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Office of the Secretary,

Clinical Endocannabinoid Deficiency (CECD)¹ is a serious condition affecting veterans with a history of PTSD, traumatic brain injuries (TBI), and other factors. It impacts the body's largest neurotransmitter system, The Endocannabinoid System (ECS) which can become impaired due to repeated stress², and can have debilitating consequences. When will the VA publicly acknowledge that veterans are facing **severe** CECD and take action to address this issue among veterans?

In order maintain homeostasis in the body with CECD, this altered lipid metabolism³ condition requires ample supplies of phytocannabinoids (fat like lipids) due to our endogenous⁴ cannabinoids (endocannabinoids) fluctuating greatly according to various factors. When the body can't make these lipids efficiently enough then this can lead to a wide range of mental health outcomes including suicide. This deficiency can be quite costly for veterans to maintain due to the costs of phytocannabinoids currently. ECS is the universal regulator of our body⁵, and as per University of California, an endocannabinoid known as anandamide (AEA) (aka the bliss molecule in sanskrit language) which was discovered in 1992, is the "bona fide" neurotransmitter involved in regulating stress and pain.⁶ Without the body's ability to produce anandamide efficiently on-demand this leads to even more brain cell loss, which is a very irritating, frustrating feeling leading to outcomes like Intermittent Explosive Disorder⁷. Yale Medical school found in clinical and pre-clinical studies⁸ that stress and depression kills our brain cells and AEA is the very neurotransmitter involved in protecting our brain and body from stress and day to day survival. Informing veterans of this concept, would likely help them cope with stress better, as it has helped me in various ways, because when you understand yourself better, it helps reduce the frustration involved in feeling this way, even when the feeling itself is out of our control. ECS regulates many other aspects of the body affected by combat & other trauma such as mood (ie. anxiety/depression), migraines, gut, body temperature, pain, skin, inflammation, and much more. Tetrahydrocannabinol (THC), a phytocannabinoid found in cannabis, mimics many of the actions found to take place with anandamide.^{9 10}

Research from 2014 by the VA National Center for Posttraumatic Stress Disorder and Yale School of Medicine New York University research has stated:

"Recently, an accumulating body of evidence has implicated the endocannabinoid system in the etiology of PTSD, and targets within this system are believed to be suitable for treatment development."

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¹ <u>https://pubmed.ncbi.nlm.nih.gov/24977967/</u>

² <u>https://pubmed.ncbi.nlm.nih.gov/20720126/</u>

³ <u>https://pmc.ncbi.nlm.nih.gov/articles/PMC2293298</u>

⁴ made from within the body

⁵ <u>https://www.jyi.org/2018-june/2018/6/1/the-endocannabinoid-system-our-universal-regulator</u>

⁶ <u>https://pubmed.ncbi.nlm.nih.gov/23954677</u>

⁷ <u>https://www.sciencedirect.com/science/article/pii/S235228952100045X</u>

⁸ <u>https://pubmed.ncbi.nlm.nih.gov/15271581/</u>

⁹ http://www.ncbi.nlm.nih.gov/pubmed/7906042

¹⁰ (pg 68) Institute of Medicine, Marijuana and Medicine: Assessing the Science

..."There is convincing evidence from multiple studies for reduced endocannabinoid availability in PTSD."..."evidence showing reduced levels of the endocannabinoid anandamide"¹¹...

In the VA research paper quoted above it says "...pharmacotherapy development to date has been largely opportunistic instead of mechanism-based." and then discusses the CECD problem facing veterans with PTSD. Why are we not focusing on a mechanism based approach to regulating veterans ECS instead of pharmacotherapy development based on a moment of opportunity? Teaching veterans how to regulate our ECS seems like a crucial step to maintaining mental health and wellbeing.

Research published in 2020 by James J. Peters Veterans' Administration Medical Center and Icahn School of Medicine at Mount Sinai found that **anandamide** plays a secondary role in preventing suicide.

"AEA appears to reduce suicidality among suicide attempters, i.e., AEA plays a part in the secondary prevention of suicide attempt. AEA may diminish suicidality because the endocannabinoid system restricts activation of the stress reaction by way of disseminated actions in limbic and hypothalamic circuits in the brain. Our research suggests that clinically detected dissimilarities between combat military veterans with vs. without a history of post deployment suicide attempts may have a neurobiological origin."¹²...

Gastrointestinal disorders (GID) such as Irritable bowel syndrome (IBS) has the potential for a fatal outcome from suicide, research suggests¹³. GIDs are a common problem with returning veterans, with U.S Veterans experiencing a GID at a rate of up to 40% or more. Our ECS regulate our gastrointestinal system as well, having CECD can greatly fluctuate and thus experiencing GID randomly.

"Mammalian cells have machinery, the so-called Endocannabinoid system (ECS), to produce and metabolize their own cannabinoids in order to control homeostasis of the gut in a rapidly adapting manner."¹⁴

-Division of Gastroenterology, Department of Medicine, University of Calgary

Based on a 2023 project outline from the VA, it doesn't look like much change has been made with regards to the number of suicides, because the VA said: "The Veterans' persistent higher rates of suicide have remained unabated challenges and, and thus, demanding new ways of understanding and engaging in preventative efforts."¹⁵

It seems like we need to start moving towards a more mechanism-based approach as the VA's research suggests. There are many more aspects to this problem, not addressed here, that hopefully can be discussed in the future. I would also like to ask about other deficiencies which in many cases don't appear to be addressed in VA standard lab protocols to include Omega-3 Deficiency/ Omega ratio, GABA, L-Arginine, Growth hormone deficiency (GHD), NAC, Glycine and more. Educating veterans on how to manage inflammation, more efficiently, would also be an important step as well, since this has been known by scientists since 1929, but never taught extensively. These can all lead to various mental health issues if not addressed, in the veteran population. ¹⁶

Sincerely, Jason Howard



¹¹<u>http://www.ncbi.nlm.nih.gov/pubmed/25456347</u>

¹² <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7524409/pdf/bjp-42-05-465.pdf</u>

¹³ <u>https://pubmed.ncbi.nlm.nih.gov/15625650/</u>

¹⁴ <u>http://www.ncbi.nlm.nih.gov/pubmed/22111567</u>

¹⁵ <u>https://reporter.nih.gov/project-details/10487844</u>

¹⁶ <u>https://pmc.ncbi.nlm.nih.gov/articles/PMC3846682</u>