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Effectiveness of Whole Green Coffee Powder (WGCP) Versus Placebo in a Double-Blind Withdrawal Design Study with Young Adults on Three Tasks of Executive Function

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ABSTRACT

Objective: This study compared relative effects of Whole Green Coffee Powder (WGCP) on cognitive functioning in neurotypical adults under 3 treatment conditions: Placebo (A), low dose 889.9 mg WGCP (B1) and moderate dose 1334.4 mg WGCP (B2).

Method: Fourteen adults aged 18-25 years, acted as their own controls in 3 treatment conditions within a 7-session withdrawal design. Participants completed the CANTAB ADHD battery at each session. The Side Effects Behavior Monitoring Scale (SEBMS), used to assess stimulant effects in individuals with ADHD, was a secondary outcome measure to assess adverse events associated with caffeine intake delivered by capsule. Self-report of qualitative effects were collected.

Results: Results indicated that moderate doses WGCP significantly improved sustained attention and working memory but had no effect on response inhibition. Low doses of WGCP showed *decreased* sustained attention and working memory. Fifty percent of subjects reported positive subjective improvement in well-being. No side effects were reported.

Conclusion: Commercially available WGCP (i.e., sold as Go Bean®) in moderate doses improved executive functioning for sustained attention and working memory but had no effect on response inhibition. Implications for individuals with attention deficits are discussed.

INTRODUCTION

Individuals progressing through academic study require concerted focused attention in order to successfully master the tasks posed by school. Control of attention is managed by executive functions which help to prioritize, organize and complete work in a timely way. Russell Barkley describes executive functions as the actions people use to control personal behavior, direct behavior toward a goal, and improve outcomes for behavior in the future [1]. The role of attention in executive functions is critical in most facets of organized daily life.

Attention wandering has been demonstrated to compromise executive functions and result in cognitive difficulties in learning [1]. For example, attention-deficit/hyperactivity disorder (ADHD) has long been recognized as a developmental disorder in children, and evidence now confirms that symptoms are experienced to varying degrees in adults as well. Prevalence rates in adult ADHD depend on whether "syndromatic" or "symptomatic" definitions of persistence are considered [2]; that is, whether or not functionally impairing symptoms are accommodated by the maturing adult. Nevertheless, clinical symptoms and functional impairments persist throughout adolescence and into adulthood in more than 50% of cases [3, 4].

The etiology of poor attention, as occurs in ADHD, for example, is multi-factorial, and the impact of problems of attention on school performance of children, adolescents and young adults is well-documented. Alternative and complementary treatments may be helpful in managing behaviors associated with attention to school tasks, thus there is need to investigate them. Also, because most subjects respond to stimulant therapy [5], stimulants used to treat attention deficits are increasingly and inappropriately diverted from their prescribed use among college students [6].

Worldwide, caffeine is the most widely consumed substance having psychoactive effects [7]. It is the neuroactive agent in coffee and tea and is a nonselective antagonist of the neuromodulator adenosine; if applied in commonly consumed doses, it generates stimulating effects by blockading adenosine receptors. Cognitive performance generally is positively influenced by caffeine ingestion and the influence of caffeine on cognitive performance is well documented [8-11]. Though some studies show limited benefit to performance [12], caffeinated coffee is the most common form of caffeine intake, increasing alertness and lowering fatigue. Caffeine is now readily available in a variety of liquid (i.e., energy drinks) and capsule forms.

Whole green coffee powder (WGCP) is a fibrous, naturally occurring endogenous substance and is a nonesterified solid source of caffeine. It is processed directly from the whole green coffee bean and contains chlorogenic acid in its natural form. It is distinct from green coffee extract in that it is a green coffee product made from the whole bean in a specified process (current patent pending). WGCP, sold commercially as Go Bean®, is an endogenous compound that delivers a solid (not from extract) form of caffeine in capsules. WGCP sponsors claim the presence of naturally occurring green coffee bean nutrients not available in coffee extract. The granularity of green coffee powder derived from the fine-grain pulverizing process of Go Bean® releases caffeine and cholinergic acid gradually, acting in an extended time-release delivery. It is purported to be well tolerated and evidence of common or frequent side effects is not reported in the current available literature.

This study investigated the effects of commercially available dietary caffeine supplement (WGCP sold as Go Bean®) on the ability of neurotypical individuals (i.e., without diagnosed ADHD) to exercise executive functions associated with sustained attention, spatial working memory, and response inhibition (i.e., impulsivity). These assessed executive functions promote cognitive activity similar in nature to academic study. To measure the effects of WGCP on core executive functions used in standard academic study, we used the ADHD Core Battery of the Cambridge Neuropsychological Test Automated Battery (CANTAB). This battery includes several modules: Motor Screening (data from this module was not used in analysis as it tests fine motor speed and is an introductory exercise to the test battery); Rapid Visual Information Processing (sustained attention); Stop Signal Task (response inhibition); and Spatial Working Memory (working memory). We also investigated the qualitative effects of WGCP via participant self-report.

The study explored the following primary research questions:

1. What are the effects of WGCP compared with placebo on *sustained attention*, *spatial working memory*, and *response inhibition*?
2. How do subjects qualitatively describe the effects of WGCP on affective presentation in daily activity?

METHOD

Rationale for a Small-N Study

The most important outcome of alternative and complementary treatment research is the evidence of effects in *individuals*. Such evidence is lost in large scale clinical trial data which focus almost exclusively on symptom reduction reported as group means. Group study designs account for variability of response by spreading variability across large numbers of subjects. However, this approach masks useful information. In single subject and small N studies, variability is experimentally controlled by using single subject designs that allow individuals to act as their own controls. This method is useful to observe variability which is critical when investigating new compounds that lead to larger, controlled trials. Experimental single-subject withdrawal designs are reliable and rigorous, efficient and inexpensive, and permit sound conclusions regarding subjects with similar behavioral repertoires.

Single subject designs do not require sample size calculations to demonstrate experimental effects. Sample size calculations are most useful in group designs. The power of well-designed single subject (repeated measures) designs is evident in that with 10 participants, receiving only 5 measurements across the study, power to detect significant differences within subjects across conditions is quite good (Power=.89) when a large effect size (f=.40; ~d=.80), moderate test-retest reliability (correlation) between repeated measurements (r=.60), and a typical Type 1 error rate (.05) are assumed. A large effect size is entirely reasonable to expect in single case research designs and the test retest correlation is likely to actually be larger, possibly as high as the reported test-retest reliability of the test (>.80) which would drive power even higher (>.99).

Assumptions of Study Design

Referenced in previous studies with caffeine products, the following characteristics of WGCP are assumed: 1) washout of WGCP effect occurs rapidly (i.e., over the period of several hours); 2) dosing may be abruptly terminated without adverse side effects; 3) WGCP effects at moderate dose are not dependent on gradual ramping up from low dose thus moderate dose may be safely administered as initial therapeutic dose; 4) onset of WGCP effect is established within one hour as is typical of caffeine products.

Procedures

We used a *withdrawal of treatment* design to examine the differential effects of a commercially available dietary supplement (Go Bean®) and placebo in neurotypical college-age adults ages 18 to 25 years. The design removes variability through improved experimental control of treatment conditions [13]. A withdrawal of treatment design allowed multiple observations of a small number of subjects (compared to randomized clinical trial designs that use few observations of many subjects). The design alternated treatment and no-treatment conditions across days within single subjects to provide sensitive examination of dose effects. The design removed variability through improved control of treatment conditions. Collection of time-series data permitted the assessment of ongoing treatment-related changes across each presentation of the dependent variable.

The trial is initiated in the baseline (BL) phase of an experimental manipulation of variables. The placebo (A) phase is alternated with the experimental phases. In this study, B_1 was the first dose of the active compound (i.e., WGCP), and B_2 is the second dose of the active compound. The A phase is an intermediary phase between BL (baseline) and active compound (B_1 and B_2) and controls for an expectancy of improvement associated with mere ingestion of a capsule as part of a trial (i.e., placebo effect). We maintained the rule central to experimental manipulation of variables—only one variable was changed at a time. This allowed for opportunity to distinguish between expectancy (i.e., placebo) and WGCP effects.

Following overnight caffeine abstinence [11], subjects received three identical capsules at each session with varying number of capsules containing WGCP. Each capsule contained placebo or 500 mg WGCP proprietary blend (Go Bean® which is 50 mg green coffee caffeine with no removal of chlorogenic acid as is typically the case in commonly sold commercial green coffee extracts and other caffeine extracts. Capsules were administered orally once each day in the presence of the study coordinator and one hour prior to CANTAB. Supplements were supplied in labeled plastic containers with study, subject randomization information (i.e., study session number and subject coded identification), and sponsor on the label. In Phase A (placebo), all three capsules contained an inert substance (i.e., corn starch); in Phase B_1, subjects received one placebo capsule and two WGCP capsules (889.9 mg); in Phase B_2, subjects received three capsules each with the same equivalent dose of WGCP (1334.4 mg) . Package label instructions for using WGCP include a three capsule dose.

The order of the dose was not randomized since the concern was not if dose improves performance but only whether WGCP improved performance. To varying degrees across subjects, this also permitted us to detect residual effects of withdrawal. Because the safety of subjects is always paramount, we did not start with a potentially high dose to which some individuals may be sensitive.

Because the order of presentation of treatment was defined a priori, placebo was counterbalanced across two orders of treatment to maintain the double-blind requirement; experimenters were unaware of the order of treatments. The counterbalanced treatment orders are indicated below:

I. $BL - A - B_1 - A - B_2 - A - B_2$
II. $BL - B_1 - A - B_2 - A - B_2 - A$

We assessed for subjects' medications, recreational drugs, or caffeine consumed through diet or other supplements prior to each administration and relied on subjects' accurate representation through verbal query.

The study focused on acute administration of WGCP, that is, subjects were provided low doses of caffeine within a short period. This was practiced because similar studies with chronic caffeine use showed diminished sustained attention and working memory compared to those who abruptly terminated chronic caffeine use [11, 12, 14].

Eligible subjects were randomly assigned in to orders I and II; 8 subjects received presentation l and 6 subjects received presentation ll. Each subject arrived at the clinic at the same time in each experimental phase; assigned times did not differ across placebo and active WGCP days. As an example, if Subject 1 arrived for her baseline visit at 8AM, she came to subsequent WGCP active and placebo visits at 8AM. After arrival, subjects were given the randomized dose of WGCP and/or placebo. In one hour, subjects were presented the CANTAB Battery which took approximately 30 minutes to complete and was administered as the same time of day, replicating baseline conditions. The CANTAB Battery was presented in a quiet, moderately lit room located in the library of a local university campus or in a similar room in a hospital setting; each subject completed the CANTAB battery in the same room the CANTAB was initiated. Sessions were separated by at least 1 day to completely eliminate carryover effects as WGCP has duration of action of 4-6 hours (as per package label). After CANTAB Battery administration, subjects completed the Side Effects Behavior Monitoring Scale (SEBMS; [15] with the study coordinator.

Statistical Analyses of CANTAB Subtests. Sustained attention was measured using the discriminability parameter of the Rapid Visual Processing subtest. Response Inhibition was measured using stop signal reaction time from the Stop Signal subtest. Spatial working memory was measured using total errors from the Spatial Working Memory subtest. For each dependent variable, a generalized estimating equations (GEE) model was computed with Treatment (placebo, low dose Go Bean®, and moderate dose Go Bean®) as fixed factor predictors and the dependent variable as the response variable. GEE is advantageous in that it flexibly accounts for repeated measurements with each participant permitting missing data and explicitly modeling relationships between repeated measures conditions. Alternative covariance structures were examined. Results are based on autoregressive structure. EE analysis assumed a Poisson distribution with loglinear link for ordinal/count data and a normal distribution with linear link for continuous data.

Measures

The CANTAB ADHD Battery was the primary outcome measure. It has been demonstrated to detect neuropsychological effects with selectivity and sensitivity, allows ready interpretation of the effects, it has a variety of applications in psychology, neurospsychology and medicine [16].

The Motor Screening Task is administered at the beginning of the CANTAB battery, and assesses whether a subject can respond to the requirements of the other tasks in the battery; it confirms appropriate visual, movement and comprehension abilities. Rapid Visual Information Processing (RVP) is a test of sustained attention and is similar to the commonly used Continuous Performance Test; it is a sensitive measure of general cognitive performance. The Stop Signal Task (SST) is a common assessment task used to assess response inhibition; it estimates an individual's reaction time and gives a measure of how well an individual can inhibit responses and resist the tendency to respond automatically. Spatial Working Memory (SWM) is a test of the participant's ability to use working memory by retaining spatial information, remembering items and manipulated them in space; this test measures global executive dysfunction.

The CANTAB subtests were administered once each session. Published studies demonstrate that the CANTAB shows very small practice effects over repeated measures [16] and parallel versions of the CANTAB allow repeated measures.

Qualitative descriptions and adverse events were assessed in each session. Side effects were assessed using the SEBMS adverse events checklist [15]. The SEBMS uses the Clinical Global Impressions-Severity (CGI-S) anchored scale (1=normal, 2= borderline, 3=mild, 4=moderate, 5=marked, 6=severe, and 7=most extreme). Subjects completed the SEBMS at the end of each session to track change in behavior. All ratings were based

on participants' subjective experience of the one hour and thirty minute period and on subjective reports between sessions. An adverse event was defined as any untoward medical or physical occurrence in a subject administered WGCP during the course of the study. Participants were probed as to the presence of the side effect.

The ADHD Rating Scale (ADHD-RS) is an 18-item scale used to rule out symptomatic attentional difficulties. It was administered at Baseline coinciding with assessment of working memory and response inhibition as measured by the CANTAB. It was used to screen for the presence of ADHD. Scores over 32 are generally considered symptomatic threshold.

Drug screening was conducted by inviting the participants to give verbal self-report of use.

Subjects

Inclusion Criteria. To be eligible for inclusion, participants met criteria at initial screening and baseline in that (a) a written consent was signed by the participant; (b) the participant was aged 18 to 25 years; (c) females of childbearing age had a negative response to a verbal inquiry for pregnancy, and were not at risk for becoming pregnant; (d) participants completed an ADHD rating scale; (e) participants had a minimum level of intellectual functioning (determined by the investigator-all participants were or had been enrolled in college courses); (f) symptom criteria for a comorbid mental health condition that could affect safety or tolerability of medication, or interfere with the participant's participation in the study were not in evidence; (g) blood pressure measurements were within the 95th percentile for age and gender at screening; and (h) participants were able to comply with the requirements of the study protocol.

Exclusion Criteria. At screening or baseline, eligibility was declined if the participant (a) had a current, controlled, or uncontrolled comorbid psychiatric diagnosis with significant symptoms, that, in the opinion of the study investigator, contraindicated treatment or assessment; (b) was suspected of substance abuse or dependence disorder within the past 12 months in accordance with *DSM-IV-TR* criteria; (c) participant admitted to the use of prescription or illegal substance; (d) had a history of seizures during the last 2 years, a severe tic disorder, and a current diagnosis or family history of Tourette's syndrome; (e) had a conduct disorder; (f) participant had taken an investigational product within 30 days prior to Screening, or participated in any other research study during the trial; (g) had any clinically significant laboratory abnormalities at Screening or Baseline, (h) had a known history of structural cardiac abnormality; (i) had a concurrent chronic or acute medical illness that would prohibit the participant from completing the study or would not be in the best interest of the participant; (j) taking any medications that are excluded, have other Central Nervous System (CNS) dysfunction, or effect performance, such as sedating antihistamines and decongestant sympathomimetics (bronchodilators were not exclusionary); and (k) the female subject was pregnant or lactating.

Subject Confidentiality & Consent**.** Subjects were interviewed by the study investigator or study coordinator. Subjects signed the consent form during the interview period and consents were obtained at least one week prior to the start of the study period. The hospital Institutional Review Board (IRB) approved the study protocol and informed consent procedures.

RESULTS

A total of 16 adults not diagnosed with ADHD or other psychiatric conditions were screened for participation; 14 enrolled in the study (see Table 1). This study population was useful due to participants' ongoing engagement with academic tasks. Academic studies require sufficient working memory and the ability to delay a response to more interesting activities in order to complete less interesting tasks (i.e., academic work).

The mean ADHD Rating Scale score was 26.4 and nonsymptomatic for ADHD. Subjects did not differ on measures of attention dysfunction. (See Table 2.)

Table 1. Subject Demographics

n	8	6	
Male (n, %)	2 (25.0%)	2 (33.3%)	.594
White non-Hispanic (n)	8	6	
Age (M, SD)	21.25 (1.49)	21.83 (1.94)	.662

Note: non-parametric statistics (Mann-Whitney U and Fisher's exact test) were computed.

Table 2. ADHD Rating Scale Measures of Attention Dysfunction

	Mean Score				
Target Symptoms	Baseline	Placebo	WGCP low dose	WGCP moderate dose	X^2 (p)
Overactivity; motor restlessness	1.29	1.36	1.34	1.34	2.89 (.409)
Impulsiveness; acting without thinking	1.33	1.26	1.27	1.26	8.58 (.035)
Distractibility; sustaining attention to tasks	1.57	1.54	1.44	1.60	3.70 (.296)
Task completion; finishing tasks	1.17	1.11	1.09	1.13	3.00 (.392)
Being on time/ Accepting limits	1.14	1.14	1.14	1.14	-
Following Instructions	1.13	1	1	1	-
Frustration tolerance; appropriately expresses frustration	1.21	1.21	1.21	1.21	-
Ability to calm self when excited	1.43	1.41	1.63	1.36	2.39 (.495)
Non-family/ Peer relations	1.07	1.07	1.07	1.07	-
Family/Close relations	1	1	1	1	-

Note: Generalized estimating equations analysis assuming Poisson distribution with loglinear link for ordinal/count data. Wald Chi-Square degrees of freedom equals 3. In many cases, the counts were of extremely low variability (almost entirely scores of 1). Therefore test statistics could not be computed or should be seen only as descriptive of the general pattern.

The study generated information on the effects of WGCP on: a) *sustained attention* (RVP), b) *response inhibition* (SST), c) *spatial working memory* (SWM), and d) qualitative description of the effects of the substance among young adults.

Results indicated a significant overall treatment effect for sustained attention (Rapid Visual Processing – total misses) ($X^2(2)=58.62$, $p<.001$). Low dose WGCP resulted in significantly worse sustained attention than placebo ($X^2(1)=5.56$, $p=.018$), but moderate dose WGCP resulted in significantly better sustained attention than placebo ($X^2(1)=5.22$, $p=.022$). Significant differences were also noted in working memory ($X^2(1)= 26.36$, $p=.001$). Working memory errors were highest in the low dose WGCP and lowest in the moderate dose WGCP. Placebo fell in between these values but pairwise comparisons were not statistically significant (low dose vs. placebo $X^2(1)=1.11$, $p=.293$ and moderate dose vs. placebo $X^2(1)=2.15$, $p=.142$). No significant differences were observed for response inhibition (impulsivity) (overall $p=.579$). See Table 3.

Table 3. Treatment Effects on CANTAB Battery

Parameter	CANTAB Task	F-value	p-value	Placebo mean (SE)	WGCP low Dose mean (SE)	WGCP moderate Dose mean (SE)
Sustained attention	RVP	58.62	p<.001	3.24 (0.58)	4.43 (0.69)	2.46 (0.49)
Response inhibition	SST	1.09	p=.579	142.8 (6.5)	145.3 (6.0)	139.0 (5.0)
Spatial working memory	SWM	26.36	p<.001	4.62 (1.39)	6.00 (1.66)	3.86 (1.38)

RVP = Rapid Visual Information Processing – Total missed targets (lower scores indicate better performance).
SST = Stop Signal Task – Reaction Time Last Half of Task (lower scores indicate faster performance).
SWM = Spatial Working Memory Task – total errors (lower scores indicate better performance).

Qualitative Results. At the end of each session, participants gave subjective accounts of their experience from the time they ingested treatment capsules until the completion of the CANTAB Battery (approximately one and a half hours). In addition, they described reactions from the previous administration of WGCP. The SEBMS probed whether any of 20 specific side effect reactions to stimulant medication were present. Participants showed no adverse events (Table 4.). When probed whether they discerned receiving an active dose or placebo, seven participants were unable to identify whether they received active ingredient or placebo, however, the other 7 participants accurately discerned they had received WGCP moderate dose but not the low dose.

Participants reported qualitative reactions to the moderate dose that are best defined in three areas: 1) increased efficiency on tasks, 2) enhanced ability to stay on task, and 3) a feeling of well-being. For example, Participant 14, stated that she felt "extra focused on the work I did in the morning." Participant 10, a college student, stated that she "felt really good and focused even though I have a lot to do today." Participant 8 reported, "I got more done in an hour today compared to yesterday." Others reported "feeling good" and the absence of feelings of malaise or intrusive emotions.

Other qualitative reports [12, 14, 17] show that acute exposure to WGCP, as administered in this study, resulted in increased alertness, improved concentration, decreased fatigue, significantly increased feelings of contentedness and satisfaction.

Side effects are summarized in Table 4. No significant side effects are reported. Side effect ratings on the CGI-S are all rated as normal or not at all present.

Table 4: Side Effects Behavior Monitoring Scale

	Mean Score				
Side Effect	Baseline	Placebo	WGCP low dose	WGCP moderate dose	X^2 (p)
Insomnia or trouble sleeping	1.43	1	1.14	1	6.00 (.112)
Nightmares	1.07	1	1	1	1.08 (.299)
Stares a lot or daydreams	1.43	1.21	1.21	1.14	5.68 (.128)
Talks less with others	1.21	1.02	1.07	1	3.64 (.303)
Uninterested in others	1.14	1.02	1	1	4.78 (.187)
Decreased Appetite	1.29	1.05	1	1	2.34 (.504)
Irritable	1.43	1.05	1.14	1.04	7.10 (.069)
Stomachaches	1.29	1.02	1.21	1.04	3.45 (.328)
Headaches	1.57	1.17	1.29	1.14	6.87 (.076)
Drowsiness	1.71	1.69	1.57	1.36	7.91 (.048)
Sad/Unhappy	1.21	1.02	1	1.07	3.52 (.318)
Prone to crying/easily upset	1.21	1	1	1	2.07 (.151)
Anxious/worried	1.43	1.02	1.07	1.11	5.17 (.160)
Perseveration (verbal or behavioral)	1.14	1	1	1	2.33 (.127)
Bites/picks skin or fingernails	1.36	1.02	1.07	1	7.77 (.051)
Euphoric/Unusually happy/Mania	1.21	1	1	1.07	3.82 (.148)
Dizziness	1.14	1.10	1.14	1.14	2.74 (.433)
Tics or nervous movements	1.07	1.07	1.07	1	2.67 (.446)
Overfocused (tunes others out)	1.21	1.19	1.21	1.18	0.04 (.998)
Hallucinosis	1	1	1	1	-
Flat affect/Emotional blunting	1	1.02	1	1	1.08 (.299)
Dry mouth	1	1	1.07	1.04	1.08 (.299)
Numbness or tingling in extremities	1.14	1.05	1	1	2.67 (.446)

Note. Wald Chi-Square degrees of freedom equals 3. In many cases, the counts were of extremely low variability (almost entirely scores of 1). Therefore test statistics could not be computed or should be seen only as descriptive of the general pattern.
1=normal, 2= borderline, 3=mild, 4=moderate, 5=marked, 6=severe, and 7=most extreme

DISCUSSION

This study confirmed the effect of improved sustained attention and spatial working memory with WGCP intake. Results indicated a negative effect on sustained attention and working memory for low dose WGCP (two capsules) contrasted with the strong positive effect for moderate dose WGCP (three capsules). This deleterious effect for low dose may indicate subjects' inability to sustain attention long enough over repeated measures. Also at a low dose, adenosine may inhibit fatigue but may not deliver enough caffeine to produce the cognitive effects that moderate doses do. The effect of being required to do a CANTAB subtest repeatedly requires more effort over time. At the moderate dose, use of effortful attention became more accessible and sustained. A similar effect was evident on working memory but not on response inhibition. In addition—as derived from qualitative inquiry, evidence from previous studies [12], and common knowledge—a deleterious effect of chronic caffeine use elicits adverse jitteriness or nervousness. Subjects in this study, however, did not report these effects with WGCP.

WGCP tended to be associated with a qualitatively positive affective response. In interview, subjects reported a sense of well-being and an ability to initiate tasks more easily. For example, use of WGCP decreased ratings of sleepy, tired, drowsy, "half awake", lazy and sluggish. Subjects reported they experienced an overall sense of contentedness and that they felt more at ease, relaxed, and satisfied. The substance induced more reportedly energetic feelings as well as heightened friendliness and sociability.

It is an interesting finding that WGCP affected spatial working memory. Working memory is a complex function that involves the ability to manipulate and control information such that information is both symbolically stored and processed in verbal and spatial forms. Neurologically, the information processed in working memory is stored throughout the brain depending on the nature of the eliciting information [18]. Caffeine effects, functionally altering the adenosine receptors, may impact the wide variety of neural pathways associated with working memory.

The finding that WGCP did not affect response inhibition is expected. Inhibitive functions are typically considered to be prefrontal, neurological events. Response inhibition is the ability to keep interfering information away from focused attention. It, too, is complex and may be outside the effects of neural pathways associated with adenosine.

The nature and mode of delivery of caffeine may influence its effect on executive performance. According to the packaging label of Go Bean®, the delivery of caffeine using WGCP provides the "natural caffeine that is deep within the fiber of the bean". Caffeine extracts are typically used in commercially sold liquid products. It is possible that the positive effect on sustained attention and the reported positive qualitative effects reported by subjects may be a function of both caffeine and the remaining nutrients that are not available in extracts. This study cannot provide information on the addition of nutrients in caffeine delivery provided by WGCP, thus, further investigation is required. In addition, effects of WGCP may also be due to the mode of ingestion. The method of delivery—taking a capsule versus drinking a liquid—may represent a distinct difference in caffeine effects [17].

Research is certainly required to fully appreciate the different effects on attention and behavior associated with WGCP. The potential adverse effect of chronic WGCP use, especially in higher doses, is necessary as it has been indicated in other studies of caffeine use. Many studies of the effects of caffeine were conducted more than a decade ago, however, and these relied on extract rather than on caffeine occurring in its natural state. Given the variety of availability of caffeine products from diet supplements to energy drinks, study of new delivery systems of the raw bean is warranted especially as this relates to adverse events.

A consideration of the study is the carryover of WGCP effects from one phase of the manipulation to the other. This problem was handled in the design of the study. In future studies, however, length of phases may be varied to determine WGCP latency effects (i.e., onset of action of WGCP), and residual effects (i.e., persisting WGCP effects during placebo phase) after active WGCP is terminated. Both latency and residual effects must be investigated in order to engage larger N trials to insure safety of subjects and to determine timeliness of active WGCP exposure.

Though many young adults studying in higher education acknowledge the beneficial effects of caffeine, further study of attention enhancers on academic tasks would be helpful. This study, for example, may have implications for well-documented stimulant diversion on college campuses. Evidence indicates significant "sharing" of prescription drugs used to treat ADHD for the purpose of enhancing performance [19, 20]. Diversion of prescribed medications to individuals without a diagnosis of ADHD has resulted in inappropriate use of prescription medications [21]. Alternatives to such diversion are likely to be helpful.

LIMITATIONS

The primary limitation to this study is the low number of subjects. Systematic investigation with a greater number of participants is warranted. Also, the study relied on subjective report of the intake of illicit substances and coffee rather than on urine drug screening. To insure that other ingested substances were not used, future studies should include drug screening prior to each administration of the dependent measure.

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