



The Millennium's Primer Series. From Inflammation to Silence: Promising Strategies for Alleviating Tinnitus through Neuroinflammation Management.

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Tinnitus is a phantom auditory perception of sound, without external stimulation, that reduces quality of life for millions worldwide and for which there has been no medical cure. Tinnitus is a prevalent condition affecting a significant number of military personnel. The underlying mechanisms of tinnitus are complex and multifactorial, but emerging research suggests a crucial role for neuroinflammation in its pathogenesis. Military personnel are particularly susceptible to neuroinflammation due to exposure to high-intensity noise, blast-related trauma, and psychological stress¹.

This paper explores the relationship between neuroinflammation and tinnitus in military personnel, highlighting the potential of nutraceutical products in alleviating tinnitus symptoms by controlling neuroinflammatory processes. Nutraceuticals, including natural compounds and dietary supplements with anti-inflammatory properties, have gained attention as potential therapeutic agents. These products target various pathways involved in neuroinflammation, including modulation of glial cell activity, suppression of pro-inflammatory cytokines, and antioxidant effects².

The use of nutraceutical products to control neuroinflammation offers a promising approach to managing tinnitus in military personnel. Several nutraceuticals, such as omega-3 fatty acids, curcumin, quercetin, and vitamins C, D, and E, have shown potential in preclinical and clinical studies for reducing neuroinflammation and ameliorating tinnitus symptoms. However, further research is needed to determine optimal dosages, treatment durations, and long-term efficacy of nutraceutical interventions^{3,4}.

Considering the challenges faced by military personnel in accessing conventional medical treatments, nutraceutical products provide a feasible and potentially cost-effective option for managing tinnitus-related neuroinflammation. Their availability and minimal side effects make them attractive alternatives or complementary options to traditional pharmacological therapies.

This report will present the results of a nutraceutical treatment protocol used to address the processes of neuroinflammation in a group of 98 Veterans with a medical history of tinnitus for more than 12 months. Dr. Mark Gordon working with the Millennium Health Centers, Inc, has developed a number of treatment strategies to address neuroinflammation that causes cognitive and emotional impairment. An unexpected, but welcome benefit to the correction of neuroinflammation has been the improvement in Tinnitus.

Introduction:

Blast wave trauma, resulting from exposure to explosive events, is a significant cause of tinnitus, a condition characterized by the perception of sound without external auditory stimuli. Military personnel, in particular, are at a heightened risk of blast-related tinnitus due to their occupational exposure to explosive devices and loud concussive events. The pathophysiology of blast-induced tinnitus involves complex mechanisms, including damage to the auditory system, neural dysfunction, and neuroinflammation.



Blast wave trauma can result in direct mechanical damage to the auditory structures, such as the cochlea, leading to sensory hair cell loss and auditory nerve damage. Additionally, the intense pressure changes generated by blasts disrupt the delicate biochemical and cellular processes in the auditory system, contributing to neuronal hyperexcitability and central auditory processing abnormalities. These alterations culminate in the perception of phantom auditory sensations, commonly manifested as tinnitus.

Neuroinflammation has emerged as a significant factor in the pathogenesis of blast-induced tinnitus. Following a blast event, a cascade of inflammatory responses occurs, involving the release of pro-inflammatory cytokines, activation of glial cells, and oxidative stress. Neuroinflammation exacerbates neuronal hyperexcitability, disrupts the balance of neurotransmitters, and contributes to the maintenance and amplification of tinnitus symptoms.

Nutraceuticals, defined as naturally occurring compounds or dietary supplements with potential health benefits, have garnered interest in managing blast-induced tinnitus due to their anti-inflammatory and neuroprotective properties. Several nutraceuticals have shown promise in modulating neuroinflammation and ameliorating tinnitus symptoms. For example, omega-3 fatty acids, found in fish oil, possess anti-inflammatory effects, and have demonstrated potential in attenuating neuroinflammation associated with blast-related injuries. Curcumin, derived from turmeric, has been shown to exhibit antioxidant and anti-inflammatory properties, potentially reducing oxidative stress and inflammation in the auditory system. Other nutraceuticals, such as quercetin, green tea extract, and vitamins C, D, and E, also possess antioxidant and anti-inflammatory activities that may be beneficial in managing blast-induced tinnitus.

While the use of nutraceuticals holds promise, it is important to note that further research is needed to establish their efficacy, optimal dosages, and potential interactions with other medications. Clinical trials focusing specifically on blast-induced tinnitus are limited, and most of the evidence comes from preclinical studies and studies conducted in other tinnitus populations. Additionally, the multifactorial nature of blast-induced tinnitus necessitates a comprehensive approach, combining nutraceutical interventions with other therapeutic strategies, such as sound therapy, cognitive-behavioral interventions, and pharmacological treatments.

What is Tinnitus?

Tinnitus, the perception of sound in the absence of external stimuli, is a complex condition with a diverse range of underlying mechanisms. While the exact pathophysiology of tinnitus is not fully understood, extensive research has provided insights into the contributing factors that shape its development and persistence. The pathophysiology of tinnitus involves a combination of peripheral and central auditory system alterations, neuroplastic changes, neuroinflammation, and emotional and cognitive influences.

At the peripheral level, tinnitus can arise from damage or dysfunction in the cochlea, the sensory organ responsible for converting sound vibrations into electrical signals. This damage can occur through exposure to excessive noise levels, ototoxic medications, aging, or other factors. When the delicate hair cells within the cochlea are damaged or destroyed, they fail to properly transduce sound waves into neural signals, resulting in reduced auditory input.

The reduced auditory input from damaged hair cells triggers compensatory changes in the central auditory system, leading to central auditory system alterations. One significant alteration is neuronal



hyperexcitability, where neurons in the auditory pathways become overly sensitive and generate spontaneous neural activity. This hyperexcitability can occur due to the loss of inhibitory input from damaged hair cells, resulting in an imbalance of excitation and inhibition.

Neuroplasticity, the brain's ability to reorganize itself in response to sensory input and environmental changes, plays a critical role in tinnitus pathophysiology. In the context of tinnitus, maladaptive neuroplasticity refers to abnormal changes in the auditory system that contribute to tinnitus perception. This can include the formation of new neural connections, increase synaptic strength, and altered patterns of neuronal firing. These neuroplastic changes occur as a result of the brain's attempt to compensate for the reduced auditory input caused by cochlear damage.

Neuroinflammation has emerged as a potential contributor to tinnitus. Inflammatory processes triggered by various factors, including noise trauma, infections, or oxidative stress, can lead to the release of pro-inflammatory cytokines, activation of glial cells, and subsequent neurochemical imbalances. The resulting neuroinflammatory responses can promote neuronal hyperexcitability, disrupt synaptic function, and contribute to the persistence of tinnitus symptoms.

Emotional and cognitive factors also influence tinnitus perception. The limbic system, which is involved in emotional processing, interacts with the auditory system, and can modulate tinnitus perception. Emotional distress, anxiety, and stress can amplify the perception of tinnitus, while negative emotional reactions to tinnitus can further heighten emotional distress. Attentional processes also play a role, as individuals who focus their attention on tinnitus sounds may experience an intensification of their perception, leading to increased distress and negative emotional reactions.

It is important to recognize that the pathophysiology of tinnitus is likely to be multifactorial and highly individualized. Different individuals may exhibit varying combinations and degrees of peripheral and central auditory alterations, neuroplastic changes, neuroinflammatory responses, and emotional and cognitive influences. Furthermore, the interaction between these factors can be complex and dynamic, contributing to the variability in tinnitus severity and presentation.

Understanding the diverse pathophysiological mechanisms involved in tinnitus is essential for developing effective treatment strategies. Targeted interventions aimed at specific aspects of tinnitus pathophysiology, such as reducing neuronal hyperexcitability, modulating neuroinflammation, or addressing emotional distress, hold promise for alleviating tinnitus symptoms. Further research is needed to refine our understanding of these mechanisms, identify reliable biomarkers, and develop personalized treatment approaches that consider the individual variations in tinnitus pathophysiology. By unraveling the complex nature of tinnitus, we can advance towards more effective management and improved quality of life for individuals living with this condition.

The Traditional Approach for Treatment of Tinnitus

The traditional treatment approaches for tinnitus aim to manage the symptoms and improve the quality of life for individuals affected by this condition. Some commonly used traditional treatments include:

Counseling and education provide information about tinnitus, its causes, and management strategies. This education helps individuals better understand their condition and develop coping mechanisms to reduce the impact of tinnitus on their daily lives.



Sound Therapy based interventions aim to provide external sounds that can distract attention from tinnitus and promote relaxation. These therapies can include the use of white noise machines, fans, or low-level background music to mask or partially cover the perception of tinnitus.

Tinnitus Retraining Therapy (TRT) combines sound therapy with counseling to help individuals habituate to the perception of tinnitus. It involves using low-level, neutral sound generators to gradually reduce the awareness and emotional response to tinnitus over time.

Cognitive-Behavioral Therapy (CBT) techniques can be beneficial for managing the emotional distress and negative reactions associated with tinnitus. This therapy helps individuals identify and modify negative thought patterns and behaviors related to tinnitus, ultimately reducing the impact of tinnitus on their well-being.

Medications in some cases may be prescribed to manage specific symptoms associated with tinnitus, such as anxiety, depression, or sleep disturbances. These medications can include antidepressants, anxiolytics, or sleep aids. However, it is important to note that medications are not universally effective for tinnitus and their use should be determined on an individual basis.

Tinnitus support groups provide a forum for individuals with tinnitus to share their experiences, learn from others, and receive emotional support. These groups can help individuals cope with the challenges of living with tinnitus and offer a sense of community.

It's important to emphasize that the effectiveness of traditional treatments for tinnitus varies among individuals, and no single treatment works for everyone. Additionally, traditional treatments often focus on symptom management rather than addressing the underlying mechanisms of tinnitus. As research continues to advance, new treatment options targeting the specific pathophysiology of tinnitus, such as neuroinflammation or neural hyperexcitability, may emerge and complement the traditional approaches. It is advisable for individuals with tinnitus to consult with healthcare professionals, such as audiologists or otolaryngologists, to determine the most suitable treatment plan based on their specific needs and circumstances.

The Millennium's Approach to Tinnitus

Dr. Mark L. Gordon is known for his work on Traumatic Brain Injury (TBI) and the damaging effects of neuroinflammation on the quality of life in our active-duty and veteran communities. Dr. Gordon has published research and discussed his approach in public forums and his protocol generally involves a comprehensive assessment, laboratory testing, and treatment that includes the following components:

A thorough review of the patient's medical history, both pre-enlistment and enlistment, including any known or suspected TBI events with or without loss of consciousness, exposure to blasts wave traumas, or other traumatic incidents.

A detailed assessment of symptoms associated with TBI, such as cognitive difficulties, memory problems, mood disturbances, sleep disturbances, and post-concussion symptoms. A comprehensive audiology evaluation with assessment by an ENT (Otorhinolaryngologist) to rule out any direct physical damage or encroachment upon the tympanic membrane (eardrum) or illnesses that will damage the three little bones (ossicles) that convey sound from the eardrum to the brain.



Measurement of hormone levels, both neurosteroids and neuroactive steroids, particularly focusing on assessing the functioning of the hypothalamic-pituitary axes and other neuroendocrine pathways affected by TBI. This will provide inference of neuroinflammation which will alter neurological pathways associated with the precipitation of phantom sounds (Tinnitus).

Biomarker testing, utilizing readily available laboratory tests, to evaluate specific biomarkers associated with TBI and neuroinflammation, such as markers of inflammation (e.g., cytokines, IL-1, IL-6, NF-alpha), neurodegeneration, oxidative stress, immune dysregulation, and steroidal hormones.

The use of various neuroimaging techniques, such as MRI or CT scans, to assess structural and functional brain abnormalities associated with TBI and potential signs of neuroinflammation. What is being specifically looked for is an acoustic neuroma, also known as vestibular schwannoma, which is a benign tumor that typically arises from the Schwann cells covering the vestibular branch of the vestibulocochlear nerve (cranial nerve VIII). While acoustic neuromas primarily affect hearing and balance, they can also cause tinnitus as a secondary symptom. The mechanisms through which an acoustic neuroma leads to tinnitus are multifaceted and involve both structural and functional changes in the auditory system.

Neuropsychological testing to evaluate cognitive performance, including attention, memory, processing speed, executive function, and other cognitive domains affected by TBI.

It's important to note that Dr. Gordon's approach to TBI and neuroinflammation assessment may evolve over time as new research and diagnostic methods emerge. For the most accurate and up-to-date information on his specific protocol, I recommend referring to Dr. Mark L. Gordon's publications, interviews, or official website.

The Millennium's Study and Results

Study Outcome

A total of 98 subjects with tinnitus were enrolled in the study, and their response to the treatment was assessed. The nutraceuticals used in the study exhibited anti-inflammatory properties and targeted neuroinflammation, a potential underlying factor in tinnitus. The results showed that a significant proportion of the subjects experienced improvements in their tinnitus symptoms, with varying degrees of benefit observed.

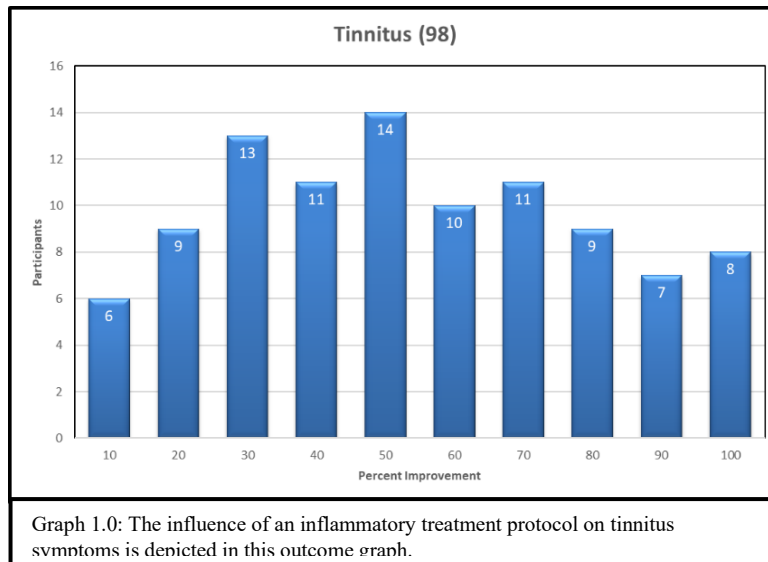
Methods

A total of 98 subjects with a history of tinnitus, present for more than 12 months, were enrolled in the study. The subjects were administered with a fixed combination of specific nutraceuticals targeting neuroinflammation ^{graph 1.0}. The severity of tinnitus symptoms was assessed before starting treatment and then every 30 days, for up to 12 months, using a subjective Tinnitus score. The scale ranged from 0% (no improvement) to 100% (complete resolution of symptoms).



Results

Following the administration of the anti-inflammatory nutraceuticals, 6 subjects (6.12%) reported a 10% improvement in their tinnitus symptoms. Nine subjects (9.18%) experienced a 20% improvement, while 13 subjects (13.27%) reported a 30% improvement. The response rate increased with higher levels of improvement: 11 subjects (11.22%) had a 40% improvement, 14 subjects (14.29%) experienced a 50% improvement, and 10 subjects (10.20%) reported a 60% improvement. Furthermore, 11 subjects (11.22%) had a 70% improvement, 9 subjects (9.18%) experienced an 80% improvement, 7 subjects (7.14%) reported a 90% improvement, and 8 subjects (8.16%) experienced a complete resolution of symptoms (100% improvement). Additionally, the level of resolution of tinnitus directly correlated with the subject's overall improvement in cognition and mood.



Discussion

The results of this study demonstrate the potential benefits of using anti-inflammatory nutraceuticals in the management of tinnitus. The observed improvements in tinnitus symptoms indicate a positive response to the treatment, suggesting that targeting neuroinflammation may play a role in mitigating tinnitus severity. The varying degrees of improvement observed in the subjects suggest that individual response and underlying factors may influence treatment outcomes. Further research is needed to elucidate the specific mechanisms by which these nutraceuticals modulate neuroinflammation and their long-term effects.

Conclusion

This study provides evidence supporting the use of anti-inflammatory nutraceuticals for the management of tinnitus. The findings demonstrate that a considerable proportion of the subjects experienced improvements in their tinnitus symptoms following treatment. These results warrant further investigation and larger-scale clinical trials to validate the efficacy of anti-inflammatory nutraceuticals in tinnitus management. The use of anti-inflammatory nutraceuticals as a complementary approach holds promise and may offer a viable option for individuals seeking relief from tinnitus symptoms.



References

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A Short Biography

Dr. Mark L. Gordon, specializing in Endocrinology since 1995, has devoted his career to understanding and treating the effects of traumatic brain injuries (TBIs). Having personally experienced multiple TBIs without loss of consciousness, he encountered the limitations of traditional treatment approaches. Driven by his own journey towards recovery, he delved into medical literature, seeking answers to the root causes of his condition and those affecting other post-concussion patients.

Dr. Gordon discovered that hormonal deficiencies, though initially evident, were merely surface manifestations of a more intricate cascade of biochemical changes triggered by trauma, particularly neuroinflammation. Recognizing the importance of addressing both inflammation and hormonal imbalances, including neurosteroids and neuroactive steroids, he pioneered a comprehensive approach that resulted in accelerated recoveries without reliance on conventional therapies.

In 2004, Dr. Gordon transitioned his expertise to the field of Neuroendocrinology, applying his knowledge to all cases of symptomatic TBI. However, it was in 2009 that his focus shifted towards the needs of the military community, driven by the alarming rise in mental health issues, depression, and suicides among veterans. A pivotal moment came with the successful treatment of Army Special Forces Sergeant First Class Andrew Marr, who experienced remarkable recovery from multiple blast wave traumas. Through Dr. Gordon's intervention, Marr was able to discontinue multiple medications, reunite with his family, pursue an MBA, and co-author a book that inspired the award-winning film "Quiet Explosions."

To date, Dr. Gordon and Mr. Marr have extended their groundbreaking protocol, known as the Millennium's protocol, to over 1200 veterans. Their work is carried out through the Millennium and Warrior Angels Foundations (501c3), providing financial support and a non-toxic treatment program that has yielded significant success. With a commitment to transforming the lives of veterans, Dr. Gordon and his team strive to make a lasting impact and offer hope through their innovative approach.

The Millennium Health Centers, Inc., is a self-funding organization that derives financial support for our Veterans' Program from the sale of our proprietary products at www.MillenniumHealthStore.com. Educational materials for our products Clear Mind & Energy, Brain Care 2, B is for Brain, Brain Rescue 1, Brain Rescue 3, and Secretropin/Dynatropin can be obtain from our education TBI site: www.TBIHelpNow.org. If you want a discount code, please use Phase2022 at check out. Make sure you are a subscriber to the **Store** for any checkout discount codes to work.



Addendum A

Brain Rescue 3

Neuroinflammation has been identified as a potential underlying factor in the development and maintenance of tinnitus. The potential benefits of specific nutraceutical products, including docosahexaenoic acid (DHA), gamma tocopherol, ascorbic palmitate, quercetin, glutathione, and epigallocatechin gallate (EGCG), in managing tinnitus associated with neuroinflammation.

Docosahexaenoic Acid (DHA), an omega-3 fatty acid, exhibits anti-inflammatory properties and has been shown to modulate inflammatory processes in the central nervous system. By reducing neuroinflammation, DHA may help alleviate tinnitus symptoms associated with inflammation-mediated damage to auditory pathways.

Gamma tocopherol, a form of vitamin E, possesses antioxidant and anti-inflammatory effects. It has the potential to counteract oxidative stress and neuroinflammatory processes implicated in tinnitus, thus providing neuroprotection and symptom relief.

Ascorbic palmitate, a fat-soluble form of vitamin C, acts as an antioxidant and anti-inflammatory agent. Its ability to scavenge free radicals and modulate immune responses may help mitigate neuroinflammation and attenuate tinnitus symptoms associated with inflammatory processes.

Quercetin, a flavonoid with antioxidant and anti-inflammatory properties, may provide benefits for tinnitus associated with neuroinflammation. By inhibiting inflammatory mediators and reducing oxidative stress, quercetin has the potential to alleviate tinnitus symptoms and protect against further neural damage.

Glutathione, a potent endogenous antioxidant, plays a vital role in maintaining cellular redox balance and reducing oxidative stress. Supplementation with glutathione or its precursors may help counteract neuroinflammatory processes, protect auditory structures, and potentially alleviate tinnitus symptoms.

Epigallocatechin Gallate (EGCG), a polyphenol found in green tea, exhibits antioxidant and anti-inflammatory properties. Its ability to modulate inflammatory pathways and scavenge free radicals may contribute to the reduction of neuroinflammation and provide relief from tinnitus symptoms.

The use of nutraceutical products targeting neuroinflammation holds promise as a complementary approach for managing tinnitus associated with inflammatory processes. DHA, gamma tocopherol, ascorbic palmitate, quercetin, glutathione, and EGCG exhibit anti-inflammatory and antioxidant properties that may help attenuate neuroinflammation and provide relief from tinnitus symptoms. Integrating these nutraceuticals into personalized treatment plans, under the guidance of healthcare professionals, may offer a holistic approach to alleviate neuroinflammation-related tinnitus and improve the well-being of affected individuals.