors, such that negative parenting styles were associated with higher PTSS in all children (regardless of parental PTSS levels), whereas positive parenting styles were associated with lower PTSS only for children with parents without PTSS (i.e., positive parenting behaviors were not protective of child PTSS among parents with PTSS). Findings suggest that joint attention must be paid to both parenting practices and to a parent's recovery from PTSS, to best assist parents with PTSS in both parenting and protect their children from intergenerational risk.

Fernando, M., Fite, R. E., & Thompson-Hollands, J. (2024). Brief family involvement enhances veteran homework quality during trauma-focused psychotherapy. *Psychological Trauma: Theory, Research, Practice, and Policy*. Advance online publication. <https://doi.org/10.1037/tra0001678>

Cognitive Processing Therapy and Prolonged Exposure, two popular evidence-based therapies for PTSD, entail between-session assignments to promote generalization of within-session learning. Many clients struggle to complete homework regularly, though, and those with low homework completion may be at risk for drop out or treatment non-response. This study examined how involving family in PTSD treatment may impact homework completion for veterans in PTSD treatment. Family members received the Brief Family Intervention for PTSD (BFI), a two-session adjunctive intervention that includes psychoeducation about PTSD and skills to provide support to their loved one during treatment. Of the 24 veteran-partner dyads who were included in the study, those whose partners received the BFI ($n = 10$) had significantly better clinician-rated homework quality than those who did not. Qualitative analysis of post-study interviews revealed themes that may promote homework engagement, such as dyads engaging in discussions about PTSD, providing check-ins about treatment, and offering more encouragement for homework. These findings support involving family early in veterans' PTSD treatment to improve homework quality.

Saraiya, T. C., Jones, A. C., Lopez-Castro, T., Hood, C. O., Flores, J., & Badour, C. L. (2024). Trauma-related shame predicts daily non-medical prescription opioid use among individuals with PTSD symptoms. *Journal of Psychiatric Research, 171*, 171–176. <https://doi.org/10.1016/j.jpsychires.2024.01.041>

Individuals who experience PTSD symptoms may be at an increased risk for non-medical prescription opioid use (NMPOU). The opioid susceptibility model suggests opioids may be used to manage trauma-related symptoms, particularly intrusive memories. Further, trauma-related shame has been associated with avoidant coping and more severe PTSD symptoms. This study therefore examined the impact of trauma-related shame on symptom severity and NMPOU in 40 community-recruited adults reporting both PTSD symptoms (PTSS) and a recent history of NMPOU. Results indicated that higher trauma-related shame at baseline was associated with higher daily NMPOU. Trauma-related shame significantly predicted NMPOU due to the following motives: managing negative emotions (e.g., depression, sadness, anxiety, worry) and getting high. These findings suggest that targeting trauma-related shame may reduce NMPOU in individuals with comorbid PTSD and NMPOU.

Diversity, Equity, and Inclusion

Cohen, G. H., Wang, R., Rosenberg, S. B., Sampson, L., Lowe, S. R., Cabral, H., Ruggiero, K., & Galea, S. (2024). Neighborhood-level economic characteristics and depression and PTSD symptoms among Houstonians who have experienced Hurricane Harvey and COVID-19. *Psychiatry Research, 333*, 115766.

Those with socioeconomic vulnerability may be exposed to additional stressors after trauma-exposure, such as financial strain, housing instability, unemployment, and low access to healthcare. This study examined the role of neighborhood-level differences in economic disparity in mental health symptoms after a mass traumatic event. Residents (N = 872) living in Houston during Hurricane Harvey and COVID-19 were surveyed regarding their trauma exposure, depression, and PTSD symptoms. Data was aggregated into 88 groups by neighborhood. Analyses found that lower neighborhood median income was associated with more severe PTSD symptoms. Within-neighborhood income inequality was associated with both PTSD and depression, though these differences appeared better accounted for by event-level exposure to stress. These findings suggest the need to consider individual, neighborhood, and community-level factors in understanding risk for post-disaster PTSD and depression.

Elbasheir, A., Fulton, T. M., Choucair, K. C., Lathan, E. C., Spivey, B. N., Guelfo, A., Carter, S. E., Powers, A., & Fani, N. (2024). Moral injury, race-related stress and post-traumatic stress disorder in a trauma-exposed Black population. *Journal of Psychiatric Research, 173*, 326–332. <https://doi.org/10.1016/j.jpsychires.2024.03.016>

Moral injury (MI) describes distress caused by an experience that severely violates personal morals or values. This construct may mediate the association between racial trauma (and consequent race-related stress) and PTSD because experiences of racism may be perceived as more disturbing if they entail betrayal from a trusted institution or person. This study examined

the relationship between MI exposure, MI-related distress, and race-related stress in a large sample of Black American civilians (N = 228). Results indicated that frequency of MI exposure and resultant MI-related distress were both positively associated with cultural, individual, and institutional race-related stress. Further, MI-related distress mediated the relationship between race-related stress and current PTSD symptoms. Findings suggests that MI may be a mechanism through which race-related stress increases the risk for PTSD among Black individuals.

Jeon, M. E., Robison, M., Robertson, L., Udupa, N. S., Potter, M. R., & Joiner, T. E. (2024). From identity-based distress to thinking "I am better off being dead:" Minority stress, posttraumatic cognitions, and suicidal ideation. *Journal of Affective Disorders, 354*, 143–151. <https://doi.org/10.1016/j.jad.2024.03.064>

Minority stress encompasses the insidious and cumulative impact of discrimination impact on those who experience marginalization. Although this model was originally developed in sexual and gender minority populations, it has broad applicability to marginalized individuals across identity domains (race, ethnicity, disability status, intersectionality of identities). This cross-sectional study examined the relationship between minority stress, suicidal ideation, and posttraumatic cognitions in minoritized young adults (N = 337). Results indicated that experiences of discrimination were positively associated with minority stress and posttraumatic cognitions. Further, minority stress was associated with increased posttraumatic cognitions, which in turn were associated with higher suicidal ideation. Findings suggest that posttraumatic cognitions within the context of discrimination may be effective treatment targets for minoritized individuals who present with minority stress and suicidal ideation.

Assessment and Diagnosis

Jia, Y. L., Yang, B. N., Yang, Y. H., Zheng, W. M., Wang, L., Huang, C. Y., Lu, J., & Chen, N. (2024). Application of machine learning techniques in the diagnostic approach of PTSD using MRI neuroimaging data: A systematic review. *Heliyon, 10*(7), e28559. <https://doi.org/10.1016/j.heliyon.2024.e28559>

Although neuroimaging data is often examined in the context of PTSD research, it is unclear if this data can be feasibly used to determine PTSD diagnostic status in clinical care. Machine learning (ML) has the potential to aid in the application of biomarkers (including those identified via neuroimaging) to diagnosis, such as by identifying unique phenotypes and structural abnormalities that distinguish between those with PTSD and those without this diagnosis. This systematic review included 13 studies that examined ML, neuroimaging, and PTSD to determine the current state of the science on this topic. Results indicated that the study and implementation of artificial neural networks (ANNs) have contributed significantly to the advancement of ML, with ML demonstrating high levels of accuracy (minimum accuracy above 70%) in discriminating participants with PTSD from both trauma-exposed healthy controls and healthy controls. Support vector machine learning was the most used ML technique. Across studies, connectivity patterns in the Insula and Amygdala appeared to have diagnostic significance. Findings suggest that the consistent use of ML algorithms based on neuroimaging in the diagnostic process of patients with PTSD may lead to increased accuracy with these techniques

and the eventual ability of clinicians to use these techniques to recognize PTSD in individuals earlier in the condition.

Legendre, M., Milot, T., Rousseau, M., Lemieux, R., Garon-Bissonnette, J., & Berthelot, N. (2024). Beyond abuse and neglect: Validation of the childhood interpersonal trauma inventory in a community sample of adults. *Frontiers in Psychiatry, 15*, 1358475. <https://doi.org/10.3389/fpsy.2024.1358475>

Childhood trauma is associated with psychiatric outcomes in adulthood. Although childhood trauma is most often operationalized as abuse or neglect in childhood, children may be exposed to a wider range of extremely adverse experiences (e.g., peer bullying, parentification, witnessing intimate partner violence, parental overcontrol). These experiences may play a pivotal role in development despite not being identified in our current measures of childhood trauma. This study presents the development of the Childhood Interpersonal Trauma Inventory (CITI), an adult measure of childhood trauma that uniquely includes a wide range of potentially traumatic experiences. When using the childhood trauma questionnaire (CTQ) as a gold standard, the CITI was 64.81-88.71% sensitive and 68.55-89.54% specific, with the CITI and the CTQ accounting for a similar percentage of the variance in PTSD symptoms. Further, the CITI identified an additional 25% of participants not captured by the CTQ, who reported a higher severity of psychiatric symptoms than participants without trauma. Findings suggest that the CITI may not only appropriately capture childhood trauma as traditionally conceptualized, but also may better identify adults with psychiatric symptoms related to less-commonly assessed negative childhood experiences than do other measures of childhood traumatic exposure.

Raines, A. M., Clauss, K. E., Seidler, D., Allan, N. P., Elhai, J. D., Vasterling, J. J., Constans, J. I., Maieritsch, K. P., & Franklin, C. L. (2024). A bifactor evaluation of self-report and clinician-administered measures of PTSD in veterans. *Assessment. Advance online publication*. <https://doi.org/10.1177/10731911241229568>

The PTSD Checklist for *DSM-5* (PCL-5), a self-report questionnaire, and the Clinician-Administered PTSD Scale for *DSM-5* (CAPS-5), a semi-structured interview, are two of the most widely used and well-validated PTSD measures providing total and subscale scores that correspond with *DSM-5* PTSD symptoms. Although both measures include items and subscales that correspond to *DSM-5* PTSD diagnostic criteria, little is known about the actual interpretability and utility of the subscale scores above and beyond the total score for either measure. This study compared the *DSM-5* four factor model to a bifactor model across both measures in a large sample of veterans (N = 1,240) presenting for treatment to VA PTSD specialty clinics. For both measures, the bifactor model – including a general PTSD factor and the individual lower order-factors (i.e., the subscales) – provided the best fit (marginal-to-acceptable) – and was retained. For both measures, the general PTSD factor accounted for the majority of reliability variance, with only a small minority of reliable variance in the lower-order factors demonstrating independence from the general factor. For the lower-order factors, individual PTSD subscales (i.e., intrusions, avoidance, negative alterations in cognitions and mood, arousal) demonstrated both small item loadings (suggesting redundancy in content) and limited utility in predicting related psychiatric outcomes (e.g., depression, alcohol use, and

substance use). While further study is needed, this study suggests that PTSD subscale scores for both the PCL-5 and the CAPS-5 provide little utility beyond the overall total score, highlighting the need to interpret subscale-level scores with caution.

Neurological, Biological, and Translational Science

Fruchter, E., Goldenthal, N., Adler, L. A., Gross, R., Harel, E. V., Deutsch, L., Nacasch, N., Grinapol, S., Amital, D., Voigt, J. D., & Marmar, C. R. (2024). Amygdala-derived-EEG-fMRI-pattern neurofeedback for the treatment of chronic post-traumatic stress disorder. A prospective, multicenter, multinational study evaluating clinical efficacy. *Psychiatry Research*, 333, 115711. <https://doi.org/10.1016/j.psychres.2023.115711>

Heightened amygdala activity has been observed when individuals with PTSD become aroused in reaction to a trauma-related stimuli. Neurofeedback therapy teaches patients to self-regulate by showing them real-time feedback of their neurological activity. Amygdala-derived-EEG-fMRI-Pattern (EFP) neurofeedback (NF) therapy combines signals from both EEG and fMRI to give the patient real-time information about their amygdala activity. This treatment was designed to be used adjunctively to trauma-focused therapy. In this open label trial, patients (N = 79) received 15 neurofeedback sessions and follow up assessments after receiving at least one month of PTSD standard of care treatment. Of the participants that completed at least 12 sessions ($n = 63$), the majority (66.7%) demonstrated a minimally clinically important difference (defined *a priori* as a 6-point or greater reduction in Clinician Administered PTSD Scale for *DSM-5* [CAPS-5] scores), with a mean reduction of 13.2 points on the CAPS-5 at the three month follow up. The dropout rate was low (16.5%; $n = 13$ participants). Although more work is needed, this study provides support for Amygdala-Derived-EFP NF therapy in reducing PTSD symptoms.

Hori, H., Fukushima, H., Nagayoshi, T., Ishikawa, R., Zhuo, M., Yoshida, F., Kunugi, H., Okamoto, K., Kim, Y., & Kida, S. (2024). Fear memory regulation by the cAMP signaling pathway as an index of reexperiencing symptoms in posttraumatic stress disorder. *Molecular Psychiatry*. Advance online publication. <https://doi.org/10.1038/s41380-024-02453-4>

Although the development of PTSD is contingent upon environmental factors (i.e., traumatic experiences), recent work has suggested that genetic factors may also play a role in the etiology. The mechanism by which these genetic factors are linked to PTSD has not been elucidated; however, recent work suggests that several candidate genes activate the cyclic adenosine monophosphate (cAMP) signaling pathway, which may have implications specifically for dysregulation associated with fear memory. PTSD is often associated with dysfunctions in fear memory, including regulation of retrieval, maintenance, and reconsolidation, and may manifest in the form of reexperiencing symptoms. In this study, the authors utilized loss- and gain-of-function procedures to demonstrate the role of cAMP signaling in both mice and human models of PTSD. In mice, for which reexperiencing symptoms were modeled through retrieval-related fear memory events, upregulation of cAMP signaling enhanced retrieval and maintenance of the fear memory, whereas downregulation impaired retrieval and maintenance. Consistent with these findings, human (female) patients with PTSD had reduced expression of phosphodiesterase 4B

(PDE4b), an enzyme that degrades cAMP, which in turn was associated with more reexperiencing symptoms. These findings suggest that the facilitation of cAMP signaling mediating the down regulation of PDE4B expression enhances trauma memory, thereby playing a key role in the manifestation of reexperiencing symptoms in PTSD.

Norred, M. A., Zuschlag, Z. D., & Hamner, M. B. (2024). A neuroanatomic and pathophysiologic framework for novel pharmacological approaches to the treatment of Post-traumatic Stress Disorder. *Drugs*, 84(2), 149–164. <https://doi.org/10.1007/s40265-023-01983-5>

Only two medications are currently US FDA-approved for the treatment of PTSD, and both are Serotonin Reuptake Inhibitors (SSRIs). However, research indicates that there are multiple non-serotonergic pathways associated with PTSD, which may be targets for drug development. This paper reviews novel and emerging pharmacological approaches for PTSD and incorporates these into a common pathophysiological framework of trauma-related disorders. The resultant framework maps associations between the HPA axis, regional brain hyperactivity (e.g., anterior cingulate cortex, amygdala, nucleus accumbens), and regional hypoactivity (e.g., prefrontal cortex, hippocampus), and notes specific drug-based mechanisms of action in these areas. This proposed framework provides a map for understanding the physiological underpinning of PTSD and how drugs – both SSRIs and non-SSRIs – can simultaneously intervene in multiple ways throughout this system.