



Canadian Psychiatric Association
Association des psychiatres du Canada

Emerging Treatments for Canadian Armed Forces and Royal Canadian Mounted Police Veterans Suffering From Operational Stress Injuries

SUBMISSION FROM THE CANADIAN PSYCHIATRIC ASSOCIATION
TO THE STANDING SENATE COMMITTEE ON
NATIONAL SECURITY, DEFENCE AND VETERANS AFFAIRS
SUBCOMMITTEE ON VETERANS AFFAIRS
MAR. 22, 2023

Introduction

The Canadian Psychiatric Association (CPA) is pleased to provide input to the Senate Subcommittee on Veterans Affairs regarding emerging treatments for Canadian Armed Forces and Royal Canadian Mounted Police veterans suffering from operational stress injuries.

Operational stress injuries are not limited to posttraumatic stress disorder (PTSD). In the treatment-seeking population, major depressive disorder is as prevalent as PTSD. Therefore, it is important to take a broad view of emerging treatments not only for PTSD, but also for major depressive disorder, substance use disorder and other psychiatric conditions that affect a veteran's overall functioning.

Most veterans continue to struggle accessing first-line evidence-based pharmacotherapy (medication) and psychotherapy, and treatment dropout remains an issue. When compared to civilian-related PTSD, military-related PTSD does not respond as well to pharmacotherapy or psychotherapy.

Many reasons have been hypothesized for this worsening outcome of military-related PTSD, including:

- The military is a primarily male population and men and women may respond differently to treatment.
- In the military population, PTSD more frequently co-occurs with other mental health problems, especially major depressive disorder and substance use disorder.
- Military-related PTSD tends to be more severe and chronic.

Emerging Treatments

Use of **esketamine** (nasal spray), or off-label use of **ketamine through infusion**, is currently indicated for treatment-resistant depression. It has also been demonstrated to assist with suicidal ideation, which is prevalent in both major depressive disorder and PTSD. There is also emerging evidence for combining ketamine with psychotherapy to assist PTSD. Across Canada, veterans still face significant challenges when trying to access this treatment, especially if they live outside a major urban centre. There are trials of at-home oral ketamine treatment to try and overcome access problems; however, oral ketamine has not been shown to be as effective as esketamine and ketamine infusions.

Repeated transcranial magnetic stimulation (rTMS) is currently indicated for treatment resistant depression, which is a very common operational stress injury, and one that often co-occurs with PTSD. There is emerging evidence that combining rTMS with psychotherapy enhances its effect. There are currently trials of **bilateral sequential theta burst stimulation**, a faster treatment option than traditional rTMS. These have demonstrated efficacy and safety in a small sample of patients with treatment resistant depression with comorbid PTSD.

Psychedelic-assisted psychotherapy using psilocybin, MDMA (3,4-Methylenedioxyamphetamine) or ketamine, shows promise in assisting those with treatment resistant PTSD and major depressive disorder. Study sample sizes are small with short follow-up and the long-term benefits and risks are not well-established. There are also questions whether this type of treatment is scalable and if it could ever be offered as a first-line treatment or whether it should be reserved for treatment resistant PTSD and major depressive disorder.

There are no current Health Canada-approved indications for use of **cannabis** or **cannabinoid products** for the treatment of mental illness. There is some limited evidence for use of cannabinoid products (excluding combustible dried cannabis and cannabis edibles) for the treatment of mental illness, but the evidence base is currently of low quality and below that required to meet Level 1 evidence. To better assess whether cannabinoid-based products have any therapeutic value, larger neuroscience-based, hypothesis-driven RCTs are needed and should include varying lower risk products (e.g., low THC concentration), dose ranges and routes of administration. Narrowing the knowledge gap with high-quality RCTs should be a priority for all stakeholders.

Innovations to Improve Outcomes with Current Treatments

Currently, most **trauma-focused psychotherapy** is offered once weekly. However, innovations such as increasing the frequency of psychotherapy in order to shorten the total treatment time and decrease dropouts has shown promise. This is called **massed prolonged exposure treatment**, or massed PE treatment.

Pharmacogenetics, which uses our understanding of how differences in our genetic make-up affect a person's response to certain medication, can help clinicians prescribe the antidepressant or mood stabilizer (atypical antipsychotics) that will best be tolerated by the patient. Use of pharmacogenetics has been shown to decrease the number of medication trials needed to find the right medication and decrease treatment dropouts.

Treatment guidelines for the veteran population need to be updated. Most current guidelines are limited to first-line treatments. More research is needed to establish guidelines beyond first-line treatments and incorporate best practice for treatment-resistant illness, as well as address common comorbidity in military-related PTSD.

The use of **machine learning, or AI**, to better match treatments to patients, is an emerging field of study. Small studies have demonstrated that machine learning can assist in predicting who will respond to an antidepressant compared to psychotherapy. With continuing improvements in advanced analytics that combine symptom profile, comorbidity and pharmacogenetics, research centres dedicated to veteran mental health, such as the MacDonald Franklin OSI Research Centre, are trying to better match a patient's profile to specific treatments in order to improve treatment outcomes.

Conclusion

Innovative and emerging treatments are important for the future. However, this must be balanced with how we can improve veterans' access to the evidence-based care of today.

About the CPA

Founded in 1951, the Canadian Psychiatric Association is the national voice of Canada's psychiatrists and psychiatrists-in-training and is the leading authority on psychiatric matters in Canada.

Psychiatrists are medical doctors who provide psychiatric assessment, treatment and rehabilitation care to people with psychiatric disorders to prevent, reduce and eliminate the symptoms and subsequent disabilities resulting from a mental illness or disorder. Psychiatrists provide direct care to patients and often act as consultants to other health professionals such as family doctors. They work in a range of settings including psychiatric and general hospitals, private offices, research units, community health centres, social agencies or in government. Psychiatrists use a mix of treatment options, including medications and psychotherapy, depending on the psychiatric condition. Often part of the treatment or rehabilitation plan will include referral to or collaboration with a range of social and support services.

As an evidence-based profession, CPA provides advice on the most effective programs, services and policies to achieve the best possible mental health care for Canadians.

References

Colic S, He JC, Richardson JD, et al. A machine learning approach to identification of self-harm and suicidal ideation among military and police Veterans. *J Mil Veteran Fam Health*. 2022;8(1):56-67.

Davis AK, Averill LA, Sepeda ND, et al. Psychedelic treatment for trauma-related psychological and cognitive impairment among US special operations forces veterans. *Chronic Stress (Thousand Oaks)*. 2020 Jul 8;4:2470547020939564.

Liu JJW, Ein N, Forchuk CA, et al. A meta-analysis of internet-based cognitive behavioral therapy for military and veteran populations. *BMC Psychiatry*. 2023. DOI: 10.1186/s12888-023-04668-1.

Liu JJW, Ein N, Plouffe RA, et al. Effectiveness of ketamine for veterans managing chronic pain and mental health conditions: a meta-analysis and systematic review. PROSPERO 2022 CRD42022339015. 2022. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022339015

Liu JJW, Nazarov A, Easterbrook B, et al. Four decades of military posttraumatic stress: Protocol for a meta-analysis and systematic review of treatment approaches and efficacy. JMIR Res Protoc. 2021 Oct 25;10(10):e33151.

Richardson JD, St. Cyr K, Forchuk CA, et al. Well-being of canadian veterans during the COVID-19 pandemic: cross-sectional results from the COVID-19 Veteran well-being study. Eur. J. Psychotraumatol. 2022 Jan 24;13(1):2012374.

Sareen J, Bolton SL, Mota N, et al. Lifetime prevalence and comorbidity of mental disorders in the two-wave 2002–2018 canadian armed forces members and veterans mental health follow-up survey (CAFVMHS): Prévalence et comorbidité de durée de vie des troubles mentaux dans l'enquête de suivi sur la santé mentale auprès des membres des forces armées canadiennes et des ex-militaires (ESSMFACM) en deux cycles de 2002 à 2018. Can J Psychiatry. 2021 Nov;66(11):951-960.

St. Cyr K, Liu J, Cramm H, et al. "You can't un-ring the bell": A mixed methods approach to understanding Veteran and family perspectives of recovery from military-related posttraumatic stress disorder. BMC Psychiatry. 2021 Jan 14;22(1):37.

Tibbo PG, McKee KA, Meyer JH, et al. Are there therapeutic benefits of cannabinoid products in adult mental illness? Can J Psychiatry. 2021 Feb;66(2):185-194.

Vaithianathan T, Blair M, Soares V, et al. Bilateral sequential theta burst stimulation in depressed veterans with service-related posttraumatic stress disorder: a feasibility study. BMC Psychiatry. 2022;22:81.

Wynn G, Jetly R, Vermetten E, et al. Pharmacogenomics: a primer for the military mental health provider. J Mil Veteran Fam Health. 2020;6(S1):44-50.

Zhang J, Richardson JD, Dunkley BT. Classifying post-traumatic stress disorder using the magnetoencephalographic connectome and machine learning. Sci Rep. 2020 Apr 3;10(1):5937.

Canadian Psychiatric Association
701 – 141 Laurier Avenue West, Ottawa ON K1P 5J3
www.cpa-apc.org