The Effect of Tablet Size on Cognitive Performance:

A Randomized Control Trial Using Caffeine

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Abstract

Background: A capsule's physical design (e.g. shape, size, and color) affects individuals' perception of drug efficacy; that is, how well a drug is likely to work. The goal of this study is to assess the effects tablet size may have on participant's performance on cognitive testing since research has found differences between preparation methods. **Method:** 120 participants will be randomly assigned to one of four groups: 1) 90 mg caffeine with a 1 mm diameter sucrose pillule; 2) no caffeine with the small sucrose pillule; 3) 90 mg caffeine with a 5 mm sucrose pillule; 4) no caffeine with the large sucrose pillule. Participants will consume the designated placebo tablet with water (caffeinated or non-caffeinated); then, participants will provide weekly caffeine intake and complete the neutral portion of Velten's Mood Induction Procedure until 30 minutes have passed to allow for caffeine activation. Participants will complete the Stroop test, Trial Making Tests A and B, and the Rey Auditory Verbal Learning Test. Previous literature, as far as the author knows, relied on evaluating drug efficacy based on appearance alone. This study aims to assess if tablet size, due to placebo effect, alters participants' performance on cognitive tests after consuming caffeinee. The Effect of Tablet Size on Cognitive Performance:

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Placebo effects are physiological changes in the brain and body brought about through treatments that have no active ingredient or active component (Geuter et al., 2017). Historically, placebo effects have been utilized as a marketing tool because the public's beliefs, expectations, experiences, and perceptions made the proposed treatments and products appealing. For example, in the 1700s, Franz Anton Mesmer developed his theory of "animal magnetism" (Hammond, 2013). His theory asserted "mesmeric" (i.e. hypnotic) motions over a patient's body would redistribute and realign magnetic fluids within the body, curing clients of their ailments. However, after much criticism, Mesmer's claim was found to be unsupported by experimental evaluation. His peers concluded that the results from his treatments were more likely due to his clients' imaginations than his theory on animal magnetism (Hammond, 2013). In other words, Mesmer took advantage of his clients' susceptibility to mesmerism, or hypnotism, to create a physiological response during treatment.

There are different methods to elicit a physiological response in individuals using placebos. Pseudo-pharmaceutical placebos include mixtures created from Galen's Pharmacopeia, a recipe book that uses plants, bacteria, worms, reptiles, fish, human organs, tissue, bone powder, or excretion to create "medicinal remedies." Before the 19th century, this recipe book was believed to provide cure all recipes for ailments (Czerniak & Davidson, 2012). If the patient died, then the ailment was incurable, and no remedy would have worked. Why have placebos endured throughout history? Literature suggests that one explanation could be how individuals perform perceptual decision making (Geuter et al., 2017).

3

Bayesian models of perceptual decision making suggest that creating biased perceptions in favor of expected values or outcomes results in outcomes that fulfill those expectations. For example, if an individual expects pain, introducing a placebo may create the expectation of experiencing less pain. If the placebo is successful, the individual will experience an analgesic effect without any active ingredient. These placebos can be applied in many different situations, where an individual's perceptions or expectations influence the outcome of their treatment or intervention.

In recent research, a placebo effect may have been responsible for differences in participant responses to experimental procedures. Initially, the placebo effect threatened the validity of previous research, because its effects were not well understood (Ross & Buckalew, 1979) among the different scientific disciplines. The placebo effect in scientific literature was still an unintentional and unexplained effect; psychological and behavioral changes were observed in different studies repeatedly (Buckalew, 1979). As more evidence surfaced, the demand to better understand the placebo effect increased. Understanding the placebo effect would not only safeguard and improve research quality; the placebo effect showed promise to be manipulated to explore possible beneficial uses.

Physical drug design

Research since then suggests that the physical design of drugs influences an individual's perception of a drug. Specifically, the color, shape, size and coating of the drug have been found to impact preferences, how strong an individual perceives a drug to be and the effect they believe a drug will have (e.g. tranquilizer, stimulant, etc.; Buckalew & Coffield, 1982).

4

Buckalew and Coffield's research on the effects of capsule size on perceived drug strength suggests that larger capsules are believed to be stronger than small capsules (Buckalew & Coffield, 1982). In their study, college students were recruited to assess the relationship between perceptual characteristics of physical drug preparation forms (i.e. formulation) and expected effects. The influence of capsule size on perceived drug strength, the influences of color on expected drug effects, and the influence of formulation on expected drug strength were all visually assessed. Their findings suggest that certain colors are related to expected pharmacological effects. Furthermore, capsules are perceived to be stronger than tablets, and capsule size is significantly related to expected drug strength. Larger capsules are perceived to be stronger compared to smaller capsules. In tablets, the same pattern might persist; however, the opposite effect might also occur. Smaller tablet sizes might result in a stronger effect than larger tablet sizes. Buckalew and Coffield's work relied on visual judgements of drug characteristics; however, this study will rely on quantitative data to evaluate tablet size's effects on participants' performances due to participant perception.

Overgaard et al.'s study aimed to assess the preferences of oral dosage forms by size, formulation (i.e. gelatin capsule, tablet, or coated tablet), and shape (Overgaard et al., 2001). The study was designed in three phases, each assessing one of the previously mentioned factors. To assess how size affects swallowability and preference, participants were each asked to swallow five differently sized oblong tablets and verbally rate how easily they were able to swallow each pill according to a 5-point Likert scale. Smaller tablets were found easier to swallow compared to larger ones. To assess what formulation is preferred, participants were asked to swallow a gelatin capsule, tablet, and coated tablet and rate which was easier to

swallow. Gelatin capsules were easiest to swallow, followed by coated tablets and non-coated tablets. Lastly, to assess the preferable shape participants were asked to visually judge small, medium, and large white tablets that were circular or oblong on swallowability. Medium and large tablets were rated the easiest to swallow if they were oblong, while small tablets were rated easiest to swallow when they were round (Overgaard et al., 2001). Overgaard et al.'s work established preferences for physical drug designs. However, little is known if those physical characteristics can influence the placebo effect influencing the performance of the drug. This study will focus on one size, specifically in tablets, to assess if that characteristic can affect cognitive outcomes in a quantifiable manner. Despite extensive library searches, no research was found that analyzed tablet-based, physical design factors, like size, that could influence a placebo effect and consequently drug performance.

Caffeine

Caffeine is a psychostimulant with three main mechanisms ofaction : 1) mobilization of intracellular calcium, 2) inhibition of phosphodiesterases, and 3) antagonism of adenosine receptors (Nehlig et al., 1992). Caffeine stimulates the release and reuptake of calcium in neurons and muscle-tissue cells; an essential process in the central and peripheral nervous systems for neuronal communication and muscle contraction in the musculoskeletal system. Caffeine inhibits the breakdown of phosphodiesterases in the central nervous system. Caffeine's molecular structure is like that of enzymes responsible for breaking down phosphodiesterases into molecules like cAMP, a messenger molecule. This action, though, occurs when there is a toxic concentration of caffeine in the blood. The mechanism of action associated with improving cognition after consuming caffeine is the antagonism of adenosine

6

receptors. Adenosine is responsible for dampening neuronal activity in the suprachiasmic nucleus (e.g. less electrical activity, less neurotransmitter release, etc.). The physiological response associated with uninhibited adenosine receptors (i.e. with no caffeine present) is feeling drowsy, sleepy, and less attentive. Caffeine has a high affinity for adenosine receptors (specifically the A₁ receptor), so adenosine receptors are blocked by caffeine molecules (Nehlig et al., 1992). Consequently, individuals can experience the opposite physiological response: better attention, feeling awake, improved attentiveness, etc. The consequences of caffeine's third mechanism of action have been thoroughly researched, making it a strong drug candidate for use in this study.

Caffeine may be a good option for testing this phenomenon for three reasons: 1) previous research already supports caffeine's improvements to cognitive functioning (EFSA, 2011); 2) caffeine use among college students is very salient, given the prominence of the caffeine across various products like energy drinks (Pettit & DeBarr, 2011); 3) using self-report measures to collect data on weekly caffeine consumption habits will allow adjustments for tolerance effects (Beaumont, et al., 2017;2016). Research on caffeine use in healthy adults has already shown significant improvement to memory, executive functioning, and processing speed (EFSA, 2011). Caffeine lends itself well to a randomized controlled trial design, allowing the introduction of tablet size as an additional factor. Previous research supports an increase in cognitive functioning after consuming caffeine; memory, executive functioning, and processing speed are improved after consuming caffeine (EFSA, 2011). The European Food and Safety Administration conducted a meta-analysis that assessed the different claims associated with consuming caffeine like increased fat oxidation, increased energy expenditure, increased

alertness, and increased attention. Their findings suggest that there is not enough data to support causal claims for caffeine causing increased fat oxidation and increased energy expenditure. However, a causal relationship between caffeine and increased alertness and increased attention is supported (EFSA, 2011). Pettit and Debarr conducted a study analyzing the association between stress and energy drink consumption, and the association between energy drink consumption and GPA in 136 college students ages 18-24 (Pettit & DeBarr, 2011). Their results show a positive correlation between perceived stress and energy drink consumption, and a negative correlation between GPA and energy drink consumption. However, the results in Pettit and DeBarr's study did not account for consumption of caffeine from other sources (e.g. coffee, tea, supplements, etc.). Heavy marketing for caffeinated products make caffeine an ideal substance to use for assessments when working with college students.

Beaumont et al.'s research on tolerance development for low doses of caffeine emphasizes the need to adjust for tolerance effects in randomized controlled trials (Beaumont, et al., 2016; 2017;). Their research examined participant physical performance after consuming small doses of caffeine. Participants experienced significant decline in performance after consuming small doses of caffeine (1.5 mg of caffeine per kg of bodyweight) for 28 consecutive days compared to placebo. Beaumont et al.'s work highlights the importance of adjusting for participants' caffeine consumption habits. Leaving scores unadjusted for caffeine consumption habits could be a confound to studies that involve participants consuming caffeine.

Lastly, age is a significant factor in caffeine metabolism. Some hepatic enzymes (Cytochrome P450s, or CYPs) become less active as individuals age (Kinirons & O'Mahony,

8

2004). There are several different CYPs that metabolize different drugs. Caffeine is metabolized by CYPs in the 1A family, specifically 1A2 CYPs. Kinirons and O'Mahony's literature analysis showed consistent decrease in enzyme activity as individuals age (Kinirons & O'Mahony, 2004). They suggest the decreases in certain enzyme activity are likely due to changes in liver size and blood flow. Livers in humans experience a size reduction and reduced blood flow with age. When conducting research that involves participants metabolizing caffeine, age should be considered. Caffeine is a good choice to examine the effects tablet size may have on participants' performances on cognitive tests.

Present Study

Previous research relied heavily on participants' perceptions to rate a drug's effectiveness and purpose; this study was designed with randomized, placebo-controlled trials to evaluate the main goal using objective quantitative data. I will use neuropsychological testing to assess if tablet size affects participants' short-term memory, executive function, and processing speed using caffeine as the drug of choice. Previous research has supported a significant cognitive boost in these cognitive functions for caffeine dosages of at least 75 mg (EFSA, 2011). If tablet size affects perceptions of how effective a dose of caffeine will be, despite doses remaining constant in the caffeinated groups, then I expect significant differences among the two tablet sizes for processing speed, executive functioning, and memory capabilities in participants. This study may prove foundational to better understanding more effective physical drug designs.

Hypotheses

There are three hypotheses for this experiment:

- caffeine will significantly improve participant's memory, executive function, and processing speed;
- there will be a significant difference in participant performance associated with tablet size;
- 3) there will be an interaction effect between caffeine content and tablet size.

Method

Participants

120 participants, primarily Psychology students fulfilling a research participation requirement for Introduction to Psychology courses, will be recruited. Ambulatory participants that are fluent in written and spoken English will be used because they should be able to complete the neuropsychological tests.

Participants that are allergic to sucrose and/or caffeine will be excluded because they are essential components to the procedure. Participants with cardiovascular disease or uncontrolled high blood pressure will be excluded because the use of caffeine may exacerbate these conditions. Participants with untreated or unresolved anxiety and/or depressive disorders will be excluded because caffeine may exacerbate symptoms related to these disorders as well. Participants that are pregnant will be excluded from this study. Lastly, participants that have a diagnosed learning disability will be excluded because the neuropsychological tests will only use scores normalized for the general population.

Participants' age will be limited to ages 18 years old through 40 years old because age is a significant factor in caffeine metabolism (Kinirons & O'Mahony, 2004). Individuals older than 40 may experience different pharmacological effects due to age; thus, age will be controlled in this study.

Measures

Processing Speed.

Stroop 1) Color and 2) Word tests.

The Color test asks participants to read the color of print on a page with columns of red, yellow, green, and blue X s. The Word test asks participants to read the printed words on a page with the words RED, YELLOW, GREEN, and BLUE printed in black ink. These tests are scored by timing, in seconds, how long participants take to correctly identify the 100 items in each test. Longer completion times indicate slower processing speed capabilities. The Stroop Test's separate 1) Color and 2) Word tests (Appendix B) test-retest reliabilities are .83 and .74, respectively (Franzen, et al., 1987)

Trail Making Task A.

This test asks participants to connect a series of numbers that are randomly distributed on the test page. The goal of these tasks is to connect the series of numbers or numbers and letters in order (e.g. 1-2-3) as quickly as possible. Scoring is done by recording the time (in seconds) participants needed to complete the test. Longer completion times indicate slower processing speed capabilities. The Chronbach's alpha reliability of Trail A is .86 (Smith, et al., 2008).

Executive Function.

Stroop 3) Color-and-Word test.

The Color-and-Word test asks participants to read the color of print for the words RED, YELLOW, GREEN, and BLUE when the print color and word conflict. This test is scored by timing, in seconds, how long it takes for participants to correctly read 100 items. Longer completion times indicate lower executive function capabilities because the conflict between the print color and printed word takes longer to overcome. The test-retest reliability of the Stroop Colorand-Word Test is .67 (Franzen, et al., 1987).

Trail Making Task B.

This test asks participants to connect a series of numbers and letters that are randomly distributed on the test page. The goal of these tasks is to connect the series of numbers and letters in order (e.g. 1-A-2-B-3-C) as quickly as possible (Appendix C). Switching between alphabetic and numeric sets and timing completion times, in seconds, is an effective measure of executive functioning capabilities. Longer completion times indicate lower executive function capabilities because participants take longer to switch between sets. The Cronbach's alpha of Trail B is .88 (Smith, et al., 2008).

Memory.

Rey Auditory Verbal Learning Test (RAVLT).

Participants are presented with 15 unrelated words and asked to recall as many as they can over five trials. This section assesses immediate recall ability. An additional 15 unrelated words are then introduced as an interference component. Participants must recall as many of the original 15 words as possible after being presented with interference. Lastly, after an interval of 30 minutes, participants are asked to recall the original 15 words again (Appendix D). The trials are scored by counting the correct number of words recalled, the % recalled (the final delayed-recall trial(A7) divided by the final immediate recall trial (A5)), and the number of intrusions (i.e. the number of incorrect words). A higher percentage of recall with little to no intrusions are considered better memory. The Cronbach's alpha reliability of the Rey Auditory Verbal learning Test is .84 (Magalhaes, et al., 2012).

Procedure

Materials for this procedure will need to be prepared beforehand. 90 mg packets of caffeine will be prepared from 200 mg pure caffeine powder capsules by opening capsules and measuring out the desired weight of caffeine using a scale that can measure accurately to the thousandths gram. The weight of each prepared packet will be recorded by hand in a notebook until it is used in a trial. Before participants arrive, the prepared caffeine packet will be mixed with distilled water and one pillule of each size will be placed into small paper cups marked A and B.

Procedures will be explained to participants at first contact, and they will sign an informed consent form to confirm eligibility (Figure 2). Participants will be randomly assigned to one of the four groups (Figure 1). Based on a power analysis conducted at 0.80 power on Pasman et al.'s work on the effects of caffeine in a home-setting, 120 participants will need to be recruited in this study to successfully detect any significant effect (Pasman et al., 2017).

Participants will be required to not have consumed caffeine the day of testing. Participants will be presented with 8 ounces of distilled water and the cups containing each sucrose placebo pill. They will be asked to drink the water and only one of the sucrose pillules (depending on the group they were placed in); half of the participants (n=60) will drink water mixed with 90 mg of dissolved caffeine (Figure 1). After consumption, participants will be asked to complete Velten's Neutral Mood Induction Procedure (Appendix A) until 30 minutes have passed to allow for caffeine activation in the body (Institute of Medicine (US) Committee on Military Nutrition Research, 2001). Participants will then begin with the series of Stroop tests. After completing the three Stroop tests, participants will complete the first section of the Rey Auditory Verbal Learning test (immediate recall). During the 30-minute waiting period

participants will complete Trail Making Tasks A and B, and fill out a demographic survey designed to collect: 1) their weekly caffeine intake using the Caffeine Consumption Questionnaire (Appendix E); 2) sex; 3) age; 4) ethnicity and race; 5) year in school (i.e. freshman, sophomore, etc.); 6) GPA; and 7) academic major. The time of day the trial begins will also be recorded. The data collected in the survey will be used to adjust scores during data analyses. If students are unable to complete the survey and caffeine questionnaire within the 30-minute waiting period allotted for the RAVLT, the survey materials will be set aside and completed after participants finish the second component of the RAVLT. After completing the second portion of the RAVLT participants will be debriefed, and the trial will conclude.

Data Analysis

Primary analysis will be done through a series of ANCOVAs, if a preliminary correlation analysis shows a significant relationship between weekly caffeine consumption and scoring for each cognitive component. If the preliminary correlation analysis does not show a significant relationship between weekly caffeine consumption and scores for each cognitive component, then a series of ANOVAs will be performed.

Proposed Timeline

Pending the approval of clinicaltrials.gov, materials will be gathered and prepared in early October. The UROP has been awarded and funds will be available once PRS has approved of this proposal. Recruitment will begin during the Fall semester. Recruitment and trials are expected to continue in through December and conclude as late as February. Course load will be kept to a minimum to allot enough time for trials every weekday during the morning.

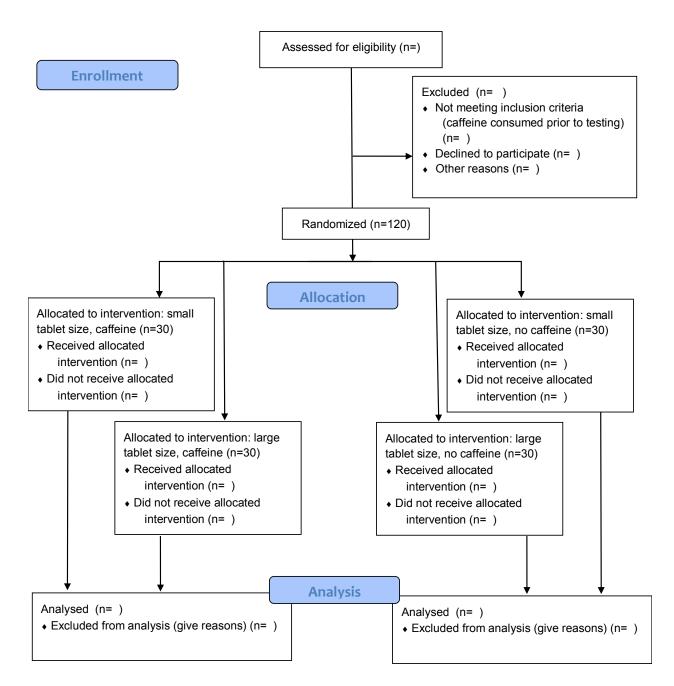
15

Weekly caffeine consumption will be calculated for each participant from their reported

caffeine consumption habits (Appendix E).

	No caffeine	90 mg caffeine
Small tablet (1 mm diameter)	Average score on cogitive test	Average score on cognitive test
Large tablet (5 mm diameter)	Average score on cognitive test	Average score on cognitive test

Figure 1. Overall study design



The Effect of Tablet Size on Cognitive Performance: A RCT Using Caffeine

Figure 2. CONSORT diagram

Appendix A

Velten's Neutral Mood Induction Procedure

MOOD STATEMENTS

CARD 1 OKLAHOMA CITY IS THE LARGEST CITY IN THE WORLD IN AREA, WITH 631.166 SQUARE MILES. CARD 2 JAPAN WAS ELECTED TO THE UNITED NATIONS ALMOST FOURTEEN YEARS AFTER PEARL HARBOR. CARD 3 AT THE END APPEARS A SECTION ENTITLED "BIBLIOGRAPHY NOTES." CARD 4 WE HAVE TWO KINDS OF NOUNS DENOTING PHYSICAL THINGS; INDIVIDUAL AND MASS NOUNS. CARD 5 THIS BOOK OR ANY PART THEREOF MUST NOT BE REPRODUCED IN ANY FORM. CARD 6 AGRICULTURAL PRODUCTS COMPRISED SEVENTY PER CENT OF THE INCOME. CARD 7 SATURN IS SOMETIMES IN CONJUNCTION, BEYOND THE SUN FROM THE EARTH, AND IS NOT VISIBLE. CARD 8 SOME STREETS WERE STILL SAID TO BE LISTED UNDER THEIR OLD NAMES.

Eight of sixty neutral mood statements on Velten's Neutral Mood Induction task. Participants will be presented one statement every thirty seconds.

Appendix B

Stroop Color test

XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX
XXXXX	XXXXX	XXXXX	XXXXX	XXXXX

Stroop Word test

GREEN	RED	YELLOW	RED	BLUE
RED	YELLOW	GREEN	YELLOW	YELLOW
GREEN	GREEN	BLUE	BLUE	GREEN
BLUE	BLUE	RED	RED	RED
RED	YELLOW	YELLOW	GREEN	YELLOW
YELLOW	BLUE	BLUE	RED	BLUE
BLUE	RED	GREEN	YELLOW	GREEN
YELLOW	GREEN	RED	GREEN	RED
GREEN	GREEN	GREEN	BLUE	GREEN
RED	BLUE	YELLOW	YELLOW	BLUE
YELLOW	YELLOW	RED	BLUE	RED
YELLOW BLUE	YELLOW RED	RED BLUE	BLUE RED	RED YELLOW
BLUE	RED	BLUE	RED	YELLOW
BLUE YELLOW	RED YELLOW	BLUE BLUE	RED GREEN	YELLOW YELLOW
BLUE YELLOW RED	RED YELLOW GREEN	BLUE BLUE YELLOW	RED GREEN YELLOW	YELLOW YELLOW RED
BLUE YELLOW RED YELLOW	RED YELLOW GREEN BLUE	BLUE BLUE YELLOW GREEN	RED GREEN YELLOW BLUE	YELLOW YELLOW RED RED
BLUE YELLOW RED YELLOW GREEN	RED YELLOW GREEN BLUE RED	BLUE BLUE YELLOW GREEN RED	RED GREEN YELLOW BLUE BLUE	YELLOW YELLOW RED RED BLUE
BLUE YELLOW RED YELLOW GREEN BLUE	RED YELLOW GREEN BLUE RED GREEN	BLUE BLUE YELLOW GREEN RED GREEN	RED GREEN YELLOW BLUE BLUE RED	YELLOW YELLOW RED RED BLUE GREEN

Stroop Color-and-Word test

RED	YELLOW	BLUE	YELLOW	GREEN		
YELLOW	BLUE	RED	BLUE	BLUE		
RED	RED	GREEN	GREEN	RED		
GREEN	GREEN	YELLOW	YELLOW	YELLOW		
YELLOW	BLUE	BLUE	RED	BLUE		
BLUE	GREEN	GREEN	YELLOW	GREEN		
GREEN	YELLOW	RED	BLUE	RED		
BLUE	RED	YELLOW	RED	YELLOW		
RED	RED	RED	GREEN	RED		
YELLOW	GREEN	BLUE	BLUE	GREEN		
BLUE	BLUE	YELLOW	GREEN	YELLOW		
GREEN	YELLOW	GREEN	YELLOW	BLUE		
BLUE	BLUE	GREEN	RED	BLUE		
YELLOW	RED	BLUE	BLUE	YELLOW		
BLUE	GREEN	RED	GREEN	YELLOW		
RED						
	YELLOW	YELLOW	GREEN	GREEN		
GREEN	YELLOW RED	YELLOW RED	GREEN YELLOW	GREEN RED		
GREEN RED						
	RED	RED	YELLOW	RED		

Name:	ame: Date:																		
the state	1	2	3		1	2	3		1	2	3		1	2	3		1	2	3
Green				Red				Yellow				Red	4			Blue			
Red				Yellow				Green				Yellow				Yellow			
Green				Green				Blue				Blue				Green			
Blue				Blue				Red				Red				Red			
Red				Yellow				Yellow				Green				Yellow			
Yellow				Blue				Blue				Red				Blue			\square
Blue				Red				Green				Yellow				Green			
Yellow				Green				Red				Green				Red			
Green				Green				Green		*		Blue				Green			
Red				Blue				Yellow				Yellow				Blue			
Yellow				Yellow			ь	Red				Blue				Red			
Blue				Red				Blue				Red				Yellow			
Yellow				Yellow				Blue				Green				Yellow			
Red				Green				Yellow				Yellow				Red			
Yellow				Blue				Green				Blue				Red			
Green				Red				Red				Blue				Blue			
Blue	T			Green				Green				Red				Green			
Green				Yellow				Red				Green				Blue			
Yellow				Blue				Yellow				Green				Yellow			
Red				Green				Blue				Blue				Red			

Scoring sheet for the Stroop Color, Word, and Color-and-Word tests

Total Part 1 (Word Reading):

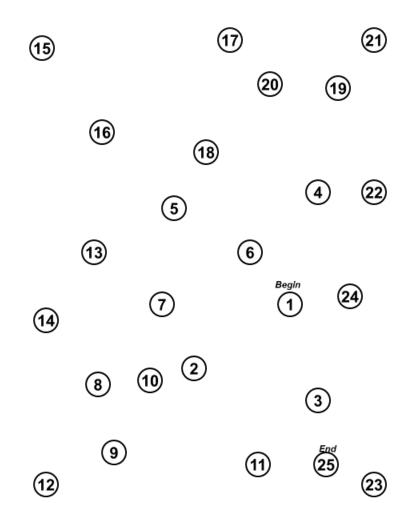
Total Part 3 (Color-Word):

Total Part 2 (Color Naming):

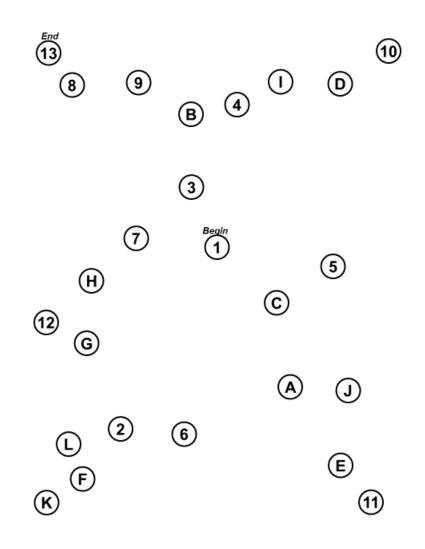
Color-Word Errors:

Appendix C

Trail Making Task A



Trail Making Task B



Appendix D

Rey Auditory Verbal Learning Test

PI: Dr. Kristin Kilbourn

Protocol #: 16-2138

Is disruption of the human gut microbial environment associated with cognitive impairment following chemotherapy for breast cancer? **REY AUDITORY VERBAL LEARNING TEST (RAVLT)**

RAVLT Scoring Sheet

Name:

Date/Time: _____

Examiner:

Learning Trials										
List A	A1	A2	A3	A4	A5	List B	B1	A6*	A7*	List A
drum						desk				drum
curtain						ranger				curtain
bell						bird				bel
coffee						shoe				coffee
school						stove				schoo
parent						mountain				parent
moon						glasses				moor
garden						towel				garder
hat						cloud				ha
farmer						boat				farme
nose						lamb				nose
turkey						gun				turkey
color						pencil				colo
house						church				house
river						fish				rive
# intrusions	-									
# correct										

Total # Correct (Learning Trials):

A1 + A2 + A3 + A**4** + A5

Percent Recall (%): A7 ÷ A5

Total # of Intrusions: A1 + A2 + A3 + A4 + A5 + B1 + A6 + A7

* Note: Do not reread List A for Recall Trial A6 or A7

Division of Health Care Policy and Research, UCHSC, Aurora, CO Chemotherapy and Cognition in Women with Breast Cancer - RAVLT Sample Scoring Sheet (01/25/05)

Appendix E

Questionnaire to Collect Weekly Caffeine Consumption

Subject ID _____ DAY 1

Date_____

CAFFEINE CONSUMPTION DIARY (CCD)

Please answer the following questions as completely and honestly as you can. This information is STRICTLY CONFIDENTIAL – do not write your name anywhere on this page. Thank you for your cooperation.

Log all item that you consume each day. Pay close attention to the size (in oz) of each product. For example, if you drink 10 oz of coffee this would count for 2 servings

(5 oz servings) 6am-12nn 12nn-6pm 6pm-2am 2am-6am Regular brewed	COFFEE	MORNING	AFTERNOON	EVENING	NIGHT
Percolated	(5 oz servings)	6am-12nn	12nn-6pm	6pm-2am	2am-6am
Percolated			<u>^</u>	<u>^</u>	
Drip-brewed					
Espresso shot	Percolated				
Regular instant	Drip-brewed				
Regular instant	Espresso shot				
Decaffeinated Brewed Instant	Regular instant				
Instant					
TEA (5 oz serv)	Brewed				
(5 oz serv)	Instant				
(5 oz serv)					
COCOA (5 oz serv)	TEA				
(5 oz serv) MORNING AFTERNOON EVENING NIGHT (2 oz serv) 6am-12nn 12nn-6pm 6pm-2am 2am-6am Diet Coca-Cola	(5 oz serv)				
CHOCOLATE (8 oz serv) MORNING 6am-12nn AFTERNOON 12nn-6pm EVENING 6pm-2am NIGHT 2am-6am Diet Coca-Cola Dr. Pepper	COCOA				
(8 oz serv) MORNING 6am-12nn AFTERNOON 12nn-6pm EVENING 6pm-2am NIGHT 2am-6am Coca-Cola	(5 oz serv)				
SOFT DRINKS (12 Oz. Serv) MORNING 6am-12nn AFTERNOON 12nn-6pm EVENING 6pm-2am NIGHT 2am-6am Diet Coca-Cola Diet Coca-Cola Dr. Pepper	CHOCOLATE				
(12 Oz. Serv) 6am-12nn 12nn-6pm 6pm-2am 2am-6am Diet Coca-Cola	(8 oz serv)				
(12 Oz. Serv) 6am-12nn 12nn-6pm 6pm-2am 2am-6am Diet Coca-Cola	SOFT DRINKS	MORNING	AFTERNOON	EVENING	NIGHT
Coca-Cola	(12 Oz. Serv)				2am-6am
Diet Coca-Cola					
Dr. Pepper					
Diet Dr. Pepper					
Mountain Dew	Dr. Pepper				
Diet Mountain Dew					
Mr. Pibb					
Diet Mr. Pibb					
Tab					
Pepsi Cola					
Diet Pepsi Cola					
RC Cola					
Mello Yello					
Diet Mello Yello Root Beer Red Bull					
Root Beer Red Bull					
Red Bull					
OVER-THE-COUNTER					
DRUGS (Tablets) Vivarin NoDoz Excedrin Vanquish Anacin Dristan	Red Bull				
DRUGS (Tablets) Vivarin NoDoz Excedrin Vanquish Anacin Dristan	OVER THE COUNTER				
(Tablets) Vivarin NoDoz					
NoDoz					
Excedrin					
Vanquish Anacin					
Anacin Dristan					
Dristan					
Dexatrim					
	Dexatrim				

Adapted from the CCQ by R.E. Landrum 1988

Participants will be asked to fill in 7 sheets, one for each day of the week.

Appendix F

Demogra	phics	Survey
00000	0	00.00,

Time of Appointment: _____

Demographics

1. How old are you?

2. Please identify your bio	logical sex:	
[] Male	[] Female	e [] Prefer not to answer
3. Please indicate the follo	owing that descr	ibe you:
[] White		
[] Black or African Ameri	can	
[] Asian		
[] American Indian or Ala	iska Native	
[] Middle Eastern or Nor	th African	
[] Native Hawaiian or Ot	her Pacific Island	der
[] Some other race, ethn	icity, or origin	
Are you Hispanic or Lating	o? []Yes	[] No
4. Please indicate the yea	r of college you a	are currently in:
[] Freshman (0-29 credit	hours passed)	[] Sophomore (30-59 credit hours passed)
[] Junior (60-89 credit ho	urs passed)	[] Senior (90+ credit hours passed)
5. What is your current GI	PA? (If this is you	ur first semester at the university, please provide high school
GPA)		

6. What is your current major? (If undecided, please write N/A) _____

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