Effects on Short-Term Object Recognition by Caffeine, Glucose, and Olfactory Cues Evaluated by Beta Wave Activity

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ABSTRACT

Studies have shown that the combination of caffeine and glucose has a positive effect on improved subjective alertness, reduced fatigue, improved reaction time, sustained attention processes, and improved learning and consolidation of memory (Serra-Grabulosa 2010). Additionally, it is known that a distinct olfactory cue can assist in memory recall. Our study looks to identify how the combination of glucose, caffeine, and olfactory cues affect short-term object recognition as compared to controls. We hypothesize that these combined treatments will improve short-term object recognition. Ten note cards with Chinese symbols will be used for object recognition. We will use measurements of accuracy, average maximum Beta wave amplitude, Beta wave activity, and average response time to demonstrate effects. Our study shows a significant statistical difference between the olfactory cues group and the other three groups in terms of response time. Our results could serve to contribute to the current body of literature or help further elucidate the connection between olfactory cues and memory.

INTRODUCTION

Caffeine and glucose are becoming increasingly more prevalent in the United States and throughout the world. Many products that contain sugar and caffeine in combination are marketed toward college students to improve alertness and reaction time. Several studies have demonstrated the beneficial results of combining glucose and caffeine, showing effects such as

improved subjective alertness, reduced fatigue, improved reaction time, sustained attention processes, and improved learning and consolidation of verbal memory (Serra-Grabulosa 2010). Due to the marked beneficial results, large quantities of caffeine are becoming a staple for many Americans, who now consume a daily average of 2.79 mg/kg of body weight for all age groups per day (Sadock 2007). When caffeine and glucose are combined, however, they have greater beneficial effects on memory and attention processes than when consumed separately (Serra-Grabulosa, et al. 2010; Adan. A, et al. 2010).

On a biochemical level, caffeine acts as an antagonist of the adenosine A_1 and A_{2A} receptors (Tarter et al.,1998). These receptors effectively inhibit the release of excitatory neurotransmitters and control vasodilatation (Koppelstaetter et al., 2008). As an antagonist, caffeine leads to an increase in neural stimulation and leads to vasoconstriction. Increased glucose, on the other hand, supplements blood to brain glucose transport and increases the rate of glucose metabolism in active regions of the brain (Jonides et al,, 1998; Stone et al., 2005). Similarly, glucose is associated with greater activation in the medial temporal and dorsolateral prefrontal cortices, which is activated during declarative verbal memory processes (Serra-Grabulosa, et at. 2010) Caffeine and glucose appear to have a synergistic effect in the body, by both working on active memory and attentional resources (Koppelstaetter et al., 2008). Caffeine increases activation related to attentional working memory which results in a need for supplementary input from the cholinergic system. Glucose facilitates cholinergic transmission ability and as a result provides the supplementary input needed to exert the effects of caffeine (Sarter et al, 2006).

While caffeine and glucose have been shown to produce improvements on short-term memory and attention, research has also indicated that olfactory cues may play a role in short-term memory. Potential reasons for this connection rely on studies that hypothesize that the hippocampus and the olfactory bulb may be linked by synapses producing a functional connection (Vanderwolf 1992). Synchronous oscillatory activity is thought to be responsible for the interaction between these two separate brain structures. As a result, "a temporal window for transient communication" is achieved, producing potential links for the crossing of sensory input of smell and the short-term memory formation process (Fries 2005). In other studies, a dramatic improvement in short-term memory has been found in mice exposed to an enriched odor environment (Christelle Rochefort, et al 2002). More specifically, olfactory cues increase the beta wave oscillations between the olfactory bulb and the hippocampus during odor sampling and improved odor guided associative learning (Martin, et al. 2007).

Visual short-term memory relies upon synchronized oscillatory activity of largely distributed neural networks over both the sensory and prefrontal cortices of the brain, which are involved in sensory processing and short-term storage of visual information. Oscillatory synchrony associated with short-term memory is specifically maintained in the Beta-range of brain activity, and during recall tasks, high Beta wave firing is found between extrastriate visual areas (Tallon-Baudry, et al. 2001). Therefore, monitoring Beta wave activity in the brain is an indirect measure of increased short-term memory and object recognition. This study will test the combined effects of caffeine, glucose, and olfactory cues on short-term memory, specifically short-term object recognition. We hypothesize that these combined effects will improve short-term object

recognition. Short-term object recognition will be measured using accuracy, Beta wave oscillations, and time to respond; thus, according to the hypothesis, we expect to see increased accuracy, higher Beta wave amplitude, increased Beta wave activity, and decreased time to respond in each of our treatment groups when compared to the control.

MATERIALS AND METHODS

Participants

Twenty healthy undergraduate students [65% percent women and 35%men, age range 20-23, mean age 21.3] were recruited from the University of Wisconsin-Madison. Subjects were instructed to fast for four hours and abstain from caffeine for twelve hours prior to the experiment. All participants were low caffeine consumers (1.54 mg/kg of body weight/ day). Consent was obtained from all participants before the administration of EEG testing began.

Study design

Each subject underwent a learning phase and a testing phase. During the learning phase, subjects were shown ten Chinese characters on flashcards and verbally told what each symbol means in English. After being given ample time (~3 seconds per card) to "learn" the meanings of the characters, we moved on to the testing phase. In order to control for a different order of cards during testing, we randomized the flashcard order in the learning phase and placed the flashcards in a predetermined order prior to the testing phase. During the testing phase, each subject underwent an EEG scan while we went through the flashcards a second time. This time, subjects were shown the flashcard with the symbol and told to verbalize the English meaning. During the this phase, subjects were allowed to choose from a word bank of English meanings, provided to

them before testing.. Each subject was told they could use words more once if they so chose. A data recorder then marks “correct” or “incorrect” on the data collection sheet after each subject’s response to keep track of their accuracy.

Treatments

We assigned subjects to one of four groups: control, olfactory cues, caffeine and glucose, and caffeine, glucose and olfactory cues. Depending on which group the subject is assigned, a different treatment procedure is followed.

Control (Group 1):

Procedure was followed according to the study design. Subjects were administered neither caffeine nor glucose and were instructed to fast 4 hours prior to the experiment and abstain from caffeine 12 hours prior to the experiment.

Olfactory Cues (Group 2):

During the learning and the testing phase, the subject followed the procedure according to the study design. In addition, they were also allowed to smell the flashcards with the Chinese symbols. Each card was assigned a random, distinct scent. During the testing phase, we went through the flashcards again, allowing the subjects to smell the scent before they verbalized their response. Subjects were administered neither caffeine nor glucose and were instructed to fast for four hours prior to the experiment and abstain from caffeine for twelve hours prior to the experiment.

Caffeine and Glucose Only (Group 3):

Procedure was followed according to the study design. In addition, one hour before the test was administered the subject was given a caffeine pill (200 mg) and a glucose tablet (4 grams). This time frame was chosen based on the fact that caffeine absorbs in the stomach lining within 45-60 minutes (Liguori 2011). Subjects were instructed to fast 4 hours prior to the experiment and abstain from caffeine 12 hours prior to the experiment.

Caffeine and Glucose and Olfactory Cues (Group 4):

Procedure was followed according to the study design. In addition, one hour before the test was administered the subject was given a caffeine pill (200 mg) and a glucose tablet (4 grams). During the learning phase, the subjects were allowed to smell the cards with the Chinese symbols. During the testing phase, we went through the flashcards again, allowing the subjects to smell the scent before they verbalized their response. Subjects were instructed to fast 4 hours prior to the experiment and abstain from caffeine 12 hours prior to the experiment.

EEG

We used EEG lesson 3 programming with Biopac Student Lab® software. We followed the setup instructions outlined in the lab manual. One evaluator placed electrodes in the same positions on the right side of the each subject's head prior to the learning phase. We then placed a swim cap on the subject's head. In order to gather Beta wave data, we connected the relay to Channel 1 on the Biopac Sytem model and clicked on the Beta icon in our Biopac Student Lab® Computer Program. Prior to the testing phase, a calibration measurement is done to gauge a

baseline measurement of brain activity. During the calibration, each subject was told to relax, keep their eyes closed, and abstain from movement during the data collection process. During the testing phase, the evaluator controlling the EEG marked the subject response period, or the period of time from the moment the card is shown until the moment the subject responds.

The EEG recording is then analyzed. We chose to examine maximum Beta wave amplitude, Beta wave activity and response time. The values for each subject were averaged and recorded in an excel spreadsheet.

Materials

Banana Extract, Peppermint Extract, Lemon Extract, Anise Extract, Strawberry Extract, Maple Extract, Almond Extract, Peanut Butter, Acqua di Gio (Giorgio Armani cologne), Light Blue (Dolce and Gabbana perfume), Jo Malone (English Pear and Freesia cologne), 10 flashcards (large note cards), EEG machine, Electrodes (adhesive, removable), swim cap.

RESULTS

A total of twenty subjects were tested and analyzed within a three-week period. Five subjects were analyzed as controls, five subjects were analyzed from the caffeine and glucose group, five subjects were analyzed from the caffeine, glucose and olfactory cues group, and four subjects were analyzed from the olfactory cues group. Each group's data was analyzed in four specific areas: short-term memory recall accuracy, EEG beta wave maximum peak amplitude, EEG beta wave activity (standard deviation), and average response time.

Short-Term Memory Accuracy

Each of the subject's correct and incorrect responses were recorded during the testing period and later analyzed in order to determine accuracy, measured by percentage correct. Group 1 displayed the highest percentage correct with 84%. Group 4 averaged 80% correct, and group 3 averaged 78%. Finally, group 2 had the lowest accuracy, with an average of only 72.5% corrects (Figure 1). Overall, there was no significant treatment effect on short-term memory accuracy, with a p-value of 0.746 as determined by one-way ANOVA analysis. Pair wise comparison using Fisher's Test of group 1 versus 2 had a p-value of 1.095, 1 versus 3 had a p-value of 0.606, 1 versus 4 was 0.404, 2 versus 3 was 0.608, 2 versus 4 was 0.486, and 3 versus 4 had a p-value of 0.843, all showed no significant treatment effect between the groups.

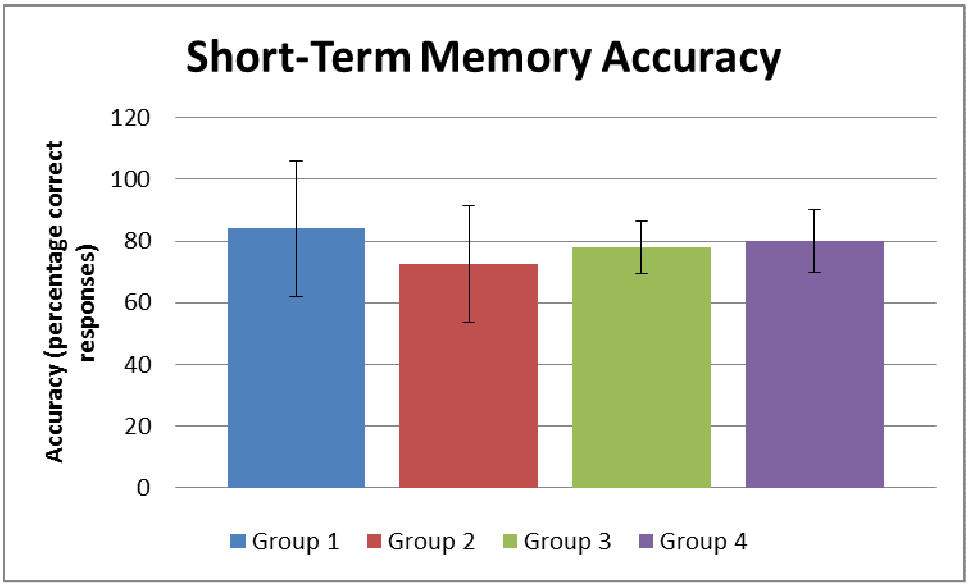

Figure 1: Comparison of short-term memory recognition accuracy between groups.

The average percentage of correct responses was used to measure short-term memory recall accuracy. *Groups were assigned as followed: Group 1= control, group 2 = olfactory cues treatment , group 3 = glucose plus caffeine treatment, and group 4 = glucose, caffeine, and olfactory cues treatment.*The average percentage correct for group 1 was 84±21.9%, group 2 was 72.5±18.9%, group 3 was 78±8.4%, and group 4 was 80±10%. Pair wise comparison using Fisher's Test of group 1 versus group 2 had a p-value of 1.095, 1 versus 3 had a p-value of 0.606, 1 versus 4 was 0.404, 2 versus 3 was 0.608, 2 versus 4 was 0.486, and 3 versus 4 had a p-value of 0.843, all showed no

significant treatment effect between the groups. There was no significant treatment effect on short-term memory accuracy overall, with a p-value of 0.746 as determined by one-way ANOVA analysis.

Maximum Beta Wave Amplitude

Maximum beta wave amplitude was measured over each response segment during the testing period of the experiment using BSL Pro 3.7.3 Biopac® software. The average maximum beta wave peak amplitude was determined by weighting the average peak amplitude of correct and incorrect responses with their corresponding accuracy fraction. The weighting of peak beta wave amplitude was calculated by using the following equation: *Average Beta Wave Amplitude=[(fraction correct* average correct beta wave amplitude) + (fraction incorrect*average incorrect beta wave amplitude)].* Using the calculation previously stated, the average beta wave amplitude for group 1 was determined to be 18.6±8.5 µV, group 2 was 20.0±4.5 µV, group 3 was 26.5±15.8 µV, and group 4 was 24.5±15.7 µV (Figure 2). Overall, there was no significant treatment effect on maximum beta wave amplitude, with a p-value of 0.736 as determined by one-way ANOVA analysis. Pair wise comparison using Fisher's Test of group 1 versus group 2 had a p-value of 0.8668, 1 versus 3 had a p-value of 0.334, 1 versus 4 had a p-value of 0.465, 2 versus 3 had a p-value of 0.453, 2 versus 4 had a p-value of 0.600, and 3 versus 4 had a p-value of 0.906; all showed no significant treatment effect between the groups.

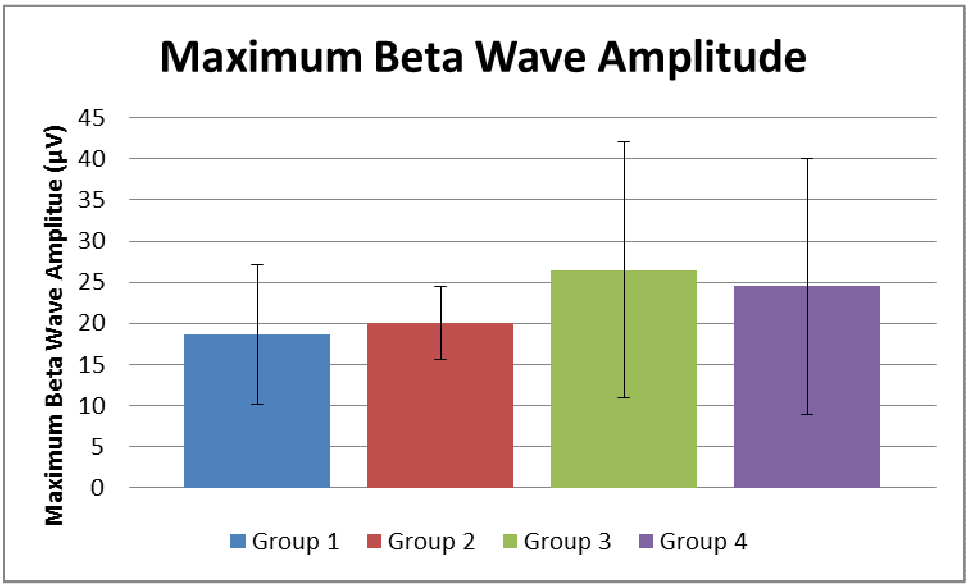

Figure 2: Group comparison of average maximum beta wave peak amplitude for responses.

The peak beta wave amplitude for each response segment was measured using BSL Pro 3.7.3 Biopac® software, measured in microvolts. *Groups were assigned as followed: Group 1= control, group 2 = olfactory cues treatment , group 3 = glucose plus caffeine treatment, and group 4 = glucose, caffeine, and olfactory cues treatment.* The average beta wave amplitude for group 1 was determined to be 18.6±8.5 µV, group 2 was 20.0±4.5 µV, group 3 was 26.5±15.8 µV, and group 4 was 24.5±15.7 µV. Overall, there was no significant treatment effect on maximum beta wave peak amplitude, with a p-value of 0.736 as determined by one-way ANOVA analysis. Pair wise comparison using Fisher's Test of group 1 versus group 2 had a p-value of 0.8668, 1 versus 3 had a p-value of 0.334, 1 versus 4 was 0.465, 2 versus 3 was 0.453, 2 versus 4 was 0.600, and 3 versus 4 had a p-value of 0.906; all showed no significant treatment effect between the groups.

Response Time

Response time was measured over each response segment during the testing period of the experiment using BSL Pro 3.7.3 Biopac® software as outlined under study design in the Materials and Methods section. Average response time calculated by weighting the correct and incorrect responses with their corresponding accuracy fraction. The weighting of response time was calculated by using the following equation: *Average Response Time =[(fraction correct* average response time for correct answers) + (fraction incorrect * average response time for incorrect answers)]* . Using this calculation, the average response time for group 1 was

determined to be 27.5±5 seconds, group 2 was 7.88±6 seconds, group 3 was 9.05±7 seconds, and 6.19±2seconds for group 4 (Figure 4). Overall, there was not a significant treatment effect on response time, with a p-value of 0.0945 as determined by one-way ANOVA analysis. Pair wise comparison using Fisher's Test of group 1 versus group 2 had a p-value of 0.0358, 1 versus 3 had a p-value of 0.864, 1 versus 4 was 0.870, 2 versus 3 was 0.049, 2 versus 4 was 0.026, and 3 versus 4 had a p-value of 0.739. There was a significant difference in treatment effect between group 1 and 2, group 2 and 3, and group 2 and 4.

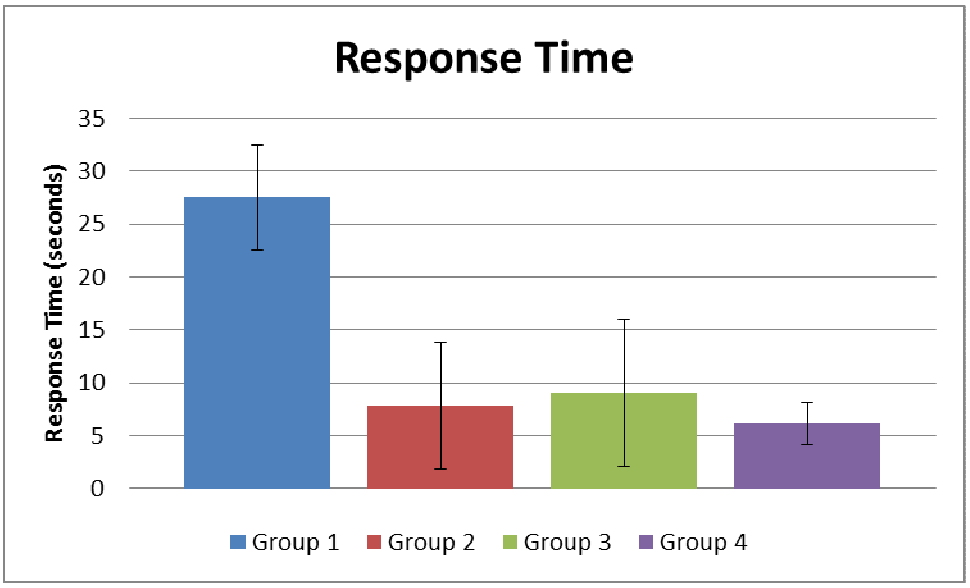

Figure 4: Group comparison of average response time.

The response time for each response segment was measured using BSL Pro 3.7.3 Biopac® software. *Groups were assigned as followed: Group 1= control, group 2 = olfactory cues treatment , group 3 = glucose plus caffeine treatment, and group 4 = glucose, caffeine, and olfactory cues treatment.* The response time for group 1 was determined to be 27.5±5 seconds, group 2 was 7.88±6 seconds, group 3 was 9.05±7 seconds, and 6.19±2seconds for group 4 (Figure 4). Overall, there was not a significant treatment effect on response time, with a p-value of 0.0945 as determined by one-way ANOVA analysis. Pair wise comparison using Fisher's Test of group 1 versus group 2 had a p-value of 0.0358, 1 versus 3 had a p-value of 0.864, 1 versus 4 was 0.870, 2 versus 3 was 0.049, 2 versus 4 was 0.026, and 3 versus 4 had a p-value of 0.739. There was a significant difference in treatment effect between group 1 and 2, group 2 and 3, and group 2 and 4.

Beta Wave Activity

Beta wave activity was measured for each response segment by using the standard deviation function of the BSL Pro 3.7.3 Biopac® software. The amount of beta wave activity for group one 5.34±3µV, group 2 was 12.2±17µV, group 3 was 15.0±7µV, and 6.8±4µV for group 4 (Figure 5). Overall, there was not a significant treatment effect on beta wave activity, with a p-value of 0.503 as determined by one-way ANOVA analysis. Pair wise comparison using Fisher's Test of group 1 versus group 2 had a p-value of 0.372, 1 versus 3 had a p-value of 0.188, 1 versus 4 was 0.837, 2 versus 3 was 0.710, 2 versus 4 was 0.480, and 3 versus 4 had a p-value of 0.261. There was no significant difference between any of the groups.

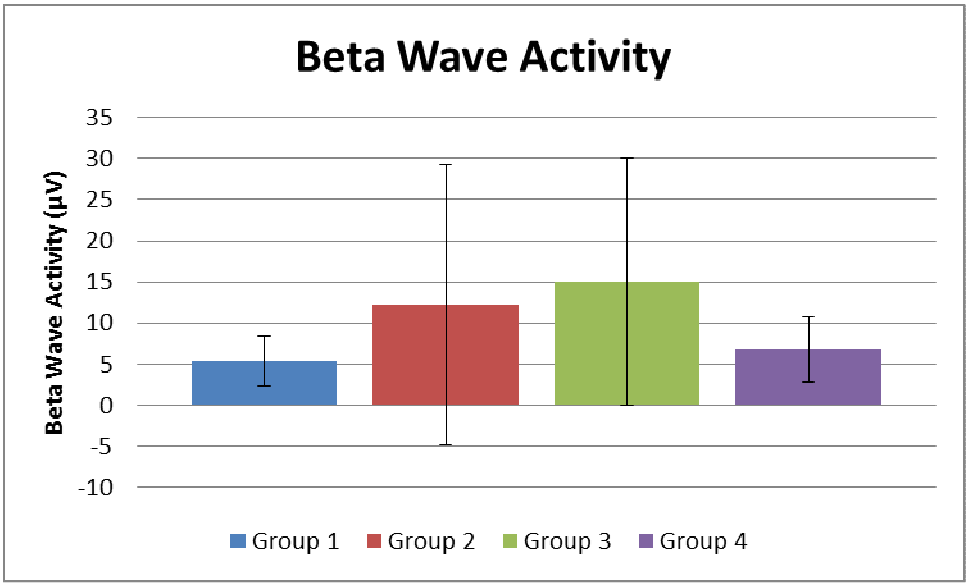

Figure 5: Group comparison of beta wave activity.

The beta wave activity was measured for each response segment by using the standard deviation function of the BSL Pro 3.7.3 Biopac® software. *Groups were assigned as followed: Group 1= control, group 2 = olfactory cues treatment , group 3 = glucose plus caffeine treatment, and group 4 = glucose, caffeine, and olfactory cues treatment.*The beta wave activity for group one 5.34±3µV, group 2 was 12.2±17µV, group 3 was 15.0±7µV, and 6.8±4µV for group 4. Overall, there was not a significant treatment effect on beta wave activity, with a p-value of 0.503 as determined by one-way ANOVA analysis. Pair wise comparison using Fisher's Test of group 1 versus group 2 had a p-value of 0.372, 1 versus 3 had a p-value of 0.188, 1 versus 4 was 0.837, 2 versus 3 was 0.710, 2

versus 4 was 0.480, and 3 versus 4 had a p-value of 0.261. There was no significant difference between any of the groups.

DISCUSSION

This study looked into the effects of caffeine, glucose and olfactory cues on short-term object recognition. Originally, we hypothesized that our chosen variables would enhance our subjects' ability to recall the meaning of ten Chinese symbols. We expected to see greater recognition of the symbols in our experimental groups compared to our control; however, our study yielded no significant differences between groups in terms of accuracy, and therefore did not agree with our hypothesis. There are many possibly reasons we may not have seen the accuracy results we expected. Using random assortment and population sizes of no more than five subjects per each group, we could not realistically expect to see the trends stated in our hypothesis. On the follow-up survey, several members of our control group reported better than average memorization abilities and performed exceedingly well during the testing phase, with several subjects achieving perfect scores. Similarly, many members of our experimental groups reported that the task was difficult and that they were not good memorizers. Additionally, several students in the olfactory cues treatment group reported that multiple sensory inputs, both sight and smell, may have diluted their concentration and detracted from their ability to memorize the symbols.

In addition, we hypothesized that subjects treated to our chosen variables of glucose, caffeine, and olfactory cues would show increased beta wave activity and a greater average maximum beta wave amplitude when compared to controls. Research has shown that increased beta wave activity, frequency and amplitude are indicative of increased concentration and memory recall.

After analyzing our results, we found that there was no statistically significant treatment effect in any of the groups on either average beta wave activity or amplitude. Also, no conclusions or interpretations can be drawn from the statistically significant differences between the groups for beta wave frequency due to data collection error from software programming restrictions. Aside from small "n" values in all of our treatment groups, we may have not seen the results we expected due to confounding factors introduced by our subjects not adhering to the fasting and caffeine abstinence guidelines. According to our follow-up surveys, several subjects from the olfactory cues treatment group and control group had just eaten a meal or drank a cup of coffee, which would reduce the impact of the caffeine pills and glucose tablets in the two caffeine and glucose treatment groups.

Lastly, in terms of response time, we hypothesized that increased stimulation of caffeine, glucose and olfactory cues would decrease our subjects' reaction time in our treatment groups. The results of the study indicated no overall significant statistical differences in treatment effects among the groups; however, in the pair-wise comparison, we found the olfactory cues to group to have a statistically significant effect. There was a statistically significant decrease in response time for the olfactory cues treatment group in comparison to the control group and caffeine plus glucose treatment group. This result may help contribute to future research in an attempt to explain the pathway between the olfactory bulb and the hippocampus. Similarly, in agreement with the hypothesis, our results yielded a statistically significant decrease in response time for the glucose, caffeine and olfactory cues group when compared to the olfactory cues treatment group. Given research on the effects of caffeine and glucose on attention span and reaction time,

we predicted that when combined with olfactory cues, the glucose, caffeine, and olfactory cues treatment group would exhibit the shortest response time. Therefore, our results are in accordance with previous findings that highlight the beneficial effects of caffeine and glucose on short term memory, as well as studies showing olfactory cues' interaction with the hippocampus in relation to short-term object recognition. This data could be used to support further studies looking to elucidate a specific biochemical pathway linking olfactory cues to the hippocampus and whether the combination of caffeine and glucose further enhances the pathway's effect.

One major error with this experiment was due to incorrectly collecting beta wave frequency as a result of misunderstanding the BSL Pro 3.7.3 Biopac® software functions. Though the frequency function for beta wave analysis of the response segments does measure the change in beta wave oscillations per second, the software calculates this number based off of the first and last portions of the segment over the its area resulting in an inaccurate measure of mean frequency. Data was collected for beta wave frequency, however due to calculation error it was disregarded from results. Instead of analyzing beta wave frequency, we chose to use an analogous measurement of beta wave activity by using the data from each subjects' standard deviation of beta wave oscillations. For future studies, the mean frequency per response segment should be calculated using the Biopac® application note 118 EMG frequency signal analysis procedure, following Part 2: Manual Scoring and Median Frequency sections (Appendix A).

Another minor problem we have encountered with our project was the difficulty of maintaining subject consistency within our four different groups. While we asked the participants to abstain from food or caffeine for 4 hours prior to our experiment, some of them had large meals close to

their trial, possibly influencing the effectiveness of the glucose pills. Similarly, if the control subjects consumed additional caffeine, it may intensify the effect of the caffeine pills. We have had to re-run some of our control trials due to excess caffeine use and large meals. In addition, we also found our sample sizes are too small to run in-depth qualitative statistical analysis, and thus the p-values determined using ANOVA analyses were easily influenced by variations within the groups. Due to the time constraint, we could only obtain twenty subjects in our study. More participants could reveal further significance of the data; future studies should pay specific attention to response time and beta wave activity. Another suggestion we had for future research groups would be to have each subject go through four different trials, allowing the same person to experience all four treatments and thus, be his or her own control. Using this method, the administrators would need to use different set of ten flashcards with new Chinese symbols, so the difficulty of the task would remain the same. Perhaps this method would eliminate the difficulty of finding subjects with equal natural memorizing ability and skills to be distributed evenly among each of the groups. With the data to compare an individual's performance across different treatments, we may be able to achieve more accurate, controlled results that could more effectively demonstrate the researched effects of caffeine, glucose and olfactory cues on short-term object recognition.

We also considered the possibility that the scents we chose for our experiment (common extracts like vanilla, orange, lemon) might be too recognizable and subjects would make associations without focusing on the symbol (i.e.: dog = orange). In order to combat this problem, we brought in less recognizable scents like random perfumes, colognes and uncommon extracts such as

almond and anise. It should further be noted that it is a possibility that some scents could have unexpected effects on beta wave oscillation. For example, common “relaxing” scents like jasmine that could be influence the patient’s beta wave oscillations to a more relaxed state, reducing their activity. Further issues with the scents chosen were that some stained the flashcards with a red, yellow, or brown hue. The subject might have been distracted by the stain or even been more able to recognize the card by the color, rather than the olfactory cue or Chinese symbol.

The last problem we sensed was that we may be giving our subjects too little or too much time to view the cards the first time through before their quiz. While we were showing the cards within a 1-3 second range, we were noticing a difference in performance between people who had less or more time with the cards. We have tried to standardize the time to about 2 seconds to strike an average between those who are in the scent groups and those who are in the control groups.

Overall, we have maintained consistency in which group members performed which tasks in order to minimize any variability in human error (ie. one person always showed the cards, one person always operated the EEG, etc). As far as group dynamics, we have all contributed evenly to independent research and duties while conducting our experiment in lab.

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