Millennium TBI Network

Rebuilding Hope one day at a time

Final Draft

2020 Summary Report on Symptomatic Neuroinflammation

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Abstract

Neuroactive steroids act as important physiological regulators of central nervous system function (1). It has been demonstrated in several experimental models of neurodegenerative disorders, that the administration of neuroactive steroids is able to promote several protective and reparative processes like inhibition of neuronal death, promotion of neurogenesis, and myelination, as well as reduction of neuroinflammation (2).

Several cytokines and chemokines are known to play important physiological roles in the brain where they act as crucial regulators of communication between neurons, glia, and microglia (3). Specifically, cytokines and chemokines can influence cellular and molecular chemical processes throughout the brain affecting long-term memory, synaptic plasticity, neurogenesis, and regulation of neurobehavioral chemical pathways (4).

This summary report will recapitulate the outcome of a year-long study where participants were laboratory assessed and subsequently placed on replenishment doses of neurosteroids and neuroactive steroids that were found to be insufficient. Additionally, a group of nutraceutical products, known for their anti-inflammatory properties and that were clinically evaluated over 16 years, were used concurrently.

Introduction

The Millennium Health Centers, Inc. began its erudition program in 2004 looking at the effects of traumatic and non-traumatic injuries on the brain's production of neurosteroids as well as neuroactive steroids, those hormones produced outside the brain. Thanks to the meticulous work of French chemist and endocrinologist Dr. Etienne-Emile Baulieu, we became aware of the brain's ability to synthesize its own steroid hormones (neurosteroids) within glial cells from cholesterol and that these neurosteroids are identical in structure as those made in the body by our endocrine glands (neuroactive steroids) (5,6). Additionally, the bench sciences were expanding our understanding of these steroid hormones as having pleiotropic effects beyond their stereotypical "sex hormone" classification. Many were being found to influence inflammatory systems based upon cytokines and chemokines (7), to enhance immunity with increases in CD4+ and CD8+ cells (8), and to improve the removal of damaging Amyloid Beta by up-regulating Neprilysin's transport of it out of cells (9). Thereafter, our patient care focus became one of improving levels of both neurosteroids and neuroactive steroids as a means of generating clinical improvement.

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Nevertheless, we kept on asking the question of "How does trauma cause the loss of neurosteroids and/or neuroactive steroids?" Reviewing the scientific literature in conjunction with our clinical findings, it became apparent that inflammation was a by-product of both traumatic and non-traumatic events and was responsible for the disruption of numerous biomolecular processes that influence cognitive and emotional well-being (10,11). So, around 2015 we changed from our initial theory that neurotrauma caused hormonal deficiencies that allows for neuroinflammation to go unchecked thereby altering the brain's chemistry (12), to our present hypothesis that neurotrauma begets neuroinflammation that basically induces a phenotypic change in Microglial cells causing chronic release of inflammatory cytokines which increase ROS (13), decreases NO, increases peroxynitrite (14), inactivates enzymes, damages mitochondrial energy production (ATP) (15), loss of gated ion channels, inhibits neurotransmitters, and impedes pre- and post-synaptic communication, damages the blood brain barrier, and increases the occurrence of neuropsychiatric and somatic complaints (16,17,18).

The Millennium's Approach to Assessment and Treatment

Each program candidate completes a comprehensive historical inventory containing all the standard data points in addition to requesting history of exposures to all forms of trauma (service and civilian related). Additionally, a subjective psychological and physical inventory is taken. The laboratory assessment uses the Millennium's Biomarker Panel-2436 which consists of 28 tests that are readily available in major commercial clinical laboratories (Access Medical Labs, Quest, and LabCorp.) Once the laboratory results are obtained, they are processed by the Millennium-TBI Office Assistant (MOA), an expert-AI system which provides for a multi-tiered, cross-correlational analysis of the results in real-time.

This system also contains subroutines that take into consideration a myriad of medications and supplements that can influence the outcome of these laboratory results. This system helps to standardize the interpretation of the results as well as to provide a consistent recommendation for treatment based upon these results. In essence, the MOA can be used as a learned tool to advance the abilities of any healthcare provider's knowledge in relationship to hormone replacement therapies affected by trauma as well as aging.

Based upon the individualized MOA reports, 156 candidates were provided with a customized treatment protocol that was recommended by the expert-AI system. Treatment recommendations might have included specific hormone replenishment protocols inclusive of Testosterone, Estrogen, Pregnenolone, Progesterone, Growth Hormone, DHEA, 7-Keto DHEA, Vitamin D3, Cortisol, and Thyroid hormones (T4/T3). Additionally, medication such as Clomiphene citrate might be offered before the use of testosterone or estrogen products in order to encourage the individual's system to provide their own hormone production. This was also true with the recommendation for use of secretagogues such as Secretropin or DynaTropin to improve one's innate growth hormone production.

Finally, a group of three nanoliposomal nutraceutical products were used to address neuroinflammation, mitochondriogenesis, and energy production (ATP) they were Clear Mind & Energy, Brain Care II and B is for Brain. Each product was used singularly or in combination over a 16-year period in a clinical environment prior to being released.

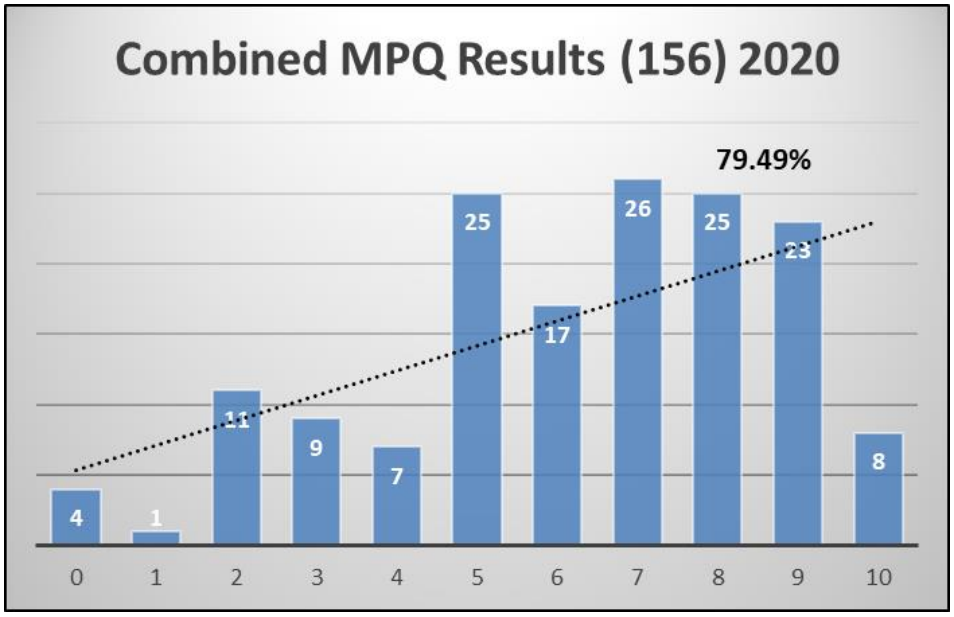
Ongoing Assessment

Since 2010, a self-assessment tool called the Monthly Program Questionnaire (MPQ) has been filled-out and submitted every 30 days by program participants. The MPQ asks questions about psychological, physiological, and physical functioning while on their treatment protocol. There are a total of 25 questions which are scored between a zero and 10 indicating the level of improvement in the particular area. The graphs that follow represent the final MPQ scores obtained from all 156 clients as of December 31, 2020.

Results

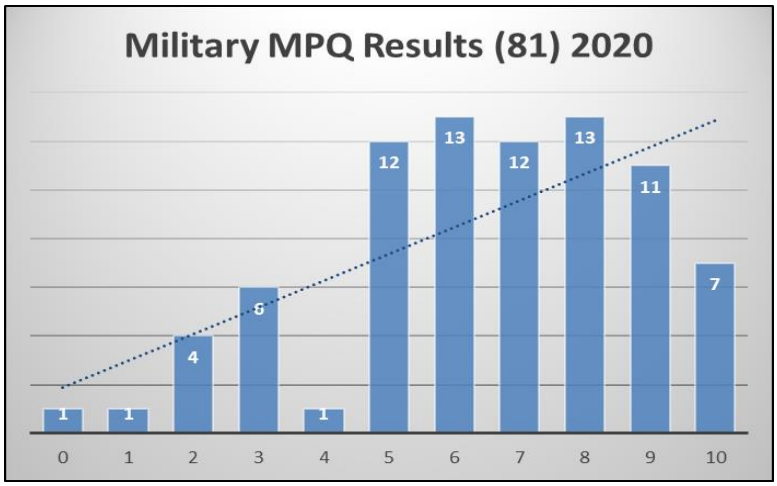
One-hundred fifty-six (156) individuals completed their initial assessment and subsequent monitoring laboratory assessments while being on their treatment protocol. Each provided a minimum of 6 separate MPQs over the course of the year adhering to a submission every 30 days. The participants were comprised of 81 military (51.9%), 75 civilians (48.1%) of which 7 had a chemically exacerbated neurotrauma due to the use of the drug finasteride. The average age of the participants was 41.7 years (range was 21 – 76yrs), 9 females (5.8%) and 147 males (94.2%).

A. Over-All Results



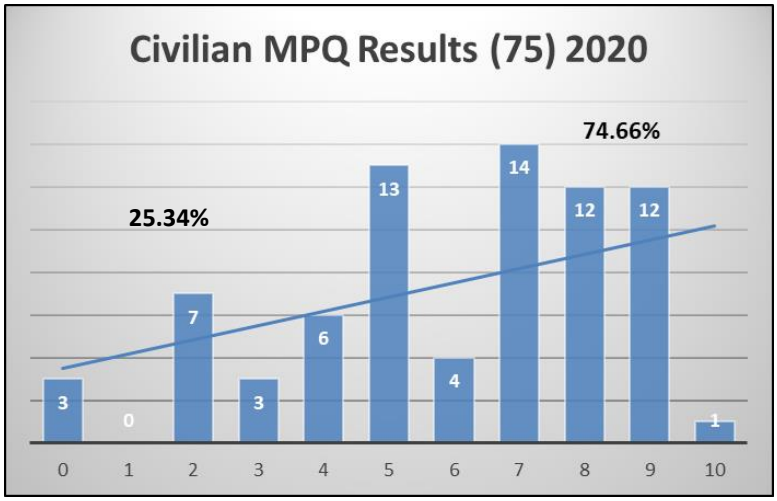
B. Active Military and Veteran Results

Of the 81 Military (active and veterans), 51 (62.96%) were exposed to one or more blast wave traumas (BWT) with 37 (72.6%) of those having had loss of consciousness. There were 55 (67.9%) participants having depression as a chief complaint, anxiety in 64 (79%), and migraines in 40 participants (49.4%).



C. Civilian MPQ Results

Of the 75 civilians, 28 (37.3%) experienced loss of consciousness, 49 (65.3%) had depression, 45 (60%) anxiety, and 31 (41.3%) had migraines. Over-all, in the civilian group, they experienced a 50% or greater improvement in 74.66% of the cases, while 25.34% experiencing less than 50% improvement.



Treatment

The Millennium Health Centers, Inc., has had the opportunity to assess and treat over 3,500 individuals from both military and civilian communities since 2004. During this time, we have added and subtracted a number of treatment protocol options that did not provide the level of improvement desired for continued use. Additionally, and as stated above, the paradigm of replenishing neurosteroids and neuroactive steroids as the mainstay of treatment, was modified based upon a greater understanding of the causation for loss of these important steroids, namely inflammation. As our treatment protocol focused more on inflammation, we saw a trend of quicker and more sustainable improvement in many of the patients' symptomatic complaints and a diminished use of prescription medication.

Furthermore, we removed the urgency to acutely supplement with growth hormone and testosterone by first addressing the causation for the loss of production and release of these important hormones. A number of articles have appeared reporting the effects of neuroinflammation on a number of pathways that lead to the production of Testosterone and Growth Hormone. In fact, inflammation can be seen as the great disruptor of all important biochemical pathways that generate not only the brain's neurosteroids, but also neurotransmitters and enzymes. Therefore, treatment that reduces inflammation has led to the improvement in measurable levels of these and other hormones.

When reduction of inflammation is associated with sub-optimal improvement in one's free testosterone level, we will add a **SERMS** to help increase the patient's hypothalamic production of gonadotropin releasing hormone (GnRH) before using an injectable testosterone. Inflammation reduces the hypothalamic production of GnRH so that the signal to the pituitary gland to release follicle stimulating hormone (FSH) and luteinizing hormone (LH) is greatly reduced (19). The finding on laboratory testing will be low FSH and LH along with a low peripheral free testosterone level. Using any form of testosterone will further diminish the hypothalamic-pituitary-gonadal circuitry's ability to regulate testosterone production (negative feedback affect). This also holds true for growth hormone.

Summary

The outcome report for 2020 has been following an annual trendline of progressive improvement over the prior years since 2018. We are attributing this to the addition to the Millennium's treatment protocol of products such as Clear Mind & Energy added in March of 2017, Brain Care II added in May 2019, and B is for Brain added in February 2020. These three products (**Tri-Pak or Brain Rescue 3**) have become our core approach to treatment where each product addresses a tactic for helping the brain reestablish a neuropermissive environment conducive to healing. The main focus is on the inflammation precipitated by trauma and complimented with an array of nutraceutical components addressing mitochondrial function with ATP production. The more energy produced the more efficient the brain can function to restore biochemical processes that have been damaged by the change in the neurochemical environment precipitated by inflammation. www.millenniumhealthstore.com

Year-by-year, we have shown progressive improvement in both neuropsychiatric and neurocognitive functioning. These are commonly represented by improvement in social habits, family unity, diminished medication, educational advancement, emotional stability, greater joy, and happiness in life.

Recommendations

The Millennium Health Centers, Inc, since 2004 has offered a comprehensive laboratory assessment utilizing the Millennium Biomarker panel (MBM panel) to direct the diagnoses and treatment of each client. This has been considered our flagship approach. In 2020, with our three core products available, we started testing their effectiveness without the benefits of initially drawing the MBM panel. Our initial group were active Marines from Camp Pendleton, California to which we added another group of veteran Marines. The final count of participants was 25 individuals, of which 65% (16) had a 50% to 100% improvement within 90 days over 20 points of assessment.

The outcome of this open study (not blinded) showed us that the treatment protocol utilizing the Brain Rescue 3 protocol could identify a population of traumatized and symptomatic individuals and improve their condition in a relatively short time frame (90days). Used as a screening tool, the Brain Rescue 3 protocol could identify those individuals that would need to have a more comprehensive assessment with performing the Millennium's Biomarker panel. (Nutraceutical MPQ @ www.TBIHELPNOW.org/the-science)

Furthermore, since June 2021, we have started looking at two pre-laboratory, nutraceutical treatment protocols identified as:

Phase 1: Brain Care 3, one sachet pre-breakfast for 90 days.

Phase 2: Brain Care 3, one sachet pre-breakfast. Then 15-30min after dinner, 50-100mg of Pregnenolone, 25mg-50mg of DHEA (males) or 15mg-25mg of DHEA (females), and 125mcg-250mcg Vitamin D3.

Conclusion

The scientific literature abounds with research that has been performed over decades addressing the biochemical changes that impact our psychiatric health and cognitive abilities. Currently, there are volumes of research associating neuroinflammation with psychiatric conditions such as depression and anxiety while advanced neuroinflammation is associated with neurodegeneration presenting as Alzheimer's, Parkinson's, Multiple Sclerosis, and Amyotrophic Lateral Sclerosis.

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