CLINICIAN'S TRAUMA UPDATE

CTU-ONLINE | www.ptsd.va.gov

ISSUE 18(2)
APRIL 2024

CTU-Online contains summaries of clinically relevant research articles.

Articles authored by staff of the National Center for PTSD are available in full text; just click the link. For other articles we provide a link to where you might be able to view or download the full text and a PTSDpubs ID for easy access. (What is PTSDpubs?)

If you have trouble accessing the full article, see the box at the bottom of the last page for help.

We welcome feedback from readers about content and format. Please email us at ncptsd@va.gov.

Subscribe to *CTU-Online*
Search past issues in PTSDpubs
Visit www.ptsd.va.gov

CTU-Online is published 6 times per year by the National Center for PTSD, Executive Division.

TREATMENT

New meta-analyses show mixed findings on cannabis and PTSD

With more states legalizing cannabis, patients commonly ask whether or assume that cannabis may treat their PTSD, whereas providers may worry that cannabis use will be a barrier to empirically supported PTSD treatments. Two recent reviews examined these questions.

In one study, a team led by investigators at University of California San Diego used the data repository Project Harmony to conduct an individual patient data meta-analysis combining data from four studies of COPE (Concurrent Treatment of PTSD and Substance Use Disorders [SUD] Using Prolonged Exposure) as compared to other non-trauma-focused studies (including relapse prevention, Seeking Safety, and SUD treatment as usual). Investigators dichotomized patients into those who had or had not used cannabis in the last 30 days prior to treatment starting, then examined differences between COPE and other non-trauma-focused treatment. Participants had greater reductions in PTSD symptoms in COPE than comparison treatments, regardless of whether they endorsed baseline cannabis use or not (d=.70 vs .73, respectively). Levels of treatment attendance were lower in COPE than other treatments, with no difference between those who used or did not use cannabis at baseline.

In a second study, a team led by investigators from Temerty Faculty of Medicine conducted a systematic review of experimental and observational studies that reported on cannabis and cannabinoid use and PTSD outcomes using a validated PTSD measure. A total of 14 studies were included, of which 2 were RCTs. Results were further divided into studies in a general PTSD population versus studies including individuals with comorbid PTSD and cannabis use disorder (CUD). For the general population studies, there were mixed findings in terms of whether cannabis use was associated with improved or worsened symptoms, with RCT evidence showing no benefit of cannabis use on PTSD. For studies that included individuals with comorbid PTSD and CUD, results were clearer: participants with CUD had slower improvement in PTSD symptoms than those without CUD. The studies included were generally at high risk of bias, with findings for cannabis use looking notably better in observational or high risk of bias studies. Further, given that it was common for patients to self-administer cannabis of unknown type, it is hard to generalize.

The lack of benefit of cannabis on PTSD symptoms in RCTs support the VA/DoD PTSD guideline's recommendation that cannabis not be used to treat PTSD. Use of cannabis alone may not decrease efficacy of COPE, but may affect response to other treatments, particularly when there is comorbid CUD. Taken together, the findings from these studies underscore the need for shared decision-making with patients who use cannabis about its efficacy and possible effect on treatment outcome.

Read the articles:

https://www.ptsd.va.gov/professional/articles/article-pdf/id1629937.pdf

Hill, M. L., Kline, A. C., Saraiya, T. C., Gette, J., Ruglass, L. M., Norman, S. B., . . . Morgan-López, A. A. (2024). Cannabis use and trauma-focused treatment for co-occurring posttraumatic stress disorder and substance use disorders: A meta-analysis of individual patient data. *Journal of Anxiety Disorders, 102,* Article 102827. PTSDPubs ID: 1629937

https://doi.org/10.4088/JCP.23r14862

Rodas, J. D., George, T. P., & Hassan, A. N. (2024). A systematic review of the clinical effects of cannabis and cannabinoids in posttraumatic stress disorder symptoms and symptom clusters. *Journal of Clinical Psychiatry, 85*(1), Article 23r14862. PTSDpubs ID: 1630877

Transcranial direct current stimulation in combination with virtual reality exposure

Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation technique that may augment behavioral interventions, such as extinction learning. Investigators at the Providence VA and Brown University conducted a randomized sham-controlled trial of tDCS combined with a standardized virtual reality (VR) intervention for PTSD. Veterans with warzone-related PTSD (*n*=55) were randomized to receive 6 sessions of VR combined with active vs. sham tDCS over 10 days, with follow-up at 1 and 3 months. The VR intervention included a set of warzone-based driving scenarios of increasing intensity. Skin conductance was measured before and during each VR session to assess for changes in psychophysiological arousal. Based on the PCL-5, active tDCS combined with VR was associated with PTSD improvement that was statistically significantly greater than in the sham group at 1-month follow-up, but not at the end of 6 sessions or at 3 months. No group differences were seen with the CAPS-5 or depression severity at any timepoint. Clinician-rated functioning was higher in the active tDCS group but only at the 3-month follow-up. Active tDCS was associated with significantly accelerated arousal habituation to VR events compared with sham tDCS. These findings support further investigation of tDCS combined with VR and potentially other behavioral interventions for PTSD.

Read the article: https://doi.org/10.1001/jamapsychiatry.2023.5661

van 't Wout-Frank, M., Arulpragasam, A. R., Faucher, C., Aiken, E., Shea, M. T., Jones, R. N., . . . Philip, N. S. (2024). Virtual reality and transcranial direct current stimulation for posttraumatic stress disorder: A randomized clinical trial. *JAMA Psychiatry.* Advance online publication. PTSDpubs ID: 1631651

New studies of adjunctive EEG-driven neurofeedback for PTSD

Neurofeedback involves training individuals to self-regulate their brain activity by displaying this activity, generated by fMRI or EEG, to them in real time while they practice mental strategies. A small sham-controlled trial found that fMRI-based neurofeedback improved patients' ability to decrease their amygdala reactivity during trauma memory recall but did not reduce PTSD symptoms (see the August 2023 issue of *CTU-Online*). Two new studies explored EEG-driven neurofeedback as an adjunctive treatment.

A team led by investigators at Tel-Aviv University in Israel examined neurofeedback among 55 women with PTSD related to childhood sexual abuse who were engaged in concurrent trauma-focused psychotherapy. They examined EEG-based amygdala electrical-finger-print neurofeedback, which is more scalable than fMRI-based neurofeedback because EEG infrastructure is less expensive and more portable. All women had been in specialized trauma-focused psychotherapy for at least one year without sufficient response; 15 were randomized to continue in this treatment only for the control condition. The other 40 participants were randomized to receive continued therapy as well as 10 50-minute sessions of adjunctive neurofeedback delivered twice per week for two weeks then weekly. The primary outcome of CAPS-5 scores did not significantly differ by group at post-treatment, but PCL-5 scores at 6-month follow-up improved more in the neurofeedback group than in the control group.

In a single-arm, open label trial, a team led by investigators at Rambam Medical Center in Israel tested amygdala-derived-EEG-fMRI-pattern neurofeedback adjunctive to treatment-as-usual among 79 participants recruited from four sites in Israel and one in the United States. This form of neurofeedback uses an algorithm based on integrated fMRI and EEG data that is intended to improve the poor spatial resolution of traditional EEG-based neurofeedback that cannot reflect brain activity in deep brain regions that are relevant to PTSD, like the amygdala. The protocol included 15 neurofeedback training sessions delivered twice per week for 25 minutes each, on non-consecutive days, over 8 consecutive weeks, along with standard of care delivered to all patients for at least one month prior to neurofeedback. There were large reductions in CAPS-5 scores at post-treatment and 3-month follow-up, with an average of 13.2-point improvement at follow-up.

Taken together, these studies suggest that EEG-based neurofeedback delivered with standard treatment may result in reduced PTSD symptom severity, but the lack of control for placebo effects prevents definitive conclusions. Next steps should include sham-controlled trials of these specific neurofeedback protocols, ideally tested as adjunctive to evidence-based psychotherapies for PTSD.

Read the articles:

https://doi.org/10.1111/pcn.13591

Fine, N. B., Helpman, L., Armon, D. B., Gurevitch, G., Sheppes, G., Seligman, Z., . . . Bloch, M. (2024). Amygdala-related electroencephalogram neurofeedback as add-on therapy for treatment-resistant childhood sexual abuse posttraumatic stress disorder: Feasibility study. *Psychiatry and Clinical Neurosciences, 78*(1), 19-28. PTSDpubs ID: 1624527

https://doi.org/10.1016/j.psychres.2023.115711

Fruchter, E., Goldenthal, N., Adler, L. A., Gross, R., Harel, E. V., Deutsch, L., . . . 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,* Article 115711. PTSDpubs ID: 1630506

Cyclobenzaprine not shown to be effective for treating PTSD but may have benefits for treating sleep disturbance

Cyclobenzaprine is a muscle relaxant that acts within the central nervous system and targets multiple neurotransmitters relevant to PTSD and especially sleep. Sleep disturbances may play a critical role in the development and maintenance of PTSD. A team led by investigators from a pharmaceutical company that makes a sublingual form of cyclobenzaprine conducted a Phase 3, randomized, placebo-controlled trial of this agent for the treatment of PTSD. Veterans with PTSD (*n*=358, 90% male, average age = 36) were randomized to receive 12 weeks of 5.6 mg cyclobenzaprine or placebo. At endpoint, after 12 weeks of treatment, there was no difference between the groups in change in PTSD severity (measured by the CAPS-5) or in overall quality of sleep (measured by the self-report PROMIS sleep disturbance scale). Certain items on the two scales suggested some

benefit for addressing sleep disturbance specifically. Also, a greater treatment effect was seen in individuals with shorter time since trauma (≤9 years). Cyclobenzaprine was well-tolerated. These data do not support the further development of cyclobenzaprine as a treatment for PTSD, although there may be a role in treating specific sleep disturbances or in subgroups of PTSD patients.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1630894.pdf

Parmenter, M. E., Lederman, S., Weathers, F. W., Davis, L. L., Vaughn, B., Engels, J., & Sullivan, G. M. (2024). A phase 3, randomized, placebo-controlled, trial to evaluate the efficacy and safety of bedtime sublingual cyclobenzaprine (TNX-102 SL) in military-related posttraumatic stress disorder. *Psychiatry Research, 334,* Article 115764. PTSDpubs ID: 1630894

Positive trial of acupuncture for combat-related PTSD

Acupuncture is a complementary and integrative therapy that has shown some preliminary efficacy as an adjunctive intervention for PTSD among active-duty Servicemembers (see the Dec 2014 issue of *CTU-Online*). Investigators at the VA in Long Beach, CA examined acupuncture as a stand-alone treatment for Veterans with combat-related PTSD in a double-blind, sham-controlled clinical trial. The sample of 93 combat Veterans aged 18-55 were randomized to 24 1-hour sessions of active or sham acupuncture (i.e., minimal needling), delivered twice weekly. Fear-conditioned extinction was assessed by fear-potentiated startle response. About 76% of Veterans completed their assigned intervention. CAPS-5 scores in the acupuncture group dropped from 37.1 at pretreatment to 22.6 at posttreatment (d = 1.2), with a smaller but medium-sized effect in the sham group (pre-treatment CAPS-5 = 36.6, post-treatment CAPS-5 = 29.1, d = 0. 7). Active acupuncture was superior to sham (between-group d = 0.6). Fear extinction was also greater in the active than the sham group. These findings provide evidence for the efficacy of acupuncture for treating combat-related PTSD. However, it is notable that neither concurrent supportive treatments nor treatment history were assessed. Future studies should examine the durability of acupuncture effects with longer-term follow-up, directly compare the efficacy of acupuncture to evidence-based treatments for PTSD, and elucidate when acupuncture is optimally delivered as adjunctive or as monotherapy.

Read the article: https://doi.org/10.1001/jamapsychiatry.2023.5651

Hollifield, M., Hsiao, A. F., Smith, T., Calloway, T., Jovanovic, T., Smith, B., . . . Cocozza, K. (2024). Acupuncture for combat-related posttraumatic stress disorder: A randomized clinical trial. *JAMA Psychiatry.* Advance online publication. PTSDpubs ID: 1631117

Enhanced Adaptive Disclosure therapy shows promise for treatment of war-related PTSD

Adaptive Disclosure (AD) is a manualized experiential psychotherapy for combat-related PTSD (see the April 2021 *CTU-Online*). Investigators from VA Boston Healthcare System led a study on an updated and enhanced version of AD (AD-E) designed specifically to address moral injury and traumatic loss from war-related trauma. Participants were 174 Veterans (77% men, 59% White) with PTSD randomized to receive 12 individual sessions (up to 90 minutes) of AD-E or Present-Centered Therapy (PCT). AD-E included experiential tasks such as letter writing, loving kindness meditation, and daily repair activities to facilitate healing and functional change. There were no differences in treatment completion between AD-E and PCT (63% and 59%, respectively). Participants in both conditions showed improvements in functioning rated by the Sheehan Disability Scale (d = 3.0 for AD-E; d = 1.9 for PCT) and clinician-rated PTSD symptoms (CAPS-5; d = 1.6 for AD-E; d= .7 for PCT), with AD-E showing greater improvement than PCT at posttreatment; however, these differences were not significant at the 6-month follow-up. There were significant improvements in anger and psychological aggression from baseline to 6-month follow-up, with no differences between treatments. Notably, because the current study did not measure changes in moral injury or grief, it is unknown if AD-E was effective in addressing these constructs. Findings suggest that AD-E may be an effective treatment for veterans with PTSD related to war-related moral injury or traumatic loss.

Read the article: https://doi.org/10.1037/ccp0000873

Litz, B. T., Yeterian, J., Berke, D., Lang, A. J., Gray, M. J., Nienow, T., . . . Rusowicz-Orazem, L. (2024). A controlled trial of adaptive disclosure-enhanced to improve functioning and treat posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology, 92*(3), 150-164. PTSDpubs ID: 1630850

Ibogaine and 5-MeO-DMT demonstrate some promise for the reduction of risky alcohol use

Psychedelic treatments have been suggested as possible interventions for Veterans with various psychological health conditions. Recent findings demonstrated preliminary support for the effects of ibogaine on neurological symptoms in Veterans (see the February 2024 issue of *CTU-Online*). A team led by investigators at The Ohio State University conducted a prospective observational study with 45 Special Operations Forces Veterans with risky alcohol use. Veterans participated in a (legal) three-day residential treatment in Mexico during which time they received psychedelic-assisted therapy with ibogaine (1st day) and 5-MeO-DMT (3rd day). At 1-month follow up, 26 Veterans (57.8%) no longer reported risky alcohol use. The "responder" group reported significantly more improvement in self-reported PTSD and cognitive functioning symptoms than those who continued to have risky alcohol use (42.8%). Although this study found positive effects of ibogaine and 5-MeO-DMT psychedelics for reduction of risky alcohol use, the lack of a control group makes it impossible to draw conclusions, especially given the novelty of the intervention. Furthermore, participants were not formally assessed for alcohol misuse, PTSD, or cognitive dysfunction, and less than half of participants reported on PTSD symptoms. Future studies with more rigorous controls and more complete follow-up are needed.

Read the article:

https://doi.org/10.1080/08995605.2022.2156200

Armstrong, S. B., Xin, Y., Sepeda, N. D., Polanco, M., Averill, L. A., & Davis, A. K. (2024). Prospective associations of psychedelic treatment for co-occurring alcohol misuse and posttraumatic stress symptoms among United States Special Operations Forces Veterans. *Military Psychology, 36*(2), 184-191. PTSDPubs ID: 1631129

Take NOTE

Synopsis of the 2023 VA/DoD Clinical Practice Guidelines for PTSD

Members of the workgroup for the latest VA/DoD clinical practice guideline for PTSD described guideline development and provided an overview of the guideline, particularly those assessments and treatments that were recommended for or against.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1631252.pdf

Schnurr, P. P., Hamblen, J. L., Wolf, J., Coller, R., Collie, C., Fuller, M. A., . . . Kelber, M. S. (2024). The management of posttraumatic stress disorder and acute stress disorder: Synopsis of the 2023 U.S. Department of Veterans Affairs and U.S. Department of Defense Clinical Practice Guideline. *Annals of Internal Medicine, 177*(3), 363-374. PTSDpubs ID: 1631252

"State of the science" of EMDR

Investigators from The Netherlands and UK provided a narrative overview of the theoretical foundations of EMDR along with its empirical support across cultures and populations.

Read the article: https://doi.org/10.1002/jts.23012

de Jongh, A., de Roos, C., & El-Leithy, S. (2024). State of the science: Eye movement desensitization and reprocessing (EMDR) therapy. *Journal of Traumatic Stress, 37*(2), 205-216. PTSDpubs ID: 1629864

Systematic review of Written Exposure Therapy for PTSD

Investigators from the National Center for PTSD conducted a systematic review of all peer-reviewed studies of Written Exposure Therapy, including randomized and open trials.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1630848.pdf

DeJesus, C. R., Trendel, S. L., & Sloan, D. M. (2024). A systematic review of written exposure therapy for the treatment of posttraumatic stress symptoms. *Psychological Trauma.* Advance online publication. PTSDpubs ID: 1630848

Systematic review of Psychological First Aid

Investigators from Kings College London conducted a systematic review of all peer-reviewed studies of psychological first aid, focusing on effectiveness and variability in implementation.

Read the article: https://doi.org/10.1177/15248380231221492

Wang, L., Norman, I., Edleston, V., Oyo, C., & Leamy, M. (2024). The effectiveness and implementation of psychological first aid as a therapeutic intervention after trauma: an integrative review. *Trauma Violence & Abuse.* Advance online publication. PTSDpubs ID: 1629869

Veterans Health Administration

Trouble Getting the Full Text of an Article?

Articles authored by National Center for PTSD staff are available in full text. For other articles we provide a link to where you might be able to view or download the full text. VA clinicians might have privileges through their VA library or university affiliation; however, VA firewalls sometimes block permissions to access reference materials. If you cannot access the full text of any of these articles, we advise that you contact your local librarian or web/internet technical person.