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TREATMENT

Novel interventions address comorbid symptoms of PTSD and TBI in Veterans

PTSD and history of traumatic brain injury (TBI) are highly comorbid conditions among military Veterans. Three new studies tested novel interventions to address these symptoms in Veteran samples.

Cognitive deficits resulting from TBI can be addressed with cognitive remediation strategies, yet these symptoms are not directly targeted in trauma-focused psychotherapies for Veterans with both history of TBI and PTSD. Investigators from the VA San Diego Healthcare System tested a novel hybrid treatment entitled SMART-CPT that combines compensatory cognitive training components of Cognitive Symptom Management and Rehabilitation Therapy (CogSMART) with CPT. One hundred returning Veterans with PTSD and a history of mild to moderate TBI with current cognitive complaints were randomized to receive weekly individually-delivered CPT or SMART-CPT over 12 weeks. SMART-CPT retained all content from CPT, plus adaptations including psychoeducation regarding TBI; compensatory strategies for attention, memory, and executive functioning; repetition of key CPT points; and simplified worksheets. Both groups showed reductions in self-reported PTSD and cognitive complaints at posttreatment, with no differences between groups. Those receiving SMART-CPT showed greater improvements in some neuropsychological domains including attention/working memory, verbal learning/memory, and novel problem solving than those assigned to CPT. Although SMART-CPT did not increase PTSD symptom improvement over standard CPT, the authors suggest that use of this integrated treatment may provide the additional benefit of improvements in some areas of cognitive functioning in a more efficient manner than delivering trauma-focused psychotherapy and cognitive remediation treatments separately.

Read the article: <https://doi.org/10.1136/jnnp-2018-319315>

A second study examined the use of cognitive remediation strategies via mobile technology combined with social support to address executive dysfunction and emotion dysregulation in a sample of Veterans with TBI and PTSD. Investigators from the VA Mid-Atlantic MIRECC randomized 112 Veteran-family/friend dyads to receive a novel intervention, Cognitive Applications for Life Management (CALM), or a brain health training control intervention. CALM consists of goal management training, context-free cueing, and attention training delivered via a mobile device. Both conditions lasted 6 months and involved three 60- to 90-minute home visits at 0, 2, and 4 months with the Veteran and support person. There was no difference between groups on executive functioning following the intervention, but Veterans randomized to CALM reported greater decreases in anger (25% vs. 8%) and engaged in fewer maladaptive interpersonal behaviors, such as aggression, than those in the control condition. Veterans in the CALM condition also demonstrated greater decreases in clinician-rated PTSD symptom severity, although this was not significant in intent-to-treat analyses. Along with the study of SMART-CPT, findings provide additional support for the benefit of cognitive remediation strategies for Veterans with TBI and PTSD.

Read the article: <https://doi.org/10.1097/HTR.0000000000000435>

Take NOTE

Commentary on study of service dogs for PTSD

Investigators from Kaiser Permanente review recent preliminary findings supporting the use of service dogs for PTSD and make the case that rigorous RCTs with adequate control conditions, long-term follow-up, and tests of mechanisms of action are needed.

Read the article: <https://doi.org/10.1037/ccp0000352>

Stumbo, S. P., & Yarborough, B. J. H. (2019). Preliminary evidence is promising, but challenges remain in providing service dogs to veterans: Commentary on preliminary efficacy of service dogs as a complementary treatment for posttraumatic stress disorder in military members and veterans (O'Haire & Rodriguez, 2018). *Journal of Consulting and Clinical Psychology, 87*, 118–121. PTSDpubs ID: 51543

Systematic review of VA and DoD mental health apps

A team of investigators at VA Palo Alto reviewed 22 articles about mental health self-management and treatment companion mobile apps created by VA and DoD. They conclude that, to date, there is limited research support for these apps with the exceptions of the National Center for PTSD's PTSD Coach and DoD's Virtual Hope Box.

Read the article: <https://www.ptsd.va.gov/professional/articles/article-pdf/id51537.pdf>

Gould, C. E., Kok, B. C., Ma, V. K., Zapata, A. M. L., Owen, J. E., & Kuhn, E. (2018). Veterans Affairs and the Department of Defense mental health apps: A systematic literature review. *Psychological Services*. Advance online publication. PTSDpubs ID: 51537

Review of internet-based CBT for PTSD

A team led by investigators at Cardiff University School of Medicine reviewed 10 RCTs of internet-based CBT for PTSD. Internet-based CBT was more effective than waitlist but not other types of internet-based psychotherapy, with the disclaimer that the studies were of low quality.

Read the article: <https://doi.org/10.1002/14651858.CD011710.pub2>

Lewis, C., Roberts, N. P., Bethell, A., Robertson, L., & Bisson, J. I. (2018). Internet-based cognitive and behavioural therapies for post-traumatic stress disorder (PTSD) in adults. *Cochrane Database of Systematic Reviews*. PTSDpubs ID: 51541

Review of neuromodulation treatments for PTSD

A team led by investigators at the David Geffen School of Medicine and VA Los Angeles reviewed the evidence base for neuromodulation treatments for PTSD: electroconvulsive therapy, repetitive transcranial magnetic stimulation, transcranial direct current stimulation, vagus nerve stimulation, trigeminal nerve stimulation, and deep brain stimulation.

Read the article: <https://doi.org/10.1016/j.pnpbp.2019.01.004>

Koek, R. J., Roach, J., Athanasiou, N., van 't Wout-Frank, M., & Philip, N. S. (2019). Neuromodulatory treatments for post-traumatic stress disorder (PTSD). *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 92*, 148–160. PTSDpubs ID: 51539

Systematic review and meta-analysis of group treatments for complex PTSD

A team led by investigators at the Edinburgh Napier University conducted a meta-analysis of 36 RCTs of group therapies for complex PTSD symptoms. They found that trauma memory processing therapies were superior to usual care but not psychoeducational approaches. Additionally, the RCTs were highly heterogeneous and many were low quality.

Read the article: <https://doi.org/10.1016/j.jad.2018.09.059>

Mahoney, A., Karatzias, T., & Hutton, P. (2019). A systematic review and meta-analysis of group treatments for adults with symptoms associated with complex post-traumatic stress disorder. *Journal of Affective Disorders, 243*, 305–321. PTSDpubs ID: 51542

Review of the health effects of service in the 1991 Persian Gulf War

The National Academies of Sciences, Engineering, and Medicine reviewed the evidence of long-term physical and mental health problems and their potential causes among Veterans who served in the Persian Gulf War and post-9/11.

Read the report: <https://doi.org/10.17226/25162>

Committee on Gulf War and Health, Volume 11: Generational Health Effects of Serving in the Gulf War, Board on Population Health and Public Health Practice, Health and Medicine Division, & National Academies of Sciences, Engineering, and Medicine. (2018). *Gulf War and Health: Volume 11: Generational Health Effects of Serving in the Gulf War*. Washington, D.C.: National Academies Press.

In contrast to these studies focused on strategies to treat cognitive problems, another study focused on a different symptom that is one of the most prevalent associated with mild traumatic brain injury (mTBI) and PTSD: sleep disturbance. Investigators from the Atlanta VA Medical Center evaluated the effect of acupuncture in treating sleep disturbance in Veterans with mTBI and PTSD. Following 4 weekly sessions of sleep education, 60 Veterans with a history of mTBI and refractory sleep disturbance (67% of whom met DSM-IV criteria for PTSD) were randomized to receive real or sham acupuncture scheduled twice weekly for 5 weeks. Conditions were stratified by PTSD status. Veterans receiving real acupuncture showed greater improvements on the Pittsburgh Sleep Quality Index than those receiving sham (4.4 vs. 2.4-points), as well as greater improvement in sleep efficiency as measured by actigraphy (2.7% improvement vs. 5.3% decrement). Although Veterans with PTSD had greater sleep disturbance at baseline than those without, acupuncture was equally effective for both groups. While sleep improvements were modest, findings suggest that acupuncture can improve sleep disturbance in Veterans with mTBI regardless of PTSD status. However, acupuncture has not been established as an effective treatment for sleep problems in PTSD overall.

Read the article: <https://doi.org/10.4088/JCP.18m12235>

Given the complex comorbidity of PTSD and TBI, no one treatment is likely to effectively address all symptoms. However, these studies highlight potential new interventions that may improve different aspects of this comorbidity in Veterans.

Elbogen, E. B., Dennis, P. A., Van Voorhees, E. E., Blakey, S. M., Johnson, J. L., Johnson, S. C., . . . Belger, A. (2019). Cognitive rehabilitation with mobile technology and social support for veterans with TBI and PTSD: A randomized clinical trial. *Journal of Head Trauma Rehabilitation, 34*, 1–10. PTSDpubs ID: 51118

Huang, W., Johnson, T. M., Kutner, N. G., Halpin, S. N., Weiss, P., Griffiths, P. C., & Bliwise, D. L. (2018). Acupuncture for treatment of persistent disturbed sleep: A randomized clinical trial in veterans with mild traumatic brain injury and posttraumatic stress disorder. *The Journal of Clinical Psychiatry, 80*. PTSDpubs ID: 51538

Jak, A. J., Jurick, S., Crocker, L. D., Sanderson-Cimino, M., Aupperle, R., Rodgers, C. S., . . . Twamley, E. W. (2019). SMART-CPT for veterans with comorbid post-traumatic stress disorder and history of traumatic brain injury: A randomised controlled trial. *Journal of Neurology, Neurosurgery, and Psychiatry*. Advance online publication. PTSDpubs ID: 51464

Residual symptoms following Prolonged Exposure and Present-Centered Therapy

Depression researchers have long recognized that some symptoms persist following a successful course of treatment, even in people who achieve remission. PTSD researchers are beginning to find similar results. Most of the focus has been on residual insomnia, but some studies have identified additional symptoms (see the [August 2018 CTU Online](#)). A new study by the National Center for PTSD points to hyperarousal symptoms as especially likely to remain. Investigators studied 235 female Veterans and Soldiers who had been randomized to either PE or Present-Centered Therapy (PCT). PE had lower conditional probabilities than PCT of retaining several symptoms, but the most striking findings were among participants who had substantial improvement:

those who no longer met PTSD diagnostic criteria, had a CAPS-IV severity score < 45, and improved ≥ 10 points (average decrease = 45). Compared with participants who did not achieve substantial improvement, those who did had much lower probabilities of retaining all symptoms. Yet the probabilities of retaining symptoms in the hyperarousal cluster, especially insomnia (51%) and anger (61%), remained high. In the context of prior studies showing residual insomnia following treatment for PTSD, these new findings raise a question about whether hyperarousal symptoms in general are difficult to treat. That question, and whether different treatments are more effective for certain symptoms, remains to be answered.

Read the article: <https://www.ptsd.va.gov/professional/articles/article-pdf/id51475.pdf>

Schnurr, P. P., & Lunney, C. A. (2018). Frontline Science: Residual symptoms following prolonged exposure and present-centered therapy for PTSD in female veterans and soldiers. *Depression and Anxiety*. Advance online publication. PTSDpubs ID: 51475

Head-to-head comparison of two types of transcranial magnetic stimulation for PTSD

Transcranial magnetic stimulation (TMS) has shown preliminary efficacy for treating PTSD (see the [August 2018 CTU-Online](#)). However, prior studies have differed significantly in which part of the brain is stimulated and stimulation parameters. Investigators at the James A. Haley VA Hospital in Tampa, FL compared two versions of TMS in Veterans with PTSD. In an open-label study, 35 participants were randomized to receive up to 36 daily sessions of either 1 Hz or 10 Hz repetitive TMS applied to the right dorso-lateral prefrontal cortex. There was no sham control condition. Both groups showed a significant reduction in PTSD severity as measured by the CAPS-5, and there was no difference in improvement between the groups. As measured by the PCL-5, improvements in PTSD in both groups were maintained over three months. Depressive symptoms also improved in both groups, but functioning improved only in the 10 Hz group. TMS was safe, and 77% of participants completed the treatment protocol. Since the two TMS arms showed similar treatment effects, it remains unclear which stimulation parameters are most effective for PTSD. Also, the lack of a sham condition limits interpretation, since improvement could have been related to non-specific factors (e.g., daily contact with treatment providers). Still, this study adds to the growing evidence base suggesting TMS may eventually have a role in the management of PTSD.

Read the article: <https://doi.org/10.1016/j.psychres.2019.01.004>

Kozel, F. A., Van Trees, K., Larson, V., Phillips, S., Hashimie, J., Gadbois, B., . . . Catalano, G. (2019). One hertz versus ten hertz repetitive TMS treatment of PTSD: A randomized clinical trial. *Psychiatry Research, 273*, 153–162. PTSDpubs ID: 51540

Additional evidence for MDMA-assisted psychotherapy for PTSD

MDMA is a psychoactive substance that has shown preliminary efficacy for the treatment of PTSD when combined with a specific form of psychotherapy (see the [June 2018 CTU-Online](#)). In a new

study, investigators compared the efficacy of two higher doses of MDMA with a lower dose of MDMA, all combined with psychotherapy. Outpatients with PTSD ($N = 28$) were randomized to receive 40, 100, or 125 mg of MDMA in conjunction with 3 preparatory psychotherapy sessions followed by 2 8-hour psychotherapy sessions combined with MDMA that were separated by 1 month. Following each psychotherapy session, there were 3 non-MDMA “integration” sessions and daily phone calls for 7 days. In ITT analyses, all groups showed decreases in PTSD severity measured with the CAPS after the 2 psychotherapy sessions, with no differences between the groups. Among patients who completed both MDMA-assisted therapy sessions, the 125 mg MDMA group showed a greater reduction in PTSD compared to the 40 mg group, with no differences between the 2 high-dose groups. Results are challenging to interpret given the lack of a placebo control group and the small sample size. Additionally, it is important to remember that this and similar studies use MDMA to enhance psychotherapy and do not offer evidence about the benefits of MDMA as a stand-alone treatment.

Read the article: <https://doi.org/10.1177/0269881118806297>

Ot'Alora G, M., Grigsby, J., Poulter, B., Van Derveer III, J. W., Giron, S. G., Jerome, L., ... & Mithoefer, M. C. (2018). 3, 4-Methylenedioxymethamphetamine-assisted psychotherapy for treatment of chronic posttraumatic stress disorder: A randomized phase 2 controlled trial. *Journal of Psychopharmacology*, 32, 1295-1307. PTSDpubs ID: 51494

Unexpected effects of nighttime prazosin in suicidal PTSD patients

Nightmares have been associated with increased suicidality, and prazosin may improve nightmares in patients with PTSD. In a small, placebo-controlled study, investigators at the Medical College of Georgia assessed effects of nighttime prazosin in PTSD patients with nightmares and mild-to-moderate suicidal ideation. Twenty patients were randomized to receive nighttime prazosin or placebo for eight weeks. Prazosin could be given up to 20 mg per night in men and 10 mg per night in women, consistent with prior dosing protocols. Most participants were civilians (90%) and women (85%). Half were diagnosed with comorbid major depressive disorder and 20% had bipolar disorder. During the study, the average highest dose of prazosin was 5.5 mg, and only six patients completed the full 8-week protocol. Across the eight weeks, nightmares and suicidal ideation generally improved, but with greater improvement noted in the placebo group. Although this study might seem consistent with a recent large, negative

study of prazosin for PTSD in Veterans (see the [February 2018 CTU-Online](#)), the small sample size, very high dropout and relatively low prazosin dose prevent drawing any definitive conclusions about the effects of prazosin on suicidal patients with PTSD.

Read the article: <https://doi.org/10.1097/JCP.0000000000000968>

McCall, W. V., Pillai, A., Case, D., McCloud, L., Nolla, T., Branch, F., ... Rosenquist, P. B. (2018). A pilot, randomized clinical trial of bedtime doses of prazosin versus placebo in suicidal posttraumatic stress disorder patients with nightmares. *Journal of Clinical Psychopharmacology*, 38, 618-621. PTSDpubs ID: 51299

More evidence supporting intensive delivery of Cognitive Processing Therapy

The evidence base for very short-term, intensive treatment for PTSD is growing, with recent support from a study of PE delivered over 2 weeks to Army Soldiers (see the [February 2018 CTU-Online](#)). Investigators from the National Center for Veterans Studies conducted an open trial of 2 weeks of daily CPT supplemented with recreation and psychoeducational sleep classes. Military Servicemembers and Veterans with PTSD or subthreshold PTSD ($N = 20$) engaged in 12 sessions of individual CPT over 2 weeks. Treatment was delivered in a novel setting: a recreational and adaptive sports center. Participants were allowed to engage in activities such as hiking, biking, and skiing and were offered 4 psychoeducational classes based on the principles of CBT for Insomnia. Participants reported declines of 18.4 points on the CAPS-5 from pre-treatment ($M = 34.6$) to post-treatment ($M = 16.2$); however, this improvement attenuated by 6-month follow-up ($M = 24.6$). Depression symptoms did not improve, but the severity of suicidal ideation declined from pre-treatment to 6-month follow-up, with the proportion of participants endorsing any suicidal ideation falling from 65.5% to 41%. Although the study lacked a comparison group, its results add to the growing literature suggesting that frequent sessions may prove to be an effective way to engage individuals for whom traditional service delivery models are less convenient.

Read the article: <https://doi.org/10.1002/jclp.22651>

Bryan, C. J., Leifker, F. R., Rozek, D. C., Bryan, A. O., Reynolds, M. L., Oakey, D. N., & Roberge, E. (2018). Examining the effectiveness of an intensive, 2-week treatment program for military personnel and veterans with PTSD: Results of a pilot, open-label, prospective cohort trial. *Journal of Clinical Psychology*, 74, 2070-2081. PTSDpubs ID: 50809

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