Effects of Caffeine on Cognitive Tasks

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Abstract

The effects of caffeine (250 mg) and placebo on healthy controls were studied in a double-blind, cross over study on 24 healthy subjects who performed a working memory n-back task. Reaction time and accuracy levels were tested using the n-back working memory measure in cognitive neuroscience. An experimental study tested on the 1, 2 and 3-back tasks under the placebo/coffee condition. Based on the empirical results obtained in this study it can be concluded that changes produced by caffeine ingestion support the hypothesis that caffeine acts as a stimulant. However, it cannot be proven that the stimulant translates into enhanced motor processes with an improvement in performance.

Keywords:. Caffeine, placebo, mean response time (MRT), accuracy (ACC) n-back, cognition, cognitive tasks, working memory (WM).

Introduction

The aim of this research was to determine whether caffeine enhances cognition in healthy subjects. Prior to this research work healthy subjects have not been assessed in sufficient detail. To this end it assesses (i) the effect of 250 mg of caffeine on mean response time (MRT) and (ii) accuracy in normal healthy human controls.

Numerous studies have examined the psychopharmacological and electrophysiological effects of caffeine on the human brain and heart (Bruce *et al.*, 1986). Caffeine has been tested to assess effects on sleep patterns, arousal, and its enhancement effectiveness in enhancing the effects of analgesics (Richardson *et al.*, 1995).

Drinking a cup of coffee is a daily pleasure for millions of people around the world with an average individual consumption estimated at around three cups per day. Caffeine has been found to enhance mental performance, mood, and vigilance (Barry *et al.,* 2005). Research findings also present a great body of evidence on the medical aspects of caffeine enhancement on patients suffering from bi-polar disorder, schizophrenia, and depression (Coffey *et al.*, 1990; Callicott and Ramsey, 1998; and Callicott *et al.*, 2003).

However, there is comparatively little literature available on the effects of caffeine on healthy subjects with no medical impediments. Hence, this research proposed to answer the following question: Can a certain dosage of caffeine ingestion measurably enhance cognitive functions? Few studies have examined the effects of caffeine on cognition on *healthy* individuals.

Caffeine is widely consumed throughout the world for a variety of reasons, including its stimulant-like effects on mood and cognitive performance (Fredholm *et al.*, 1999 and Liberman *et al.*, 1987). The purpose of this study was to investigate the possible effect of *caffeine* on cognitive neural function in healthy human volunteers.

Caffeine absorption from the gastrointestinal tract is rapid and reaches 99% in humans in about 45 minutes after ingestion (Marks and Kelly, 1973). Peak plasma caffeine concentration is reached between 15 and 120 minutes (mins) after oral dosage, and therefore, it can be estimated that peak concentration is reached after 30 mins of ingestion.

One effect of caffeine is the ability to manifests itself in lengthening the post firing duration in the hippocampus; this effect lasts longer than the changes induced by caffeing on the EEG (Kenemans and Lorist, 1995).

Working Memory

Working memory (WM) refers to a system which enables temporary storage and manipulations of information within the context of cognitive activity (Baddeley and Hitch, 1974). Baddeley and Hitch characterised WM as a type of mental workspace composed of 3 sub-systems:

(a) Central executive involved in control and selection process
(b) A buffer responsible for maintaining acoustically-coded information
(c) A buffer responsible for maintaining visual and spatial information.

The present study attempted to clarify whether WM is improved or enhanced in any way with ingestion of a controlled amount of caffeine. The fundamental characteristic of WM, are well known. Working memory capacity to handle information is limited; the physiological

basis of this limitation has not been explained and is still being explored extensively.

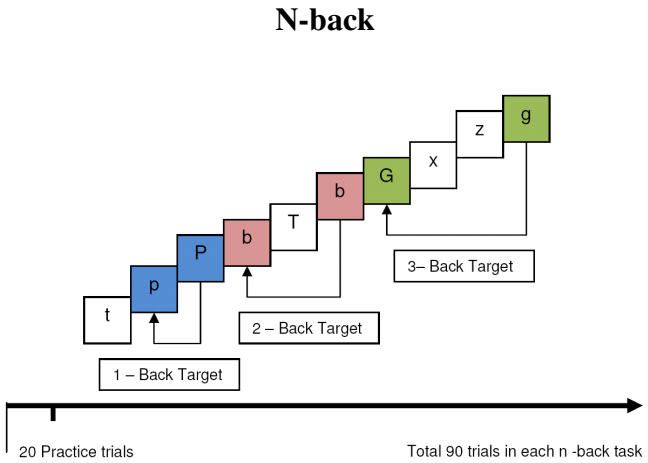

Figure 1: An example of a trial illustrating the schematic representation of the 3WM (n-back task). Each subject performed 20 practice trials, before performing 90 trials in the test, re-test sessions.

The n-back was used to test WM. The task involved a number of stimuli that must be held in the mind at any one time, to be varied parametrically (Owen *et al.*, 2005). Figure 1 outlines a series of stimuli, in the present case letters, and participant had to match and identify the stimuli 1, 2, or 3 previously seen.

Methodology

Twenty four healthy (non smoking) volunteers aged between (19-38 years) participated in this experiment with a mean age of (26.5), with no history of psychiatric disease. All subjects gave written informed consent to take part in the study, which was approved by the Human Research Ethics Committee, Swinburne University of Technology.

Study Design

A double blind, counter-balanced, placebo controlled, cross-over was used. Each participant was tested under two different drug conditions [placebo and caffeine (250mg)] separated by a seven-day 'wash-out' period. The doses selected were based on previous research that found significant behavioral effects at this dose (Barry *et al.*, 2005), but being low enough to minimize the possibility of side-effects, such as nausea, which could confound the results. Upon arrival, participants were provided with a standard lunch to reduce the possible nausea caused by caffeine administration.

N-back task was a stimuli, which in this study was a single white consonant presented for 500 ms each every 3s in the middle of a black computer screen (Koivisto, Krause *et al.*, 2000). The letter case was alternated at each appearance of each particular letter of the alphabet (e.g. z-b-Z-B). Letter case was treated as irrelevant, e.g., "g" and "G" were defined as matching. The rationale for alternating letter-case is to force participants to remember letters by their meaning rather than their shape (Levin et al., 2002). The 1, 2 and 3-back tasks were also administered in a counterbalanced order, so that the effects of memory load were not confounded by caffeine/placebo condition.

Results

Mean reaction time and accuracy data were collected and analysed by a two-way analysis of variance (ANOVA) testing the effects of 'groups' (A and B). Group A consisted of participants consuming placebo first and coffee in the second session. Group B involved participants who consumed coffee first in session one and placebo in session two. The term 'drug' will refer to coffee or placebo.

ANOVA testing was conducted to determine any significant differences between MRTs for the groups, n-backs, treatments, and their interactions. The data was split into the four groups (placebo first, coffee first, placebo second, coffee second), with all passing the Kolmogorov-Smirnov normality tests ($p > 0.05$), meeting one of the underlying assumptions of the ANOVA test. Posthoc analysis was conducted utilising Tukey's Honestly Significant Difference (HSD) test. Significant differences were found amongst all 3 n-back task comparisons (1 versus 2: $p<.012$, 1 versus 3: $p<.001$, 2 versus 3: $p<.01$).

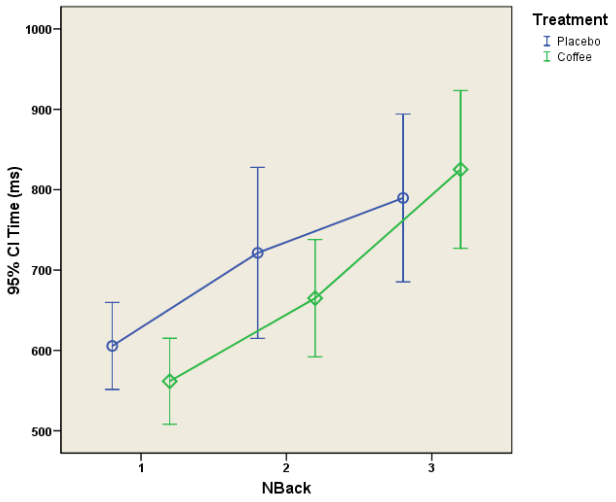

Figure 2: Behavioural data presented for visual comparison: 95 % Confidence Interval for the mean response time MRT for placebo and coffee ingestion, estimated by n-back: (1-, 2-, and 3- back). Data was collapsed across the different treatment conditions (coffee or placebo for all 24 participants over 2 sessions = 48 experiments). The error bar range suggests that reaction time increased with working memory load.

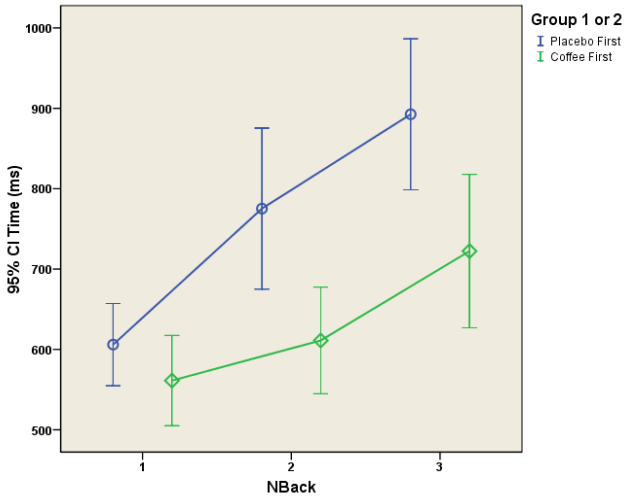

Figure 3: Percentage increase in response time. MRTs for all 3 trials: 95% confidence interval for the MRT for coffee first vs. placebo first by n-back: 1-back, 2-back, and 3-back, across task conditions. Participants taking coffee first (green bar) had a significantly lower MRT for all n-back experiments. This does not account for whether or not the group ingested coffee or placebo, Group A or B, rather provides the MRT of all their experiments. This indicates that being in the coffee first group significantly impacts MRT, irrespective of treatment.

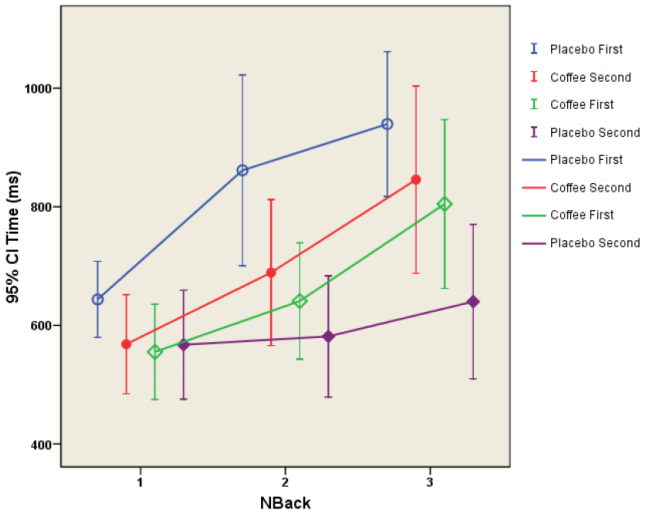

Figure 4**:** Activity data for n-back – MRT of performance across the levels of the n-back task for all 4 sessions.

These results depict the trend irrespective of coffee ingestion, first or second. However, the placebo plot shows that the placebo first group exhibited a markedly higher MRT compared to the coffee first group. Placebo first and Placebo second, exhibits an inverse result with placebo being quicker than coffee, (a lower MRT). This weakness was identified in the previous figure (Fig. 2).

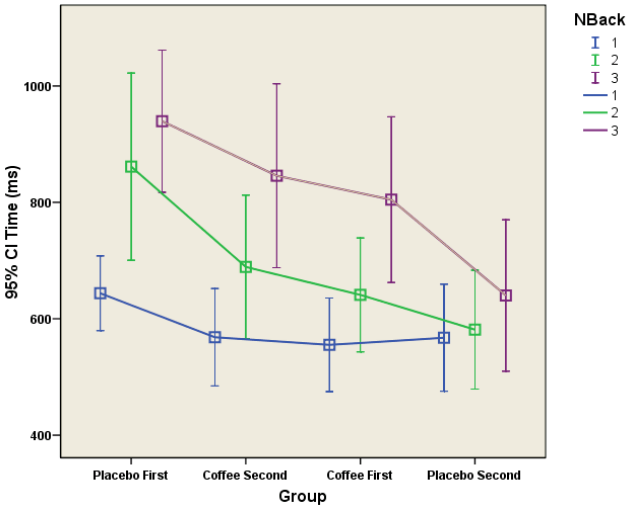

Figure 5: Behavioural data presented for visual comparison: 95% confidence interval of the mean response time for all subjects (grouped) by n-back: 1-back, 2-back, and 3-back. Data displayed across task conditions and collapsed across working memory task.

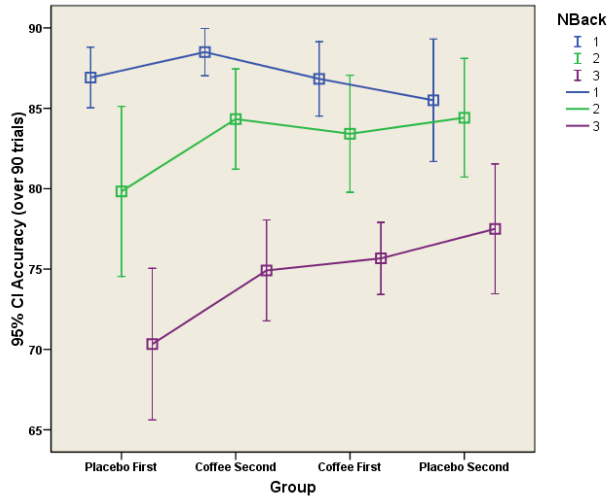

Figure 6: Average mean percentage accuracy levels of Group A and B (4 sessions) by n-back task. Accuracy Data for the 3 levels of task difficulty. This provides a pictorial image where the coffee second group performed better than coffee first.

MRT gradually increased with WM load and 3-back proving the most difficult task, with the longest MRT. Retrieval decreased as n increased in all variants of the n-back task.

As previously plotted n-back 1, has the highest level of accuracy. Figure 6 illustrates the mean percentage accuracy for each of the four sessions by n-back. The coffee second group had the highest mean accuracy for n-back 1, whereas the placebo second had the highest accuracy for n-back 2 and 3.

An ANOVA was conducted on mean accuracy levels to determine if there was any significant difference between the groups. A full interaction model was utilised. The only significant difference occurred in relation to the 3-back $F(2, 143) = 64.241$, $p = .001$ indicating, as shown in the Fig. 7. Treatment (coffee or placebo) and Group (1 or 2) showed no significant differences in mean accuracy level $F(1,143) = 2.834$, $p = .095$; $F(1,143) = 2.437$, $p = .121$.

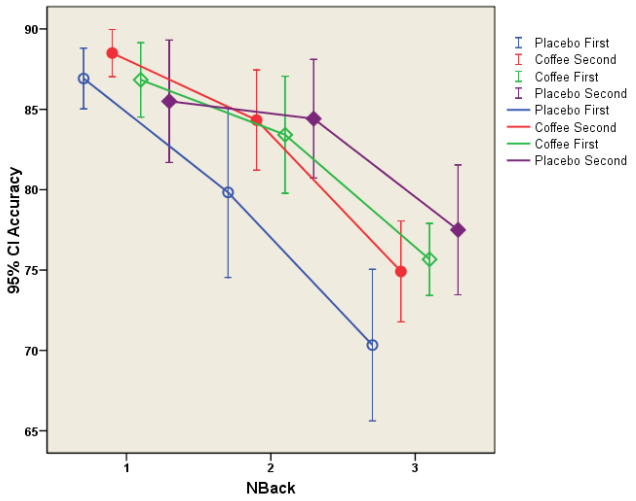

Figure 7: Plots the n-back by groups. Visual complexity of accuracy levels within the groups. Average accuracy for each of the groupings presented and the proportion of drop in accuracy levels whilst performing 3-back which had the greatest difficulty.

Discussion

Caffeine was associated with a significant increase in alertness. However, there was no significant enhancement on cognition. There was no significant relationship between the intake of caffeine and cognitive task. Analyses between caffeine/placebo conditions, found significant results in 1-back and 2-back. On the other hand, results were not significant with n-back 3. This performance decrement could be due to familiarity of content, and counteracted by caffeine (Deslandes *et al.*, 2005). Briefly summarising, across subjects, accuracy was higher, and RT faster, in the low-load WM task compared with the high-load WM tasks.

Optimal level of performance was achieved with caffeine, when comparing the two groups in Fig. 2, providing support for the hypothesis, that caffeine improved response time. Whereas MRT was slightly higher for the coffee group in the 3-back task, this could be attributed to memory load or other variables. It can be clearly observed that MRT increases with memory load of n-back 3 in both group conditions. As the task difficulty and memory load increased, reaction time also increased. The 3-back task required judging whether an item matched any item up to and including 3-back. Reduced MRT suggests that three items could not be effectively maintained in focal attention. These results indicate that focal attention has a much smaller capacity than has typically been assumed (Cowan, 2008).

The ANOVA results supports earlier findings which indicated that taking coffee first, then a placebo had some effect in the second test. Although the task was counterbalanced across subjects so as to control for task practice effects, it still seemed that group B fully or partially were alert in session one to enable familiarity in Session 2. This however did not occur when the group ingested Placebo first. There was no speed-accuracy trade off and accuracy since all subjects found the 3-back task difficult in all 4 sessions and RTs were slower. Data shows that the n-back judgements are in part mediated by a search process, and that the complexity of the search depends on 'n'. Inter-subject variability poses a different problem, in that no standard method has emerged for reliably comparing activity across subjects (Braver *et al.*, 1997).

A possible explanation of these results could be due to testing bias, that is, exposure to the n-back test originally leads to better results the second time. This could be due to the nature of the test, rather than any treatment effects. Therefore, it is reasonable to conclude that having practised the n-back task over 90 trails, thrice, familiarity of content, enables participants to improve MRT in group having placebo second, rather than the effects of treatment? Perhaps the measures are not reflective of arousal rather indicators of task related difficulty.

As expected, increasing WM load was associated with declining accuracy and performance tended to decrease as memory load increased. Performance declines continuously with increased task load. The behavioural findings also indicate that both accuracy and speed declined monotonically with increases in task load. Note that the 3-back task differs considerably. The statistical analysis of Smith and Jonides stated that there are 22 significant sites of activation in both 2-back and 3-back tasks, but only 2 significant areas in 0, and 1-back (Smith and Jonides, 1997). These results support previous studies that as memory load increases, more areas in the brain are recruited to perform the task.

As was mentioned above, the primary purpose of this study was to determine whether caffeine improved cognition. The empirical results obtained did not support a strong correlation. The second aim was to test whether caffeine improved accuracy and this objective was accomplished by comparing the behavioural data obtained during the WM task performance (Gevins et al., 1996 and Gevins et al., 2000). With respect to the performance data, significantly shorter response times were recorded for the caffeine rather than the placebo condition.

Koppelstaetter *et al.* (2008) concluded that the modulations seen in specific cortical regions suggest an effect on brain areas engaged in specific cognitive processes rather than a general effect due to the influence of caffeine on the vasculature. The Koppelstaetter study used functional magnetic resonance imaging (fMRI) with a focus on

caffeine users. The most relevant aspect of Koppelstaetters' study was the confirmation that "caffeine had no significant effect on cognitive performance," which matched our experimental results. Our study differs from the Koppelstaetter study in that it used healthy subjects and an increased dosage of 250 mg (as against 100 mg).

Conclusions

Based on the empirical results obtained in this study it can be concluded that changes produced by caffeine ingestion support the hypothesis that caffeine acts as a stimulant. However, it cannot be proven that the stimulant translates into enhanced motor processes with an improvement in performance. Improved performance through ingestion of caffeine may be evident in a fatigue situation. However, to verify this assumption additional studies are needed to better understand the mechanisms of how caffeine influences WM, as the underlying fundamental processes are still unclear. In the present work, caffeine showed little effect on performance and it can be suggested that caffeine had no large effects on cognitive tasks.

Future Work

Coffee as a beverage and its popularity in society definitely warrants additional investigation. Consequently, large scale studies need to be undertaken to affirm caffeine's possible effectiveness on specific cognitive functions and working memory. Testing would require replication, and inclusion of a third session that would result in a broader range of scores. Investigators would have to be mindful that the dual-task nature of the n-back, such as encoding, matching, responding, updating, storing and rehearsing demands, vary greatly between individuals due to (demographics, education and social status). This perhaps may pose as a potential problem. To date, little is known about the sequence of events or neural pathways whilst performing the WM task. Although calculation of response times and accuracy levels assist to a degree, further studies are required to account for subtleties. This thesis offered one more account to add to its underlying processes.

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