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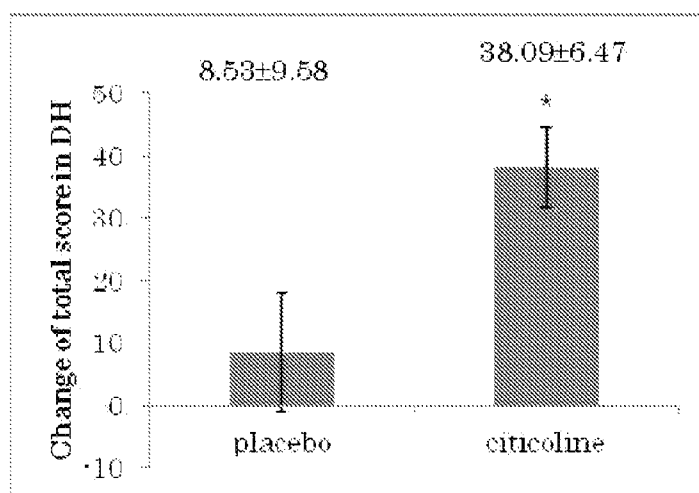
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- (54) **Title:** ADMINISTRATION OF CITICOLINE TO IMPROVE COGNITIVE PERFORMANCE, ATTENTIONAL PERFORMANCE, AND MOTOR FUNCTION

Figure 1. Visit Difference Scores of Finger Tap Test

* $P < 0.05$ significantly different from the placebo.

(57) **Abstract:** A method of improving both motor function and cognitive function of healthy human subjects through administration of citicoline or its salt in high dosage or low dosage for a period of time, resulting in improved motor function and cognitive function.

ADMINISTRATION OF CITICOLINE TO IMPROVE COGNITIVE PERFORMANCE, ATTENTIONAL PERFORMANCE, AND MOTOR FUNCTION

CROSS-REFERENCE TO RELATED APPLICATIONS

5 The present application claims priority to U.S. Provisional Patent Application Serial No. 61/986,502, the contents of which are hereby incorporated by reference.

BACKGROUND OF THE INVENTION

Cytidine 5'-diphosphocholine, also known as citicoline, is a choline-containing compound made up of choline and cytidine, and is a nucleotide that is
10 integral to cellular metabolism. A recognized precursor to acetylcholine, citicoline promotes the synthesis and transmission of neurotransmitters important to memory and attention. As a supplement, citicoline has been used in Japan, Europe, and the United States to ameliorate cognitive impairment and memory dysfunction in populations not generally considered in good health, such as the elderly, Alzheimer's patients, stroke
15 victims, and victims of traumatic brain injury. There remains a need for a supplement that prevents the decline of cognitive function and motor function in healthy adults.

BRIEF SUMMARY OF THE INVENTION

The present invention addresses the aforementioned need. The present invention provides an agent, citicoline, and a method of mitigating cognitive decline or
20 improving cognitive function and mitigating decline motor function or improving motor function by administering citicoline to a subject in need, increasing the utilization of cellular energy reserves and increasing phospholipid membrane production needed for cellular repair.

In one embodiment of the present invention, a method for improving motor
25 function of a healthy human subject comprising a step of administering an effective amount of citidine-5'-diphosphocholine (hereinafter referred to as citicoline) or a salt thereof to a healthy human subject is provided.

In another embodiment of the present invention, the effective amount of citicoline or a salt thereof being administered is an amount that is 5 mg or more and 4.0
30 g or less per day.

In another embodiment of the present invention, the effective amount of citicoline or a salt thereof being administered is an amount that is 100 mg or more and 1.0 g or less per day.

5 In another embodiment of the present invention, the effective amount of citicoline or a salt thereof being administered is an amount that is 250 mg or more and 500 mg or less per day.

In another embodiment of the present invention, the effective amount of citicoline or a salt thereof being administered is an amount that is less than 500 mg per day.

10 In yet another embodiment of the present invention, the citicoline or a salt thereof is administered orally.

In another embodiment of the present invention, the citicoline or a salt thereof is administered alone in an amount that is 5 mg or more and 4.0 g or less per day.

15 In one embodiment of the present invention, the citicoline or a salt thereof is administered for at least 1 day and at most 1 year.

In another embodiment, citicoline or a salt thereof is administered for at least 1 day and at most 4 weeks.

20 BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows the effects of citicoline administration on motor speed and control compared to a control group receiving placebos. The citicoline-treated group (N=51) were administered 250 mg/day (N=24) or 500 mg/day (N=27). Three finger tap tests were administered over a period of 28 days to measure motor speed and control.

25 Results are expressed as mean $\pm$ SD. Statistical analysis was performed using Student's t test. The $p < 0.05$ was considered statistically significant.

FIG. 2 shows the effects of citicoline administration on attentional capacity compared to a control group receiving placebos.

30 DETAILED DESCRIPTION OF THE INVENTION

A detailed description of the various tests and studies conducted and the results of each of these studies are listed. The studies conducted involve healthy

subject groups generally administered with either high dose of citicoline (500 mg/day) or low dose of citicoline (250 mg/day).

EXAMPLE

5 Materials and Methods

Study participants were screened by telephone prior to study enrollment. Healthy subjects, ages 13-18, with no significant medical conditions and no history of co-morbid psychiatric disorder, current Axis I or II diagnosis, or previous participation in a pharmacotherapeutic trial, were selected. Use of any psychotropic medication or
10 any previous head injury resulting in loss of consciousness for 5 or more minutes were used as exclusion criteria. While no participant met criteria for a neuropsychiatric disorder at enrollment, clinical assessments were still completed throughout the study to evaluate changes in mood state. In addition, self-reports of sleep habits, lifestyle, and exercise routines were also administered at baseline as well as at each study visit to
15 assess changes in health habits during study participation.

Participants also provided a urine sample for drug screening and a blood sample for comprehensive chemistry panel (sodium, potassium, chloride, BUN, creatinine, glucose, calcium, magnesium, phosphorus), liver function tests (SGOT, SGPT, GGT, total bilirubin, albumin), a full blood count (WBC, RBC, platelet count).

20 A visual acuity test was given in addition to weight and height measurements. Participants then completed a diagnostic interview, lifestyle questionnaires, and neuropsychological testing.

Following the completion of Visit 1 assessment, participants were given their 28-day supply of citicoline (250 mg or 500 mg) or placebo, which was randomly
25 assigned. They were instructed to take one capsule a day every day for the next 28 days.

Visit 2 occurred fourteen days after Visit 1. At Visit 2, the remaining study pills were counted and participant dosage calendars were checked to ensure compliance with the protocol. Additional neuropsychological measures and clinical assessments were
30 administered during this visit.

Participants returned for Visit 3 fourteen days later, on the 28th day of their study participation. The pill bottle and the dosage calendar were collected from each

participant. Urine and blood were again obtained. Participants also participated in similar clinical and neuropsychological testing and clinical measures that were given during visit 1.

5 *Clinical Ratings and Assessment*

Schedule for Affective Disorders and Schizophrenia for School-Age Children/Present and Lifetime Version (KSADS-PL)

The KSADS-PL was administered to each participant during the first visit. The KSADS-PL is a structured diagnostic interview used to assess current functioning and to determine whether participants met study inclusion criteria, including absence of a lifetime Axis I or Axis II psychiatric disorder both currently and lifetime. None of the 75 participants who completed the study met criteria for any past or current Axis I or II disorder.

Columbia-Suicide Severity Rating Scale (C-SSRS)

15 The C-SSRS is an investigator-administered scale that assesses suicidal ideation and identifies behaviors that may indicate intent to commit suicide. The C-SSRS was administered at each of the three visit to assess for presence or absence of suicidal ideation.

The Positive and Negative Affect Scale for Children (PANAS-C)

20 The PANAS-C is a self-report questionnaire on which participants rate to what extent they are currently experiencing a variety of positive and negative emotions such as “excited” and “mad.” The PANAS was administered during each of the three visits to assess participant affect prior to taking the study drug as well as after taking the study drug over a period of 28 days.

25 *Children’s Depression Rating Scale (CDRS)*

The CDRS is an investigator-administered scale that is widely used as observational measures of depressive symptoms in children. The scale was administered at each of the three visits to assess presence or absence of depressive symptoms.

30 *Barratt Impulsiveness Scale (BIS)*

The BIS is a questionnaire is a scale used to measure impulsiveness. It includes three subscales: attentional, motor, and non-planning impulsiveness. A total score, or a

sum of the three factors, was also calculated. The scale was administered at the first and third visits to assess presence or absence of symptoms of impulsiveness.

ADHD Rating Scale (ARS)

The ARS is a questionnaire assessing the frequency of DSM-IV-TR symptoms of ADHD in children including inattention, impulsivity, and hyperactivity. The scale was administered at each of the three visits to assess presence or absence of ADHD symptoms.

Conner-Wells Self-Report Scale (L) (Conners)

The Conners is a self-report questionnaire assessing a range of problem behaviors in children, including family problems, emotional problems, conduct problems, cognitive problems/inattention, anger control problems, hyperactivity, ADHD Index, and DSM-IV symptom subscales. The scale was administered at the first and third visits to assess presence or absence of a range of problem behaviors.

Pittsburgh Sleep Quality Index (PSQI)

The PSQI is a self-report sleep questionnaire designed to assess usual sleep habits during the past month. The PSQI was administered at each of the three study visits to assess alterations to sleep quality during the 28 days of study participation.

General Questionnaire, Exercise and Life Style Questionnaire

The General Questionnaire and Exercise and Life Style Questionnaire are self-report questionnaires designed to assess a variety of symptoms, behaviors, and self-perceptions, including mood, complexion, exercise, food, and alcohol habits of each of the participants. The General Questionnaire was administered during each of the three study visits; the Exercise and Life Style Questionnaire was administered during each of the three study visits.

Neuropsychological Measures

Wechsler Adult Intelligence Scale-Revised (WASI-R)

Two subtests were included from the WASI-R test to generate estimates of Verbal Comprehension and Perceptual Reasoning. The vocabulary subtests were completed to estimate verbal abilities, which has also been supported as a strong predictor of overall intellectual ability. The Matrix Reasoning subtest was also

administered as an estimate of perceptual reasoning. The two WASI-R subtests were administered during the first visit.

WAIS-IV Vocabulary Subtest:

- 5 This subtest measures the participants' verbal ability and has been shown to correlate with measures of general intellectual ability.

WAIS-IV Matrix Reasoning Subtest:

- 10 The Matrix Reasoning subtest primarily measures nonverbal abstract problem solving. It also assesses inductive and spatial reasoning abilities.

Motor Function

Finger Tap Test

- 15 The finger tap test is used to measure motor speed and control. It is a common assessment measure administered by neuropsychologists to detect cognitive impairment. During the finger tap test, the participant is instructed to use his/her index finger to press a lever attached to a mechanical counter as many times as s/he can within the designated time period. The participant is instructed to move only their index finger, not the entire hand. The same process is completed using the index finger of the dominant and non-dominant hand. The finger tap test was administered at each of the three visits.
- 20

Assessment of Cognitive Domains

Memory

- 25 *California Verbal Learning Test I (CVLT-I) and California Verbal Learning Test II (CVLT-II)*

- These verbal learning tests assess the subject's immediate and delayed recall, as well as suggesting the strategy utilized for retrieval of newly-learned information. Subjects are asked to remember a 16-item word list, which is presented on five trials. After each trial, the subject is asked to recall all of the words that they can remember. A second list is then presented to provide an interference condition. The subject is then asked to recall the first word list. After a temporal delay, the subject is again asked to
- 30

recall the first word list. Test results provide scores for assessing verbal learning, strength of memory following interfering tasks, proactive interference, accuracy of recognition memory and storage versus retrieval of newly learned information. The CVLT was administered at all three visits.

5 *Rey-Osterreith Complex Figure Test (ROCFT) and Modified Taylor Complex Figure (MTCF)*

10 The ROCFT is an assessment of visuo-organizational ability, visual attention, and visual memory. The participant is asked to copy a complex 2-dimensional figure with the stimulus or complex figure in front of them (Copy Trial), immediately after the stimulus has been removed (Short Delay Trial), and after 30 minutes without the stimulus present (Long Delay Trial). The figure produced at each trial is then evaluated for the strategy used in reproducing the figure, constructional accuracy, and placement of elements within the figure. The Copy, Short Delay, and Long Delay trials are each scored on the number of elements that have been correctly recalled and the accuracy and placement of each element. The Difference Score between immediate and delayed performance scores is a measure of temporary decay for visuospatial memory. This test was administered on both the first and the third visits. The Modified Taylor Complex Figure (MTCF) is an alternate form of the ROCFT to assess visuo-organizational ability, visual attention, and visual memory. The same procedure was used to administer the MTCF. The MTCF was administered at the second visit instead of the ROCFT to minimize the effect of repeat testing on copy and retention of the figure across visits.

25 *Attention*

Stroop Color Word Test

30 The Stroop measures the ability to inhibit incorrect responses and to resist interference. The three conditions, Color Naming, Word Reading, and Interference, are designed to establish competing response tendencies. Outcome variables include time to complete each condition, as well as total errors per condition. The Stroop test was administered at each of the three visits.

Continuous Performance Test (CPT)

The CPT is a test of sustained attention that has been adapted for computerized administration. The test requires participants to attend vigilantly to a series of target and distracter stimuli for a 14-minute duration. Attention scores include reaction time, omission errors during which the participant should have responded but did not, and commission errors during which the participant failed to inhibit a response. The CPT was administered at all three visits.

Ruff 2 & 7

The Ruff 2 & 7 measures two aspects of visual attention: sustained attention and selective attention. There are a series of 20 trials involving visual searching in which the respondent detects and marks through all given stimuli the digits “2” and “7”. In the 10 Automatic Detection trials, the target digits are embedded among alphabetical letters that serve as distractors. In the 10 Controlled Search trials, the target digits are embedded among other numbers that serve as distractors. Correct hits and errors are counted for each trial and serve as the basis for scoring the test. Accuracy scores evaluate the number of targets identified in relation to the number of possible targets. The Ruff 2 & 7 was administered at all three visits.

Mental Flexibility

Wisconsin Card Sorting Task (WCST)

The WCST assess a person’s ability to form abstract concepts, utilize feedback, and to shift and maintain set. This test has been shown to be sensitive to frontal lobe dysfunction. The WCST involves 4 stimulus cards that vary in color, geometric form, and number. Without knowing the criterion, participants are asked to match cards from a deck to the stimulus cards. After the participant places each card, she is told whether she is correct or incorrect and should change the element she is matching based on this feedback. Dependent variables include total number of cards used, categories achieved (color, form, or number), and perseverative errors during which the individual did not adjust matching strategy according to feedback. The WCST was given on the third visit of the study.

Trail Making Test

The Trail Making Test is designed to measure visual conceptual and visuomotor tracking, as well as maintenance of cognitive set. On Trial A the participant must draw lines to connect consecutively numbered circles on one work sheet (1-2-3-4 etc.). For Part B she must connect numbered and lettered circles by alternating between the two sequences (i.e., 1-A-2-B etc.). Part B is the more sensitive of the two tests -- particularly to frontal-lobe dysfunction -- as scores on this section are indicative of the participant's ability to shift sets (numeric to alphabetical order) and process concurrent stimuli. This test was administered on all three visits.

Measurement of Adverse Events

Monitoring of Side Effects Scale (MOSES)

The MOSES is a scale designed to assess common symptoms or adverse events associated with psychopharmacological medications. This scale is divided into nine body areas representing a typical physical examination. The interviewer asks subjects whether they have each symptom on the measure and, if so, asks them to report the level of severity of the symptom on a scale from 0 (not present) to 4 (severe). This scale was administered on the second and third visits to assess presence or absence of adverse events.

Results and Discussion

The Positive and Negative Affect Scale (PANAS-C)

Comparisons within Groups for Difference scores

On the PANAS-C, the 250 mg/day group showed significant declines in feeling positive emotions ($p < 0.01$) and showed improvement in feeling less negative emotions ($p < .01$) between visit 1 and visit 3 (Table 3).

The Placebo group showed a trend toward declines in positive emotion ($p=0.09$) and showed improvement in feeling less negative emotions ($p=.03$) between visit 1 and visit 3 (Table 4).

On the PANAS-C, the 500 mg/day group showed significant declines in feeling positive emotions ($p=.04$) and showed improvement in feeling less negative emotions ($p<.01$) between visit 1 and visit 3 (Table 5).

Comparisons between Groups at Time 3

5 At visit 3, no significant differences were evident between the 250 mg/day group and the 500 mg/day group on both positive emotional attributes ($p=0.95$) or negative emotional attributes ($p=0.18$) (Table 5).

10 No significant effect was seen between the Placebo group and the 500 mg/day group during visit 3 for positive emotional attributes ($p=0.39$). The 500 mg/day group showed less negative emotional attributes compared to the 500 mg/day group ($p=0.03$) (Table 6).

At visit 3, no significant effects were seen between the 250 mg/day group and the Placebo group in positive emotional attributes ($p=0.44$) and negative emotional attributes ($p=.45$) (Table 6a).

15 When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall analysis, there was a trend toward significant differences between groups on negative emotional attributes ($p=0.06$). Post-hoc analyses showed that at visit 3 individuals in the 500 mg/day group showed a trend toward feeling less negative emotions compared to individuals in the Placebo group ($p=0.05$) (Table 7).

20 *Comparisons between Groups for Difference Scores*

On the PANAS-C, there were no significant differences between the 250 mg/day group and the 500 mg/day group from visit 1 to visit 3 on positive emotional attributes ($p=0.18$) or negative emotional attributes ($p=.89$) (Table 5).

25 There were no significant differences between the Placebo group and the 500 mg/day group from visit 1 to visit 3 on positive emotional attributes ($p=0.97$) or negative emotional attributes ($p=.41$) (Table 6).

30 There were no significant differences between the 250 mg/day group and the Placebo group from visit 1 to visit 3 on positive emotional attributes ($p=0.23$) or negative emotional attributes ($p=.43$) (Table 6a).

No overall between group differences were detected for positive emotional attribute differences ($p=0.15$) or negative emotional attribute differences ($p=.32$) between visit 1 and visit 3 (Table 8).

5 Children's Depression Rating Scale (CDRS)

Comparisons within Groups for Difference scores

On the CDRS, the 250 mg/day group showed significant declines in depressive symptoms ($p=0.02$) between visit 1 and 3 (Table 9).

There were no significant differences for the Placebo group between visit 1 and 10 3 on the CDRS ($p=0.42$) (Table 10).

On the CDRS, the 500 mg/day group showed significant declines in depressive symptoms ($p=0.03$) between visit 1 and 3 (Table 11).

Comparisons between Groups at Time 3

At visit 3, no significant difference was evident between the 250 mg/day 15 and the 500 mg/day group on the CDRS ($p=0.29$) (Table 12). No significant difference was detected between the Placebo group and the 500 mg/day group during visit 3 on CDRS ($p=0.30$) (Table 13).

At visit 3, no significant difference was evident between the 250 mg/day and the Placebo group on the CDRS ($p=0.93$) (Table 13a).

20 When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall analysis, no significant differences between groups were detected on the CDRS ($p=0.27$) (Table 14).

Comparisons between Groups for Difference Scores

On the CDRS, there were no significant differences between the 250 mg/day group 25 and the 500 mg/day group from visit 1 to visit 3 on depressive symptoms ($p=0.22$) (Table 12). There were no significant differences between the Placebo group and the 500 mg/day group from visit 1 to visit 3 on depressive symptoms ($p=0.40$) (Table 13).

On the CDRS, there were no significant differences between the 250 mg/day group and the Placebo group from visit 1 to visit 3 on depressive symptoms ($p=0.10$) (Table 30 13a).

There was a trend toward significant differences between group difference scores ($p=0.07$). Post-hoc analyses showed that at individuals in the 250 mg/day group showed a

trend toward greater declines in depressive symptoms compared to individuals in the Placebo group ($p=0.07$) (Table 15).

Barratt Impulsiveness Scale (BIS)

5 The BIS included three summary categories of attention, motor, and non-planning impulsiveness, each of which had multiple individual items. Within and between group analyses are reported below for the three summary categories, as well as the total score.

10 *Comparisons within Groups for Difference scores*

The 250 mg/day group showed no improvement between visit 1 and visit 3 on attention ($p=0.44$), motor ($p=0.36$), non-planning ($p=0.30$), or the total score ($p=0.35$) (Table 16).

The Placebo group showed no improvement between visit 1 and visit 3 on
15 attention ($p=0.45$), motor ($p=0.40$), or the total score ($p=0.33$). There was a trend
toward improvement in scores on non-planning from visit 1 to 3 ($p=.09$) (Table
17).

The Placebo group showed no improvement between visit 1 and visit 3 on attention ($p=0.47$), motor ($p=0.40$), or the total score ($p=0.17$). There was a trend toward improvement in scores on non-planning from visit 1 to 3 ($p=.09$) (Table 18).

Comparisons between Groups at Time 3

At visit 3, the 500 mg/day group showed a significantly lower total score than the 250 mg/day group ($p=0.03$). There was a trend toward significant differences in the 250 mg/day and 500 mg/day group on attention ($p=0.07$) and motor ($p=0.05$), with the 500 mg/day group showing a lower score compared to the 250 mg/day group on both scores. There were no significant differences in the non-planning score between the 250 mg/day and 500 mg/day group ($p=0.12$)(Table 19).

At visit 3, no significant difference was detected between the Placebo group and the 500 mg/day group on attention ($p=0.82$), motor ($p=0.47$), non-planning ($p=0.56$), or the total score ($p=0.91$) (Table 20).

At visit 3, the Placebo group showed a significantly lower total score ($p=0.02$) and non-planning score ($p=0.04$) than the 250 mg/day group. There was a trend toward significant differences in the 250 mg/day and Placebo group on attention ($p=0.08$), with the Placebo group showing a lower score compared to the 250 mg/day group. There were
5 no significant differences in the motor score between the 250 mg/day and Placebo group ($p=0.13$)(Table 20a).

When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall analysis, there were significant differences between groups on attention ($p=0.05$), motor ($p=0.04$), non-planning ($p=0.04$), and the total score ($p=0.01$). Post-hoc analyses
10 showed that at visit 3 individuals in the 500 mg/day group showed a trend toward lower scores on attention compared to individuals in the 250 mg/day group ($p=0.06$). The 500 mg/day group showed a significantly lower motor score ($p=0.04$) and the total score ($p=0.02$) than the 250 mg/day group at visit 3. The Placebo group showed a significantly lower non-planning score ($p=0.04$) and total score ($p=0.03$) than the 250 mg/day group at
15 visit 3 (Table 21).

Comparisons between Groups for Difference Scores

No significant differences were detected between the 250 mg/day group and the 500 mg/day group on differences in scores from visit 1 to visit 3 for attention ($p=0.88$), motor ($p=0.44$), non-planning ($p=0.98$), or the total score ($p=0.67$) (Table
20 19).

No significant differences were detected between the Placebo group and the 500 mg/day group on differences in scores from visit 1 to visit 3 for attention ($p=0.89$), motor ($p=0.42$), non-planning ($p=0.58$), or the total score ($p=0.85$) (Table 20).

No significant differences were detected between the 250 mg/day group and the
25 Placebo group on differences in scores from visit 1 to visit 3 for attention ($p=0.99$), motor ($p=0.95$), non-planning ($p=0.60$), or the total score ($p=0.81$) (Table 20a).

When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall analysis, no significant differences between groups were detected on attention ($p=0.49$), motor ($p=0.32$), non-planning ($p=0.42$), and the total score
30 ($p=0.45$) (Table 22).

ADHD Rating Scale (ARS)

The ARS included two summary categories of inattention and impulsivity, each of which had multiple individual items. Within and between group analyses are reported below for the two summary categories.

5 Comparisons within Groups for Difference scores

The 250 mg/day group showed no improvement between visit 1 and visit 3 on inattention ($p=0.17$). There were significant declines in impulsivity between visit 1 and visit 3 for the 250 mg/day group ($p<0.01$) (Table 23).

The Placebo group showed significant declines in inattention between visit 1 and visit 3 ($p=0.03$). There were no improvements between visit 1 and 3 for impulsivity for the Placebo group ($p=0.10$) (Table 24).

The 500 mg/day group showed no improvement between visit 1 and visit 3 on inattention ($p=0.28$). There were significant declines in impulsivity between visit 1 and visit 3 for the 250 mg/day group ($p=0.02$) (Table 25).

Comparisons between Groups at Time 3

The 500 mg/day group showed significantly lower scores on inattention at visit 3 compared to the 250 mg/day group ($p=0.01$). There were no significant differences detected between the 250 mg/day group and the 500 mg/day group on impulsivity ($p=0.13$) (Table 26).

At visit 3, no significant difference was detected between the Placebo group and the 500 mg/day group on inattention ($p=0.46$) or impulsivity ($p=0.48$) (Table 27).

The Placebo group showed significantly lower scores on inattention at visit 3 compared to the 250 mg/day group ($p<0.01$). There were no significant differences detected between the 250 mg/day group and the Placebo group on impulsivity ($p=0.56$) (Table 27a).

When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall analysis, there were significant differences at visit 3 on inattention ($p<0.01$). Post-hoc analyses showed that the 500 mg/day group ($p<0.01$) and the Placebo group ($p<0.01$) showed significantly lower scores on inattention than the 250 mg/day group. No significant differences between groups were detected on impulsivity at visit 3 ($p=0.20$) (Table 28).

Comparisons between Groups for Difference Scores

No significant differences were detected between the 250 mg/day group and the 500 mg/day group on differences in scores from visit 1 to visit 3 for inattention ($p=0.27$) or impulsivity ($p=0.77$) (Table 26).

5 No significant differences were detected between the Placebo group and the 500 mg/day group on differences in scores from visit 1 to visit 3 for inattention ($p=0.61$) or impulsivity ($p=0.39$) (Table 27).

10 No significant differences were detected between the 250 mg/day group and the Placebo group on differences in scores from visit 1 to visit 3 for inattention ($p=0.10$) or impulsivity ($p=0.26$) (Table 27a).

When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall analysis, no significant differences between groups were detected for inattention ($p=0.11$) or impulsivity ($p=0.25$) (Table 29).

15 *Conner-Wells Self-Report Scale (L) (Conners)*

Comparisons within Groups for Difference scores

On the Conners, the 250 mg/day group showed significant *increases* between visit 1 and visit 3 in problem behaviors, with visit 3 having higher scores than visit 1 ($p=0.02$) (Table 30).

20 The Placebo group showed a trend toward a significant declines in problem behaviors between visit 1 and visit 3 ($p=0.07$) (Table 31).

The 500 mg/day group showed significant declines in problem behaviors between visit 1 and visit 3 ($p<0.01$) (Table 32).

25 *Comparisons between Groups at Time 3*

At visit 3, the 500 mg/day group showed significantly lower scores on problem behaviors than the 250 mg/day group ($p=0.01$) (Table 33).

30 No significant difference was detected between the Placebo group and the 500 mg/day group during visit 3 on the Conners in problem behaviors ($p=0.28$) (Table 34).

At visit 3, no significant difference was detected between the 250 mg/day group and the Placebo group on the Conners in problem behaviors ($p=0.10$) (Table 34a).

When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall analysis, there were significant differences between groups on problem behaviors on the Conners ($p=0.01$). Post-hoc analyses showed that the 500 mg/day group had significantly lower scores on problem behaviors than the 250 mg/day group ($p=0.01$). There was also a trend toward the Placebo group having lower scores on problem behaviors at visit 3 compared to the 250 mg/day group ($p=0.09$) (Table 35).

Comparisons between Groups for Difference Scores

There were no significant differences between visit 1 and visit 3 in problem behaviors when the 250 mg/day and 500 mg/day group were compared ($p=0.36$) (Table 33).

There were no significant differences between visit 1 and visit 3 in problem behaviors when the Placebo and 500 mg/day group were compared ($p=0.17$) (Table 34).

There were no significant differences between visit 1 and visit 3 in problem behaviors when the 250 mg/day and Placebo group were compared ($p=0.66$) (Table 34a).

On the Conners, when the visit 1 to visit 3 difference scores for the 250 mg/day, Placebo and 500 mg/day groups were compared, there was no significant difference detected between groups in problem behaviors ($p=0.20$) (Table 36).

Pittsburgh Sleep Quality Index (PSQI)

Comparisons within Groups for Difference scores

On the PSQI, the 250 mg/day group showed a significant difference in sleep quality between visit 1 and visit 3 ($p<0.01$) (Table 37).

The Placebo group showed a significant difference in sleep quality between visit 1 and visit 3 ($p<0.01$) (Table 38).

On the PSQI, the 500 mg/day group showed a significant difference in sleep quality

Between visit 1 and visit 3 ($p<0.01$) (Table 39).

Comparisons between Groups at Time 3

At visit 3, no significant difference was evident between the 250 mg/day and the 500 mg/day group on the PSQI in sleep quality ($p=0.77$) (Table 40).

No significant difference was detected between the Placebo group and the
5 500 mg/day group during visit 3 on the PSQI in sleep quality ($p=0.83$) (Table 40).

No significant difference was detected between the 250 mg/day group and the Placebo group during visit 3 on the PSQI in sleep quality ($p=0.60$) (Table 41a).

When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall analysis, no significant differences between groups were detected in sleep
10 quality on the PSQI ($p=0.44$) (Table 42).

Comparisons between Groups for Difference Scores

The 250 mg/day group did not demonstrate a significant difference in sleep quality on the PSQI than the 500 mg/day group between visit 1 and visit 3 ($p=0.82$) (Table 40).

15 On the PSQI, there was no significant difference between the Placebo group and the 500 mg/day group from visit 1 to visit 3 in sleep quality ($p=0.92$) (Table 41).

The 250 mg/day group did not demonstrate a significant difference in sleep quality on the PSQI than the Placebo group between visit 1 and visit 3 ($p=0.72$) (Table 41a).

20 On the PSQI, when the visit 1 to visit 3 difference scores for the 250 mg/day, Placebo and 500 mg/day groups were compared, there was no significant difference detected between groups in sleep quality ($p=0.47$) (Table 43).

General Questionnaire

25 The General Questionnaire included five summary categories (Vision, Depression, Attention, Sleep, and Complexion) each of which had multiple individual items. Within and between group analyses are reported below for each of the summary categories.

Comparisons within Groups for Difference scores

30 The 250 mg/day group showed improvement between visit 1 and visit 3 on total vision ($p<0.01$), depression ($p<0.01$), attention ($p=0.04$), and sleep ($p<0.01$). The

250 mg/day group also demonstrated a trend toward improved complexion ($p=0.09$) (Table 44).

The Placebo group showed improvement between visit 1 and visit 3 on total vision ($p<0.01$), depression ($p<0.01$), attention ($p<0.01$), sleep ($p<0.01$), and complexion ($p<0.01$) (Table 45).

The 500 mg/day group showed improvement between visit 1 and visit 3 on total vision ($p<0.01$), depression ($p<0.01$), attention ($p=0.01$), sleep ($p<0.01$), and complexion ($p<0.01$) (Table 46).

Comparisons between Groups at Time 3

At visit 3, the 500 mg/day group showed lower scores on depression ($p=0.03$) and attention ($p=0.04$) compared to the 250 mg/day group. No significant differences were evident between the 250 mg/day and the 500 mg/day group in vision ($p=0.24$), sleep ($p=0.50$) and complexion ($p=0.12$) (Table 47).

No significant differences were detected between the Placebo group and the 500 mg/day group during visit 3 for scores on vision ($p=0.60$), depression ($p=0.28$), attention ($p=0.58$), sleep ($p=0.57$), and complexion ($p=0.31$) (Table 48).

At visit 3, no significant differences were detected between the 250 mg/day group and the Placebo group for scores on vision ($p=0.13$), depression ($p=0.15$), attention ($p=0.11$), sleep ($p=0.24$), and complexion ($p=0.49$) (Table 48a).

When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall analysis, there were significant differences between groups on depression ($p=0.02$) and attention ($p=0.03$). Post-hoc analyses showed that the 500 mg/day group showed lower scores on depression ($p=0.02$) and attention ($p=0.04$) on visit 3 compared to the 250 mg/day group. There was also a trend toward lower scores in the Placebo group on attention compared to the 250 mg/day group ($p=0.09$) (Table 48a).

Comparisons between Groups for Difference Scores

Difference scores were created by subtracting individual scores at visit 1 from individual scores at visit 3. There were no significant differences between the 250 mg/day group and the 500 mg/day group on improvement from visit 1 to visit 3 for vision ($p=0.38$), depression ($p=0.40$), attention ($p=0.91$), sleep ($p=0.17$), and complexion ($p=0.23$) (Table 47).

There were no significant differences between the Placebo group and the 500 mg/day group on improvement from visit 1 to visit 3 for vision ($p=0.51$), depression ($p=0.91$), attention ($p=0.94$), sleep ($p=0.79$), and complexion ($p=0.80$) (Table 48).

There were no significant differences between the 250 mg/day group and the Placebo group on improvement from visit 1 to visit 3 for vision ($p=0.84$), depression ($p=0.48$), attention ($p=0.95$), sleep ($p=0.24$), and complexion ($p=0.21$) (Table 48a).

When the visit 1 to visit 3 difference scores for the 250 mg/day, Placebo and 500 mg/day groups were compared overall, there were no significant differences between groups on vision ($p=0.33$), depression ($p=0.32$), attention ($p=0.50$), sleep ($p=0.14$), and complexion ($p=0.16$) (Table 50).

Exercise/Lifestyle Questionnaire

The Exercise/Lifestyle Questionnaire included four summary categories (Exercise, Appetite, Smoke, and Alcohol), each of which consisted of multiple individual items.

Within and between group analyses are reported below for each of the summary categories.

Comparisons within Groups for Difference scores

The 250 mg/day group showed a trend toward differences between visit 1 and visit 3 for appetite ($p=0.08$). There was no significant change in exercise ($p=0.29$) or smoking ($p=0.16$) from visit 1 to visit 3. Comparisons could not be calculated for alcohol use due to mean scores being unchanged from visit 1 to visit 3 (Table 51).

The Placebo group showed significant differences between visit 1 and visit 3 for appetite ($p<0.01$). There was no significant change in exercise ($p=0.20$) or alcohol use ($p=0.16$) from visit 1 to visit 3. Comparisons could not be calculated for smoking due to mean scores being unchanged from visit 1 to visit 3 (Table 52).

The 500 mg/day group showed significant differences between visit 1 and visit 3 for exercise ($p<0.01$). There was also a trend toward changes in appetite from visit 1 to visit 3 ($p=0.09$). Comparisons could not be calculated for smoking and alcohol use due to mean scores being unchanged from visit 1 to visit 3 (Table 53).

Comparisons between Groups at Visit 3

Between group comparisons for scores at visit 3 indicated significant differences between 250 mg/day and 500 mg/day for appetite ($p=0.04$). There were no

significant differences between the 250 mg/day group and the 500 mg/day group for exercise ($p=0.83$), smoking ($p=0.35$), or alcohol consumption ($p=0.35$) (Table 54).

No significant differences were found between the Placebo and the 500 mg/day group at visit 3 in exercise ($p=0.47$) or appetite ($p=0.53$). Comparisons could not be
5 calculated for smoking and alcohol use due to mean scores being identical across groups at visit 3 (Table 55).

At visit 3, there were significant differences between the 250 mg/day and Placebo group on appetite ($p<0.01$). No significant differences were found between the 250 mg/day and the Placebo group at visit 3 in exercise ($p=0.39$), smoking ($p=0.35$), or alcohol use
10 ($p=0.35$) (Table 55a).

When all three groups were included in an analysis of variance, there were significant differences between the 250 mg/day, Placebo, and 500 mg/day group on appetite ($p=.01$). Post-hoc analyses showed that the 250 mg/day group had significantly higher scores on appetite compared to the 500 mg/day ($p=0.04$) and Placebo ($p=0.01$)
15 groups. No significant differences were detected at visit 3 on exercise ($p=0.41$), smoking ($p=0.21$), or alcohol ($p=0.21$) (Table 56).

Comparisons between Groups For Difference Scores

There were no significant differences in scores from visit 1 to visit 3 between the 250 mg/day group and 500 mg/day group on exercise ($p=0.27$), appetite ($p=0.74$),
20 or smoking ($p=0.35$). Comparisons could not be calculated for alcohol use due to difference scores being unchanged from visit 1 to visit 3 (Table 54).

There were no significant differences in scores from visit 1 to visit 3 between the Placebo group and 500 mg/day group on exercise ($p=0.44$), appetite ($p=0.34$), or alcohol use ($p=0.32$). Comparisons could not be calculated for smoking due to difference scores
25 being unchanged from visit 1 to visit 3 (Table 55).

There were no significant differences in scores from visit 1 to visit 3 between the 250 mg/day group and Placebo group on exercise ($p=0.79$), appetite ($p=0.11$), smoking ($p=0.35$), or alcohol use ($p=0.29$) (Table 55a).

When all three groups were included in an analysis of variance, no significant
30 differences were detected for change between visit 1 and visit 3 on exercise ($p=0.28$), appetite ($p=0.17$), smoking ($p=0.21$), or alcohol ($p=0.18$) (Table 57).

Neuropsychological Assessments*Finger Tap Test**Comparisons within Groups for Difference scores*

The 250 mg/day group showed significant increases in scores between visit 1 and
 5 visit 3 on mean dominant hand ($p < 0.01$) and the mean non-dominant hand ($p < 0.01$)
 (Table 58).

For the Placebo group, there were significant increases in scores between visit 1 and visit
 3 on mean non-dominant hand ($p = 0.04$). There were no significant differences between
 visit 1 and 3 for mean dominant hand ($p = 0.19$) (Table 59).

10 The 500 mg/day group showed significant increases in scores between visit 1 and
 visit 3 on mean dominant hand ($p < 0.01$) and the mean non-dominant hand ($p < 0.01$)
 (Table 60).

Comparisons between Groups at Time 3

At visit 3, no significant differences were found between the 250 mg/day and
 15 the 500 mg/day group on mean dominant hand ($p = 0.75$) or mean non-dominant hand
 ($p = 0.96$) (Table 61).

No significant differences were found between the Placebo and the 500 mg/day
 group at visit 3 on mean dominant hand ($p = 0.68$) or mean non-dominant hand ($p = 0.88$)
 (Table 62).

20 At visit 3, no significant differences were found between the 250 mg/day and the Placebo
 group on mean dominant hand ($p = 0.88$) or mean non-dominant hand ($p = 0.85$) (Table 62a).
 When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall
 analysis, no significant differences between groups were detected on mean dominant hand
 ($p = 0.45$) or mean non-dominant hand ($p = 0.49$) (Table 63).

25

Comparisons between Groups for Difference Scores

The 250 mg/day group demonstrated a trend toward greater increases from visit 1
 to visit 3 for the dominant hand compared to group 500 mg/day ($p = 0.08$). There were no
 significant differences in scores for the non-dominant hand from visit 1 to 3 between the
 30 250 mg/day and 500 mg/day groups ($p = 0.78$) (Table 61).

There were no significant differences in scores from visit 1 to 3 between the Placebo and 500 mg/day groups on mean dominant hand ($p=0.16$) or mean non-dominant hand ($p=0.64$) (Table 62).

5 The 250 mg/day group showed significantly greater increases from visit 1 to visit 3 for the mean dominant hand score compared to group Placebo ($p<0.01$). There were no significant differences in scores for the non-dominant hand from visit 1 to 3 between the 250 mg/day and Placebo groups ($p=0.47$) (Table 62a).

10 When the visit 1 to visit 3 difference scores for the 250 mg/day, Placebo and 500 mg/day groups were compared, there were significant differences detected between groups on mean dominant hand ($p<0.01$). Post-hoc analyses showed that the 250 mg/day group showed greater differences in scores from visit 1 to 3 on dominant hand compared to the Placebo group. There were no significant differences in scores from visit 1 to 3 between groups for mean non-dominant hand ($p=0.37$) (Table 64).

15 *California Verbal Learning Test I & II (CVLT I & II)*

Comparisons within Groups for Difference scores

The 250 mg/day group showed significant improvement between visit 1 and visit 3 on CVLT List A Trial 1 ($p<0.01$), List A Short Delay ($p=0.01$), and List A Long Delay ($p=0.04$). There was a trend toward increases in scores for List A Trials 1-5 ($p=0.06$)
20 between visit 1 and 3. There were no significant improvements detected on the List A Trial 5 ($p=0.10$) and List B ($p=0.12$) (Table 65).

The Placebo group showed significant improvement on the CVLT between visit 1 and visit 3 on List A Trial 1 ($p<0.01$), List A Trials 1-5 ($p=0.01$) and List A Long Delay ($p<0.01$). There was no significant improvement for the Placebo group on the CVLT
25 between visit 1 and visit 3 on List A Trial 5 ($p=0.20$), List B ($p=0.46$), or List A Short Delay ($p=0.12$) (Table 66).

The 500 mg/day group showed significant improvement on the CVLT between visit 1 and visit 3 on List A Trial 1 ($p=0.02$), List A Trial 5 ($p=0.04$), List A Trials 1-5 ($p=0.02$), List A Short Delay ($p=0.03$) and List A Long Delay ($p=0.01$). There was no
30 significant improvement for the Placebo group on the CVLT between visit 1 and visit 3 on List B ($p=0.25$) (Table 67).

Comparisons between Groups at Time 3

At time 3, no significant differences between the 250 mg/day group and the 500 mg/day group were found for CVLT performance on List A Trial 1 ($p=0.81$), List A Trial 5 ($p=0.85$), List A Trials 1-5 ($p=0.80$), List B ($p=0.90$), List A Short Delay ($p=0.67$), and List A Long Delay ($p=0.87$) (Table 68).

At time 3, there was a trend toward greater improvement in the Placebo group compared to the 500 mg/day group for List A Long Delay ($p=0.07$). No significant differences between the Placebo group and the 500 mg/day group were found for CVLT performance on List A Trial 1 ($p=0.60$), List A Trial 5 ($p=0.41$), List A Trials 1-5 ($p=0.21$), List B ($p=0.80$), or List A Short Delay ($p=0.25$) (Table 69).

At time 3, no significant differences between the 250 mg/day group and the 500 mg/day group were found for CVLT performance on List A Trial 1 ($p=0.82$), List A Trial 5 ($p=0.60$), List A Trials 1-5 ($p=0.35$), List B ($p=0.68$), List A Short Delay ($p=0.51$), and List A Long Delay ($p=0.15$) (Table 69a).

Analyses including all three groups, the Placebo group, the 250 mg/day group and the 500 mg/day group, indicated no significant differences for List A Trial 1 ($p=0.45$), List A Trial 5 ($p=0.37$), List A Trials 1-5 ($p=0.24$), List B ($p=0.46$), List A Short Delay ($p=0.28$), or List A Long Delay ($p=0.10$) (Table 70).

Comparisons between Groups for Difference Scores

There were no significant differences in performance between visits 1 and 3 between groups 250 mg/day and 500 mg/day on List A Trial 1 ($p=0.33$), List A Trial 5 ($p=0.56$), List A Trials 1-5 ($p=0.81$), List B ($p=0.20$), List A Short Delay ($p=0.90$), and List A Long Delay ($p=0.63$) (Table 68).

There were no significant differences in performance between visits 1 and 3 between groups Placebo and 500 mg/day on List A Trial 1 ($p=0.79$), List A Trial 5 ($p=0.50$), List A Trials 1-5 ($p=0.91$), List B ($p=0.65$), List A Short Delay ($p=0.69$), and List A Long Delay ($p=0.71$) (Table 69).

There were no significant differences in performance between visits 1 and 3 between groups 250 mg/day and Placebo on List A Trial 1 ($p=0.43$), List A Trial 5 ($p=0.87$), List A Trials 1-5 ($p=0.72$), List B ($p=0.37$), List A Short Delay ($p=0.59$), and List A Long Delay ($p=0.40$) (Table 69a).

Analyses including all three groups, the Placebo group, the 250 mg/day group and the 500 mg/day group, indicated no significant differences for List A Trial 1 ($p=0.28$), List A Trial 5 ($p=0.38$), List A Trials 1-5 ($p=0.47$), List B ($p=0.20$), List A Short Delay ($p=0.42$), or List A Long Delay ($p=0.35$) (Table 71).

5

Rey-Osterreith Complex Figure Test (ROCFT)

Comparisons within Groups for Difference scores

The 250 mg/day group showed significant improvement between visit 1 and visit 3 on the Immediate Raw Score ($p<0.01$), Delayed Raw Score ($p<0.01$), and the Difference Raw Score ($p=0.03$). There was no significant improvement detected on the Copy Raw Score ($p=0.38$) (Table 72).

The Placebo group showed significant improvement between visit 1 and visit 3 on the Immediate Raw Score ($p<0.01$), Delayed Raw Score ($p<0.01$). There were no significant improvements detected on the Copy Raw Score ($p=0.35$) or the Difference Raw Score ($p=0.27$) (Table 73).

The 500 mg/day group showed significant improvement between visit 1 and visit 3 on the Immediate Raw Score ($p<0.01$), Delayed Raw Score ($p<0.01$). There were no significant improvements detected on the Copy Raw Score ($p=0.38$) or the Difference Raw Score ($p=0.44$) (Table 74).

Comparisons between Groups at Time 3

At time 3, no significant differences between the 250 mg/day group and the 500 mg/day group were found for ROCFT performance on the Copy Raw Score ($p=0.68$), the Immediate Raw Score ($p=0.26$), the Delayed Raw Score ($p=0.14$) or the Difference Raw Score ($p=0.31$) (Table 75).

At time 3, no significant differences between the Placebo group and the 500 mg/day group were found for ROCFT performance on the Copy Raw Score ($p=0.43$), the Immediate Raw Score ($p=0.25$), the Delayed Raw Score ($p=0.24$) or the Difference Raw Score ($p=0.96$) (Table 76).

At time 3, no significant differences between the 250 mg/day group and the 500 mg/day group were found for ROCFT performance on the Copy Raw Score ($p=0.69$), the Immediate Raw Score ($p=0.99$), the Delayed Raw Score ($p=0.60$) or the Difference Raw Score ($p=0.30$) (Table 76a).

Analyses including all three groups, the Placebo group, the 250 mg/day group and the 500 mg/day group, indicated no significant differences for ROCFT performance on the Copy Raw Score ($p=0.36$), the Immediate Raw Score ($p=0.19$), the Delayed Raw Score ($p=0.11$) or the Difference Raw Score ($p=0.25$) (Table 77).

5 *Comparisons between Groups for Difference Scores*

There were no significant differences in performance between visits 1 and 3 between groups 250 mg/day and 500 mg/day for ROCFT performance on the Copy Raw Score ($p=1.00$), the Immediate Raw Score ($p=0.86$), the Delayed Raw Score ($p=0.26$) or the Difference Raw Score ($p=0.26$) (Table 75).

10 There were no significant differences between the Placebo group and the 500 mg/day group for ROCFT performance between visits 1 and 3 on the Copy Raw Score ($p=0.64$), the Immediate Raw Score ($p=0.92$), the Delayed Raw Score ($p=0.88$) or the Difference Raw Score ($p=0.78$) (Table 76).

15 There were no significant differences in performance between visits 1 and 3 between groups 250 mg/day and Placebo for ROCFT performance on the Copy Raw Score ($p=0.65$), the Immediate Raw Score ($p=0.79$), the Delayed Raw Score ($p=0.34$) or the Difference Raw Score ($p=0.35$) (Table 76a).

20 Analyses including all three groups, the Placebo group, the 250 mg/day group and the 500 mg/day group, indicated no significant differences for ROCFT performance between visits 1 and 3 on the Copy Raw Score ($p=0.44$), the Immediate Raw Score ($p=0.48$), the Delayed Raw Score ($p=0.23$) or the Difference Raw Score ($p=0.23$) (Table 78).

Stroop Color Word Test

25 *Comparisons within Groups for Difference scores*

On the Stroop, the 250 mg/day group showed significant improvement between visit 1 and visit 3 on the word trial ($p=0.04$), the color trial ($p<0.01$), the interference trial ($p<0.01$), and the difference between the interference trial and the word trial ($p<0.01$) (Table 79).

30 The Placebo group showed significant improvement between visit 1 and visit 3 on the color trial ($p<0.01$), the interference trial ($p<0.01$), and the difference between the

interference trial and the word trial ($p < 0.01$). There was a trend toward improvement on the word trial ($p = 0.06$) (Table 80).

The Placebo group showed significant improvement between visit 1 and visit 3 on the color trial ($p < 0.01$), the interference trial ($p < 0.01$), and the difference between the
 5 interference trial and the word trial ($p < 0.01$). There was a trend toward improvement on the word trial ($p = 0.07$) (Table 81).

Comparisons between Groups at Time 3

At visit 3, there were no significant differences between the 250 mg/day group and the 500 mg/day group in Stroop performance for the word trial ($p = 0.65$), the color
 10 trial ($p = 0.69$), the interference trial ($p = 0.68$), and the difference between the interference trial and the color trial ($p = 0.28$) (Table 82).

There were no significant differences between the Placebo group and the 500 mg/day group in Stroop performance during visit 3 for the word trial ($p = 0.98$), the color
 15 trial ($p = 0.46$), the interference trial ($p = 0.56$), and the difference between the interference trial and the color trial ($p = 0.46$) (Table 83).

At visit 3, there were no significant differences between the 250 mg/day group and the Placebo group in Stroop performance for the word trial ($p = 0.62$), the color trial
 ($p = 0.72$), the interference trial ($p = 0.84$), and the difference between the interference trial and the color trial ($p = 0.81$) (Table 83a).

Analyses that included all three groups showed no significant differences between
 20 groups during visit 3 for the word trial ($p = 0.43$), the color trial ($p = 0.38$), the interference trial ($p = 0.41$), and the difference between the interference trial and the color trial ($p = 0.27$) (Table 84).

Comparisons between Groups For Difference Scores

In Stroop performance between visit 1 and visit 3, there were no significant
 25 differences between the 250 mg/day group and the 500 mg/day group on the word trial ($p = 0.68$), the color trial ($p = 0.25$), the interference trial ($p = 0.53$), and the difference between the interference trial and the color trial ($p = 0.61$) (Table 82).

In Stroop performance between visit 1 and visit 3, there were no significant
 30 differences between the Placebo group and the 500 mg/day group on the word trial ($p = 0.96$), the color trial ($p = 0.91$), the interference trial ($p = 0.38$), and the difference between the interference trial and the color trial ($p = 0.45$) (Table 83).

In Stroop performance between visit 1 and visit 3, there were no significant differences between the 250 mg/day group and the Placebo group on the word trial ($p=0.63$), the color trial ($p=0.17$), the interference trial ($p=0.12$), and the difference between the interference trial and the color trial ($p=0.21$) (Table 83a).

5 Analyses including all three groups showed no significant differences between groups from visit 1 and visit 3 for the word trial ($p=0.43$), the color trial ($p=0.17$), the interference trial ($p=0.16$), and the difference between the interference trial and the color trial ($p=0.23$) (Table 85).

Continuous Performance Test (CPT)

10 *Comparisons within Groups for Difference scores*

The 250 mg/day group showed a significant difference between visit 1 and visit 3 on hit reaction time ($p<0.01$). A trend toward a difference was detected on number of omission errors ($p=0.08$). There were no changes between visit 1 and 3 on commission errors ($p=0.15$) (Table 86).

15 The Placebo group showed significant improvement between visit 1 and visit 3 on number of commission errors ($p=0.03$). No significant change was detected on number of omission errors ($p=0.13$) or hit reaction time ($p=0.18$) (Table 87).

The 500 mg/day group showed a significant difference between visit 1 and visit 3 on commission errors ($p<0.01$) and hit reaction time ($p<0.01$). A trend toward a
20 difference was detected on number of omission errors ($p=0.06$) (Table 88).

Comparisons Between Groups for Time 3 scores

At visit 3, there were no significant differences between the 250 mg/day and the 500 mg/day group for omission errors ($p=0.89$), commission errors ($p=0.45$), or hit reaction time ($p=0.78$) (Table 89).

25 There were no significant differences between the Placebo and the 500 mg/day group for omission errors ($p=0.55$), commission errors ($p=0.87$), or hit reaction time ($p=0.98$) during visit 3 (Table 90).

At visit 3, there were no significant differences between the 250 mg/day and the Placebo group for omission errors ($p=0.39$), commission errors ($p=0.36$), or hit
30 reaction time ($p=0.79$) (Table 90a).

Analyses including all three groups indicated no significant between group differences at visit 3 on omission errors ($p=0.35$), commission errors ($p=0.31$), or hit reaction time ($p=0.48$) (Table 91).

Comparisons between Groups For Difference Scores

5 Between visit 1 and visit 3, there were no significant differences between the 250 mg/day group and the 500 mg/day group in omission errors ($p=0.93$), commission errors ($p=0.10$), or hit reaction time ($p=0.68$) (Table 89).

There were no significant differences between the Placebo group and the 500 mg/day group in omission errors ($p=0.67$), commission errors ($p=0.35$), or hit reaction
10 time ($p=0.18$) between visit 1 and visit 3 (Table 90).

Between visit 1 and visit 3, there were no significant differences between the 250 mg/day group and the Placebo group in omission errors ($p=0.75$), commission errors ($p=0.49$), or hit reaction time ($p=0.12$) (Table 90a).

When analyses were conducted including all three groups, no significant
15 differences in difference scores between visit 1 and 3 were detected for omission errors ($p=0.46$), commission errors ($p=0.13$), or hit reaction time ($p=0.12$) (Table 92).

Ruff 2 & 7 Test

20 *Comparisons within Groups for Difference scores*

The 250 mg/day group showed significant differences between visit 1 and visit 3 on the total speed score ($p<0.01$) and total accuracy score ($p<0.01$). No significant differences were detected on the speed difference score ($p=0.43$), accuracy difference score ($p=0.26$), or total difference score ($p=0.40$) (Table 93).

25 The Placebo group showed significant differences between visit 1 and visit 3 on the total speed score ($p<0.01$), total accuracy score ($p<0.01$), and total difference score ($p<0.01$). No significant differences were detected on the speed difference score ($p=0.26$) or accuracy difference score ($p=0.30$) (Table 94).

30 The 500 mg/day group showed significant differences between visit 1 and visit 3 on the total speed score ($p<0.01$), total accuracy score ($p<0.01$), speed difference score ($p=0.05$), and accuracy difference score ($p=0.01$). No significant differences were detected on the total difference score ($p=0.22$) (Table 95).

Comparisons between Groups at Time 3

At time 3, there were no significant differences between the 250 mg/day and 500 mg/day group on the total speed score ($p=0.72$), total accuracy score ($p=0.10$), speed difference score ($p=0.38$), accuracy difference score ($p=0.14$), or the total difference score ($p=0.37$) (Table 96).

At time 3, there were significant differences between Placebo group and 500 mg/day group on the total difference score ($p=0.04$), and there was a trend toward a difference in the accuracy difference score ($p=0.09$). There were no significant differences between the Placebo and 500 mg/day group on the total speed score ($p=0.23$), total accuracy score ($p=0.60$), or speed difference score ($p=0.32$) (Table 97).

At time 3, there were no significant differences between the 250 mg/day and Placebo group on the total speed score ($p=0.13$), total accuracy score ($p=0.30$), speed difference score ($p=0.87$), accuracy difference score ($p=0.81$), or the total difference score ($p=0.15$) (Table 97a).

Analyses including all three groups showed a trend toward significant differences between the 250 mg/day, Placebo, and 500 mg/day groups for the total difference score ($p=0.06$). Post-hoc analyses indicated a trend toward differences between the Placebo and 500 mg/day group ($p=0.05$). No significant differences were found between groups on the total speed score ($p=0.14$), total accuracy score ($p=0.14$), speed difference score ($p=0.26$), or accuracy difference score ($p=0.12$) (Table 98).

Comparisons between Groups for Difference Scores

There were no significant differences between the 250 mg/day and 500 mg/day group in scores between visit 1 and visit 3 on the total speed score ($p=0.84$), total accuracy score ($p=0.51$), speed difference score ($p=0.26$), accuracy difference score ($p=0.19$), or the total difference score ($p=0.61$) (Table 96).

Between visit 1 and 3, there were significant differences between Placebo group and 500 mg/day group on the total difference score ($p=0.02$), and there was a trend toward a difference in the total speed score ($p=0.05$). There were no significant differences between the Placebo and 500 mg/day group on the total accuracy score ($p=0.89$), the speed difference score ($p=0.13$), or the accuracy difference score ($p=0.19$) (Table 97).

There were significant differences between 250 mg/day group and Placebo group between visit 1 and 3 on the total difference score ($p=0.02$), and there was a trend toward a difference in the total speed score ($p=0.05$). There were no significant differences between the 250 mg/day and Placebo group on the total accuracy score ($p=0.42$), the speed difference score ($p=0.52$), or the accuracy difference score ($p=0.96$) (Table 97a).

Comparison of differences between the three groups on differences in scores from visit 1 to visit 3 indicated significant differences between groups on the total difference score ($p=0.01$), and a trend toward differences on the total speed score ($p=0.05$). Post-hoc analyses revealed significant differences in the total difference score between the Placebo and 500 mg/day groups ($p=0.01$), as well as a trend toward differences in the total speed score between the Placebo and 500 mg/day groups ($p=0.06$) and the 250 mg/day and Placebo groups ($p=0.08$). There were no differences between the three groups on the total accuracy score ($p=0.36$), the speed difference score ($p=0.31$), or the accuracy difference score ($p=0.16$) (Table 99).

Wisconsin Card Sorting Test (WCST)

Comparisons between Groups at Time 3

There were no significant differences between the 250 mg/day group and the 500 mg/day group in WCST performance during visit 3 for total cards used ($p=0.81$), number of categories achieved ($p=0.39$), total number of errors ($p=0.87$), total number of perseverative errors ($p=0.68$), number of trials to get into category ($p=0.68$), or number of trials to complete the categories ($p=0.84$) (Table 100).

There was a trend toward increased total errors at visit in the 500 mg/day group compared to the Placebo group ($p=0.08$). There were no significant differences between the Placebo group and the 500 mg/day group during visit 3 for total cards used ($p=0.42$), number of categories achieved ($p=0.39$), total number of perseverative errors ($p=0.25$), number of trials to get into category ($p=0.18$), and number of trials to complete the categories ($p=0.72$) (Table 101).

There were no significant differences between the 250 mg/day group and the Placebo group in WCST performance during visit 3 for total cards used ($p=0.30$), number of categories achieved ($p=0.16$), total number of errors ($p=0.14$), total number

of perseverative errors ($p=0.44$), number of trials to get into category ($p=0.25$), or number of trials to complete the categories ($p=0.88$) (Table 101a).

Between the Placebo group, the 250 mg/day group and the 500 mg/day group, no significant differences were detected between groups during visit 3 of the WCST for total number of cards used ($p=0.28$), number of categories achieved ($p=0.14$), total number of errors ($p=0.13$), total number of perseverative errors ($p=0.26$), number of trials to get into category ($p=0.22$), or number of trials to complete the categories ($p=0.47$) (Table 102).

Trail Making Test

Comparisons within Groups for Difference scores

On the Trail Making Test, the 250 mg/day group showed significant improvements in scores between visit 1 and visit 3 in performance times for test A ($p=0.03$), test B ($p<0.01$), and B-A test difference ($p<0.01$) (Table 104).

The Placebo group showed significant improvements in scores between visit 1 and visit 3 in performance times for test A ($p<0.01$), test B ($p<0.01$), and B-A test difference ($p=0.03$) (Table 105).

Between visit 1 and 3, the 500 mg/day group showed significant improvements in scores in performance times for test A ($p<0.01$) and test B ($p=0.03$). There were no significant improvements in the B-A test difference between visit 1 and visit 3 for the 500 mg/day group ($p=0.25$) (Table 106).

Comparisons between Groups at Time 3

During visit 3, there were no significant differences between the 250 mg/day group and the 500 mg/day group in Trail Making performance times for test A ($p=0.93$), test B ($p=0.15$), and the B-A test difference ($p=0.14$) (Table 107).

There were no significant differences between the Placebo group and the 500 mg/day group during visit 3 for the performance times for test A ($p=0.48$), test B ($p=0.20$), and the B-A test difference ($p=0.26$) (Table 108).

During visit 3, there were no significant differences between the 250 mg/day group and the Placebo group in Trail Making performance times for test A ($p=0.48$), test B ($p=0.98$), and the B-A test difference ($p=0.69$) (Table 108a).

Analyses including all three groups at visit 3 showed significant differences between groups in performance times for test A ($p=0.37$), test B ($p=0.10$), and the B-A test difference ($p=0.11$) (Table 109).

Comparisons between Groups For Difference Scores

5 In differences in performance times between visit 1 and visit 3, there was a trend toward a difference between the 250 mg/day and 500 mg/day groups on the B-A test difference score ($p=0.08$). There were no significant differences between the 250 mg/day group and the 500 mg/day group in performance time differences for test A ($p=0.16$) or test B ($p=0.17$) (Table 107).

10 In differences in performance times between visit 1 and visit 3, there were no significant differences between the Placebo group and the 500 mg/day group in performance time differences for test A ($p=0.90$), test B ($p=0.51$), or the B-A test difference score ($p=0.57$) (Table 108).

15 In differences in performance times between visit 1 and visit 3, there were no significant differences between the 250 mg/day group and the Placebo group in performance time differences for test A ($p=0.16$), test B ($p=0.35$), or the B-A test difference score ($p=0.14$) (Table 108a).

20 Between the Placebo group, the 250 mg/day group and the 500 mg/day group, there was a positive trend towards improvement between visit 1 and visit 3 on the B-A test difference score ($p=0.06$). Post-hoc analyses showed a trend toward a difference in 250 mg/day and 500 mg/day groups ($p=0.06$). No significant differences from visit 1 to visit 3 were detected between the Placebo group, the 250 mg/day group and the 500 mg/day group for test A ($p=0.12$) or test B ($p=0.15$) difference scores between visit 1 and 3 (Table 110).

25

Adverse Events

Monitoring of Side Effects Scale (MOSES)

Comparisons within Groups for Difference scores

30 On the MOSES, there were no significant differences for the 250 mg/day group ($p=0.34$) between visit 2 and 3 (Table 111).

There were no significant differences for the Placebo group between visit 2 and 3 on the MOSES ($p=0.42$) (Table 112).

On the MOSES, there was a trend toward significant differences for the 500 mg/day group ($p=0.07$) between visit 2 and 3 (Table 113).

5 Comparisons between Groups at Time 3

At visit 3, no significant difference was evident between the 250 mg/day and the 500 mg/day group on the MOSES ($p=0.11$) (Table 114).

No significant difference was detected between the Placebo group and the 500 mg/day group during visit 3 on MOSES ($p=0.85$) (Table 115).

At visit 3, no significant difference was evident between the 250 mg/day and the Placebo group on the MOSES ($p=0.21$) (Table 115a).

When the 250 mg/day, Placebo, and the 500 mg/day groups were included in an overall analysis, no significant differences between groups were detected on the MOSES ($p=0.23$) (Table 116).

15 *Comparisons between Groups for Difference Scores*

On the MOSES, there were no significant differences between the 250 mg/day group and the 500 mg/day group from visit 1 to visit 3 ($p=0.64$) (Table 114).

There were no significant differences between the Placebo group and the 500 mg/day group from visit 1 to visit 3 ($p=0.30$) (Table 115).

20 On the MOSES, there were no significant differences between the 250 mg/day group and the Placebo group from visit 1 to visit 3 ($p=0.70$) (Table 115a).

There were no significant differences between group difference scores for groups 250 mg/day, Placebo, and 500 mg/day on the MOSES ($p=0.66$) (Table 117).

Table 1

	250 mg/day group (N=27)	Placebo group (N=24)	500 mg/day group (N=24)
Age (+ SD)	15.33 + 1.69	15.71 + 1.73	15.50 + 1.75
Education (years)	8.96 + 1.65	9.42 + 1.82	9.04 + 1.90
Height (in) (baseline)	66.96 + 3.90	67.70 + 4.24	67.86 + 3.34
Weight (lbs) (baseline)	129.48 + 26.16	138.38 + 31.55	142.98 + 37.84
IQ (baseline)	105.00 + 11.11	107.33 + 9.50	107.21 + 9.48

Subject Demographics

Table 2
PANAS-C Visit 1 to Visit 3: 250 mg/day group

PANAS-C	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Positive Score V1	45.74	6.68	< .01	.01
Positive Score V3	41.93	8.77		
Negative Score V1	23.15	5.15	< .01	< .01
Negative Score V3	19.81	5.29		

Table 3
PANAS-C Visit 1 to Visit 3: Placebo group

5

PANAS-C	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Positive Score V1	45.42	6.35	.09	.19
Positive Score V3	43.83	8.48		
Negative Score V1	23.08	4.91	.03	.06
Negative Score V3	20.92	4.93		

Table 4
PANAS-C Visit 1 to Visit 3: 500 mg/day group

PANAS-C	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Positive Score V1	43.30	7.39	.04	.08
Positive Score V3	41.78	7.58		
Negative Score V1	21.55	6.26	< .01	.01
Negative Score V3	18.00	3.57		

Table 5
PANAS-C Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Positive Score	41.93	8.77	41.78	7.58	.95
V3 Negative Score	19.81	5.29	18.00	3.57	.18
V3-V1 Positive Score	-3.81	7.25	-1.52	4.02	.18
V3-V1 Negative Score	-3.33	5.20	-3.55	5.93	.89

5

Table 6
PANAS-C Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Positive Score	43.83	8.48	41.78	7.58	.39
V3 Negative Score	20.92	4.93	18.00	3.57	.03
V3-V1 Positive Score	-1.58	5.72	-1.52	4.02	.97
V3-V1 Negative Score	-2.17	5.26	-3.55	5.93	.41

10

Table 6a
PANAS-C Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Positive Score	41.93	8.77	43.83	8.48	.44
V3 Negative Score	19.81	5.29	20.92	4.93	.45
V3-V1 Positive Score	-3.81	7.25	-1.58	5.72	.23
V3-V1 Negative Score	-3.33	5.20	-2.17	5.26	.43

Table 7
PANAS-C Visit 3: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
Positive Score	.63	-	.32	-
500 mg/day vs. 250 mg/day	-	1.00	-	.50
500 mg/day vs. Placebo	-	.68	-	.34
250 mg/day vs. Placebo	-	.69	-	.35
Negative Score	.12	-	.06	-
500 mg/day vs. 250 mg/day	-	.38	-	.19
500 mg/day vs. Placebo	-	.10	-	.05
250 mg/day vs. Placebo	-	.68	-	.34

Table 8
5 PANAS-C Visit Difference Scores: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
Positive Score	.29	-	.15	-
500 mg/day vs. 250 mg/day	-	.36	-	.18
500 mg/day vs. Placebo	-	1.00	-	.50
250 mg/day vs. Placebo	-	.37	-	.19
Negative Score	.65	-	.32	-
500 mg/day vs. 250 mg/day	-	1.00	-	.50
500 mg/day vs. Placebo	-	.67	-	.33
250 mg/day vs. Placebo	-	.73	-	.36

Table 9
CDRS Visit 1 to Visit 3: 250 mg/day group

CDRS	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 CDRS	16.89	1.42	.02	.03
V3 CDRS	16.22	.58		

Table 10
CDRS Visit 1 to Visit 3: Placebo group

5

CDRS	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 CDRS	16.25	.85	.42	.85
V3 CDRS	16.21	.51		

Table 11

CDRS	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 CDRS	16.33	.76	.03	.06
V3 CDRS	16.08	.28		

CDRS Visit 1 to Visit 3: 500 mg/day group

Table 12
CDRS Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 CDRS	16.22	.58	16.08	.28	.29
V3-V1 Score	-.67	1.52	-.25	.61	.22

5

Table 13

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 CDRS	16.21	.51	16.08	.28	.30
V3-V1 Score	-.04	1.04	-.25	.61	.40

CDRS Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

Table 13a
CDRS Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 CDRS	16.22	.58	16.21	.51	.93
V3-V1 Score	-.67	1.52	-.04	1.04	.10

Table 14
CDRS Visit 3: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall p (2-tailed)	Between Groups p (2-tailed)	Between Groups Overall p (1-tailed)	Between Groups p (1-tailed)
CDRS Score	.53	-	.27	-
500 mg/day vs. 250 mg/day	-	.56	-	.28
500 mg/day vs. Placebo	-	.64	-	.32
250 mg/day vs. Placebo	-	.99	-	.50

Table 15
CDRS Visit Difference Scores: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
CDRS Score	.14	-	.07	-
500 mg/day vs. 250 mg/day	-	.40	-	.20
500 mg/day vs. Placebo	-	.80	-	.40
250 mg/day vs. Placebo	-	.13	-	.07

Table 16
BIS Visit 1 to Visit 3: 250 mg/day group

BIS	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Attention V1	18.52	3.17	.44	.89
Attention V3	18.59	3.96		
Motor V1	22.22	4.72	.36	.73
Motor V3	22.00	5.43		
Non-planning V1	24.85	5.10	.30	.60
Non-planning V3	24.44	4.85		
Total V1	65.59	9.31	.35	.70
Total V3	65.04	11.35		

Table 17
BIS Visit 1 to Visit 3: Placebo group

5

BIS	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Attention V1	16.67	3.75	.45	.91
Attention V3	16.75	3.15		
Motor V1	20.21	3.65	.40	.80
Motor V3	20.04	3.37		
Non-planning V1	22.67	3.28	.09	.17
Non-planning V3	21.71	4.17		
Total V1	59.54	8.45	.22	.44
Total V3	58.50	7.52		

Table 18
BIS Visit 1 to Visit 3: 500 mg/day group

BIS	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Attention V1	16.54	3.70	.47	.94
Attention V3	16.50	4.17		
Motor V1	20.21	3.65	.40	.80
Motor V3	20.04	3.37		
Non-planning V1	22.67	3.28	.09	.17
Non-planning V3	21.71	4.17		
Total V1	59.63	8.38	.17	.34
Total V3	58.21	9.68		

Table 19
BIS Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Attention	18.59	3.96	16.50	4.17	.07
V3 Motor	22.00	5.43	19.29	3.79	.05
V3 Non-planning	24.44	4.85	22.42	4.13	.12
V3 Total	65.04	11.35	58.21	9.68	.03
V3-V1 Attention	.07	2.63	-.04	2.87	.88
V3-V1 Motor	-.22	3.27	-1.00	3.83	.44
V3-V1 Non-planning	-.41	4.03	-.38	3.90	.98
V3-V1 Total	-.56	7.41	-1.42	7.05	.67

5

Table 20
BIS Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Attention	16.75	3.15	16.50	4.17	.82
V3 Motor	20.04	3.37	19.29	3.79	.47
V3 Non-planning	21.71	4.17	22.42	4.13	.56
V3 Total	58.50	7.52	58.21	9.68	.91
V3-V1 Attention	.08	3.49	-.04	2.87	.89
V3-V1 Motor	-.17	3.16	-1.00	3.83	.42
V3-V1 Non-planning	-.96	3.32	-.38	3.90	.58
V3-V1 Total	-1.04	6.43	-1.42	7.05	.85

Table 20a
BIS Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Attention	18.59	3.96	16.75	3.15	.08
V3 Motor	22.00	5.43	20.04	3.37	.13
V3 Non-planning	24.44	4.85	21.71	4.17	.04
V3 Total	65.04	11.35	58.50	7.52	.02
V3-V1 Attention	.07	2.63	.08	3.49	.99
V3-V1 Motor	-.22	3.27	-.17	3.16	.95
V3-V1 Non-planning	-.41	4.03	-.96	3.32	.60
V3-V1 Total	-.56	7.41	-1.04	6.43	.81

Table 21
BIS Visit 3: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2- tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1- tailed)	Between Groups <i>p</i> (1-tailed)
Attention	.10	-	.05	-
500 mg/day vs. 250 mg/day	-	.13	-	.06
500 mg/day vs. Placebo	-	.97	-	.49
250 mg/day vs. Placebo	-	.20	-	.10
Motor	.08	-	.04	-
500 mg/day vs. 250 mg/day	-	.07	-	.04
500 mg/day vs. Placebo	-	.82	-	.41
250 mg/day vs. Placebo	-	.25	-	.12
Non-planning	.08	-	.04	-
500 mg/day vs. 250 mg/day	-	.24	-	.12
500 mg/day vs. Placebo	-	.84	-	.42
250 mg/day vs. Placebo	-	.08	-	.04
Total	.02	-	.01	-
500 mg/day vs. 250 mg/day	-	.04	-	.02
500 mg/day vs. Placebo	-	.99	-	.50
250 mg/day vs. Placebo	-	.05	-	.03

Table 22
BIS Visit Difference Scores: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2- tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1- tailed)	Between Groups <i>p</i> (1-tailed)
Attention	.99	-	.49	-
500 mg/day vs. 250 mg/day	-	.99	-	.50
500 mg/day vs. Placebo	-	.99	-	.49
250 mg/day vs. Placebo	-	1.00	-	.50
Motor	.64	-	.32	-
500 mg/day vs. 250 mg/day	-	.70	-	.35
500 mg/day vs. Placebo	-	.68	-	.34
250 mg/day vs. Placebo	-	1.00	-	.50
Non-planning	.83	-	.42	-
500 mg/day vs. 250 mg/day	-	1.00	-	.50
500 mg/day vs. Placebo	-	.85	-	.43
250 mg/day vs. Placebo	-	.86	-	.43
Total	.91	-	.45	-
500 mg/day vs. 250 mg/day	-	.90	-	.45
500 mg/day vs. Placebo	-	.98	-	.49
250 mg/day vs. Placebo	-	.97	-	.48

Table 23
ARS Visit 1 to Visit 3: 250 mg/day group

ARS	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Inattention V1	1.30	1.64	.17	.34
Inattention V3	1.56	2.08		
Impulsivity V1	1.44	1.45	< .01	.01
Impulsivity V3	.85	1.29		

Table 24
ARS Visit 1 to Visit 3: Placebo group

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ARS	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Inattention V1	.46	.83	.03	.06
Inattention V3	.21	.59		
Impulsivity V1	.88	1.30	.10	.21
Impulsivity V3	.63	1.47		

Table 25
ARS Visit 1 to Visit 3: 500 mg/day group

ARS	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Inattention V1	.50	.89	.28	.56
Inattention V3	.38	.92		
Impulsivity V1	.88	1.62	.02	.03
Impulsivity V3	.38	.88		

Table 26
ARS Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Inattention	1.56	2.08	.38	.92	.01
V3 Impulsivity	.85	1.29	.38	.88	.13
V3-V1 Inattention	.26	1.38	-.13	1.03	.27
V3-V1 Impulsivity	-.59	1.15	-.50	1.06	.77

5

Table 27
ARS Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Inattention	.21	.59	.38	.92	.46
V3 Impulsivity	.63	1.47	.38	.88	.48
V3-V1 Inattention	-.25	.61	-.13	1.03	.61
V3-V1 Impulsivity	-.25	.94	-.50	1.06	.39

Table 27a
ARS Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Inattention	1.56	2.08	.21	.59	< .01
V3 Impulsivity	.85	1.29	.63	1.47	.56
V3-V1 Inattention	.26	1.38	-.25	.61	.10
V3-V1 Impulsivity	-.59	1.15	-.25	.94	.26

Table 28
ARS Visit 3: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
Inattention	< .01	-	< .01	-
500 mg/day vs. 250 mg/day	-	.01	-	< .01
500 mg/day vs. Placebo	-	.91	-	.46
250 mg/day vs. Placebo	-	< .01	-	< .01
Impulsivity	.40	-	.20	-
500 mg/day vs. 250 mg/day	-	.36	-	.18
500 mg/day vs. Placebo	-	.77	-	.38
250 mg/day vs. Placebo	-	.79	-	.40

Table 29
ARS Visit Difference Scores: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
Inattention	.21	-	.11	-
500 mg/day vs. 250 mg/day	-	.41	-	.21
500 mg/day vs. Placebo	-	.91	-	.46
250 mg/day vs. Placebo	-	.21	-	.11
Impulsivity	.50	-	.25	-
500 mg/day vs. 250 mg/day	-	.95	-	.47
500 mg/day vs. Placebo	-	.69	-	.35
250 mg/day vs. Placebo	-	.49	-	.24

Table 30
Conners Visit 1 to Visit 3: 250 mg/day group

Conners	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 Conners	49.26	10.25	.02	.03
V3 Conners	49.52	10.90		

5

Table 31
Conners Visit 1 to Visit 3: Placebo group

Conners	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 Conners	43.92	7.02	.07	.14
V3 Conners	41.96	7.71		

Table 32
Conners Visit 1 to Visit 3: 500 mg/day group

Conners	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 Conners	43.83	9.25	< .01	< .01
V3 Conners	39.54	7.64		

Table 33
Conners Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 Conners	46.52	10.90	39.54	7.64	.01
V3-V1 Score	-2.74	6.38	-4.29	5.39	.36

5

Table 34
Conners Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 Conners	41.96	7.71	39.54	7.64	.28
V3-V1 Score	-1.96	6.20	-4.29	5.39	.17

10

Table 34a
Conners Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 Conners	46.52	10.90	41.96	7.71	.10
V3-V1 Score	-2.74	6.38	-1.96	6.20	.66

Table 35
Conners Visit 3: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
Conners Score	.02	-	.01	-
500 mg/day vs. 250 mg/day	-	.02	-	.01
500 mg/day vs. Placebo	-	.62	-	.31
250 mg/day vs. Placebo	-	.17	-	.09

Table 36
Conners Visit Difference Scores: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
Conners Score	.40	-	.20	-
500 mg/day vs. 250 mg/day	-	.63	-	.32
500 mg/day vs. Placebo	-	.38	-	.19
250 mg/day vs. Placebo	-	.89	-	.44

Table 37
PSQI Visit 1 to Visit 3: 250 mg/day group

PSQI	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 PSQI	3.41	1.65	< .01	.01
V3 PSQI	2.59	1.53		

Table 38
PSQI Visit 1 to Visit 3: Placebo group

5

PSQI	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 PSQI	3.30	1.52	< .01	< .01
V3 PSQI	2.35	1.72		

Table 39
PSQI Visit 1 to Visit 3: 500 mg/day group

PSQI	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 PSQI	3.38	1.53	< .01	.01
V3 PSQI	2.46	1.77		

Table 40
PSQI Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 PSQI	2.59	1.53	2.46	1.77	.77
V3-V1 Score	-.81	1.55	-.92	1.61	.82

5

Table 41
PSQI Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 PSQI	2.35	1.72	2.46	1.77	.83
V3-V1 Score	-.96	1.19	-.92	1.61	.92

Table 41a
PSQI Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 PSQI	2.59	1.53	2.35	1.72	.60
V3-V1 Score	-.81	1.55	-.96	1.19	.72

Table 42
PSQI Visit 3: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
PSQI Score	.87	-	.44	-
500 mg/day vs. 250 mg/day	-	.96	-	.48
500 mg/day vs. Placebo	-	.97	-	.49
250 mg/day vs. Placebo	-	.86	-	.43

Table 43
PSQI Visit Difference Scores: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
PSQI Score	.94	-	.47	-
500 mg/day vs. 250 mg/day	-	.97	-	.48
500 mg/day vs. Placebo	-	1.00	-	.50
250 mg/day vs. Placebo	-	.94	-	.47

General Questionnaire Statistics for 250 mg/day group Paired Samples Statistics

Example	Never	1	2	3	4	5	6	7	8	9	Always yawning
I yawn often.						5					10

Please circle like this based on your answer.

Questions	Never	1	2	3	4	5	6	7	8	9	Always
1 My eyes often feel strained.	Never	1	2	3	4	5	6	7	8	9	Constant eyestrain 10
2 I find it hard to focus on distant objects.	Never	1	2	3	4	5	6	7	8	9	Always have difficulty focusing 10
3 I find it hard to focus on nearby objects.	Never	1	2	3	4	5	6	7	8	9	Always have difficulty focusing 10
4 I feel heavy-headed.	Never	1	2	3	4	5	6	7	8	9	Always drowsy 10
5 My whole body feels tired.	Never	1	2	3	4	5	6	7	8	9	Whole body always tired 10
6 My legs feel tired or ache.	Never	1	2	3	4	5	6	7	8	9	Legs severely tired and achy 10
7 I yawn often.	Never	1	2	3	4	5	6	7	8	9	Always yawning 10
8 I often feel disoriented or muddled.	Never	1	2	3	4	5	6	7	8	9	Always foggy-brained 10
9 I become drowsy during the daytime.	Never	1	2	3	4	5	6	7	8	9	Always drowsy 10
10 I have headaches.	Never	1	2	3	4	5	6	7	8	9	Always headache 10
11 I feel anxious or troubled.	Never	1	2	3	4	5	6	7	8	9	Feel strong anxiety 10
12 I have a hard time organizing my thoughts.	Never	1	2	3	4	5	6	7	8	9	Difficulty organizing thoughts 10
13 I get confused/mixed up when I am talking.	Never confused in conversation	1	2	3	4	5	6	7	8	9	Always confused in conversation 10
14 I get irritated easily.	Never irritated	1	2	3	4	5	6	7	8	9	Always irritated 10
15 I find it hard to remember details.	Never	1	2	3	4	5	6	7	8	9	Always 10
16 I make careless mistakes at work, at home, or in other activities.	Never make mistakes	1	2	3	4	5	6	7	8	9	Consistently make mistakes 10

Test Code () ID NO. ()
Date () Time ()
Study Day No. ()

General Questionnaire (Pre)

For the listed questions, please circle the number that best corresponds to your answer. "1" or "10" is the maximum(strongest) or minimum(weakest) feeling you can imagine. Please follow the example provided below.

Test Code
()General Questionnaire
Page 2ID NO. ()
Date ()
Time()

Study Day No. ()

I have difficulty keeping my attention on tasks or recreational activities.	No trouble focusing 1 2 3 4 5 6 7 8 9 10 Difficulty concentrating
I am told that I do not seem to listen when spoken to directly.	Never 1 2 3 4 5 6 7 8 9 10 Always
19 I follow through on instructions to finish chores, or duties in the workplace?	Never 1 2 3 4 5 6 7 8 9 10 Always
20 I have difficulty organizing tasks and activities.	Never 1 2 3 4 5 6 7 8 9 10 Always
21 I avoid or dislike tasks that require sustained mental effort (such as problem solving).	Never 1 2 3 4 5 6 7 8 9 10 Always
22 I lose things necessary for carrying out tasks or activities (such as calculators, tools, etc).	Never 1 2 3 4 5 6 7 8 9 10 Always
23 I am easily distracted by extraneous stimuli.	Never distracted 1 2 3 4 5 6 7 8 9 10 Easily distracted
24 I am forgetful in daily activities.	Never 1 2 3 4 5 6 7 8 9 10 Always
25 I fall asleep easily.	Fall asleep easily 1 2 3 4 5 6 7 8 9 10 Difficulty falling asleep or can't sleep at all
26 I wake in the middle of the night.	Never 1 2 3 4 5 6 7 8 9 10 Often wakes in the middle of the night
27 I wake before I have to, and have difficulty falling back asleep.	Never 1 2 3 4 5 6 7 8 9 10 Wake much earlier than desired
28 How do you feel about the total amount of sleep you get?	Sufficient 1 2 3 4 5 6 7 8 9 10 Not enough at all, or cannot sleep at all
29 How do you feel about your overall quality of sleep? (Unrelated to amount of sleep)	Satisfied 1 2 3 4 5 6 7 8 9 10 Not satisfied at all
30 How do you feel during the day?	Content 1 2 3 4 5 6 7 8 9 10 Severely depressed
31 How is your social activity in the day time (physical and mental)?	Very active 1 2 3 4 5 6 7 8 9 10 Severely impaired
32 I feel sleepy during the daytime.	Never 1 2 3 4 5 6 7 8 9 10 Always feel severe sleepiness
33 How do you feel about your complexion of your face?	Has a good complexion 1 2 3 4 5 6 7 8 9 10 Pale
34 The skin on my cheek and jaw feels rough.	No, and not concerned 1 2 3 4 5 6 7 8 9 10 Yes, and very concerned
Please comment freely about your general physical and mental condition, as well as your feelings about these areas (e.g. vision, memory, fatigue, concentration, sleep, headaches, etc).	

Thank you for your cooperation.

2

Table 44
General Questionnaire Visit 1 to Visit 3: 250 mg/day group

Questionnaire	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Vision Q1 V1	3.44	1.95	< .01	< .01
Vision Q1 V3	2.33	1.30		
Vision Q2 V1	3.26	2.26	< .01	< .01
Vision Q2 V3	2.44	1.93		
Vision Q3 V1	2.15	1.35	.07	.14
Vision Q3 V3	1.81	1.21		
Vision Total V1	8.85	4.60	< .01	< .01
Vision Total V3	6.59	4.01		
Depression Q4 V1	2.59	1.45	.02	.03
Depression Q4 V3	1.81	1.33		
Depression Q5 V1	3.26	1.91	.01	.02
Depression Q5 V3	2.30	1.46		
Depression Q6 V1	2.85	1.98	.02	.03
Depression Q6 V3	2.00	1.04		
Depression Q7 V1	4.26	2.12	.01	.03
Depression Q7 V3	3.33	2.09		
Depression Q8 V1	2.74	2.16	< .01	.01
Depression Q8 V3	1.81	1.21		
Depression Q9 V1	3.74	2.23	.01	.02
Depression Q9 V3	2.89	1.81		
Depression Q10 V1	2.85	1.83	< .01	< .01
Depression Q10 V3	2.07	1.33		
Depression Q11 V1	2.85	2.27	.03	.06
Depression Q11 V3	2.15	1.63		
Depression Q12 V1	3.26	1.91	.04	.08
Depression Q12 V3	2.67	1.98		
Depression Total V1	28.41	12.27	< .01	< .01
Depression Total V3	21.04	10.73		
Attention Q13 V1	3.52	2.29	.04	.08
Attention Q13 V3	2.74	1.83		
Attention Q14 V1	2.37	1.25	.36	.73
Attention Q14 V3	2.48	1.58		
Attention Q15 V1	3.89	2.50	.08	.16
Attention Q15 V3	3.15	2.11		
Attention Q16 V1	3.19	1.50	.04	.07
Attention Q16 V3	2.63	1.71		
Attention Q17 V1	3.30	2.30	.03	.05
Attention Q17 V3	2.48	1.53		
Attention Q18 V1	2.63	2.19	.08	.15
Attention Q18 V3	2.26	1.87		
Attention Q19 V1	6.59	2.75	.41	.81
Attention Q19 V3	6.41	2.72		
Attention Q20 V1	3.48	2.49	.24	.47
Attention Q20 V3	3.22	2.52		

Attention Q21 V1	3.22	2.06	.38	.75
Attention Q21 V3	3.15	2.35		
Attention Q22 V1	4.00	2.38	.05	.10
Attention Q22 V3	3.35	2.59		
Attention Q23 V1	4.15	2.37	.19	.38
Attention Q23 V3	3.70	2.51		
Attention Q24 V1	3.67	1.84	.04	.08
Attention Q24 V3	2.96	2.14		
Attention Total V1	44.31	16.58	.04	.07
Attention Total V3	38.73	17.66		
Sleep Q25 V1	3.19	1.88	< .01	.02
Sleep Q25 V3	2.33	1.52		
Sleep Q26 V1	2.78	2.21	.04	.07
Sleep Q26 V3	2.15	2.05		
Sleep Q27 V1	3.26	2.68	.01	.02
Sleep Q27 V3	2.07	2.02		
Sleep Q28 V1	3.63	1.84	< .01	.01
Sleep Q28 V3	2.78	1.81		
Sleep Q29 V1	3.48	2.14	< .01	< .01
Sleep Q29 V3	2.19	1.42		
Sleep Q30 V1	2.11	1.12	.28	.57
Sleep Q30 V3	1.96	1.32		
Sleep Q31 V1	1.96	1.02	.42	.84
Sleep Q31 V3	1.93	1.14		
Sleep Q32 V1	4.15	1.99	.04	.08
Sleep Q32 V3	3.56	1.99		
Sleep Total V1	24.56	8.13	< .01	< .01
Sleep Total V3	18.96	7.66		
Complexion Q33 V1	2.78	1.76	.03	.05
Complexion Q33 V3	2.30	1.59		
Complexion Q34 V1	1.85	1.32	.28	.57
Complexion Q34 V3	1.67	1.30		
Complexion Total V1	4.63	2.66	.09	.19
Complexion Total V3	3.96	2.53		

Table 45
General Questionnaire Visit 1 to Visit 3: Placebo group

Questionnaire	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Vision Q1 V1	2.54	1.22	< .01	< .01
Vision Q1 V3	1.83	.92		
Vision Q2 V1	2.92	1.74	.03	.05
Vision Q2 V3	2.00	1.35		
Vision Q3 V1	1.79	1.35	.04	.09
Vision Q3 V3	1.33	.57		
Vision Total V1	7.25	3.48	< .01	< .01
Vision Total V3	5.17	2.12		
Depression Q4 V1	2.04	1.60	.08	.16
Depression Q4 V3	1.58	.93		
Depression Q5 V1	2.75	1.57	< .01	< .01
Depression Q5 V3	1.92	.97		
Depression Q6 V1	2.71	1.63	< .01	< .01
Depression Q6 V3	1.79	.93		
Depression Q7 V1	3.71	1.43	< .01	< .01
Depression Q7 V3	2.75	1.23		
Depression Q8 V1	1.88	1.26	.10	.21
Depression Q8 V3	1.50	.83		
Depression Q9 V1	2.58	1.61	.37	.73
Depression Q9 V3	2.67	1.49		
Depression Q10 V1	2.54	1.59	< .01	< .01
Depression Q10 V3	1.67	.96		
Depression Q11 V1	2.29	1.68	.03	.07
Depression Q11 V3	1.71	1.20		
Depression Q12 V1	2.33	1.66	.05	.11
Depression Q12 V3	1.75	.94		
Depression Total V1	22.83	11.01	< .01	< .01
Depression Total V3	17.33	6.24		
Attention Q13 V1	2.63	1.31	.01	.03
Attention Q13 V3	2.04	.86		
Attention Q14 V1	2.58	1.89	.16	.32
Attention Q14 V3	2.13	1.33		
Attention Q15 V1	3.29	1.97	< .01	< .01
Attention Q15 V3	2.67	2.01		
Attention Q16 V1	2.83	1.40	.05	.11
Attention Q16 V3	2.46	1.14		
Attention Q17 V1	2.67	1.58	.04	.08
Attention Q17 V3	2.21	1.53		
Attention Q18 V1	2.04	1.40	.22	.45
Attention Q18 V3	1.83	1.01		
Attention Q19 V1	7.00	2.60	.48	.96
Attention Q19 V3	6.96	3.03		
Attention Q20 V1	2.79	1.62	< .01	< .01
Attention Q20 V3	1.92	.97		

Attention Q21 V1	2.88	1.70	.03	.05
Attention Q21 V3	2.17	1.47		
Attention Q22 V1	2.58	1.91	.01	.03
Attention Q22 V3	2.00	1.35		
Attention Q23 V1	2.96	1.63	.45	.90
Attention Q23 V3	2.92	1.91		
Attention Q24 V1	2.79	1.41	.04	.09
Attention Q24 V3	2.38	1.47		
Attention Total V1	37.04	13.08	< .01	< .01
Attention Total V3	31.67	11.73		
Sleep Q25 V1	2.67	1.49	< .01	< .01
Sleep Q25 V3	1.79	.83		
Sleep Q26 V1	2.38	1.35	.01	.02
Sleep Q26 V3	1.75	1.39		
Sleep Q27 V1	2.29	1.65	< .01	.01
Sleep Q27 V3	1.58	1.14		
Sleep Q28 V1	3.04	1.71	.03	.07
Sleep Q28 V3	2.33	1.66		
Sleep Q29 V1	2.29	1.52	.33	.66
Sleep Q29 V3	2.21	1.84		
Sleep Q30 V1	1.96	1.08	.32	.63
Sleep Q30 V3	1.83	.76		
Sleep Q31 V1	1.83	1.05	.26	.52
Sleep Q31 V3	1.71	.91		
Sleep Q32 V1	3.58	1.59	.10	.21
Sleep Q32 V3	3.21	1.62		
Sleep Total V1	20.04	7.11	< .01	< .01
Sleep Total V3	16.42	7.41		
Complexion Q33 V1	3.13	1.70	< .01	.01
Complexion Q33 V3	2.04	1.27		
Complexion Q34 V1	1.96	1.40	.03	.06
Complexion Q34 V3	1.46	.66		
Complexion Total V1	5.08	2.41	< .01	< .01
Complexion Total V3	3.50	1.67		

Table 46
General Questionnaire Visit 1 to Visit 3: 500 mg/day group

Questionnaire	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Vision Q1 V1	2.75	1.65	< .01	.01
Vision Q1 V3	1.92	.93		
Vision Q2 V1	2.54	1.82	.03	.06
Vision Q2 V3	2.08	1.18		
Vision Q3 V1	1.71	1.08	.10	.20
Vision Q3 V3	1.50	.66		
Vision Total V1	7.00	4.11	< .01	.02
Vision Total V3	5.50	2.25		
Depression Q4 V1	1.75	1.29	.23	.46
Depression Q4 V3	1.58	1.02		
Depression Q5 V1	2.46	1.50	.03	.06
Depression Q5 V3	1.88	1.08		
Depression Q6 V1	2.21	1.38	.04	.08
Depression Q6 V3	1.67	.87		
Depression Q7 V1	3.13	1.65	< .01	< .01
Depression Q7 V3	2.25	1.36		
Depression Q8 V1	1.92	1.21	.03	.05
Depression Q8 V3	1.46	.66		
Depression Q9 V1	3.04	1.88	.01	.02
Depression Q9 V3	2.00	1.32		
Depression Q10 V1	2.00	1.56	.06	.12
Depression Q10 V3	1.54	.93		
Depression Q11 V1	2.00	1.10	< .01	.01
Depression Q11 V3	1.38	.77		
Depression Q12 V1	2.04	1.37	.03	.07
Depression Q12 V3	1.58	.83		
Depression Total V1	20.54	9.99	< .01	< .01
Depression Total V3	15.33	6.49		
Attention Q13 V1	2.42	1.21	.03	.05
Attention Q13 V3	1.96	1.08		
Attention Q14 V1	2.21	1.32	.09	.18
Attention Q14 V3	1.83	.92		
Attention Q15 V1	2.63	1.79	.03	.05
Attention Q15 V3	1.92	1.06		
Attention Q16 V1	2.83	1.49	< .01	.02
Attention Q16 V3	1.92	1.02		
Attention Q17 V1	1.96	1.04	.21	.41
Attention Q17 V3	1.75	.74		
Attention Q18 V1	2.79	2.32	.05	.11
Attention Q18 V3	1.92	1.79		
Attention Q19 V1	7.29	2.63	.06	.13
Attention Q19 V3	8.42	2.32		
Attention Q20 V1	2.54	1.79	.05	.09

Attention Q20 V3	1.92	1.14		
Attention Q21 V1	3.25	2.15	< .01	< .01
Attention Q21 V3	2.42	1.89		
Attention Q22 V1	1.83	.76	.13	.26
Attention Q22 V3	1.63	.77		
Attention Q23 V1	2.92	1.74	.01	.03
Attention Q23 V3	2.13	1.36		
Attention Q24 V1	2.46	1.56	.14	.28
Attention Q24 V3	2.17	1.40		
Attention Total V1	35.13	12.78	.01	.02
Attention Total V3	29.96	9.62		
Sleep Q25 V1	3.54	2.04	< .01	.01
Sleep Q25 V3	2.50	1.10		
Sleep Q26 V1	2.54	1.87	.02	.05
Sleep Q26 V3	1.71	1.43		
Sleep Q27 V1	2.00	1.41	.31	.62
Sleep Q27 V3	1.83	1.58		
Sleep Q28 V1	2.96	1.60	.02	.03
Sleep Q28 V3	2.29	1.23		
Sleep Q29 V1	2.00	1.45	.41	.82
Sleep Q29 V3	1.96	1.23		
Sleep Q30 V1	2.04	1.20	.38	.75
Sleep Q30 V3	1.96	.96		
Sleep Q31 V1	2.33	1.13	.31	.61
Sleep Q31 V3	2.21	1.50		
Sleep Q32 V1	3.54	1.79	.09	.18
Sleep Q32 V3	3.13	1.92		
Sleep Total V1	20.83	5.48	< .01	< .01
Sleep Total V3	17.58	6.85		
Complexion Q33 V1	2.58	1.28	< .01	< .01
Complexion Q33 V3	1.75	.94		
Complexion Q34 V1	1.88	1.26	< .01	.01
Complexion Q34 V3	1.29	.62		
Complexion Total V1	4.46	2.13	< .01	< .01
Complexion Total V3	3.04	1.40		

Table 47
General Questionnaire Visit 3 and Visit Difference Scores:
250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
Vision Total V3	6.59	4.01	5.50	2.25	.24
Depression Total V3	21.04	10.73	15.33	6.49	.03
Attention Total V3	38.48	17.37	29.96	9.62	.04
Sleep Total V3	18.96	7.66	17.58	6.85	.50
Complexion Total V3	3.96	2.53	3.04	1.40	.12
Vision Total V3-V1 Difference	-2.26	3.11	-1.50	2.92	.38
Depression Total V3-V1 Difference	-7.37	9.53	-5.21	8.42	.40
Attention Total V3-V1 Difference	-5.58	15.16	-5.17	10.10	.91
Sleep Total V3-V1 Difference	-5.59	6.76	-3.25	5.03	.17
Complexion Total V3-V1 Difference	-.67	2.54	-1.42	1.69	.23

Table 48
General Questionnaire Visit 3 and Visit Difference Scores:
Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
Vision Total V3	5.17	2.12	5.50	2.25	.60
Depression Total V3	17.33	6.24	15.33	6.49	.28
Attention Total V3	31.67	11.73	29.96	9.62	.58
Sleep Total V3	16.42	7.41	17.58	6.85	.57
Complexion Total V3	3.50	1.67	3.04	1.40	.31
Vision Total V3-V1 Difference	-2.08	3.19	-1.50	2.92	.51
Depression Total V3-V1 Difference	-5.50	9.07	-5.21	8.42	.91
Attention Total V3-V1 Difference	-5.38	8.32	-5.17	10.10	.94
Sleep Total V3-V1 Difference	-3.63	4.73	-3.25	5.03	.79
Complexion Total V3-V1 Difference	-1.58	2.62	-1.42	1.69	.80

Table 48a
General Questionnaire Visit 3 and Visit Difference Scores:
250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
Vision Total V3	6.59	4.01	5.17	2.12	.13
Depression Total V3	21.04	10.73	17.33	6.24	.15
Attention Total V3	38.48	17.37	31.67	11.73	.11
Sleep Total V3	18.96	7.66	16.42	7.41	.24
Complexion Total V3	3.96	2.53	3.50	1.67	.45
Vision Total V3-V1 Difference	-2.26	3.11	-2.08	3.19	.84
Depression Total V3-V1 Difference	-7.37	9.53	-5.50	9.07	.48
Attention Total V3-V1 Difference	-5.58	15.16	-5.38	8.32	.95
Sleep Total V3-V1 Difference	-5.59	6.76	-3.63	4.73	.24
Complexion Total V3-V1 Difference	-.67	2.54	-1.58	2.62	.21

Table 49
General Questionnaire Visit 3: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Vision Total	.21		.10	
500 mg/day vs 250 mg/day		.40		.20
500 mg/day vs Placebo		.92		.46
250 mg/day vs Placebo		.21		.10
Depression Total	.05		.02	
500 mg/day vs 250 mg/day		.04		.02
500 mg/day vs Placebo		.68		.34
250 mg/day vs Placebo		.25		.12
Attention Total	.06		.03	
500 mg/day vs 250 mg/day		.07		.04
500 mg/day vs Placebo		.90		.45
250 mg/day vs Placebo		.18		.09
Sleep Total	.47		.23	
500 mg/day vs 250 mg/day		.78		.39
500 mg/day vs Placebo		.85		.42
250 mg/day vs Placebo		.44		.22
Complexion Total	.25		.13	
500 mg/day vs 250 mg/day		.22		.11
500 mg/day vs Placebo		.70		.35
250 mg/day vs Placebo		.68		.34

Table 50
General Questionnaire Visit Difference Scores: 250 mg/day, Placebo, and 500
mg/day

	groups			
	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Vision Total	.66		.33	
500 mg/day vs 250 mg/day		.66		.33
500 mg/day vs Placebo		.79		.39
250 mg/day vs Placebo		.98		.49
Depression Total	.65		.32	
500 mg/day vs 250 mg/day		.67		.34
500 mg/day vs Placebo		.99		.50
250 mg/day vs Placebo		.74		.37
Attention Total	.99		.50	
500 mg/day vs 250 mg/day		.99		.50
500 mg/day vs Placebo		1.00		.50
250 mg/day vs Placebo		1.00		.50
Sleep Total	.28		.14	
500 mg/day vs 250 mg/day		.31		.15
500 mg/day vs Placebo		.97		.49
250 mg/day vs Placebo		.43		.22
Complexion Total	.33		.16	
500 mg/day vs 250 mg/day		.49		.24
500 mg/day vs Placebo		.97		.48
250 mg/day vs Placebo		.35		.17

Test Code:

Exercise and Life Style Questionnaire
(Pre)

(ID NO.)

Date _____

Time _____

Study Day No. _____

For the listed questions, please circle the number that best corresponds to your answer.

"1" or "10" is the maximum (strongest) or minimum (weakest) feeling you can imagine.

Please follow the example provided below.

Example	Never	1	2	3	4	5	6	7	8	9	Always
I sweat often.							6				Always sweating

Please circle like this based on your answer.

Questions	Answers
1 Do you exercise regularly?	Yes No
2 If yes, how much do you exercise per week?	hrs / week
3 Do you feel exhausted during exercise?	Never 1 2 3 4 5 6 7 Always exhausted during exercise 8 9 10
4 Are you fatigued after exercising?	Never 1 2 3 4 5 6 7 Always exhausted after exercise 8 9 10
Please comment freely about your physical condition and fatigue, related to exercise or daily performance (e.g. duration of load, mobility of the body)	
5 What is your appetite like?	Always hungry 1 2 3 4 5 6 7 8 9 Never hungry 10
6 Do you feel you eat more than you intend to?	Never 1 2 3 4 5 6 7 8 9 Always 10
7 Do you smoke? If yes, how many cigarettes do you consume per day?	Yes No / day
8 How do you feel when you cannot smoke or have to reduce smoking?	No problem 1 2 3 4 5 6 7 8 9 Crave cigarettes 10
9 Do you feel you smoke more than you intend to?	Never 1 2 3 4 5 6 7 8 9 Always 10
10 How many alcoholic drinks do you consume per week?	/ week
11 How do you feel when you cannot drink alcohol or have to reduce drinking?	No problem 1 2 3 4 5 6 7 8 9 Crave alcohol 10
12 Do you drink alcohol more than you intend to?	Never 1 2 3 4 5 6 7 8 9 Always 10
Please comment freely about your life style habits (e.g. smoking, alcohol, eating)	

Table 51
Exercise/Lifestyle Questionnaire Visit 1 to Visit 3: 250 mg/day group

Questionnaire	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Exercise Q1 V1	1.15	.36	.16	.33
Exercise Q1 V3	1.07	.27		
Exercise Q2 V1	6.35	4.78	.37	.73
Exercise Q2 V3	6.80	6.13		
Exercise Q3 V1	3.56	1.81	.07	.14
Exercise Q3 V3	3.11	1.63		
Exercise Q4 V1	3.81	2.04	.05	.10
Exercise Q4 V3	3.11	1.72		
Exercise Total V1	14.87	5.46	.29	.58
Exercise Total V3	14.09	7.15		
Appetite Q5 V1	4.11	2.03	.46	.92
Appetite Q5 V3	4.15	1.96		
Appetite Q6 V1	4.44	2.29	.04	.07
Appetite Q6 V3	3.81	2.35		
Appetite Total V1	8.56	2.68	.08	.15
Appetite Total V3	7.96	2.78		
Smoke Q7 V1	.00	.01	na	na
Smoke Q7 V3	.00	.01		
Smoke Q8 V1	1.00	.00	na	na
Smoke Q8 V3	1.00	.00		
Smoke Q9 V1	1.07	.39	.16	.33
Smoke Q9 V3	1.00	.00		
Smoke Total V1	2.08	.39	.16	.33
Smoke Total V3	2.00	.01		
Alcohol Q10 V1	.07	.38	na	na
Alcohol Q10 V3	.07	.38		
Alcohol Q11 V1	1.00	.00	na	na
Alcohol Q11 V3	1.00	.00		
Alcohol Q12 V1	1.00	.00	na	na
Alcohol Q12 V3	1.00	.00		
Alcohol Total V1	2.07	.38	na	na
Alcohol Total V3	2.07	.38		

Table 52
Exercise/Lifestyle Questionnaire Visit 1 to Visit 3: Placebo group

Questionnaire	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Exercise Q1 V1	1.13	.34	.16	.33
Exercise Q1 V3	1.04	.36		
Exercise Q2 V1	8.77	6.13	.44	.89
Exercise Q2 V3	8.96	7.95		
Exercise Q3 V1	3.33	1.88	.12	.25
Exercise Q3 V3	2.83	1.52		
Exercise Q4 V1	4.00	2.23	.01	.02
Exercise Q4 V3	3.08	1.72		
Exercise Total V1	17.23	7.36	.20	.39
Exercise Total V3	15.92	7.90		
Appetite Q5 V1	4.08	1.69	.04	.09
Appetite Q5 V3	3.63	1.56		
Appetite Q6 V1	3.38	1.93	< .01	< .01
Appetite Q6 V3	2.29	1.71		
Appetite Total V1	7.46	2.55	< .01	< .01
Appetite Total V3	5.92	2.47		
Smoke Q7 V1	.00	.00	na	na
Smoke Q7 V3	.00	.00		
Smoke Q8 V1	1.00	.00	na	na
Smoke Q8 V3	1.00	.00		
Smoke Q9 V1	1.00	.00	na	na
Smoke Q9 V3	1.00	.00		
Smoke Total V1	2.00	.00	na	na
Smoke Total V3	2.00	.00		
Alcohol Q10 V1	.00	.00	na	na
Alcohol Q10 V3	.00	.00		
Alcohol Q11 V1	1.04	.20	.16	.33
Alcohol Q11 V3	1.00	.00		
Alcohol Q12 V1	1.00	.00	na	na
Alcohol Q12 V3	1.00	.00		
Alcohol Total V1	2.04	.20	.16	.33
Alcohol Total V3	2.00	.00		

Table 53
Exercise/Lifestyle Questionnaire Visit 1 to Visit 3: 500 mg/day group

Questionnaire	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Exercise Q1 V1	1.17	.38	.16	.33
Exercise Q1 V3	1.13	.34		
Exercise Q2 V1	8.50	6.56	.11	.22
Exercise Q2 V3	7.54	5.59		
Exercise Q3 V1	3.71	1.81	.01	.02
Exercise Q3 V3	2.96	1.63		
Exercise Q4 V1	3.75	1.96	< .01	.01
Exercise Q4 V3	2.75	2.07		
Exercise Total V1	17.24	7.07	< .01	.02
Exercise Total V3	14.46	5.49		
Appetite Q5 V1	3.96	1.40	.13	.26
Appetite Q5 V3	3.50	1.47		
Appetite Q6 V1	3.25	2.13	.20	.40
Appetite Q6 V3	2.88	1.83		
Appetite Total V1	7.21	2.93	.09	.18
Appetite Total V3	6.38	2.50		
Smoke Q7 V1	.00	.00	na	na
Smoke Q7 V3	.00	.00		
Smoke Q8 V1	1.00	.00	na	na
Smoke Q8 V3	1.00	.00		
Smoke Q9 V1	1.00	.00	na	na
Smoke Q9 V3	1.00	.00		
Smoke Total V1	2.00	.00	na	na
Smoke Total V3	2.00	.00		
Alcohol Q10 V1	.00	.00	na	na
Alcohol Q10 V3	.00	.00		
Alcohol Q11 V1	1.00	.00	na	na
Alcohol Q11 V3	1.00	.00		
Alcohol Q12 V1	1.00	.00	na	na
Alcohol Q12 V3	1.00	.00		
Alcohol Total V1	2.00	.00	na	na
Alcohol Total V3	2.00	.00		

Table 54
Exercise/Lifestyle Questionnaire Visit 3 and Visit Difference Scores:
250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
Exercise Total V3	14.09	7.15	14.48	5.37	.83
Appetite Total V3	7.96	2.78	6.38	2.50	.04
Smoke Total V3	2.00	.01	2.00	.00	.35
Alcohol Total V3	2.07	.38	2.00	.00	.35
Exercise Total V3-V1	-.78	7.17	-2.78	5.25	.27
Appetite Total V3-V1	-.59	2.10	-.83	2.94	.74
Smoke Total V3-V1	-.07	.38	.00	.00	.35
Alcohol Total V3-V1	.00	.00	.00	.00	na

Table 55
Exercise/Lifestyle Questionnaire Visit 3 and Visit Difference Scores:
Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
Exercise Total V3	15.92	7.90	14.48	5.37	.47
Appetite Total V3	5.92	2.47	6.38	2.50	.53
Smoke Total V3	2.00	.00	2.00	.00	na
Alcohol Total V3	2.00	.00	2.00	.00	na
Exercise Total V3-V1	-1.31	7.37	-2.78	5.25	.44
Appetite Total V3-V1	-1.54	2.02	-.83	2.94	.34
Smoke Total V3-V1	.00	.00	.00	.00	na
Alcohol Total V3-V1	-.04	.20	.00	.00	.32

Table 55a
Exercise/Lifestyle Questionnaire Visit 3 and Visit Difference Scores:
250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
Exercise Total V3	14.09	7.15	15.92	7.90	.39
Appetite Total V3	7.96	2.78	5.92	2.47	< .01
Smoke Total V3	2.00	.01	2.00	.00	.35
Alcohol Total V3	2.07	.38	2.00	.00	.35
Exercise Total V3-V1	-.78	7.17	-1.31	7.37	.79
Appetite Total V3-V1	-.59	2.10	-1.54	2.02	.11
Smoke Total V3-V1	-.07	.38	.00	.00	.35
Alcohol Total V3-V1	.00	.00	-.04	.20	.29

Table 56
Exercise/Lifestyle Questionnaire Visit 3: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Exercise Total	.62		.31	
500 mg/day vs 250 mg/day		.98		.49
500 mg/day vs Placebo		.75		.38
250 mg/day vs Placebo		.62		.31
Appetite Total	.02		.01	
500 mg/day vs 250 mg/day		.08		.04
500 mg/day vs Placebo		.81		.41
250 mg/day vs Placebo		.02		.01
Smoking Total	.42		.21	
500 mg/day vs 250 mg/day		.49		.25
500 mg/day vs Placebo		1.00		.50
250 mg/day vs Placebo		.49		.25
Alcohol Total	.42		.21	
500 mg/day vs 250 mg/day		.49		.25
500 mg/day vs Placebo		1.00		.50
250 mg/day vs Placebo		.49		.25

Table 57
Exercise/Lifestyle Questionnaire Visit Difference Scores:
250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Exercise Total	.56		.28	
500 mg/day vs 250 mg/day		.55		.27
500 mg/day vs Placebo		.73		.37
250 mg/day vs Placebo		.96		.48
Appetite Total	.35		.17	
500 mg/day vs 250 mg/day		.93		.47
500 mg/day vs Placebo		.56		.28
250 mg/day vs Placebo		.34		.17
Smoking Total	.42		.21	
500 mg/day vs 250 mg/day		.49		.25
500 mg/day vs Placebo		1.00		.50
250 mg/day vs Placebo		.49		.25
Alcohol Total	.35		.18	
500 mg/day vs 250 mg/day		1.00		.50
500 mg/day vs Placebo		.43		.21
250 mg/day vs Placebo		.41		.20

Table 58
Finger Tap Test Visit 1 to Visit 3: 250 mg/day group

Finger Tap Test	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 Mean Dominant Hand	46.72	7.48	< .01	< .01
V3 Mean Dominant Hand	51.59	4.97		
V1 Mean Non-Dominant Hand	44.52	7.15	< .01	< .01
V3 Mean Non-Dominant Hand	47.01	6.47		

Table 59
Finger Tap Test Visit 1 to Visit 3: Placebo group

Finger Tap Test	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 Mean Dominant Hand	50.49	8.11	.19	.38
V3 Mean Dominant Hand	51.34	6.40		
V1 Mean Non-Dominant Hand	45.68	5.66	.04	.08
V3 Mean Non-Dominant Hand	47.34	5.70		

Table 60
Finger Tap Test Visit 1 to Visit 3: 500 mg/day group

Finger Tap Test	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V1 Mean Dominant Hand	49.44	6.10	< .01	< .01
V3 Mean Dominant Hand	52.05	5.10		
V1 Mean Non-Dominant Hand	44.89	7.10	< .01	< .01
V3 Mean Non-Dominant Hand	47.10	5.58		

Table 61
Finger Tap Test Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Mean Dominant Hand	51.59	4.97	52.05	5.10	.75
V3 Mean Non-Dominant Hand	47.01	6.47	47.10	5.58	.96
V3-V1 Mean Dominant Hand	4.87	5.09	2.61	3.78	.08
V3-V1 Mean Non-Dominant Hand	2.49	3.74	2.21	3.48	.78

5

Table 62
Finger Tap Test Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Mean Dominant Hand	51.34	6.40	52.05	5.10	.68
V3 Mean Non-Dominant Hand	47.34	5.70	47.10	5.58	.88
V3-V1 Mean Dominant Hand	.85	4.69	2.61	3.78	.16
V3-V1 Mean Non-Dominant Hand	1.66	4.43	2.21	3.48	.64

10

Table 62a
Finger Tap Test Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Mean Dominant Hand	51.59	4.97	51.34	6.40	.88
V3 Mean Non-Dominant Hand	47.01	6.47	47.34	5.70	.85
V3-V1 Mean Dominant Hand	4.87	5.09	.85	4.69	< .01

V3-V1 Mean Non-	2.49	3.74	1.66	4.43	.47
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Dominant Hand

Table 63
Finger Tap Test Visit 3: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
Mean Dominant Hand	.90	-	.45	-
500 mg/day vs. 250 mg/day	-	.95	-	.48
500 mg/day vs. Placebo	-	.90	-	.45
250 mg/day vs. Placebo	-	.99	-	.49
Mean Non-Dominant Hand	.98	-	.49	-
500 mg/day vs. 250 mg/day	-	1.00	-	.50
500 mg/day vs. Placebo	-	.99	-	.49
250 mg/day vs. Placebo	-	.98	-	.49

5 **Table 64**
Finger Tap Test Visit Difference Scores: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
Mean Dominant Hand	.10	-	< .01	-
500 mg/day vs. 250 mg/day	-	.19	-	.10
500 mg/day vs. Placebo	-	.38	-	.19
250 mg/day vs. Placebo	-	< .01	-	< .01
Mean Non-Dominant Hand	.75	-	.37	-
500 mg/day vs. 250 mg/day	-	.96	-	.48
500 mg/day vs. Placebo	-	.88	-	.44
250 mg/day vs. Placebo	-	.73	-	.37

Table 65
CVLT I & II Visit 1 to Visit 3: 250 mg/day group

CVLT I & II Lists	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
List A Trial 1 V1	6.11	1.91	< .01	< .01
List A Trial 1 V3	7.74	2.38		
List A Trial 5 V1	12.33	2.53	.10	.20
List A Trial 5 V3	12.85	3.01		
List A Trials 1-5 V1	50.52	11.23	.06	.11
List A Trials 1-5 V3	53.63	11.99		
List B V1	5.78	1.91	.12	.25
List B V3	6.26	1.97		
List A Short Delay V1	10.56	2.89	.01	.02
List A Short Delay V3	11.59	3.40		
List A Long Delay V1	10.26	2.74	.04	.08
List A Long Delay V3	11.07	3.74		

Table 66
CVLT I & II Visit 1 to Visit 3: Placebo group

CVLT I & II Lists	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
List A Trial 1 V1	6.71	1.33	< .01	< .01
List A Trial 1 V3	7.88	1.60		
List A Trial 5 V1	12.83	1.93	.20	.41
List A Trial 5 V3	13.25	2.17		
List A Trials 1-5 V1	52.33	5.93	.01	.03
List A Trials 1-5 V3	56.38	8.41		
List B V1	6.54	1.44	.46	.92
List B V3	6.50	2.11		
List A Short Delay V1	11.50	1.56	.12	.24
List A Short Delay V3	12.17	2.67		
List A Long Delay V1	11.04	1.73	< .01	.01
List A Long Delay V3	12.42	2.60		

Table 67
CVLT I & II Visit 1 to Visit 3: 500 mg/day group

CVLT I & II Lists	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
List A Trial 1 V1	6.58	1.64	.02	.05
List A Trial 1 V3	7.58	2.21		
List A Trial 5 V1	11.83	2.01	.04	.07
List A Trial 5 V3	12.71	2.33		
List A Trials 1-5 V1	49.04	9.29	.02	.05
List A Trials 1-5 V3	52.79	10.87		
List B V1	6.67	1.74	.25	.50
List B V3	6.33	2.33		
List A Short Delay V1	10.25	2.67	.03	.05
List A Short Delay V3	11.21	3.01		
List A Long Delay V1	9.79	3.27	.01	.02
List A Long Delay V3	10.92	3.05		

Table 68
CVLT I & II Visit 3 and Visit Difference Scores: 250 mg/day group and 500
mg/day
group

	250 mg/day		500 mg/day		<i>p</i> -value
	Mean	Std. Deviation	Mean	Std. Deviation	
V3 CVLT I & II List A Trial 1	7.74	2.38	7.58	2.21	.81
V3 CVLT I & II List A Trial 5	12.85	3.01	12.71	2.33	.85
V3 CVLT I & II List A Trial 1-5	53.63	11.99	52.79	10.87	.80
V3 CVLT I & II List B Trial 1	6.26	1.97	6.33	2.33	.90
V3 CVLT I & II List A Short Delay	11.59	3.40	11.21	3.01	.67
V3 CVLT I & II List A Long Delay	11.07	3.74	10.92	3.05	.87
V3-V1 CVLT I & II Difference List A Trial 1	1.63	2.22	1.00	2.32	.33
V3-V1 CVLT I & II Difference List A Trial 5	.52	2.05	.88	2.27	.56
V3-V1 CVLT I & II Difference List A Trials 1-5	3.11	9.82	3.75	8.64	.81
V3-V1 CVLT I & II Difference List B Trial 5	.48	2.12	-.33	2.37	.20
V3-V1 CVLT I & II Difference List A Short Delay	1.04	2.16	.96	2.31	.90
V3-V1 CVLT I & II Difference List A Long Delay	.81	2.34	1.13	2.23	.63

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Table 69
CVLT I & II Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		<i>p</i> -value
	Mean	Std. Deviation	Mean	Std. Deviation	
V3 CVLT I & II List A Trial 1	7.88	1.60	7.58	2.21	.60
V3 CVLT I & II List A Trial 5	13.25	2.17	12.71	2.33	.41
V3 CVLT I & II List A Trial 1-5	56.38	8.41	52.79	10.87	.21
V3 CVLT I & II List B Trial 1	6.50	2.11	6.33	2.33	.80
V3 CVLT I & II List A Short Delay	12.17	2.67	11.21	3.01	.25
V3 CVLT I & II List A Long Delay	12.42	2.60	10.92	3.05	.07
V3-V1 CVLT I & II Difference List A Trial 1	1.17	1.93	1.00	2.32	.79
V3-V1 CVLT I & II Difference List A Trial 5	.42	2.41	.88	2.27	.50
V3-V1 CVLT I & II Difference List A Trials 1-5	4.04	8.30	3.75	8.64	.91
V3-V1 CVLT I & II Difference List B Trial 1	-.04	2.01	-.33	2.37	.65
V3-V1 CVLT I & II Difference List A Short Delay	.67	2.71	.96	2.31	.69
V3-V1 CVLT I & II Difference List A Long Delay	1.38	2.39	1.13	2.23	.71

Table 69a
CVLT I & II Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 CVLT I & II List A Trial 1	7.74	2.38	7.88	1.60	.82
V3 CVLT I & II List A Trial 5	12.85	3.01	13.25	2.17	.60
V3 CVLT I & II List A Trial 1-5	53.63	11.99	56.38	8.41	.35
V3 CVLT I & II List B Trial 1	6.26	1.97	6.50	2.11	.68
V3 CVLT I & II List A Short Delay	11.59	3.40	12.17	2.67	.51
V3 CVLT I & II List A Long Delay	11.07	3.74	12.42	2.60	.15
V3-V1 CVLT I & II Difference List A Trial 1	1.63	2.22	1.17	1.93	.43
V3-V1 CVLT I & II Difference List A Trial 5	.52	2.05	.42	2.41	.87
V3-V1 CVLT I & II Difference List A Trials 1-5	3.11	9.82	4.04	8.30	.72
V3-V1 CVLT I & II Difference List B Trial 1	.48	2.12	-.04	2.01	.37
V3-V1 CVLT I & II Difference List A Short Delay	1.04	2.16	.67	2.71	.59
V3-V1 CVLT I & II Difference List A Long Delay	.81	2.34	1.38	2.39	.40

Table 70
CVLT I & II Visit 3: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
List A Trial 1 Total	.89		.45	
500 mg/day vs 250 mg/day		.96		.48
500 mg/day vs Placebo		.88		.44
250 mg/day vs Placebo		.97		.49
List A Trial 5 Total	.75		.37	
500 mg/day vs 250 mg/day		.98		.49
500 mg/day vs Placebo		.74		.37
250 mg/day vs Placebo		.84		.42
List A Trials 1- 5 Total	.47		.24	
500 mg/day vs 250 mg/day		.96		.48
500 mg/day vs Placebo		.47		.24
250 mg/day vs Placebo		.63		.31
List B Total	.92		.46	
500 mg/day vs 250 mg/day		.99		.50
500 mg/day vs Placebo		.96		.48
250 mg/day vs Placebo		.92		.46
List A Short Delay Total	.55		.28	
500 mg/day vs 250 mg/day		.90		.45
500 mg/day vs Placebo		.53		.26
250 mg/day vs Placebo		.78		.39

List A Long Delay Total	.20		.10	
500 mg/day vs 250 mg/day		.98		.49
500 mg/day vs Placebo		.24		.12
250 mg/day vs Placebo		.30		.15

Table 71
CVLT Visit Difference Scores: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
List A Trial 1 Total	.56		.28	
500 mg/day vs 250 mg/day		.56		.28
500 mg/day vs Placebo		.96		.48
250 mg/day vs Placebo		.73		.36
List A Trial 5 Total	.76		.38	
500 mg/day vs 250 mg/day		.84		.42
500 mg/day vs Placebo		.76		.38
250 mg/day vs Placebo		.99		.49
List A Trials 1- 5 Total	.93		.47	
500 mg/day vs 250 mg/day		.97		.48
500 mg/day vs Placebo		.99		.50
250 mg/day vs Placebo		.93		.46
List B Total	.40		.20	
500 mg/day vs 250 mg/day		.38		.19
500 mg/day vs Placebo		.89		.44
250 mg/day vs Placebo		.67		.33
List A Short Delay Total	.85		.42	
500 mg/day vs 250 mg/day		.99		.50

500 mg/day vs Placebo		.91		.45
250 mg/day vs Placebo		.85		.42

List A Long Delay Total	.69		.35	
500 mg/day vs 250 mg/day		.88		.44
500 mg/day vs Placebo		.93		.46
250 mg/day vs Placebo		.67		.33

Table 72
ROCFT Visit 1 to Visit 3: 250 mg/day group

ROCFT	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Copy Raw Score V1	29.72	4.67	.38	.76
Copy Raw Score V3	30.00	4.23		
Immediate Raw Score V1	21.39	5.22	< .01	< .01
Immediate Raw Score V3	26.54	4.39		
Delayed Raw Score V1	21.63	5.34	< .01	< .01
Delayed Raw Score V3	25.43	4.73		
Difference Raw Score V1	-.24	2.20	.03	.07
Difference Raw Score V3	1.11	2.75		

Table 73
ROCFT Visit 1 to Visit 3: Placebo group

ROCFT	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Copy Raw Score V1	30.21	3.76	.35	.70
Copy Raw Score V3	29.96	3.96		
Immediate Raw Score V1	21.38	4.17	< .01	< .01
Immediate Raw Score V3	26.94	5.13		
Delayed Raw Score V1	20.94	3.67	< .01	< .01
Delayed Raw Score V3	26.04	4.95		
Difference Raw Score V1	.48	2.69	.27	.54
Difference Raw Score V3	.90	2.40		

Table 74
ROCFT Visit 1 to Visit 3: 500 mg/day group

ROCFT	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Copy Raw Score V1	29.13	5.53	.38	.77
Copy Raw Score V3	29.40	5.06		
Immediate Raw Score V1	19.48	6.79	< .01	< .01
Immediate Raw Score V3	24.88	6.46		
Delayed Raw Score V1	19.00	7.11	< .01	< .01
Delayed Raw Score V3	24.31	6.58		
Difference Raw Score V1	.44	2.51	.44	.88
Difference Raw Score V3	.56	2.87		

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Table 75
ROCFT Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
Copy Raw Score V3	29.722	4.67	29.13	5.53	.68
Immediate Raw Score V3	21.39	5.22	19.48	6.79	.26
Delayed Raw Score V3	21.63	5.34	19.00	7.11	.14
Difference Raw Score V3	-.24	2.20	.44	2.51	.31
V3-V1 Copy Raw Score	.28	4.74	.27	4.40	1.00
V3-V1 Immediate Raw Score	5.15	5.00	5.40	4.90	.86
V3-V1 Delayed Raw Score	3.80	4.92	5.31	4.58	.26
V3-V1 Difference Raw Score	1.35	3.70	.13	4.02	.26

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Table 76
ROCFT Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
Copy Raw Score V3	30.21	3.76	29.13	5.53	.43
Immediate Raw Score V3	21.38	4.17	19.48	6.79	.25
Delayed Raw Score V3	20.94	3.67	19.00	7.11	.24
Difference Raw Score V3	.48	2.69	.44	2.51	.96
V3-V1 Copy Raw Score	-.25	3.16	.27	4.40	.64
V3-V1 Immediate Raw Score	5.56	5.81	5.40	4.90	.92
V3-V1 Delayed Raw Score	5.10	4.82	5.31	4.58	.88
V3-V1 Difference Raw Score	.42	3.25	.13	4.02	.78

Table 76a
ROCFT Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
Copy Raw Score V3	29.722	4.67	30.21	3.76	.69
Immediate Raw Score V3	21.39	5.22	21.38	4.17	.99
Delayed Raw Score V3	21.63	5.34	20.94	3.67	.60
Difference Raw Score V3	-.24	2.20	.48	2.69	.30
V3-V1 Copy Raw Score	.28	4.74	-.25	3.16	.65
V3-V1 Immediate Raw Score	5.15	5.00	5.56	5.81	.79
V3-V1 Delayed Raw Score	3.80	4.92	5.10	4.82	.34
V3-V1 Difference Raw Score	1.35	3.70	.42	3.25	.35

Table 77
ROCFT Visit 3: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Copy Raw Score	.73		.36	
500 mg/day vs 250 mg/day		.89		.45
500 mg/day vs Placebo		.71		.35
250 mg/day vs Placebo		.93		.46
Immediate Raw Score	.38		.19	
500 mg/day vs 250 mg/day		.43		.22
500 mg/day vs Placebo		.46		.23
250 mg/day vs Placebo		1.00		.50
Delayed Raw score	.23		.11	
500 mg/day vs 250 mg/day		.22		.11
500 mg/day vs Placebo		.45		.23
250 mg/day vs Placebo		.90		.45
Difference Raw Score	.50		.25	
500 mg/day vs 250 mg/day		.59		.30
500 mg/day vs Placebo		1.00		.50
250 mg/day vs Placebo		.55		.28

Table 78
ROCFT Visit Difference Scores: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Copy Raw Score	.88		.44	
500 mg/day vs 250 mg/day		1.00		.50
500 mg/day vs Placebo		.90		.45
250 mg/day vs Placebo		.89		.45
Immediate Raw Score	.96		.48	
500 mg/day vs 250 mg/day		.98		.49
500 mg/day vs Placebo		.99		.50
250 mg/day vs Placebo		.96		.48
Delayed Raw score	.47		.23	
500 mg/day vs 250 mg/day		.50		.25
500 mg/day vs Placebo		.99		.49
250 mg/day vs Placebo		.64		.32
Difference Raw Score	.46		.23	
500 mg/day vs 250 mg/day		.46		.23
500 mg/day vs Placebo		.96		.48
250 mg/day vs Placebo		.64		.32

Table 79
Stroop Visit 1 to Visit 3: 250 mg/day group

Stroop Trials	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Word Trial V1	48.32	7.76	.04	.08
Word Trial V3	46.34	8.40		
Color Trial V1	61.05	8.93	< .01	< .01
Color Trial V3	53.34	8.97		
Interference Trial V1	91.85	21.66	< .01	< .01
Interference Trial V3	72.82	15.01		
Difference V1	43.53	19.41	< .01	< .01
Difference V3	26.00	8.71		

Table 80
Stroop Visit 1 to Visit 3: Placebo group

Stroop Trials	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Word Trial V1	46.58	6.92	.06	.11
Word Trial V3	45.25	7.04		
Color Trial V1	58.04	8.99	< .01	< .01
Color Trial V3	52.45	8.68		
Interference Trial V1	86.32	18.51	< .01	< .01
Interference Trial V3	71.97	15.48		
Difference V1	39.74	14.71	< .01	< .01
Difference V3	26.72	11.73		

Table 81
Stroop Visit 1 to Visit 3: 500 mg/day group

Stroop Trials	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Word Trial V1	46.69	7.03	.07	.15
Word Trial V3	45.30	7.57		
Color Trial V1	60.12	10.61	< .01	< .01
Color Trial V3	54.35	9.13		
Interference Trial V1	91.62	21.34	< .01	< .01
Interference Trial V3	74.68	16.42		
Difference V1	44.93	18.02	< .01	< .01
Difference V3	29.38	12.91		

Table 82
Stroop Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Stroop Word Trial	46.34	8.40	45.30	7.57	.65
V3 Stroop Color Trial	53.35	8.97	54.35	9.13	.69
V3 Stroop Interference Trial	72.82	15.01	74.68	16.42	.68
V3 Stroop Difference	26.00	8.71	29.38	12.91	.28
V3-V1 Stroop Word Trial	-1.98	5.57	-1.40	4.58	.68
V3-V1 Stroop Color Trial	-7.71	5.82	-5.77	6.05	.25
V3-V1 Stroop Interference Trial	-19.03	11.95	-16.95	11.48	.53
V3-V1 Stroop Difference	-17.53	14.62	-15.55	12.76	.61

Table 83
Stroop Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 Stroop Word Trial	45.25	7.04	45.30	7.57	.98
V3 Stroop Color Trial	52.45	8.68	54.35	9.13	.46
V3 Stroop Interference Trial	71.97	15.48	74.68	16.42	.56
V3 Stroop Difference	26.72	11.73	29.38	12.91	.46
V3-V1 Stroop Word Trial	-1.33	3.91	-1.40	4.58	.96
V3-V1 Stroop Color Trial	-5.59	4.95	-5.77	6.05	.91
V3-V1 Stroop Interference Trial	-14.35	8.84	-16.95	11.48	.38
V3-V1 Stroop Difference	-13.02	10.17	-15.55	12.76	.45

Table 83a
Stroop Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Stroop Word Trial	46.34	8.40	45.25	7.04	.62
V3 Stroop Color Trial	53.35	8.97	52.45	8.68	.72
V3 Stroop Interference Trial	72.82	15.01	71.97	15.48	.84
V3 Stroop Difference	26.00	8.71	26.72	11.73	.81
V3-V1 Stroop Word Trial	-1.98	5.57	-1.33	3.91	.63
V3-V1 Stroop Color Trial	-7.71	5.82	-5.59	4.95	.17
V3-V1 Stroop Interference Trial	-19.03	11.95	-14.35	8.84	.12
V3-V1 Stroop Difference	-17.53	14.62	-13.02	10.17	.21

Table 84
Stroop Visit 3: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Word Trial	.85		.43	
500 mg/day vs 250 mg/day		.88		.44
500 mg/day vs Placebo		1.00		.50
250 mg/day vs Placebo		.87		.44
Color Trial	.76		.38	
500 mg/day vs 250 mg/day		.91		.46
500 mg/day vs Placebo		.74		.37
250 mg/day vs Placebo		.93		.47
Interference Trial	.83		.41	
500 mg/day vs 250 mg/day		.91		.45
500 mg/day vs Placebo		.82		.41
250 mg/day vs Placebo		.98		.49
Difference Time	.54		.27	
500 mg/day vs 250 mg/day		.53		.27
500 mg/day vs Placebo		.69		.34
250 mg/day vs Placebo		.97		.49

Table 85
Stroop Visit Difference Scores: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Word Trial	.86		.43	
500 mg/day vs 250 mg/day		.90		.45
500 mg/day vs Placebo		1.00		.50
250 mg/day vs Placebo		.88		.44
Color Trial	.33		.17	
500 mg/day vs 250 mg/day		.44		.22
500 mg/day vs Placebo		.99		.50
250 mg/day vs Placebo		.38		.19
Interference Trial	.32		.16	
500 mg/day vs 250 mg/day		.78		.39
500 mg/day vs Placebo		.69		.34
250 mg/day vs Placebo		.28		.14
Difference Time	.46		.23	
500 mg/day vs 250 mg/day		.85		.42
500 mg/day vs Placebo		.77		.39
250 mg/day vs Placebo		.42		.21

Table 86
CPT Visit 1 to Visit 3: 250 mg/day group

CPT Responses	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Omissions V1	9.59	12.07	.08	.15
Omissions V3	14.52	17.51		
Commissions V1	18.22	7.95	.15	.29
Commissions V3	16.96	9.26		
Hit Reaction Time V1	362.62	61.02	< .01	.01
Hit Reaction Time V3	397.19	83.16		

Table 87
CPT Visit 1 to Visit 3: Placebo group

CPT Responses	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Omissions V1	6.79	7.81	.13	.26
Omissions V3	10.25	17.90		
Commissions V1	16.83	8.17	.03	.05
Commissions V3	14.42	10.49		
Hit Reaction Time V1	381.77	68.26	.18	.36
Hit Reaction Time V3	390.68	89.97		

Table 88
CPT Visit 1 to Visit 3: 500 mg/day group

CPT Responses	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Omissions V1	8.42	9.96	.06	.11
Omissions V3	13.75	22.18		
Commissions V1	18.79	8.30	< .01	.01
Commissions V3	14.92	9.73		
Hit Reaction Time V1	363.58	55.67	< .01	.01
Hit Reaction Time V3	391.30	65.52		

Table 89
CPT Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 CPT Omissions	14.52	17.51	13.75	22.18	.89
V3 CPT Commissions	16.96	9.26	14.92	9.73	.45
V3 CPT Hit Reaction Time	397.19	83.16	391.30	65.52	.78
V3-V1 CPT Omissions	4.93	17.32	5.33	15.71	.93
V3-V1 CPT Commissions	-1.26	6.05	-3.88	4.94	.10
V3-V1 CPT Hit Reaction Time	34.57	66.00	27.71	48.82	.68

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Table 90
CPT Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 CPT Omissions	10.25	17.90	13.75	22.18	.55
V3 CPT Commissions	14.42	10.49	14.92	9.73	.87
V3 CPT Hit Reaction Time	390.68	89.97	391.30	65.52	.98
V3-V1 CPT Omissions	3.46	14.63	5.33	15.71	.67
V3-V1 CPT Commissions	-2.42	5.79	-3.88	4.94	.35
V3-V1 CPT Hit Reaction Time	8.91	46.27	27.71	48.82	.18

Table 90a
CPT Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 CPT Omissions	14.52	17.51	10.25	17.90	.39
V3 CPT Commissions	16.96	9.26	14.42	10.49	.36
V3 CPT Hit Reaction Time	397.19	83.16	390.68	89.97	.79
V3-V1 CPT Omissions	4.93	17.32	3.46	14.63	.75
V3-V1 CPT Commissions	-1.26	6.05	-2.42	5.79	.49
V3-V1 CPT Hit Reaction Time	34.57	66.00	8.91	46.27	.12

Table 91
CPT Visit 3: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Omissions Total	.71		.35	
500 mg/day vs 250 mg/day		.99		.49
500 mg/day vs Placebo		.80		.40
250 mg/day vs Placebo		.71		.36
Commissions Total	.62		.31	
500 mg/day vs 250 mg/day		.74		.37
500 mg/day vs Placebo		.98		.49
250 mg/day vs Placebo		.63		.31
Hit Reaction Time Total	.95		.48	
500 mg/day vs 250 mg/day		.96		.48
500 mg/day vs Placebo		1.00		.50
250 mg/day vs Placebo		.96		.48

Table 92
CPT Visit Difference Scores: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Omissions Total	.91		.46	
500 mg/day vs 250 mg/day		1.00		.50
500 mg/day vs Placebo		.91		.46
250 mg/day vs Placebo		.94		.47
Commissions Total	.26		.13	
500 mg/day vs 250 mg/day		.23		.11
500 mg/day vs Placebo		.64		.32
250 mg/day vs Placebo		.75		.37
Hit Reaction Time Total	.24		.12	
500 mg/day vs 250 mg/day		.90		.45
500 mg/day vs Placebo		.47		.23
250 mg/day vs Placebo		.23		.11

Table 93
Ruff 2 & 7 Visit 1 to Visit 3: 250 mg/day group

Ruff 2 & 7	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Total Speed T Score V1	45.74	11.45	< .01	< .01
Total Speed T Score V3	54.85	11.63		
Total Accuracy T Score V1	47.41	7.49	< .01	< .01
Total Accuracy T Score V3	53.00	4.42		
Speed Difference Score V1	.01	.02	.43	.86
Speed Difference Score V3	.01	.03		
Accuracy Difference Score V1	.02	.03	.26	.51
Accuracy Difference Score V3	.01	.03		
Total Difference Score V1	.01	.02	.40	.80
Total Difference Score V3	.02	.02		

Table 94
Ruff 2 & 7 Visit 1 to Visit 3: Placebo group

Ruff 2 & 7	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Total Speed T Score V1	43.58	8.72	< .01	< .01
Total Speed T Score V3	50.13	10.20		
Total Accuracy T Score V1	44.29	9.71	< .01	< .01
Total Accuracy T Score V3	51.13	8.01		
Speed Difference Score V1	.02	.03	.26	.53
Speed Difference Score V3	.01	.02		
Accuracy Difference Score V1	.02	.04	.30	.59
Accuracy Difference Score V3	.02	.03		
Total Difference Score V1	.03	.04	< .01	.01
Total Difference Score V3	.01	.01		

Table 95
Ruff 2 & 7 Visit 1 to Visit 3: 500 mg/day group

Ruff 2 & 7	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Total Speed T Score V1	44.33	12.11	< .01	< .01
Total Speed T Score V3	53.75	10.34		
Total Accuracy T Score V1	42.71	9.16	< .01	< .01
Total Accuracy T Score V3	49.88	8.41		
Speed Difference Score V1	.01	.02	.05	.10
Speed Difference Score V3	.02	.04		
Accuracy Difference Score V1	.02	.04	.01	.02
Accuracy Difference Score V3	.00	.01		
Total Difference Score V1	.02	.02	.22	.43
Total Difference Score V3	.02	.03		

Table 96
Ruff 2 & 7 Visit 3 and Visit Difference Scores: 250 mg/day group and 500
mg/day
group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
Total Speed T Score V3	54.85	11.63	53.75	10.34	.72
Total Accuracy T Score V3	53.00	4.42	49.88	8.41	.10
Speed Difference Score V3	.01	.03	.02	.04	.38
Accuracy Difference Score V3	.01	.03	.00	.01	.14
Total Difference Score V3	.02	.02	.02	.03	.37
Total Speed T Score V3-V1	9.11	4.93	9.42	5.82	.84
Total Accuracy T Score V3-V1	5.59	5.93	7.17	10.54	.51
Speed Difference Score V3-V1	.00	.03	.01	.04	.26
Accuracy Difference Score V3-V1	-.01	.04	-.02	.04	.19
Total Difference Score V3-V1	.00	.03	.01	.04	.61

5

Table 97
Ruff 2 & 7 Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
Total Speed T Score V3	50.13	10.20	53.75	10.34	.23
Total Accuracy T Score V3	51.13	8.01	49.88	8.41	.60
Speed Difference Score V3	.01	.02	.02	.04	.32
Accuracy Difference Score V3	.02	.03	.00	.01	.09
Total Difference Score V3	.01	.01	.02	.03	.04
Total Speed T Score V3-V1	6.54	3.89	9.42	5.82	.05
Total Accuracy T Score V3-V1	6.83	4.93	7.17	10.54	.89
Speed Difference Score V3-V1	-.01	.04	.01	.04	.13
Accuracy Difference Score V3-V1	-.00	.04	-.02	.04	.19
Total Difference Score V3-V1	-.02	.04	.01	.04	.02

Table 97a
Ruff 2 & 7 Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		<i>p</i> -value
	Mean	Std. Deviation	Mean	Std. Deviation	
Total Speed T Score V3	54.85	11.63	50.13	10.20	.13
Total Accuracy T Score V3	53.00	4.42	51.13	8.01	.30
Speed Difference Score V3	.01	.03	.01	.02	.87
Accuracy Difference Score V3	.01	.03	.02	.03	.81
Total Difference Score V3	.02	.02	.01	.01	.15
Total Speed T Score V3-V1	9.11	4.93	6.54	3.89	.05
Total Accuracy T Score V3-V1	5.59	5.93	6.83	4.93	.42
Speed Difference Score V3-V1	.00	.03	-.01	.04	.52
Accuracy Difference Score V3-V1	-.01	.04	-.00	.04	.96
Total Difference Score V3-V1	.00	.03	-.02	.04	.02

Table 98
Ruff 2 & 7 Visit 3: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Total Speed T Score	.28		.14	
500 mg/day vs 250 mg/day		.93		.47
500 mg/day vs Placebo		.48		.24
250 mg/day vs Placebo		.27		.13
Total Accuracy T Score	.29		.14	
500 mg/day vs 250 mg/day		.26		.13
500 mg/day vs Placebo		.81		.41
250 mg/day vs Placebo		.62		.31
Speed Difference Score	.51		.26	
500 mg/day vs 250 mg/day		.61		.30
500 mg/day vs Placebo		.54		.27
250 mg/day vs Placebo		.99		.50
Accuracy Difference Score	.25		.12	
500 mg/day vs 250 mg/day		.38		.19
500 mg/day vs Placebo		.27		.13
250 mg/day vs Placebo		.96		.48
Total Difference Score	.12		.06	
500 mg/day vs 250 mg/day		.54		.27
500 mg/day vs Placebo		.09		.05
250 mg/day vs Placebo		.51		.25

Table 99
Ruff 2 & 7 Visit Difference Scores: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Total Speed T Score	.09		.05	
500 mg/day vs 250 mg/day		.97		.49
500 mg/day vs Placebo		.12		.06
250 mg/day vs Placebo		.16		.08
Total Accuracy T Score	.73		.36	
500 mg/day vs 250 mg/day		.74		.37
500 mg/day vs Placebo		.99		.49
250 mg/day vs Placebo		.83		.41
Speed Difference Score	.26		.31	
500 mg/day vs 250 mg/day		.57		.28
500 mg/day vs Placebo		.24		.12
250 mg/day vs Placebo		.78		.39
Accuracy Difference Score	.33		.16	
500 mg/day vs 250 mg/day		.40		.20
500 mg/day vs Placebo		.39		.19
250 mg/day vs Placebo		1.00		.50
Total Difference Score	.02		.01	
500 mg/day vs 250 mg/day		.87		.43
500 mg/day vs Placebo		.03		.01
250 mg/day vs Placebo		.07		.04

Table 100
WCST Visit 3: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Total Cards Used	90.88	20.17	89.57	18.50	.81
V3 Number of Categories Achieved	5.69	.88	5.87	.46	.39
V3 Total Errors	19.73	18.03	19.00	12.05	.87
V3 Total Perseverative Errors	8.54	4.76	9.13	5.18	.68
V3 Number of Trials to Get into Category	15.19	14.91	13.78	7.05	.68
V3 Number of Trials to Complete Category	71.15	10.80	70.57	9.31	.84

Table 101
WCST Visit 3: Placebo group and 500 mg/day group

	Placebo		500 mg/day		<i>p</i> -value
	Mean	Std. Deviation	Mean	Std. Deviation	
V3 Total Cards Used	85.46	15.91	89.57	18.50	.42
V3 Number of Categories Achieved	5.96	.20	5.87	.46	.39
V3 Total Errors	13.83	7.35	19.00	12.05	.08
V3 Total Perseverative Errors	7.54	4.22	9.13	5.18	.25
V3 Number of Trials to Get into Category	11.58	3.53	13.78	7.05	.18
V3 Number of Trials to Complete Category	71.63	10.50	70.57	9.31	.72

Table 102
WCST Visit 3: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	p-value
V3 Total Cards Used	90.88	20.17	85.46	15.91	.30
V3 Number of Categories Achieved	5.69	.88	5.96	.20	.16
V3 Total Errors	19.73	18.03	13.83	7.35	.14
V3 Total Perseverative Errors	8.54	4.76	7.54	4.22	.44
V3 Number of Trials to Get into Category	15.19	14.91	11.58	3.53	.25
V3 Number of Trials to Complete Category	71.15	10.80	71.63	10.50	.88

Table 103
WCST Visit Difference Scores: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Total Cards Used	.56		.28	
500 mg/day vs 250 mg/day		.97		.48
500 mg/day vs Placebo		.72		.36
250 mg/day vs Placebo		.55		.28
Number of Categories Achieved	.28		.14	
500 mg/day vs 250 mg/day		.56		.28
500 mg/day vs Placebo		.87		.43
250 mg/day vs Placebo		.27		.13
Total Errors	.25		.13	
500 mg/day vs 250 mg/day		.98		.49
500 mg/day vs Placebo		.39		.19
250 mg/day vs Placebo		.27		.14
Total Perseverative Errors	.51		.26	
500 mg/day vs 250 mg/day		.90		.45
500 mg/day vs Placebo		.49		.24
250 mg/day vs Placebo		.74		.37
Number of Trials to Get into Category	.44		.22	
500 mg/day vs 250 mg/day		.87		.44
500 mg/day vs Placebo		.73		.37
250 mg/day vs Placebo		.41		.21

Number of Trials to Complete Category	.94		.47	
500 mg/day vs 250 mg/day		.98		.49
500 mg/day vs Placebo		.93		.47
250 mg/day vs Placebo		.99		.49

Trail**Table 104**

Trail Making	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Trail Making A V1	11.16	3.36	.03	.07
Trail Making A V3	9.37	3.87		
Trail Making B V1	29.15	13.31	< .01	< .01
Trail Making B V3	18.40	5.80		
Trail Making B-A V1	17.99	13.77	< .01	< .01
Trail Making B-A V3	9.00	3.95		

Making Test Visit 1 to Visit 3: 250 mg/day group

5

Trail

Table

Trail Making	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Trail Making A V1	12.47	5.50	< .01	< .01
Trail Making A V3	8.71	2.45		
Trail Making B V1	26.10	12.06	< .01	< .01
Trail Making B V3	18.36	8.16		
Trail Making B-A V1	13.62	11.74	.03	.06
Trail Making B-A V3	9.67	7.56		

105

Trail Making	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
Trail Making A V1	12.89	3.91	< .01	< .01
Trail Making A V3	9.28	3.12		
Trail Making B V1	28.60	12.16	.03	.05
Trail Making B V3	23.02	15.40		
Trail Making B-A V1	15.71	10.45	.25	.50
Trail Making B-A V3	13.73	15.69		

Making Test Visit 1 to Visit 3: Placebo group

Table

Trail Making Test Visit 1 to Visit 3: 500 mg/day group

106

Table 107
Trail Making Test Visit 3 and Visit Difference Scores:
250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 Trail Making A	9.37	3.87	9.28	3.12	.93
V3 Trail Making B	18.40	5.80	23.02	15.40	.15
V3 Trail Making B-A	9.00	3.95	13.73	15.69	.14
V3-V1 Trail Making A	-1.80	4.87	-3.60	4.05	.16
V3-V1 Trail Making B	-10.75	13.13	-5.58	13.40	.17
V3-V1 Trail Making B-A	-8.99	13.42	-1.98	14.07	.08

Table 108
Trail Making Test Visit 3 and Visit Difference Scores:
Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 Trail Making A	8.71	2.45	9.28	3.12	.48
V3 Trail Making B	18.36	8.16	23.02	15.40	.20
V3 Trail Making B-A	9.67	7.56	13.73	15.69	.26
V3-V1 Trail Making A	-3.76	4.98	-3.60	4.05	.90
V3-V1 Trail Making B	-7.74	8.81	-5.58	13.40	.51
V3-V1 Trail Making B-A	-3.96	9.73	-1.98	14.07	.57

Table 108a
Trail Making Test Visit 3 and Visit Difference Scores:
250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i>-value
V3 Trail Making A	9.37	3.87	8.71	2.45	.48
V3 Trail Making B	18.40	5.80	18.36	8.16	.98
V3 Trail Making B-A	9.00	3.95	9.67	7.56	.69
V3-V1 Trail Making A	-1.80	4.87	-3.76	4.98	.16
V3-V1 Trail Making B	-10.75	13.13	-7.74	8.81	.35
V3-V1 Trail Making B-A	-8.99	13.42	-3.96	9.73	.14

Table 109
Trail Making Test Visit 3: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Trail Making A	.74		.37	
500 mg/day vs 250 mg/day		1.00		.50
500 mg/day vs Placebo		.81		.41
250 mg/day vs Placebo		.75		.38
Trail Making B	.21		.10	
500 mg/day vs 250 mg/day		.26		.13
500 mg/day vs Placebo		.28		.14
250 mg/day vs Placebo		1.00		.50
Trail Making B-A	.21		.11	
500 mg/day vs 250 mg/day		.23		.11
500 mg/day vs Placebo		.35		.18
250 mg/day vs Placebo		.97		.49

Table 110
Trail Making Test Visit Difference Scores: 250 mg/day, Placebo, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between groups <i>p</i> (1-tailed)
Trail Making A	.25		.12	
500 mg/day vs 250 mg/day		.36		.18
500 mg/day vs Placebo		.99		.50
250 mg/day vs Placebo		.30		.15
Trail Making B	.31		.15	
500 mg/day vs 250 mg/day		.28		.14
500 mg/day vs Placebo		.81		.40
250 mg/day vs Placebo		.65		.32
Trail Making B-A	.13		.06	
500 mg/day vs 250 mg/day		.12		.06
500 mg/day vs Placebo		.85		.42
250 mg/day vs Placebo		.33		.17

Table 111
MOSES Visit 1 to Visit 3: 250 mg/day group

MOSES	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V2 MOSES	1.30	1.61	.17	.34
V3 MOSES	1.04	1.58		

Table 112
MOSES Visit 1 to Visit 3: Placebo group

5

MOSES	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V2 MOSES	.59	1.14	.21	.42
V3 MOSES	.45	1.53		

Table 113
MOSES Visit 1 to Visit 3: 500 mg/day group

MOSES	Mean	Std. Dev.	Sig (1-tailed)	Sig (2-tailed)
V2 MOSES	.81	1.40	.04	.07
V3 MOSES	.38	.97		

Table 114
MOSES Visit 3 and Visit Difference Scores: 250 mg/day group and 500 mg/day group

	250 mg/day		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 MOSES	1.04	1.58	.38	.97	.11
V3-V2 Score	-.26	1.29	-.43	1.03	.64

5

Table 115
MOSES Visit 3 and Visit Difference Scores: Placebo group and 500 mg/day group

	Placebo		500 mg/day		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 MOSES	.45	1.53	.38	.97	.85
V3-V2 Score	-.14	.77	-.43	1.03	.30

10

Table 115a
MOSES Visit 3 and Visit Difference Scores: 250 mg/day group and Placebo group

	250 mg/day		Placebo		
	Mean	Std. Deviation	Mean	Std. Deviation	<i>p</i> -value
V3 MOSES	1.04	1.58	.45	1.53	.21
V3-V2 Score	-.26	1.29	-.14	.77	.70

Table 116
MOSES Visit 3: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
MOSES Score	.23	-	.11	-
500 mg/day vs. 250 mg/day	-	.27	-	.13
500 mg/day vs. Placebo	-	.98	-	.49
250 mg/day vs. Placebo	-	.34	-	.17

Table 117
MOSES Visit Difference Scores: 250 mg/day, Placebo groups, and 500 mg/day groups

	Between Groups Overall <i>p</i> (2-tailed)	Between Groups <i>p</i> (2-tailed)	Between Groups Overall <i>p</i> (1-tailed)	Between Groups <i>p</i> (1-tailed)
MOSES Score	.66	-	.33	-
500 mg/day vs. 250 mg/day	-	.86	-	.43
500 mg/day vs. Placebo	-	.64	-	.32
250 mg/day vs. Placebo	-	.92	-	.46

CLAIMS

What is claimed is:

1. A method for improving motor function of a healthy human subject comprising a step of
5 administering an effective amount of citidine-5'-diphosphocholine (hereinafter referred to as
citicoline) or a salt thereof to a healthy human subject.
2. The method according to claim 1, wherein the effective amount of citicoline administered is 5
mg or more and 4.0 g or less per day.
- 10 3. The method according to claim 1, wherein the effective amount of citicoline administered is
100 mg or more and 1.0 g or less per day.
4. The method according to claim 1, wherein the effective amount of citicoline administered is
15 250 mg or more and 500 mg or less per day.
5. The method according to claim 1, wherein the effective amount of citicoline administered is
250 mg per day.
- 20 6. The method according to claim 1, wherein the effective amount of citicoline administered 500
mg or less per day.
7. The method according to claim 1, wherein the citicoline is administered for at least 1 day and
at most 1 year.
- 25 8. The method according to claim 1, wherein the citicoline is administered for at least 1 day and
at most 4 weeks.
9. The method according to claim 1, wherein the motor function involves performing a complex
30 and precise movement.

10. The method according to claim 1, wherein the motor function involves performing detailed work by using a hand or finger of the subject.

11. The method of claim 1, wherein the citicoline or a salt thereof is administered alone in an amount of 5 mg or more and 4.0 g or less per day.

12. The method of claim 1, wherein the citicoline or a salt thereof is administered orally.

13. A method for improving cognitive function of a healthy human subject comprising a step of administering an effective amount of citicoline to a healthy human subject.

14. The method according to claim 13, wherein the effective amount of citicoline administered is 5 mg or more and 4.0 g or less per day.

15. The method according to claim 13, wherein the effective amount of citicoline administered is 100 mg or more and 1.0 g or less per day.

16. The method according to claim 13, wherein the effective amount of citicoline administered is 250 mg or more and 500 mg or less per day.

20

17. The method according to claim 13, wherein the effective amount of citicoline administered is 250 mg per day.

18. The method according to claim 13, wherein the effective amount of citicoline administered is 25 500 mg or less per day.

19. The method according to claim 13, wherein the improved cognitive function results in making few mistakes in routine work and performing said work continuously without being distracted.

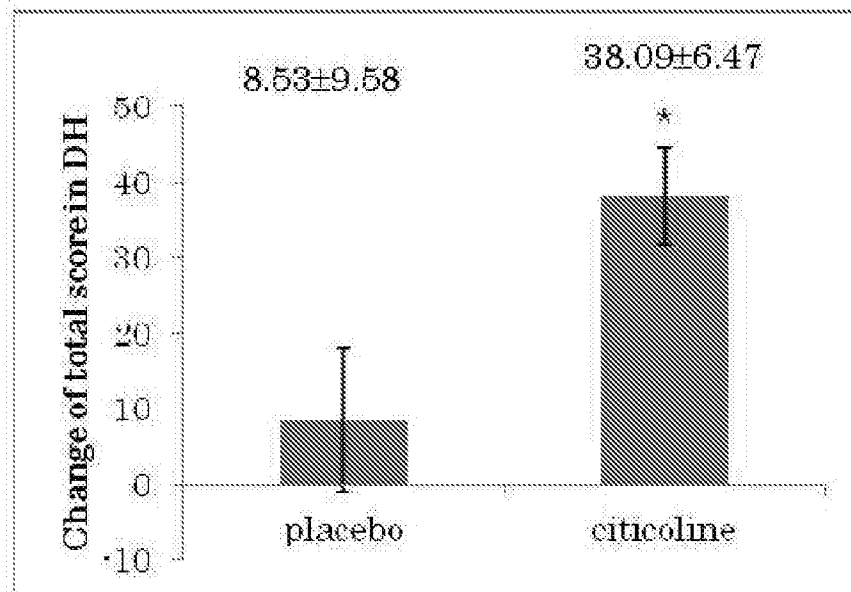
30

20. The method according to claim 13, wherein the improved cognitive function results in the ability to instantly distinguishing between right and wrong.

21. The method according to claim 13, wherein the citicoline or a salt thereof is administered 5 alone in an amount of 5 mg or more and 4.0 g or less per day.

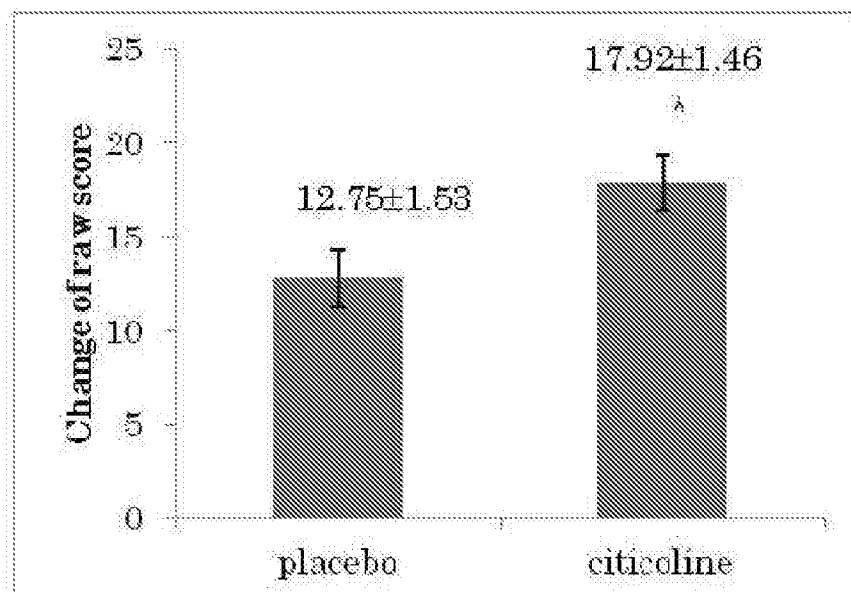
22. The method according to claim 13, wherein the citicoline or a salt thereof is administered orally.

Figure 1. Visit Difference Scores of Finger Tap Test



* $P < 0.05$ significantly different from the placebo.

Figure 2. Visit Difference Scores of Ruff2&7 speed task



* $P < 0.05$ significantly different from the placebo.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2015/053178

A. CLASSIFICATION OF SUBJECT MATTER

Int.Cl. A61K31/14 (2006.01) i, A61P43/00 (2006.01) i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int.Cl. A61K31/14, A61P43/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Published examined utility model applications of Japan 1922-1996
 Published unexamined utility model applications of Japan 1971-2015
 Registered utility model specifications of Japan 1996-2015
 Published registered utility model applications of Japan 1994-2015

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

JSTPlus/JMEDPlus/JST/580 (JDreamIII), CAPplus/REGISTRY/MEDLINE/EMBASE/BIOSIS (STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	Steven E. Bruce, Improvements in quantitative EEG following consumption of a natural citicoline-enhanced beverage, Int J Food Sci Nutr., 2012, 63(4), 421-5 See Results, Conclusions	13-22 1-12
X	Silveri M. M., et al., Citicoline enhances frontal lobe bioenergetics as measured by phosphorus magnetic resonance spectroscopy, NMR Biomed., 21(10), 2008, 1066-75 See ABSTRACT, page 1073, right column, line 18-40	13-22



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

09.06.2015

Date of mailing of the international search report

23.06.2015

Name and mailing address of the ISA/JP

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2015/053178

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Alvarez X. Anton, et al., Citicoline improves memory performance in elderly subjects, Methods Find Exp Clin Pharmacol., 1997, 19(3), 201-10 See page 202, left column, line 16-right column, line 8, RESULTS	13-22
Y	Toshimasa Sato, et al., Time courses of brain activation and their implications for function: A multichannel near-infrared spectroscopy study during finger tapping, Neurosci Res., 2007, 58(3), 297-304 See page 300, left column, line 1-right column, line 28	1-12