A Proof of Concept for a Randomized, Double Blind, Placebo Controlled, Parallel Group, Efficacy Study of Alpha Brain(TM) Administered Orally

Todd M. Solomon[1,2,3], Andrew E. Budson[2,3], Guy B. deBros[1] Cynthia A. Murphy[1,2], Elizabeth Vassey[2] & Paul R. Solomon[1,2,4]

[1]The Memory Clinic, Bennington, VT; [2]Boston Center for Memory, Boston, MA; [3]Boston University School of Medicine, Boston, MA, [4]Williams College, Williamstown, MA

Introduction

Sales of medical foods, dietary supplements and nutraceuticals totaled an estimated 30 billion dollars in 2012[1].

Within this market, numerous medical foods and nutraceuticals now purport to improve cognitive functioning[2].

While some medical foods are meant to be used under a doctor's supervision, neither medical foods nor nutraceuticals are regulated by the United States Food and Drug Administration (FDA) in the same manner as pharmaceuticals.

Further, despite claims made by their manufacturers, medical foods and nutraceuticals are not subject to the same rigorous scientific study as FDA-approved medications.

Given the continued growth of the supplement industry as well as the claims made by manufacturers and the lack of available scientific data, it is paramount that supplements whose manufactures claim they improve cognitive functioning are subjected to the same rigorous scientific study as pharmaceuticals.

Alpha Brain™ is manufacured by Onnit Labs and is marketed as a cognitive enhancing supplement or nootropic for healthy adults. While Alpha Brain™ does contain several ingredients associated with increased acetylcholine function and cognitive enhancement[3-7], its efficacy has not yet been demonstrated using a randomized, double-blind, placebo controlled trial.

Thus, the goal of this study was to investigate the efficacy of a self-described cognitive enhancing nutraceutical, Alpha Brain™, on cognitive functioning and sleep in a group of healthy adults by using a randomized, double-blind, placebo-controlled design.

Methods

A total of seventeen 18- to 35-year-old treatment naïve individuals were screened for inclusion and were randomized for participation. Inclusion criteria included MMSE score ≥ 28; no current or past diagnosis of ADD, ADHD, major depression, learning disabilities or concussions with loss of consciousness; not taking any psychoactive medication or cognitive enhancer within the past 6 months; and not currently dependent on any illicit substance (according to ICD-10 criteria). All participants completed a two-week placebo run-in before being randomized to receive either active product, Alpha Brain™, or new placebo.

After the placebo run-in phase, participants completed a comprehensive battery of neuropsychological tests. Participants then followed the manufacturer's instructions for use of Alpha Brain™ for six weeks, at which time they repeated the neuropsychological battery. Primary outcome measures included neuropsychological tests from the WMS-IV, DKEFS, CVLT-II, Trails A & B, and PASAT.

Results

Following the two-week placebo run-in, significant differences were found between groups on scores for Logical Memory I, Logical Memory II, and Trails B ($p < .05$).

After six weeks, these initial differences diminished. However, significant improvements in performance were seen on CVLT-II long-delay verbal recall and D-KEFS Color-Word Inhibition score ($p < .05$) among those participants randomized to the treatment group.

Overall, the control group neither deteriorated nor improved on neuropsychological tests, while the treatment group showed significant improvement on several outcome measures (see Table 1). No differences between groups were observed on measures of sleep.

Overall compliance with treatment was excellent for both groups (94% at 2weeks and 96% at 6 weeks) and the product was well-tolerated by all participants.

Table 1. Mean Neuropsychological Test Raw Scores by Time Point & Group

	BASELINE		+45 DAYS	
Outcome Measure	AlphaBrain™	Placebo	AlphaBrain™	Placebo
Logical Memory I Total	*M = 30.30	*M = 26.14	M = 33.33	M = 31.00
Logical Memory II Total	*M = 26.70	*M = 22.00	M = 32.77	M = 26.83
BVMT-R Immediate Recall	M = 30.30	M = 30.42	M = 31.44	M = 34.33
BVMT-R Delayed Recall	M = 10.90	M = 11.42	M = 16.33	M = 11.66
FAS Total	M = 48.20	M = 50.28	M = 57.22	M = 50.16
D-KEFS Animals + Names Total	M = 46.70	M = 49.57	M = 46.55	M = 42.83
D-KEFS Fruits + Furniture Total	M = 16.30	M = 15.28	M = 17.77	M = 15.66
Trails A Time	M = 16.70	M = 23.00	M = 17.11	M = 19.33
Trails B Time	*M = 40.90	*M = 57.33	M = 36.00	M = 41.00
D-KEFS Color-Word Inhibition Time	M = 45.50	M = 50.71	*M = 45.33	*M = 52.83
CVLT Total	M = 48.20	M = 50.00	M = 57.22	M = 50.16
CVLT List B	M = 7.60	M = 6.85	M = 8.66	M = 7.00
CVLT Short Delay	M = 13.10	M = 11.71	M = 13.88	M = 12.00
CVLT Long Delay	M = 12.00	M = 11.28	M = *14.20	M = *11.16
PASAT Trial I	M = 47.00	M = 43.28	M = 51.11	M = 46.16
PASAT Trial II	M = 37.90	M = 36.00	M = 42.80	M = 38.16

* = $p < .05$

Discussion

The use of the nutraceutical Alpha Brain™ for 6 weeks improved scores on neuropsychological measures associated with verbal memory and executive functioning compared to placebo in healthy a group of adults aged 18-35.

Specifically, significant differences were found between groups on mean scores for both the CVLT-II long delay verbal recall and the D-KEFS Color-Word Inhibition score. While these were only two measures that reached statistical significance, out of 16 analyzed, several other measures also demonstrated trends towards significance.

While the small study sample size limits generalizability to a larger population, these preliminary data do indicate the potential for efficacy in several areas of cognitive functioning. Given the lack of prior rigorous scientific testing, this proof of concept study justifies a subsequent larger clinical trial.

Table 2. Mean Z-Scores by Time Point & Group

	BASELINE		+45 DAYS	
Outcome Measure	AlphaBrain™	Placebo	AlphaBrain™	Placebo
Logical Memory I Total	Z = .23	Z = -.33	Z = .10	Z = -.16
Logical Memory II Total	Z = .25	Z = -.36	Z = .27	Z = -.40
BVMT-R Immediate Recall	Z = -.01	Z = .01	Z = -.19	Z = .29
BVMT-R Delayed Recall	Z = -.13	Z = .01	Z = .17	Z = -.25
FAS Total	Z = -.06	Z = .19	Z = .21	Z = -.32
D-KEFS Animals + Names Total	Z = -.08	Z = .09	Z = .22	Z = -.33
D-KEFS Fruits + Furniture Total	Z = .93	Z = .11	Z = .25	Z = -.38
Trails A Time	Z = -.45	Z = -.13	Z = -.20	Z = .30
Trails B Time	Z = -.30	Z = .76	Z = -.14	Z = .21
D-KEFS Color-Word Inhibition Time	Z = -.14	Z = .50	Z = -.15	Z = .22
CVLT Total	Z = - .18	Z = .21	Z = .50	Z = -.76
CVLT List B	Z = .15	Z = .25	Z = .32	Z = -.49
CVLT Short Delay	Z = .34	Z = -.22	Z = .29	Z = -.44
CVLT Long Delay	Z = -.09	Z = -.49	Z = .39	Z = -.59
PASAT Trial I	Z = .17	Z = -.13	Z = .17	Z = -.25
PASAT Trial II	Z = .07	Z = -.24	Z = .14	Z = -.22

Table 3. Mean Sleep Measure Scores by Time Point & Group

	BASELINE		+45 DAYS	
Outcome Measure	AlphaBrain™	Placebo	AlphaBrain™	Placebo
Epworth Sleepiness Scale	M = 7.4	M = 6.7	M = 7.1	M = 7.3
Mentation Question 1	M = 3.8	M = 3.2	M = 3.7	M = 2.5
Mentation Question 2	M = 2.5	M = 2.7	M = 2.4	M = 2.5

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