CALIFORNIA STATE UNIVERSITY, NORTHRIDGE

ACTIVATIONAL EFFECTS OF ESTROGEN ON COGNITIVE PERFORMANCE IN WOMEN DURING DIFFERENT PHASES OF MENSES

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Arts in Psychology, Clinical Psychology

By

Jaime Ann Sanam

May 2014
The thesis of Jaime Ann Sanam is approved:

________________________________________  __________________

Luciana Laganà, Ph.D.  Date

________________________________________  __________________

Gary S. Katz, Ph.D.  Date

________________________________________  __________________

Jill Razani, Ph.D., Chair  Date

California State University, Northridge
DEDICATION

This thesis is dedicated to:

My family

A special thank you to my father, Roy, for instilling in me the compassion and drive that I have to accomplish my goals. To never give up, even when things get rough because perseverance is essential in life. He taught me that there are multiple ways in solving one problem; tenacity is within the mind. Furthermore, a special thank you to my mother, Rita, for providing the support and strength for me to continue in my course of academia. During times of defeat, my mother gave me her strength in order to find my own, without her willingness to sacrifice herself, I would have been crushed long ago. Additionally, my brother, Sean, who has provided me with the insight and realization that regardless of whatever barriers or struggles we may face, we have the power to get up and try again. His courage to endure a new day, regardless of what battles the previous day held, is an admirable trait that one can only wish to maturate into. Lastly, a special thank you to my sister, Marcelle, whose relentless ambition has inspired me to push through. She has proven that determination overcomes almost any challenge or stigmatizing label that tries to hinder success.

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TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signature page</td>
<td>ii</td>
</tr>
<tr>
<td>Dedication</td>
<td>iii</td>
</tr>
<tr>
<td>Acknowledgment</td>
<td>iv</td>
</tr>
<tr>
<td>List of Tables</td>
<td>vii</td>
</tr>
<tr>
<td>Abstract</td>
<td>viii</td>
</tr>
<tr>
<td>CHAPTER I – INTRODUCTION</td>
<td></td>
</tr>
<tr>
<td>General Information about Gender Specific Hormones and Cognition</td>
<td>1</td>
</tr>
<tr>
<td>Definitions</td>
<td>1</td>
</tr>
<tr>
<td>Female Menstrual Cycle</td>
<td>4</td>
</tr>
<tr>
<td>Specific Cognitive Effects of Sex Hormones and Female Menstrual Cycle</td>
<td>6</td>
</tr>
<tr>
<td>Oral Contraceptives and Specific Cognitive Effects of Sex Hormones</td>
<td>9</td>
</tr>
<tr>
<td>Purpose of the Present Study</td>
<td>11</td>
</tr>
<tr>
<td>Hypotheses</td>
<td>11</td>
</tr>
<tr>
<td>Assumptions</td>
<td>12</td>
</tr>
<tr>
<td>CHAPTER II- METHODOLOGY</td>
<td></td>
</tr>
<tr>
<td>Procedure</td>
<td>13</td>
</tr>
<tr>
<td>Participants</td>
<td>14</td>
</tr>
<tr>
<td>Measurements</td>
<td>15</td>
</tr>
<tr>
<td>CHAPTER III – RESULTS</td>
<td></td>
</tr>
<tr>
<td>Statistical Analysis</td>
<td>20</td>
</tr>
<tr>
<td>CHAPTER IV – DISCUSSION</td>
<td></td>
</tr>
<tr>
<td>REFERENCES</td>
<td>28</td>
</tr>
<tr>
<td>APPENDIX A: Figures</td>
<td></td>
</tr>
<tr>
<td>1: Displaying Means of All Measures</td>
<td>34</td>
</tr>
<tr>
<td>2: Displaying Marginal Significance of the Stress Arousal Checklist</td>
<td></td>
</tr>
<tr>
<td>APPENDIX B</td>
<td></td>
</tr>
<tr>
<td>1: Human Subject Approval Form</td>
<td>35</td>
</tr>
</tbody>
</table>
LIST OF TABLES

Table 1- Participant Demographics 38
ABSTRACT

ACTIVATIONAL EFFECTS OF ESTROGEN ON COGNITIVE PERFORMANCE IN WOMEN DURING DIFFERENT PHASES OF MENSES

By

Jaime Ann Sanam

Master of Arts in Psychology,

Clinical Psychology

The purpose of this study is to examine the effect of sex hormones on non-reproductive behavior and cognitive abilities in younger women. The current project included the examination of the effects of estrogen on cognitive performance during the midluteal and menses phase of menstruation. Specifically, we (a) examined whether oral contraceptives affect cognitive performance and depressive symptomology during these two phases (b) examined whether differences in performance levels occur between women who use oral contraceptives and women who take a natural course of menstruation, and (c) whether other cognitive functions, such as memory, information processing, and mood are affected by estrogen during both phases of menses. The researchers used a repeated measures design to test younger women (n=6 women who used some form of hormonal influence, n=31 women who do not use any method of hormonal influence) with a normal functioning menstrual cycle (28-32 days) using Vandenberg’s Mental Rotation Task, the Stroop, the Stress Arousal Checklist, the
California Verbal Learning Test, and the Center for Epidemiological Studies-Depression Scale during both phases of menstruation. A multivariate analyses of variance was conducted and showed a main effect in assessment measures, however we found no main effect in phase or the interaction of assessment and phase. A paired samples t-test showed a marginally significant result with the stress arousal checklist, specifically negative arousal. This study seems to imply that neither the phase of estrogen in women, nor the level of estrogen can be directly linked to cognitive performance.
General Information about Gender Specific Hormones and Cognition

Hormonal secretion has been observed between genders to differentiate specific cognitive strengths. While testosterone has an influential impact on spatial ability and mathematical reasoning for men, estrogen has a positive effect on verbal memory and fluency, perceptual speed, and fine motor skill for women (Kimura & Hampson 1993; Kimura 1996). However, the largest gender difference produced is characterized by spatial ability when comparing men to women. This difference has also been shown when factoring in menstrual phases in women with a decrease in mental rotation tasks during the late follicular and midluteal phases (elevated estrogen levels), while higher performance has been shown during menses (low gonadal hormone levels). This hormonal influence or “activational effect” on non-reproductive behavior can be further explored to provide preventative solutions of cognitive decline or impairment during later years of one’s lifespan. For example, the use of estrogen replacement therapy has shown a decrease in the risk of Alzheimer’s disease in healthy postmenopausal women (Vranić & Hromatko, 2008). Research has also suggested that high estrogen levels (HEL) suppress right hemisphere functions (spatial ability) while enhancing the left hemisphere (verbal ability and memory) of the brain (Hatta & Nagaya, 2009).

Memory and information processing are crucial to one’s well-being. Working memory serves the moment-to-moment monitoring, processing, and maintenance of information in everyday tasks and self-care (Vranić, & Hromatko, 2008). How individuals’ process information gives insight to attention and the filtration of stimuli,
while showing deficits in this area can be harmful to normal human functioning (Groth-Marnat, 2009; Kolb & Whishaw, 2009). For instance, inadequate results may reflect neurological decline involving the level of distraction, incoherent thinking, impaired judgment, loss of insight, high agitation, and delusions (Gitelman, 2003). Memory and information processing are important hemispheric functions; exploration of both and preventing such cognitive tasks from becoming impaired during later years is imperative. However, most research has been conducted on older adults, those coming close to premenopausal symptoms or already having begun the menopause process; therefore, research on younger women is needed. Furthermore, the usage of contraceptives are increasing, as postponing childbirth from early twenties to early thirties has become a common trend and is socially acceptable in Western societies (Wharton, Merritt, Paris, Hirshman, Doyle, & Gleason, 2008). Therefore, the need to investigate the effects of contraceptives with younger women and cognition is critical and may also be significant when compared to natural effects (Wharton, Merritt, Paris, Hirshman, Doyle, & Gleason, 2008).

Definitions

Prior to presenting all the research some definitions need to be established. To begin, the term activational effects was coined after some research conducted by Doreen Kimura in order to term sex-hormones influence on non-reproductive behavior; studies on non-reproductive gender differences suggested that cognitive tests might have been influenced by the variations of estrogen and testosterone blood levels (Kimura, 1996). Activational effects of these hormones, specifically estrogen in this case, act upon brain patterns and behavior, which are synced prenatally, known as organizing effects (Kimura
& Hampson, 1994; Moody, 1997; O’Connor, Archer, Hair, & Wu, 2004; Hausmann, Slabbekoorn, Van Goozen, Cohen-Kettenis, & Güntürkün, 2000). For example, animal studies have shown that early exposure to estrogen in both men and women, has produced long term organizational effects on visuo-spatial abilities, however, these abilities are phasic and occur during puberty and throughout adulthood (Slabbekoorn et al., 1998; Williams, Barnett, & Meck, 1990).

Additionally, human subjects who have been exposed to diethylstilbestrol (DES) and children with congenital androgen hyperplasia (CAH), in relation to these organizing effects has been studied. DES is a non-steroidal estrogen, which has an androgenizing effect on the brain when taken orally, resulting in DES exposed women having more masculine patterns of lateralization when compared to their control group of unexposed women (Hines & Shipley, 1984). In comparison, DES exposure in men ended up reducing their hemispheric laterality and lowered spatial ability when compared to their control group of unexposed men (Reinisch & Sanders, 1992). Lastly, CAH leads to increased levels of adrenal androgens in both boys and girls, which resulted in degrees of masculinization in female genitalia in women and precocious puberty in men (Reinisch, Gandelman, Spiegel, 1979). Helleday and colleagues observed CAH women in relation to cognitive patterns on spatial ability and verbal tasks and found a more masculine cognitive pattern in these women when compared to their matched control group (Helleday, Bartfai, Ritze´n, Forsman, 1994).

Organizing effects are the permanent structures and changes in brain activity during fetal development when the brain is exposed to different levels of sex hormones, but activational effects refers to the changes these sex hormones induce from the pubertal
stage, when there is an increase of hormone levels (Torres, Gómez-Gil, Vidal, Puig, Boget, & Salamero, 2006). In other words, the way in which we are wired at birth changes during times of menstruation for women due to the fluctuation of sex hormones. Further explanation on the interaction of these sex hormones and their levels during phasic menstruation is presented in the female menstrual cycle section below.

Next, spatial ability is the capacity to understand the relations among objects (e.g., to think about objects in a 3-dimensional form and draw conclusions with a limited amount of information). This would include mentally rotating the object in order to see how it would look from a different angle. In sum, spatial ability is a task that requires spatial orientation as well as mental rotation (Eals & Silverman, 1992). Furthermore, information processing corresponds to the attention involving manipulating, storing, and retrieving information, along with the processing speed of such activities (Hatta & Nagaya, 2009). Lastly, verbal memory, which includes tasks associated with verbal pairings, verbal learning, and logical memory (Torres et al., 2006) is considered a female favoring tasks, according to Kimura (1996).

**Female Menstrual Cycle**

The female menstrual cycle is regulated by two hormones, which are secreted by the pituitary gland. These hormones are known as the follicle-stimulating hormone (FSH) and luteinizing hormone (LH). However, research findings supporting the effects of these hormones on cognitive functioning have been debated and inconsistent (Hatta & Nagaya, 2009; Kozaki & Yusachouchi, 2009; Vranic & Hromatko, 2008). With that being said, one study has reported evidence suggesting that FSH is negatively correlated to visuospatial scores, whereas LH is positively correlated (Hausmann et al., 2000).
Furthermore, these two hormones regulate the production of estrogen and progesterone in a woman’s ovaries. The average menstrual cycle lasts around 28 days; however, it can range from 24 to 42 days (The menstrual cycle, 2013). In relation to the female menstrual cycle, three major phases occur, which will be explained below separately, in order, beginning with the menstrual phase.

The menstrual phase is defined as the time in which the endometrium - consisting of blood, mucus, and tissue - sheds; this time is commonly known as a period. This is considered day one in the menstrual cycle process and lasts approximately 3 to 7 days. Moreover, reduced levels of estrogen and progesterone from the previous menstrual cycle trigger menstruation, which is why this phase is generally considered as a phase for testing in studies that are based upon women’s menstrual cycles (Hatta & Nagaya, 2009; Kozaki & Yusachouchi, 2009; Vranic & Hromatko, 2008; Hausmann et al., 2000; Slabbekoorn et al., 1998). Additionally, FSH is secreted, which initiates the next phase of menstruation known as the follicular phase (Vranic, & Hromatko, 2008; Wharton, Hirshman, Merritt, Doyle, Paris, & Gleason, 2008).

The follicular and proliferative phase is when the follicles in the ovaries develop and mature in preparation for ovulation, which is caused by an increase in FSH. During this time the ovaries produce estrogen in order to thicken the uterus wall. Once estrogen peaks, the secretion of FSH decreases, while LH begins to flow. This process releases the ovum from the ovary in order to travel through the fallopian tubes, which is known as ovulation. Ovulation usually occurs 14 days before the next menstrual phase and is considered the time in which estrogen is at its highest level (HEL) in women, which is why this time frame is typically chosen by researchers as an optimal time for cognitive

Thus, the luteal phase or secretory phase of menstruation occurs after ovulation. This causes the follicle to burst and develop into the corpus luteum, which is a small yellow structure in the ovary that secretes estrogen and progesterone. During the secretory phase, both hormones of estrogen and progesterone are high in order to nourish the fertilized egg. However, if no fertilization occurs, LH will be reduced and FSH will begin to be produced. In contrast, the absence of LH will destroy the corpus luteum, in turn lowering the levels of estrogen and progesterone and simultaneously preparing the body for the menstrual phase once again (Vranić, & Hromatko, 2008; Wharton, et al., 2008).

**Specific Cognitive Effects of Sex Hormones and Female Menstrual Cycle**

Sex hormones and the effects on cognition have been studied since the early 1990’s (Kimura & Hampson, 1994; Kimura, 1996; Moody, 1997; Chipman & Kimura, 1998). Research in this area began with a study on animals, as researchers found an influence on cognition during critical periods in development, such as just before and after birth, during sexual encounters, and in adulthood (Kimura & Hampson, 1994; Kimura, 1996; Moody, 1997; Chipman & Kimura, 1998). For example, high levels of ovarian hormones, estrogen and progesterone facilitate sexual activity in many species, during the fertile phase, as well as high levels of testosterone in males. These effects seemed to alter an animal’s behavior when the animal came across sexual encounters, as well as in neural circuits and problem solving abilities (Kimura & Hampson, 1994). These findings suggest that sex hormones could have a variety of effects on
neurochemistry, modulating neurotransmitters, as well as induce structural changes.
Studies of the impact of hormonal fluctuation on cognitive abilities in human subjects followed, resulting in similar observations in both men and women. In women, studying such activational effects on cognition was provided by the menstrual cycle because it is a natural paradigm to investigate such influences, providing phases with both high and low levels of estrogen for a comparison between phases. For instance, Kimura compared men’s and women’s spatial abilities and found that women with high levels of testosterone and men with low levels of testosterone completed their task on the mental rotation task (MRT) better than their counterparts. Furthermore, women performed better on spatial ability tasks using the MRT during the menstrual phase (low levels of estrogen) than when they experienced high levels of estrogen (during midluteal phase). In contrast, women’s performance on female-favoring tasks, such as verbal memory and fine motor skills during high levels of estrogen was much better than during times of low estrogen. This suggests that sex hormones play a vital role in specific gender-favoring tasks. It appears that estrogen enhances verbal, memory, and fine motor abilities while testosterone improves spatial ability and mathematical reasoning (Kimura, 1996). On a similar note, Hausmann and colleagues reported a decrease in spatial ability with increased estrogen levels, whereas spatial performance seemed to increase for women if testosterone levels increase, but not for men, when testing research participants with the MRT (Hausmann et al., 2000). Moreover, Hausmann and colleagues found that performance during the midluteal phase decreased a women’s spatial ability tasks score when compared with their results during the menses phase, which concluded that spatial ability is sensitive to fluctuations of sex hormones (Hausmann et al., 2000).
Additional research has contributed to the notion that women perform better on female-favoring tasks and worse on male-favoring tasks during menstrual phases of high estrogen levels (late follicular and midluteal phases). For example, Sherwin (2012) conducted a study using a cross sectional longitudinal design in which estrogen replacement therapy in healthy premenopausal women protected them from verbal ability decline and decreased their risk of Alzheimer’s disease. In comparison, a study done by Slabbekoorn and colleagues on activating effects on cognitive function in transsexuals and showed that female-to-male (FM) individuals (i.e., females undergoing sexual reassignment to become biological males) after hormonal therapy eventually did better on spatial ability tasks, whereas, male-to-female (MF) individuals eventually did better on female-favoring tasks (Slabbekoorn et al., 1999). Additionally, Sherwin (2012) found that menopausal women increased their spatial ability test scores following oophorectomy (Sherwin, 2012). Furthermore, estrogen replacement therapy (ET) in women before the age of 65 years old was 50% less likely to develop some form of dementia (Sherwin, 2012). However, this finding by Sherwin was not affected by timing, age of participant, or duration of treatment, which left Sherwin to explain such effects of ET as a neuro-protective effect or the healthy cell bias of estrogen action. Sherwin (2012) describes this, healthy cell bias, as a theory of “beneficial effects of estrogen on the survival of neurons that are healthy at the time of their exposure to this sex hormone, but that an exacerbation of neurological demise occurs if exposure to estrogen occurred in previously compromised neurons” (Sherwin, 2012).

In contrast, studies have shown that this sex difference does not remain stable over the course of one’s lifetime and that these hormonal influences may be associated to
age-related sex differences (Hatta & Nagaya, 2009; Vranic & hromatko, 2009; Kimura & hampson, 1994). Additionally, these activational effects of sex hormones on non-reproductive behavior may depend on the individuals’ cognitive abilities to begin with, such as attention, memory, and verbal fluency (Hatta & Nagaya, 2009). Female-favoring tasks increase during high levels of estrogen and the same for men, according to the aforementioned researchers. Hatta and Nagaya (2009) speculate that high estrogen levels during the midluteal phase will suppress the right hemisphere function, while enhancing the function of the left hemisphere. Hatta and Nagaya found that estrogen levels affected attention and suggested this was due to the hemispheric influences that sex hormones have on the brain (Hatta & Nagaya, 2009).

**Oral Contraceptives and Specific Cognitive Effects of Sex Hormones**

Oral contraceptives (OCs) contain synthetic estrogen that is similar across a variety of different OCs (Wharton, et al., 2008). On the other hand, the androgenic activity, which is a synthetic creation of progesterone, greatly varies across all forms of OCs (Batur, Elder, and Mayer, 2003; Wharton, et al., 2008). Women who use oral contraceptives are exposed to higher levels of progesterone and do not fluctuate into high levels of estrogen during the midluteal and late follicular phases, as do women who choose a natural course. Batur, Elder, and Mayer (2003) found that women using OCs perform better on mental rotation tasks when compared to women who take a natural course due to higher levels of androgens (Batur, Elder, and Mayer, 2003). However, in contrast, Wharton and colleagues have found a decrease in verbal reaction time occurring due to low levels of estrogen in OC users (Wharton et al., 2008).
Oral contraceptives can be divided into three groups based on the level of androgenic activity in each; second-generation pills, third generation pills, and anti-androgenic pills. Second generation pills have progestin, which is derived from testosterone and third generation pills were built in order to lower the androgenic activity, so they have less progestin when compared to second-generation pills. In contrast, the anti-androgenic pill has the least amount of androgenic activity of all three groups. What is important about these three forms of OCs is not only the grouping of androgenic activity, but the way in which progestin is released throughout the menstrual cycle. For instance, monophasic pills provide a consistent does of progestin throughout the 28-day cycle, whereas triphasic pills increase the amount of progestin released throughout the cycle, replicating a more natural cycle and having the highest amount of progestin toward the end of the cycle. Second generation pills are typically monophasic, while third generation pills are generally triphasic, while anti-androgenic pills have the least amount of progesterone and are also static across the cycle (Batur, Elder, and Mayer, 2003).

When examining the differences among anti-androgenic users, non-users, third generation users, and second-generation users on mental rotation tasks, the anti-androgenic users performed poorly when compared to nonusers. Whereas second generation users outperformed non-users on mental rotation tasks, engaging in high androgenic activity that may enhance visuospatial performance, equaling better performance on spatial ability tasks (Wharton, et al., 2008). Other studies have not been able to identify the hormone specifically influencing test results, whether progesterone or estrogen. However, high levels of estrogen appeared to significantly influence visuospatial and motor skills (Kimura & Hampson, 1994). Furthermore, in a study on
individuals with a condition of congenital adrenal hyperplasia (CAH), where there is an excess of androgens during fetal life, Van Goozen and colleagues (2002) found a significant enhancement in spatial ability when compared to those unaffected, in addition to, androgen administration increasing spatial ability tasks in female-to-male transsexuals (Van Goozen, Slabbekoorn, Gooren, Sanders, & Cohen-Kettenis, 2002; Resnick, Berenbaum, Gottesman, & Bouchard, 1986). This also suggests an influence of androgens on cognitive skills with high levels increasing on male-favoring tasks, while decreasing on female-favoring ability tasks.

**Purpose of the Present Study**

In the current project, we examined activational effects on spatial ability, memory, and information processing in women during the midluteal and menses phase of menstruation. In comparison to previous research, we seek to test influences of sex hormones on non-reproductive behavior, such as cognitive performance. Currently, the gender gap regarding spatial ability has been shown in several different studies and tested using the MRT between menstrual and midluteal phases (Wharton, et al., 2008; Hatta & Nagaya, 2009; Vranic & hromatko, 2009; Kimura & hampson, 1994; Kozaki & Yasukouchi, 2009; Hausmann, et al., 2000; Hampson, 1990a, 1990b; Phillips & Silverman, 1997). In the current project, we explored whether fluctuations of estrogen would decrease spatial ability performance as well as two other important cognitive functions that are relevant to cognitive decline as one increases in age, memory and information processing.

**Hypotheses**
First it is hypothesized that spatial ability performance during the midluteal phase will be significantly lower when compared to the menses phase in women. Secondly, we hypothesized that memory and information processing during the midluteal phase will also be significantly lower when compared to cognitive performance during the menses phase in women. In addition, we intend to explore in more depth factors such as differences in cognitive performance between the midluteal and menses phase in women using oral contraceptives. Furthermore, we explored whether a difference will be present between women who use oral contraceptives and women who choose no method of hormonal influence concerning cognitive performance.

Assumptions

This research study was created based upon certain assumptions, with the first being that participants will answer all questionnaires and checklists honestly and that the measures given are appropriate for the age group and ethnicity of the subject pool provided. Additionally, we assumed that no errors would be made during data entry and during the data analyses. This project is also under the assumption that participants have a normal functioning menstrual cycle (28-32 days) and fall within the age group specified prior to conducting assessments.
CHAPTER II

METHODOLOGY

Procedures

Participants were recruited by convenient and snowball sampling (i.e., word of mouth). Data was collected in the Los Angeles area with the majority of participants being University students in the San Fernando Valley. At California State University, Northridge, students were recruited from the Psychology Department Participant Pool. As for snowball sampling, those already participating from CSUN were asked to “spread the word” about the current study to fellow classmates, friends, and family members who fit the criteria (age, gender, and menstruation cycle length). Additionally, the researcher used forms of social networking (Facebook, classmates, Twitter) to recruit potential candidates as well.

This project was conducted over a 3-day period; the first day consisting of participants being told about the current study, given consent forms, and administered the one-time menstrual cycle questionnaire, which is averaged around 10 minutes to complete in a group setting. The counting method within a 28-day cycle was used to assess the menstrual phase for each participant starting with her last menstrual date provided within the questionnaire. Days one through five were considered the menses phase in which the participant will have low estrogen levels (LEL) and days fifteen through twenty-eight were the midluteal phases where the participants will have high estrogen levels (HEL) (Wharton et al., 2008). Ovulation occurs approximately fourteen days before the next menstrual cycle in women, which correlates with the counting method being used (Vranić & Hromatko, 2008).
The second day of this project began the first trials of assessments during either menses phase of menstruation (individually dependent) in which the participants were asked to be available for an estimated hour and a half. This day will started in a group setting with the administration of the Center for Epidemiological Studies - Depression Scale (CES-D, Knight, Williams, McGee, & Olaman, 1997; Radloff, 1977) followed by the California Verbal Learning Test - Short Form (CVLTMOD-SF, (Delis, Kramer, Kaplan, & Ober, 1987; Woods, Delis, Scott, Kramer, & Holdnack, 2006) with the ten-minute delay. In the meantime, participants were asked to fill out the Stress Arousal Checklist, upon completion, they were then asked to recall the CVLTMOD-SF word list on a piece of paper with their assigned identification number. After all materials were collected the subjects were given a ten-minute break in order to relax, get refreshments or food, or use the restroom. Once the ten-minute break was over, the respondents were given the MRT followed by the Stroop color word test, which is the only assessment that was administered on an individual basis. Upon completion of the MRT, participants were asked to step outside and wait while researchers conducted the Stroop color word test individually. Once that task was completed, subjects were able to leave. The third day of assessments was constructed around the opposite phase, individually dependent, and consisted of the same procedure of assessments described above, with the addition of the contraceptive checklist.

Participants

We received a total of 42 participants, but only 37 subjects were able to complete the experiment. The remaining five subjects were eliminated from the study due to not completing all measures (absent during phase testing N=3), not fulfilling all
qualifications (not having a normal menstrual cycle N=1), and/or insufficient results (with the CES-D N=1). The studied population was women between the ages of 18 to 35 who experienced a normal functioning menstrual cycle (i.e., 28-32 day cycle). The mean age of women was 19 years old with an average menstrual cycle lasting 28 days, which fit the normal menstrual cycle requirement to participate in this study. The average age in beginning puberty was 12 years old with the majority of participants referring themselves as celibate. The participant demographic information is listed in Table 1.

**Measurements**

The instruments used will be employed for the two menstrual phases, menses and midluteal phases in women. All measures are listed in the order that they will be administered administration.

*Menstrual Cycle Questionnaire*

This questionnaire consists of 20 questions revolving around menstruation, which took approximately five minutes to complete and will be administered only once to the respondents. This questionnaire is contained in a public file online and is commonly used to assess menstrual phase, use of contraceptives, and functioning of menstrual cycle (28-32 day cycle).

*California Verbal Learning Test-Short Form*

This measure is a 9-word item list that is repeated several times aloud by the test administrator followed by the participant and ending with a 30-second distractor interval. However, this tool was changed for this project to the 9-word item list being stated aloud, one by one, first by the administrator and then repeated by the participant and recalled after a 10-minute delay. Due to this change the CVLT-SF will be referred to as the
CVLT-MOD. The scoring will result in receiving one point per correct word recalled on the list and will serve to quantify one’s memory. The test-retest correlation ranges from .80 to .84; however, practice effects may occur (Delis, Kramer, Kaplan, & Ober, 1987; Woods, et al., 2006). The CVLT-II short form reliability coefficients range from .72-.79 with a test-retest reliability of .82 (Delis, Kramer, Kaplan, & Ober, 1987).

Cronbach’s alpha .615.

Contraceptive Questionnaire

This is a checklist of multiple forms of contraception that can be used today in order to normalize an abnormal menstrual cycle, as well as to avoid pregnancy and/or sexually-transmitted diseases, or for other medical and contraceptive reasons. This original tool is a list of contraceptive methods created in collaboration with Dr. Luciana Laganà. It was used in order to assess the participant’s method of contraceptive, if any, in addition to information that could be used in post-hoc analyses, including brand, frequency, and dosage of the contraceptive used. This is important to assess due to the various forms of hormonal influences that some methods of contraceptives may have. Furthermore, via administering this questionnaire, we will assess issues of side effects that may serve as a confounded explanation to testing results. Cronbach’s alpha was at .475.

Center For Epidemiological Studies-Depression Scale

This instrument is a 20-item depression scale to assess the number, types, and duration of depressive symptoms across racial, gender, and age categories within the last 7 days (Knight, Williams, McGee, & Olaman, 1997; Radloff, 1977). Depressive symptomology is rated using a 4-point rating scale, where 0 equals “rarely” and 3 equals
“most or all of the time” (Radloff, 1977). This is one of the most popular measures used to assess depressive symptomology; it has a strong Cronbach’s alpha for internal consistency is .83. This tool was used in this project to assess mood change symptomology that could serve as a confound affecting one’s performance scores between phases.

*Stress Arousal Checklist- Form A and B*

The stress arousal checklists consist of a 30-item instrument, with 18 items on stress and the other 12 items on arousal, revolving around the individual’s mood and psychological experience within the last 7 days. The categories of stress and arousal are broken up into subcategories for further investigation. For instance, the 18 items under the stress category are subcategorized into ten positive stress items (e.g. distressed, nervous, uptight) and eight negative stress items (i.e. calm, relaxed, content). Furthermore, the 12 arousal items are broken up in a similar fashion, seven positive (e.g. alert, active, lively) and five negative items (e.g. sleepy, tired, drowsy). Each form has the exact same word list, however, words are rearranged in a different order to avoid practice effects between both assessment days. Both variables are assessed using a 4-point rating scale, where (++) equals “definitely feel”, one (+) sign equaling “likely applies to feelings, a question mark (?) representing “not clear or cannot decide”, and last, a minus (-) sign equaling “definitely not feeling” (McCormick, Walkey, & Taylor, 1985). The Cronbach’s alphas of internal consistency are .65. Cronbach’s alphas for the two item scales are .57 for stress and .52 for arousal. Additionally, the reliability for the four subscales are stress positive .66, stress negative .87, arousal positive .68, and arousal negative at .56.
This checklist was used in order to assess any stress arousal confound that could affect one’s performance during assessments.

**Vandenberg Mental Rotation Task- Form A**

The Vandenberg Mental Rotation Task (MRT) assesses spatial ability. This is done using adjoining cube drawings conveying a 3-dimensional target figure following four similar figures in different rotations in which participants must identify two figures that match the target figure. This is a 24-item scale divided into two trials, 12-items each trial, with a timed limit of 4 minutes per trial to complete, following a 4-minute break in between trials. For the purpose of this project, however, this scale was divided between menstrual phases (Caissie, Vigneau, & Bors, 2009). Specifically, the first 12 items were administered during day one of assessments and the following 12 items were given on the second day of assessments. In order to avoid practice effect confounds within this experiment, the MRT trails were given interchangeably during both days of assessments; some participants were given trial one and others were given trial two. This is the most widely used spatial ability assessment showing the highest gender gap difference (Kimura, 1998). One point per correct answer was given within the time limit, with a maximum of 48 points being received upon completion. Cronbach’s alpha for internal consistency is .88.

**Stroop Color Word Test**

This measure consists of three trials in order to assess attention and information processing speed. To begin, participants were asked about impairments revolving around color blindness prior to conducting this assessment. The first trial is a congruent task in which participants read the color patch names aloud to the administrator with of a time of
90 seconds (i.e. red, green, and blue). The next trial consists of word reading, where subjects read the words written in black ink aloud to the administrator within 90 seconds. Lastly, in the incongruent task, known as the inhibition condition, respondents were asked to name the color of the printed ink rather than the conflicting printed color word within a 180 second time constraint (i.e. the word “red” printed in blue ink). For the sake of this project, times between each trial was compared between phases in order to justify any cognitive difference in testing results. The test-retest correlation reported in the literature is .80 (Oosthuizen & Phipps, 2012) and Cronbach’s alpha is .83.
CHAPTER III
RESULTS

Statistical Analysis

Multivariate Analyses of Variance (MANOVA) were conducted in order to compare both phases of menstruation and cognitive performance, as well as to compare performance levels across women who use contraceptives during both phases of menstruation. Although the expectation while starting this experiment was to compare both groups of women (those using some form of hormonal influence and those who use no method of hormonal influence), there were not a sufficient amount of participants in the hormonal group for comparison. All data analyses were based specifically on the comparison between menstrual phases and cognitive performance in women only.

A MANOVA was conducted in order to assess cognitive performance on five different measures, known as the California Verbal Learning Test-Modification, Center for Epidemiological Studies-Depression Scale, the Stress Arousal Checklist, Mental Rotation Task-3D, and the Stroop color word test, during two different phases of menses, known as the midluteal phase and follicular phase. Wilks’Lambda, the most commonly used test statistic, according to Tabachnick and Fidell (2012) was used in the present study. Results revealed a significant main effect of the assessment measures, $F(4, 32)=215.482, p<0.05$. However, there was no main effect of estrogen levels, $F(1, 35)=.666, p>0.05$; nor was there a significant interaction effect of assessment and estrogen levels, $Measures \times Phase F(4, 32)= .228, p>0.05$. The main effect of assessment measures may be due to the method variance; the Stroop shows the most differentiation in scores (see Figure 1), being a timed score to represent speed in this task, while using a summed score...
assessed the other measures. Nonetheless, given that the focus of this study was not on different performance of the five measures when averaged over the two phases, no follow-up analysis was performed.

*Paired Sample T-Test*

The main effect in the assessments (measures), however, did pique interest in more closely examining differences between the two phases for the four subscales of the Stress Arousal Checklist (SACL) created for this study. The four subscales of this checklist are referred to as positive and negative stress and arousal. T-tests did not reveal a difference between the two phases for three of the four subscales of the SACL; positive stress, $t(38)=-1.199, p>.05$, negative stress, $t(38)=-.136, p>.05$, and positive arousal, $t(38)=-.692, p>.05$. It should be noted, however, that negative arousal showed marginally significant results, with phase two (HEL) scoring higher ($M=2.7692$) on this subscale when compared to phase one’s (LEL) score ($M=2.3590$), $t(38)=-1.709, p=.096$. 
CHAPTER IV
DISCUSSION

The purpose of this study was to examine the effects of estrogen on cognitive performance in women during different phases of menses. Although previous research has suggested that the fluctuation of estrogen levels between menstrual phases has had an impact on cognitive performance (Chipman & Kimura, 1998; Collins & Kimura, 1997; Slabbekoorn, et al., 1991; Gomez, et al., 2009), we found no such evidence. Assessing scores on measures of spatial ability, memory, processing speed, and emotional competence, we found no difference in scores between high and low levels of estrogen.

This discrepancy between the current study and those of previous ones may be due to the fact that those others studied the difference in cognitive scores between men and women, while the current study focused on cognition and behavior during two estrogen phases in women. For instance, Chipman and Kimura (1998) found significant differences between scores of men and women on specific tasks, such that women scored higher than men on verbal memory tasks, while men scored higher than women with spatial ability. Furthermore, another reason for the discrepancy between our findings and that of others may be due to task complexity. Collins and Kimura (1997) found significant results in spatial ability when comparing men to women on levels of MRT difficulty favoring men (i.e. 2D task vs. 3D task), whereas in this experiment, spatial ability was only assessed using the MRT 3D measure. Additionally, Slabbekoorn and colleagues (1999) and Gómez-Gil and his colleagues (2009) not only tested participants on both levels of difficulty on the MRT (2D & 3D), they also provided tools to assess fine motor skills, verbal memory, visual memory, and processing speed over the course
of 3 to 6 months. Slabbekoorn et al. (1999) and Gomeź et al. (2009) found significant results in male-to-female (MF) transsexuals and female-to-male transsexuals (FM) over the course of their hormone treatment; FM had increased scores on spatial ability, while MFs excelled after treatment in verbal memory and processing speed (Slabbekoorn, et al., 1999; Gómez-Gil et al., 2009).

In contrast, Hatta and Nagaya (2009) provided similar tests to this project however found significance only in attention with women when compared to their male counterparts, specifying that attention may also be a gender specific task. In comparison, Wharton et al. (2008) found significant results in measures while factoring in levels of androgens (testosterone) in men and women, suggesting androgenic activity may have more of an effect alone or in combination with estrogen on cognitive performance.

Other research examining estrogen levels have provided support for the findings of this current study. For instance, Kozaki and Yasukouchi (2009) studied both high and low levels of estrogen and found no significant results on the MRT task and Vranić and Hromatko (2008) found no significant difference in performance on memory during different phases of menstruation. Similar to the current study, both studies tested estrogen levels indirectly, which may have contributed to their insignificant results.

Taken that previous studies have found differences between males and females on cognitive performance, some of those studies have been able to directly link these differences to hormonal variations between the genders. Our study and that of other researchers that indirectly measured estrogen seem to imply that neither the phase of estrogen in women, nor the level of estrogen can be directly linked to cognitive performance.
Further analyses were conducted on the four subscales of the stress and arousal checklist (SACL). The findings indicated marginal differences in the negative arousal subscales of the SACL. With a larger sample size, this effect may have reached statistical significance. The results showed that between phase one (LEL) and phase two (HEL) the negative arousal scale increased for participants, which means that during high levels of estrogen our respondents felt more tired, drowsy, sluggish, and/or sleepy. Hatta and Nagaya (2009) found that differences in cognitive performance due to the modulation of sex hormones were unlikely to be related to mood status. While we did not examine the relationship between negative mood and cognition impairment, we believe it warrants further investigation.

**Limitations**

As with every study, current research does present some limitations. The first limitation in this study is the small sample size of participants for a multivariate analysis. The small sample size for this study could have possibly lead to reduced statistical power, which in turn may not have allowed us to find small effect sizes between groups. A second limitation may have been the set requirements to participate in this study, as well as the age group needed for comparison and research. Although age was not apart of either hypothesis, the mean age group (M=19) is typically inexperienced in contraceptives and usage (see Table 1), which resulted in the dismissal of the goals stated previously. This limitation did not allow us to fully test the hypothesis that the form of contraceptive used affects cognitive scores between hormonal phases.

There was also a third limitation of time constraint. Assessments were given within a month of each other and only repeated once for comparison. This short time
period may have lead to practice effects on some measures, specifically with the Center for Epidemiological Studies-Depression Scale (Radloff, 1977) and the Stroop color word test (Bohen, 1991; Homack & Riccio, 2004). Although, due to the unlimited influence of hormones on cognition, conducting research on this topic quickly is essential to providing markers for future experiments. Lastly, having a more reliable source of assessing estrogen levels in women would be critical in receiving accurate results. While the counting method may have been used reliably in prior research, it is difficult to quantify high or low levels of estrogen during each menstrual phase.

**Future Research**

Overall, these findings may potentially expand our understanding of how sex hormones affect cognition by eliminating variables and/or directing research in the future. It is be suggested, due to the limitations of this project, to first have a larger sample size in order to increase statistical power. Secondly, seek a wider age range in the research participants so that age effects in relation to hormonal influences on cognition can be explored. Furthermore, it is suggested to conduct a longitudinal repeated measures design with possibly longer time between testing intervals.

Additionally, androgen effects need to be studied in this type of study. For instance, testosterone alone and combined with estrogen showed both strong and positive influences on the MRT, as shown by Slabbekoorn and colleagues (Slabbekoorn, et al., 1999). The effects of androgens in female to male transsexuals, resulted in high performance scores on spatial ability with high levels of testosterone, in comparison to low scores on spatial ability with high levels of estrogen (Slabbekoorn, et al., 1999). In prior research, as participants went through androgen treatment, spatial ability scores
increased slowly while the combination of estrogen and testosterone occurred and increase significantly once these individuals transitioned fully (within 3 months of treatment). Three months of treatment is considered a sufficient amount of time for an individual to have sex hormones in the same range of the opposite sex (Meyer, Webb, Stuart, Finkelstein, Walker, 1986). However, this induction of hormones in transsexuals is difficult to compare to non-transsexual women due to the extreme enhancement of testosterone when compared to the natural production of testosterone in women. Further research on the contribution of each hormone individually and in combination with one another is essential to this research. Additionally, hormonal effects on cognition, as shown in research mentioned above, varies by level of testosterone and estrogen, but individuals are known to have higher or lower levels of each hormone naturally. With that being said, the natural levels of testosterone and estrogen, unique to each individual, should be further explored and Ethnicity may be a great contributor to this natural hormonal bias. Therefore, it is lastly suggested to begin conducting this research on one ethnicity to start.

To conclude, further investigation of the effects of sex hormones in relation to cognitive performance is critical in not only understanding specific gender strengths and weaknesses, but also in order to understand the effects of such hormones on mental abilities in later years. Additional research in the area of cognitive decline and the hormonal influences associated with it is imperative in the advancement of preventative solutions. In order to understand how we cognitively age, we must first understand how we are mechanically wired. Insight and further investigation on both activational and
organizational effects would provide more understanding to the complexity of these biological influences.
REFERENCES


A study of short-term and long-term hormone effects in transsexuals.


performance in younger individuals. *Experimental and Clinical Psychopharmacology*,
16(2), 156-164. doi:10.1037/1064-1297.16.2.156


Figure 1: Displaying Means of All Measures
APPENDIX B

Human Subjects Approval Form

Student Researcher

HUMAN SUBJECTS PROTOCOL APPROVAL FORM
CALIFORNIA STATE UNIVERSITY, NORTHRIDGE

1. Title of research
   Activational Effects of Estrogen on Cognitive Performance in Women During Different Phases of Menses

2. Principal Investigator
   Jaime Sanam
   Major or Department Psychology

3. Home Address
   18111 Nordoff Street
   Northridge, CA
   Mobile phone 909-908-7571
   Email Address jaime sanam 67@my.csun.edu

4. Co-Investigators:
   1. Student: [Student ID]
   2. Student: [Student ID]

5. Name of Faculty Advisor
   Jill Razani
   Faculty Advisor ext. 4623
   Faculty Advisor email address: jill.razani@csun.edu

6. Projected Dates of Data Collection:
   Begin Subject Recruitment/Data Collection: October/November 2013
   End Data Collection: January/February 2014

7. Course prefix and number for thesis/grad.
   Psy 698C
   Course title Thesis or Graduate project

8. Check one:
   ☒ Unfunded
   ☐ Funded
   Name of Funding Source: [Funding source]
   Date (to be) submitted

9. History of Protocol:
   ☒ New
   ☐ Continuing (Previous Approval Date)

10. Existing Data: Will this study involve the use of existing data or specimens (Data/specimens currently existing at the time you submitted this project)?
    ☒ No
    ☐ Yes
    If Yes, attach documentation indicating the authorization to access the data if not publicly available and if accessing from an agency outside of CSUN.

11. Subjects to be recruited (Check all that apply)
   a. ☒ Adults (18+ years)
   b. ☐ Minors specify age: [Age]
   c. ☐ Cognitively or Emotionally Impaired Persons
   d. ☒ CSUN Students
   e. ☒ Others (describe) non-CSUN student, 18 years or older, women only.
   f. ☐ Using existing data

12. Data will include (check all variables that apply): You must specify all of this information in the Project Information form.
   a. ☒ names of people
   b. ☒ email address
   c. ☒ street address
   d. ☒ phone numbers
   e. ☒ age
   f. ☒ gender
   g. ☒ ethnicity
   h. ☐ marital status
   i. ☐ income
   j. ☐ social security number
   k. ☐ job title
   l. ☐ names of employers
   m. ☐ types of employers
   n. ☐ physical health report
   o. ☒ zip code
   p. ☐ other, specify: [Specify other]
   Date of birth: [Date]

13. Will subjects be identified by a coding system(i.e., other than by name)?
    YES ☒ NO ☐
14. Is compensation offered? YES □  NO ☒
15. If yes, describe (e.g., gift cert., cash, research credit). ____________________________

16. Number of Subjects: 30-50

17. Method of recruiting (elaborate in Section 2 of Project Information Form): convenient sampling, snowball sampling.

18. Will there be any deception (that is, not telling subjects exactly what is being tested)? YES □  NO ☒
(Provide justification for deception and explain how subjects are debriefed in Section 2 of the Project Information form)

19. Potential Risk Exposure (cannot leave blank): ☒Physical □Psychological □Economic □Legal □Social □Other, specify: fatigue (cannot be “none” or “N/A”)
(Elaborate in Section 4 of the Project Information Form)

20. Data Collection Instruments (Check all that apply) 21. Recorded by (Check all that apply)
   a. ☒standardized tests  a. ☒written notes
   b ☒questionnaire  b. □audio tape
c. □interview  c. □video tape/film
d. □other (specify)__________________________ d. □photography
e. □observation

22. Administered by (Check all that apply) 23. Findings used for (Check all that apply)
   a. ☒in person (group setting)  a. ☒publication
   b. ☒in person (individual)  b. □evaluation
   c. □telephone  c. □needs assessment
d. □text message  d. ☒thesis/dissertation
e. □email/website e. □other (specify): ____________________________
f. □mail
g. □other (specify): ____________________________

24. Are drugs or radioactive materials used in this study? YES □  NO ☒
   If yes, then list the drugs or radioactive materials used in Section 1 of the Project Information form and provide a detailed description of each, with justification for its use.

25. Are any medical devices or other equipment to be used in this study? YES □  NO ☒
   If yes, describe in detail the medical devices or equipment to be used in Section 2 of the Project Information Form.

26. Did you attach a copy of any questionnaire(s), survey instrument(s) and/or interview schedule(s) referred to in this protocol?  
   YES ☒  NO □

27. Is a letter of permission for subject recruitment attached (if recruiting from an organization outside of CSUN)?  
   YES □  NO ☒

28. SIGNATURES:
   **All Signatures must be obtained prior to submission. Student projects must have faculty advisor’s signature.**
   Faculty signature on this Protocol Approval Form indicates that:
   • You and your student are familiar with the regulations for human subject research as defined by California State University, Northridge's Standing Advisory Committee for the Protection of Human Subjects (SACPHS) and you and your student intend to follow those regulations when conducting this study. You have reviewed and approve of this Protocol Approval Form and accompanying documentation.
You approve of the manner in which human subjects will be involved in this study.

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<th>Date</th>
<th>Student Investigator's Signature</th>
<th>Date</th>
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FOR SACPHS AND RESEARCH OFFICE USE ONLY
- [ ] Noted, exempt
- [ ] Approved, Minimal Risk
- [ ] Approved, Greater than Minimal Risk
- [ ] Approved, Expedited Review

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**LIST OF TABLES**

Table 1

*Participant Demographics*

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<td>( SD )</td>
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