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TREATMENT

Recent studies provide insight into which treatments might be best for which patients

Despite the range of effective treatments for PTSD, not all treatments work equally well for all people. Investigators are increasingly focused on identifying which patients respond best to certain treatments. This knowledge can eventually be used to match patients to the treatments to which they are most likely to respond. Five recently published studies tested whether patient characteristics prior to treatment predicted differential treatment outcomes, with three of the studies leveraging data from completed clinical trials. The first three studies examined how emotion regulation difficulties, severe depression, and sleep disorders affected treatment outcomes. Two medication studies showed that treatment outcomes vary for patients with different genetic predispositions, trauma histories, and levels of symptom severity. Taken together, these studies suggest that better understanding of which variables predict response vs. non-response can eventually lead to personalized and optimized treatment planning for PTSD and related problems.

Patients with both PTSD and substance abuse can have difficulty managing strong emotions. Given that trauma-focused therapies require patients to confront painful memories, and that substance use is often triggered by negative emotions, patients with poorer emotion regulation skills when starting treatment may show less response to treatment than patients with better skills. Investigators at Adelphi University and the City College of New York tested the role of baseline emotion regulation skills in predicting treatment outcomes in a randomized clinical trial of Concurrent Treatment with Prolonged Exposure (COPE), a treatment for comorbid PTSD and SUD. In this trial, COPE ($n = 39$) was compared to Relapse Prevention Therapy (RPT) for SUD ($n = 43$) and an active monitoring control group ($n = 28$; see the [June 2017 CTU-Online](#)). Among patients with greater difficulties in emotion regulation, COPE was more effective than RPT for reducing PTSD symptoms. Among patients with lesser difficulties in emotion regulation, RPT was associated with fewer days of substance use than COPE. Findings suggest that a measure of emotion regulation could be used for treatment matching, although patient goals (e.g., reducing PTSD vs. substance use) could also be important in determining the optimal treatment for a given patient.

Read the article: <https://doi.org/10.1016/j.janxdis.2017.10.003>

In another study that focused on comorbidity, investigators at the National Center for PTSD re-analyzed data from a randomized clinical trial in which they investigated the effects of an intervention that teaches emotion regulation and interpersonal coping skills before trauma-focused treatment. In the original study, 104 female participants who had experienced child abuse were randomly assigned to receive Skills Training in Affect and Interpersonal Regulation (STAIR) followed by narrative exposure therapy, STAIR followed by supportive counseling, or supportive counseling followed by narrative exposure therapy (see the [October 2010 CTU-Online](#)). At the beginning of treatment, participants with the most severe PTSD also had the most severe depression. Among participants with moderate or severe depression, STAIR followed by supportive counseling had the best immediate outcomes, but the effects eroded over time. By 6-month follow-up, participants who had received STAIR followed by narrative exposure therapy had the greatest gains. Results suggest that individuals with severe PTSD and depression can benefit from all of these treatments, but that long term gains are best

maintained with STAIR followed by narrative exposure therapy. Additionally, the finding that STAIR/narrative exposure therapy outperformed STAIR/supportive counseling provides more support for the therapeutic effects of exposure.

Read the article: <https://www.ptsd.va.gov/professional/articles/article-pdf/id49172.pdf>

Adequate sleep supports many processes that are critical to trauma-focused treatments, such as learning, memory, and emotional processing. Obstructive sleep apnea (OSA) disrupts sleep quality and therefore may interfere with treatment response. Investigators at the Cincinnati VA examined whether Veterans with PTSD and OSA ($n = 68$) exhibited poorer treatment outcome in Cognitive Processing Therapy than Veterans without OSA ($n = 276$). PTSD diagnoses were made with the Clinician-Administered PTSD Scale. Chart reviews were used to determine OSA diagnosis, the number of CPT sessions (range 1-14, average 7-8), access to continuous positive airway pressure (CPAP), and self-reported PTSD symptom severity at each CPT session. OSA-positive Veterans had less PTSD symptom reduction throughout treatment and greater symptom severity at post-treatment than OSA-negative Veterans. OSA-positive Veterans with access to CPAP before initiating CPT had better treatment response than those who were given access after starting CPT. However, the investigators could not determine whether Veterans who had access to CPAP were compliant with it, nor whether Veterans who were given access to CPAP *after* the start of CPT also used it. These results suggest that OSA may interfere with treatment response and raise the possibility that treatment for OSA before or while engaging in evidence-based psychotherapies for PTSD may help Veterans to maximally benefit from treatment.

Read the article: <http://dx.doi.org/10.1002/jts.22245>

In another study examining factors that may interfere with treatment response, investigators at Yale University and the National Center for PTSD conducted a secondary analysis of a double-blind randomized clinical trial of risperidone, an antipsychotic medication, for 276 Veterans with chronic, antidepressant resistant PTSD. The original trial revealed no differences in outcomes for six months of adjunctive risperidone versus placebo (see the [August 2011 CTU-Online](#)). The current study focused on factors related to non-improvement and delayed improvement in the full sample collapsed across risperidone versus placebo (since there was no effect of medication in the original trial). A total of 194 Veterans (70%) exhibited improvement (i.e., ≥ 10 point reduction in CAPS), with 49% of these Veterans showing delayed improvement between 12 and 24 week follow-up. Delayed response was predicted only by greater functional impairment related to emotional difficulties. Participants who had more severe PTSD symptoms at the beginning of treatment were less likely to show improvement, with follow-up analyses revealing specific contributions of more severe re-experiencing (i.e., nightmares) and emotional numbing (i.e., foreshortened future) symptoms to non-improvement. Findings are challenging to interpret since they are based on participants who were administered either risperidone or placebo while already prescribed a variety of psychiatric medications. The authors conclude by encouraging the development of treatments that target specific PTSD symptom clusters associated with non-improvement.

Read the article: <https://www.ptsd.va.gov/professional/articles/article-pdf/id49196.pdf>

Take NOTE

Review of inhibitory learning approach to enhancing exposure

A recent review by investigators at Washington University in St. Louis summarizes the evidence supporting inhibitory learning therapy, versus habituation, as the mechanism underlying exposure therapy and proposes novel exposure augmentation techniques.

Read the article: <https://doi.org/10.1016/j.cpr.2017.10.010>

Weisman, J. S., & Rodebaugh, T. L. (2017). Exposure therapy augmentation: A review and extension of techniques informed by an inhibitory learning approach. *Clinical Psychology Review*. Advance online publication. PILOTS ID: 49399

Meta-analysis of the effects of yoga and meditation on PTSD

Investigators at the University of Rochester conducted a meta-analysis of 19 randomized controlled trials of yoga and meditation for PTSD. Results suggest that these comple-

mentary approaches have a small to medium effect on PTSD symptoms compared to control conditions.

Read the article: <https://doi.org/10.1016/j.cpr.2017.10.004>

Gallegos, A. M., Crean, H. F., Pigeon, W. R., & Heffner, K. L. (2017). Meditation and yoga for posttraumatic stress disorder: A meta-analytic review of randomized controlled trials. *Clinical Psychology Review*, 58, 115-124. PILOTS ID: 49400

Review of mobile apps for PTSD

A team led by investigators at Texas A&M University reviewed the availability and usage of mobile health apps relevant to PTSD, including apps developed by the National Center for PTSD and VA.

Read the article: <http://doi.org/10.2196/mhealth.7318>

Rodriguez-Paras, C., Tippey, K., Brown, E., Sasangohar, F., Creech, S., Kum, H.-C., . . . Benzer, J. K. (2017). Posttraumatic stress disorder and mobile health: App investigation and scoping literature review. *JMIR mHealth and uHealth*, 5, e156. PILOTS ID: 49401

Alterations in hypothalamic-pituitary-adrenal (HPA) axis functioning is frequently observed in PTSD. Corticotrophin-releasing factor (CRF) is key to HPA axis functioning, suggesting that medications targeting CRF may reduce PTSD symptoms. Investigators at Emory University were the first to examine the efficacy of a CRF₁ receptor antagonist, GSK561679, in PTSD. They also explored how variation in a gene that regulates CRF functioning (rs110402) predicted treatment outcome. Investigators randomized 128 women with PTSD to GSK561679 or placebo; 96 completed the double-blind 6-week trial. There were no differences between treatments in either PTSD or depression severity in intent-to-treat and completer analyses. In exploring further, the investigators found that GSK561679 led to greater improvement in self-reported PTSD symptoms than placebo only among women with histories of moderate to severe childhood abuse who also had a specific rs110402 genetic variation (the G/G genotype), with strongest effects on hyperarousal and re-experiencing. Although the overall effect of GSK561679 was negative, the gene (rs110402) X environment (history of child abuse) interaction suggests that targeting CRF receptors could be a promising strategy for some patients.

Read the article: <http://dx.doi.org/10.1016/j.biopsych.2017.06.024>

Byrne, S. P., Krystal, J. H., Rosenheck, R. A., Vessicchio, J., & Pietrzak, R. H. (2017). Correlates of nonimprovement to pharmacotherapy for chronic, antidepressant-resistant, military service-related posttraumatic stress disorder: Insights from the Veterans Affairs Cooperative Study No. 504. *Journal of Clinical Psychopharmacology*, 37, 717–721. PIILOTS ID: 49196

Cloitre, M., Garvert, D. W., & Weiss, B. J. (2017). Depression as a moderator of STAIR Narrative Therapy for women with post-traumatic stress disorder related to childhood abuse. *European Journal of Psychotraumatology*, 8, 1377028. PIILOTS ID: 49172

Dunlop, B. W., Binder, E. B., Iosifescu, D., Mathew, S. J., Neylan, T. C., Pape, J. C., . . . Mayberg, H. S. (2017). Corticotropin-releasing factor receptor 1 antagonism is ineffective for women with posttraumatic stress disorder. *Biological Psychiatry*, 82, 866–874. PIILOTS ID: 49315

Hien, D. A., Lopez-Castro, T., Papini, S., Gorman, B., & Ruglass, L. M. (2017). Emotion dysregulation moderates the effect of cognitive behavior therapy with prolonged exposure for co-occurring PTSD and substance use disorders. *Journal of Anxiety Disorders*, 52, 53–61. PIILOTS ID: 49368

Mesa, F., Dickstein, B. D., Wooten, V. D., & Chard, K. M. (2017). Response to Cognitive Processing Therapy in Veterans with and without obstructive sleep apnea. *Journal of Traumatic Stress*. Advance online publication. PIILOTS ID: 49402

Mobile app improves homework completion time but not clinical outcomes in anger treatment

Mobile applications can be used to improve patient engagement and treatment efficacy for PTSD, as well as associated problems like difficulty managing anger (see Take Note in this issue). A randomized clinical trial led by investigators at the National Center for PTSD investigated the efficacy of a mobile app for enhancing outcomes in an anger management treatment (AMT) program. Fifty-eight male Veterans with elevated anger and moderate

PTSD symptoms were randomized to one of two parallel treatment arms: a 12-week, 90-minute group AMT alone, or AMT plus Remote Exercises for Learning Anger and Excitation Management (RELAX). RELAX is an interactive mobile platform that includes skills practice, symptom monitoring, and physiological data tracking using a synced wearable heart rate monitor. There were no differences between groups in treatment dropout or completion. Participants in both conditions reported less anger over time. The addition of the RELAX app was not associated with better anger outcomes, as expected, but participants in the AMT+RELAX group spent less time completing homework than those receiving AMT alone. Effect sizes for reductions in anger were similar between groups, suggesting that the lack of group differences in outcomes was not due to low statistical power. Findings suggest that the RELAX app may be a useful addition to AMT for patients who have concerns about the time commitment of participating in treatment.

Read the article: <https://www.ptsd.va.gov/professional/articles/article-pdf/id49343.pdf>

Mackintosh, M.-A., Niehaus, J., Taft, C. T., Marx, B. P., Grubbs, K., & Morland, L. A. (2017). Using a mobile application in the treatment of dysregulated anger among Veterans. *Military Medicine*, 182, e1941–e1949. PIILOTS ID: 49343

Preliminary evidence for a group exercise program to address PTSD symptoms in Veterans

Complementary and integrated health practices may offer promise to Veterans with PTSD, but evidence on these alternative treatments is still emerging. A new study by investigators from the San Francisco VAMC examined exercise, which may be appealing especially to Veterans because of the emphasis on fitness as part of military service. This pilot trial included 47 Veterans randomized to an Integrative Exercise Program (IE) or waitlist control. The 12-week IE intervention included three 1-hour group sessions per week of aerobic exercise, strength training, and yoga within a mindfulness-based framework. Participants could participate in psychotherapy or receive psychotropic medication if they remained on a stable dosage throughout the trial. At posttreatment, the IE group had greater reductions than the waitlist group in PTSD symptoms measured by the CAPS ($d = -.90$). The IE group also had greater increases in psychological quality of life ($d = .53$). Surprisingly, groups did not differ in physical quality of life, perhaps suggesting that non-physical aspects of the intervention (e.g., mindfulness, behavioral activation) are most important for improving mental health. Findings provide preliminary evidence that IE could be a feasible and acceptable treatment for PTSD in Veterans. A possible next step is a larger trial that controls for placebo effects and the non-specific benefits of treatment and clarifies whether IE is effective as a stand-alone treatment.

Read the article: <http://dx.doi.org/10.1016/j.jad.2017.11.002>

Goldstein, L. A., Mehling, W. E., Metzler, T. J., Cohen, B. E., Barnes, D. E., Choucroun, G. J., . . . Neylan, T. C. (2017). Veterans Group Exercise: A randomized pilot trial of an Integrative Exercise program for Veterans with posttraumatic stress. *Journal of Affective Disorders*, 227, 345–352. PIILOTS ID: 49403

Posttraumatic Cognitions Inventory shown to be valid and reliable in a Veteran sample

The Posttraumatic Cognitions Inventory (PTCI) is a measure of trauma-related beliefs that has the potential for clinical use with Veterans who experienced military-related trauma. But because the measure had not been validated in this population, a team led by investigators from the VA Ann Arbor Healthcare System tested the validity and reliability of the PTCI in a sample of treatment-seeking Veterans. A sample of 949 Veterans who reported experiencing combat or military sexual trauma completed the 36-item PTCI. Factor analyses revealed that a 4-factor model (negative view of self, negative view of the world, self-blame, and negative beliefs about coping competence) fit better than the original 3 factors identified in a civilian sample. Both models demonstrated construct validity (i.e., the PTCI measures what it

is purported to measure) and internal reliability. There were no gender differences in PTCI scores after controlling for trauma type, but Veterans endorsing MST reported higher PTCI scores across all 4 factors regardless of gender. These findings support the use of the PTCI to measure negative beliefs related to military trauma that may be addressed in PTSD treatment. Identifying and tracking changes in these beliefs, such as self-blame and coping competence, may help to guide treatment and monitor therapeutic progress of Veterans with military trauma.

Read the article: <http://dx.doi.org/10.1016/j.jad.2017.09.048>

Sexton, M. B., Davis, M. T., Bennett, D. C., Morris, D. H., & Rauch, S. A. M. (2018). A psychometric evaluation of the Posttraumatic Cognitions Inventory with Veterans seeking treatment following military trauma exposure. *Journal of Affective Disorders*, 226, 232–238. PILOTS ID: 49404



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