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Improved cognitive performance in human volunteers following administration of guarana (*Paullinia cupana*) extract: comparison and interaction with *Panax ginseng*

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Abstract

Extracts from the plant guarana (*Paullinia cupana*) feature as putatively stimulating ingredients in a number of foods, drinks and dietary/herbal supplements. To date, little research in humans has examined the potential psychoactive effects of these extracts. Extracts of *Panax ginseng*, which are often sold in combination with guarana, contain similar potentially active components, and have been shown to modulate cognitive performance.

In this double-blind, counterbalanced, placebo-controlled study, the cognitive and mood effects of separate single doses of: 75 mg of a dried ethanolic extract of guarana (approx 12% caffeine), 200 mg of *Panax ginseng* (G115), and their combination (75 mg/200 mg), were assessed in 28 healthy young (18–24) participants. On each day of the study (separated by a 7-day washout), cognitive performance and subjective mood were assessed pre-dose and at 1, 2.5, 4 and 6 h post-dose using the Cognitive Drug Research computerised assessment battery, Serial subtraction tasks and Bond–Lader mood scales.

In comparison to placebo, all three treatments resulted in improved task performance throughout the day. In the case of guarana, improvements were seen across 'attention' tasks (but with some evidence of reduced accuracy), and on a sentence verification task. While also increasing the speed of attention task performance, both ginseng and the ginseng/guarana combination also enhanced the speed of memory task performance, with little evidence of modulated accuracy. Guarana and the combination, and to a lesser extent ginseng, also led to significant improvements in serial subtraction task performance.

These results provide the first demonstration in humans of the psychoactive effects of guarana, and confirmation of the psychoactive properties of ginseng. Given the low caffeine content (9 mg) of this dose of guarana extract, the effects are unlikely to be attributable to its caffeine content.

Keywords: Guarana; Panax ginseng; *Paullinia cupana*; Memory; Attention; Caffeine; Psychopharmacology

1. Introduction

An extensive range of products that include guarana (*Paullinia cupana*) seed extracts as ingredients are commercially available. Examples include confections (e.g. chocolate products), fruit-juice based drinks, 'energy' drinks, dietary and herbal supplements, and, most controversially, natural weight loss products.

The plant species guarana originates from the central Amazonian Basin, and has a long history of local usage, initially as a stimulant by indigenous tribespeople (Henman, 1982) and more latterly as an ubiquitous ingredient in Brazilian soft drinks. The putative stimulant properties are generally taken to reflect the presence of caffeine, which comprises 2.5–5% of the

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extract's dry weight, although other purine alkaloids (theophylline and theobromine) are present in smaller quantities (Weckerle et al., 2003). The psychoactive properties of guarana have also been attributed to a high content of both saponins and tannins (Espinola et al., 1997), the latter of which may well underlie the demonstrated antioxidant properties of the plant (Mattei et al., 1998).

While guarana is becoming progressively more common as a putatively psychoactive food additive in Western markets, there is a paucity of evidence as to its specific behavioural effects. Two studies in rodents have included behavioural measures. In one (Mattei et al., 1998), both acute and chronic administration of guarana were found to have no toxic effects, but also failed to modulate motor activity or pentobarbital-induced sleep parameters. A subsequent analysis of the same guarana extract revealed relatively low levels of caffeine (2.1%). In a further study, Espinola et al. (1997) demonstrated that chronic (9 months) administration of a lower (but not a higher) dose of guarana improved swimming time in mice, and reversed performance deficits in rats on a passive avoidance task. Acute administration of both low (3 mg/kg) and high (30 mg/kg) doses of guarana and 1 mg/kg of caffeine also reversed scopolamine-induced deficits on passive avoidance performance in mice (Espinola et al., 1997). Given that the lower dose of guarana contained only 10% of the caffeine in the higher guarana dose, and approximately 6% of the 1-mg/kg pure caffeine treatment, the authors concluded that the behavioural effects of guarana are not likely to be attributable to its caffeine content alone, but rather to its saponin and tannin content.

Panax ginseng is a member of the plant genus *Panax* (Araliaceae family). It is indigenous to the Far East (most notably China and Korea), was first cultivated around 11 BC, and has a medical history (originally as a wild herb) stretching back more than 5000 years (Yun, 2001). It is currently consumed worldwide for its putative beneficial properties, which include positive effects on physical parameters, cognitive performance and well-being.

The major active constituents of the *Panax* genus are also thought to be saponins, in this case species-specific triterpenoid glycosides known as ginsenosides, of which over 30 individual examples have been identified, many of which exist only in minute amounts (Tachikawa et al., 1999). The individual and combined ginsenosides have been shown to exhibit both a plethora of physiological effects in vitro, and to modulate physical and mnemonic performance in animals (for review see: Kennedy and Scholey, 2003).

A number of recent double-blind, placebo-controlled, crossover studies have also examined the behavioural effects of acute administration of a standardised ginseng extract (G115) to humans. In the first of these experiments (Kennedy et al., 2001a), the cognitive and mood effects of three separate single doses (comparing 200, 400 and 600 mg) of ginseng were assessed in healthy young participants. The results showed benefits in memory performance following all three doses of ginseng, with this effect most apparent following the middle dose. The two less mnemonically beneficial doses were, however, associated with slower performance on attention tasks. This finding of longer response latency on attention tasks was in contrast to the findings of a subsequent electroencephalography (EEG) experiment in which a 200-mg dose of ginseng was shown to significantly shorten evoked P300 response latency, and provoke a stronger pattern of beneficial topographic EEG effects than *Ginkgo biloba* (Kennedy et al., 2003a). Similarly, a recent study (Reay et al., 2004) reported speeded performance on a mental arithmetic task, with concomitant reduction in blood glucose levels, following this dose. While the contradictory nature of these findings with regards 200 mg doses of G115 have not as yet been addressed, the mnemonic effects of 400 mg and treatments combining G115 with *Ginkgo biloba* have been confirmed (Kennedy et al., 2001b, 2002a, Wesnes et al., 1997; 2000).

Guarana is rarely taken alone, and one of its most common herbal combinations is with ginseng. While the mechanisms of action of both herbal extracts are, as yet, undelineated, the therapeutic effects of both guarana (Mattei et al., 1998) and ginseng (Brekhman and Dardymov, 1969) have been attributed to their ability to attenuate the physiological consequences of physical or psychological stressors. This has been suggested on the basis that both contain saponins (high molecular weight glycosides combining a sugar element and a steroid aglycone or triterpene molecule) as active components. Guarana has the additional potential benefit of being a source of caffeine. As the cognitive and mood effects of guarana have received little attention in humans, it seemed timely to investigate potential nootropic properties both in guarana, and in a product combining guarana with *Panax ginseng*.

In the current double-blind, placebo-controlled, counterbalanced experiment, the cognitive and mood effects of single doses of guarana (75 mg Pharmaton extract), ginseng (200 mg G115) and their combination (75 mg/200 mg) were assessed in 28 healthy participants utilising the Cognitive Drug Research (CDR) computerised assessment battery, Serial Subtraction tasks and Bond–Lader visual analogue mood scales. In order to assess potential differential time course effects, testing took place pre-dose and at 1, 2.5, 4 and 6 h thereafter. To allow a sufficient 'washout' between treatments, testing was conducted at 7-day intervals.

This study, therefore, not only provided an examination of the cognitive and mood effects of guarana in humans, but also assessed the potential for additive or

synergistic effects following the common, commercially available, combination of guarana with *Panax ginseng*.

2. Methods

2.1. Participants

Nineteen female and nine male undergraduate volunteers (mean age 21.4 years, S.E.M. 0.77) took part in the study, which was approved by the ethics committee of Northumbria University Division of Psychology, and was carried out in accordance with the Declaration of Helsinki. Prior to participation, each volunteer signed an informed consent form and completed a medical health questionnaire. All participants reported that they were in good health, and were taking no illicit social drugs. Additionally, they were free of any 'over-the-counter' or prescribed medications, with the exception, for some female volunteers, of the contraceptive pill. Regular smokers were excluded from the study. All participants abstained from alcohol and caffeine for a minimum of 12 h prior to the first testing session of the morning and throughout the day.

2.2. Cognitive and mood measures

2.2.1. Cognitive Drug Research computerised assessment battery

The Cognitive Drug Research (CDR) computerised assessment battery has been used in over 500 European and North American drug trials.

The tailored version of the CDR battery utilised here, including a detailed description of the constituent tasks, is described in detail by Kennedy et al. (2000, 2001a,b, 2002a,b). This battery has previously been found to be sensitive to modulation of cognitive function as a consequence of acute ingestion of herbal extracts, including *Melissa officinalis* (Kennedy et al., 2002b, 2003b), *Ginkgo biloba* (Kennedy et al., 2000, 2002a) and *Panax Ginseng* (Kennedy et al., 2001a, 2002a), and acute and chronic administration of a *Ginkgo biloba/ Panax ginseng* combination (Kennedy et al., 2001b, 2002a; Wesnes et al., 1997, 2000). In the case of the current study, an additional 'logical reasoning' task was included in the battery. The running order of the tasks from the CDR battery is shown in Table 1. The selection of computer controlled tasks from the system was administered with randomly ordered parallel forms of the tests being presented at each testing session. Presentation was via desktop computers with high-resolution VGA colour monitors, and, with the exception of written word recall tests, all responses were recorded via two-button (YES/NO) response boxes. The entire selection of tasks took approximately 20 min to perform.

2.2.2. Primary cognitive outcome measures

As with the previous studies assessing herbal treatments, the single task outcomes from the CDR battery were collapsed into the five cognitive outcome factors derived from the battery by a factor analysis conducted and described by Wesnes et al. (2000) and subsequently confirmed in data from healthy young adults (unpublished data). The factor composition is described briefly below.

'*Speed of Attention*' *factor:* derived by combining the reaction times of the three attentional tasks—simple reaction time, choice reaction time and digit vigilance (units are summed milliseconds for the three tasks).

'*Speed of Memory*' *factor:* derived by combining the reaction times of numeric working memory, spatial memory, delayed word recognition, and delayed picture recognition (units are summed milliseconds for the four tasks).

'*Accuracy of Attention*' *factor:* derived by calculating the combined percentage accuracy across the choice reaction time and digit vigilance tasks. 100% accuracy across the two tasks would generate a maximum score of 100.

'*Secondary Memory*' *factor:* derived by combining the percentage accuracy scores from delayed word recognition, delayed picture recognition, immediate word recall and delayed word recall tasks. One hundred percent accuracy across the four tasks would generate a maximum score of 400 on this index.

'*Working Memory*' *factor:* derived by combining the percentage accuracy scores from the two working memory tests—spatial working memory and numeric working memory. One hundred percent accuracy across the two tasks would generate a maximum score of 200 on this index.

2.2.3. Other measures

2.2.3.1. Logical reasoning task. This task within the CDR battery was not previously utilised or described. In this task, a series of statements referring to the relationships between two letters appeared on the screen one at a time. Participants were required to decide if each statement correctly described the order of two letters that followed it. If they thought the statement was true they pressed the 'YES' button and if they thought it was false, they presented the 'NO' button. Task measures were accuracy (%) and reaction time (ms).

2.2.3.2. Sentence Verification Task. This task measures speed of retrieval of information. A series of simple statements were presented on screen. The participant indicates whether they are true (e.g. forks are manufactured goods) or false (e.g. dogs have wings) by pressing designated keys on the keyboard. Thirty stimuli were presented and performance was measured as number correct and mean reaction time.

Table 1
Effects of the treatments on the individual task outcome measures from the CDR battery

Measure		Pre-dose baseline score	Change from baseline score			
			1 h post-dose	2.5 h post-dose	4 h post-dose	6 h post-dose
Immediate word recall (% accuracy)	Placebo	$50.36_{2.63}$	$-5.71_{2.29}$	$-6.79_{2.37}$	$-5.71_{2.62}$	$-6.79_{2.11}$
	Guarana	$49.88_{2.82}$	$-4.52_{3.18}$	$-4.05_{2.48}$	$-7.26_{1.93}$	$-7.26_{2.46}$
	Ginseng	$45.24_{3.15}$	$-6.55_{1.90}$	$-2.86_{2.49}$	$-3.93_{3.10}$	$-0.12_{3.44}$
	Guar/Gin	$49.76_{2.67}$	$-3.81_{2.40}$	$-6.67_{2.79}$	$-5.12_{2.58}$	$-9.17_{2.95}$
Simple reaction time (ms)	Placebo	$286.43_{10.33}$	$10.28_{7.08}$	$8.63_{9.09}$	$21.29_{8.70}$	$11.54_{8.60}$
	Guarana	$279.82_{5.95}$	$10.09_{4.82}$	$12.16_{6.17}$	$18.00_{5.59}$	$18.41_{5.82}$
	Ginseng	$280.37_{6.75}$	$8.14_{4.28}$	$12.07_{6.54}$	$23.43_{7.25}$	$18.28_{6.23}$
	Guar/Gin	$285.72_{7.28}$	$5.58_{6.63}$	$2.35_{7.03}$	$9.39_{7.63}$	$7.28_{5.81}$
Digit vigilance accuracy (%)	Placebo	$94.45_{1.37}$	$0.56_{0.78}$	$0.08_{0.83}$	$-4.21_{1.62}$	$-3.49_{1.90}$
	Guarana	$94.60_{1.39}$	$-0.71_{1.09}$	$-1.75_{1.40}$	$-0.71_{0.98}$	$-0.63_{1.00}$
	Ginseng	$95.00_{1.29}$	$-1.27_{1.21}$	$-1.82_{1.11}$	$-2.94_{1.89}$	$-3.81_{1.11}$
	Guar/Gin	$94.21_{1.44}$	$-0.56_{1.65}$	$-1.35_{1.73}$	$-2.78_{1.47}$	$-0.63_{1.44}$
Digit vigilance false alarms (number)	Placebo	$1.29_{0.26}$	$-0.04_{0.29}$	$0.21_{0.33}$	$-0.21_{0.20}$	$0.04_{0.34}$
	Guarana	$0.96_{0.25}$	$-0.04_{0.27}$	$0.61_{0.33}$	$0.04_{0.26}$	$0.21_{0.27}$
	Ginseng	$1.21_{0.24}$	$-0.29_{0.22}$	$-0.07_{0.32}$	$-0.04_{0.28}$	$0.21_{0.37}$
	Guar/Gin	$1.14_{0.28}$	$-0.04_{0.25}$	$-0.04_{0.31}$	$-0.18_{0.30}$	$-0.14_{0.25}$
Digit vigilance reaction time (ms)	Placebo	$\mathbf{426.24_{8.23}}$	$\mathbf{21.52_{4.63}}$	$\mathbf{13.78_{5.89}}$	$\mathbf{24.84_{6.08}}$	$\mathbf{36.79_{6.39}}$
	Guarana	$\mathbf{431.95_{7.03}}$	$\mathbf{5.42_{5.48}}^{*}$	$\mathbf{14.38_{6.55}}$	$\mathbf{9.86_{5.93}}^{*}$	$\mathbf{10.15_{6.13}}^{*****}$
	Ginseng	$\mathbf{435.55_{10.33}}$	$\mathbf{18.38_{5.73}}$	$\mathbf{19.89_{6.35}}$	$\mathbf{15.31_{7.60}}$	$\mathbf{18.97_{6.83}}^{***}$
	Guar/Gin	$\mathbf{433.16_{9.10}}$	$\mathbf{11.01_{6.62}}$	$\mathbf{3.01_{6.70}}$	$\mathbf{10.64_{7.48}}^{*}$	$\mathbf{16.34_{7.71}}^{****}$
Choice reaction time accuracy (%)	placebo	$\mathbf{95.29_{0.69}}$	$\mathbf{0.71_{0.84}}$	$\mathbf{0.21_{0.48}}$	$\mathbf{0.00_{0.74}}$	$\mathbf{0.00_{0.63}}$
	Guarana	$\mathbf{96.50_{0.67}}$	$\mathbf{-1.36_{0.58}}^{**}$	$\mathbf{-0.93_{0.71}}$	$\mathbf{-1.79_{0.84}}^{**}$	$\mathbf{-0.64_{0.65}}$
	Ginseng	$\mathbf{94.71_{0.90}}$	$\mathbf{2.00_{0.74}}$	$\mathbf{0.64_{0.65}}$	$\mathbf{0.07_{0.59}}$	$\mathbf{0.21_{0.79}}$
	Guar/Gin	$\mathbf{95.57_{0.63}}$	$\mathbf{0.36_{0.71}}$	$\mathbf{-0.50_{0.63}}$	$\mathbf{0.00_{0.76}}$	$\mathbf{-0.14_{0.82}}$
Choice reaction time (ms)	placebo	$\mathbf{421.95_{11.66}}$	$\mathbf{12.59_{9.17}}$	$\mathbf{15.50_{7.19}}$	$\mathbf{24.74_{10.89}}$	$\mathbf{17.82_{11.71}}$
	Guarana	$\mathbf{426.45_{13.16}}$	$\mathbf{-5.60_{6.92}}^{*}$	$\mathbf{0.95_{9.23}}$	$\mathbf{6.73_{10.89}}^{*}$	$\mathbf{7.32_{10.90}}$
	Ginseng	$\mathbf{434.28_{11.64}}$	$\mathbf{4.17_{6.03}}$	$\mathbf{6.71_{9.52}}$	$\mathbf{-8.16_{8.95}}^{****}$	$\mathbf{1.23_{8.51}}^{*}$
	Guar/Gin	$\mathbf{425.43_{9.59}}$	$\mathbf{12.95_{9.82}}$	$\mathbf{-0.02_{6.80}}$	$\mathbf{11.69_{7.09}}$	$\mathbf{14.78_{6.59}}$
Spatial memory (%>chance)	placebo	$95.49_{1.08}$	$-0.58_{1.67}$	$-4.33_{4.55}$	$-1.74_{1.76}$	$-4.60_{2.08}$
	Guarana	$94.55_{1.61}$	$-4.60_{2.86}$	$-5.31_{1.77}$	$-5.31_{3.44}$	$-4.15_{2.63}$
	Ginseng	$94.42_{1.07}$	$-6.71_{3.02}$	$-3.17_{1.69}$	$-0.80_{1.31}$	$-10.31_{4.00}$
	Guar/Gin	$91.88_{2.18}$	$0.13_{2.01}$	$-1.43_{2.51}$	$-2.41_{4.40}$	$-0.85_{2.91}$
Spatial memory reaction time (ms)	Placebo	$610.83_{21.76}$	$-7.79_{27.32}$	$-14.88_{15.29}$	$-7.74_{32.56}$	$19.05_{31.85}$
	Guarana	$621.08_{29.58}$	$16.51_{36.77}$	$-14.59_{14.90}$	$-32.80_{15.73}$	$7.633_{6.82}$
	Ginseng	$614.84_{36.15}$	$-34.82_{32.98}$	$-29.54_{33.54}$	$-59.58_{34.59}$	$13.05_{53.15}$
	Guar/Gin	$622.47_{30.63}$	$40.52_{31.84}$	$-26.82_{22.24}$	$-55.16_{28.21}$	$-2.81_{31.29}$
Logical reasoning reaction time (ms)	Placebo	$2856.1_{311.66}$	$-138.9_{182.79}$	$-67.80_{179.09}$	$-123.8_{129.59}$	$-339.4_{254.63}$
	Guarana	$2802.5_{260.16}$	$-199.7_{111.20}$	$-431.7_{185.74}$	$-261.4_{138.82}$	$-266.8_{210.23}$
	Ginseng	$2858.2_{283.44}$	$-26.76_{222.34}$	$-167.4_{208.76}$	$-495.1_{192.28}$	$-242.4_{220.89}$
	Guar/Gin	$3106.1_{338.89}$	$-279.4_{287.21}$	$-462.3_{237.57}$	$-414_{222.11}$	$-496.2_{182.35}$
Logical reasoning accuracy (%)	Placebo	$76.04_{4.34}$	$-1.34_{1.66}$	$0.60_{2.26}$	$1.64_{1.80}$	$1.49_{1.44}$
	Guarana	$76.64_{3.86}$	$-0.30_{1.74}$	$0.46_{1.42}$	$-0.59_{1.83}$	$1.64_{2.15}$
	Ginseng	$75.30_{4.34}$	$3.13_{1.51}$	$2.53_{1.90}$	$0.89_{1.80}$	$0.75_{2.14}$
	Guar/Gin	$77.53_{4.13}$	$0.89_{1.24}$	$2.23_{1.61}$	$1.49_{1.74}$	$0.30_{1.65}$
Numeric working memory (%>chance)	Placebo	$\mathbf{89.60_{1.68}}$	$\mathbf{-2.46_{1.97}}$	$\mathbf{-1.59_{2.15}}$	$\mathbf{-1.51_{2.02}}$	$\mathbf{-1.03_{1.59}}$
	Guarana	$\mathbf{88.10_{1.73}}$	$\mathbf{1.59_{1.84}}^{*}$	$\mathbf{1.35_{2.06}}$	$\mathbf{-1.43_{2.15}}$	$\mathbf{-0.40_{2.34}}$
	Ginseng	$\mathbf{91.35_{1.63}}$	$\mathbf{-2.30_{1.31}}$	$\mathbf{-1.35_{1.41}}$	$\mathbf{-4.52_{1.30}}$	$\mathbf{-1.43_{1.53}}$
	Guar/Gin	$\mathbf{91.75_{1.02}}$	$\mathbf{-3.97_{2.28}}$	$\mathbf{-3.65_{0.96}}$	$\mathbf{-0.56_{1.06}}$	$\mathbf{-3.57_{1.47}}$
Numeric working memory reaction time (ms)	Placebo	$\mathbf{600.65_{23.91}}$	$\mathbf{5.99_{13.12}}$	$\mathbf{-2.17_{19.87}}$	$\mathbf{5.60_{21.53}}$	$\mathbf{-14.82_{17.75}}$
	Guarana	$\mathbf{607.87_{26.62}}$	$\mathbf{3.39_{12.74}}$	$\mathbf{-13.62_{10.07}}$	$\mathbf{-4.49_{22.61}}$	$\mathbf{-27.25_{17.52}}$
	Ginseng	$\mathbf{635.90_{30.64}}$	$\mathbf{-20.27_{24.11}}$	$\mathbf{-47.48_{25.61}}^{**}$	$\mathbf{-43.92_{26.34}}^{****}$	$\mathbf{-59.99_{27.72}}^{***}$
	Guar/Gin	$\mathbf{611.53_{21.34}}$	$\mathbf{-3.10_{21.02}}$	$\mathbf{-2.41_{13.23}}$	$\mathbf{-11.34_{12.58}}$	$\mathbf{-42.29_{14.81}}$
Delayed word recall (% accuracy)	Placebo	$35.95_{2.49}$	$-10.48_{2.63}$	$-14.64_{3.20}$	$-15.00_{2.58}$	$-14.52_{2.53}$
	Guarana	$35.00_{2.74}$	$-7.62_{2.60}$	$-10.71_{2.88}$	$-12.98_{3.11}$	$-14.76_{3.07}$
	Ginseng	$32.26_{3.15}$	$-11.07_{2.76}$	$-9.29_{2.85}$	$-12.74_{2.93}$	$-8.33_{3.74}$
	Guar/Gin	$35.95_{3.16}$	$-12.26_{2.93}$	$-14.64_{3.04}$	$-11.90_{2.78}$	$-15.83_{2.89}$
Word recognition (%>chance)	Placebo	$63.33_{4.33}$	$-6.43_{4.43}$	$-11.67_{3.83}$	$-9.29_{4.22}$	$-7.62_{2.86}$
	Guarana	$58.81_{3.93}$	$-2.38_{3.31}$	$-1.90_{3.91}$	$-6.90_{4.95}$	$-7.38_{4.02}$
	Ginseng	$60.71_{4.55}$	$-9.76_{5.00}$	$-8.57_{4.60}$	$-10.24_{5.69}$	$-9.76_{4.30}$
	Guar/Gin	$62.14_{3.76}$	$-5.95_{4.29}$	$-8.57_{2.95}$	$-7.14_{4.24}$	$-9.76_{3.81}$

Table 1 (*continued*)

Measure		Pre-dose baseline score	Change from baseline score			
			1 h post-dose	2.5 h post-dose	4 h post-dose	6 h post-dose
Word recognition reaction time (ms)	Placebo	**691.38**$_{24.08}$	**113.7**$_{42.02}$	**10.91**$_{17.52}$	**76.00**$_{42.04}$	**53.02**$_{27.68}$
	Guarana	**718.08**$_{27.40}$	**48.75**$_{30.86}$	**42.78**$_{30.24}$	**63.61**$_{39.00}$	**−7.09**$_{28.92}$
	Ginseng	**761.19**$_{30.81}$	**−0.94**$_{33.59}$**	**−47.68**$_{37.33}$	**−18.32**$_{34.49}$*	**−12.96**$_{29.04}$
	Guar/Gin	**748.79**$_{37.93}$	**66.95**$_{64.13}$	**−21.17**$_{36.85}$	**−27.83**$_{32.00}$*	**−27.74**$_{24.72}$
Picture recognition (%>chance)	Placebo	**60.89**$_{4.84}$	**−10.18**$_{4.12}$	**−11.07**$_{3.91}$	**−8.75**$_{3.71}$	**−10.36**$_{4.69}$
	Guarana	**55.18**$_{4.91}$	**0.71**$_{3.25}$***	**1.96**$_{4.60}$****	**−3.39**$_{3.40}$	**−1.61**$_{3.74}$*
	Ginseng	**59.29**$_{4.66}$	**−6.61**$_{3.41}$	**−3.75**$_{4.29}$	**−7.50**$_{3.03}$	**−3.75**$_{4.39}$
	Guar/Gin	**58.57**$_{4.83}$	**−5.36**$_{3.53}$	**−9.82**$_{4.57}$	**−6.61**$_{4.87}$	**−4.46**$_{4.19}$
Picture recognition reaction time (ms)	Placebo	**788.98**$_{27.41}$	**47.62**$_{23.59}$	**19.71**$_{23.22}$	**51.76**$_{18.08}$	**21.77**$_{29.55}$
	Guarana	**827.42**$_{29.10}$	**−6.28**$_{33.24}$*	**−45.51**$_{21.54}$*	**−33.96**$_{20.80}$****	**−28.18**$_{26.11}$
	Ginseng	**804.61**$_{26.13}$	**50.32**$_{34.04}$	**14.85**$_{22.37}$	**−2.43**$_{23.88}$*	**−7.15**$_{21.66}$
	Guar/Gin	**827.31**$_{28.03}$	**8.97**$_{35.11}$	**9.16**$_{31.36}$	**−6.16**$_{27.53}$*	**−14.25**$_{26.08}$

Mean baseline and change from baseline scores (with standard errors) are presented. Tasks are displayed in order of completion. Bold font indicates measures that reached significance on the initial ANOVA. Asterisks denote significance on the subsequent planned comparisons (*p=0.05; **p=0.01; ***p=0.005, *****p=0.0005 compared to placebo).

2.2.3.3. '*Serial Threes*' *and* '*Serial Sevens*' *Subtraction Tasks.* A modified computerised version of the Serial Sevens test was utilised. The original verbal Serial Sevens test (Hayman, 1942) has appeared in a number of forms, including as part of the Mini-Mental State Examination (Folstein et al., 1975). It has been used to assess cognitive impairment during hypoglycaemia (e.g. Hale and Margen, 1982; Taylor and Rachman, 1988), and has also been used to investigate the relationship between increased blood glucose levels and cognitive performance (Kennedy and Scholey, 2000; Scholey et al., 2001; Scholey, 2001). In the current study, computerised versions of serial subtractions were implemented (see Scholey et al., 2001 for details), here using tests of 2 min duration. For the Serial Sevens task, a standard instruction screen informed the participant to count backwards in sevens from the given number, as quickly and accurately as possible, using the numeric keypad to enter each response. Participants were also instructed verbally that if they were to make a mistake they should carry on subtracting from the new incorrect number. A random starting number between 800 and 999 was presented on the computer screen, which was cleared by the entry of the first response. Each three-digit response was entered via the numeric keypad with each digit being represented on screen by an asterisk. Pressing the enter-key signalled the end of each response and cleared the three asterisks from the screen. The task was scored for total number of subtractions and number of errors. In the case of incorrect responses, subsequent responses were scored as positive if they were correct in relation to the new number.

The Serial Threes task was identical to Serial Sevens, except that it involved serial subtraction of threes.

2.2.4. Subjective mood measure

The Bond–Lader Visual Analogue Scales (Bond and Lader, 1974), consisting of sixteen 100-mm visual analogue scales anchored by antonyms (e.g. Alert–Drowsy, Lethargic–Energetic, etc.), were combined as recommended by the authors to form three mood factors: alertness, calmness and contentedness.

2.3. Extracts and treatments

2.3.1. Extracts

2.3.1.1. Panax ginseng—standardised extract G115. Extraction from selected roots of *Panax ginseng* C.A. Meyer was undertaken by exhaustive percolation in a 40% ethanol–60% water solvent at temperatures below 40 °C. Following quantitative analysis of the resultant dry extract, standardization was performed by the addition of excipients (lactose at a range of 43–68%, and 2% silicon dioxide), bringing the concentration of ginsenosides to 4%. This process results in root/extract ratios of between 3 and 7 parts root to one part extract depending on the concentration of ginsenosides in the root.

2.3.1.2. Guarana—standardised extract. Extraction from *Paullinia Cupana* H. B. et Kunth seeds was undertaken by exhaustive percolation in a 50% ethanol–50% water solvent at temperatures below 50 °C. Following quantitative analysis of the resultant dry extract, standardization was performed by the addition of maltodextrine (in the range 10–20%), bringing the concentration of alkaloids (caffeine and theobromine) to 11–13%. This process results in seed/extract ratios of between 3 and 7 parts seed to one part extract depending on the concentration of alkaloids in the root.

2.3.2. Treatments

On each study day participants received two capsules that were of identical appearance on each occasion. The individual capsules contained a total of either: 75 mg guarana extract; 200 mg *Panax ginseng* G115; a combination of 75 mg guarana and 200 mg ginseng; or

0 mg guarana and 0 mg ginseng (placebo). To maintain the double-blind, coded treatments were provided by the manufacturer in identical hard gelatine capsules. A disinterested third party was then responsible for preparing treatments as per the study's Latin square. The code remained unbroken until initial statistical analysis had been completed. All treatments were identical in appearance and scent.

2.4. Procedure

Each participant was required to attend a total of five study days that were conducted 7 days apart to ensure a sufficient washout between conditions. Testing took place, commencing at the same time on each day (between 8:30 and 9:30 a.m.), in a suite of laboratories with participants visually isolated from each other.

On arrival at their first session on the first day, participants were randomly allocated to a treatment regime using a Latin square design which counterbalanced the order of treatments across the four active days of the study.

Each completion of the cognitive assessment comprised the CDR battery, sentence verification task, serial subtraction tasks and mood scales.

The first day was identical to the following four, except that no treatment (active or placebo) was offered. This allowed familiarisation with the test battery and procedure, and dissipation of practice effects. Data from the four sessions of this practice day were not included in any analysis. Each of the subsequent four active study days comprised five identical testing sessions. The first was a pre-dose testing session which established baseline performance for that day, and was immediately followed by the day's treatment. Further testing sessions began at 1, 2.5, 4 and 6 h following consumption of the day's treatment.

Each testing session comprised completion of the Bond–Lader visual analogue scales, the CDR test battery, sentence verification task and serial subtraction tasks. Total testing time was approximately 30 min per session.

2.5. Statistics

Scores on the individual task outcomes, the four primary factors and the two memory sub-factors were analysed as 'change from baseline' using the Minitab statistical package.

The primary statistical analysis of the 'change from baseline' data for each measure was carried out using planned comparisons, utilising *t* tests with MSError from an omnibus ANOVA as an error term (Kepple, 1991). At each time point (1, 2.5, 4 and 6 h post-dose), data from the placebo condition were compared to that for each of the three treatments (guarana, ginseng, guarana/ginseng). Prior to carrying out planned comparisons, an ANOVA (General Linear Model), with terms fitted to the model for dose, visit, Dose × Visit and subject (Kirk, 1968), was carried out to identify main effects and interaction effects on change from baseline data for each measure (statistic not reported). To ensure the overall Type I error protection level only those planned comparisons associated with measures that generated a significant main effect ($p<0.05$) or interaction effect, or a trend towards the same, on this initial ANOVA are reported. Furthermore, all testing was two-tailed, comparisons were strictly planned prior to the study, were restricted to the number of conditions minus one at each time-point, and only probabilities associated with these pre-planned comparisons were calculated.

3. Results

3.1. Baseline scores

Prior to analysis of change from baseline data, mean pre-dose raw baseline scores for all four conditions (placebo, guarana, ginseng, guarana/ginseng) for each outcome (single task outcomes, cognitive factor scores, and mood scale scores) were subjected to a one-way, repeated-measures ANOVA. There were no significant baseline performance differences for any measure.

3.2. Individual task outcome measures

Task outcomes contributing to the factors (in chronological order), and performance data on these individual task outcome measures are presented in Table 1. Where appropriate, the results of the planned comparisons of individual task outcomes that generated a significant result on the initial ANOVA (statistic not reported) are described in relationship to the overall factor to which they contribute below.

3.3. Cognitive factor outcome measures

Mean raw baseline scores and change from baseline scores for each condition across each session are presented in the tables and graphs of Fig. 1.

3.3.1. Speed of Attention factor

Planned comparisons showed that there was a significant effect of treatment on the Speed of Attention factor, with this effect apparent following guarana at 1 h [$t(243)=2.56$, $p=0.011$], 4 h [$t(243)=2.7$, $p=0.007$] and 6 h [$t(243)=2.25$, $p=0.025$] post-dose; following ginseng at 4 h [$t(243)=2.99$, $p=0.003$] and 6 h [$t(243)=2.06$, $p=0.04$]; and following the combination at 2.5 h [$t(243)=2.42$,

Factor		Pre-dose Baseline score	Change from baseline score			
			1 hr post-dose	2.5hr post-dose	4 hr post-dose	6hr post-dose
Speed of Attention	placebo	1134.62 24.63	44.39 13.19	37.91 13.73	70.87 18.28	66.14 19.60
	Guarana	1138.21 23.47	9.92 10.27	27.49 16.12	34.59 16.40	35.87 16.85
	Ginseng	1150.20 26.45	30.68 11.90	38.68 18.83	30.58 17.97	38.48 15.17
	Guar/Gins	1144.31 21.34	29.54 14.54	5.33 16.37	31.72 17.66	38.39 13.71
Speed Of Memory	placebo	2691.84 80.18	159.52 73.38	13.57 49.95	125.6 84.30	79.02 76.88
	Guarana	2774.44 91.94	62.37 60.33	-30.93 47.96	-7.64 66.63	-54.89 60.40
	Ginseng	2816.53 93.13	-5.71 81.75	-109.8 69.69	-124.2 75.12	-67.05 90.69
	Guar/Gins	2810.10 94.00	113.33 113.37	-41.24 55.73	-100.5 73.78	-87.08 65.77
Accuracy Of Attention	placebo	88.86 0.86	0.64 0.60	-0.07 0.63	-1.68 0.88	-1.61 0.91
	Guarana	89.86 0.90	-0.96 0.59	-1.86 0.71	-1.25 0.59	-0.82 0.49
	Ginseng	88.89 0.84	0.71 0.63	-0.43 0.68	-1.25 0.87	-1.82 0.56
	Guar/Gins	89.04 0.94	-0.04 0.79	-0.82 1.04	-1.07 0.67	-0.21 0.93
Quality of Memory	placebo	392.77 11.01	-36.79 9.44	-52.94 12.82	-45.09 9.16	-47.29 9.20
	Guarana	378.66 12.74	-19.20 10.70	-21.52 10.02	-42.28 10.34	-39.13 9.16
	Ginseng	379.46 14.33	-44.90 10.92	-32.56 10.61	-41.87 11.11	-36.09 13.59
	Guar/Gins	386.24 12.13	-31.22 7.98	-45.50 7.64	-34.45 10.90	-44.36 9.80
Secondary Memory	placebo	207.68 10.14	-33.75 8.39	-47.02 10.06	-41.84 8.28	-41.67 7.97
	Guarana	196.01 11.19	-16.19 8.70	-17.56 9.57	-35.53 9.01	-34.58 8.98
	Ginseng	193.69 13.13	-35.89 9.49	-28.04 9.82	-36.55 10.84	-24.35 12.57
	Guar/Gins	202.62 10.72	-27.38 7.57	-40.42 7.36	-31.49 9.06	-39.94 8.54
Working Memory	placebo	185.09 2.06	-3.04 2.47	-5.92 5.79	-3.25 2.36	-5.63 3.02
	Guarana	182.65 2.44	-3.01 3.37	-3.96 3.32	-6.74 4.45	-4.55 3.77
	Ginseng	185.77 2.37	-9.01 4.12	-4.52 2.50	-5.33 2.07	-11.74 4.56
	Guar/Gins	183.62 2.56	-3.84 2.72	-5.08 2.29	-2.97 4.41	-4.42 3.57

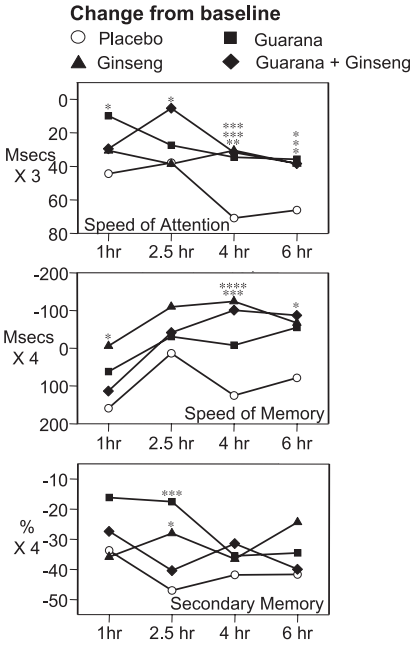

Fig. 1. Effects of the treatments on the primary outcome cognitive factors derived from the CDR battery outcomes. Mean baseline and change from baseline scores (with standard errors) are presented, with a graphical representation of the factors generating significant differences on the initial ANOVA and subsequent planned comparisons (*p=0.05; **p=0.01; ***p=0.005, ****p=0.001 compared to placebo).

p=0.016], 4 h [t(243)=2.91, p=0.004] and 6 h [t(243)= 2.06, p=0.04] post-dose.

In line with this, reference to the planned comparisons of individual outcome measures showed that reaction times were significantly faster following guarana on the digit vigilance task at 1 h [t(243)=2.56, p=0.011], 4 h [t(243)=2.39, p=0.018] and 6 h [t(243)=4.24, p<0.001] post-dose. Speed was also increased for ginseng at 6 h [t(243)=2.84, p=0.005] and for the combination at 4 h [t(243)=2.26, p=0.025] and 6 h [t(243)=3.26, p=0.001] post-dose. Similarly, speed on the choice reaction time task was increased following guarana at 1 h [t(243)=2.19, p=0.029]and 4 h [t(243)=2.17, p=0.031], and following ginseng at 4 h [t(243)=3.97, p<0.001] and 6 h [t(243)=2, p=0.047].

3.3.2. Accuracy of Attention factor

While there was no significant difference on the Accuracy of Attention factor following any treatment, accuracy of performance of the choice reaction time task was reduced following guarana at 1 h [t(243)=3.04, p=0.003] and 4 h [t(243)=2.63, p=0.009] post-dose.

3.3.3. Speed of Memory factor

Planned comparisons showed that performance was enhanced following ginseng at 1 h [t(243)=2.18, p=0.03] and 4 h [t(243)=3.293, p=0.001] with a strong trend towards the same at 6 h [t(243)=1.93, p=0.055], and following the combination at 4 h [t(243)=2.98, p=0.003] and 6 h [t(243)=2.19, p=0.029] post-dose.

With regards the single outcomes contributing to this factor, planned comparisons showed that following ginseng performance was faster on the numeric working memory task at 2.5 h [t(243)=2.99, p=0.003], 4 h [t(243)=3.26, p=0.004] and 6 h [t(243)=2.98, p=0.003] post-dose; on the word recognition task at 1 h [t(243)=2.69, p=0.008]and 4 h [t(243)=2.21, p=0.028]; and on the picture recognition task at 4 h post-dose [t(243)=2.05, p=0.042]. Following guarana, performance speed was increased on the picture recognition task at 1 h [t(243)=2.04, p=0.043], 2.5 h [t(243)=2.46, p=0.014] and 4 h [t(243)=3.24, p=0.001], with a strong trend towards improvement at 6 h post-dose [t(243)=1.88, p=0.06]. Following the combination, speed was increased at 4 h post-dose on both the word recognition [t(243)=2.44, p=0.015] and picture recognition [t(243)=2.19, p=0.03] tasks.

3.3.4. Secondary Memory factor

Secondary Memory performance was enhanced for both guarana [t(243)=3.18, p=0.002] and ginseng [t(243)=2.05, p=0.04] at the 2.5-h testing session, with trends towards the same for the former at 1 h [t(243) =1.9, p=0.06] and for the latter at 6 h [t(243)=1.87, p=0.062] post-dose. Reference to the single task measures making up the factor showed that performance was significantly affected on the picture recognition task following guarana at 1 h [t(243)=2.81, p=0.005], 2.5 h [t(243)=3.37, p=0.001] and 6 h [t(243)=2.26, p=0.025] post-dose.

3.3.5. Working Memory factor

The initial ANOVA suggested that this factor was not significantly affected by the treatment.

Mood Factor		Pre-dose Baseline score	Change from baseline score 1 hr post-dose	2.5hr post-dose	4 hr post-dose	6hr post-dose
Sentence Verification (No. correct)	placebo	**28.86***0.20*	**-0.21***0.22*	**-0.25**0.26	**-0.43**0.26	**-0.21**0.24
	Guarana	**28.79***0.29*	**-0.54***0.42*	**0.11**0.22	**-0.46**0.33	**-0.07**0.24
	Ginseng	**28.46***0.34*	**0.04***0.35*	**0.07**0.32	**0.25**0.30	**-0.32**0.28
	Guar/Gin	**28.71***0.27*	**-0.36***0.37*	**0.25**0.23	**-0.43**0.30	**0.00**0.35
Sentence Verification (Reaction time)	placebo	**1273.2***58.9*	**-26.4**21.6	**22.4**39.9	**-3.6**41.4	**-33.8**40.7
	Guarana	**1351.6***69.8*	**-35.3**44.8	**-92.9**32.7	**-86.7**45.1	**-112.8**43.3
	Ginseng	**1359.6***90.1*	**-129.9**57.8	**-100.2**72.0	**-119.5**62.1	**-141.1**47.7
	Guar/Gin	**1302.9***50.3*	**-11.1**51.7	**-83.8**31.6	**-46.7**30.4	**-15.3**27.2

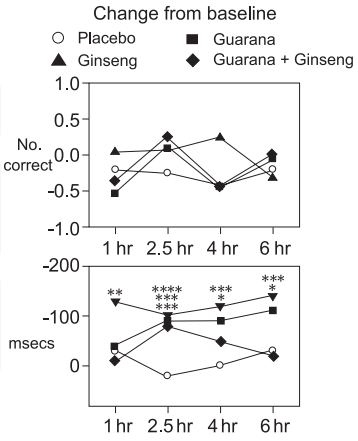

Fig. 2. Effects of the treatments on the sentence verification task. Mean baseline and change from baseline scores (with standard errors) are presented (*p=0.05; **p=0.01; ****p=0.001, *****p=0.0005 compared to placebo on the planned comparisons).

3.4. Individual tasks (not contributing to factors)

3.4.1. Logical reasoning

Performance of this task was not significantly affected.

3.4.2. Sentence verification

Planned comparisons showed that performance of the sentence verification task was significantly speeded for all three conditions. For the guarana condition, this effect was evident at 2.5 h [t(243)=3.05, p=0.003], 4 h [t(243)=2.2, p=0.029] and 6 h [t(243)=2.09, p=0.038]. Ginseng led to increased speed at all time points: 1 h [t(243)=2.73, p=0.007], 2.5 h [t(243)=3.24, p=0.001], 4 h [t(243)=3.06, p=0.002], 6 h [t(243)=2.84, p=0.005]. The same effect for the combination was restricted to the 2.5-h time point [t(243)=2.81, p=0.005].

Mean raw baseline scores and change from baseline scores for each condition across each session on the sentence verification task are presented in the tables and graphs of Fig. 2.

3.4.3. Serial threes subtraction task

While there was no effect on the total number of subtractions generated, both guarana and the guarana/

Factor		Pre-dose Baseline score	Change from baseline score 1 hr post-dose	2.5 hr post-dose	4 hr post-dose	6 hr post-dose
Serial 3 Total	placebo	**42.46***2.40*	**2.18***0.99*	**2.57***1.45*	**0.75***1.43*	**2.93***1.22*
	Guarana	**39.89***2.80*	**2.50***1.49*	**4.86***1.03*	**4.04***1.21*	**4.11***1.67*
	Ginseng	**41.86***2.46*	**1.57***1.10*	**3.29***1.41*	**2.46***1.38*	**4.00***1.43*
	Guar/Gin	**41.32***2.39*	**1.89***0.90*	**3.32***1.48*	**1.25***1.46*	**3.96***0.99*
Serial 3 Errors	placebo	**2.57***0.36*	**1.14***0.36*	**1.04***0.45*	**1.36***0.62*	**0.64***0.44*
	Guarana	**2.93***0.37*	**0.25***0.54*	**-0.14***0.36*	**0.29***0.47*	**0.36***0.51*
	Ginseng	**2.96***0.31*	**0.82***0.41*	**0.36***0.41*	**0.50***0.47*	**0.46***0.52*
	Guar/Gin	**3.36***0.39*	**0.11***0.49*	**0.64***0.51*	**-0.04***0.56*	**-0.61***0.42*
Serial 7 Total	placebo	**27.25***2.40*	**-1.46***0.73*	**1.07***0.72*	**1.50***0.56*	**0.93***0.68*
	Guarana	**24.64***2.53*	**2.61***0.97*	**3.54***0.77*	**3.39***0.99*	**3.36***1.08*
	Ginseng	**25.57***2.19*	**1.79***1.39*	**2.21***1.29*	**1.96***0.95*	**3.11***0.96*
	Guar/Gin	**24.96***2.22*	**2.00***0.83*	**2.04***0.84*	**1.64***0.82*	**3.25***1.08*
Serial 7 Errors	placebo	**3.04***0.31*	**0.86***0.35*	**0.96***0.50*	**-0.04***0.42*	**0.29***0.44*
	Guarana	**2.79***0.31*	**1.39***0.47*	**0.32***0.30*	**1.07***0.56*	**0.50***0.44*
	Ginseng	**2.82***0.42*	**0.18***0.56*	**0.43***0.48*	**0.89***0.41*	**0.68***0.45*
	Guar/Gin	**3.82***0.68*	**-0.57***0.74*	**-0.75***0.73*	**-0.36***0.62*	**-0.36***0.84*

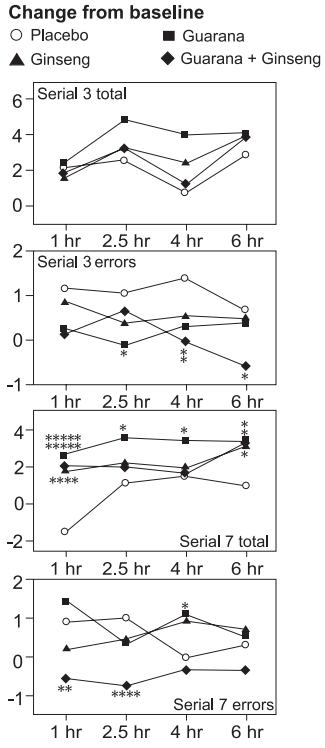

Fig. 3. Effects of the treatments on the serial subtraction tasks. Mean baseline and change from baseline scores (with standard errors) are presented (*p=0.05; **p=0.01; ****p=0.001, *****p=0.0005 compared to placebo on the planned comparisons).

ginseng combination led to a significant reduction in errors during the task. For the former this effect was evident at 2.5 h [$t(243)=2.17$, $p=0.03$] and 4 h [$t(243)=1.97$, $p=0.049$], and for the latter at 4 h [$t(243)=2.57$, $p=0.011$] and 6 h [$t(243)=2.3$, $p=0.022$].

3.4.4. Serial sevens subtraction task

All three treatments resulted in an increase in the total number of subtractions on the serial subtractions task. Following guarana, this effect was evident during all four post-dose testing sessions: 1 h [$t(243)=4.25$, $p<0.001$], 4 h [$t(243)=2.57$, $p=0.011$], 2.5 h [$t(243)=1.97$, $p=0.05$], 6 h [$t(243)=2.53$, $p=0.012$]. Following both ginseng and the guarana/ginseng combination, more subtractions were performed at the 1 h (ginseng [$t(243)=3.39$, $p=0.001$], combination [$t(243)=3.61$, $p<0.001$]) and 6 h (ginseng [$t(243)=2.27$, $p=0.024$], combination [$t(243)=2.42$, $p=0.016$]) testing sessions.

Accuracy of performance (reduced errors) was also improved following the guarana/ginseng combination at the 1 h [$t(243)=2.77$, $p=0.006$] and 2.5 h [$t(243)=3.33$, $p=0.001$] testing sessions. In contrast to this, following guarana, participants under-performed at three time points, with this effect reaching significance at a single time point (4 h) [$t(243)=2.15$, $p=0.032$].

Mean raw baseline scores and change from baseline scores for each condition across each session on the serial subtraction tasks are presented in the tables and graphs of Fig. 3.

3.5. Mood assessment

3.5.1. Bond–Lader mood scales

There was no significant effect of the treatments on mood as assessed by the Bond–Lader mood scales.

4. Discussion

The results of the current study showed that single doses of both guarana and ginseng, and a combination of the two, improved cognitive performance in comparison to placebo in healthy young participants. These improvements took the form both of gross improvement of performance on several tasks, and an attenuation of the decline in performance invariably seen in placebo conditions during multiple completions of elements of the CDR test battery.

With regard to guarana, this study provides the first empirical evidence confirming its reputed psychotropic properties in humans. Most notably, improvements in the speed of task performance were observed following 75 mg of the extract during the tasks making up the ‘Speed of Attention’ factor, the more difficult serial subtraction task (serial sevens); and during the sentence verification task. In the case of the former and the latter, improvements were seen at three out of four time points. For serial sevens, significant improvements were found at all four post-dose testing sessions, albeit with increased errors at 4 h, suggesting that there may have been a speed–accuracy tradeoff at this time point. Although less pronounced, performance on the ‘Secondary Memory’ factor was also improved at one time point, with improvements seen at three time points on the (contributing) picture recognition task.

Given that the guarana extract contained only 11% to 12% caffeine, it seems unlikely that the potential maximum dose of under 10 mg caffeine could itself account for the performance effects seen here. Furthermore, improved speed of task performance on all measures was still apparent at 6 h. Caffeine, including when derived from guarana, has a half-life of approximately 6 h in nonsmoking humans (Haller et al., 2002; Cheng et al., 1990), and would have presumably decayed to subactive levels by this time point. The suggestion that guarana’s caffeine content alone does not account for all of its cognitive effects is supported by Espinola et al.’s (1997) observations in rodents. Doses of guarana with minimal total caffeine content were more beneficial than 10-fold doses of guarana (where the caffeine fraction may have been approaching pharmacological levels). Additionally, the lower doses were as effective as pure caffeine administered at a 16-fold higher dose (by caffeine content alone) on fatigue and memory tasks.

The likelihood that caffeine is not the only psychoactive component of guarana does also raise questions of the advisability of standardising extracts to caffeine content (as in the extract used here). We are currently embarking on research directly comparing guarana with an equivalent pure caffeine doses using a similar experimental structure to that utilised here. It is hoped that this will allow a direct comparison of caffeine with an equivalent dose of guarana, with an ultimate aim of delineating the relative contributions of caffeine and the saponin/tannin content in guarana.

In the case of ginseng, the results again replicate a direct mnemonic effect for this dose (Kennedy et al., 2001a). In terms of accuracy, improvement was restricted to a single time point on the Secondary Memory factor. However, the effect of this dose on the speed of task performance was somewhat more marked and extended across the CDR battery, with faster performance during two post-dose testing sessions on both the ‘Speed of Attention’ and ‘Speed of Memory’ factors. Reaction times were also improved at all time points on the sentence verification task, extending the range of memory tasks shown to be sensitive to ginseng. Taken with the ‘Secondary Memory’ and ‘Speed of Memory’ effects, the latter could be interpreted as reflecting a beneficial effect of ginseng on memory per se, with faster performance on the timed tasks reflecting more efficient retrieval of stored information.

The results also clarify the discrepancy in findings regarding speed of task performance for this dose. The results are consistent with the demonstration of significantly reduced P300 latency (Kennedy et al., 2003a), and are also broadly in agreement with a preliminary report showing both reduced blood glucose levels and speeded task performance following a 200-mg dose of G115 in young volunteers (Reay et al., 2004). The lack of any correlational relationship between the modulation of blood glucose and cognitive performance in the latter study highlights the fact that while ginseng would appear to exert a wide range of physiological and cognitive effects, the mechanisms underlying them are complex, and to date, poorly understood. Potential candidate mechanisms include effects on the cardiovascular and HPA systems, acceleration of platelet aggregation, cardio- and neuroprotective effects, modulation of neurotransmission, and promotion of nitric oxide synthesis (see Kennedy and Scholey, 2003). The reason for the slight impairment in attention task speed in the original study (Kennedy et al., 2001a) is also unclear, although it should be viewed in the light of far stronger patterns of improved memory performance for all three doses used in that study. Thus it appears that, while the memory-enhancing effects of ginseng are robust following a single dose, any attentional effects may be more fragile. The reasons for the latter are not known but may reflect subtle differences in cohorts, task parameters or even subjective factors such as participants' understanding of which aspects of performance should be prioritised.

The ginseng/guarana combination was associated with faster 'Speed of Attention' and 'Speed of Memory'. Interestingly, the effects of the combination on the 'Speed of Attention' factor are most similar to those of guarana alone (three significant time points each). Conversely, the 'Speed of Memory' effects are more similar to those associated with ginseng alone. The combination also led to improved performance on both the serial threes and serial sevens subtraction tasks. On these, 200 mg of ginseng had little effect, whereas 75 mg of guarana resulted in some improvement in serial threes speed and accuracy, but with some reduced accuracy on the serial sevens task. The ginseng/guarana combination, on the other hand, was wholly beneficial on both tasks, with increased accuracy on both tasks and increased serial sevens subtractions at the 1-h time point. As these tasks (in particular, serial sevens) have previously been rated as the most subjectively demanding tasks within the entire battery utilised here, this does potentially signal a utility for the combination in situations of intense cognitive demand. Indeed, given that guarana is often consumed for its stimulant properties at times of increased mental demand, this possibility should be further explored. Beyond this, while the general pattern of effects following the combination could be described as reflecting elements of the effects from the single ingredients, it could not be described on the basis of the current data as offering clear evidence for a synergistic relationship between the two. Indeed, while the a priori statistical approach adopted here did not allow for a direct comparison of the effects of the treatments, the overall pattern of results for all three treatments are notable in their general similarity. However, this similarity does not preclude the possibility of synergistic effects at different doses. The current study employed a typical dose of guarana (75 mg), which was substantially lower than that of ginseng (200 mg)—although this is not an untypical dose. It is possible that changing the ratios of the two might potentiate any behavioural effects. It should also be noted that the cognitive and mood effects of chronic administration of ginseng have not been adequately addressed as yet, and that this is the first investigation of the cognitive effects of guarana in healthy young humans. It is entirely feasible that the effects of extracts of either or both might increase with chronic dosage. Mattei et al. (1998) note that, on the basis of their saponin contents and observations from animal studies, guarana and ginseng might both be classed as 'resistogens' or 'adaptogens' (i.e. offering protection against the physiological effects of physical or psychological stressors). If this is the case, then the effects of both may increase with chronic dosage, and the possibility exists for a synergistic relationship between their components which would confer an added advantage over time, potentially both in terms of general health and cognitive performance.

The results here were obtained in a sample of young healthy participants, and therefore it may not be possible to generalise them to other populations. However, given its increasing inclusion in foodstuffs, beverages and herbal supplements, the demonstration of cognitive effects seen here following acute administration of guarana to this population suggests that its behavioural effects warrant further investigation.

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