

# Dose Dependent Effects of Caffeine on Cognitive Performance and Neuronal Activation

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## Abstract

Many students assume that the more caffeine you drink, the better your cognitive performance. Overconsumption of caffeine has many negative effects, so if there are no dose related cognitive benefits to large amounts of caffeine, then college students should limit their intake. This study looked at whether ingesting a medium dose (200 mg) versus a lower dose (100 mg) of caffeine improved short term memory as measured by Flanker and n-back tests, compared to a control group. In addition, we looked at whether larger doses of caffeine produced a difference in neuronal activation during these tests as measured by functional near-infrared spectroscopy (fNIR). There were no differences in cognitive performance observed between the treatment groups, although the 200 mg caffeine group did have significantly more neuronal activation during higher cognitive load tasks. If increased neuronal activation does not correlate to increased performance, it may not reflect an actual benefit of increased caffeine consumption.

## Introduction

Caffeinated beverages are the most popular beverages enjoyed worldwide. In America, alone, over 90% of people consume a form of caffeine on a daily basis<sup>1</sup>. With this, it comes as no surprise that numerous studies have focused on the cognitive benefits of caffeine. Several positive features include its propensity to provide an increase in subjective alertness and to reduce fatigue<sup>1</sup>. Caffeine also has beneficial effects on reaction time<sup>3</sup>, sustained attention tasks<sup>4</sup>, simulated driving tasks<sup>4</sup>, and other life-oriented motor tasks, such as handwriting<sup>6</sup>. Cognitive benefits seem to be greatest when the subject is fatigued<sup>3</sup>. Benefits in cognition have been shown at dosages as low as 50 mg<sup>7</sup> and a study by Lieberman et al. (2002) showed little statistical increase in cognitive performance (short term spatial memory or pattern recognition) and reaction time between 100 and 200 mg of caffeine consumption<sup>8</sup>. A study using fMRI showed that there was not a significant increase in neuronal activation after consumption of 75 mg caffeine<sup>4</sup>, but this has not been studied at increased dosages or using an fNIR.

To understand why these benefits occur, it is helpful to look at the structural similarity of caffeine to adenosine, a naturally occurring inhibitory neurotransmitter that occurs in the brain. Throughout the day, neurons continue firing in the brain, causing adenosine to be released. Adenosine then attaches to adenosine receptors, which naturally decreases the amount of neuronal firing that occurs throughout the day, until one falls asleep<sup>9</sup>. Adenosine is the body's natural braking system for neuronal firing. Caffeine, on the other hand, is able to mimic adenosine in a nonselective antagonistic manner due to its similarity in structure to adenosine, which can most easily be seen by the purine rings that appear in both structures<sup>9</sup>. This likeness in similarity is what allows caffeine

to block the same adenosine receptors, effectively removing the brain's natural braking system<sup>9</sup>. As a result, neuronal firing is not inhibited and continues to increase. As neuronal firing continues to increase, the pituitary gland reacts the same way as it would to an emergency. Hormones are released into the bloodstream that cause the adrenal gland to release epinephrine, which activates the body's "fight or flight" response. Soon, the heart beats drastically faster, muscles tense, and the liver releases increased amounts of sugar into the blood stream for added energy<sup>9</sup>. The symptoms one normally feels after consuming a large cup of coffee occur due to this process.

Caffeine can lead to a host of negative effects including nausea, gastrointestinal upset, as well as cardiovascular issues that arise from the increased heart rate due to the release of epinephrine. With this in mind, it makes sense that if there is no dose-related cognitive benefit to consuming excess amounts of caffeine, consumption should be limited. The purpose of this study was to see if there is a difference in cognitive performance after consuming 200 mg caffeine compared to 100 mg caffeine or control, as well as observe the degree of neuronal activation in the prefrontal cortex using fNIR brain imaging during cognitive assessments.

It was hypothesized that accuracy measurements on cognitive tasks would be higher for the both caffeine groups compared to the control while there would be no significance difference between the caffeine groups. It was also hypothesized that greater neuronal activation would be seen during high cognitive load tasks for both caffeine groups when compared to the control with higher neuronal activation seen at the higher dose of caffeine.

## Methods

Twenty-seven healthy, USC Aiken undergraduates were selected for this study. Subjects taking any form of stimulant, including prescriptions and/or nicotine were excluded from

the study. Prior to the trial, participants were asked to fast for four hours to assure rapid absorption of the caffeine as well as fast from any form of caffeine for 48 hours and obtain at least six hours of sleep. Three treatment groups were used: 1) 100 mg of Vitamin C (control), 2) 100 mg caffeine and 3) 200 mg caffeine. Each treatment was allocated through random assignment and the entire study was done as a double blind procedure, so neither the participants nor the experimenters knew what dose was given to each participant until post analysis.

Two types of cognitive tests were used to measure cognitive performance. A Flanker test was used to measure reaction speed, which required participants to differentiate between congruent and incongruent stimuli. As purely a reactionary target, it served as a low cognitive load measure. The second test was the n-Back Test that measured working memory on a range of low to high cognitive load (1-back through 3-back). In this test participants were asked to differentiate between targets seen either 1, 2, or 3 slides back. Both tests were designed and presented using E-Prime Software.

Neuronal measures were assessed using a functional near infrared brain imaging system that measured cerebral blood flow changes in the prefrontal cortex. Extremely noninvasive, the subject wears a headband while the fNIR emits and records a near infrared light, akin to a pulse oximeter, to measure the changes in oxygenated and deoxygenated blood. This correlates to neuronal activation, as increasingly higher load tasks require more oxygen<sup>9</sup>. Neuronal activation was visibly apparent through a color spectrum that ranged from cool (low activation) colors to warm (high activation) colors. Quantitatively, the values obtained from an initial baseline were compared to values obtained during each cognitive task. A one way ANOVA was conducted to detect significance between the groups.

## Results

There was a large amount of variation in accuracy on all cognitive tasks for subjects in the control treatment group as well as for all subjects during the 1-back task (Figure 1). Although not significant, both caffeine groups did better than

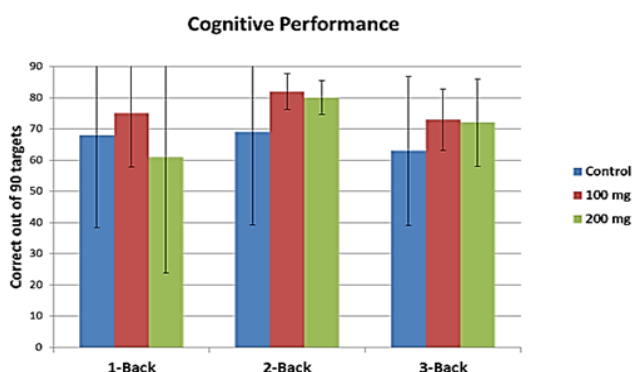


Figure 1. Cognitive function of test subjects.

the control on the 2-back and 3-back task and there was virtually no difference in accuracy between the caffeine groups on these tasks.

When looking at changes in neuronal activation across all tasks (Figure 2) certain marginal trends can be observed. During the Flanker task, the control group had less neuronal activation than they did baseline, although the control group showed a lot of variation across all cognitive tasks.

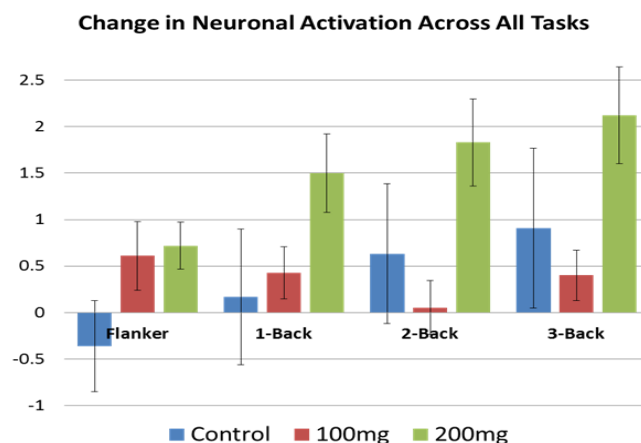


Figure 2. Changes in neuronal activation.

Additionally, there was a slight increase in neuronal activation within the 200 mg caffeine group as the level of cognitive load increased. There was a significant increase in neuronal activation between the 200 mg caffeine group and 100 mg caffeine group across all n-back tasks.

## Discussion

There was no significant difference in accuracy between groups on any cognitive task. This could indicate no cognitive benefit to caffeine at these doses but this is highly unlikely based on past findings. This more likely indicates a probable need for more subjects, better control of subject alertness, screening for individual caffeine dependence/withdrawal as well as more practice sessions before the actual experimental tasks are conducted. A lot of variation was found within the control group. This is believed to have been due to varying degrees of alertness for the un-caffeinated participants. Although subjects were asked to get adequate sleep the night before the test, we relied on self-reporting to assure that they did so. We also did not run tests at the same time each day so there were participants scheduled for early morning as opposed to early afternoon. Variation found within all subjects for the 1-back data set is believed to be due to inadequate familiarity with the testing procedures. Although there were practice sessions and subjects were encouraged to ask for help, some of the subjects scored extremely poorly on this task which increased variance.

Except for the Flanker test, increases in neuronal activation were observed in all groups during the cognitive tasks as compared to baseline. The 200 mg caffeine group had a significantly greater increase in neuronal activation, compared to the 100 mg caffeine group, in the higher cognitive load

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tasks (n-back). Given how caffeine works in the brain this was not unexpected. Increased activation did not correlate to increased cognitive performance however. Some researchers contend that greater neuronal activation does not necessarily equate to greater cognitive performance. For instance, greater increases in neuronal activation over a certain threshold may be associated with over-arousal and inefficiency<sup>4, 11</sup>.

Future work will focus on increasing the subject pool and modifying the testing procedures. The procedure will be adjusted to a within-subject format, where neuronal activation and cognitive performance will be recorded on the same participant both before and after taking the caffeine or placebo pill. Additionally, researchers will improve the initial training procedures to guarantee participants thoroughly understand the N-back before starting the experimental trail.

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