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TREATMENT

Repeated ketamine infusions safe and effective for PTSD

Few medications have demonstrated effectiveness for treating PTSD. A previous study by investigators at the Icahn School of Medicine at Mount Sinai found that a single, intravenous (IV) infusion of the anesthetic agent ketamine led to a substantial decrease in PTSD severity within 24 hours (see the [June 2014 CTU-Online](#)). In the current study, these investigators assessed the safety and efficacy of repeated ketamine infusions in 30 individuals with PTSD. Participants were randomized to receive six IV infusions of ketamine or midazolam, a medication with psychoactive properties that mimic some of ketamine's effects, over two weeks. PTSD severity was assessed at baseline and after two weeks of treatment. Response was defined as a 30% or greater decrease in CAPS-5 score by posttreatment. Participants receiving ketamine had a greater decrease in CAPS-5 scores compared with those receiving midazolam, and a greater proportion were defined as treatment responders (67% vs. 20%). The median time to loss of response in treatment responders was 28 days. Ketamine was well-tolerated, and there were no serious adverse events. Limitations of this study include a small sample size, exclusion of patients with common comorbidities, and a higher rate of dissociative symptoms during ketamine than midazolam administration that may have affected the adequacy of blinding. However, these findings provide the first evidence that repeated doses of IV ketamine may be safe and effective in treating PTSD.

Read the article: <https://doi.org/10.1176/appi.ajp.2020.20050596>

Feder, A., Costi, S., Rutter, S. B., Collins, A. B., Govindarajulu, U., Jha, M. K., . . . Charney, D. S. (2021). A randomized controlled trial of repeated ketamine administration for chronic posttraumatic stress disorder. *American Journal of Psychiatry*, 178, 193-202. PTSDpubs ID: 1563573

Unclear benefit of cannabis for individuals with PTSD

Cannabis is frequently used by Veterans with PTSD, and PTSD is increasingly considered an eligible diagnosis in US medical cannabis programs. However, the safety and efficacy of medical cannabis for PTSD is unknown. A prospective, observational study of Colorado residents assessed the effects of dispensary-provided cannabis in individuals with PTSD. Adults with PTSD were categorized as using cannabis at least once per week from a licensed or recreational cannabis dispensary ($n = 75$) or as having not used cannabis in the prior six months ($n = 75$). Participants were evaluated at baseline and then every three months for one year. Wrist actigraph data were collected for one week following each evaluation. Cannabis users showed a greater decrease in CAPS-5 PTSD severity over time, although the effect size was small. Cannabis users were also 2.6 times more likely to not meet PTSD diagnostic criteria at the one-year endpoint. The groups did not differ on changes in functioning, physical activity or sleep quality. This study did not assess safety outcomes. Because this study was not randomized and individuals had already chosen to use cannabis or not, it is impossible to conclude that the difference in change in PTSD severity was due to cannabis use. RCTs with long-term follow-up are needed to rigorously assess the safety and efficacy of cannabis as a treatment for PTSD.

Read the article: <http://www.ptsd.va.gov/professional/articles/article-pdf/id1563675.pdf>

Bonn-Miller, M. O., Brunstetter, M., Simonian, A., Loflin, M. J., Vandrey, R., Babson, K. A., & Wortzel, H. (2020). The long-term, prospective, therapeutic impact of cannabis on post-traumatic stress disorder. *Cannabis and Cannabinoid Research*. Advance online publication. PTSDpubs ID: 1563675

Loss of PTSD diagnosis tied to best functional outcomes

A prior study of women Veterans found that loss of diagnosis, assessed using the CAPS-IV, was an optimal benchmark for improved functioning and quality of life in PTSD (see the [April 2016 CTU-Online](#)). A team led by investigators at the University of Melbourne in Australia has now replicated the study in a predominantly male Veteran sample. Australian Veterans ($N = 472$, 93% male) who attended hospital-based PTSD treatment between 2014 and 2019 completed the PCL-5 at intake and discharge. The Veterans were divided into four groups based on changes in PCL-5 scores: No response (<10-point reduction), Response (≥ 10 -point decrease but final score ≥ 33), Loss of Diagnosis (final score <33 but ≥ 20), and Remission (final score <20). Veterans reported on quality of life, relationships, distress, and physical health at pre- and post-treatment. The investigators determined thresholds for clinically meaningful change and good end-point functioning for each domain. Clinically meaningful improvements were more likely among Veterans reporting any response to treatment (46%) vs. no response. Those who lost their diagnosis (13.1%) were significantly more likely to report good end-point functioning in several domains than those who experienced symptom relief but retained their diagnosis (26.5%). These findings, which parallel the previous finding in women Veterans, suggest that providers consider adopting a clinically meaningful threshold like loss of diagnosis in order to optimize treatment outcome.

Read the article: <https://doi.org/10.1002/smi.3019>

Hinton, M., O'Donnell, M., Cowlshaw, S., Kartal, D., Metcalf, O., Varker, T., . . . Phelps, A. J. (2020). Defining post-traumatic stress disorder recovery in veterans: Benchmarking symptom change against functioning indicators. *Stress & Health*. Advance online publication. PTSDpubs ID: 1562532

Head injury from interpersonal violence does not impact PTSD treatment response

Head injuries may occur during a traumatic event, raising the possibility that any resulting cognitive symptoms could interfere with treatment response. Investigators from the National Center for PTSD assessed the influence of head injury on recovery from PTSD and depression following CPT. This secondary analysis included data from a repository of three RCTs examining CPT. Participants were 306 community outpatients (92% women) with PTSD resulting from interpersonal violence. They were assessed with the CAPS at pretreatment, posttreatment, and at 3-6-month follow-up. Participants reported whether they had sustained any of 13 different injuries as a result of interpersonal violence and were classified according to whether they reported head injury, severe physical non-head injuries, or no injury. Nearly 75% of the sample reported head injury; this group had slightly higher baseline CAPS scores (7 points). There were substantial improvements in PTSD (mean CAPS change = 42-45 points) and depression (mean BDI change = 16-18 points) for all three groups with no significant differences between them. These findings suggest that patients may benefit from CPT regardless of having experienced a head injury. However, the results may not generalize

to patients with diagnosed traumatic brain injury, to men, or to patients with head injuries due to blast-related events.

Read the article: <http://www.ptsd.va.gov/professional/articles/article-pdf/id1562046.pdf>

Galovski, T. E., Smith, B. N., Micol, R. L., & Resick, P. A. (2020). Interpersonal violence and head injury: The effects on treatment for PTSD. *Psychological Trauma*. Advance online publication. PTSDpubs ID: 1562046

First study of therapist-assisted, web-based PE

Web-based interventions for PTSD could offer symptom relief with fewer barriers to access than traditional in-person treatments. Investigators at the National Center for PTSD developed and tested Web-PE, first in a small RCT and then in an uncontrolled trial. Web-PE is a 10-session online intervention that closely follows the PE protocol. In both studies, therapists facilitated participant engagement in Web-PE via feedback and phone calls. The RCT, which was suspended due to slow recruitment, included 40 active-duty Service members and Veterans randomized to either Web-PE or 10 60-minute, in-person sessions of Present-Centered Therapy (PCT). PTSD symptoms measured with the PCL-5 improved from before to after treatment in both groups (d s: Web-PE = .6, PCT = .7), with no difference between them. Engagement in Web-PE was poorer than in PCT, with 52.6% of participants dropping out of Web-PE by post-treatment compared to 23.8% in PCT. The investigators then conducted an open trial in order to target individuals specifically interested in web-based treatment. The pre-post effect size on the PCL-5 ($d = 1.8$) for these 34 Veterans and Service members was three times that observed in the RCT. Therapist-facilitated Web-PE appears promising, especially for patients who are interested in web-based care, but better powered, controlled studies that test Web-PE against in-person PE are needed to more fully determine its efficacy.

Read the article: <http://www.ptsd.va.gov/professional/articles/article-pdf/id1561431.pdf>

McLean, C. P., Foa, E. B., Dondanville, K. A., Haddock, C. K., Miller, M. L., Rauch, S. A. M., . . . Peterson, A. L. (2020). The effects of web-prolonged exposure among military personnel and veterans with posttraumatic stress disorder. *Psychological Trauma*. Advance online publication. PTSDpubs ID: 1561431

Additional evidence supports benefits of consultation following CPT training

A study reported in *CTU-Online* in [2018](#) found that therapists who received weekly consultation following CPT training obtained better patient outcomes than therapists attending training alone. In order to understand the factors leading to better outcomes, investigators from the National Center for PTSD used data from that study to examine relationships among therapist self-efficacy, treatment fidelity, and patient outcomes. Eighty therapists who completed CPT training had been randomized to receive standard weekly consultation, weekly consultation with audio review of CPT sessions, or no consultation. The therapists treated 188 patients throughout the 6-month training period, completing monthly surveys of self-efficacy in delivering CPT. Independent raters assessed session

fidelity at 4 time points. Therapist self-efficacy improved over the course of the training period, with no differences between consultation conditions. Surprisingly, therapist self-efficacy was not associated with treatment fidelity, although high levels of treatment adherence across therapists may have limited the ability to find a relationship. Therapists receiving standard consultation achieved better patient outcomes regardless of level of self-efficacy compared to those in the other conditions. Among therapists with low-self efficacy, those who received consultation had much larger patient improvement relative to those without consultation. This suggests that self-efficacy may be an important factor to consider when identifying therapists who could benefit most from consultation.

Read the article: <http://www.ptsd.va.gov/professional/articles/article-pdf/id1561724.pdf>

Pace, B. T., Song, J., Suvak, M. K., Shields, N., Monson, C. M., & Wiltsey Stirman, S. (2020). Therapist self-efficacy in delivering cognitive processing therapy in a randomized controlled implementation trial. *Cognitive and Behavioral Practice*. Advance online publication. PTSDpubs ID: 1561724

Examining the impact of video visits on retention of MST survivors in treatment for PTSD

New research led by investigators at VA Ann Arbor Healthcare System examined MST survivors' dropout from PE and CPT when delivered in person versus via clinical video technology (CVT). Delivering treatment through CVT can address barriers such as logistical challenges that may lead to treatment dropout. Participants were 171 Veterans (73.5% women) who initiated either PE or CPT between 2010 and 2016 to target MST-related PTSD. The Veterans chose their treatment and whether to receive it in person or via CVT; 31 (18.1%) chose CVT, most of whom had their sessions at a community-based outpatient clinic rather than at home. Contrary to expectation, CVT participants were less likely than those in the in-person condition to receive a "minimally adequate" dose of 8 sessions (41.9% CVT vs. 62.1% in-person). CVT patients also tended to drop out earlier than those who received in-person care, with higher attrition roughly coinciding with the introduction of imaginal exposures or written narratives. The investigators speculated that patients who chose CVT may have also been facing more logistical constraints to care than those who chose in-person treatment, which may have further contributed to premature termination. The investigators concluded that additional efforts may be necessary to fully engage MST survivors in trauma-focused treatment via CVT.

Read the article: <https://doi.org/10.1177/1357633x19832419>

Valentine, L. M., Donofry, S. D., Broman, R. B., Smith, E. R., Rauch, S. A., & Sexton, M. B. (2020). Comparing PTSD treatment retention among survivors of military sexual trauma utilizing clinical video technology and in-person approaches. *Journal of Telemedicine and Telecare*, 26, 443-451. PTSDpubs ID: 1562946

Using CPT worksheets to assess fidelity shows promise

Fidelity to a psychotherapy protocol is typically assessed using audio or video review of therapy sessions. In an effort to develop a more efficient method, a team led by investigators at the National Center for PTSD took a novel approach: assessing therapists' fidelity by rating the worksheets that patients complete in CPT. Investigators developed the rating system using CPT worksheets from two previous RCTs of CPT and then evaluated the system using worksheets from 93 Service Members who participated in a third RCT of CPT (see the [December 2016 CTU-Online](#)). The 5 raters, who took an average of 7 minutes to complete ratings of worksheets for each session, found the rating system to be low to moderately difficult to use and moderately representative of the session content, therapist skills, and patient skill. Fidelity ratings of worksheets were not correlated with observer ratings of the full videotaped sessions but were highly correlated with observer ratings of audio-recorded cognitive interventions reflected on worksheets. Quality of worksheets completed outside of session, but not within session, was related to PTSD symptom reduction. Although this rating system does not capture elements of CPT that are not reflected in worksheets, rating of worksheets could provide a scalable method of assessing fidelity to key cognitive interventions in CPT that is less time-intensive than reviewing full sessions and less subjective than therapist self-report.

Read the article: <http://www.ptsd.va.gov/professional/articles/article-pdf/id1561375.pdf>

Wiltsey Stirman, S., Gutner, C. A., Gamarra, J., Suvak, M. K., Vogt, D., Johnson, C., . . . Resick, P. A. (2020). A novel approach to the assessment of fidelity to a cognitive behavioral therapy for PTSD using clinical worksheets: A proof of concept with cognitive processing therapy. *Behavior Therapy*. Advance online publication. PTSDpubs ID: 1561375

Take NOTE

Virtual reality exposure treatment for PTSD

A team led by investigators at the University of Amsterdam reviewed RCTs of virtual reality exposure therapy (VRET) and augmented reality exposure therapy for PTSD, then conducted a meta-analysis on the 11 studies of VRET.

Read the article: <https://doi.org/10.1016/j.jpsychires.2020.11.030>

Eshuis, L. V., van Gelderen, M. J., van Zuiden, M., Nijdam, M. J., Vermetten, E., Olf, M., & Bakker, A. (2020). Efficacy of immersive PTSD treatments: A systematic review of virtual and augmented reality exposure therapy and a meta-analysis of virtual reality exposure therapy. *Journal of Psychiatric Research*. Advance online publication. PTSDpubs ID: 1561743

TMS for PTSD

Investigators at the University of Calgary carried out a systematic review and network meta-analysis of 10 RCTs of transcranial magnetic stimulation (TMS) for PTSD.

Read the article: <https://doi.org/10.1177/0706743720982432>

McGirr, A., Devoe, D. J., Raedler, A., Debert, C. T., Ismail, Z., & Berlim, M. T. (2020). Repetitive transcranial magnetic stimulation for the treatment of post-traumatic stress disorder: A systematic review and network meta-analysis. *Canadian Journal of Psychiatry*. Advance online publication. PTSDpubs ID:1562864

MDMA-assisted psychotherapy for PTSD

A team led by investigators at Peterborough City Hospital in the UK conducted a systematic review and meta-analysis of 4 RCTs of MDMA-assisted psychotherapy for PTSD.

Read the article: <https://doi.org/10.1177/0269881120965915>

Illingworth, B. J., Lewis, D. J., Lambarth, A. T., Stocking, K., Duffy, J. M., Jelen, L. A., & Rucker, J. J. (2020). A comparison of MDMA-assisted psychotherapy to non-assisted psychotherapy in treatment-resistant PTSD: A systematic review and meta-analysis. *Journal of Psychopharmacology*. Advance online publication. PTSDpubs ID: 1562888



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