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A Phytonutrient Based Brain Activation Complex and Short-Term Brain Function Changes: An Initial Investigation

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Abstract

Purpose: Over the last ten years, ketogenic diets have demonstrated increasing health and athletic applications. They generally consist of moderate protein, a slightly higher intake of positive lipid sources, and significantly reduced carbohydrate consumption. Since ketogenic diets have proven to be challenging to maintain, the appeal of exogenous ketone products may provide similar results with just one dose rather than an extensive and total dietary modification. Phytonutrient compounds have become popular due to increased brain energy based on the relationship between these compounds and ketone production, especially for older individuals or low-carbohydrate diets. However, little evidence exists to demonstrate that these products positively affect short-term brain function. In this pilot study, subject measurements occurred before ingestion of a proprietary phytonutrient product formula (Activate) and then 90 minutes later using the same electroencephalographic (EEG) device.

Methods: Eight volunteers, aged 49-68 years old (male = 5, female =3) were studied and compared to three control subjects, aged from 48 to 68 years old (male = 3). Study subjects completed standard EEG testing (WaviMed, Boulder, CO) before ingesting the compound and 90 minutes after consuming the compound using the same EEG system. The testing included a P300 audio reaction time test with recorded voltage/evoke readings, and two visual decision-making measures, specifically trail making. Control subjects received only placebo supplementation.

Results: The subjects in the intervention group increased overall brain function as measured with evoke potentials, time to task, and graphic representations compared to the control group. There was a decrease in reaction time for the group in the P300 audio reaction time test of 340 milliseconds to 314 milliseconds. In addition, microvolt(μV) activation during the auditory reaction time test increased from 7.5 μV to 12.9 μV, indicating increased brain functional activity from the intervention supplement. The control group showed essentially no voltage changes. The intervention group also decreased times in the first trail-making test score from 94 to 62 seconds and decreased the time to complete the second trail-making test from 113 to 93 seconds. All parameters showed positive improvement trends for the intervention group compared to control subjects. Topographic brain maps from the test revealed a more representative picture of the changes from taking the supplement.

Conclusion: In this pilot study, consumption of a concentrated, proprietary brain activation compound produced a marked enhancement in functional brain activity 90 minutes after ingestion with significant increases concerning topographical brain maps and related performance criteria. Optimal ingestion conditions and time to effect for this and similar products across various populations are being investigated. In addition, EEG measurements show promise as assessment biomarkers for the effects of nutritional supplements on brain function, especially for topographic maps of brain activity and response.

Keyword: Medium Chain Triglycerides; Ketones; EEG; Evoke potential; Reaction time; Brain function; Brain activity

Study Description

Introduction

By definition, ketogenic diets, commonly termed "keto," advocate moderate protein consumption while significantly reducing carbohydrate intake. In addition, many of these plans increase fat intake, especially of those fats which are considered "healthy." The initial goal of these programs was to put patients/individuals into ketosis, where the body would have to utilize stored fat for most energy needs [1-3]. The initial appeal of these programs was in weight loss and then quickly became popular in athletic performance [4-6]. As research emerged on the importance of ketones for brain function and ameliorating cognitive decline in aging, these approaches received another boost [8,9]. These nutritional plans do work yet suffer from the critical observation that they are challenging in adherence. They spur increased ketone production, which influences brain function and has been demonstrated in ameliorating several brain and cognitive conditions [10,11]. With the difficulty of adherence, exogenous ketogenic compounds, or agents which can be ingested and provide a ketone increase, became popular to address the same conditions. As alternatives to ketogenic diets have been utilized in recent years, these agents have purported increased brain function based on the relationship between these products and ketone production [12-14]. Part of the rationale for compounds that mimic a ketogenic diet is that the individual does not have to radically change nutritional intake to derive the

same effects from adding the supplement/compound. In addition, similar phytonutrient compounds and related supplements have been used by various endurance athletes to shift fuel usage to fat sources during moderate to intense exertion and demonstrate some strength benefits [15-18].

Medium Chain Triglyceride (MCT) compounds, which influence ketone production, have been demonstrated to be absorbed into the bloodstream and body tissues at a rapid rate comparable to that of glucose [19]. This relatively immediate absorption and availability for use are essential for product efficacy in competitive situations or those requiring intense focus or reaction. However, little evidence exists to demonstrate that these products positively affect brain function in the short term. From available research, the speed at which these compounds are absorbed is not well established. Limited studies indicate that the speed of absorption results in reasonably rapid brain function, cognitive enhancement, and mild endurance performance improvement [20-22]. In this pilot study, subjects were tested before ingestion of a proprietary phytonutrient brain activation compound and then 90 minutes later using the same EEG device compared to a control group.

Methods

Eight volunteer subjects aged 49-68 years old (male = 5, female =3), were studied compared to three volunteer controls, aged 48 to 68 years old (male = 3). The guidelines given to the subjects were not to exercise within one hour of the testing and to have their last meal completed at least 60 minutes before the scheduled testing time. Upon entering, subject health conditions were reviewed, and subjects were presented an informed consent for testing. No subjects were excluded based upon not adhering to test guidelines or regarding metabolic or nutrition conditions or medications, which would have indicated participation was inadvisable. A WaviMed EEG System (WaviMed, Boulder, CO) was powered to ensure functionality according to the manufacturer's specifications. The appropriate size head cap and ear lobe grounds were administered to the subject using specified protocols, then checked to ensure adequate electrical contact and measurement. Electrode sock placement in this system uses the standard 10/20 system. Testing consisted of monitoring evoke potentials and other information in three different measures [23]. The same head cap and electrode socks were utilized for the second measurement to further ensure test consistency in placement 90 minutes after ingestion of the study compound (Figure 1). In the three control subjects, the test timing was the same, with the only difference being that they received only a placebo supplement. The cap and electrodes were sealed to prevent evaporation of the saline solution for conductivity, and the electrode socks received additional saline solution if determined to have varied in potential conductivity from the first test. This was verified for each subject before the start of the second measurement.

The specific test protocol and order for the pre-supplement test and the post-supplement test were closely monitored and were comparable. Subjects were placed in a comfortable seated position just in front of the system computer screen. Contacts were verified to ensure an adequate signal, and then the subject was instructed to sit quietly to determine baseline waveforms and signals. The testing started with a standard P300 audio reaction time test [24], where the subject listens to two types of tones and notes via mouse pad interface when the higher tone occurs. This measurement also recorded the electrical potential for that result as well as reaction time. Two visual tests were then administered, including a trail making test where the subject connects numbers in random placement on the screen from one to 25, and a second trail making test where numbers and letters are linked (1-A, 2-B, and so on) until 25 total responses are recorded [25-27]. In each instance, the subject is given a practice test with instructions on scoring best and most consistently. Between trials, subjects received instructions to sit quietly and occupy their time with work, study, or reading. All subjects used the same space with the same conditions.

Figure 1: Label from Brain Activation Product.

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Results & Discussion

The subjects in the intervention group increased functional brain activity overall as measured with evoke potentials, time to task, and graphic representations compared to the control group. There was a decrease in reaction time for the group in the P300 audio reaction time test of 340 milliseconds to 314 milliseconds. In addition, microvolt (μV) activation during the auditory reaction time test increased from 7.5 μV to 12.9 μV, indicating increased brain function. The intervention group also decreased time in the first trail-making test from 94 to 62 seconds and decreased time to complete the second trail-making test from 113 to 93 seconds. The descriptive analysis demonstrated that the active product cohort received positive, beneficial effects compared to the placebo group (Table 1).

Table 1: Intervention vs. Control Group: Individual Study Data.

Intervention Subjects	Reaction Time 1(MSEC)	RT 2(MSEC)	RT Voltage 1 (μV)	RT Volage 2 (μV)	Trail Making A 1 (seconds)	TM A 2	TM B 1	TM B 2
1	338	344	1.8	3.8	111	80	175	116
2	320	319	7.4	13.8	78	62	97	73
3	320	274	7.9	8.8	66	60	102	109
4	272	260	13.2	15.1	133	72	107	89
5	330	336	10.1	17.4	77	47	114	90
6	320	317	8.5	8.3	75	44	79	61
7	465	362	5.8	18.3	129	81	128	105
8	357	303	5.3	18	81	54	104	102
Average	340.5	314.4	7.5	12.9	93.8	62.5	113.25	93.13
Control Subjects	**Reaction Time 1(MSEC)**	**RT 2(MSEC)**	**RT Voltage 1 (μV)**	**RT Volage 2 (μV)**	**Trail Making A 1 (seconds)**	**TM A 2**	**TM B 1**	**TM B 2**
1	306	296	15.7	17.7	57	55	69	67
2	381	394	8.2	5.9	68	70	83	85
3	337	424	4.6	4.8	83	82	70	79
Average	341.3	371.33	9.5	9.47	69.3	69	74	77

All measurements in the intervention group attained strongly positive beneficial effect trends compared to the control group. An extensive variation in the subjects' baseline status precluded traditional statistical analysis. For example, EEG measurements may rely on a combination of a trait (age, sex, heredity) and state (training, nutrition, rest, mental stimulation), resulting in a broader mean and median distribution than other physiological variables or medicine. A subsequent conformational trial with a more extensive study cohort is in process and anticipated to diminish the effect of this wide baseline variability.. While the measured parameters indicate that the proprietary brain activation compound had an effect in just 90 minutes, the individual topographic representations and the composite are more indicative of the net increased functional brain activation (Figures 2-10) & (Table 2).

Table 2: Subject Demographics and Brain Scan Impact.

Subject	Sex	Age	Occupation	Brain Impact
1	M	69	Artist	Increased R frontal (cognition) and L parietal lobes (sensory, awareness)
2	M	62	Writer	Marked increased central frontal (higher integration)
				and R parietal cortex (spatial orientation)
3	F	59	Travel Agent	Increased R temporal lobe (motor, language, memory)
4	F	68	Teacher	Increased R temporal and parietal lobe (motor, somatosensory)
5	M	49	Consultant	Dramatic increase central frontal cortex (higher cognition)
				and R, L parietal lobes (sensory, orientation)
6	M	62	Marketing	Dramatic increase central frontal cortex (cognition, integration)
				and R, L temporal/parietal lobes (sensory, memory, motor, awareness)
7	F	63	Financial Services	Increased R temporal lobe (motor, sensory, memory)
8	M	62	Manager	Increased L frontal cortex (higher integration) and parietal lobe (sensory, motor)
				and parietal lobe (sensory, motor)

Conclusions & Future Direction

In this pilot study, consumption of a concentrated, proprietary phytonutrient compound produced enhanced functional brain activity 90 minutes after ingestion with significant increases concerning topographical brain maps. Optimal ingestion conditions and time to effect for this and similar products across various populations are being investigated. In addition, EEG measurements show promise as analytical tools to measure the effects of nutritional supplements on brain function. The inherent

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variability in baseline functional brain status appears to warrant a modified statistics assessment of response for future nutritional interventions regarding brain activity as measured with EEG devices.

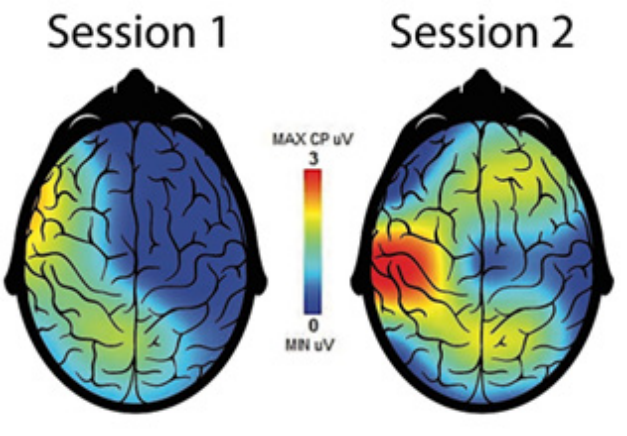

Figure 2: Subject #1.

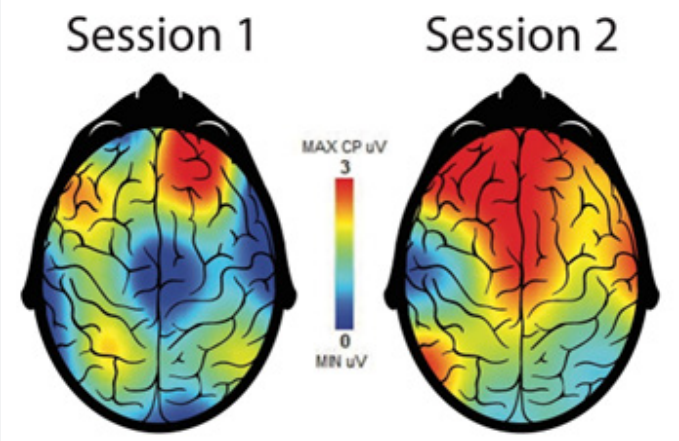

Figure 3: Subject #2.

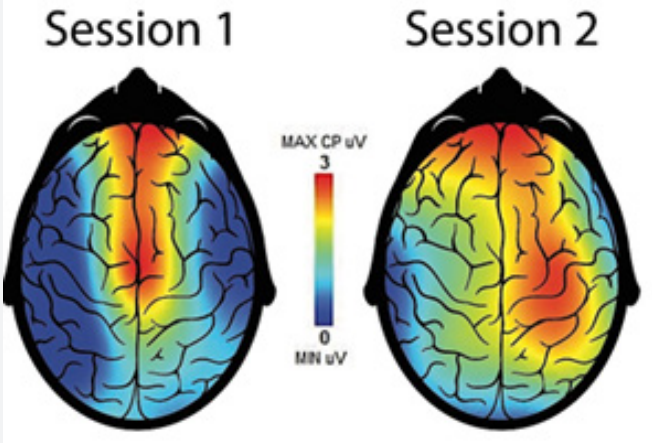

Figure 4: Subject #3.

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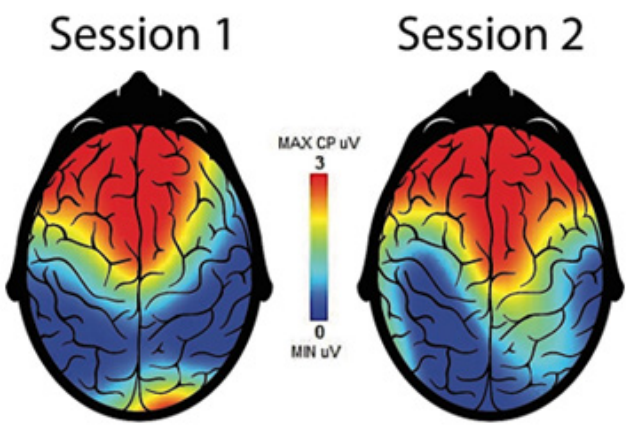

Figure 5: Subject #4.

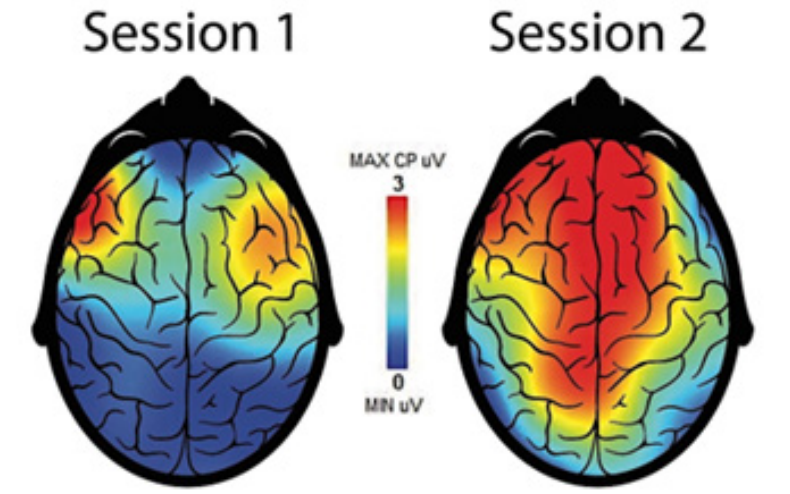

Figure 6: Subject #5.

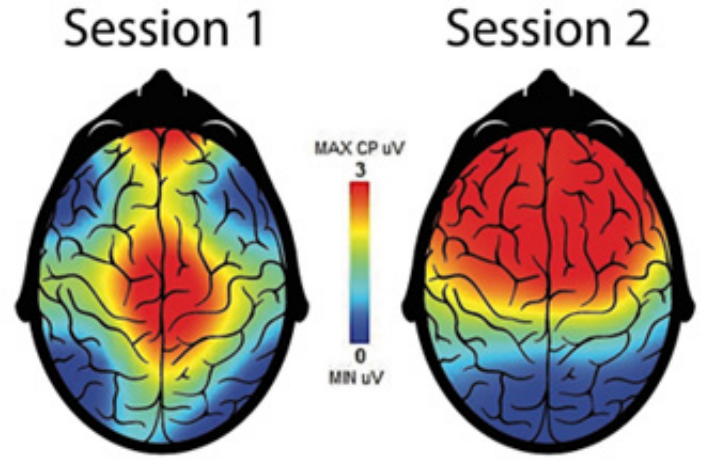

Figure 7: Subject #6.

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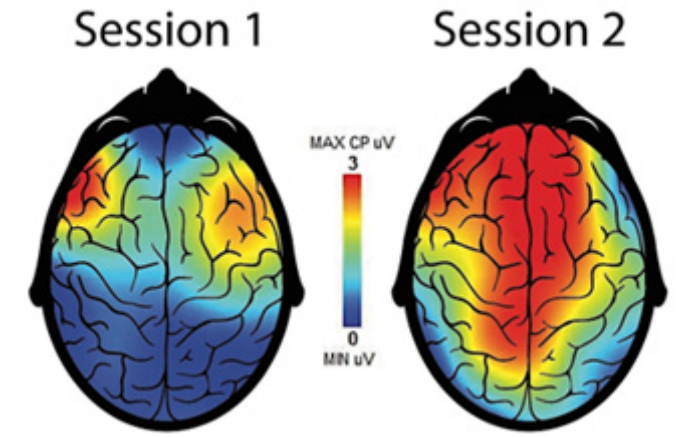

Figure 8: Subject #7.

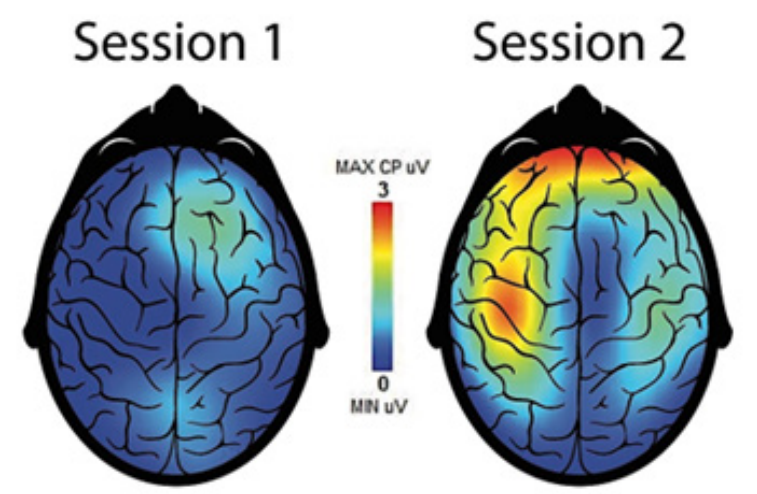

Figure 9: Subject #8.

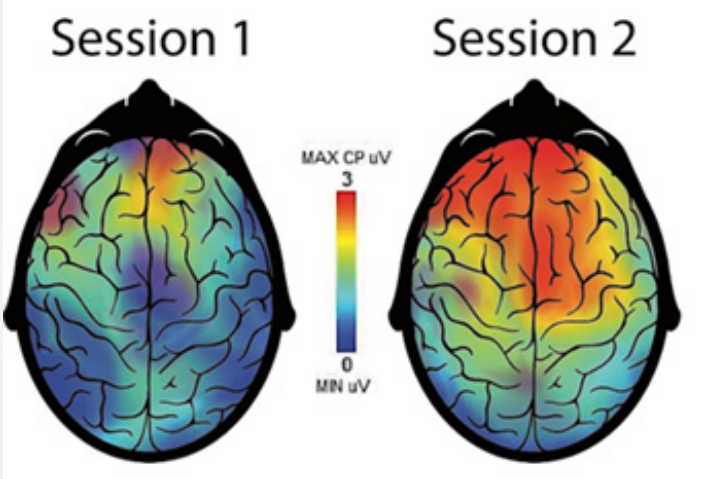

Figure 10: Composite Topographic Brain Image Based on Median Voltage Values Dramatic Generalized Increase in Functional Activity.

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