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Case Report

Improved Brain Function with Deep Spectrum Biotherapeutics

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Abstract: In this case series, we examine the impact of the Titan-iR Pro® deep spectrum biotherapeutic device on brain function in healthy individuals. Here we present 15 participants, aged 26-68 years, who enrolled in this open-label study, designed to assess the effect of a single 15-minute course of deep spectrum biotherapy on brain function. Although symptom-free upon enrollment, participants had diverse medical histories with some displaying early signs of cognitive decline. As part of the evaluation, all participants engaged in electroencephalogram (EEG) recording sessions that focused on assessing event-related potential (ERP) evaluations, including audio P300 amplitudes and latencies (speeds), neurocognitive testing, and physical reaction times. Following the Titan-iR Pro intervention an improvement in EEG-based cognitive markers was observed. These results underscore the importance of further investigation into the potential of advanced and deep spectrum photobiomodulation in the prevention and treatment of cognitive decline and other neurological disorders.

Keywords: electroencephalogram (EEG); event related potential (ERP); advanced & deep biotherapeutics; photobiomodulation (PBM); mild cognitive impairment (MCI)

1. Introduction

This case series aims to understand the impact of Titan-iR Pro advanced & deep spectrum biotherapeutic intervention on brain function in individuals at risk for cognitive decline and further neurological disorders. Here we present 15 subjects who underwent clinical EEG-ERP testing before, and following, a 15-minute session of photobiomodulation therapy.

2. Materials and Methods

Event-related potential measurements using electroencephalogram

Event-related potentials (ERPs) are a measurement of the electroencephalogram (EEG) signal that is time-locked to the onset of a provided stimulus and consists of different components labelled by their polarity (P for positive or N for negative) as well as their time of occurrence after the stimulus in milliseconds (e.g. P300). Here we focus specifically on the audio oddball P300 amplitude and latency (speed) assessments, which are relevant to age-related cognitive decline, as well as measuring a physical reaction time.

The oddball P300 protocol, one of the most widely studied, utilizes measurements of amplitude and latency to assess the brain's cognitive ability to recognize the odd tone as different. P300 amplitude (P300V) is thought to be proportional to the number of attentional resources devoted to a given task, whereas P300 latency (P300T, the delay between stimulus delivery and recognition of the oddball tone as different) is a measure of stimulus classification speed [1]. An increase in the P300T and/or a decrease in P300V peak amplitude are observed in various conditions, accompanied by a decline in cognitive function including ageing, dementia, mild traumatic brain injury (mTBI), substance abuse, depressive disorders, PTSD, cardio health, pre-Alzheimer's, responsiveness to pharmaceuticals, and trauma [2,3].

Procedure

After clinical interviews and assessments, the participants (n=15) received an EEG scan with an oddball P300 stimulus, using the WAVi™ system. Details of the scan, system, procedure, and EEG extraction have been detailed elsewhere and include a 4-min oddball audio ERP [4]. The EEG study was approved by the Solutions Institutional Review Board and written informed consent was obtained from the participant before scanning.

The intervention was administered using the Titan-iR Pro™ Deep Biotherapeutic Device. The interventional platform focuses on utilizing a proprietary array of advanced + deep spectrum wavelengths to specific areas of the pre-frontal cortex that are responsible for mood and cognition. Participants underwent a single 15-minute, high-powered, continuous treatment protocol, which was controlled using the Titan-iR Mobile Application. The Titan-iR Mobile Application allows the hardware to administer a pre-specified dose of therapy as determined by the energy delivered over a set period. During treatment, participants were allowed to resume normal relaxed measures and did not perform any extra movements or activities.

3. Results

Because of the small sample size, the difference in pre-intervention and post-intervention EEG results was analyzed using McNemar's test to evaluate the change in state to test the null hypothesis that the treatment had no effect. The subjects were categorized into 2 groups: below and above normal on the two ERP metrics discussed above, plus physical reaction time which is also known to correspond with conditions affecting cognition [1]. Below normal constituted previously published target values for P300 amplitude (14uV here); latency (300ms); and reaction time (300ms) [5]. Subjects who scored above normal for 2 out of these 3 were classified as high and those who were 1 or below (out of 3) were classified as low.

Before treatment, 3 subjects scored high (again, above normal in 2/3 categories); and post-treatment 10 subjects scored high resulting in chi-squared values of 3.8 and a P-value near our $P < 0.05$ cutoff used to reject the null hypothesis that the treatment had no effect. Concluding the treatment had a statistically significant effect amongst participants.

3.1. Observations of an Individual Participant

A 44-year-old former Division One college football player, who had received numerous concussions during his career, was measured pre- and post-intervention to evaluate the effects of Titan-IR Pro on his cognitive performance (Table 1).

Table 1. Effect of Intervention on WAVi Metrics for an Individual Participant.

	P300V	P300T	Reaction Time	Score (#>target)
Target	14uV	300ms	300ms	
Pre-intervention	18uV	328ms	384ms	1
Post-intervention	24uV	276ms	210ms	3

Further analysis of this individual shows changes in peak alpha amplitudes in front, mid, and rear brain regions (Figure 1). Alpha is the dominant frequency of the human EEG and, as with the P300, the frequency and power of the alpha band provide information on brain function.

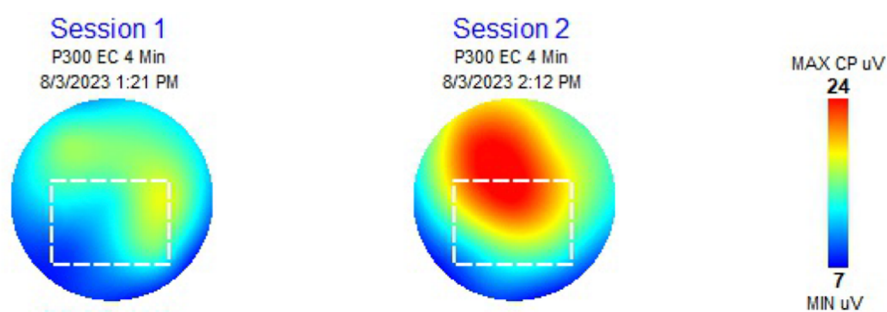


Figure 1. Topography of P300 amplitude across the scalp pre-and post-intervention.

Figure 2 shows the topography of the alpha distribution across the scalp for this subject before and after intervention. As often seen in PPCS recovery, this subject showed a healthy return to occipital dominance post-intervention.

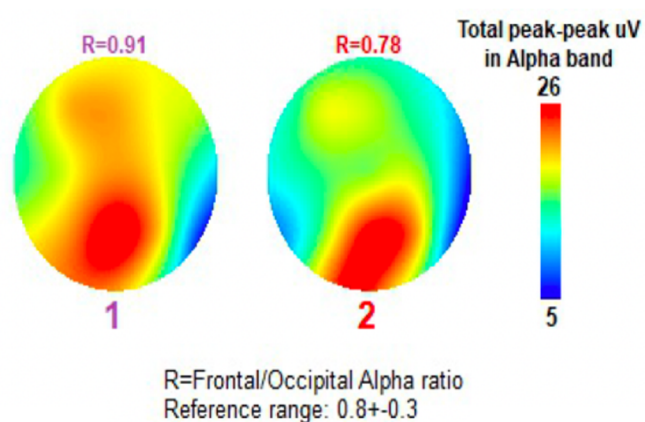


Figure 2. Topography of alpha amplitude across the scalp pre-and post-intervention.

4. Discussion

This heterogeneous sample of participants showed improved cognition following Titan-iR Pro® interventional treatment as measured by EEG-evoked responses and reaction time. It is important to consider the diverse medical histories within this population. Alongside concussions, individuals may have experienced other medical conditions or injuries that could have influenced their cognitive abilities. These additional factors must be considered when interpreting the findings, as they may contribute to the lower-than-expected number of high performers in the study.

This individual case study is particularly significant due to the cumulative impact of multiple concussions experienced throughout their athletic career, while also suffering from mild-to-moderate cognitive fog and depressive episodes. While frontal locations of F3-FZ-F4 are responsible for mood and cognition, alpha power is normally occipitally dominant in resting states. It has been shown to move frontal with conditions such as prolonged-post concussion syndrome (PPCS) where symptom resolution may coincide with a return to occipital dominance [6]. Concussions and traumatic brain injuries are known to increase the risk of long-term cognitive impairments, such as memory deficits, attention problems, executive dysfunction, and depression. The intervention implemented in this study aimed to address the specific cognitive challenges faced by former athletes with a history of concussions. The goal was to optimize brain function, promote neural recovery in brain regions, and improve overall cognitive performance.

This research holds broader implications beyond the individual case. It contributes to our understanding of the potential long-term consequences of repeated concussions in athletes and highlights the need for targeted interventions and comprehensive support systems for those at risk. By identifying effective strategies for cognitive rehabilitation, healthcare professionals can better

assist individuals with a history of concussions in regaining optimal cognitive functioning and improving their overall quality of life.

Given that most of these participants are considered healthy, it would be interesting to expand this study on a more homogeneous sample of patients suffering from a single condition such as depression or PPCS. Whilst the participant with a history of concussion did show point of care improvement following the intervention, along with long-term durability with the treatment (up to 60 days), it is important to conduct further research, with a larger sample size, to validate these findings.

Author Contributions: Conceptualization, D.O. and I.S.; methodology, D.O.; formal analysis, D.O.; data curation, D.O. and A.P.; writing—original draft preparation, D.O. and I.S.; writing—review and editing, I.S.; supervision, D.O.; project administration, D.O. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The EEG study was approved by the Solutions Institutional Review Board.

Informed Consent Statement: Written informed consent was obtained from all subjects involved in the study. Recruitment began on the 1st of July 2023 and ended on the 15th of August 2023. The study was completed between the 28th of July and the 26th of August.

Data Availability Statement: The raw data and any other materials presented in this manuscript are available upon request from the corresponding author.

Conflicts of Interest: David Oakley is an employee of WAVi Co., the company that provided the EEG equipment and data analysis. Iain Strickland and Anna Parievsky are employees of Medify Inc. and contributed to the statistical analysis applied to the data and the writing of the manuscript.

References

1. Polich J. Clinical application of the P300 event-related brain potential. *Physical Medicine and Rehabilitation Clinics*. 2004 Feb 1;15(1):133-61.
2. Golob EJ, Ringman JM, Irimajiri R, Bright S, Schaffer B, Medina LD, Starr A. Cortical event-related potentials in preclinical familial Alzheimer disease. *Neurology*. 2009 Nov 17;73(20):1649-55.
3. Gordeev SA. The use of endogenous P 300 event-related potentials of the brain for assessing cognitive functions in healthy subjects and in clinical practice. *Human physiology*. 2007 Apr;33:236-46.
4. Clayton G, Davis N, Holliday A, Joffe D, Oakley DS, Palermo FX, Poddar S, Rueda M. In-clinic event related potentials after sports concussion: A 4-year study. *Journal of pediatric rehabilitation medicine*. 2020 Jan 1;13(1):81-92.
5. Oakley DS, Fosse K, Gerwick E, Joffe D, Oakley DA, Prather A, Lucini FA, Palermo FX. P300 Parameters Over the Lifespan: Validating Target Ranges from an In-Clinic Platform. *bioRxiv*. 2021 Oct 26:2021-10.
6. Mortazavi M, Lucini FA, Joffe D, Oakley DS. Electrophysiological trajectories of concussion recovery: From acute to prolonged stages in late teenagers. *Journal of pediatric rehabilitation medicine*. 2023 Jan 23(Preprint):1-3.

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