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The effect of oral contraceptives on performance in sexually dimorphic cognitive tasks

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by

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Abstract

The goal of the current study was to further extend limited research assessing the effects of sex, menstrual phase, and oral contraceptive use on sexually dimorphic cognitive tasks, as well as emotional regulation. Studies have found that menstrual cycle phases have cognitive and physiological effects on women's brains depending on the concentration of female sex hormones, progesterone and estrogen (Epting & Overman, 1998). Oral Contraceptive pills (OC) contain a concentration of these female sex hormones that have been shown to alter gray matter volume to resemble men's brains in areas associated with learning, memory, spatial navigation, and emotional regulation (Pletzer et al., 2010). Participants for this study were 21 undergraduates from the University of Richmond, comprised of men (N=7) , naturally cycling women (N=5), and women taking oral contraceptives (N=9). Participants reported to the lab on two occasions, two weeks apart so as to assess the performance differences on the three tasks during the hormonal fluctuations of women's menstrual and luteal phases. The mental rotations task (MRT), a male favored task, the reading span task (RSPAN), a female favored task, and a perceived stress scale (PSS) were administered on both occasions. There were no significant group or cycle phase differences for the MRT, RSPAN, or PSS. There was a main effect for time for the MRT and the RSPAN, such that participants in all groups performed better during the second session. Future research can further examine this relationship with a larger sample and more reliable methods of assessing hormone levels in order to better understand the relationship between physiological changes in the brain and associated cognitive effects due to oral contraceptive use.

Keywords: oral contraceptives, emotional regulation, cognition, menstrual cycle phase, hormones

The Effect of Oral Contraceptives on Performance on Sexually Dimorphic Cognitive Tasks

Hormone fluctuations of estrogen and progesterone occur naturally during women's menstrual cycle (Kinsley & Meyer, 2010). During the menstrual phase, these hormone levels are the lowest, higher during the follicular phase, and highest during midluteal/luteal phase (Hausmeann et al., 2000). Research has found that sex hormones influence sex differences on performance on cognitive tasks, such that women perform better on tasks involving verbal fluency, manual speed and coordination, and articulation and men perform better on visual-spatial tasks, spatial perception, and spatial-temporal tasks (Epting & Overman, 1998).

Oral contraceptives (OC), also commonly referred to as birth control pills, are comprised of combined progesterone and estrogen female sex hormones that suppress ovulation by diminishing the frequency of gonadotropin-releasing hormone pulses and restricting the luteinizing hormone surge (Burkman, 2001). When taken as directed, oral contraceptives have 99% effectiveness in preventing pregnancy, as well as other associated health benefits, such as preventing ovarian and cervical cancers and reducing acne (Burkman, 2001). However, OC use has also been associated with adverse side effects, such as weight gain, mood changes, and breast tenderness (Burkman, 2001). Until recently, research has neglected to investigate the long-term consequences of OC use on brain anatomy, as well as the associated cognitive effects.

Kinsley & Meyer (2010) reported on the neurobiological effects of birth control on female rat brains and found that OCs keep natural progesterone and estrogen hormone levels low so that they don't fluctuate as drastically as naturally cycling females. Research done by Pletzer et al. (2010) found that oral contraceptives may also have physiological effects on areas of the brain that are associated with higher-order cognitive tasks. In general, males have greater gray matter volumes in the hippocampal regions, compared to naturally cycling females who show an increase in gray matter in these areas only during phases of their menstrual cycles where levels of estrogen and progesterone are low versus as opposed to higher (Pletzer et al., 2010). However, Pletzer et al. (2010) also found that these gray matter volumes are enhanced overall in women taking oral contraceptives. As a result, researchers have recently started to investigate the associated cognitive effects of these physiological changes.

Maki, Rich, & Rosenbaum (2002) studied the implicit memory variations across the menstrual cycle to find that women perform better during their midluteal phase compared to follicular phase on the category exemplar generation test, a test of conceptual implicit memory. Compared to the follicular phase, female sex hormone levels are higher during midluteal phase. In the follicular phase of their cycles, women performed better on the fragmented object identification task, a test of implicit memory. In addition, this study found no significant differences in performance on tests of explicit memory. This suggests that high levels of female sex hormones may inhibit perceptual object priming (Maki, Rich, & Rosenbaum, 2002). Other studies have also examined cognitive performance differences in men and women on sex-sensitive tasks during the different phases of women's menstrual cycles. In their study, Mordecai, Rubin, & Maki (2008) explored the effects of menstrual cycle phase and oral contraceptives on verbal memory, a female favored task, using the California Verbal Learning Test in naturally cycling women and OC users. Naturally cycling women showed no changes in verbal memory when comparing follicular and midluteal phases, whereas OC users showed enhanced memory during active pill phases, when estrogen and progesterone levels are highest. Previous studies evaluating OC users' performance on tasks of reaction time, short-term memory, and sustained attention found significant between-group differences between OC users and non-users for reaction time and short-term memory task, such that OC users performed better (Griksiene & Ruksenas, 2009). These differences were also more pronounced during the luteal phases (high progesterone and estrogen) compared to phases when these hormones were low. No significant differences were found for sustained attention.

Taken together, research has shown that women perform better on cognitive tasks involving verbal articulation and memory compard to men. In addition, research has demonstrated that women's performance on verbal working memory tasks can be enhanced during phases of high female sex hormones, such as the luteal phase, yielding greater sex differences. Research has also shown that sex differences are maintained for women who use oral contraceptives, which keep female sex hormones low and decrease the extent to which these hormones naturally fluctate with the menstrual cycle. Performance on male favored cognitive tasks has also been found to vary by menstrual cycle phase for women.

Moody (1997) assessed women's performance on the Mental Rotations Test (MRT), a male favored task evaluating spatial navigation abilities, once during their menstrual phase and once during their luteal phase. Men scored higher than the women during the initial testing, but not significantly higher than those who were in their menstrual phase during first testing. This supports previous research findings that women perform similarly to men during their menstrual phase on male favored tasks when female sex hormones are lowest. Respectively, research has found that women perform poorly during follicular and midluteal phases on male favored tasks when sex hormone levels are highest (Hausman et al., 2000). Specifically, Kimura & Hampson (1994) found that during phases where women's sex hormones are highest, women perform more poorly on perceptual-spatial tasks compared to males. The findings suggest that ovarian hormones may provide an advantage to women on tasks that they are naturally better at, such as verbal working memory, but can be a disadvantage on tasks that usually demonstrate male advantage.

Rosenberg & Park (2002) investigated both the verbal and spatial functions across menstrual cycle in women that were naturally cycling or on non-tricyclic birth control pills for at least three months. These women were test four times during their menstrual cycle, once on the first day and then three times once a week after. Confirmation of ovulation was provided through basal body temperature. The results of this study show no main effect of the group on the verbal span, but a main effect of cycle only for the naturally cycling group. Specifically, for naturally cycling women, verbal span increased in the middle of the cycle. It was concluded that increased estrogen levels improve verbal working memory but had no effect on the spatial task.

A more recent study has compared the effects of androgenicity of modern oral contraceptives on sex-sensitive tasks favoring men (Wharton, Hirshman, Merritt, Doyle, Paris, & Gleason, 2008). Androgenicity refers to the concentration of androgens which are typically male sex hormones, such as testosterone. Wharton et al. (2008) found that OC androgenicity influenced performance on the MRT, such that performance was enhanced in women who were more exposed to androgens. Taken together, this suggests that the concentration of male sex hormones in relation to female sex hormones in a woman's oral contraception, coupled with her phase in the menstrual cycle, could impact her performance on respective sex-sensitive tasks.

Due to the limited research evaluating the effects of oral contraception on women's performance on sex-sensitive cognitive tasks relative to men and naturally cycling women at phases of both high and low ovarian hormones, the current study intended to contribute to the current literature. In addition, the aim of the current study was to determine the effects oral contraception may have on emotion regulation, given that the amygdala, an area of the brain associated with emotion, showed changes in gray matter volume as well (Pletzer et al., 2010). This study is of relevance due to the expanding literature on the cognitive effects of birth control and it is important to evaluate how this medication impacts women's brains, especially if it can help explain sex differences in performance on cognitive tasks. In addition, with the emerging prospect in the media of scientists developing a male equivalent to oral contraceptives, it is of particular interest to study the degree to which these medications can alter our brains.

The current study investgiated the the effect of oral contraceptives on two sexually dimorphic cognitive tasks and a scale that assesses emotional regulation primarily with reactivity to stress. The study also investigated the extent to which menstrual cycle phase also mediated the effects between men, women taking oral contraceptives, and naturally cycling women. It was hypothesized that men will perform better than women on the male favored task, but women taking oral contraceptives will perform better than naturally cycle women, especially during the menstrual phase when female sex hormones are lowest. It was also hypothesized that women will perform better than men on the female favored task, especially during the luteal phase when female sex hormones are highest. Last, it was hypothesized that men will endorse lower perceived stress than women, but women taking oral contraptives will also endorse lower perceived stress compared to naturally cycling women, specficially during the luteal phase.

Method

Participants

The participants of this study were comprised of 21 undergraduates from the University of Richmond between the ages of 18 and 24 (N_{OC} = 9; N_{NOC} = 5; N_{MEN} = 7). A questionnaire was utilized in order to screen for those we wished to exclude from the study.

Measures

Mental Rotations Task. One of the three tasks that were administered was the Mental Rotations Test (MRT) (see Appendix). This test yields large and reliable gender differences favoring males and shows consistent gender differences despite paper or electronic test form (Monahan, Harke, & Shelley, 2008). These strong gender differences may be attributed to the MRT being a cognitive test of spatial abilities (Hausmann et al., 2000). The design of the test includes 20 items in five sets of four items (see Appendix B). Each item has a criterion figure and two correct alternatives and two incorrect alternatives or “distractors” (Vandenberg & Kuse, 1978). The correct alternatives are structurally exact replications of the criterion, but are displayed in a vertically rotated position. The distractors are either mirror images of the criterion that have also been rotated or rotated images of one or two of the other criteria. In order to correct for guessing, one point is given if both the items that match the figure are identified correctly, whereas no points are given if they are not (Vandenberg & Kuse, 1978). Participants completed the MRT using paper and pencil and manual instructions from the experimenter. This particular task was time-sensitive. Participants were given three minutes to accurately complete as much of the two pages as possible. Following the first three minute period, participants were then given a two minute break, and then once again three minutes to accurately complete as much of the last two pages as possible. The proportion of correct responses was scored. My secondary advisor, Dr. David Landy, provided access to a pdf version of the MRT.

Reading Span Task. The second cognitive task, Reading Span Test (see Appendix), has been proven to be both reliable and valid in measuring verbal working memory capacity (Conway, Kane, Bunting, Hambrick, Wilhelm, & Engle, 2005). In general, verbal tasks also tend to favor women (Conway et al., 2005). During this task, programmed in Eprime 2.0 and downloaded from the Georgia Tech Attention and Working Memory lab at http://psychology.gatech.edu/renglelab/english-tasks.html (Unsworth et al., 2005), participants viewed a series of short sentences on a screen for six seconds, one at a time. The participant was instructed to read the sentence and respond by either (D) True or (L) False to the statement and then was asked to try to remember the last word at the end of each (Tirre & Peña, 1992). After a few sentences, the participant was asked to recall in order the last words of the sentences they were instructed to remember. This process repeated unsystematically, so that participants did not recall the same number of words each time. The total correct RPSAN score was utilized with consideration of reading errors, accuracy errors, and speed errors, but not correct order for words recalled (Redick et al., 2012).

Perceived Stress Scale. The third measure was a modified version of the Perceived Stress Scale (PSS). The PSS is a questionnaire that measures the perception of stress and participants' appraisal of how controllable they find their lives (Cohen, Kamarck, & Mermelstein, 1983). The test was modified from instructing participants to rate feelings and thoughts during the past month to ratings of the past week. Participants indicated their rankings by selecting a value on a Likert scale from 0-4, where 0 indicated never and 4 indicated very often. Higher scores yielded greater perceived stress and therefore, less efficient emotional regulation. The Chronbach's alpha for the first and second sessions was .89 and .90 respectively, indicating high internal consistency.

Procedure

All procedures were reviewed and approved by the Institutional Review Board at the University of Richmond.

Inclusion and exclusion criteria. Two groups of female participants were recruited: females taking oral contraceptives and females not taking contraceptives. Female participants were excluded from both groups if they had been taking oral contraceptives for less than one month, if they were using another form of prescribed contraception (e.g., IUD), or if they were pregnant at the time of the study. Male participants were not excluded from the study for any reason.

Screening: Participants were given a web link on study flyers and email advertisements directing them to fill out screening questionnaires on www.qualtrics.com (see *Appendix)* and results were stored on HIPAA-compliant, secure servers. This enabled us rule out those participants who did not meet inclusion criteria. Participants first read an IRB-approved study description and consent form and indicated their consent before proceeding. The questionnaire collected participant demographic information, such as gender, age, ethnicity, class year, and religiosity, as well as an email address in order to contact them if they qualified for the study. Women were asked to report the date of their most recent period or the anticipated date of their upcoming menstruation. They were asked to report whether they were taking oral contraceptives consistently for at least the past month. In addition, for women who identified as oral contraceptive users, they were asked to specify their brand of oral contraception. If a participant passed the screening process, they were then emailed to set up an appointment for their first session. For those who qualified, data were downloaded and ID numbers were added to hard copies. Participants' profiles and corresponding ID numbers were locked in a lab-secured filing cabinet so that accurate records could be kept since participants returned on two occasions. This also ensured that confidentiality of participant information was maintained.

Study sessions: All participants came to the lab on two occasions, Part I and Part II of the experiment, which were two weeks apart. Female participants were grouped as OC users and non-OC users (NOC). Similar to the study done by Moody (1997), women who passed the screening process were contacted and assigned to either an M-L (Menstruation to Luteal) or L-M (Luteal to Menstruation) group, depending on their current menstrual cycle phase. If they were in the M-L group they reported to Part I during their menstrual phase or while they were currently going through a menstrual cycle and then were scheduled to return two weeks later during their luteal phase. If they were in the L-M group, they came to Part I of the experiment two weeks prior to their anticipated menstruation and then were scheduled to return two weeks later once they had began menstruation. OC users were scheduled similarly, but with greater reliability since their phase could be indicated by their inactive pills (menstrual phase) and during the second week of their active pills (luteal phase) (Mordecai, Rubin, & Maki, 2008). Men's study sessions were scheduled two weeks apart as well.

During Part I of the experiment, participants reported to the lab and were given an IRB-approved consent form to read and sign. Completion of Part I resulted in compensation of $5 for 35 minutes. If for some reason the participant decided to withdraw from the study, they were allowed to do so without penalty. Once consent was provided, the researcher led the participant to a private computer lab and logged the participant into the computer with the participant ID number. After being seated at a personal computer, participants read the instructions for and completed three tasks. Two of the tasks, the Mental Rotations Task and the Perceived Stress Scale, were completed with paper and pencil with instructions provided by the experimenter.

Part II of the experiment was a replication of Part I without an additional consent procedure. Participants were reminded that they could withdraw without penalty. Following the completion of Part II, participants were escorted to a private room for debriefing. Completion of Part II resulted in compensation of $10.

Across sessions, the tasks were counterbalanced for order effects so that participants do not receive the tasks in the same order as they did their first time. Participants always completed the PSS first and the RSPAN and MRT were counterbalanced between Part I and Part II in order to account for order effects. Counterbalancing also incorporated cycle phase for women.

Results

The primary analyses were a series of two-way mixed factor ANOVAs with one within subjects factor (session or cycle phase) and one between-subjects factor (group) for each dependent variable. Descriptive statistics and histograms were examined for all dependent variables and judged to be suitable for parametric analysis.

Mental Rotations Task

A two-way mixed factor analysis of variance yielded a main effect for session for the MRT, $F(1,20) = 11.41$, $p < .05$, such that on average all groups performed better during the second session ($M = .46$, $SD = .23$) compared to the first ($M = .34$, $SD = .19$). The main effect of group was non-significant, $F(2,19) = .26$, $p > .05$, and the interaction effect was not significant, $F(2, 19) = 2.58$, $p > .05$ (see *Figure 1)*.

A two-way mixed factor analysis of variance did not yield a significant main effect for phase on the MRT, $F(1, 13) = .03$, $p >.05$, a significant main effect for group (OC vs. NOC), $F(1, 13) = .85$, $p > .05$, or a significant interaction effect $F(1, 13) = 1.19$, $p > .05$ (*Figure 2)*.

Reading Span Task

A two-way mixed factor analysis of variance yielded a main effect for session for the RSPAN, $F(1,20) = 5.29$, $p < .05$, such that on average all groups performed better during the second session (*M* = 42.89, *SD* = 9.81) compared to the first (*M* = 38.79, *SD* = 10.26). The main effect of group was non-significant, $F(2,19) = .10$, $p > .05$, and the interaction effect was not significant, $F(2, 19) = 1.53$, $p > .05$ (see *Figure 3)*.

A two-way mixed factor analysis of variance did not yield a main effect for phase for the RSPAN, $F(1, 13) = 1.15$, $p > .05$. The main effect of group was non-significant, $F(1, 13) = .07$, $p > .05$, and the interaction effect was not significant, $F(1, 13) = 1.61$, $p > .05$ (see *Figure 4)*.

Perceived Stress Scale

A two-way mixed factor analysis of variance did not yield a main effect for group on the PSS, $F(2, 19) = 1.74$, $p > .05$. The main effect of time was non-significant, $F(1, 20) = .95$, $p > .05$, and the interaction effect was not significant, $F(2, 19) = .09$, $p > .05$ (see *Figure 5*).

A two-way mixed factor analysis of variance did not yield a main effect for phase on the PSS, $F(1, 13) = .83$, $p > .05$. The main effect of group was non-significant, $F(1, 13) = .01$, $p > .05$, and the interaction effect was not significant, $F(1, 13) = .10$, $p > .05$ (see *Figure 6)*.

Discussion

Although none of the hypotheses was significant, there were main effects of session for both the MRT and RSPAN, such that all groups performed better during the second session compared to the first. Due to these results, I was not able to detect any cognitive or emotion regulation differences based on gender, oral contraceptive use, or cycle phase. Nevertheless, this study still yielded interesting findings. Contrary to what was expected, the lack of group differences on perceived stress on the PSS suggested that perhaps men and women are not as different as anticipated in terms of perceived ability to cope with stressors. In addition, the expectation of there being gender differences for perceived stress could also imply a social bias favoring men as better emotional regulators than women. Despite the lack of significant group differences on the MRT, it was interesting to see that for the first session, the oral contraceptives group performed less similar to men than the naturally cycling group, which was contrary to what was hypothesized.

There were several limitations to this study. First, there was a power issue due to the small sample sizes of the groups, making it difficult to gather conclusive results. In particular, the repeated measures design of the study made obtaining a larger sample size problematic due to the difficulty in retention of participants. Second, the use of self-report of menstrual cycles for women was not as reliable as more intrusive methodologies that would yield accurate hormone concentrations. In regards to the RSPAN task, the consideration of correctly recalled words may have yielded more significant results. The study by Rosenburg & Park (2002) found significant effects for menstrual cycle phase, but not group, when taking into account correct recall order. Last, the use of a homogenous college campus sample could have contributed to the lack of group differences. Perhaps such differences are more pronounced outside of a college population or at a University with students of more diverse demographic backgrounds and cognitive abilities. In order to fully understand the cognitive effects of oral contraceptives on women's brains further research should address these limitations.

Future directions may include replication of the current study with consideration of the aforementioned limitations. Specifically, a more diverse and larger sample size could yield more conclusive results. In addition, using more reliable methods of measuring hormone concentration, such as basal body temperature (Rosenburg & Park, 2002) or blood samples (Hausman et al., 2000). The use of tasks that also involve the intersection of cognition and emotion may also be better at teasing out potential gender differences and associated cognitive effects of birth control on women's brains. In fact, the use of separate tasks tapping cognition and emotion may not be as valid since studies have found that the relationship between cognition and emotion is bidirectional, such that it is nearly impossible to distinguish between them (Gray, 1990). In the future, it would also be of interest to explore the cognitive effects between different brands of oral contraception and other forms of prescribed contraception altogether since studies have found that androgenicity, the concentration of androgens or male sex hormones, of oral contraceptives have associated cognitive effects. Specifically, the study by Wharton et al. (2008) found that androgenicity of oral contraceptive pills enhances women's performance on the MRT (Wharton et al., 2008). It would be of interest to investigate potential mediating cognitive effects of oral contraceptive androgenicity in the relationship between gender, oral contraceptive use, and menstrual cycle phase.

Overall, this area of research has extraordinary relevance to women today, especially to young adults where oral contraception is the main form of birth control. In addition, the use of oral contraception over extended periods of time is becoming more and more prevalent as women are marrying and having children later in life. Thus, it is extremely important to better understand the prolonged cognitive effect of these medications on women's brains, especially since physiological changes have been found (Pletzer et al., 2010). Research will not only explain these potential effects, but also provide insight into the extent to which gender differences in cognition exist.

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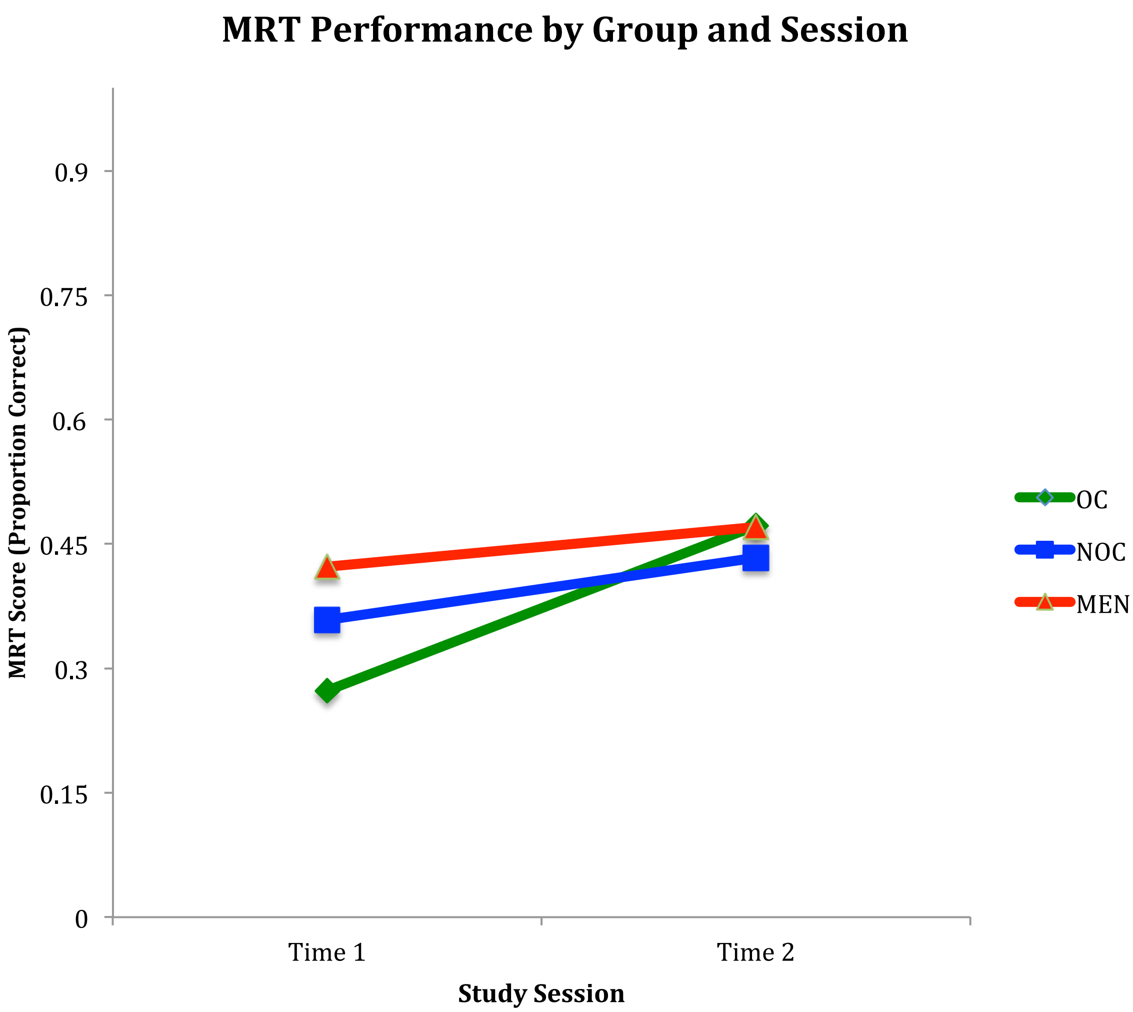


Figure 1: The figure above shows a non-significant main effect and interaction for group, but a main effect for session.

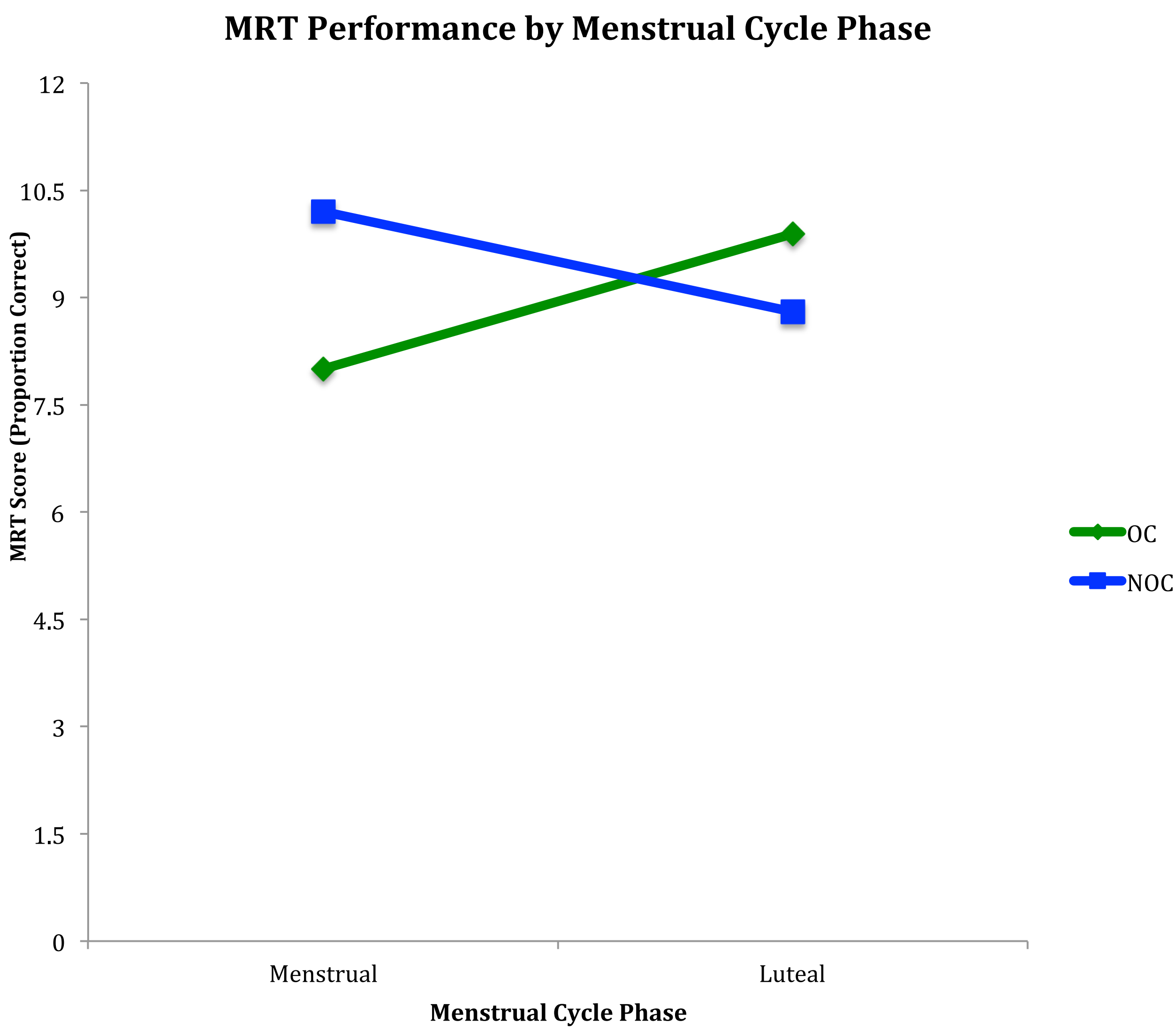


Figure 2: The figure above shows a non-significant main effect of menstrual cycle phase or OC use on MRT performance for women.

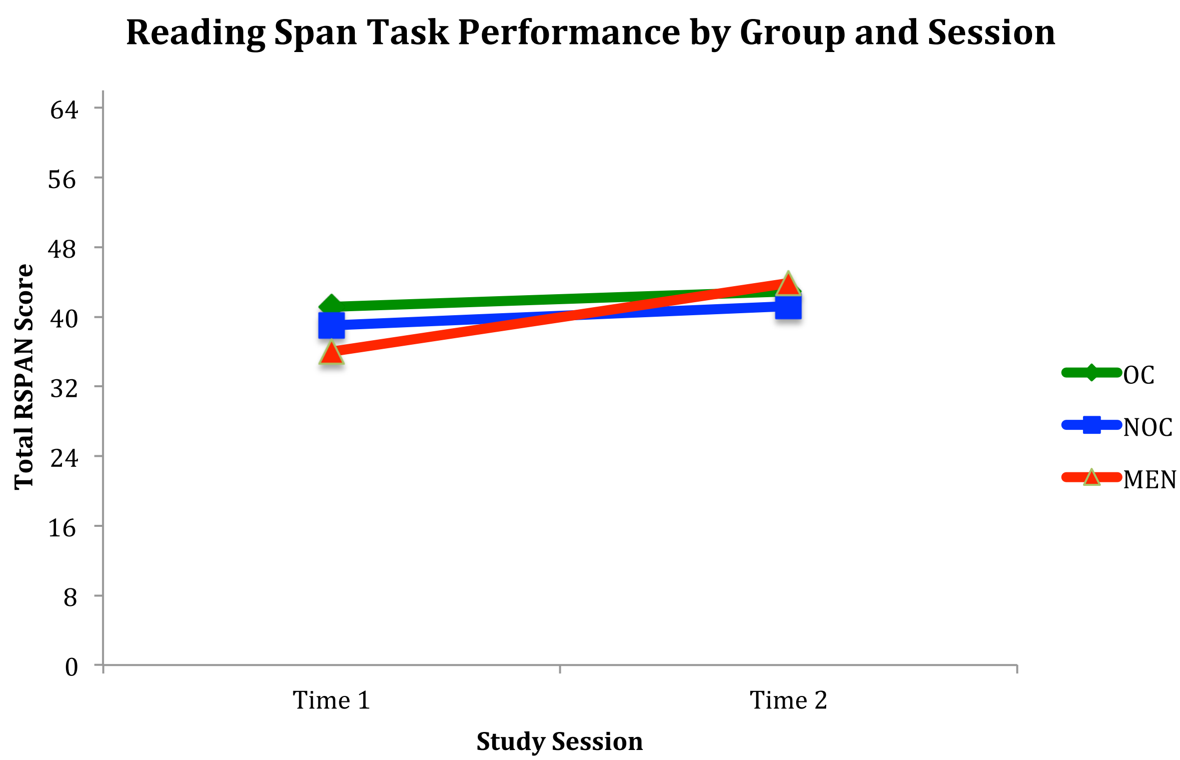


Figure 3: The figure above shows a non-significant main effect and interaction for group, but a main effect for session. Participants in all groups performed better the second time for the verbal working memory task.

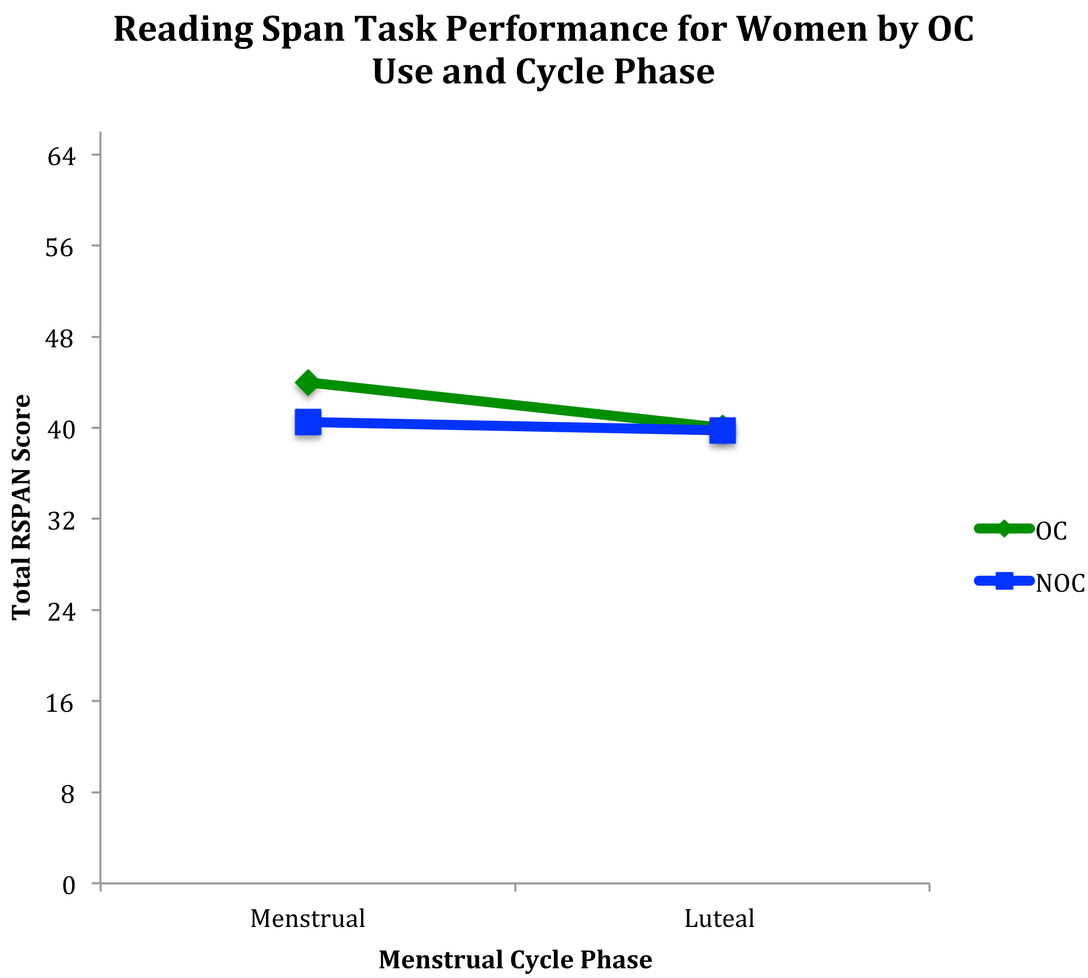


Figure 4: The figure above shows a non-significant main effect and interaction for menstrual cycle phase and OC use for women.

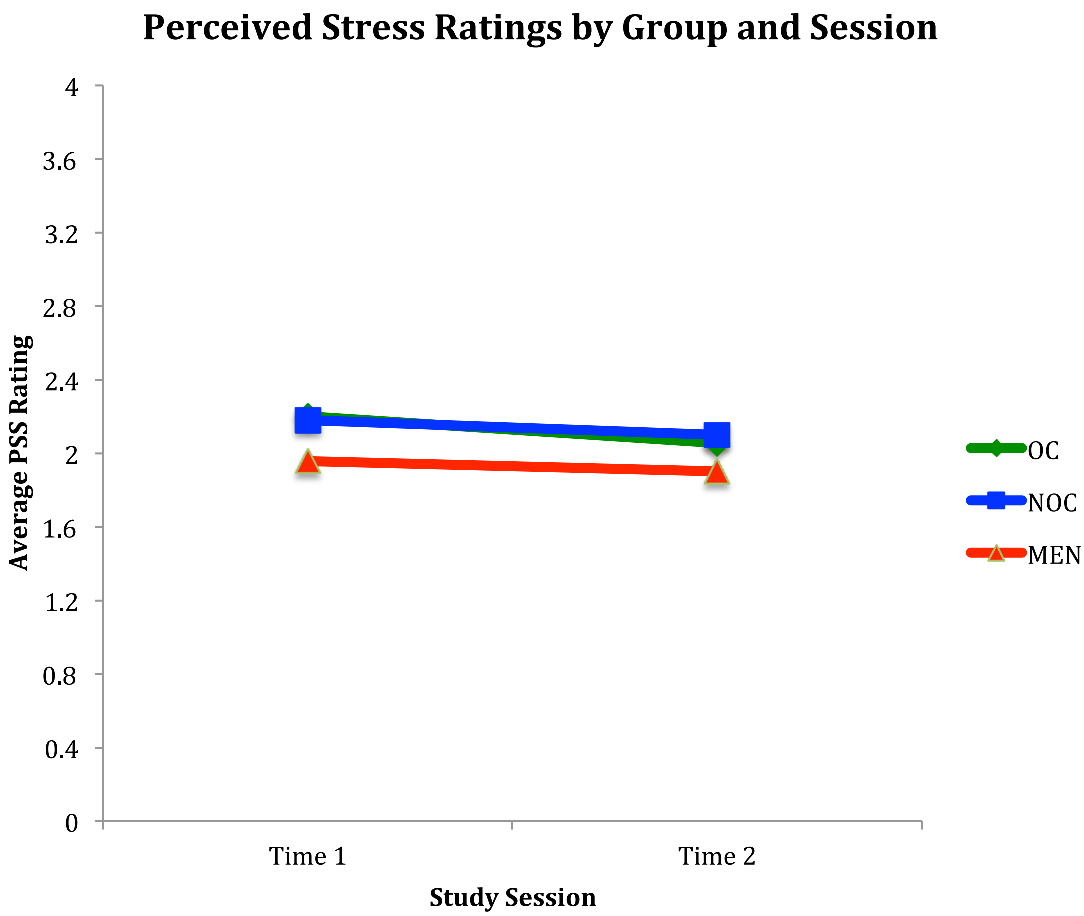


Figure 5: The figure above shows a non-significant main effect for study session and group for self-reported ratings of ability to cope with perceived stress.

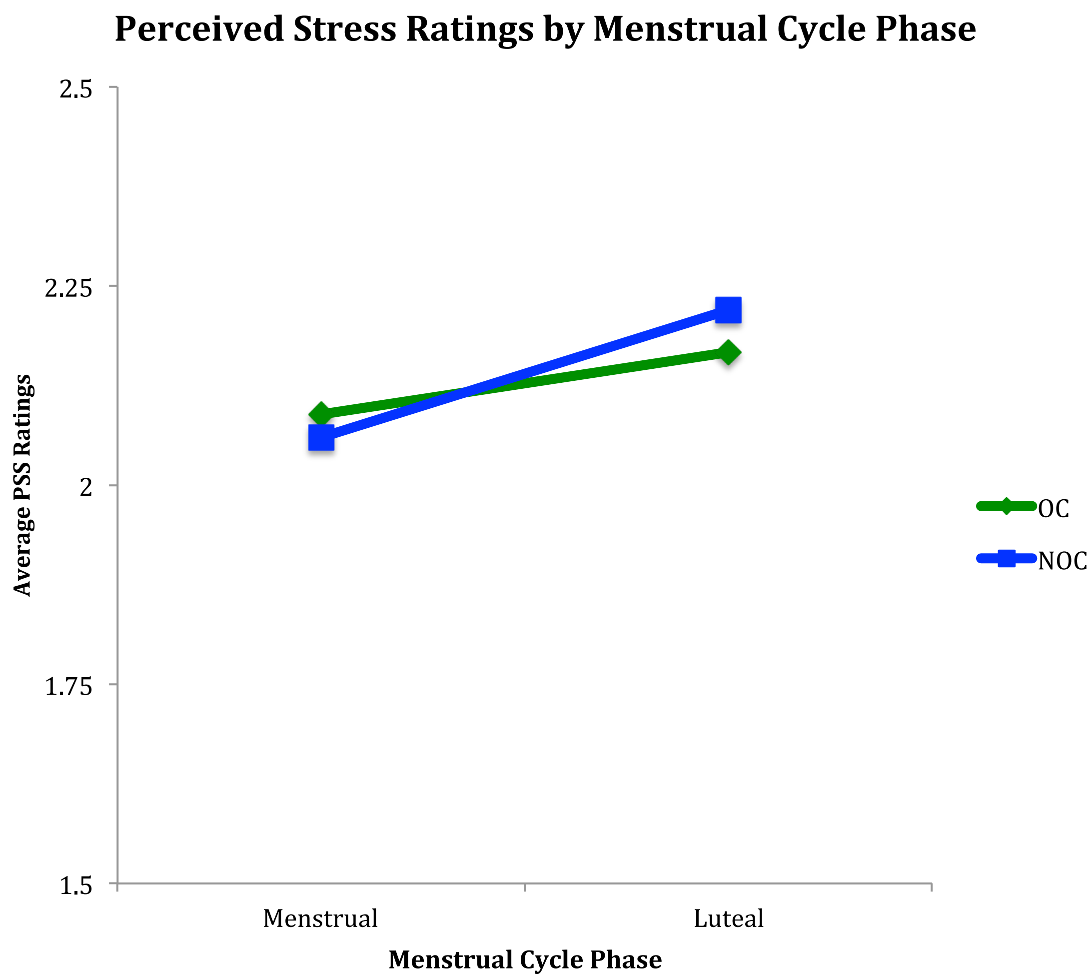


Figure 6: The figure above shows a non-significant main effect for menstrual cycle phase and OC use for women on self-reported abilities to cope with perceived stress.

Appendix

Screening Demographic Questionnaire

1. Name:

2. Age:

3. Sex (M/F):

4. Email address: ______________________________

5. Circle the race that best describes you.

A. Caucasian

B. African American

C. Latino/Latina

D. Asian

E. Other (Please describe): _____________

6. Circle the religious orientation that best describes you.

A. Christian

B. Jewish

C. Muslim

D. Atheist

E. Other (Please describe): _______________

7. Please indicate on the scale below your level of religiosity.

0	1	2	3	4
Not at all	**Somewhat**	**Moderately**	**Very**	**Extremely**

Screening Questionnaire- WOMEN ONLY

1. What was the first date of your late menstrual period? _____________

2. What is the anticipated date of your next menstrual period? ____________

3. Are you currently on prescribed birth control (If no, skip questions 4, 5, & 6)? ________________

4. If you answered yes to the previous question, please circle which method of birth control you use.

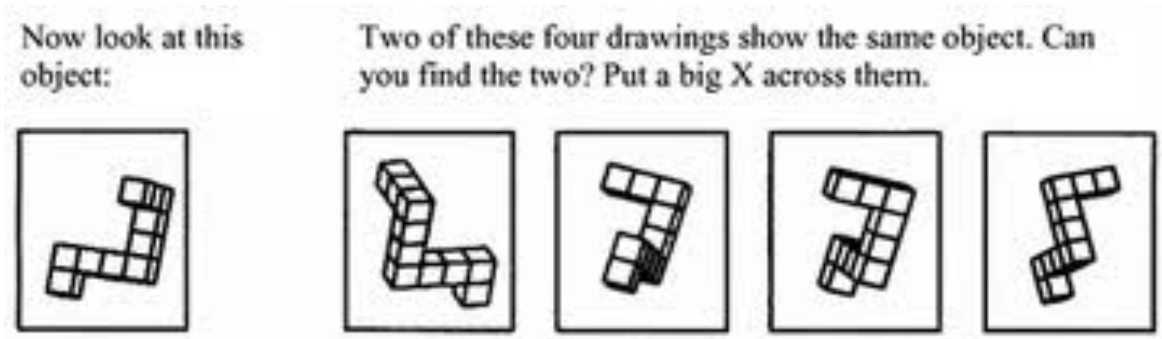
A. Oral Contraceptives (the pill)

B. Depo-Provera (the shot)

C. Other (Please describe):_______________

5. If using oral contraception, have you been taking it for at least one month? (Check the answer that applies)
Yes ___ No ___

6. If using oral contraception, do you take your pills regularly? (Check the answer that applies)
Yes___ No___



The figure above displays a sample of an MRT question that participants viewed. The figure to the left is the target figure for which they were asked to select the two correct vertically rotated images of from the four figures to the right. They were only given a point for selecting both correct answers.

Reading Span Test Sample

Indicate whether the following sentences are True or False by pressing the corresponding key

The bird lays eggs.

(true) (false)

A dog is blue.

(true) (false)

Cars have wheels.

(true) (false)

Recall the final word of each of the previous sentences in order.

George Washington was a president.

(true) (false)

Penguins can fly.

(true) (false)

Recall the final word of each of the previous sentences in order.