The Effects of Exogenous Sex Hormones on Cognition in Female College Students

Lily Otto

Sponsor: Lauren Harburger, Ph.D.

Second Reader: Yanine Hess, Ph.D.

Submitted to the department of Natural Sciences

Purchase College, State University of New York

Abstract

The current study examined differences between women taking hormonal contraceptives and naturally cycling women on object memory using 2-dimensional object arrays and in spatial memory by using the 3D Vandenberg Mental Rotation Task (Vandenberg & Kuse, 1978). The HC group had higher mean scores for all object array conditions and the mental rotation task compared to the NC group. The sample size for this study was small and therefore, results are not final or conclusive.

The Effects of Exogenous Sex Hormones on Cognition in Female College Students

Hormones are chemical substances, secreted by glands and transported through the bloodstream to specific receptors on target cells. They can be secreted endogenously (naturally within the body) or taken exogenously (hormones put into the body). Exogenous sex hormones are typically known as oral contraceptives, or birth control, containing forms of estrogen and/or progesterone. Oral contraceptives are medications taken by mouth to aid in preventing pregnancy or regulating the hormones involved with the menstrual cycle. According to the American College Health Association, about 40% of college women are on the pill to prevent pregnancy. Furthermore, other forms of hormonal contraceptives include: the pill (combination or progesterone only), the patch, nuvaring, IUD, and injections. Sex Hormones can also be used in a treatment called hormone replacement therapy (HRT). This is used when a woman's hormone levels (estrogens/progesterone) decrease, typically after menopause. Previous studies examined the effects of HRT on cognition; however, limited research has been conducted on young college-aged females taking hormonal contraceptives. This study will contribute to the limited research on exogenous sex hormones (estrogen and progesterone) on cognition in college-aged females. In addition, this is the first study to examine the effects of exogenous hormones in college females on an object array task and a spatial ability task. It is hypothesized that hormones will increase performance on both the object array and spatial ability task. Thus, it is important to study the effects of exogenous hormones on cognition in hopes to better understand the chemicals that individuals are putting into their bodies.

Cognitive Effects of Estrogen

In rodents.

Several studies have found cognitive effects of exogenous estrogen treatments in rodents. Luine et al., (2003) tested ovariectomized rats using injections (before and after tasks) of various types of estrogens. They wanted to see whether estrogen would have an effect on object recognition and object placement. Rats had to distinguish between old and new places, as well as old and new presented objects. Researchers determined if rats were interested by the amount of time they spent with each object/place. The study concluded that both object and place task performance was enhanced when estrogens were given immediately after sample trials, but not when injections were delayed (Luine, Jacome, & Maclusky, 2003).

Another study examined the relationship of estrogens on executive functioning, memory, and inhibitory control. Wang et al., (2008) investigated young adult ovariectomized rats and tested their delayed spatial alternation (DSA), delayed alteration working memory task, and differential reinforcement of low rates of responding (DRL). Researchers state that in past literature, estradiol administration improves spatial working memory tasks, including the radial arm maze. Furthermore, researchers suggest that both the prefrontal cortex and the hippocampus are generally affected by extensive hormonal treatment when looking at learning and memory. The study examined 30 young adult rats that were separated into three groups: ovariectomized with long-term estradiol implants, ovariectomized with cholesterol implants, and sham ovariectomies and cholesterol implants acting as a control group. Rats were tested on behavioral actions such as response shaping and lever-pressing using cued alterations, noncued alterations and delayed spatial alterations for 25 sessions. Few significant differences were found, however, estradiol-treated rats performed significantly worse than cholesterol-treated rats in the cued alterations and the DSA task. High estradiol levels appeared to heighten responses to lever-pressing which then impaired performance on the task (making more errors). In addition,

estradiol-treated rats did not differ from intact rats on the DRL and pressed more levers. This study states that estrogen generally has been reported to have positive effects on the prefrontal cortex (Wang, Sable, Ju, Allred, Helferich, Korol, & Schantz, 2008). More research should be done to study the effects of estrogens on executive function, memory and inhibitory control.

In humans.

Beneficial effects of estrogen have been shown on cognition in elderly women. Duka et al., (2000) investigated frontal lobe function and the effects of estradiol on memory. Thirty-seven women over the age of 50 were tested. The unique aspect of this study is that the estrogen hormone replacement was not for therapeutic reasons and the women were completely healthy. Researchers had women take either estrogen hormone replacement (transdermally) or a placebo. They were tested on frontal lobe functional tasks such as: CANTAB (intradimensional/extradimensional attention shifts), the Stroop Task, Random Number Generation Task, and a Mental Rotation Task. Each task was tested before and after the administration of estrogen or placebo. The study found that estradiol levels in the estrogen hormone replacement group increased to that of a fertile woman. Additionally, the mental rotation task improved greatly with the estrogen group compared to the placebo. This is important to note because the mental rotation task has a known male advantage, and this study shows that the estrogen enhanced performance for this task (Duka, Tasker, & McGowan, 2000). Thus, additional research should be conducted on estrogen administration alone and its effects on cognition.

Cognitive Effects of Estrogen and Progesterone

In rodents.

Estrogen and Progesterone may also have an effect on cognition in rodents. One study investigated sex differences and female sex hormones in object and spatial cognition in rats. Cost et al., (2012) stated that male rodents usually show an advantage over females in tasks that assess memory for the recognition or location of objects. Additionally, sex hormones such as estradiol and progesterone tend to influence the performance of female rodents on object recognition and object location tasks. Two experiments were conducted to compare the performance of male rats to female rats in various hormone states on the object-in-place task. This was done to see if various hormones affect cognition. The object-in-place task consisted of putting the rat in the center of an open space and allowed them to investigate four objects in an arrangement for three minutes. The position of two of the objects were switched, and the rats were measured on how long they spent investigating the objects. Results show that female rats outperform males on a memory task that combines object recognition and location. However, this is only when enhanced levels of the ovarian steroids, estradiol and progesterone, are presented (Cost, Williams–Yee, Fustok, & Dohanich, 2012).

Harburger, Bennett, & Frick (2007) examined whether estrogen, or estrogen and progesterone, affects consolidation of spatial memory in female ovariectomized mice. Two experiments were conducted, one including just estradiol, and the other including estrogen and progesterone to see if it would further enhance spatial memory. The mice completed eight training trials in the spatial Morris Water Maze before receiving injections of either 17-estradiol (control), or estrogen and progesterone (10 mg/kg or 20 mg/kg dose). All mice learned to find the platform on day one. On day two, both groups were tested again in the maze to determine whether or not the post-training hormone injections improved memory. Results suggested that estrogen enhanced memory for platform location; however, performance was not affected, or

decreased, with the addition of progesterone. The 10 mg/kg dose of progesterone did not affect estrogen's ability to enhance consolidation of spatial memory, but the 20 mg/kg dose blocked estrogen's effects. This indicated that estrogen can enhance spatial memory consolidation, but not in combination with progesterone (Harburger, Bennett, & Frick, 2007).

In humans.

Previous literature explored the effects of estrogen plus progestin on cognitive function in postmenopausal women. The Women's Health Initiative Memory Study (WHIMS) is an addition to the Women's Health Initiative (WHI) hormone therapy trials. Rapp et al., (2003) wanted to investigate whether estrogen plus progestin effects global cognitive function in postmenopausal women over the age of 65. A placebo-controlled, randomized, double-blind clinical trial was conducted by researchers to examine 4,381 women. Participants took either one daily tablet containing estrogen and progestin, or the placebo pill. A Modified Mini-Mental State Examination was given to assess global cognitive function and measured 15 parts comprised of 46 items. The total score could range from 0-100, with a higher score representing better cognitive performance. The examination measured: temporal and spatial orientation, all aspects of recall and memory, executive functioning, naming, verbal fluency, abstract reasoning, obeying commands, writing, and copying. Additionally, women took a demographic questionnaire, health and behavioral questionnaire, and a 34-question menopausal symptoms inventory. The purpose of this study was to evaluate hormone therapy with respect to baseline characteristics and health problems such as stroke, or dementia. Results show that women assigned to estrogen plus progestin therapy were more likely to have decreases in exam scores. In addition, memory skills in menopausal women do not considerably differ from postmenopausal women. Furthermore, the combined treatment increased risk of coronary heart disease, breast cancer, stroke, pulmonary

embolism, etc. In conclusion, this study contributes to the research examining effects of estrogen and progestin on cognitive functioning on postmenopausal women (Rapp, Espeland, Shumaker, Henderson, Brunner, Manson, ... & Johnson, 2003).

Another study contributing knowledge to the Women's Health Initiative Memory Study explored the effects of estrogen plus progestin on dementia and mild cognitive impairment with a placebo. Shumaker et al., (2003) examined postmenopausal women aging from 65-75 years, in hopes to better understand estrogens effects on the brain. They designed a randomized, double-blind, placebo controlled trial, giving participants either one daily tablet of conjugated equine estrogen, or a placebo. This eight-and-a-half- year trial was discontinued after about five years due to increased risk for other health problems. Participants were given a series of tests, standardized interviews, and clinical examinations to assess their cognitive functioning, baseline characteristics, behavioral symptoms and eligibility. The dementia protocol was divided into four phases, each containing mental and physical examinations. No significant differences were apparent between hormone and placebo groups at the baseline. Researchers concluded that the risk of being diagnosed with probable dementia was about three times greater in the estrogen and progestin group compared to the placebo. The risk of being diagnosed with mild cognitive impairment or dementia increased by about 37% for the hormonal group compared to the placebo. Thus, this study is useful in providing knowledge on estrogen and progestin effects on postmenopausal women (Shumaker, Legault, Rapp, Thal, Wallace, Ockene ... & Kotchen, 2003).

Duff & Hampson, (2000) examined the effects of estrogen in the prefrontal cortex using dependent or working memory tasks. They studied three groups of postmenopausal women (estrogen group, estrogen and progesterone group, and women not taking HRT) using a cross-sectional design. A series of tasks were given evaluating verbal working memory, spatial

memory, logical memory, and recognition memory. Results showed that women in the estrogen or estrogen/progesterone group had significantly better performance than women not on HRT. This demonstrated that estrogen may affect the prefrontal cortex and is capable of influencing functions dependent on this region. The results of this study raise the possibility that estrogen may play a role in maintaining certain frontal lobe functions in women.

Previous studies of older women receiving estrogen replacement therapy and studies of sexually dimorphic skills in young women express that estrogen and progesterone may affect cognition. Maki, Rich, & Rosenbaum, (2002) experimented on sixteen young women (ages 18–28) and initiated tests of memory (implicit category exemplar generation, category-cued recall, implicit fragmented object identification) and sexually dimorphic skills (fine motor coordination, verbal fluency, mental rotations). All participants were at the early follicular (low estrogen and progesterone) and midluteal (high estrogen and progesterone) phases of their menstrual cycle. Results suggest that increased levels of ovarian hormones might inhibit perceptual object preparation. In addition, these hormones decreased mental rotations and increased motor skills and fluency in the mid luteal phase. Estradiol levels associated positively with verbal fluency and negatively with mental rotations and perceptual priming. This suggest that estrogen, and not progesterone, was important when looking at changes in cognition (Maki, Rich, & Rosenbaum, 2002).

Recent literature examined the relationship between post-learning stressors, retention of memory (gist and detail), and sex hormones (women naturally cycling or women on hormonal contraceptives). Nielsen, Ahmed, & Cahill, (2014) hypothesized that women on hormonal contraceptives would have less hypothalamic-pituitary-adrenal reactivity when exposed to physical stress, compared to naturally cycling women. In addition, they predicted that post-

learning stress would not affect emotional memory for gist or detail for women on hormonal contraceptives. Researcher's hypothesis includes that in naturally cycling women, post-learning stress would improve emotional memory for gist and detail. Researchers inspected 60 naturally cycling women and 49 women on hormonal contraceptives. Participants filled out a screening questionnaire and three cognitive assessments (Bem Sex Roles Inventory, Positive and Negative Affect Schedule, and Mehrabian Test). Furthermore, participants provided multiple saliva samples, read a narrative story (either emotional or neutral), were assigned to either a CPS or control group (warm or cold water), and a 5-point calibration eye-tracking system. The study indicated that naturally cycling women produced significantly larger cortisol responses than hormonal contraceptive women. Additionally, only naturally cycling women in the stress condition expressed enhanced memory recall of gist and detail; hormonal contraceptive women had no emotional memory enhancement. Furthermore, women in the luteal phase of their menstrual cycle (where estrogen and progesterone are higher) expressed improved emotional memory for gist and detail. Overall a valuable contribution to research on post-learning stressors and memory recall with both naturally cycling and hormonal contraceptive women (Nielsen, Ahmed, & Cahill, 2014).

Cognitive Effects of Progesterone

In rodents.

Harburger, Pechenino, Saadi, & Frick, (2008) examined how progesterone modulates object and spatial memory consolidation in young ovariectomized mice. Object memory was tested in an object recognition task (24- and 48-h delays) while spatial memory was tested in the Morris water maze (Retention 24 or 48 h after training). Directly after training in each task, mice were given an injection of vehicle or 5, 10, or 20 mg/kg water-soluble progesterone.

Additionally, mice were tested 24 or 48 h later in the absence of circulating progesterone. Results conclude that post-training injections (10 and 20 mg/kg progesterone) enhanced object recognition, but not spatial memory. This proposes that young female mice may be more sensitive to the effects of progesterone on object memory consolidation than spatial memory consolidation. Thus, it is important to further research the effects of progesterone on cognition (Harburger, Pechenino, Saadi, & Frick, 2008).

Researchers suggest that progesterone may be negatively affecting cognition in women taking hormone replacement therapy. Bimonte-Nelson, Singleton, Williams, & Granholm, (2004) evaluated aged sham ovariectomized rats to see whether progesterone disturbs these cognitive-enhancing effects. Researchers examined working and reference memory of a water radial arm maze. They found that rats made more working memory errors on testing days compared to rats not given progesterone. Results suggest that progesterone inhibits aspects of performance regardless of how well female rats exercise spatial memory. This study gives insight to the effects of progesterone on cognition (Bimonte-Nelson, Singleton, Williams, & Granholm, 2004).

In humans.

Progesterone may have an effect on cognition in humans. Limited research has been conducted on progesterone alone in object memory and spatial ability tasks, however, it has been looked at in combination with estrogens. A study conducted by Wingen et al., (2007) examined progesterone's metabolite, allopregnanolone, in relation to amygdala activity and cognition. A single progesterone dose or a placebo was given orally to health young women. Participants were examined under functional magnetic resonance imaging (fMRI) and asked to memorize different human faces. Results of the study showed that progesterone decreased responses in the amygdala

to faces but increased hippocampal responses. This is interesting because the amygdala is important for the modulation of emotional memories while the hippocampus is responsible for the formulation and retrieval of working memory. (Wingen, Broekhoven, Verkes, Petersson, Backstrom, Buitelaar, & Fernandez, 2007).

Cognitive Tasks to Examine the Effects of Hormone Birth Control on Memory

Exogenous sex hormones may have an effect on cognitive tasks that contribute to memory. Hausmann et al., (2000) aimed to show that spatial cognition is influenced by fluctuating estrogen levels of the menstrual cycle. Participants donated blood samples in three-day intervals over six weeks to measure levels of estradiol, progesterone, luteinizing hormone, etc. They also took a mental rotation test, mirror picture test and hidden figure test to assess their spatial memory during different phases of their menstrual cycle. The Mental Rotation Test found a significant cycle difference in spatial ability, with high scores during the menstrual phase and low scores during the midluteal phase. Thus, results indicated that spatial performance is susceptible to hormonal fluctuations over the menstrual cycle. It is interesting to consider which brain regions mediate the beneficial effects of estrogen and progesterone on memory tasks. Hayes, Ryan, Schnyer, & Nadel (2004) analyzed frontal and medial temporal lobe structures during tasks of episodic memory. Sixteen participants were tested on their object, spatial and temporal memory as they watched a video of a house tour containing different objects and their spatial locations. In addition, participants were monitored via fMRI. Results suggested that during the retrieval of spatial-location information, the right parahippocampal gyrus expressed preferential activation. Furthermore, the right dorsolateral prefrontal cortex was associated with the retrieval of contextual information. Greater activation was also shown to be associated with processing visual scenes regardless of memory judgement in bilateral posterior parietal regions.

The study suggests that the hippocampal complex has a particular role in spatial-location memory, as well as the importance of frontal and medial temporal regions in episodic memory (Hayes, Ryan, Schnyer, & Nadel, 2004). Thus, different brain regions are linked to object and spatial memory that may be associated with fluctuating hormone levels.

Present Research

Endogenous sex hormones, such as estrogen and progesterone, may have an effect on cognition. These chemical substances are found in oral contraceptives, which is often used to regulate the menstrual cycle or prevent pregnancy and frequently used in college students. There is conflicting evidence in the literature regarding whether or not exogenous hormones benefit cognition. Thus, more research needs to be done to better understand its effects of exogenous hormone use on cognition in young women.

This study will contribute to the limited research on exogenous sex hormones (estrogen and progesterone) on cognition in college aged females. In addition, this is the first study to examine the effects of exogenous hormones in college females on an object array task and a mental rotation task. These tasks measures object memory and spatial ability. The overall purpose of this study is to evaluate whether estrogen and/or progesterone affect object and spatial memory.

Method

Participants

Participants included college undergraduate students from Purchase College. Thirty-four subjects were recruited through emails to students in psychology courses. There were 25 females and their ages ranged from 19-27 (M = 20.12, SD = 1.704). Participants were compensated with one credit for their psychology class.

Materials

Informed Consent Form. An informed consent form was created to state any important debriefing information such as: purpose of the study, procedure, confidentiality, voluntary, and risks/benefits. (See Appendix A).

Personal Information Questionnaire. A personal information questionnaire was developed to ask about hormonal contraceptive use and information regarding women's menstrual cycle. (See appendix B).

Object Array Task. The object array task measures object memory and consists of thirty-one black-and-white line drawings of familiar objects (Levy, Astur, & Frick, 2005). The participant was given the original array, and then given three different conditions (object-exchange condition, object-shift condition, and object-novel condition). They had one minute to circle either the exchanged object, shifted object, or new object depending on the condition given. The maximum possible score on each array is fourteen. This task typically has a female advantage. (See Appendix C).

Mental Rotation Task. The mental rotation task measures spatial ability and consists of twenty three-dimensional images produced by a computer (Vandenberg, & Kuse, 1978). Each question contains a target figure, and four stimulus figures. Two of the four choices are correct; the two correct are simply rotated. Participants had two minutes for three practice problems and then four minutes for 12 problems, a 4-minute break and then 4 minutes for the final 12 problems. Participants much chose the two correct stimulus that matches the target figure. This task typically has a male advantage. (See Appendix D).

Procedure

Participants first read and signed a consent form. Participants then were asked to complete an online survey (personal information questionnaire) in Qualtrics. At the end of the Qualtrics survey, participants were given a subject number and were asked to bring that to the in-person part of the experiment. Once they finished the questionnaire and signed up for a time, they came into the lab to complete the object array task and mental rotation task, using a pen and paper. Once completed, participants were debriefed, given credit and thanked for their time.

Results

Consistent with predictions, mean scores for women taking hormone contraceptives (HC) were higher for all object array conditions compared to naturally cycling women (NC; See figure 1). Independent t-tests were conducted for each array condition to examine differences between the two groups (HC vs NC). In the object exchange condition, there was no significant difference in the scores for HC group (M = 7.75, SD = 2.71) and NC group (M = 5.12, SD = 3.64); t (23) = 1.815, p = .083. In the object shift position, there was no significant differences in scores for the HC group (M = 4.38, SD = 2.72) and NC group (M = 4.06, SD = 1.95); t (23) = .333, p = .742. There was a significant difference in the object novel condition between the HC group (M =11.63 SD = .916) and the NC group (M = 9.41 SD = 2.12); t (23) =2.803, p = .010. Consistent with predictions, mean scores for women taking hormone contraceptives (HC) were slightly higher in the mental rotation task compared to naturally cycling women (NC; See figure 2). There was no significant differences between the HC group (M = 8.88 SD = 3.40) and the NC group (M = 8.71 SD = 5.43); t (23) =.080, p = .937.

In order to control for the effects of menstruation, we also compared women who were menstruating (n = 7) and women who are not menstruating (n = 17) during the time of testing. In the object exchange condition, there was no significant differences in performance between

women who were menstruating (*M* = 7.14, *SD* = 3.24) and women who were not menstruating (*M* = 5.47, *SD* = 3.74); t (22) = 1.031, p = .314. In the object shift condition, there was no significant differences in performance between women who were menstruating (*M* = 4.71, *SD* = 1.60) and women who were not menstruating (*M* = 4.06, *SD* = 2.38); t (22) = .664, p = .514. In the object novel condition, there was no significant differences in performance between women who were menstruating (*M* =10.0, *SD* = 2.38) and women who were not menstruating (*M* =10.18, *SD* = 2.10); t (22) = -.180, p = .859. In the MRT, there was no significant differences in performance between women who were menstruating (*M* = 7.43, *SD* = 3.91) and women who were not menstruating (*M* = 8.65, *SD* = 4.49); t (22) = -.626, p = .538.

Discussion

This study will contribute to the limited research on exogenous sex hormones (estrogen and progesterone) on cognition in college-aged females. In addition, this is the first study to examine the effects of exogenous hormones in college females on an object array task and a spatial ability task. It was hypothesized that hormones will increase performance on both the object array and spatial ability task.

The results showed an increase in scores for women taking hormonal contraceptives compared to naturally cycling women on the object array and mental rotations task. However, results were only significant for the object novel condition in the object array task. Although results were not significant for the other object array conditions, there was a noticeable trend in increasing scores of the HC group compared to the NC group Though mean scores for the MRT were higher in the HC group, it is possible that the MRT did not improve because of the floor effect (males perform better than females) on this task. In addition, both tasks may employ

different brain regions which could have skewed the results; the object array uses the perirhinal cortex and the mental rotation uses the hippocampus (Hayes, Ryan, Schnyer, & Nadel, 2004).

Previous research is inconclusive in stating whether estrogen and/or progesterone increases/decreases cognition. The beneficial effects of sex hormones in this study are consistent with previous reports demonstrating enhanced performance (Duff et al.,. (2000), Duka et al., (2000), Luine et al., (2003). Contrastingly, past literature was not consistent with the results of this study, showing no effect or decrease in scores on various tasks with the addition of female sex hormones (Bimonte-Nelson et al., (2004), Maki et al., (2002), Rapp et al., (2003), Wang et al., (2008). Multiple studies also stated that either estrogen and/or progesterone have differing effects on cognition depending on the task, dose and timing (Harburger et al., (2007), Harburger et al., (2008), Nielsen et al., (2014). Most previous studies have examined estrogen and/or progesterone on cognition in older populations in the form of hormone replacement therapy or HRT (Duff et al., 2000), Rapp et al., (2003).

This is the first study to report beneficial effects of estrogen and/or estrogen and progesterone as combined hormonal contraceptives in a young undergraduate female population. Nevertheless, other studies show benefits of female sex hormones on spatial tasks (Duff et al.,. (2000), Harburger et al., (2007). We found no effect on the MRT however, this is the first study to examine spatial memory in young undergraduate females. Perhaps, different results in the present study are due to the fact that hormone contraceptive regimens in young women are very different from hormone replacement therapy regimens in older populations. Furthermore, the present results may also differ from previous studies because we had a low sample size.

Our hypothesis was confirmed in that mean scores were increased on all tasks in the HC group compared to the NC group. However, the only significant results were in the object novel

condition of the object array task. In a larger sample size, results may have significantly shown differences between the two groups in all tasks and conditions. Therefore, future studies should have more participants.

When conducting the study, participants were asked specifics about their birth control and menstrual cycle however, it is important to note for future studies, the effects of each type of hormonal contraceptive, as well as controlling for whether or not the participant takes them as instructed (dose and timing). In addition, intervention studies should be considered. This would control for participants taking the same brand of birth control, having the same demographics, or ruling out certain confounds. Thus, future studies should continue to examine the effects of sex hormones on cognition in college-aged individuals.

References

Bimonte-Nelson, H. A., Singleton, R. S., Williams, B. J., & Granholm, A. E. (2004). Ovarian Hormones and Cognition in the Aged Female Rat: II. Progesterone Supplementation Reverses the Cognitive Enhancing Effects of Ovariectomy. *Behavioral Neuroscience, 118*(4), 707-714. doi:10.1037/0735-7044.118.4.707

Cost, K. T., Williams–Yee, Z. N., Fustok, J. N., & Dohanich, G. P. (2012). Sex differences in object-in-place memory of adult rats. *Behavioral Neuroscience, 126*(3), 457-464. doi:http://dx.doi.org/10.1037/a0028363

Duff, S. J., & Hampson, E. (2000). A Beneficial Effect of Estrogen on Working Memory in Postmenopausal Women Taking Hormone Replacement Therapy. *Hormones and Behavior, 38*(4), 262-276. doi:10.1006/hbeh.2000.1625

Duka, T., Tasker, R., & McGowan, J. F. (2000). The effects of 3-week estrogen hormone replacement on cognition in elderly healthy females. *Psychopharmacology, 149*(2), 129. http://ezproxy.purchase.edu:2048/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=a9h&AN=4693566&site=eds-live

Harburger, L. L., Bennett, J. C., & Frick, K. M. (2007). Effects of estrogen and progesterone on spatial memory consolidation in aged females. *Neurobiology of Aging, 28*(4), 602-610. doi:10.1016/j.neurobiolaging.2006.02.019

Harburger, L. L., Pechenino, A. S., Saadi, A., & Frick, K. M. (2008). Post-training progesterone dose-dependently enhances object, but not spatial, memory consolidation. *Behavioural Brain Research,194*(2), 174-180. doi:10.1016/j.bbr.2008.07.014

Hausmann, M., Slabbekoorn, D., van Goozen, S. H. M., Cohen-Kettenis, P. T., & Gu¨ntu¨rku¨n, O. (2000). Sex hormones affect spatial abilities during the menstrual cycle. Behavioral Neuroscience, 114, 1245–1250

Hayes, S. M., Ryan, L., Schnyer, D. M., & Nadel, L. (2004). An fMRI study of episodic memory: Retrieval of object, spatial, and temporal information. *Behavioral Neuroscience, 118*(5), 885-896. doi:http://dx.doi.org/10.1037/0735-7044.118.5.885

Luine, V. N., Jacome, L. F., & Maclusky, N. J. (2003). Rapid Enhancement of Visual and Place Memory by Estrogens in Rats. *Endocrinology, 144*(7), 2836-2844. doi:10.1210/en.2003-0004

Maki, P. M., Rich, J. B., & Rosenbaum, R. S. (2002). Implicit memory varies across the menstrual cycle: Estrogen effects in young women. *Neuropsychologia, 40*(5), 518-529. doi:10.1016/s0028-3932(01)00126-9

Mecklinger, A., Gruenewald, C., Weiskopf, N., & Doeller, C. F. (2004). Motor affordance and its role for visual working memory: Evidence from fMRI studies.*Experimental Psychology, 51*(4), 258-269. doi:http://dx.doi.org/10.1027/1618-3169.51.4.258

Nielsen, S. E., Ahmed, I., & Cahill, L. (2014). Postlearning stress differentially affects memory for emotional gist and detail in naturally cycling women and women on hormonal contraceptives.

Behavioral Neuroscience, 128(4), 482-493. doi:http://dx.doi.org/10.1037/a0036687

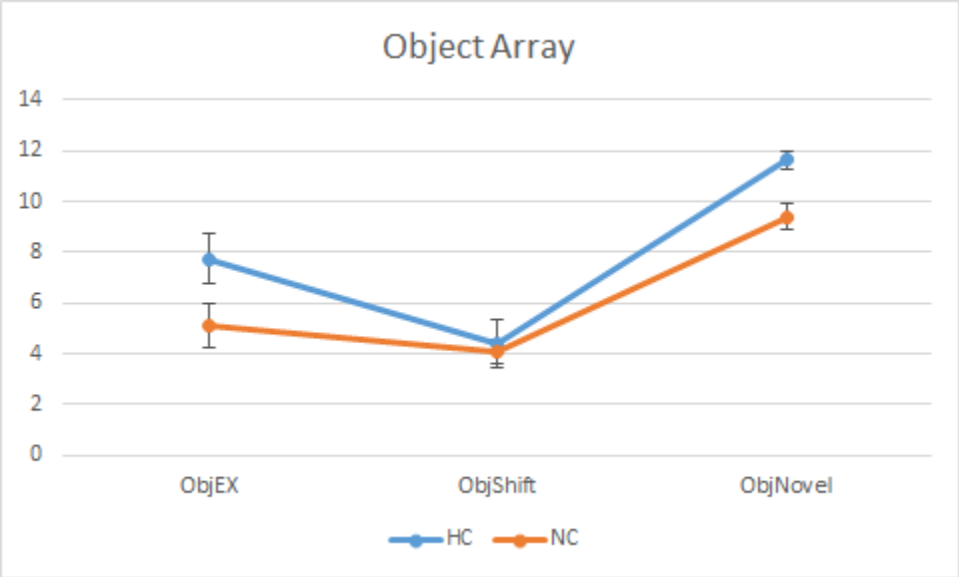
Rapp, S. R., Espeland, M. A., Shumaker, S. A., Henderson, V. W., Brunner, R. L., Manson, J. E., ... & Johnson, K. C. (2003). Effect of estrogen plus progestin on global cognitive function in postmenopausal women: the Women's Health Initiative Memory Study: a randomized controlled trial. *Jama, 289*(20), 2663-2672.

Shumaker, S. A., Legault, C., Rapp, S. R., Thal, L., Wallace, R. B., Ockene, J. K., ... & Kotchen, J. M. (2003). Estrogen plus progestin and the incidence of dementia and mild cognitive impairment in postmenopausal women: the Women's Health Initiative Memory Study: a randomized controlled trial. *Jama*, *289*(20), 2651-2662.

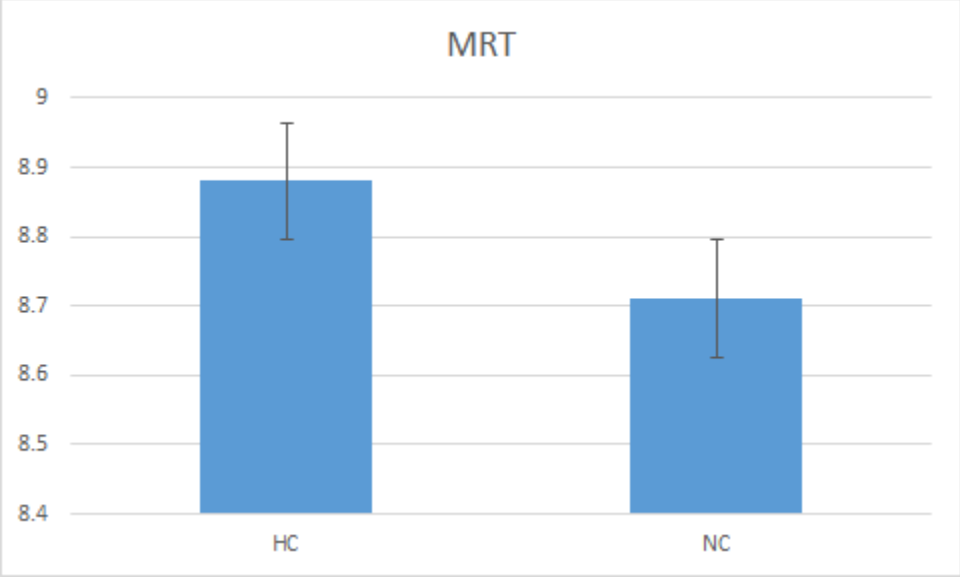
Wang, V. C., Sable, H. J. K., Ju, Y. H., Allred, C. D., Helferich, W. G., Korol, D. L., & Schantz, S. L. (2008). Effects of chronic estradiol treatment on delayed spatial alternation and differential reinforcement of low rates of responding. *Behavioral Neuroscience*, *122*(4), 794-804. doi:http://dx.doi.org/10.1037/a0012513

Wingen, G. V., Broekhoven, F. V., Verkes, R. J., Petersson, K. M., Backstrom, T., Buitelaar, J., & Fernandez, G. (2007). How Progesterone Impairs Memory for Biologically Salient Stimuli in Healthy Young Women. Journal of Neuroscience, 27(42), 11416-11423. doi:10.1523/jneurosci.1715-07.2007

(Figure 1)



(Figure 2)



Appendix A

Informed Consent Form

Informed Consent Form

Name of Study: The Effects of Exercise, Nicotine and Exogenous Hormone Use on Object Memory and Mental Rotation in Young Men and Women

Researchers: Principal Investigators: Kathleen Beach, Ethan Sua, Lily Otto, Nadia Shadi

Sponsor: Harburger

Contacts: Lauren.harburger@purchase.edu

Sponsor Email: Lauren.harburger@purchase.edu

Purpose: We would like permission to enroll you as a participant in a research study. This study investigates how multiple variables affect cognitive performance.

Procedure: In this experiment, you will be asked to complete a personal information questionnaire. The questionnaire will ask you personal questions ranging from drug and exercise habits to questions about your hormones. After the personal information questionnaire you will be asked to complete two cognitive performance tests. All information collected will be kept anonymous. The study should take approximately 60 minutes.

Costs, risks, and discomforts: This study has minimal risks. The personal information questionnaire may evoke some discomfort from reporting any personal information that one does not wish to share. This study is not mandatory and you can opt out at any time. Your identity will not be reported and will remain anonymous.

Benefits and compensation: The general benefit of participating in scientific research is the satisfaction that comes from contributing to science and the pursuit of knowledge. If applicable, participation in this research will allow college student participants to be compensated through class credit.

Confidentiality: The results of this study may be published in a scholarly book or journal or used for teaching purposes. However, your name and other identifiers will not be used in any publication or teaching materials. Your data will never be associated with your name or any other information that would make it possible to identify you.

Refusal or withdrawal of participation: You do not have to participate in this study. If you decide to participate, you can change your mind and drop out of the study at any time without affecting your present or future interactions with the experimenters and with no loss of credit for participation.

Signature: I confirm that the purpose of the research, the study procedures, the possible risks and discomforts, as well as potential benefits that I may experience have been explained to me. All my questions have been answered. I have read this consent form. My signature below indicates my willingness to participate in this study. I understand that I may contact the chair of the Institutional Review Board if I experience any problems during this experiment or have concerns about the ethics of this research [**irb.chair@purchase.edu**].

Type in your full name as your signature:

Appendix B

Personal Information Questionnaire

Q2

Personal Information Questionnaire

Age:

Q3

Sex:

- Male
- Female
- Non-Binary

Q4

Assigned sex at birth:

- Male
- Female

Page Break

Q5

Race (Choose all that apply):

- White/Caucasian
- African-American/Black
- Mexican-American
- Asian-American/Asian
- Puerto-Rican American
- Pacific-Islander
- Middle-Eastern
- American Indian
- Other Latino/Hispanic Origin
- Other

Page Break

Q6

Relevant Background Information

What were your scores on the SAT? (Type N/A if not applicable)

Reading and Writing

Q7
Math

Q8
What was your score on the ACT? (Type N/A if not applicable)

Page Break

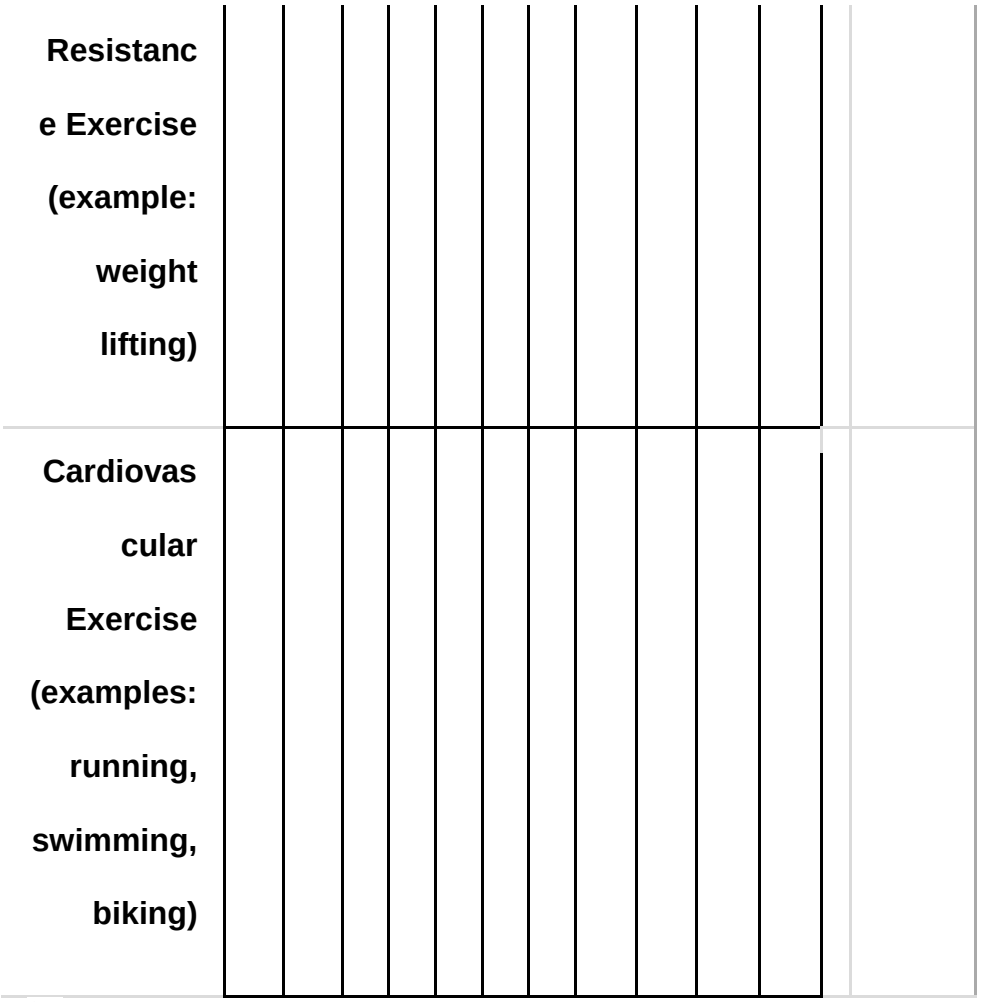
Q9
How many times per week do you exercise? (If none, type 0):

Display This Question:

If How many times per week do you exercise? (If none, type 0): Text Response Is Greater Than 0

Q10
How many minutes do you spend doing each type of exercise per week?

	0	15	30	45	60	75	90	105	120	135	150	Not Applicable
Stretch Exercise (examples: yoga, a type of dance, zumba)												



Q11
Are you currently part of a sports club, sports team or a dance program?

- Yes
- No

Page Break

Q12
Do you use (or have you used) any Nicotine products?

- Yes
- No

Display This Question:

If Do you use (or have you used) any Nicotine products? Yes Is Selected

Q13
What forms of nicotine delivery do/did you use? (Choose all that apply):

- Cigarette/Cigar Smoking

- Vaping
- E-Cig
- Hookah/Water Pipe
- Nicotine Gum
- Nicotine Patch
- Chewing Tobacco
- Other

Display This Question:

If Do you use (or have you used) any Nicotine products? Yes Is Selected

Q14
How long have you been a nicotine user? (Amount in years, months, weeks, or days):

Display This Question:

If Do you use (or have you used) any Nicotine products? Yes Is Selected

Q15
How many times a day do you use nicotine?

Display This Question:

If Do you use (or have you used) any Nicotine products? Yes Is Selected

Q16
How many times a week do you use nicotine?

Display This Question:

If Do you use (or have you used) any Nicotine products? Yes Is Selected

Q17
When was the last time you used nicotine? (Amount in minutes, hours, days, weeks, months, or years):

Page Break

Display This Question:

If Assigned sex at birth: Female Is Selected

Q18
Females Only:

What was the date of your last menstrual period? (Type N/A if you prefer not to answer):

Display This Question:

If Assigned sex at birth: Female Is Selected

Q19
Are you currently menstruating?

- Yes
- No
- Prefer not to answer

Display This Question:

If Assigned sex at birth: Female Is Selected

Q20
Do you have regular menstrual cycles?

- Yes
- No
- Prefer not to answer

Display This Question:

If Assigned sex at birth: Female Is Selected

Q21
Are you currently pregnant?

- Yes
- No
- Prefer not to answer

Page Break

Display This Question:

If Assigned sex at birth: Female Is Selected

Q22
Are you currently taking any type of birth control that uses artificial hormones including birth control pills or patch, Norplant, Depo Provera, or others?

- Yes

- No
- Prefer not to answer

Display This Question:

If Are you currently taking any type of birth control that uses artificial hormones including birth...Yes Is Selected

Q23
If so, what type and brand?

Page Break

Display This Question:

If Assigned sex at birth: Female Is Selected

Q24
Are you currently taking any type of estrogen and/or progesterone as prescription hormone therapy?

- Yes
- No
- Prefer not to answer

Display This Question:

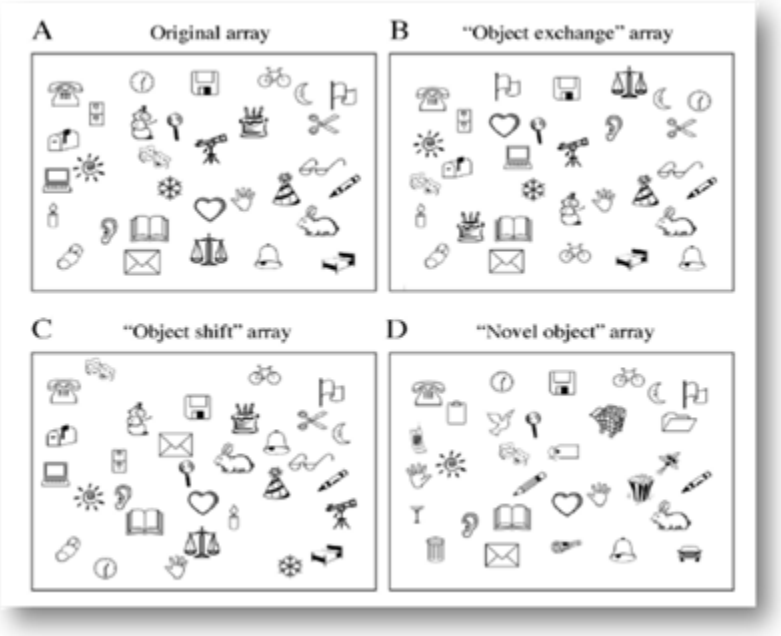
If Are you currently taking any type of estrogen and/or progesterone as prescription hormone therapy? Yes Is Selected

Q25
If so, what type and brand?

Page Break

Appendix C

Object Array Task



Appendix D

Mental Rotation Task