CLINICIAN'S TRAUMA UPDATE

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TREATMENT

Smoked cannabis appears ineffective in treating PTSD

Cannabis is frequently used by Veterans with PTSD, but the safety and effective of cannabis for PTSD has not been established. A recent study funded by the Colorado Department of Public Health and Environment and the Multidisciplinary Association for Psychedelic Studies tested three formulations of smoked cannabis in a two-stage, randomized, placebo-controlled trial. The three formulations of active cannabis included a high tetrahydrocannabinol version (THC), a high cannabidiol version (CBD) and a version with equal amounts THC and CBD (THC-CBD). In the first stage, 80 men and women with PTSD (2/3 with combat-related PTSD) were randomized to receive one of these three formulations or placebo for three weeks. In the second stage, 74 of the participants were re-randomized to receive one of the three active cannabis formulations for an additional three weeks; this stage had no placebo condition. In stage 1, there was no difference in efficacy for PTSD measured with the CAPS-5 in any of the three active cannabis conditions compared to placebo. In stage 2, the combined THC-CBD group showed a greater reduction in PTSD symptoms at the end of three weeks compared to the THC and CBD conditions, but there was no difference between the groups at the final post-treatment follow-up visit. The lack of a placebo group in this stage limits interpretation. Taken together, this evidence does not support the use of smoked cannabis for the treatment of PTSD.

Read the article: http://www.ptsd.va.gov/professional/articles/article-pdf/id1566890.pdf

Bonn-Miller, M. O., Sisley, S., Riggs, P., Yazar-Klosinski, B., Wang, J. B., Loflin, M. J. E., . . . Doblin, R. (2021). The short-term impact of 3 smoked cannabis preparations versus placebo on PTSD symptoms: A randomized cross-over clinical trial. *PLoS One, 16*, Article e0246990. PTSDpubs ID: 1566890

Safety and effectiveness of CPT among Veterans at risk for suicide

EBPs for PTSD reduce suicidal ideation (see the June 2013 *CTU-Online*), but research with Veterans at more acute risk for suicide, such as those who previously attempted suicide, has remained sparse. A team led by investigators at the VAMC in Salt Lake City used medical record data to evaluate CPT outcomes among Veterans at increased suicide risk. Analyses were based on data from 290 Veterans (88.3% male) who completed at least one session of CPT in a VA PTSD outpatient clinic. Charts were reviewed for the dates of Veterans' most recent suicidal ideation and history of any suicide attempts. Veterans without recent suicidal ideation or a history of suicide attempt were considered low risk (46.0%), while Veterans with recent and/or current ideation or a previous attempt were categorized as at acute risk (10.0%). Three Veterans (1.0%) reported a post-CPT suicide attempt ($n = 2$ within 7 months after CPT, $n = 1$ in the month following their only CPT session). Suicide risk level did not predict completion of CPT nor response to CPT. Improvements on the PCL-5 were observed in all risk groups. These results support the use of CPT among Veterans at risk for suicide.

Read the article: https://doi.org/10.1002/jts.22662

Roberge, E. M., Harris, J. A., Weinstein, H. R., & Rozek, D. C. (2021). Treating veterans at risk for suicide: an examination of the safety, tolerability, and outcomes of cognitive processing therapy. *Journal of Traumatic Stress*. Advance online publication. PTSDpubs ID: 1566279

New study compares Adaptive Disclosure to CPT

Adaptive Disclosure, an emotion-focused therapy for combat-related PTSD, was previously found to improve PTSD in an uncontrolled study but had not yet been tested in a randomized controlled trial. Investigators from the VA Boston Healthcare System led a non-inferiority study comparing Adaptive Disclosure to CPT. Participants were 122 Marines and Sailors randomized to receive Adaptive Disclosure or CPT. Adaptive Disclosure uses experiential change techniques such as imaginal dialogues to address sequelae of combat trauma including life threat, traumatic loss, and moral injury. Adaptive Disclosure was delivered in 8 90-minute sessions; CPT was delivered in 12 60-minute sessions. Adaptive Disclosure was non-inferior to CPT for reducing PTSD severity at posttreatment (d = .01), according to a noninferiority margin of 10 points on the CAPS-IV. Treatment dropout was roughly 40% and did not differ between treatments. Dropout from measurement was high—43% at posttreatment—but the authors performed sensitivity analyses to demonstrate the robustness of their finding. However, the amount of dropout from measurement at 3 months (77%) and 6 months (84%) was too low to permit analysis. Findings suggest that Adaptive Disclosure could be an effective treatment option for individuals who have experienced combat and wish to pursue an alternative to current trauma-focused psychotherapies for PTSD. Future work is needed to determine longer-term benefit and whether (or for whom) Adaptive Disclosure is superior to other evidence-based treatments for some outcomes.

Read the article: https://doi.org/10.1016/j.psychres.2021.113761

Litz, B. T., Rusowicz-Orazem, L., Doros, G., Grunthal, B., Gray, M., Nash, W., & Lang, A. J. (2021). Adaptive disclosure, a combat-specific PTSD treatment, versus cognitive-processing therapy, in deployed marines and sailors: A randomized controlled non-inferiority trial. *Psychiatry Research, 297*, Article 113761. PTSDpubs ID: 1564968

Efficacy of CPT among Veterans who experienced moral injury

A team led by investigators from Rush University Medical Center examined whether exposure to a morally injurious event or targeting a morally injurious index event during CPT was associated with higher symptom severity or impacted treatment response. Some authors have suggested that existing EBPs for PTSD may not be as effective among Veterans who have experienced moral injury, yet prior studies had not directly tested this idea. Participants were 161 Service members and Veterans (91% male) enrolled in a 3-week CPT intensive treatment program involving daily individual and group CPT, as well as adjunctive interventions including mindfulness and yoga. The majority of participants (80%) reported exposure to a morally injurious event, and 51% addressed an index trauma involving moral injury during CPT. Neither moral injury history nor index trauma type was associated with baseline self-report PTSD or depression symptoms, completion rates, or treatment days completed. Changes in PTSD and depression symptoms pre- to post-treatment also did not differ based on moral injury history (d = .03 and .07 for PTSD and depression, respectively) or index trauma type (d = .22 and .16, respectively). Because the treatment in this study was intensive and included adjunctive interventions, these findings should be replicated with standard delivery CPT alone to determine whether moral injury is associated with differential outcomes.

Read the article: https://doi.org/10.1080/20008198.2021.1877026

Held, P., Klassen, B. J., Steigerwald, V. L., Smith, D. L., Bravo, K., Rozek, D. C., . . . Zalta, A. (2021). Do morally injurious experiences and index events negatively impact intensive PTSD treatment outcomes among combat veterans? *European Journal of Psychotraumatology, 12,* Article 1877026. PTSDpubs ID: 1567077

Vortioxetine not effective in the treatment of PTSD

Antidepressants targeting the serotonin neurotransmitter system comprise the few medications demonstrating efficacy in treating PTSD. Vortioxetine is an antidepressant medication that affects the serotonin system in several novel ways. A research team led by investigators at Emory University and the University of Miami tested the efficacy of vortioxetine in patients with PTSD. In a 12-week trial, 41 adults with PTSD were randomized to receive vortioxetine versus placebo. PTSD severity was measured using the CAPS-5. Although there was statistically greater efficacy for vortioxetine after eight weeks of treatment, there was no difference compared to placebo at 12 weeks. Vortioxetine was well tolerated, and 78% of participants completed the trial. However, the lack of difference from placebo at 12 weeks suggests that vortioxetine is not an effective medication for PTSD.

Read the article: https://doi.org/10.1097/jcp.0000000000001363

Dunlop, B. W., Rakofsky, J. J., Newport, D. J., Mletzko-Crowe, T., Barone, K., Nemeroff, C. B., & Harvey, P. D. (2021). Efficacy of vortioxetine monotherapy for posttraumatic stress disorder: A randomized, placebo-controlled trial. *Journal of Clinical Psychopharmacology, 41*, 172-179. PTSDpubs ID: 1565688

Dropout in trials comparing treatments for PTSD

Predicting dropout from effective PTSD treatment continues to be a critical challenge for the field (see Take Note in this issue of *CTU-Online*). In two new studies, teams led by an investigator at Case Western Reserve University examined dropout from several treatments for PTSD: PE and sertraline in one study and COPE and Seeking Safety in the other.

The first study evaluated predictors of dropout from a doubly randomized preference trial comparing PE to sertraline in 200 non-Veterans (see the October 2018 *CTU-Online*) in which 33.0% (n = 66) of participants terminated before starting treatment. The 19 "nonstarters," patients who did not initiate treatment after randomization (PE n = 7, sertraline n = 12), had less severe baseline PTSD than patients who started treatment (d = .6). Nonstarters were also less likely to have been assigned to their preferred intervention, with 68.4% of nonstarters having a mismatch compared to only 21.0% of participants who started treatment. Starters in the PE group and nonstarters in the sertraline group reported more positive beliefs toward PE than sertraline (both ds = 1.0). A similar pattern emerged when comparing nonstarters to patients who started treatment but later dropped out. None of the other factors, including enabling factors like income and

social support, need factors such as depression severity, and current and past mental health treatment, predicted pretreatment dropout status.

The second study evaluated predictors of dropout from a trial comparing two integrated treatments for PTSD and alcohol use disorder (AUD), COPE and Seeking Safety, in a sample of 110 Veterans. The treatments were equally effective for AUD outcomes, but COPE was more effective than Seeking Safety for PTSD (see the June 2019 *CTU-Online*). Participants completed an average of 8.1 sessions in COPE and 11.2 in Seeking Safety. Dropout (defined as completion of fewer than 12 sessions) was 67.2% in COPE and 36.5% in Seeking Safety. The only predictor of dropout was the interaction of treatment type and changes in alcohol use between sessions. An increase of one drink per day in the previous 2-3 weeks since the last assessment was associated with a 5-fold increase in likelihood of dropout in COPE but not in Seeking Safety, suggesting that exacerbations of alcohol misuse have less impact on treatment continuation in Seeking Safety than in COPE. The investigators also reported Veterans' reasons for dropout, with "practical barriers" (e.g., work/school commitments) and "therapy/therapist-related barriers" (e.g., poor perceived treatment fit) cited most frequently across treatments.

The results of both studies illustrate the complex and heterogenous reasons for patients' early termination from treatments for PTSD. Both studies suggest that treatment preference and perceived fit, which can be addressed during shared decision-making, are important for engagement in treatment. The findings from the first study in particular may be generalizable since the treatment options available in many settings are inherently limited.

Read the articles:

http://www.ptsd.va.gov/professional/articles/article-pdf/id1565968.pdf

Kline, A. C., Panza, K. E., Harlé, K. M., Angkaw, A. C., Trim, R. S., Back, S. E., & Norman, S. B. (2021). Within-treatment clinical markers of dropout risk in integrated treatments for comorbid PTSD and alcohol use disorder. *Drug and Alcohol Dependence, 221*, Article 108592. PTSDpubs ID: 1565968

https://doi.org/10.1016/j.brat.2020.103750

Kline, A. C., Baier, A. L., Klein, A. B., Feeny, N. C., & Zoellner, L. A. (2020). Differentiating "types" of treatment dropout: Nonstarters in an RCT of prolonged exposure versus sertraline. *Behaviour Research and Therapy, 135,* Article 103750. PTSDpubs ID: 1559437

Further evidence that PE does not worsen PTSD symptoms PE

Patients and providers often cite concerns that exposure-based therapies will worsen PTSD symptoms, despite little evidence for this claim (see the February 2014 *CTU-Online*). A new study by investigators at the University of Washington provides more evidence of a lack of symptom exacerbation in PE. The investigators conducted a secondary analysis of data from the same randomized preference trial of PE versus sertraline delivered via weekly medication management described above ($N = 151$, 71.8% women; see the October 2018 *CTU-Online*) to determine whether PTSD symptoms worsened following the initiation of imaginal exposure. Reliable worsening was defined as an increase of >6.2 points on the PTSD Symptom Scale-Self-Report, which measures DSM-IV PTSD symptoms. Reliable worsening did not differ between the PE group (13.0%) and the sertraline group (6.8%), which not statistically significant. Across the sample, reliable worsening was not linked to treatment dropout or PTSD and depressive symptoms at posttreatment or at 3- or 6-month follow-up. Within the PE group, the investigators found no associations between symptom exacerbation and characteristics such as mental health comorbidities, childhood sexual/physical abuse, or index trauma type. Although it will be important to replicate the findings in larger samples and with Veterans, these results provide further evidence that PE does nor differentially increase symptom exacerbation.

Read the article: https://doi.org/10.1016/j.brat.2020.103747

Walker, R. S. W., Marks, E. H., Jaeger, J., Duax, J. M., Feeny, N. C., & Zoellner, L. A. (2020). Imaginal exposure exacerbation revisited: Deconstructing patient characteristics associated with worse reactions to the initiation of imaginal exposure in PTSD. *Behaviour Research and Therapy, 135*, Article 103747. PTSDpubs ID: 1559966

ASSESSMENT

PC-PTSD screen for DSM-5 validated for use in primary care

Screening for PTSD in primary care is mandatory in VHA, so it is crucial to have PTSD screening instruments adapted for this setting. Investigators at the National Center for PTSD have now validated the Primary Care Posttraumatic Stress Disorder Screen updated for DSM-5 (PC-PTSD-5) against the CAPS-5, the gold-standard assessment for PTSD. Participants included Veterans who sought primary care at two VHA sites between May 2017 and September 2018 ($N = 396$, 84.1% men). Veterans completed the PC-PTSD-5, which assesses exposure to lifetime trauma and has five items assessing past-month PTSD symptoms. An investigator blinded to the Veterans' PC-PTSD-5 scores assessed PTSD with the CAPS-5. PC-PTSD-5 scores range from 0 to 5. In the overall sample, a cutoff score ≥ 4 optimally balanced identifying true PTSD cases while screening out true PTSD-negative cases (area under the curve = .9; 95% CI, 0.9-1.0). However, this cutoff resulted in almost twice as many false-negative cases in women versus men. The investigators recommended using a cutoff of 4 for men and women, but suggested that a cutoff score of ≥ 3 may be useful for women Veterans in some settings. These findings show the PC-PTSD-5 is a valid screening tool for PTSD in primary care, but the best cutoff scores may vary based on the populations served and resources available for those who screen positive.

Read the article: http://www.ptsd.va.gov/professional/articles/article-pdf/id1564989.pdf

Bovin, M. J., Kimerling, R., Weathers, F. W., Prins, A., Marx, B. P., Post, E. P., & Schnurr, P. P. (2021). Diagnostic accuracy and acceptability of the Primary Care Posttraumatic Stress Disorder Screen for the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) among US veterans. *JAMA Network Open, 4,* Article e2036733. PTSDpubs ID: 1564989

Take NOTE

Dropout from PTSD treatment

Two new papers report on dropout from PTSD treatment. A team led by investigators at the Psychological Health Center of Excellence in Washington conducted a systematic review and meta-analysis of dropout from RCTs of psychotherapies for PTSD among military and Veteran samples. Investigators at the Michael E. DeBakey VA Medical Center carried out a systematic review of factors associated with PTSD treatment dropout among OIF/OEF Veterans.

Read the articles:

https://doi.org/10.1002/jts.22653

Edwards-Stewart, A., Smolenski, D. J., Bush, N. E., Cyr, B. A., Beech, E. H., Skopp, N. A., & Belsher, B. E. (2021). Posttraumatic stress disorder treatment dropout among military and veteran populations: A systematic review and meta-analysis. *Journal of Traumatic Stress*. Advance online publication. PTSDpubs ID: 1565044

https://doi.org/10.1037/ser0000519

Sciarrino, N. A., Bartlett, B. A., Smith, L. J., Martin, C. E., & Williams, W. (2021). Factors contributing to PTSD treatment dropout in veterans returning from the wars in Iraq and Afghanistan: A systematic review. *Psychological Services.* Advance online publication. PTSDpubs ID: 1566234

Network meta-analysis of expressive writing for PTSD

A team led by investigators at the University of Basel in Switzerland conducted a systematic review and network meta-analysis of RCTs examining outcomes for expressive writing interventions for PTSD.

Read the article: https://doi.org/10.1017/s0033291721000143

Gerger, H., Werner, C. P., Gaab, J., & Cuijpers, P. (2021). Comparative efficacy and acceptability of expressive writing treatments compared with psychotherapy, other writing treatments, and waiting list control for adult trauma survivors: A systematic review and network meta-analysis. *Psychological Medicine.* Advance online publication. PTSDpubs ID: 1565900

Meta-analysis of third wave CBT for PTSD

Investigators at Auburn University carried out a meta-analysis of studies of third wave cognitive-behavioral interventions for PTSD, such as ACT, DBT, Mindfulness-Based Cognitive Therapy, and Behavioral Activation.

Read the article: https://doi.org/10.1016/j.janxdis.2021.102360

Benfer, N., Spitzer, E. G., & Bardeen, J. R. (2021). Efficacy of third wave cognitive behavioral therapies in the treatment of posttraumatic stress: A meta-analytic study. *Journal of Anxiety Disorders, 78,* Article 102360. PTSDpubs ID: 1564242

Systematic reviews of cannabinoids for PTSD

Two new systematic reviews address cannabinoids for PTSD. The first, conducted by investigators at McMaster University, review physical and mental health outcomes associated with cannabis use in Veterans; the second, by investigators at the Geisel School of Medicine at Dartmouth, is a review of RCTs testing the effects of cannabinoids on PTSD, mood disorders, and anxiety.

Read the articles:

https://doi.org/10.1016/j.cpr.2021.101958

Turna, J., & MacKillop, J. (2021). Cannabis use among military veterans: A great deal to gain or lose? *Clinical Psychology Review, 84,* Article 101958. PTSDpubs ID: 1564238

https://doi.org/10.1176/appi.ps.202000189

Stanciu, C. N., Brunette, M. F., Teja, N., & Budney, A. J. (2021). Evidence for use of cannabinoids in mood disorders, anxiety disorders, and PTSD: A systematic review. *Psychiatric Services, 72*, 429-436. PTSDpubs ID: 1565010

Mental health care for Service members living away from military bases

In a new report, RAND investigators examined access to mental health care and the quality of care for Service members with PTSD, depression, or substance use who live off base from military facilities.

Read the report: https://www.rand.org/pubs/research_reports/RR2788.html

Hepner, K. A., Brown, R. A., Roth, C. P., Ruder, T., & Pincus, H. A. (2021*). Behavioral health care in the military health system: Access and quality for remote service members* (Report No. RR-2788) Rand Corporation. PTSDpubs ID: 1567778

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