The Effect of Post-Learning Caffeine Consumption on the Learning and Retrieval of Non-Verbal Stimuli

Verbal Stimuli**,** Bond University, Australia
Andrew Garas, Bond University, Australia

Asian Conference on Psychology and the Behavioural Sciences 2015
Official Conference Proceedings

Abstract
The present study aimed to conceptually replicate a recent study showing improvements in cognition when caffeine was consumed following learning. Thirty-two non-naive participants were administered 200mg of caffeine either: Pre-Learning, Post-Learning, or At-Retrieval, and compared to non-caffeine administered Controls. The learning and retrieval of non-verbal stimuli was assessed using a Korean Characters Non-Verbal Learning task, derived from the Shum Visual Learning task. Participants administered caffeine Pre-Learning and At-Retrieval were found to have significantly better initial learning of target stimuli than the Post-Learning and non-administered Controls. There was no significant difference found between groups on retrieval of the learned stimuli following a 20 minute interval between learning and retrieval. The findings suggested that the timing of caffeine consumption did not influence retrieval. While the improvements in initial learning of target stimuli demonstrated by the groups administered caffeine Pre-Learning and At-Retrieval appeared to be a potential placebo or expectancy effect.

Keywords: caffeine consumption, cognition, learning and retrieval, recognition

Caffeine is the most commonly used stimulant globally (Gilbert, 1984; Gray, 1998). Reports indicate that the average amount of caffeine consumed by individuals from all dietary sources is approximately 75 mg per day in Non-Western countries, and approximately 200 mg per day in Western countries (Barone & Roberts, 1996; Gilbert, 1984; Gray, 1998). Globally, caffeine is predominantly consumed through drinking coffee with the estimated dose of caffeine contained within a single cup of coffee varying between 20 mg to 175 mg depending on the serving size, preparation and type of coffee bean used (D'Amicis & Viani, 1993). Previous research has shown that approximately 100mg of caffeine can be sufficient to induce possible behavioural and cognitive changes in animals and humans (Glade, 2010; Nehlig, 1999). The effect of caffeine consumption on cognition was initially demonstrated using animals (Fredholm, Bättig, Holmén, Nehlig, & Zvartau, 1999). These cognitive effects have not reliably replicated in humans, however, as findings were often mixed and inconclusive (Herz, 1999; Maia & Mendonça, 2002; Nehlig, 2010; Rees, Allen, & Lader, 1999; Ryan, Hatfield, & Hofstette, 2002).

Caffeine is believed to cause behavioural changes in animals and humans as it is a type of stimulant known as a Methyltheobromine (Arnaud, 1987; Blanchard & Sawers, 1983; Smith, 2002). Studies originally examining the behavioural effects of caffeine consumption revealed there to be no blood-brain barrier to caffeine in animals after absorption (Lachance, Marlow, & Waddell, 1983). Once consumed, Methyltheobromines are also rapidly absorbed through the gastrointestinal tract (Bonati, Latini, Galetti, Young, Tognoni, & Garattini, 1982; Mandel, 2002). Peak concentration of caffeine has been recorded within the first 15 minutes of ingestion with an estimated half-life ranging between 2.5 – 4.5 hours for doses of 5mg/kg in humans (Arnaud, 1993; Arnaud & Welsch, 1982; Fredholm et al., 1999).

Physiologically, caffeine has been shown to elevate excitability in the hippocampus of animals and humans during peak concentration (Arushanian & Belozertsev, 1978; Dunwiddie, Hoffer, & Fredholm, 1981; Lorist & Tops, 2003; Phillis & Kostopoulos, 1975). The hippocampus contains highly concentrated levels of adenosine receptors which are responsible for decreasing the rate at which neurons fire, thereby, inhibiting synaptic transmission and subsequent release of most neurotransmitters (Dunwiddie, Hoffer, & Fredholm, 1981; Nehlig, Daval, & Derby, 1992; Nehlig, Lucignani, Kadekaro, Porrino, & Sokoloff, 1984). Caffeine is believed to act as an antagonist for adenosine receptors (Mandel, 2002; Nehlig et al., 1992; Nehlig et al., 1984).

Therefore, caffeine appears to increase the turnover of neurotransmitters, especially in areas of the brain where adenosine receptors are highly concentrated (Nehlig, 1999; Nehlig et al., 1984; Nehlig et al., 1992). The hippocampus has consistently been implicated in learning and retrieval dating back to early clinical observations of patients with memory and learning deficits attributed to hippocampal damage (Penfield & Pérot, 1963; Scoville & Milner, 1957). Following these early clinical observations, research targeting the hippocampus showed it to be specifically involved in storing and processing learned information as well as the consolidation of memory (Izquierdo, 1974; Landfield, Tusa, & McGaugh, 1974; McGaugh & Dawson, 1971; McGaugh, 2000; Penfield & Pérot, 1963). Therefore, caffeine consumption appears to influence learning and retrieval by modulating the function of the hippocampus.

A recent study by Borota et al. (2014) suggested that caffeine consumed after learning a set of stimuli subsequently improved the memory consolidation of participants. The Borota et al. (2014) finding suggested timing of caffeine ingestion as an important and previously unexplored variable in the investigation of the effect of caffeine on cognitive performance. This finding offered a new paradigm to consider when conducting research on the effect of caffeine on cognition. Subsequently, the present study also aimed to investigate the relationship between the timing of caffeine consumption and cognition. The Borota et al. (2014) study found that participants administered caffeine following the learning hippocampal memory dependent non-verbal stimuli, reported subsequent improved memory consolidation. However, the stimuli used in the Borota et al. (2014) study were pictures of commonplace items that participants would have likely had prior exposure to. It may then be argued that the stimuli used in the Borota et al. (2014) were not in fact non-verbal as there would have been pre-existing verbal mapping of these commonplace items. Therefore, an alternative task using uncommon stimuli would be more appropriate in order to remove the internal threat of pre-existing verbal mapping of common items used as stimuli.

The overall aim of the present study was to conceptually replicate the Borota et al. (2014) study. The present study employed a similar methodology but did not incorporate a typical placebo administered group as it was argued that this group was not required due to the methodological problems typical placebo controls can sometimes create (Kaptchuk, 1998; Kienle & Keine, 1996; McDonald, Mazzuca, & McCabe, 1983). As well as the practical problem of obtaining a suitable placebo tablet not containing glucose, a potentially confounding substance also previously shown to influence cognition (Gold, 1995). Rather, the proposed design of the current study used four groups for comparison, administered caffeine at varying times throughout the study; prior to the learning of non-verbal stimuli, immediately following the learning of non-verbal stimuli and immediately prior to the retrieval of non-verbal stimuli.

Commonplace items used as stimuli and potentially confounding the results of the Borota et al. (2014) study was addressed using a learning and retrieval task labelled the Shum Visual Learning Test (SLVT) which used characters of an unfamiliar language as stimuli (Eadie and Shum 1995). A modified version of the SLVT would ensure participants had an equal level of previous exposure to the stimuli and counter the threats to internal validity when compared to the Borota et al. (2014) study. The modified SLVT contained a primary measure of the accuracy of correctly selecting targets (hit rate) in proportion with incorrectly selecting distractors (false positive) on each trial, referred to as the Recognition score. As participants progressed through the task and were repeatedly presented with the target stimuli, initial learning and would be demonstrated by an increase in the proficiency of correctly identifying the target stimuli amongst the distractors across the learning phase. This was labelled the Initial-Learning score of participants in the present study. A measurement assessing participant's consistency of positive hits of the target stimuli during the learning phase, labelled Initial-Retention score, was also used in the replacement task. To assess retrieval, the replacement task contained two further measures. The first measure was the degree of retention of target stimuli in the retrieval phase, following the release of any potential interference from the distractor stimuli presented during the learning phase labelled the Retention-Post-Interference score.

The second measure of retrieval was the measure of retention following the release from the interference created by the newly introduced distractor stimuli in the retrieval phase, or Delayed-Retention score. This would indicate the extent to which participants could continue to correctly distinguish target stimuli amongst the newly introduced distractors in the retrieval phase of the task.

In summary, the first hypothesis aimed to address the equivocal nature of previous caffeine and cognition research. Therefore, the present study aimed to find be a significant improvement in learning of non-verbal stimuli, measured using Initial-Learning and Initial-Retention scores, for the Pre-Learning caffeine administered group compared to the non-caffeine administered Control group. The second hypothesis, similar to the Borota et al. (2014) study, aimed at demonstrating a significant improvement in retrieval of non-verbal stimuli, measured using Retention-Post-Interference and Delayed-Retention scores, for the group administered caffeine Post-Learning compared to participants administered caffeine Pre-Learning. To measure any potential effect of caffeine administration directly prior to retrieval the third hypothesis, similar to the first, stated that there would be a significant improvement in retrieval, again measured using Retention-Post-Interference and Delayed-Retention scores, for the group administered caffeine At-Retrieval compared to the group administered caffeine Post-Learning.

Method

Participants

A total of 32 participants completed the study, ranging in age between 18 and 60 (M = 27.03, SD = 10.60) and sex (males n = 8 and females n = 24). Participants reported an approximate period of 24 hours (M = 21.61, SD = 26.89), on average, since last caffeinated drink and an average caffeine intake of approximately 2 cups (M = 1.88, SD = .97) of caffeinated beverages per day.

Materials

Korean Characters Non-Verbal Learning task (KCNVL). Learning and retrieval was measured using the computerised KCNVL task. The KCNVL is derived from the SLVT which uses Chinese characters that were originally argued to be relatively unfamiliar due to minimal exposure in Western society (Shum, Gorman, & Eadie, 1999). The SLVT has previously been used as a suitable alternative to non-verbal learning tasks by demonstrating stable criterion and predictive validity in studies of children with head injuries (Shum et al., 1999). However, considering there are almost 1.3 billion native speaking Chinese people, Korean Hangeul characters are argued to be more appropriate stimuli as previous exposure is expected to be far less with a Korean speaking population of less than 50 million (United Nations – Department of Economic and Social Affairs, 2012).

The KCNVL involves the learning of characters of an unfamiliar alphabet, the Korean Hangeul alphabet. The KCNVL comprises of two phases: an initial learning phase containing five trials and a retrieval phase containing three trials, with a 20 minute interval in-between.

Figure 1. Example Korean Hangeul target character used in the KCNVL task.

The learning phase is completed first and involves five individual trials. At the beginning of each trial a standard output box is presented containing instructions for a masking task in which participants are asked to count the number of strokes that constitute the presented characters with no input required. Ten simplified Korean characters are then presented in a randomised order at a rate of one per two seconds, separated by a one second black screen. Following this, a similarly styled output box instructs participants that a grey cursor appearing at the top left hand corner of the screen is a signal for the participant to respond. Participants are instructed to press the 'Y' key if the character is recognised or 'N' if the character is unfamiliar. The ten Korean characters used earlier in the trial are then randomly presented amongst ten distractors at a rate of one per two seconds, separated by a one second blank black screen and the grey cursor input screen. The grey cursor input screen is displayed for 2 seconds. Following the 20 character presentations, the individual trial concludes and participants are returned to the trial selected screen. Participants complete trials one - five in a similar fashion with an output box following the completion of the fifth trial alerting the participants of the 20 minute required interval before beginning the subsequent trials in the retrieval phase.

Trial six is then completed in a similar fashion using the same target and distractor stimuli with participants expected to learn the distractor set gradually after the repeated exposure. Trial seven and eight are also completed in a similar fashion using the same target stimuli with a different set of distractors. Over the course of the six earlier trials the participant is repeatedly exposed to the same set of distractors and inadvertently begins to learn the distractor set implicitly, which leads to a gradual increase in interference from the original set of distractors. The new distractors are, therefore, introduced to release the participant from this interference. The complete stimulus set (n = 30) consists of 10 Korean Hangul characters for learning, ten distracter characters for trials one – six, and ten new distracters for trials seven and eight.

Scoring of the eight trials of the KCNVL task is based on a measure of Recognition, $p(A)$, incorporating both hit rate (HR) and the false positive rate (FP). The formula for calculating $p(A)$ is:

$$p(A) = 0.5\ (1 + HR - FP)\ .$$

Four learning measures are calculated using the $p(A)$ obtained from each of the eight trials. An Initial-Learning score measuring the degree which target stimuli are learned

in the initial learning phase of the KCNVL task using the mean recognition over the first five trials:

$$\frac{(trial1\ p(A) + \ trial2\ p(A) + \ trial3\ p(A) + \ trial4\ p(A) + \ trial5\ p(A))}{5}.$$

An Initial-Retention score calculated by comparing the hit rate of the target stimuli on trial one with the hit rate of the target stimuli on trial five, with the hit rate on trial one expected to be more accurate than trial five as a result of the subsequent repeated exposure to the distractors:

$$\frac{trial5\ \ (HR)}{trial1\ (HR)}.$$

A Retention-Post-Interference score measuring the extent of which distractors from the first five trials of the learning phase of the task interfered with retrieval in trial seven when the ten new distractors were presented:

$$\frac{p(A)trial\ 7}{p(A)trial\ 5}.$$

Finally, a Delayed-Retention score measuring the extent to which the ten newly introduced distractors interfered with retrieval during the retrieval phase by comparing the recognition scores of trials seven and eight:

$$\frac{p(A)trial8}{p(A)trial7}.$$

During the task each character in the entire stimulus set is presented as white on a black background filling the entire screen. Each target and distractor character is centred with a resolution of 145 by 135 pixels and a height of 6.1cm by width of 5.7cm.All instructions are presented in black font on a grey background as part of standard input boxes which are also used for entry of demographic information.

Caffeine. A standard 200mg dose of NoDoz® branded caffeine tablets administered with 250 ml of water. NoDoz® branded caffeine was used as it contained the least amount of impurities allowing for higher internal validity.
Filler task. A paper-based word find task is used as a filler task in the 20 minute interval between the learning and retrieval phase of the KCNVL.

Procedure
The five trials in the initial learning phase of the KCNVL task were completed first by each participant. Participants randomly assigned to the Pre-Learning administration condition were administered 250ml of water and two, 100mg caffeine NoDoz® tablets to ingest orally prior to commencement. Once completed, participants alerted the researcher and those participants randomly pre-assigned to the Post-Learning administration condition were administered 250ml of water and two 100mg caffeine NoDoz® tablets to ingest orally.

Prior to the retrieval phase, a 20 minute break period was observed, in which participants were given a pen and the filler task word-find puzzle to complete. Upon the conclusion of the 20 minute interval, participants randomly pre-assigned to the At-

Retrieval administration condition were administered 250ml of water and two 100mg caffeine NoDoz® tablets to ingest orally. All participants then completed the three trials in the retrieval phase of the KCNVL task. At the conclusion of the study, those participants pre-assigned to the non-administered control group were advised of their random allocation to the group. These participants were offered two 100mg caffeine NoDoz® tablets to ingest if they so desired.

Results

Preliminary Analysis

Learning and retrieval.

A four (*caffeine-timing*: Pre-Learning, Post-Learning, At-Retrieval and Control) by two (*gender:* male and female) way Multivariate Analysis of Covariance was used to examine the between subject effect of caffeine-timing on participants' combined learning and retrieval measures including: Initial-Learning, Initial-Retention, Retention-Post-Interference and Delayed-Retention with age, hours since last caffeinated drink and average daily caffeine intake as covariates. There was no significant effect of the covariates: age $F(4, 19) = 1.14$, $p = .37$, hours since last caffeinated drink $F(4, 19) = .37$, $p = .83$ and average daily caffeine intake per cup $F(4, 19) = .78$, $p = .78$. There was also a no significant effect of gender $F(4, 19) = 2.04$, $p = .13$. Consequently, gender, age, hours since last caffeinated drink, and average daily caffeine intake per cup variables were dropped from the analysis.

A four (*caffeine-timing*: Pre-Learning, Post-Learning, At-Retrieval and Control) by one way Multivariate Analysis of Variance (MANOVA) again examining the between subject effect of caffeine-timing on participants' combined learning and retrieval scores including: Initial-Learning, Initial-Retention, Retention-Post-Interference and Delayed-Retention, revealed a significant main effect of caffeine-timing $F(12, 66) = 2.94$, $p < .01$, partial $\eta^2 = .31$, observed power = .95.

Follow-up analyses revealed a significant main effect of caffeine-timing on participants' Initial-Learning scores $F(3, 28) = 11.67$, $p < .01$, partial $\eta^2 = .56$, observed power approaching 1 (see Figure 2). No significant effects of caffeine-timing were found between participants' Initial-Retention scores $F(3, 28) = 1.02$, $p = .40$, Retention-Post-Interference scores $F(3, 28) = 1.80$, $p = .17$ and Delayed-Retention scores $F(3, 28) = .44$, $p = .73$. The range of obtained Initial-Learning, Initial-Retention, Retention-Post-Interference and Delayed-Retention scores are presented in Table 1.

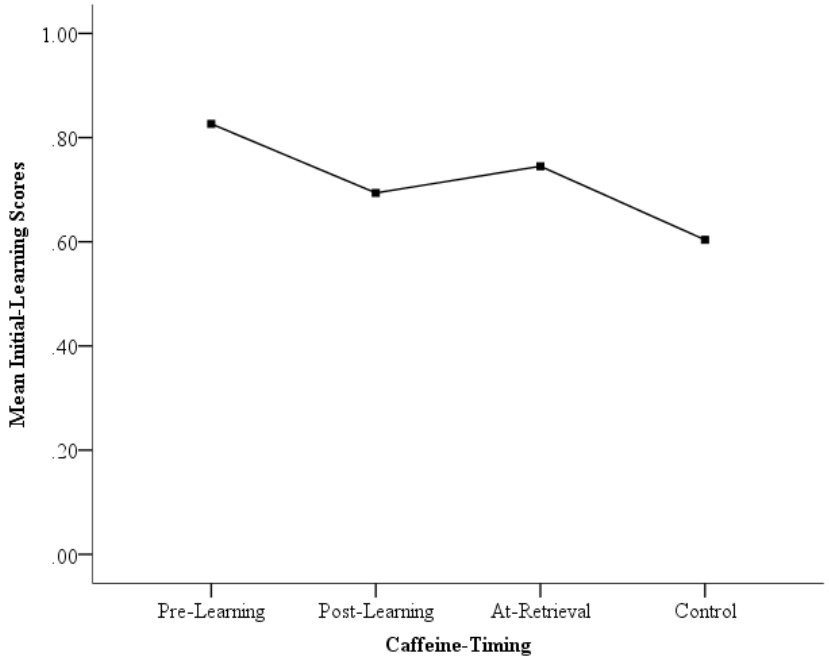

Figure 2. Initial-Learning means of participants across the four levels of caffeine-timing.

Table 1.
Ranges of obtained scores for the four learning variables

Measure	Minimum	Maximum
Initial-Learning	.50	.94
Initial-Retention	.60	1.44
Retention-Post-Interference	.63	1.90
Delayed-Retention	.50	1.09

Note. $n = 32$

Follow-up comparisons to assess for significant differences between the four caffeine-timing groups on mean Initial-Learning scores were completed using a Tukey b post hoc analysis. The Tukey b technique controls for family wise error inflation and therefore reduces the risk of making a Type 1 error, whilst avoiding a Type 2 error. This revealed the Pre-Learning administered group to have significantly higher mean Initial-Learning scores when compared to the Post-Learning caffeine administered group and the non-administered Control group (see Table 2).

There was no significant difference between the Pre-Learning administered group mean Initial-Learning scores and the At-Retrieval administered group mean Initial-Learning scores. There was also no significant difference between the At-Retrieval mean Initial-Learning scores and the Post-Learning administered group mean Initial-Learning scores. Finally, there was no significant difference between the Post-Learning administered group mean Initial-Learning scores and the non-administered Control group mean Initial-Learning scores.

Table 2.
Learning measure means and standard deviations across caffeine-timing conditions.

Measure	Pre-Learning *M (SD)*	Post-Learning *M (SD)*	At-Retrieval *M (SD)*	Control *M (SD)*
Overall Learning	.83 (.09)	.69 (.10)	.75 (.06)	.60 (.06)
Initial-Retention	1.01 (.17)	.95 (.09)	.94 (.28)	1.08 (.13)
Retention-Post-Interference	1.01 (.14)	1.33 (.39)	1.05 (.30)	1.21 (.35)
Delayed-Retention	.75 (.12)	.80 (.19)	.80 (.15)	.85 (17)

Note. $n = 32$

Discussion

The rational for the current study arose from the previous inconclusive research regarding the effect of the consumption of caffeine on cognition (Herz, 1999; Maia & Mendonça, 2002; Nehlig, 2010; Rees et al., 1999; Ryan et al., 2002). It was firstly hypothesised that there would be a significant improvement in learning of non-verbal stimuli, measured using Initial-Learning and Initial-Retention scores, for the Pre-Learning caffeine administered group when compared to the non-caffeine administered Control group. This was partially supported as there was found to be a significant difference in Initial-Learning of target stimuli for those administered caffeine prior to learning when compared to the non-administered controls. There was no significant difference, however, between the Pre-Learning caffeine administered group and the non-caffeine administered Control group on the Initial-Retention of target stimuli over the first five learning trials.

Secondly, it was hypothesised that there would be a significant improvement in the retrieval of non-verbal stimuli, measured using Retention-Post-Interference and Delayed-Retention scores, for the group administered caffeine Post-Learning compared to the group administered caffeine Pre-Learning. This was rejected, as there was no significant difference between those administered caffeine Post-Learning on the retrieval of target stimuli, relative to those administered caffeine Pre-Learning in the present study. Participants in the group administered caffeine Post-Learning were not significantly better than those administered caffeine Pre-Learning at identifying the learned target stimuli in the retrieval phase, following the 20 minute interval and expected release from interference caused by initial distractors.

Participants in the Post-Learning caffeine administered group were also not found to demonstrate significantly improved Delayed-Retention than those in the Pre-Learning caffeine administered group. Thirdly, it was hypothesised that there would be a significant improvement in retrieval, again measured using Retention-Post-Interference and Delayed-Retention scores, for the group administered caffeine At-Retrieval compared to the group administered caffeine Post-Learning. This was not supported as there was no significant difference between the At-Retrieval caffeine administered group and the Post-Learning caffeine administered group on both retrieval measures.

The non-significant findings of the present study did not support the new model proposed by Borota et al. (2014) claiming that post learning caffeine consumption would improve memory consolidation. Interestingly, the Pre-Learning caffeine group demonstrated the highest initial learning of the target stimuli in the present study, providing some evidence for prior research showing improvements in participant's cognition when caffeine was consumed prior to the completion of cognitive tasks (Herz, 1999; Ryan et al., 2002). Even more surprising was that participants that were administered caffeine much later on in the task, At-Retrieval, also showed equally high initial learning of target stimuli in the learning phase.

One possible explanation for the improved initial learning of the target stimuli demonstrated by the group administered caffeine prior to the learning was that this was due to an expectancy or placebo effect. For ethical reasons, participants in the present study were informed of the aim of the study, specifically, the goal of examining the effect of caffeine on cognition. Once informed of the aim of the study, participants then went on to complete the learning phase of the KCNVL task. The learning phase of the KCNVL task incorporated the Initial-Learning measure which assessed the extent to which the target stimuli had been learned, calculated from the average Recognition scores over the first five trials of the KCNVL task.

When considering the pharmacology of caffeine, however, the group administered caffeine prior to the learning phase of the KCNVL task may be argued to have completed the learning phase without the physiological effect of caffeine as it would not have manifested until approximately 15 minutes after ingestion (Fredholm et al., 1999). Or, the approximate time taken to complete the initial learning phase of the KCNVL task. Therefore, any initial learning improvements for the Pre-Leaning caffeine administered group compared to non-caffeine administered Control group, also not experiencing the physiological effect of caffeine, would indicate the potential existence of a placebo effect. In the current study, participants in Pre-Learning caffeine administration group, having just been informed of the nature of the study and not yet experiencing the physiological effect of caffeine, went on to record the highest mean Initial-Learning scores. The simple act of ingesting the tablets or the anticipation of being assessed cognitively appears to have improved their cognition.

While plausible, the equally high mean Initial-Learning scores of the group administered caffeine 20 minutes after the learning at the retrieval phase of the KCNVL task somewhat discount this explanation. The At-Retrieval group showed equally high Initial-Learning of the target stimuli, while having not yet been administered caffeine during the learning phase of the KCNVL task. Therefore, a placebo effect does not explain why these participants demonstrated improved initial learning of target stimuli. The non-naive At-Retrieval caffeine administered group was not yet subject to the physiological effects of caffeine in the learning phase as they would have experienced these effects much later on in the retrieval phase. Interestingly, when administered caffeine immediately prior to retrieval, these participants did not demonstrate improved Retention-Post-Interference or Delayed-Retention scores similar to the placebo induced immediate improvements as the Pre-Learning caffeine administered group. Therefore, while a placebo effect may explain the unexpected performance for the Pre-Learning caffeine administered group, an expectancy effect appears to explain the unusual performance on the initial learning of the target stimuli for the group administered caffeine At-Retrieval.

When compared with the Borota et al. (2014) study, one potential limitation of the current study was the threat to internal validity created by the absence of a direct measure of participant's caffeine metabolite levels to control for individual differences in caffeine absorption. Conversely, it may be argued that any possible confounds created from prior caffeine contamination were seen to be adequately controlled for in the present study as participants reported an average period of approximately 24 hours since last caffeinated drink. When considering the 4.5 hour half-life of caffeine in humans, it could also be assumed that participants were relatively free of any residual caffeine effects that may have influenced performance regardless of individual caffeine metabolising rates (Fredholm et al., 1999).

Also of note was the self-reported caffeine consumption expressed as average cups of coffee (or other caffeinated beverages such as tea or soft drink) consumed per day. The present sample contained similar daily consumption averages to the current estimated population average daily caffeine consumption (D'Amicis & Viani, 1993; Mandel, 2002; Nehlig, 2010). This suggests that the participants in the present study where representative of the population with regards to daily caffeine consumption. The threat to internal validity arising from prior caffeine consumption was argued to be effectively addressed, while still maintaining ecological validity in terms of population caffeine consumption. A factor not considered by Borota et al.'s (2014) use of only caffeine naïve participants.

As caffeine is such a widely used substance, the potential implications of any findings of the current study were expected to have a high degree of generalizability (Gilbert, 1984; Nehlig, 2010). The findings of this study, instead, suggest that more methodologically sound experimental research is required. Additionally, the suspected placebo or expectancy effect found for the groups administered caffeine Pre-Learning and At-Retrieval showed that caffeine consumed and not yet physiologically active, as well as the anticipation of cognitive assessment may have improved initial learning of target stimuli. Adding to the previous mixed research regarding the effect of caffeine consumption on cognition (Herz, 1999; Maia & Mendonça, 2002; Nehlig, 2010; Rees et al., 1999; Ryan et al., 2002). Although the findings in the present study were inconclusive, the increasing consumption of caffeine in the population, combined with the mixed evidence on cognitive effects, provide a strong basis for researchers to continue examining the cognitive effects of caffeine consumption.

References

Arnaud, M. J. (1987). The pharmacology of caffeine. *Progress in Drug Research, 31,* 273-313. doi:10.1007/978-3-0348-9289-6_9

Arnaud, M. J. (1993). Metabolism of caffeine. In Garattini, S. (Ed.), *Caffeine, coffee and health* (pp. 43-95). New York: Raven Press.

Arnaud, M. J., & Welsch, C. (1982). Theophylline and caffeine metabolism in man. In Reitbrock, N., Woodcock, B. G., & Staib, A. H. (Eds.), *Theophylline and other methylxanthines* (pp. 135-148). Zurich: Vieweg.

Arushanian, E. B., & Belozertsev, Y. B. (1978). The effect of amphetamine and caffeine on neuronal activity in the neocortex of the cat. *Neuropharmacology, 17,* 1-6. doi:10.1016/0028-3908(78)90166-1

Barone, J. J., & Roberts, H. R. (1996). Caffeine consumption. *Food and Chemical Toxicology, 34,* 119-129. doi:10.1016/0278-6915(95)00093-3

Blanchard, J., & Sawers, J. A. (1983). The absolute bioavailability of caffeine in man. *European Journal of Clinical Pharmacology, 24,* 93-98. doi:10.1007/BF00613933

Bonati, M., Latini, R., Galetti, F., Young, J. F., Tognoni, G., & Garattini, S. (1982). Caffeine disposition after oral doses. *Clinical Pharmacology and Therapeutics, 32,* 98-106. doi:10.1038/clpt.1982.132

Borota, D., Murray, E., Keceli, G., Chang, A., Watabe, J. M., Ly, M., … Yassa, M. A. (2014). Post-study caffeine administration enhances memory consolidation in humans. *Nature Neuroscience, 17,* 201-203. doi:10.1038/nn.3623

D'Amicis, A., & Viani, R. (1993). The consumption of coffee. In Garattini S. (Ed.), *Caffeine, coffee and health* (pp. 1-16). New York: Raven Press.

Dunwiddie, T. V., Hoffer, B. J., & Fredholm, B. B. (1981). Alkylxanthines elevate hippocampal excitability. *Naunyn-Schmiedeberg's Archives of Pharmacology, 316,* 326-330. doi:10.1007/BF00501365

Eadie, K., & Shum, D. (1995). Assessment of visual memory: A comparison of Chinese characters and geometric figures as stimulus materials. *Journal of Clinical and Experimental Neuropsychology, 17,* 731-739. doi:10.1080/01688639508405163

Fredholm, B. B., Bättig, K., Holmén, J., Nehlig, A., & Zvartau, E. (1999). Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. *Pharmacological Reviews, 51*(1)*,* 83-133. Retrieved from: http://pharmrev.aspetjournals.org/content/51/1/83.l

Gilbert, R. M. (1984). Caffeine consumption. *Progress in Clinical and Biological Research, 158*(1)*,* 185-213. Retrieved from: http://europepmc.org/abstract/MED/6396645

Glade, M. J. (2010). Caffeine – Not just a stimulant. *Nutrition, 26,* 932-938. doi:10.1016/j.nut.2010.08.004

Gold, P. E. (1995). Role of glucose in regulating the brain and cognition. *The American Journal of Clinical Nutrition, 61,* 987 – 999. Retrieved from http://ezproxy.library.usyd.edu.au/login?url=http://search.proquest.com/docview/231938033?accountid=14757

Gray, J. (1998). Caffeine, coffee and health. *Nutrition and Food Science, 6,* 314-319. doi:10.1108/00346659810235215

Herz, R. S. (1999). Caffeine effects on mood and memory. *Behavior, Research and Therapy, 37,* 869-879. doi:10.1016/S0005-7967(98)00190-9

Izquierdo, I. (1974). The hippocampus and learning. *Progress in Neurobiology, 5,* 37-75. doi:10.1016/0301-0082(75)90007-6

Kaptchuk, T. J. (1998). Powerful placebo: the dark side of the randomised control trial. *The Lancet, 351,* 1722-1725. doi:10.1016/S0140-6736(97)10111-8

Kienle, G., & Keine, H. (1996). Placebo effect and placebo concept - a critical methodological and conceptual analysis of information on the extent of the placebo effect. *Research in Complementary Medicine, 3,* 121-128. doi:10.1159/000210214

Lachance, M. P., Marlow, C., & Waddell, W. J. (1993). Autoradiographic disposition of [1-methyl-^{14}C]- and [2-^{14}C] caffeine in mice. *Toxicology Applied Pharmacology, 71,* 237-241. doi: 10.1016/0041-008X(83)90340-X

Landfield, P. W., Tusa, R. J., & McGaugh, J. L. (1974). Effects of post-trial hippocampal stimulation on memory storage and EEG activity. *Behavioral Biology, 8,* 485-505. doi:10.1016/S0091-6773(73)80042-2

Lorist, M. M., & Tops, M. (2003). Caffeine, fatigue and cognition. *Brain and Cognition, 53,* 82-94. doi:10.1016/S0278-2626(03)00206-9

Maia L., & Mendonça, A. D. (2002). Does caffeine intake protect from Alzheimer's disease? *European Journal of Neurology, 9,* 377-382. doi:10.1046/j.1468-1331.2002.00421.x

Mandel, H. G. (2002). Update on caffeine consumption, disposition and action. *Food and Chemical Toxicology, 40,* 1231-1234. doi:10.1016/S0278-6915(02)00093-5

McDonald, C. J., Mazzuca, S. A., & McCabe, G. P. (1983). How much of the placebo 'effect' is really statistical regression? *Statistics in Medicine, 2,* 417-427. doi:10.1002/sim.4780020401

McGaugh, J. L. (2000). Memory – a century of consolidation. *Science, 287,* 248-251. doi:10.1126/science.287.5451.248

McGaugh, J. L., & Dawson, R. G. (1971). Modification of memory storage processes. *Behavioral Science, 16,* 45-63. doi:10.1002/bs.3830160105

Nehlig, A. (1999). Are we dependent upon coffee and caffeine? A review on human and animal data. *Neuroscience & Biobehavioral Reviews, 23,* 563-576. doi:10.1016/S0149-7634(98)00050-5

Nehlig, A. (2010). Is caffeine a cognitive enhancer? *Journal of Alzheimer's Disease, 20,* 85-94. doi:10.3233/JAD-2010-091315

Nehlig, A., Daval, J. L., & Derby, G. (1992). Caffeine and the central nervous system: mechanisms for action, biochemical, metabolic and psychostimulant effects. *Brain Research Reviews, 17,* 139-170. doi:10.1016/0165-0173(92)90012-B

Nehlig, A., Lucignani, G., Kadekaro, M., Porrino, L. J., & Sokoloff, L. (1984). Effects of acute administration of caffeine on local cerebral glucose utilization in the rat. *European Journal of Pharmacology, 101,* 91-100. doi:10.1016/0014-2999(84)900347

Penfield, W., & Pérot, P. (1963). The brain's record of auditory and visual experience: A final summary and discussion. *Brain, 86,* 595-696. doi:10.1093/brain/86.4.595

Phillis, J. W., & Kostopoulos, G. K. (1975). Adenosine as a putative transmitter in the cerebral cortex. Studies with potentiators and antagonists. *Life Sciences, 17,* 1085-1094. doi:10.1016/0024-3205(75)90329-X

Rees, K., Allen, D., & Lader, M. (1999). The influences of age and caffeine on psychomotor and cognitive function. *Psychopharmacology, 145,* 181-188. doi:10.1007/s002130051047

Ryan, L., Hatfield, C., & Hofstetter, M. (2002). Caffeine reduces time-of-day effects on memory performance in older adults. *Psychological Science, 13,* 68-71. doi:10.1111/1467-9280.00412

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery & Psychiatry, 20,* 11-21. doi:10.1136/jnnp.20.1.11

Shum, D. H., Gorman, J. G., & Eadie, K. (1999). Normative data for a new memory test: The Shum Visual Learning Test. *The Clinical Neuropsychologist, 13,* 121-135. doi:10.1076/clin.13.2.121.1967

Smith, A. (2002). Effects of caffeine on human behavior. *Food and Chemical Toxicology, 40,* 1243-1255. doi:10.1016/S0278-6915(02)00096-0

United Nations, Department of Economic and Social Affairs. (2012). *Overall total population – Both Sexes.* Retrieved from http://esa.un.org/wpp/excel-data/population.htm