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Assessing the effects of caffeine and theanine on the maintenance of vigilance during a sustained attention task

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ABSTRACT

Caffeine and L-theanine, both naturally occurring in tea, affect the ability to make rapid phasic deployments of attention to locations in space as reflected in behavioural performance and alpha-band oscillatory brain activity (8–14 Hz). However, surprisingly little is known about how these compounds affect an aspect of attention that has been more popularly associated with tea, namely *vigilant attention*: the ability to maintain focus on monotonous tasks over protracted time-periods. Twenty-seven participants performed the Sustained Attention to Response Task (SART) over a two-hour session on each of four days, on which they were administered caffeine (50 mg), theanine (100 mg), the combination, or placebo in a double-blind, randomized, cross-over fashion. Concurrently, we recorded oscillatory brain activity through high-density electroencephalography (EEG). We asked whether either compound alone, or both in combination, would affect performance of the task in terms of reduced error rates over time, and whether changes in alpha-band activity would show a relationship to such changes in performance. When treated with placebo, participants showed a rise in error rates, a pattern that is commonly observed with increasing time-on-task, whereas after caffeine and theanine ingestion, error rates were significantly reduced. The combined treatment did not confer any additional benefits over either compound alone, suggesting that the individual compounds may confer maximal benefits at the dosages employed. Alpha-band oscillatory activity was significantly reduced on ingestion of caffeine, particularly in the first hour. This effect was not changed by addition of theanine in the combined treatment. Theanine alone did not affect alpha-band activity.

1. Introduction

Any compound that could potentially enhance the ability to maintain attention over protracted periods of time could have potentially profound importance in everyday life where lapses in attention are a common occurrence, from the relatively trivial broken cup on the floor to the far more crucial failure to step on the brakes when a child runs onto the roadway ahead.

The "relaxed state of alertness" commonly attributed to tea-drinking by the general population has important implications for sustained attention, or "vigilance." Research based on subjective alertness and anxiety ratings has provided evidence to support the notion that tea (*Camellia Sinensis*) affords a good compromise between facilitated alertness and arousal (see e.g. Quinlan et al., 2000; Hindmarch et al., 1998, 2000). However, to properly address the mechanism underlying the effects of tea on attention and vigilance, a more systematic examination of its constituent elements in isolation and their effects on brain networks responsible for sustaining attention is required. To this end, there have been considerable efforts to understand the neural effects of the two major psychoactive components of tea in isolation; namely the methylxanthine caffeine and the non-proteinic amino acid L-theanine (5-N-ethylglutamine).

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Caffeine is well known to improve arousal and alertness (e.g. Bryan, 2008; Hewlett and Smith, 2007; see Brice and Smith, 2001 for a review), and the effects of caffeine on EEG measures have been studied in the context of a varied array of cognitive and attentional paradigms. Clear effects on cognitive performance and associated brain physiology are a near ubiquitous finding in the ERP literature.

However, there have been comparatively few investigations of caffeine's effects on oscillatory brain activity, and very little investigation of caffeine's effects on oscillatory brain activity during demanding attention tasks. Studies of caffeine's effects on oscillatory activity at rest have revealed conflicting results, with studies demonstrating both reduced overall alpha power (Barry et al., 2008a,b; Deslandes et al., 2006; Dimpfel et al., 1993) and finding no overall effect of caffeine on oscillatory mechanisms (Keane and James, 2008; Keane et al., 2007). In one study using the sustained attention to response (SART) task, 1.75 mg/kg caffeine (equivalent to about 115 mg caffeine) was found to have modest effects on theta and alpha power (Keane et al., 2007). However, no obvious performance benefits were noted, although the authors did not directly assess response speed or errors.

In a series of studies from this laboratory, a clear link between theanine ingestion and alpha-band oscillatory brain activity during demanding selective attention tasks has been established (Gomez-Ramirez et al., 2007, 2009; Kelly et al., 2008). Earlier work had pointed to effects of theanine on alpha-band brain activity during recordings from participants who were in a passive resting state (e.g. Juneja et al., 1999; see also Nobre et al., 2008). More recently, a synergistic effect of theanine in combination with caffeine has also been shown and this combination treatment also clearly improved humans' ability to perform a very challenging visual spatial attention task (Kelly et al., 2008). That oscillations in the alpha-band are important in a number of critical selective attentional processes is now well established (see Foxe et al., 1998; Worden et al., 2000; Fu et al., 2001; Kelly et al., 2005, 2006, 2009; Rihs et al., 2007; Romei et al., 2008a, 2008b, 2010; Snyder and Foxe, 2010; Banerjee et al., 2011; Foxe and Snyder, 2011), and as such, natural compounds such as theanine and caffeine that have clear effects on this rhythm are of significant interest to attention researchers. A common finding from our studies of theanine and its role in attention is that its greatest effect appears to be a substantial attenuation of ongoing background alpha activity when participants who have ingested theanine are engaged in demanding attention tasks.

A potentially important implication of this series of studies is that the greatest effect of theanine may be upon vigilance. In this study, we aim to investigate a task context where the major challenge in task performance lies in the maintenance of vigilant focus on a cognitively undemanding task over protracted periods of time. Our central thesis, based on our previous studies (Gomez-Ramirez et al., 2007, 2009; Kelly et al., 2008) was that a moderate dosage of theanine and caffeine would enhance the ability to maintain concentration on a task over sustained periods and that this would be reflected in sustained attenuation of tonic alpha-band oscillatory activity in key nodes of the cortical attention network.

We chose a well-established paradigm, the Sustained Attention to Response Task (SART), as our main assay of sustained attention (see Manly et al., 1999). The SART has proven very effective in assessing this type of sustained attentive responding (Manly et al., 1999, 2002, 2003; Robertson et al., 1997; Smilek et al., 2010). In the most common version of the SART, a predictable series of single digits are presented (1–9) and participants are required to make a response to each number (go-trials) with the exception of the number 3 (no-go trial). Neuroimaging has shown increased activation in both the right dorsolateral prefrontal cortex and the right superior/posterior parietal cortex compared to a more challenging version of the SART in which the numbers were presented randomly (Manly et al., 2003). These findings suggest that right fronto-parietal regions are responsible for maintaining a goal-directed focus in unarousing contexts. Electrophysiological work in humans has established event-related potential analogues of these activations (Dockree et al., 2005) and spectral analysis of the EEG during SART performance has drawn a clear link between optimal performance and ongoing tonic alpha-band activity (Dockree et al., 2007). Thus, the SART presents an ideal means of assessing the relationship of alpha-band activity to performance on a sustained attention task, in the context of potential theanine and caffeine effects upon these related processes.

2. Methods

2.1. Participants

Twenty-seven medically healthy participants were initially recruited into this study via word of mouth or through the volunteer participant pool at the Nathan S. Kline Institute for Psychiatric Research. Each participant was screened during a comprehensive intake interview for the following exclusionary criteria: 1) Any history of psychiatric or neurological disorders, 2) any previous or current substance abuse disorders, including cigarette use, 3) any current or previous severe medical problems, 4) any instance of head trauma with loss of consciousness, 5) HIV positive status, 6) any current or previous psychotropic medication use. All participants reported normal or corrected-to-normal vision. Participants who completed the study were run across five separate test days (see Kelly et al., 2008 for an essentially identical approach). The five days consisted of the administration of questionnaires and a simple 1-h training session on day 1 that did not involve the recording of electrical activity, followed by four separate test days where electrical activity was recorded and all four possible treatments administered. The 4 days of testing were separated by an average range of 13 days in between test session 1 and 4, with an average of 4 days between each of the individual test sessions. Participants fell between the ages of 18 and 40 y (Mean age = 26 y). Eight of the participants were female, and two participants were left-handed as assessed by the Edinburgh Handedness inventory. Ultimately, data from 21 participants were entered into the analyses reported here. Three participants were excluded before completing the five-day sequence (one after revealing a substance abuse disorder, the other two because of poor performance on the task). Data from three additional participants who did complete all testing days were eventually excluded following detailed analyses of their behavioural data, where it became clear that two of them were responding in an essentially random fashion and that a third had ceased to perform the task midway through each of the test days. Each participant served as their own control (within-participants design) such that they received one of the three active compound treatments (100 mg theanine, 50 mg caffeine, or 100 mg theanine plus 50 mg caffeine) separately on each of three days and a placebo on the fourth day. The order of treatment across days was randomized and counterbalanced across participants in a double-blind design. Participants were asked to refrain from drinking tea, coffee or soft-drinks (soda-pop) for at least 24 h before each test. A questionnaire was also administered to determine each participant's typical daily consumption rates of such products. Participants received a modest fee (circa $18 per hour) for participation in this study. All experimental procedures were approved by the institutional review board of the Nathan Kline Institute and each participant provided written informed consent. All procedures complied with the tenets of the Declaration of Helsinki.

2.2. Typical caffeine & theanine intake

Fourteen of the 21 participants reported consuming no coffee or tea at all as part of their daily routine. Three subjects reported consuming just one cup of coffee and no tea on an average day. Two subjects reported consuming just one cup of tea per day and no coffee. Just two subjects in the sample reported greater than a single beverage per day, and both were exclusively coffee drinkers (one averaging 2 cups per day, the other 3).

2.3. Sustained attention to response inhibition task (SART)

Digits were presented sequentially from '1' through '9'. For each block of trials, 225 digits were presented sequentially (25 of each of the nine digits) over a period of 3.9 min. Participants undertook a total of 13 blocks over the course of a recording session with each block timed to begin at precisely 12-min inter-block intervals. Performance of the SART block was immediately followed by a 6-min sustained attention task (the Continuous Temporal Expectancy Task (CTET) – see O'Connell et al., 2009). Results of this CTET task will be reported elsewhere. Following the CTET, a 2-min break ensued before participants began the sequence again. After the 7th block, a fixed break of 11 min replaced the standard 2-min break. Participants then completed the remaining 5 blocks as before, in 12-min increments. The

experimental blocks were run on a very strict schedule that was kept as close to identical as possible across days. Time of day was also matched across participants, in order to assess performance as a function of time-on-task, as well as ruling out contributions from differential circadian rhythms. On each of the testing days, electrode application began at 9:30 am and the treatment was consumed at exactly 10:05 am. The first block of the SART began at 10:30 am and the sequence proceeded thereafter as described above until 13:15 pm. Caffeine is rapidly absorbed and distributed throughout the body including the brain (Dager and Friedman, 2000), and reaches maximum plasma concentrations at about 30 min post consumption (Magkos and Kavouras, 2005). Theanine peaks in plasma at 50 min post consumption (Van der Pijl et al., 2010), and affects alpha activity from 45 until at least 105 min after consumption (Nobre et al., 2008). The timing of the EEG recording period from 25 until 185 min after treatment consumption was chosen to span this period. Participants were asked to refrain from eating during the entire testing period and were provided lunch when testing was completed. Two subjects, however, requested, and were provided a small snack during the break.

Participants were seated in a dimly lit, sound-attenuated, electrically shielded room at a distance of 1.5 m from the computer monitor on which the digits were presented. For each trial, a digit was presented for 150 ms followed by an Inter-Stimulus-Interval (ISI) that varied randomly between 800 and 1250 ms. A variable ISI was included to prevent participants succumbing to a speed-accuracy trade-off that can occur when ISIs are regularly paced. That is, participants are inclined to anticipate the occurrence of a stimulus when completely regular pacing is used. Participants were instructed to respond with a left mouse button press with their right forefinger upon presentation of each digit (go-trials) with the exception of the 25 occasions per block when the digit 3 (target) appears, where they were required to withhold/inhibit their response. The basic design is illustrated in Fig. 1.

Five randomly allocated digit sizes were presented to increase the demands for processing the numerical value and to minimize the possibility that participants could simply set a search template for some perceptual feature of the target trial ('3'). Digit font sizes were 100, 120, 140, 160 and 180 in Arial font. The five allocated digit sizes therefore subtended 1.39°, 1.66°, 1.92°, 2.18° and 2.45° of visual angle respectively, at a viewing distance of 150 cm. Digits were presented 0.25° above a central yellow fixation cross on a grey background. Stimuli were delivered using the stimulus delivery program, Presentation® software package (Version 0.75, www.neurobs.com). More details of the task can be found in Dockree et al. (2005) or in Dockree et al. (2007).

2.4. Pharmacological manipulation

The theanine and caffeine solutions were prepared by dissolving 100 mg theanine and/or 50 mg caffeine into 200 ml of cool potable water. The placebo solution was 200 ml of cool potable water without any additional substance. The solutions were prepared just prior to the arrival of the participant in the laboratory. The experimenter was blinded as to which compound was to be administered on each day of testing.

2.5. High-density EEG recordings

Participants were seated in a sound-attenuated, electrically shielded and dimly illuminated recording chamber and asked to keep head and eye-movements to a minimum, while maintaining central fixation. Recordings were made from a custom designed 168-channel electrode array. Biosemi ActiveTwo electrodes were applied at the scalp surface. A filter bandpass of DC to 100 Hz and a sampling rate of 512 Hz were used. EEG was recorded continuously and epoched and averaged offline. The nose was used as the reference. Trials with blinks and large eye-movements were rejected offline on the basis of horizontal and vertical electro-oculographic recordings. An artefact rejection criterion of ±70 μV was used at all other electrode sites to exclude periods of high EMG and other noise-transients. From the remaining artefact-free trials, averages were computed for each participant. These averages were then visually inspected for each individual to ensure that clean recordings with sufficient numbers of trials were obtained and that no artifacts were still included. Data were ultimately averaged across all participants (grand mean averages) for comparison between treatment conditions and for display purposes. Applying the above artefact rejection criteria resulted in a mean trial rejection rate of 7.2% (standard deviation = ±3.6).

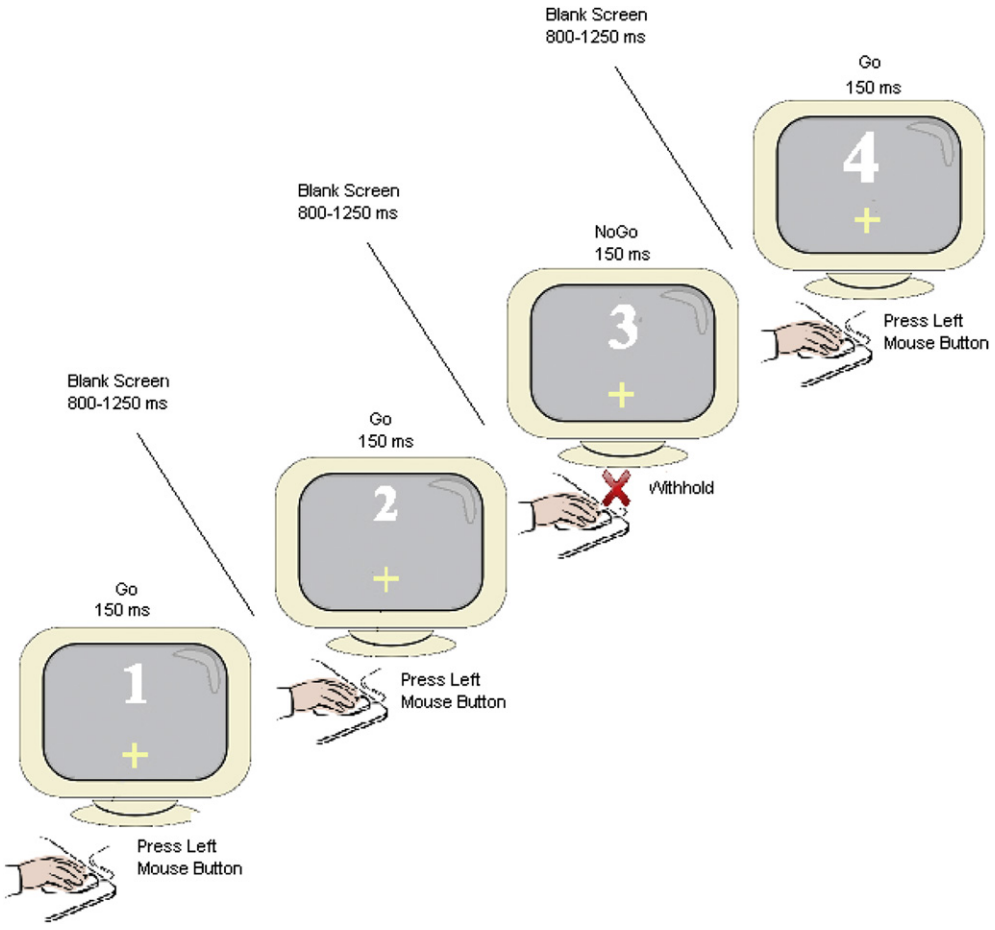

Fig. 1. The basic fixed-sequence SART paradigm is depicted schematically here. Subjects push a mouse button to each occurrence of a digit stimulus as the sequence cycles from 1 through 9, but they are required to withhold responding to occurrences of the digit "3".

2.6. Behavioural data analysis

The behavioural dependent variables were omission and commission errors and reaction times. Omission errors were defined as missing responses to any digit but 3 (binary), and commission errors as false responses to digit 3 (binary). All reaction times except those to digit 3 were included provided that the values were in the range of 100–800 ms. Reaction times were log-transformed to fit a Gaussian probability distribution, and then averaged to obtain a single observation per block.

2.7. Neurophysiological data analysis

Alpha-band activity (8–14 Hz) was calculated on a subject-by-subject basis by computing a fast Fourier transform (FFT) on a 500-ms window of data immediately preceding the presentation of each digit, thus largely avoiding the early visual evoked potential to the digits. A topographical approach was then used to identify the site of maximal alpha-amplitude for each participant and to identify individualized alpha peak frequency (see e.g. Dockree et al., 2007). This approach was applied to spectra averaged across all stimuli, all blocks and all treatments to eliminate bias. The following strategy was employed: 1) the spectra from all 160 channels were overlaid in a butterfly plot; 2) this allowed for easy identification of those channels where alpha-band activity was elevated above the otherwise 1/f decreasing function of frequency (for the majority of subjects, this was a single frequency bin at 10 Hz, for others a range of 8–10 or 10–12 Hz, 3 subjects showed a single elevated bin at 12 Hz); 3) the cluster of 4–5 channels at which alpha showed maximal activity were then identified and a center-of-activity in this cluster was identified for each subject (see inset head in Fig. 2). Alpha was log-transformed to fit a Gaussian distribution, and then averaged across all stimuli to obtain a single observation per block.

2.8. Statistical analyses

Analyses were based upon a range of Generalized Linear Mixed Models, assuming normal residuals in the case of log(alpha) and log(reaction time), and a Poisson distribution for numbers of Omissions and Commission Errors.

Treatment order, Caffeine, Theanine, and the interaction of Caffeine × Theanine were fitted as fixed effects, and Subject was included as a random effect. Time was fitted as a continuous covariate, and an additional quadratic term (Time2) was added to reflect curvature in the response where appropriate. An additional two-level categorical factor Rest was also tested to describe the effect of the additional rest experienced between blocks 7 and 8 on performance at block 8, and included if appropriate. Treatment × Time interactions were included where necessary to describe time-related treatment effects. Subsequent exploratory analyses investigated effect of digit presented.

Degrees of freedom were Kenward-Roger adjusted, and a 5% significance level was used throughout. The analysis of reaction times was weighted for the number of trials contributing to the per block mean. Omission and commission errors were weighted by inclusion of number of trials as the offset parameter. For alpha, the number of observations did not vary.

Key requirements of the covariance structure were the description of within-subject correlations of an autoregressive nature between blocks in the same visit, and the accommodation of the additional time interval between blocks 7 and 8. A "spatial power" covariance structure was employed to achieve these. A compound symmetric (or exchangeable) covariance element was also added at the Subject × Visit level, in order to allow the fitted correlations between blocks within a visit to be higher where necessary. A random effect was also fitted for Subject, to describe compound-symmetric correlations between blocks for the same subject on different visits. This error structure was employed with respect to all endpoints.

Figures depict transformed proportions (GLSMEANS) ± standard errors based on models treating Time as categorical variable for illustrative purposes.

3. Results

3.1. Behavioural data

3.1.1. Omission errors

Caffeine decreased omission errors by 50% relative to placebo (comparison of Caffeine only to Placebo $t_{53.5} = -5.4$, $p < .0001$). Theanine also decreased omission errors, but to a lesser extent (36% relative to placebo; comparison of Theanine-alone to Placebo $t_{53.3} = -3.8$, $p < .001$). There was evidence of a Caffeine × Theanine interaction ($F_{1,53.6} = 5.0$, $p < .05$); however, the effect of the combined treatment of caffeine and theanine was essentially the same as that of caffeine alone. Subsequent modelling suggested a Theanine × Caffeine × Time interaction ($F_{1,222} = 6.16$), which would indicate that the extent to which the effects of Caffeine and Theanine appeared not to be additive, as described above, varied over time. However interpretation of Omission errors was complicated by the presence of a number of outliers reporting Omission Error rates in excess of 50% under Placebo, the effects of which are evident in Fig. 3 from Block 9 onwards. A subsequent assessment focusing only on data up to and including Block 8 suggested a more straightforward additive effect of the two treatments in the first half of the session. Exploratory statistics restricted to blocks 1 through 8 showed that omission errors were reduced by 37.4% after caffeine [95% CI: (22.6%, 49.3%); $F_{1,56.4} = 19.5$, $p < .0001$] and by 21.6% after theanine [95% CI: (3.4%, 36.4%); $F_{1,56.5} = 5.5$, $p < .05$].

3.1.2. Commission errors

Similarly, caffeine decreased commission errors by 30% relative to placebo (comparison of Caffeine only to Placebo $t_{56.4} = -4.2$, $p < .0001$), and theanine decreased commission errors to a lesser extent (23% relative to placebo; comparison of Theanine-alone to Placebo $t_{56.5} = -3.1$, $p = .0033$). There was evidence of a Caffeine × Theanine interaction ($F_{1,56.4} = 7.7$, $p < .01$) suggesting that the effect of the combined treatment of caffeine and theanine was

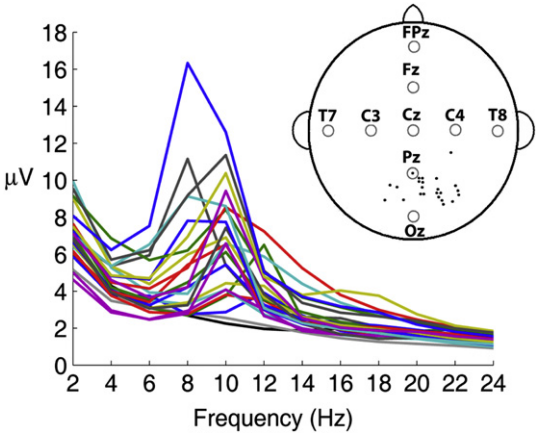

Fig. 2. Individual frequency spectra are plotted for each of the 21 participants from the scalp-site of maximal alpha-amplitude. The scalp-site of maximal alpha-amplitude is plotted on the insert cartoon head for each participant to illustrate the general parieto-occipital distribution of these maxima and the high inter-subject variability.

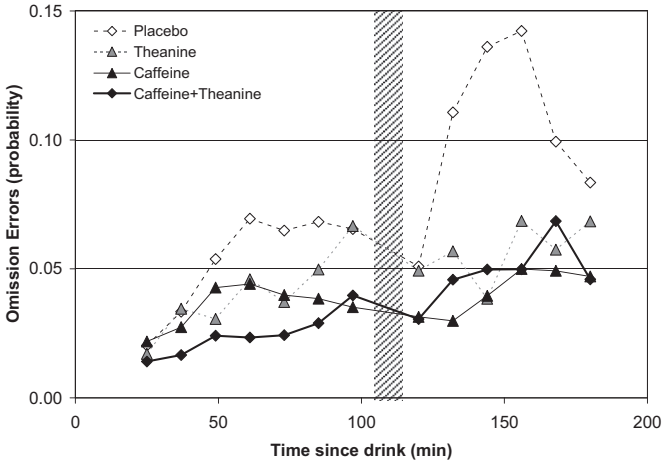

Fig. 3. The probability of omission errors is plotted as a function of treatment and time. Caffeine decreased omission errors by 50% relative to placebo. Theanine also decreased omission errors, but to a lesser extent (36% relative to placebo). There was evidence of a Caffeine × Theanine interaction; however, the effect of the combined treatment of caffeine and theanine was essentially the same as that of caffeine alone.

similar to that of caffeine alone. Treatment effects on commission errors did not change over time (see Fig. 4).

3.1.3. Reaction times

Caffeine decreased reaction times by 3% relative to placebo on average (main effect of caffeine: $F_{1,57.1} = 5.0$, $p < .05$; see Fig. 5). There was no evidence of main or interaction effects involving theanine. The effect of caffeine did not change over time.

The 11-min break after block 7 systematically decreased reaction times by 2% in block 8 (main effect of Rest $F_{1,915.4} = 5.2$, $p < .05$), suggesting recovery after the break. Subsequent exploratory analysis suggested that reaction times to digit 1 were considerably slower than to any other digit (main effect of Stimulus $F_{7,7570} = 142.7$, $p < .001$; data not shown).

3.2. Electrophysiological data

Caffeine decreased alpha (main effect of Caffeine $F_{1,57.0} = 7.5$, $p < .01$). There were no main or interaction effects involving theanine. Further exploratory analysis suggested that the effect of caffeine was to initially decrease alpha by an estimated 12% (see Fig. 6). This effect attenuated at around one hour after the drink (Caffeine × Time interaction: $F_{1,250.9} = 9.9$, $p < .01$; no effect of Theanine, Theanine × Caffeine, or Time).

The 11-min break after block 7 systematically increased alpha by 8% in block 8 (main effect of Rest $F_{1,948.4} = 24.4$, $p < .001$). Further exploratory analysis suggested that Alpha to digit 2 was considerably higher than to any other digit (main effect of Stimulus $F_{8,8648} = 31.2$, $p < .001$; data not shown); this may reflect preparation for the upcoming inhibitory trial with digit 3. Treatment effects on alpha did not interact with the factor Digit.

Fig. 7 displays topographic maps of alpha-band amplitude for each of the treatments. These topographies are plotted for the anticipatory alpha period, that is, the 500 ms epoch immediately preceding the presentation of all digit stimuli. The maps show a typical bilateral parieto-occipital alpha-topography. These maps are displayed for two main time-periods; Panel A shows the topographies collapsed across the first 5 blocks (up to 85 min after ingestion of the treatment) where clear alpha-band suppression was evident for both treatment conditions that included caffeine; Panel B displays the remainder of the blocks where this effect was much attenuated.

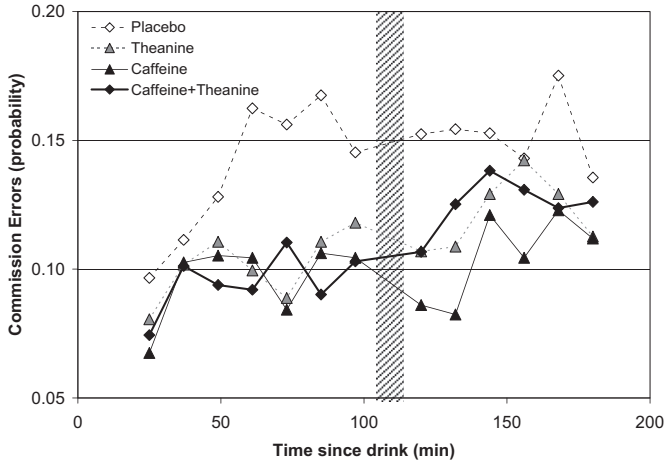

Fig. 4. The probability of commission errors is plotted as a function of treatment and time. Caffeine decreased commission errors by 30% relative to placebo. Theanine decreased commission errors to a lesser extent (23% relative to placebo). There was evidence of a Caffeine × Theanine interaction suggesting that the effect of the combined treatment was similar to that of caffeine alone.

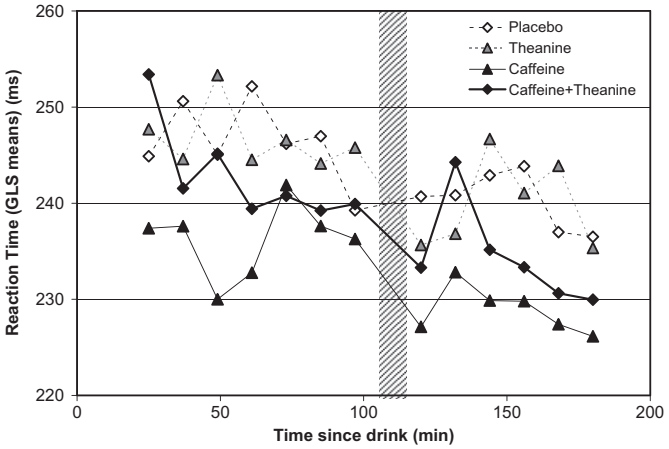

Fig. 5. Reaction times are plotted as a function of treatment and time. Caffeine decreased reaction times by 3% relative to placebo on average. There was no evidence of main or interaction effects involving theanine.

4. Discussion

To our knowledge, this was the first study to use high-density electrophysiology to explicitly examine the effects of theanine and caffeine on sustained attention. The amount of caffeine used here corresponded to a typical cup of tea. We used an amount of theanine corresponding roughly to five cups of tea in order to maximize any potential effects, since theanine's effects on sustained attention have not yet been explored to our knowledge. We will begin with a brief description of the basic pattern of behavioural effects that was observed across time for the placebo condition and then summarize the main findings for each of the treatments as they relate to this baseline performance.

A) An interesting pattern of behavioural results was associated with performance of the SART across the approximately two-hour block of time during which participants were required to engage in the task. The rates of both omission errors (failures to push the button to the regular occurrence of the digit stimuli) and commission errors (failures to inhibit a responses to the occasional digit "3" stimuli) were very low at the beginning of testing. However, as the testing period wore on, these rates climbed fairly consistently. The increase in errors with time was

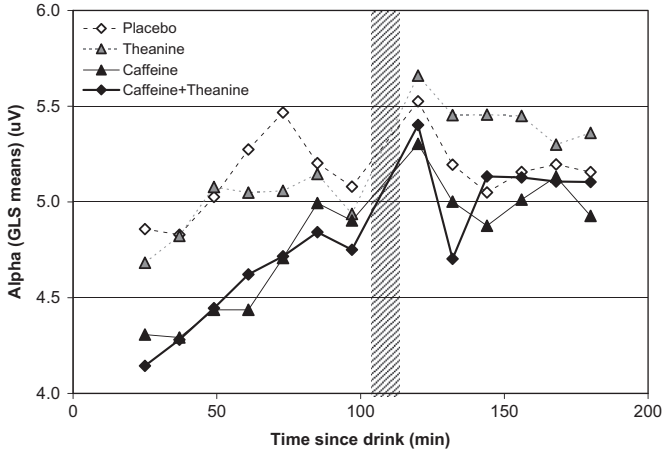

Fig. 6. Alpha-band activity is plotted as a function of treatment and time. Caffeine decreased alpha-band power. There were no main or interaction effects involving theanine.

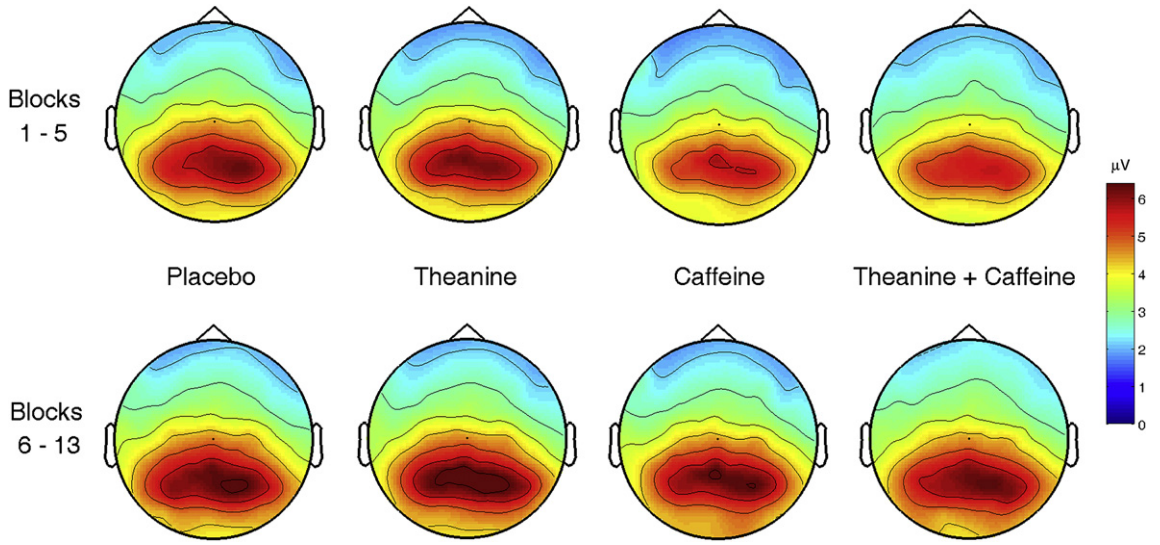

Fig. 7. Topographic maps of alpha-band activity during the 500-ms epoch preceding any digit stimulus showing that the suppression in the caffeine conditions was stronger in block 1–5 than in later blocks.

especially evident in the case of commission errors, where an initial tendency to make an error at a rate of approximately 1-in-10 instances climbed to a rate of about 1-in-6 by just the fourth block of trials, a level at which it stabilized for the remaining 10 blocks of the experiment. Omission errors, on the other hand, showed a somewhat different temporal trajectory, increasing modestly over the initial 4 blocks, then levelling off, before increasing dramatically in the blocks following the 11-min rest break (i.e. after block 8). Taken together, it is clear that participants showed a general, if modest, decline in their ability to sustain attentional focus as the 2-h testing period progressed.

B) Theanine consumed in isolation (100 mg) significantly reduced the rate of both commission errors and omission errors. That is, participants were less likely to incorrectly push the button on the occurrence of the digit "3" than when they had consumed the placebo, and they were also less likely to fail to press the button to the other digits in the sequence. Theanine alone did not affect reaction times. Turning to the electrophysiological results, it was somewhat surprising to us that these significant improvements in the ability to maintain performance over time were not accompanied by any significant change in background alpha-band activity for the theanine-alone treatment, which was found to be indistinguishable from the activity recorded during the placebo condition, a matter we will return to below.

C) Caffeine alone (50 mg) also significantly reduced omission and commission error rates relative to the placebo condition, a pattern of effects closely resembling those seen for the theanine-alone condition. As with theanine, caffeine appeared to suppress error rates and significantly shortened reaction times, a speeding that was seen consistently across the testing period. Electrophysiologically, caffeine also resulted in a significant attenuation of tonic alpha power, an effect that was seen over approximately the first hour of the task, but that then returned to levels seen during placebo for the second half of the testing period. That is, there appears to be an uncoupling of timing of the behavioural and electrophysiological effects here, in that the behavioural effects were sustained across the entire 2-h test period, whereas the alpha-band effects were only seen for the first half of the period.

D) The combined theanine-caffeine intervention (100 mg plus 50 mg respectively) resulted in a largely similar set of behavioural effects to those observed for the caffeine-alone treatment. Both reduced omission and commission error rates were observed, but these were no greater than those seen for either compound delivered alone. Alpha-band activity was significantly reduced for the combined treatment, but as with caffeine alone, this effect was mainly evident over the first hour of testing and returned to levels seen during placebo for the second hour. Reaction times, on the other hand, were not reduced by the theanine-caffeine combination, although Fig. 5 suggests that the combination increasingly diminished reaction times towards the end of the session.

Our main thesis here was that the greatest effect upon sustained attentional processing would be observed for the theanine-caffeine combination treatment, a prediction based on one of our previous studies where this combination treatment showed the greatest effects upon performance of a spatial attention task and upon tonic alpha-band activity (Kelly et al., 2008). However, this was not the case in the current study, where there were no differences between the theanine-caffeine combination and the caffeine-alone condition in terms of either performance or tonic alpha-band activity. As such, all behavioural effects in these two conditions seem to have been mainly mediated by caffeine, with no obvious additional effect of theanine, in contrast to the findings of Kelly et al. (2008).

However, although theanine confers no additional advantage during the combined treatment, when administered in isolation, there was a significant effect on performance, with clear improvements in the resistance to both forms of error over time (i.e. errors of commission and omission). Perhaps one plausible explanation here is that the caffeine dose used caused as much improvement as was possible (a ceiling effect), leaving no room for further improvement when theanine was added. There is some support in the data for this contention since one might reasonably assume that participants were highly alert and optimally sustaining attention during the first block of the task at the beginning of the test day. The effect of caffeine and the combined treatment was to lower error rates across the ensuing blocks to levels very close or identical to this initial rate. The positive effect of theanine-alone on error rates found here is also noteworthy relative to somewhat more negative results reported by Haskell et al. (2008). In that study, participants were administered 250 mg of theanine or a caffeine–theanine combination of 150–250 mg respectively. Across a battery of tests, the

only psychophysical finding regarding theanine-alone was a slight reduction in performance of a mental calculation task. On the other hand, the combination treatment showed positive effects on a host of cognitive functions such as memory for digits and words. Expanding on this, the combination treatment was also shown to improve attention as measured with the switch task compared to a placebo drink (Einöther et al., 2010; Giesbrecht et al., 2010; Owen et al., 2008). Also noteworthy is the fact that the theanine-alone condition here did not result in a slowing of reaction speed, since this had been reported in two previous studies (Gomez-Ramirez et al., 2007; Rogers et al., 2008). It needs to be pointed out though that dosages of theanine across studies are not consistent (100 mg in this study; 250 mg in Gomez-Ramirez; and 200 mg in Rogers). Thus, the slowing effect of theanine may be a function of higher dosages. There is clear need for a systematic dose–response study, including lower natural concentration levels typically found in tea, to unpack this issue. One obvious implication of the results across these studies is that theanine may have distinct effects on different aspects of cognitive performance.

We also found no effect whatsoever of the theanine treatment upon alpha-band activity, whether consumed alone or in combination with caffeine. Our original prediction was based on our previous findings of a synergistic effect of these two compounds during performance of a taxing spatial attention task. In Kelly et al. (2008), where we used precisely the same dosages as were employed here, we found an increase both in accuracy and in target discriminability (d′) for the combined theanine–caffeine treatment (100–50 mg). Caffeine alone (50 mg) also resulted in an increase in d′ but not in accuracy. There were no significant behavioural effects detected for the theanine-alone treatment (100 mg) though. The current results also stand in apparent contrast to two previous studies by our group where clear effects of theanine-alone treatments were observed on alpha-band activity. However, one obvious difference between the current study and this previous work is the differences in dosage used. In Gomez-Ramirez et al. (2007) and Gomez-Ramirez et al. (2009), robust alpha-suppression effects were observed while participants performed taxing intersensory selective attention tasks, but a dose of 250 mg of theanine was used in both these studies. Here, the dose of theanine used was only 100 mg and this seems likely to be the reason for the attenuated effects we observed.

Another consideration here deserving mention pertains to the tea and coffee drinking habits of our participants. A persistent issue in studies that assess the effects of caffeine or theanine on performance of cognitive tasks concerns the issue of putative withdrawal effects (e.g. James and Rogers, 2005). That is, participants are often asked to refrain from caffeine intake for a day or more before the active intervention, and as such, when these subjects receive a caffeine dosage (or a placebo), they may well already be in a state of caffeine withdrawal if they are regular tea or coffee drinkers. When this is the case, it becomes difficult to interpret results in terms of improvements in performance, since it is entirely plausible that any effects simply represent a return to baseline performance. The young American adults who served in the present study, however, were neither regular tea nor coffee drinkers, as was the case in our previous studies (e.g. Gomez-Ramirez et al., 2007). The majority of them drank neither beverage at all, and those that did consume one or the other were likely to drink only a single cup per day. Only two of the 21 participants reported drinking more than a single cup of coffee per day, and no participant reported drinking more than a single cup of tea per day. Of the subset of participants that did drink these beverages, all drank exclusively one or the other. As such, the current participants had minimal to no previous exposure to theanine and only two participants could be classed as habitual caffeine users (i.e. more than one beverage per day). Thus, the current findings contradict the withdrawal hypothesis and suggest a net positive effect of caffeine alone or in combination with theanine on sustained attention.

5. Conclusion

Sustained attention, or the ability to maintain vigilance over protracted periods of time, is an integral part of cognitive performance in daily life. Whereas caffeine has repeatedly been shown to improve sustained attention, theanine, another ingredient naturally present in tea has received less attention. Based on our previous studies assessing selective attention (Gomez-Ramirez et al., 2007, 2009; Kelly et al., 2008), we hypothesized that caffeine and theanine would also improve sustained attention abilities, and that the combination would confer even greater benefits. Using the well-characterized SART paradigm, caffeine and theanine, both alone and in combination, were indeed shown to improve vigilance as evidenced by sustained attenuation of errors that naturally occur over time. These findings concurred with reduced tonic alpha-band activity suggesting improved attentional processing. The combination treatment, however, did not confer any additional benefits over either ingredient alone, suggesting that either 50 mg of caffeine or 100 mg theanine already provides a maximal effect on sustained attention. In the context of the previous studies, it is clear that dose plays an important role, and a logical next step would be to investigate this in a dose–response study.

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