

## ORIGINAL ARTICLE

# A Randomized Controlled Trial (RCT) on the Effect of Caffeine on Working Memory and Sustained Attention of Bachelor of Medicine and Bachelor of Surgery (MBBS) Students in University of Cyberjaya (UoC), Cyberjaya, Selangor.

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## ABSTRACT

**Introduction:** Caffeine is the most widely consumed psychoactive substance across the world reported to improve cognitive performance. Hence, this study aims to assess the effect of caffeine on working memory and sustained attention of undergraduate medical students. **Methods:** A randomized controlled trial (RCT) study was conducted within 2 months in the University of Cyberjaya, Cyberjaya, Selangor. Sixty-three students volunteered to participate and were randomized into two groups; caffeinated and controlled. Subjects with known medical illnesses (e.g., peptic ulcer disease, severe anxiety, seizure, metabolic diseases, and heart diseases), sleep less than 6 hours, and last caffeine intake less than 12 hours were excluded from this study. The subjects completed two tests (pre- and post- intervention) each for working memory and sustained attention, i.e., Hopkins Verbal Learning Test and Serial Seven Subtraction Ttest respectively after filling a survey form on caffeine consumption. **Results:** Out of 32 students in the caffeinated group, only 37.5% ( $p = 0.719$ ) showed improvements in working memory, whereas 71.9% ( $p = 0.721$ ) showed improvements in sustained attention. **Conclusion:** The results from this study suggest that acute ingestion of low doses of caffeine is not statistically significant to improve working memory and sustained attention.

**Keywords:** Caffeine, Memory, Attention, Cognition

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## INTRODUCTION

Over 2.25 billion cups of coffee are consumed worldwide (1), and multiple studies have been done to uncover the truth on the benefits of coffee on different aspects. Studies have shown that there is an association between coffee consumption and overall decreases in mortality rate (2). There are also studies being done on the effect of coffee consumption on cognitive functions of the human mind (3).

According to the Department of Electrical Engineering at American University of Sharjah, UAE, a review was made on cognitive enhancement techniques and their impact on performance improvements (4). The term “cognitive enhancement” is usually characterized

by human interventions which aim to improve the essential operation of mental for sustaining or restoring good health (4). Such intervention is employed to enhance the cognitive functioning of the brain such as learning improvement, focus enhancement, attentional control, memory enhancement, faster reaction time, better perception and reasoning capacity.

The European Food Safety Authority (EFSA) stated that 75 mg serving of caffeine which is the average amount of caffeine in a typical cup of coffee leads to both increased attention and alertness (5). EFSA concluded that both selective attention and sustained attention which focuses on relevant stimulus and maintaining focused attentions over an extended period of time respectively are improved with caffeine consumptions (5). According to Smit et al (2000), caffeine concentration as low as 12.5 mg to 100 mg can improve cognitive performance (6). Hence, this study aims to assess the effect of caffeine on working memory and sustained attention

of University of Cyberjaya MBBS undergraduates at Persiaran Bestari, Cyber 11, 63000 Cyberjaya, Selangor.

## MATERIALS AND METHODS

### Subjects

Sample size was calculated using two proportions formula. Based on the calculations using prevalence of previous studies, the sample size for this study was 52. After taking into consideration 20% of non-respondents, the sample size for this study has been increased to 63. Sixty-three (63) MBBS students (22 males, 41 females) from University of Cyberjaya were recruited to participate through convenience sampling. Subjects were excluded through a series of exclusion criteria, i.e., subjects with known medical illnesses such as peptic ulcer disease, severe anxiety, seizures, metabolic diseases, and heart diseases, female subjects who are pregnant, subjects who did not get at least six hours of sleep the night prior, and subjects who did not abstain from caffeine consumption for at least 12 hours. Informed consents were obtained before the study and all subjects were allowed to withdraw at any given time. This study was approved, and ethical clearance was received from CUCMS Research Ethics Review Committee (CRERC) [Reference No.: UOC/CRERC/ER/248]. Subjects were also required to fill in a survey form on the frequency of caffeine consumption in a day and days per week, last caffeine intakes by hours, last meal intake by hours, and exercise. Subjects were then randomised into two groups, i.e., caffeinated and decaffeinated (control) groups using online true random number generator software.

### Beverage

Subjects were given instant caffeinated and decaffeinated coffee (NESCAFÉ Classic and NESCAFÉ Classic Decaf respectively) during the test sessions according to their assigned groupings. Two teaspoons (approximately 4 g) of either caffeinated or decaffeinated coffee powders were mixed with 100 ml of plain drinking water. Subjects were then given 150 ml of plain drinking water after administration of coffee beverages. According to NESCAFÉ, the approximate amount of caffeine is more than 50 mg per 2 g of caffeinated coffee and less than 30 mg per 100 g for decaffeinated coffee. Both the caffeinated and decaffeinated were administered black and unsweetened.

### Working Memory

Hopkins Verbal Learning Test (HVLT) was first introduced by Brandt (1991). HVLT is suitable as a brief assessment due to its simplicity as well as it is well-tolerated by both demented and neurologically

healthy individuals (8). HVLT is also an ideal test to assess memory during maximal drug effect as it can be administered rapidly. For the purpose of this study, two different sets of HVLTs were administered each for pre-intervention and post-intervention. HVLT is used in this study to assess subjects' working memories. HVLT comprises a 12-item word list, made up of 4 words from each of the 3 semantic groups. Instructions were given to the subject to listen attentively as the researchers pronounce the word list and attempt to memorize the words. The rate for each word read to the subject is approximately 2 seconds. Free recall of the list from the subjects was recorded. This procedure was done for 3 attempts. Next, the subjects were requested to say "yes" to the 24 words read to them if they were similar or "no" to the other words that did not belong to the 12-item word list (8).

### Sustained Attention

The Serial Seven Subtraction Test (S7ST) has been described in literature as a measure of concentration (9,10). In this study, the test was slightly modified to assess participants before and after intervention. Hence, the starting number for pre-intervention was "100" and for post-intervention was "102". Time of completion was taken to make comparisons during statistical analysis. S7ST in this study is used to evaluate subjects' sustained attention. Each subject will be given a three-digit number before and after administration of caffeine or placebo, which is 100 and 102 respectively. The subjects are then instructed to subtract seven from the numbers given, one at a time for 10 times. The time of completion for subjects to subtract seven for 10 times consecutively from the number given will be recorded. If subjects fail to get the correct answers at any point of assessment, they will be asked to start over from the beginning, however, the time recording will not be stopped.

### Pilot Study

Pilot study was not done due to time limitation and commencement of Movement Control Order (MCO) by the Malaysian government during the COVID-19 pandemic.

### Statistical Analysis

The collected data was analyzed using Statistical Package for the Social Sciences (SPSS) software v26. Since there are 2 instruments that are involved in the collection of data which are Serial Seven Subtraction Test and Hopkins Verbal Learning Test, chi-square was used to test for association between the caffeine effect on working memory and sustained attention. For all tests, a p value of  $\leq 0.05$  is statistically significant and thus, the null hypothesis will be rejected.

## RESULTS

### Working Memory

Among 32 subjects from the caffeinated group, 12 (37.5%) subjects had improvements in HVLТ that test for working memory whereas 20 (62.5%) subjects had no improvement.

In the decaffeinated group, 13 (52.0%) had improvements in HVLТ while 18 (47.4%) had no improvement. However, there is no statistical significance of the effect of caffeine and working memory with a P-value of 0.72. Hence, there is no association between caffeine and working memory of MBBS students of UoC in this study (Table I).

### Survey Parameters

The frequency of caffeine intake in a day and days per week, last caffeine intake by hours, last meal intake by hours and exercise were analyzed. It was found that all the parameters were statistically not significant with p-value of more than 0.05 (Table III).

## DISCUSSION

This study investigated the effect of acute administration of low-dose caffeine on the working memory and sustained attention. Many other well-established studies demonstrated positive effects of caffeine on cognitive function (6,10).

**Table I : Association between Caffeine and Working Memory**

Coffee Group	Working memory		Total, n (%)	Chi Square Value (df)	P Value
	Improved, n (%)	Not Improved, n (%)			
<b>Caffeinated</b>	12 (37.5)	20 (62.5)	32 (100)		
<b>Decaffeinated</b>	13 (52.0)	18 (47.4)	31 (100)	0.13 (1)	0.72
<b>Total, n(%)</b>	25 (39.7)	38 (60.3)	63 (100)		

### Sustained Attention

Twenty-three (71.9%) from a total of 32 subjects from the caffeinated group showed improvements in S7ST that tested for sustained attention while 9 (28.1%) showed no improvement. Among 31 subjects from the decaffeinated group, 21 (67.7%) had improvements in S7ST as opposed to 10 (32.2%) had no improvement. This study demonstrated that there is no statistical significance of the effect of caffeine and sustained attention with a P-value of 0.72. This shows that there is no association between caffeine and sustained attention of MBBS students of UoC (Table II).

### Working memory

Based on this study conducted using the Hopkins Verbal Learning Test towards 63 undergraduate MBBS students from University of Cyberjaya (UoC), the data analysis from chi-square tests showed that there is no statistical significance in the association between caffeine and working memory. This was shown by a p-value of more than 0.05 (P = 0.72). However, a previous study disagreed with the findings of this study as they showed that there were positive effects of caffeine on memory performance of undergraduate students (ages 18-21 years old) from the University of

**Table II : Association between Caffeine and Sustained Attention**

Coffee Group	Sustained Attention		Total, n (%)	Chi Square Value (df)	P Value
	Improved, n (%)	Not Improved, n (%)			
<b>Caffeinated</b>	23 (71.9)	9 (28.1)	32 (100)		
<b>Decaffeinated</b>	21 (67.7)	10 (32.2)	31 (100)	0.13 (1)	0.72
<b>Total, n (%)</b>	44 (69.8)	19 (30.2)	62 (100)		

**Table III : Survey parameters**

Parameters			Coffee Group		Chi-square (df)	P-value
			Caffeinated, n (%)	Decaffeinated, n (%)		
<b>Frequency of caffeine intake</b>	<b>In a day (times)</b>	0	11 (55.0)	9 (45.0)	1.18 (2)	0.55
		1-2	21 (50.0)	21 (50.0)		
		3-4	0 (0.0)	1 (100.0)		
	<b>Days per week (days)</b>	0	9 (50)	9 (50)		
		1-2	11 (52.4)	10 (47.6)		
		3-4	8 (61.5)	5 (38.5)		
<b>Last caffeine intake (hours)</b>	None	11 (52.4)	10 (47.6)	0.03 (2)	0.98	
	12-24	7 (50.0)	7 (50.0)			
	>24	14 (50.0)	14 (50.0)			
<b>Last meal intake (hours)</b>		21 (48.8)	22 (51.2)	0.21 (1)	0.65	
	>8	11 (55.0)	9 (45.0)			
<b>Exercise</b>	No	18 (60.0)	12 (40.0)	1.94 (1)	0.16	
	Yes	14 (42.4)	19 (57.6)			

Arizona (10). However, the study specifically selected participants with a moderate amount of caffeine consumption weekly. On the contrary, this study included participants who abstained from caffeine for at least 12 hours regardless of their habitual caffeine consumption. This is a particularly important factor to consider as regular coffee drinkers were reported to have higher scores in cognitive assessments (11).

In another study, regular coffee consumers (2 to 3 cups per day) showed a higher mean number of words remembered in learning, recall, and word recognition tests as compared to those never/almost never consumed coffee in the last 12 months (12). In comparison to this study, authors did not take into account on the duration of coffee consumption or abstinence to be able to analyse in detail and postulate such findings. Furthermore, all of the terminologies used in HVLТ were in English and the English language is not the first and dominant language for the majority of the subjects. This is a major disadvantage to this study as proficiency of a language plays an important role in an individual's recall in working memory (13,14). This could possibly explain the discrepancies of the findings in this study with other studies.

To our knowledge, one of the studies that is comparable to this study is by Warburton et al. (2001),

conducted on 424 participants aged 18-24 years old using verbal and non-verbal memory tests, has shown that caffeine has no effect on memory (15). Child and Witt (2006) found that caffeine causes memory task performance to be impaired in short-term memory tests (16). Similarly, Oei and Hartley (2005) concluded that caffeine did not benefit short term memory among undergraduates aged 19-47 years old from Murdoch University using a memory scanning experiment (17).

#### **Sustained attention**

Serial Seven Subtraction Tests had been used to test for sustained attention among 63 undergraduate MBBS students from the University of Cyberjaya and showed that there is no statistical significance in the data analysis in association between caffeine consumption and sustained attention ( $P = 0.72$ ). Hence, caffeine has no effect on sustained attention. This data, however, is contradictory to other studies because various studies showed that caffeine has an effect on sustained attention. According to a study, as little as 40 mg of caffeine in chewing gum also has proven to show performance on tasks requiring sustained attention (18). However, they also excluded participants who smoke more than five cigarettes in the daytime to eliminate the possible effects of nicotine withdrawal, which this study did not take into account in its exclusion criteria. Other than that, it was concluded that

habitual coffee users (at least 1 cup/day) reported to have a higher mean scores all cognitive domains assessed with significant positive correlation for items that measure attention, working memory, and concentration. It is postulated that caffeine influences stimulus processing and increases activation of the cortex and the rate of information gathering, hence improves vigilance (11). As many other evidence have shown that caffeine in fact improves attention, the contradictory findings of this study may also be attributed to the fact that the study was conducted at different times of day, thus explaining the possible differences in the level of attention affected by the subjects' individual circadian rhythm (19).

Even so, according to a study that was conducted on the first year students at a university in Indonesia using Stroop Test to measure attention showed that caffeine consumption had no significant effect on attention level, after controlling sleep duration (21).

## CONCLUSION

As a conclusion from a total of 32 students from the caffeinated group, 12 (37.5%) of them showed improvements in working memory whereas 23 (71.9%) of them showed improvement in sustained attention among a total of 63 Bachelor of Medicine and Bachelor of Surgery (MBBS) students in University of Cyberjaya, Cyberjaya, Selangor. However, the results from this study suggested that acute ingestion of low doses of caffeine is not statistically significant to improve working memory and sustained attention even after confounding parameters are controlled.

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