CLINICIAN'S TRAUMA UPDATE

CTU-ONLINE | www.ptsd.va.gov

ISSUE 15(3)
JUNE 2021

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

Another study of MDMA-assisted therapy for PTSD

MDMA-assisted psychotherapy has shown potential benefit for PTSD in preliminary studies (see the February 2019 *CTU-Online*). With the aim of collecting data to support FDA approval of this intervention, investigators at the Multidisciplinary Association for Psychedelic Studies coordinated a 15-site, randomized, placebo-controlled trial of MDMA-assisted psychotherapy for PTSD. Male and female Veteran and non-Veteran participants ($N = 90$) with PTSD were randomized to receive MDMA versus an inactive placebo combined with manualized, supportive psychotherapy delivered by a two-person therapist team as in previous studies. From baseline to endpoint 8 weeks after the final session with MDMA or placebo, the MDMA group showed a greater reduction in CAPS-5 scores compared to the placebo group (24.4 points vs. 13.9 points), higher response and remission rates, and a greater proportion of participants who no longer met criteria for a PTSD diagnosis. Depression also improved more with MDMA than placebo. One challenge in interpreting these findings is that participants may not have been adequately blinded due to the psychoactive effects of MDMA, which could have increased expectancy effects. Still, this trial provides additional evidence that MDMA-assisted psychotherapy may have benefit in treating PTSD.

Read the article: https://doi.org/10.1038/s41591-021-01336-3

Mitchell, J. M., Bogenschutz, M., Lilienstein, A., Harrison, C., Kleiman, S., Parker-Guilbert, K., . . . Doblin, R. (2021). MDMA-assisted therapy for severe PTSD: A randomized, double-blind, placebo-controlled phase 3 study. *Nature Medicine, 27,* 1025-1033. PTSDpubs ID: 1569198

Flexible-length CPT linked to greater treatment response among active-duty military

A prior study found that flexing the number of sessions of CPT rather than adhering strictly to the original 12-session protocol improved outcomes among civilians (see the December 2012 *CTU-Online*). New research led by investigators at the STRONG STAR Consortium tested this approach with active-duty Service members. The 127 Service members (14% female) participated in individual CPT sessions twice a week for up to 18 weeks. PTSD symptoms were measured weekly using the PCL-5. Participants remained in treatment until they reached "good end-state" (PCL-5 ≤ 19 and patient-provider agreement on outcome) or engaged in a maximum of 24 sessions. More severe baseline depressive symptoms and identifying as African American were linked with needing more than 12 sessions or non-response. The investigators also compared results to a previous study of fixed-length CPT with a sample from the same population. Participants in the variable-length study were more likely to reach good end-state (48% vs. 22%, $d = 0.7$) and show clinically significant improvement than those in the fixed-length study (76% vs. 46%). Although it will be important to compare fixed versus flexible-length CPT within the same trial, these findings suggest that personalized treatment and addressing comorbid depression and barriers faced by African American patients (e.g., stigma, discrimination) could enhance outcomes among active-duty military.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1568341.pdf

Resick, P. A., Wachen, J. S., Dondanville, K. A., LoSavio, S. T., Young-McCaughan, S., Yarvis, J. S., . . . Mintz, J. (2021). Variable-length cognitive processing therapy for posttraumatic stress disorder in active duty military: Outcomes and predictors. *Behaviour Research and Therapy, 141,* Article 103846. PTSDpubs ID: 1568341

Test of a predictive strategy to inform PTSD treatment matching

One of the unanswered questions in PTSD treatment is which treatment works best for which patients? A team led by investigators at the National Center for PTSD addressed this question using a novel multivariate analytic strategy with data from a large trial of PE versus PCT among women Veterans and Service members (see the April 2007 *CTU-Online*). The original study found that PE was superior to PCT. The authors developed a prognostic index to predict good versus poor outcomes among the 267 participants. The prognostic index included variables associated with lower posttreatment PTSD severity (greater perceived treatment credibility and better physical and mental functioning) and higher posttreatment PTSD severity (higher baseline PTSD symptoms, more time since trauma, and exposure to military sexual trauma). However, the prognostic index also moderated treatment response: among participants with the best prognoses (64%), PE outperformed PCT, but among participants with poorer prognoses, PE and PCT did not differ. Although findings need replication in other samples, they suggest that information tailored to an individual based on their characteristics before treatment could be useful in optimizing treatment response.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1569426.pdf

Wiltsey Stirman, S. W., Cohen, Z. D., Lunney, C. A., DeRubeis, R. J., Wiley, J. F., & Schnurr, P. P. (2021). A personalized index to inform selection of a trauma-focused or non-trauma-focused treatment for PTSD. *Behaviour Research and Therapy, 42,* Article 103872. PTSDpubs ID: 1569426

Examining complementary and integrative practices for PTSD

There is strong interest in using practices such as yoga and meditation to address symptoms of PTSD, yet evidence of their efficacy and how they compare with established treatments is not definitive. Two recent randomized clinical trials add to the growing evidence.

A study by investigators at the Atlanta VA Healthcare System presented interim findings from one of two VA sites in an RCT assessing the effectiveness of Trauma Center Trauma-Sensitive Yoga compared to group CPT for treating PTSD related to military sexual trauma. The intent-to-treat sample included 104 women Veterans (91% African American) randomized to receive the yoga intervention (n = 58) or CPT (n = 46). Yoga was delivered by certified yoga facilitators in 10 weekly 60-minute group sessions. CPT was conducted in 12 90-minute weekly group sessions by trained clinicians in a PTSD clinic. Both groups showed improvement on clinician-rated PTSD symptoms, with large effect sizes at 2-weeks posttreatment (d = 1.2 yoga; 0.9 CPT) and 3-month follow-up (d = 1.2 yoga; 1.4 CPT). Although these differences were not statistically significant, low completion of follow-up assessments (n = 28 for yoga, n = 19 for CPT at 3-months) may have limited the ability to detect differences. Notably, the CPT group continued to improve over time, so longer term follow-up might have revealed differences over time. Additionally, the completion rate in the CPT group (35% completed more than 9 sessions) was lower than typically seen in practice, compared to 60% completion (≥ 7/10 sessions) of the yoga intervention. It is possible that this difference is related to preference for yoga over CPT in this sample, but preference data were not presented. As these are interim findings, results should be interpreted with caution.

A second RCT compared Loving Kindness Meditation (LKM) to CPT in a sample of 184 Veterans diagnosed with PTSD receiving VA care (83% men). LKM involves silent repetition of phrases intended to elicit feelings of kindness to self and others. Both interventions were delivered in 12 90-minute group sessions and included 30 minutes of homework 6 days per week between sessions. Both treatments demonstrated medium effects on the CAPS-5 from pre- to post-treatment (d = .5 for both) and at 6-month follow-up (d = .7 for LKM and .5 for CPT). Differences did not exceed the non-inferiority margin of 5 points, indicating no difference between the conditions, although effects were modest for both. Notably, baseline CAPS-5 scores were relatively low in this sample (M = 35) and the average reduction in PTSD symptoms was only 5 points for both conditions at posttreatment. For depression, effect sizes were smaller (pre-post d = .4 for LKM and .1 for CPT), with greater reductions in the LKM condition. Participants randomized to LKM attended more treatment sessions than those randomized to CPT (7.4 vs. 6.0, respectively) although overall treatment completion was low, with only 54% and 60% of participants attending 6 or more sessions of CPT or LKM, respectively.

Taken together, these studies suggest that complementary and integrative health interventions show promise for the treatment of PTSD and depression. However, methodological limitations in these studies make it difficult to draw definitive conclusions. Furthermore, as group CPT is less effective than individual CPT, comparison of these interventions with individual CPT and other gold standard treatments is warranted.

Read the articles:

https://doi.org/10.1001/jamanetworkopen.2021.6604

Kearney, D. J., Malte, C. A., Storms, M., & Simpson, T. L. (2021). Loving-kindness meditation vs cognitive processing therapy for posttraumatic stress disorder among veterans: a randomized clinical trial. *JAMA Network Open, 4*(4), Article e216604. PTSDpubs ID: 1568095

https://doi.org/10.1089/acm.2020.0417

Kelly, U., Haywood, T., Segell, E., & Higgins, M. (2021). Trauma-sensitive yoga for post-traumatic stress disorder in women veterans who experienced military sexual trauma: Interim results from a randomized controlled trial. *Journal of Alternative and Complementary Medicine, 27*(S1), S45-S59. PTSDpubs ID: 1567680

Variants of exposure therapy effective for patients with complex PTSD

A recent clinical trial conducted by a team at Leiden University in the Netherlands found that weekly PE, PE preceded by STAIR (STAIR+PE), and PE delivered intensively (iPE) were equally effective (with no differences in dropout across conditions) among survivors of childhood trauma. In a new analysis, the investigators examined whether treatment outcomes varied for patients

with complex PTSD. Complex PTSD is a diagnosis in the ICD-11 that includes PTSD symptoms plus disturbance in self-organization (i.e., poor emotion regulation, interpersonal problems, and negative self-concept). A total of 80 of the 149 participants (54%) met criteria for complex PTSD based on the International Trauma Questionnaire. Patients with complex PTSD had more severe PTSD symptoms and more psychiatric comorbidities at baseline than patients without complex PTSD. The complex PTSD group showed a similar rate of improvement to the PTSD group on the CAPS-5 through 12-month follow-up within each treatment and in an analysis combining the 3 treatment conditions. Complex PTSD patients also did not drop out more frequently than patients without complex PTSD (24% versus 26%, respectively). Findings indicate that patients with complex PTSD did not experience less benefit than patients without complex PTSD from three variants of exposure therapy, and in particular, did not benefit more from STAIR+PE. Future research can examine whether patients with complex PTSD require more treatment sessions to reach the same end-state functioning as those without complex PTSD.

Read the article: https://doi.org/10.1016/j.janxdis.2021.102388

Hoeboer, C. M., de Kleine, R. A., Oprel, D. A. C., Schoorl, M., van der Does, W., & van Minnen, A. (2021). Does complex PTSD predict or moderate treatment outcomes of three variants of exposure therapy? *Journal of Anxiety Disorders, 80,* Article 102388. PTSDpubs ID: 1567885

Comparison of two transcranial magnetic stimulation protocols for depression and PTSD

Intermittent theta burst stimulation (iTBS) is a form of transcranial magnetic stimulation (TMS) that may have similar antidepressant effects as standard TMS and can be delivered over a much shorter time period. It is unknown if iTBS is effective for patients with comorbid MDD and PTSD. Investigators at the Providence VA Healthcare system assessed effects of iTBS versus standard TMS in Veterans with MDD and comorbid PTSD. Using retrospective chart review, the investigators compared changes in depression and PTSD severity in 10 iTBS patients with MDD and PTSD and 10 patients who received standard TMS treatment for depression (5 hz) who were matched for age, sex and symptom severity . Both groups received up to 30 treatment sessions. iTBS was performed August 2019 to October 2020, and standard TMS was performed September 2014 to June 2016. Self-reported depressive and PTSD symptoms improved in both groups, but contrary to *a priori* hypotheses, patients receiving iTBS had smaller improvements than patients who received standard TMS. Limitations of this study include the retrospective, non-randomized design, the collection of data during different time periods and reliance on self-report measures. Still, these findings suggest that iTBS may be less effective than standard TMS in MDD patients with comorbid PTSD.

Read the article: https://doi.org/10.1002/jts.22686

Philip, N. S., Doherty, R. A., Faucher, C., Aiken, E., & van 't Wout-Frank, M. (2021). Transcranial magnetic stimulation for posttraumatic stress disorder and major depression: Comparing commonly used clinical protocols. *Journal of Traumatic Stress.* Advance online publication. PTSDpubs ID: 1569196

Reduced suicidal ideation following intensive PTSD treatment

Treating PTSD among Veterans with suicidal ideation in traditional outpatient care is safe and effective for PTSD and suicidal ideation (see the April 2021 *CTU-Online*). New research led by investigators at Emory University and Rush University Medical Center examined whether this is also the case for Veterans participating in short-term, intensive treatment programs. The investigators analyzed data from 684 Veterans (32.3% women) who completed intensive treatment programs at either institution between February 2016 and April 2019. Veterans at one site completed a two-week PE program ($N = 376$); Veterans at the other site completed a three-week CPT program ($N = 308$). Both programs involved daily group and individual treatment. At baseline and throughout treatment, Veterans self-reported PTSD symptoms via the PCL-5; SI was measured with item 9 from the Patient Health Questionnaire-9. Veterans in both programs reported large pre-post reductions in PTSD and suicidal ideation ($ds = 1.1$-1.5). Reductions in PTSD symptoms predicted SI reductions across sessions at both sites. Although the study did not have a control group, these findings demonstrate that it is feasible to reduce suicidal ideation through intensive, short-term treatment. They also provide further evidence that treating PTSD can help Veterans struggling with suicidal ideation. It will be important to examine whether these gains are maintained over time.

Read the article: https://doi.org/10.1037/ser0000518

Post, L. M., Held, P., Smith, D. L., Black, K., Van Horn, R., Pollack, M. H., . . . Rauch, S. A. M. (2021). Impact of intensive treatment programs for posttraumatic stress disorder on suicidal ideation in veterans and service members. *Psychological Services.* Advance online publication. PTSDpubs ID: 1567891

Stronger therapeutic alliance predicts lower dropout from CPT

The quality of the therapeutic alliance between patients and providers is associated with dropout from psychotherapy in general. A team led by investigators at Ryerson University examined whether therapeutic alliance also predicts dropout from CPT. The original randomized controlled hybrid implementation/effectiveness trial found that therapists who received weekly consultation following CPT training obtained better treatment outcomes than therapists who attending training alone (see the October 2018 *CTU-Online*). For this study, therapeutic alliance was assessed by independent raters who listened to the audio-recorded CPT sessions from 169 patients. The investigators examined whether initial alliance (session 1), late alliance (session 12), average alliance, and change in alliance predicted dropout, which was defined as completing fewer than 12 CPT sessions. A total of 33.1% of participants dropped out of CPT. Greater average alliance was associated with lower likelihood of dropout; however, there was no effect of initial alliance, late alliance, or change in alliance. Alliance also did not change over time. These results are largely in line with previous research showing that therapeutic alliance may be important for retention in treatment, but the lack of findings for early, late, and change in

alliance makes it challenging to know when to most closely monitor alliance to prevent dropout. Having patients and providers report on alliance in addition to independent observers could help clarify this picture.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1567223.pdf

Sijercic, I., Liebman, R. E., Wiltsey Stirman, S., & Monson, C. M. (2021). The effect of therapeutic alliance on dropout in cognitive processing therapy for posttraumatic stress disorder. *Journal of Traumatic Stress*. Advance online publication. PTSDpubs ID: 1567223

Take NOTE

Transcranial magnetic stimulation for PTSD

A team led by investigators at the Carl T. Hayden VAMC in Phoenix carried out a systematic review of RCTs of TMS for PTSD.

Read the article: https://doi.org/10.1016/j.jpsychires.2021.05.011

Belsher, B. E., Beech, E. H., Reddy, M. K., Smolenski, D. J., Rauch, S., Kelber, M., Issa, F., Lewis, C., & Bisson, J. I. (2021). Advances in repetitive transcranial magnetic stimulation for posttraumatic stress disorder: A systematic review. *Journal of Psychiatric Research, 138*, 598–606. PTSDpubs ID: 1569116

Investigators at the College of Applied Psychology in Australia conducted a meta-analysis of 19 studies of TMS for PTSD.

Read the article: https://doi.org/10.1016/j.jad.2021.04.003

Harris, A., & Reece, J. (2021). Transcranial magnetic stimulation as a treatment for posttraumatic stress disorder: A meta-analysis. *Journal of Affective Disorders, 289,* 55-65. PTSDpubs ID: 1569043

Treating comorbid PTSD and borderline personality disorder

A team at Ryerson University in Canada carried out a systematic review of studies examining treatment outcomes for patients with co-occurring PTSD and borderline personality disorder. The article includes recommendations for most effectively treating this population.

Read the article: https://doi.org/10.1016/j.cpr.2021.102030

Zeifman, R. J., Landy, M. S. H., Liebman, R. E., Fitzpatrick, S., & Monson, C. M. (2021). Optimizing treatment for comorbid borderline personality disorder and posttraumatic stress disorder: A systematic review of psychotherapeutic approaches and treatment efficacy. *Clinical Psychology Review, 86,* Article 102030. PTSDpubs ID: 1568344

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.