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**RELATIONSHIP BETWEEN MENSTRUAL CYCLE PHASES AND COGNITIVE
FUNCTION IN FEMALES WHO USE AND DO NOT USE ORAL
CONTRACEPTIVES**

BY

MEREDITH G. COCKERELL

A THESIS

**Submitted to
Michigan State University
in partial fulfillment of the requirements
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ABSTRACT

RELATIONSHIP BETWEEN MENSTRUAL CYCLE PHASES AND COGNITIVE FUNCTION IN FEMALES WHO USE AND DO NOT USE ORAL CONTRACEPTIVES

By

Meredith G. Cockerell

Purpose: The purpose of this study was to evaluate the cognitive function of females who use oral contraceptives and do not use oral contraceptives during the three phases of the menstrual cycle. Cognitive function was measured using the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) neuropsychological test battery.

Methods: A total of 32 participants (19 females not taking oral contraceptive, 13 females taking oral contraceptives) volunteered for this study. Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) was administered during each phase of the menstrual cycle, follicular, luteal and menses.

Results: There were no differences in ImPACT scores during the different phases of the menstrual cycle for females who do and no not take oral contraceptives.

Conclusion: Results suggest that there is no cognitive impairment throughout the different phases of the menstrual cycle. This is true for females who take and who do not take oral contraceptives.

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CHAPTER 1

INTRODUCTION

Overview of Problem

The menstrual cycle is a natural monthly event in young women, influenced by physiological and pathological changes that occur during a female's life (Redman, Scroop, & Norman, 2003). The female menstrual cycle has been studied using a variety of different research methods. One main focus of research has concentrated on symptoms women experience during the different phases of the menstrual cycle (Friedman, Hurt, Arnoff & Clarkin, 1980; Brooks, Ruble, & Clark, 1977; Keenan, Lindsmer, & Jong, 1995; Olasov & Jackson, 1987; Abplanalp, Donnelly, & Rose, 1979). Another area that has been researched concentrates on the cognitive function of females during phases of the menstrual cycle (Shaywitz et al., 1999; Sommer, 1972; Sherwin, 2003; Dietrich et al., 2001; Owens, Matthews, & Everson, 2002; Morgan & Rapkin, 2002). However, most menstrual cycle and cognitive function research concentrates on irregular menstrual cycles of females, or females who have problems such as pain or negative moods during their menstrual cycle (Keenan et al., 1995). Very few researchers have investigated, cognitive function of normally cycling females during the menstrual cycle.

The primary function of the menstrual cycle is to allow females to reproduce. The menstrual cycle occurs in all healthy females and has specific hormonal changes throughout the cycle. The main female sex hormones that regulate the menstrual cycle are progesterone and estradiol. Progesterone and

estradiol are responsible for the start and cessation of bleeding (Gruhn & Kazer, 1989). These hormones may play a role in cognitive function; as a result they need to be more closely examined to determine if cognitive function changes during the menstrual cycle.

The menstrual cycle has historically been associated with discomfort and pain. Several studies tested menstrual pain through the use of questionnaires such as the Social-Sexual Activities Log (SSAL), Profile of Mood States (POMS), Menstrual Distress Questionnaire (MDQ), Zung Self-Rating Anxiety Scale, and Daily monitoring forms (Abplanalp et al., 1979; Keenan et al., 1995; Olasov & Jackson, 1987; Collins, Eneroth, & Landgren, 1985; Brooks, Ruble, & Clark, 1977). Some of the symptoms studied were tension/anxiety, depression, anger, fatigue, and confusion (Abplanalp et al., 1979). However, none of these studies examined if cognitive function changes during the menstrual cycle.

Cognitive function is the ability to use reasoning, judgment, memory, and perception effectively and in a timely manner (Saladin, 2001). Cognitive function has previously been assessed through learning tests such as the California Verbal Learning Test (CVLT), stroop test, Digit Span-Backward, Symbol Digit-Correct and the Wechsler Memory Scale (Keenan et al., 1995). Recently, cognitive function has been examined through computerized neurocognitive test batteries or functional magnetic resonance imaging (fMRI) (Maki & Resnick, 2001). To date there have been no studies that have investigated the use of a computerized neurocognitive test battery during the phases of the menstrual cycle.

There are many discrepancies in the literature on menstrual cycle and cognitive function. Some researchers suggest that cognitive function is affected by different phases of the menstrual cycle (Shaywitz et al., 1999; Maki & Resnick, 2001; Dietrich et al., 2001; Schoning et al., 2007) whereas other research studies reported no difference in cognitive function during the different phases of the menstrual cycle (Sommer, 1972; Owens et al., 2002; Morgan & Rapkin, 2002; Owens, Matthews, & Everson, 2002). Shaywitz et al. (1999) found that postmenopausal females who were administered estrogen performed better on working memory tasks than postmenopausal females not taking estrogen supplements. The researchers suggest that pre-menopausal estrogen levels are depleted during the menses phase of the menstrual cycle. In another study by Morgan and Rapkin (2002), hormone replacement therapy was found to influence the brain function and cognition status across phases of the menstrual cycle. In contrast, Sommer (1972) concluded that there are no declines in intellectual performance across phases of the menstrual cycle. Due to these discrepancies in the literature more research is needed to determine if cognitive function differs during the different menstrual cycle phases.

Oral contraceptives are the most used form of reversible contraception in the United States and throughout most of the world (Abraham, Luscombe, & Soo, 2003). Oral contraceptives are small tablets taken orally for either 21, 24, or 28 days or longer each month. Oral contraceptives release synthetic hormones that prevent the release of eggs from the ovaries (Ernst, Baumgartner, Bauer, & Janssen, 2002). Due to the high rate of oral contraceptive usage among females

the positive and negative side effects of oral contraceptives have been widely studied. However, most of the literature has concentrated on physical or mental pain and not on cognitive function.

Significance of the Problem

The menstrual cycle occurs in all females and is individualized to every woman. The three different menstrual cycles include menses, follicular, and luteal phase. Research has shown that many females have problems during at least one phase of the menstrual cycle (Keenan et al., 1995). Problems such as pain, arousal, negative moods and the inability to focus during daily activities all commonly occur during the menstrual cycle (Abplanalp et al., 1979). Some researchers have tried to determine if problems during the menstrual cycle such as negative moods are due to the negative connotations of the menstrual cycle or an outside source (Olasov & Jackson, 1987). For example, Olasov and Jackson (1987) found that expectancies regarding the mood-menstrual relationship could be altered by means of a brief lecture on the menstrual cycle. Results found changes in the mood-menstrual relationship could still be detected as long as 40 days post-lecture.

Female sex hormones such as progesterone and estradiol have been evaluated during different phases of the menstrual cycle. Estradiol is a steroid hormone produced primarily by the ovaries and adrenal gland. Estradiol is the most active form of estrogen in the human body and is responsible for a normal monthly cycle. Estradiol is also known to play a role in quite a number of important physiological processes such as bone mineral density and

osteoporosis prevention. Progesterone is the other important female hormone. Like estradiol, progesterone is responsible for a normal monthly cycle. Progesterone is a precursor for most other hormones including Dehydroepiandrosterone (DHEA), estradiol, testosterone and cortisol. However, more research is needed on progesterone to determine all functions this hormone plays in the human body. It is important to study hormone fluctuations according to the different menstrual phases, because the difference in hormone levels may affect cognitive function and in turn may have an affect on the females' daily life.

Oral contraceptives work by controlling the release of hormones. There are two main types of birth control pills: the combination pills and the progestin-only pill. Combination oral contraceptives consist of synthetic versions of estrogen and progestin and are taken daily to block the usual hormone messages that direct ovulation. As a result, egg development is blocked preventing conception. Other effects of combination oral contraceptives help prevent sperm from reaching the egg and reduce the chance of the egg implanting in the uterus (O'Connell, Davis, & Kerns, 2007). Unlike combination oral contraceptives, progestin-only pills contain no estrogen and have a lower dose of progestin than combined birth control pills. Progestin-only oral contraceptives work in three different ways: (1) they make the cervical mucus at the entrance to the uterus too thick for the sperm to get through to the egg; (2) they prevent ovulation in about half of the users; and (3) they affect other hormones, the fallopian tubes, and the lining of the uterus (O'Connell et al.,

2007). Since oral contraceptives pharmacologically control the hormones estrogen and progesterone, it is important to study the effects of oral contraceptives on cognitive function. Very little research has been conducted in the past two decades on cognitive function and menstrual cycle. Furthermore, there have only been a few studies that have evaluated the use of oral contraceptives on cognitive function during different phases of the menstrual cycle (Brooks et al., 1977; Wright & Badia, 1999).

Statement of the Problem

The purpose of this study was to evaluate the cognitive function of females who use oral contraceptives and do not use oral contraceptives during the three phases of the menstrual cycle. Cognitive function was measured using the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) neuropsychological test battery.

Hypothesis

There will be no difference in cognitive function during the three different phases of the menstrual cycle for females who do not take oral contraceptives and females who take oral contraceptives.

Definition of terms

Estradiol: The most active naturally occurring estrogen (Gruhn and Kazer, 1989)

Follicular Phase: Phase in the menstrual cycle where levels of estradiol are high, the first day of the menstrual cycle usually lasting 14 days until ovulation (Walpurger, Pietrowsky, Kirschbaum, & Wolf, 2004)

Luteal Phase: Phase in the menstrual cycle where estradiol and progesterone are high, the time from when the egg is released until the first day of menstruation (Walpurger et al., 2004)

Menses phase: Phase in the menstrual cycle where levels of estradiol and progesterone are low, usually occurring in the second to fourth day of bleeding (Walpurger et al., 2004)

Menstrual Cycle: The number of days between the beginning menstrual bleeding to the day preceding the onset of the next bleeding (Abplanalp et al., 1979)

Neurocognitive Function: The ability to use reasoning, judgment, memory, and perception effectively and in a timely manner (Saladin, 2001)

Progesterone: A sex hormone that regulates the menstrual cycle (Gruhn and Kazer, 1989)

Verbal Memory: recall of word lists (Kolb & Wishaw, 2003)

Visual Memory: recall of geometric shapes and faces (Kolb & Wishaw, 2003)

Reaction Time: The time between the onset of a stimulus and the beginning of a movement response (Haywood & Getchell, 2005)

CHAPTER 2

LITERATURE REVIEW

This section will outline background information pertaining to anatomy of the menstrual cycle, menstrual cycle and cognitive function, menstrual cycle and mood disorders, hormone replacement, oral contraceptive use, and the importance of ImPACT.

Anatomy of the Menstrual Cycle.

The menstrual cycle is made up of many changes that take place inside the body. These changes help prepare a female's body for pregnancy each month. The progression of the cycle from one to the next is caused by the rise and fall of hormones throughout a specific interval, usually about 28 days, or one month. Although the typical menstrual cycle lasts 28 days, it can range anywhere from 21 to 38 days, and it can vary from female to female. The follicular phase is the time from the first day of the menstrual cycle until ovulation, when a mature egg is released from the ovary. It's called the follicular phase because growth or maturation of the egg is taking place inside the follicle, a small sac where the egg matures. Ovulation occurs around day 14 of the cycle, in response to a surge of luteinizing hormone (LH) when the egg is released from the ovary. The luteal phase is the time from when the egg is released (ovulation) until the first day of menstruation. It is named after the corpus luteum, and is a structure that grows in the ovary where a mature egg was released at ovulation. (Gruhn & Kazer, 1989). The declining levels of progesterone at the end of the normal menstrual cycle causes a process that allows the inner layer of the uterus, the endometrium, to

becomes necrotic and then discarded, leading to menstruation (Gruhn & Kazer, 1989).

Menstrual Cycle and Cognitive Function.

There have been several studies that have investigated cognitive function and the menstrual cycle. Some studies have found that the menstrual cycle causes changes in cognitive function across all the different phases of the menstrual cycle (Maki & Resnick, 2001; Dietrich et al., 2001). For example, Maki and Resnick (2001) conducted a review of studies pertaining to the activational effects of estrogen on cerebral activity during rest and during performance of cognitive tasks in pre and postmenopausal women. The researchers found that specific neuroimaging outcomes fluctuate across the menstrual cycle in young women. Dietrich et al., (2001) used fMRI and blood oxygenation level-dependent (BOLD) contrast to study hemodynamic menstrual cycle dependant changes for a verbal, spatial, and motor task. Six females with a normal menstrual cycle participated in the study. The participants were scanned twice, once during menses and once on the 11/12th day of the menstrual cycle. Results found that blood estrogen level strongly influenced cerebral hemodynamics and that these changes dramatically alter the size but not the pattern of cortical activation during performance of cognitive task.

Schoning et al., (2007) conducted a study that investigated gender differences in mental rotation performance and brain activation patterns measured through fMRI. In addition, variations in gender differences to

menstrual cycle phases were also evaluated. Twelve women and 12 men were scanned once in the fMRI while performing a mental rotation task. Results revealed men and women exhibited significant differences of brain activation patterns. The researchers also found differences across menstrual cycle in females. Several regions such as the left middle temporal gyrus, left lentiform nucleus and thalamus, left and right cingulated gyrus, corpus callosum, right middle temporal gyrus, superior occipital and angular gyrus, and right middle and superior frontal gyrus, exhibit enhanced activation patterns when female hormones are at their peak (midluteal). The researchers concluded that estrogen might enhance vasoreactivity and therefore lead to an increased activation of the (Schoning et al., 2007).

Keenan et al. (1995) conducted a study to determine if memory impairment on the California Verbal Learning test (CVLT) was generalizable to memory for narrative or nonverbal material. Thirty-six women were analyzed that had PMS. Keenan et al. (1995) suggests that women with prospectively documented premenstrual syndrome have a subtle, yet consistent, relative memory impairment. These findings were consistent regardless of phase the participants were in during their menstrual cycle. However, Collins et al. (1985) conducted a study to examine whether there is a difference in psychoneuroendocrine reactivity to psychologic stress as a function of the normal menstrual cycle. Fifteen normally cycling females were participated in this study. The participants were induced with a stressful activity such as cognitive-conflict task, mental arithmetic test or a computer game. Hormone levels were taken

during different menstrual cycle phases. The researchers concluded that although some women do report an impairment of their mental capacity before or during menstruation, when objective measures of performance were employed the majority of studies have failed to demonstrate significant phase-related changes.

When the Watson-Glaser Critical Thinking Appraisal test was used to determine intellectual performance, it failed to show an association between menstrual cycle phase and test performance (Sommer, 1972). Sommer (1972) conducted a study with college aged females using the Watson-Glaser Critical Thinking Appraisal test to determine if intellectual performance was altered during different menstrual cycle phases. Sommer (1972) found no difference in intellectual performance, however, the author suggest that there may be changes in other subdivisions of intellectual function. Owens et al. (2002) conducted another study that did not find any differences in cognitive function across the phases of the menstrual cycle. This study utilized the Welchler Adult Intelligence Scale-Revised Information Subset, California Verbal Learning Test, Digit Span Test, and Verbal Fluency Test to assess cognitive function. Results revealed no differences in test score across the phases of the menstrual cycle. In a study done by Morgan and Rapkin (2002), cognitive function was evaluated throughout the menstrual cycle in women who suffer from premenstrual dysphoric disorder and controls. Participants included 37 women who met prospectively documented criteria of premenstrual dysphoric disorder and 32 control women who did not have the disorder. Cognitive function was examined using the Digit Span test,

Extended Digit Symbol test, California Computerized Assessment Package, and Simple reaction time test. The researchers found that females who suffer from premenstrual dysphoric disorder exhibit no difference when compared to a control group in the late luteal phase of the menstrual cycle (Morgan & Rapkin, 2002).

Owen, Matthews, and Everson (2002) conducted a study to evaluate the effects of a pharmacologically induced, temporary suppression of ovarian hormones on healthy women's cognitive function. The researchers used tests such as the Wechsler Adult Intelligence Scale, California Verbal Learning Test, Digit Span test and Verbal Fluency Test. Sixteen healthy women were tested three times, once during normal follicular phase, a second time after four monthly injections of gonadotropin-releasing hormone (GnRH) agonist, and a third time after either 3 more GnRH agonist injections or after resuming follicular cycles. Experimental participants were compared to a control group that were tested three times during the normal follicular phases. Results showed no evidence that a decline in ovarian hormones was associated with change in short-term verbal memory, concentration, attention, or mood.

Menstrual Cycle and Mood Disorders

The menstrual cycle has commonly been associated with negative moods and symptoms. Abplanalp et al. (1979) conducted a study to better understand the psychological function of women during the menstrual cycle. Mood was assessed with the POMS and SSAL questionnaires and revealed that there was no relationship between cycle phase and mood or enjoyment of activities

(Abplanalp et al., 1979). Abplanalp et al. also suggested that daily events had a greater impact on moods and enjoyment of daily life than the menstrual cycle. The results of their study might have been affected by the participants knowing that they were being tested for menstrual cycle symptoms, which is a common problem in most menstrual cycle studies (Abplanalp et al.).

Olasov and Jackson (1987) found that expectancies regarding the mood-menstrual relationship could be altered by means of a brief lecture on the topic. Olasov and Jackson took four groups of college aged females and had them listen to a lecture that either associated the menstrual cycle as a negative experience, a positive experience, not related to the menstrual cycle, or no lecture at all. Results indicated that females who received the lecture associated the menstrual cycle with negative experiences had more negative feelings toward their own menstrual cycle.

Brooks et al. (1977) conducted a study to explore the range of expectations and attitudes associated with menstruation. The self-reported study included 191 college-aged females who reported experiencing more severe symptoms in premenstrual phase than intramenstrual phase. The researchers suggest these findings may reflect stereotypical expectations. However some researchers have stated that self-reporting is not a reliable source of information. According to Friedman et al. (1980) self-reporting symptoms and attitudes cause too much discrepancy, therefore, alternative methods should be used to test symptoms such as anxiety and cognitive function.

Hormone Replacement

Post-menopausal women have been widely studied due to the loss of estrogen they experience during menopause. The effects of estrogen may have positive effects on the brain and cognitive function. Shaywitz et al. (1999) performed a study to determine the effects of estrogen on brain activation patterns in post-menopausal women as they performed verbal and nonverbal working memory task. The study was conducted in a hospital setting using forty-six post-menopausal women. Results indicated that estrogen produces significant alterations in brain activation patterns as seen by an fMRI as post-menopausal women performed a working memory task. Sherwin (2003) conducted a review a literature investigating estrogen and its role in cognitive function. It was found that estrogen replacement therapy (ERT) aids in protecting verbal memory in post-menopausal women. Dietrich et al. (2001) examined if hemodynamic menstrual cycle dependant changes for verbal, spatial and motor task. An fMRI using blood oxygenation level-dependent contrast was used to examine cognitive function. Results revealed normal cycling females blood estrogen level have a significant difference between the sizes of activation in an fMRI for cognitive task when estrogen is at peak levels (Dietrich et al., 2001).

In contrast to previous research, one study found that during high levels of the sex hormones (estrogen and progesterone) spatial test score decreased (Hausmann, Slabbekoorn, Van Goozen, Cohen-Kettenis, & Gunturkun, 2000). Hausmann et al. (2000) administered a mental rotation test during the menses

and midluteal phase and found that all women had higher test scores in the menses phase, specifically when estrogen levels are at its lowest point during the menstrual cycle. Hausmann et al. concluded that spatial performance is sensitive to hormonal fluctuations across the menstrual cycle and that different aspects of spatial performance are related to different hormones. Similarly, in another study that suppressed estrogen in normally functioning females it was found that a decline in ovarian hormones was associated with change in short-term verbal memory concentration and attention (Owens et al., 2002).

Oral Contraceptives

Oral contraceptives have been a widely studied topic for their use in protecting women against pregnancy. There are two primary types of oral contraceptives, combination and progestin-only pills. Combination oral contraceptives consist of synthetic versions of estrogen and progestin taken daily, which block the usual hormone interaction that directs ovulation. Estrogen and progestin, the active ingredients in the pill, are similar to the hormones that a female's body naturally makes. Females taking oral contraceptives results in egg development being blocked, preventing conception (Darney, 1997). Unlike combination oral contraceptives, progestin-only pills contain no estrogen and have a lower dose of progestin than combined birth control pills. Progestin-only oral contraceptives work in 3 different ways: (1) they make the cervical mucus at the entrance to the uterus too thick for the sperm to get through to the egg; (2) they prevent ovulation in about half of the users; and (3) they affect other hormones, the fallopian tubes, and the lining of the uterus (Graham, Ramos,

Bancroft, Maglaya, & Farley, 1995). There have been several studies that have examined the possible side effects of oral contraceptives which include nausea, breast pain, and headache (O'Connel, Davis, & Kerns, 2006; Ernst, Baumgartner, Bauer, & Janssen, 2002). However oral contraceptives have not been widely investigated for their affect on cognitive function during different menstrual cycle phases.

Brooks et al. (1977) conducted a study to explore the range of expectations and attitudes associated with menstruation. The researchers found that women who were taking oral contraceptives had the same attitudes and accepted the same cycle-related symptoms as women who were not taking oral contraceptives. Abraham et al., (2003) conducted a study to examine the cyclicity and group differences in daily menstrual cycle mood and physical experiences of three groups of healthy women using monophasic, triphasic OC or non-hormonal contraception. It was found that there were no differences between oral contraceptive users and non-oral contraceptive users in mood and physical experiences (Abraham et al.). In contrast, Wright and Badia (1999) conducted a study to examine the influence of menstrual cycle phase and oral contraceptives on nighttime alertness and performance on the circadian rhythms and body temperature. Oral contraceptive users had higher alertness and performance in the follicular phase when compared to non-oral contraceptive users.

Review of Method Literature

Phases of the menstrual cycle have been determined by either self-reporting when the first day of bleeding occurred, ovulation tests, or by taking blood samples. Ablanalp et al. (1979) found that taking blood samples was much more accurate in determining the stage of menstrual cycle. Hausmann et al. (2000) also determined that by taking blood samples the researcher is then certain that the female is in the correct menstrual cycle phase. However, taking blood samples is extremely costly and invasive to the participant. Therefore, many studies have used self-reporting to determine which menstrual cycle phase the participants are in (Abplanalp et al., 1979; Brooks et al., 1977). Furthermore self-reporting is commonly used when there is a large sample size due to the cost involved in blood samples.

The ovulation test is a good method to determine phase of the menstrual cycle, because it considered non-invasive and not as costly as blood samples. An ovulation test can confirm that ovulation has occurred and the participant has moved from the follicular phase to the luteal phase by identifying a surge in urinary luteinising hormone (LH). Once the LH surge has been shown to occur, it can be assumed with a confidence level of 95% that ovulation will take place within the next 14 to 26 hours (Janse de Jonge, 2003).

Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT)

Neuropsychological testing has evolved from the traditional paper and pencil test to the computerized test. Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) is a computer-based program used to assess

neurocognitive function. The neurocognitive test, ImPACT has been most widely used for establishing neurocognitive deficits after sustaining a concussion. The ImPACT test consists of a demographic section, self-report concussion symptoms, and six individual test modules that measure aspects of cognitive function including attention, memory, reaction time, and processing speed (Iverson, Lovell, & Collins, 2003). Detailed information and psychometric properties of ImPACT are covered under the methods section.

Summary

Overall it has been shown that there are many discrepancies in the literature regarding the menstrual cycle and cognitive function. Furthermore, oral contraceptives have not been widely investigated for their effect on cognitive function during different menstrual cycle phases. The main female sex hormones that regulate the menstrual cycle are progesterone and estradiol. These hormones may play a role in cognitive function; as a result they need to be more closely examined to determine if cognitive function changes during the menstrual cycle. Therefore, the purpose of this study was to evaluate the cognitive function of females who use oral contraceptives and do not use oral contraceptives during the three phases of the menstrual cycle.

CHAPTER 3

METHODS

This chapter describes the design, procedures, and methodology used in this research. Included in this chapter are the following: Research Design, Participants, Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT), First Response Ovulation Test, Data Collection Procedures, Management, and Analysis, and Threats to Internal and External Validity.

Research Design

This study was a quasi-experimental two group counterbalance research design. This study is considered a two group counterbalance design because there will be two groups; oral contraceptives and no oral contraceptives. The participants acted as their own control for this study. The independent variable is phase of the menstrual cycle. It has three levels: menses phase, follicular phase, and luteal phase. The dependent variable is the ImPACT neurocognitive test battery. ImPACT consists of verbal memory composite score, visual memory composite score, reaction time composite score, and processing speed composite score.

Participants

Thirty-two adult females were asked to volunteer for this study. Specifically, 19 females who were not taking oral contraceptives and 13 females who were taking ortho tri-cyclen lo (norgestimate/ethinyl estradiol). Ortho tri-cyclen lo (norgestimate/ethinyl estradiol) is comprised of a combination of progestational compound norgestimate and the estrogenic compound ethinyl

estradiol. Participants were between the ages of 18 to 28 years. Prior to taking part in the study participants signed an informed consent. Females had no history of menstrual cycle problems, or history of pregnancy. All participants had no history of concussions within the past six months. Participants taking oral contraceptives were all taking the same dosage birth control pill, ortho tri-cyclen lo (norgestimate/ethinyl estradiol). The participants took a different pill every week. First the white pill was comprised of 0.18mg of progestational compound and 0.025mg of the estrogenic compound. The light blue pill was comprised of 0.215mg of the progestational compound and 0.025 mg of the estrogenic compound. The dark blue pill was comprised of 0.250 mg of the progestational compound and 0.025 mg of the estrogenic compound. The dark green pill has no active ingredients.

Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT)

ImPACT version 5.0 (ImPACT Applications Inc.) is a computer-based program that was used to assess neurocognitive function (Lovell et al., 2006). The software program is run from either a desktop PC or laptop using Windows NT operating system or higher (Lovell, Collins, Podell, Powell & Maroon, 2000). The program uses a keyboard and external mouse to allow participants to select responses and navigate through the six test modules.

The ImPACT protocol consists of three categories. The first category included a demographic information section. The user was asked to navigate through a series of instructional screens where they are asked to enter

descriptive information about themselves, such as years in school, presence of learning disabilities, and neurological disorders.

The second category consists of 22 symptoms that participant's rate using a seven point Likert scale. These symptoms include headache, nausea, vomiting, balance problems, dizziness, fatigue, trouble falling asleep, sleeping more than usual, sleeping less than usual, drowsiness, sensitivity to light, sensitivity to noise, irritability, sadness, nervousness, feeling more emotional, numbness or tingling, feeling slowed down, feeling mentally foggy, difficulty concentrating, difficulty remembering, and visual problems. Participants self-rated their symptoms by clicking on a number between zero (not experiencing) and six (severe) using an external mouse.

The third category consists of six neurocognitive test modules. It is important to note that ImPACT has multiple built-in word/design groups. This is important to limit practice effects. A different word/design group was administered to the participant for each ImPACT test. Module one of the neurocognitive test battery focuses on word discrimination. This section is used to evaluate verbal memory and attentional processes. Subjects are presented with 12 words two times each for 750 milliseconds. Individuals are then tested to recall words from a 24 word list. There are 12 target words and 12 non-target words. Using the mouse, subjects are prompted to select "yes" or "no" depending on whether or not the word was presented in the original list. After a 20 minute delay, subjects are asked again to recall this list of words. A total score of percent correct is given at the end of the battery.

Module two evaluates attention and visual recognition through design memory. Similar to module one, 12 target designs are presented twice for 750 milliseconds. Following the presentation subjects are asked to recall these designs, choosing from the 12 target and 12 non-target designs presented. Subjects are prompted to click “yes” or “no” depending on whether or not the design was originally presented. After a 20 minute delay, subjects are asked again to recall this list of designs. A total score of percent correct is given at the end of the battery.

Module three is designed to measure visual working memory, visual processing speed, and visual memory. This section incorporates a distracter which is a reaction time test that asks the subject to click the left mouse button if a blue square appears, and the right mouse button if a red circle appears. For the memory test, a random assortment of X's and O's are displayed for one and one-half seconds. Of this random assortment, three X's and O's are illuminated in yellow. The subject is instructed to remember the placement of these illuminated objects. Immediately following the presentation of the three illuminated X's and O's, the subject is asked to complete the distractor task. After the completion of the distractor task, the memory screen reappears and the subject is asked to click on the X's and O's that were originally highlighted. Four trials are completed for this section. Scores for this section include percent correct for identification of the X's and O's and reaction time scores for the distractor task.

Module four is a symbol-matching task that evaluates processing speed, learning, and memory. A grid with nine common symbols and accompanying

numbers is presented to the subject. The subject is presented with a symbol below the grid, and is asked to click the number of the corresponding design. After 27 trials, the symbols are removed from the grid. The symbols are presented below the grid, and the subject is asked to recall the correct symbol/number pairing by clicking the appropriate button. Reaction time scores and memory scores are both calculated.

Module five measures choice reaction time and impulse control. Subjects are presented with the words red, green, and blue each written in their respective color. Subjects are instructed to click the mouse when the word correctly matches with the color ink. For this section, a reaction time score and task error score are provided.

The sixth and final module examines working memory and visual motor response speed. This module is comprised of both a distractor task and memory component. Participants are presented with and asked to remember three letters. Once the letters are removed from the screen, the participant is presented with the distractor task. A 5x5 grid appears on the screen consisting of 25 numbered boxes. The participant is asked to count backwards, clicking on the corresponding numbered box with the mouse. Following the completion of the distractor task, the participant must input the three letters in the exact order they were previously presented. There are five trials for this test module.

Reliability and Validity of ImPACT

Test-retest reliability for ImPACT was assessed over eight days across four administrations, yielding correlation coefficients ranging from 0.66 to 0.85 for

the verbal memory index, 0.75 – 0.88 for the processing speed index, and 0.62 to 0.66 for the reaction time index (Lovell, Collins, Fu, Burke & Podell, 2001). Using reliable change indices, repeated administrations over a 2-week period revealed no practice effects (Iverson, Lovell, Collins & Norwig, 2002). In another study, one week test-retest reliability coefficients were as follows: 0.70 for verbal memory, 0.67 for visual memory, 0.79 for reaction time, and 0.86 for processing speed, with significant test-retest differences for only the processing speed composite scores on with-in subject comparisons (Iverson, Lovell & Collins, 2005). Concurrent validation of ImPACT revealed correlations with the Symbol-Digit Modalities test (SDMT) which ranged from 0.37 and 0.46 for visual and verbal memory indices, to 0.60 and 0.70 for reaction time and processing speed indices (Iverson, Lovell & Collins, 2005). Since the SDMT is believed to measure scanning and tracking aspects of attention, as well as processing speed (Spreen & Strauss, 1998), these coefficients represent good convergent and divergent validity. Correlations between ImPACT visual and verbal memory composites with the Brief Visual Spatial Memory Test-Revised total score ($r=.50$) and the delayed recall score ($r=.85$) have been established (Iverson, Franzen, Lovell & Collins, 2004); the processing speed composite was shown to correlate with the Trailmaking Tests A ($r= -.49$) and B ($r= -.60$), and the SDMT ($r=.68$). Schatz and colleagues documented a combined sensitivity of 81.9% for ImPACT indices and total symptom score, and a specificity of 89.4%; positive likelihood ratio was approximately 8:1 and negative likelihood ratio was 2:1 (Schatz, Pardini, Lovell, Collins & Podell, 2006).

First Response Ovulation Test

In order to confirm that ovulation has occurred in naturally cycling females, and, the participant has moved from the follicular phase to the luteal phase, an ovulation test was taken. The ovulation test identified a surge in urinary luteinising hormone (LH). Once the LH surge occurred, it can be assumed with a confidence level of 95% that ovulation took place within the next 14 to 26 hours (Janse de Jonge, 2003). This is important because ovulation marks the end of the follicular phase and the start of the luteal phase.

Data Collection Procedures

Michigan State University's Institutional Review Board approved this study prior to data collection. Participants were chosen solely on a volunteer basis. The participants were recruited by word of mouth and through fliers. The fliers were posted in IM Circle and IM West in the women's locker room. Once participants were recruited, they were selected by a convenience sampling method.

Participants were asked to sign an informed consent form prior to testing and data collection (see Appendix A). The consent included: the purpose of research, the duration of data collection, the testing procedure, the potential risk and/or benefits of the testing, confidentiality, contact information for myself, my advisor, as well as Michigan State University's UCRIHS office, and a place for the participant to sign and date. The Participant was also given a health history questionnaire to determine if they met the requirements for this study (see Appendix B)

Testing for this research was done over the course of each participant's menstrual cycle. All tests were done at approximately the same time of day. The participant was asked to report the start of her last menstrual cycle. Based on the first date of the last menstrual cycle, the follicular, luteal, and menses was then approximated. Ovulation was confirmed by the First Response Ovulation test to ensure the change from the follicular phase to the luteal phase. In 15 out of the 19 participants ovulation was confirmed, the other three participants' luteal phase was approximated. Each participant's menstrual cycle was calculated and a testing schedule was determined.

Participants taking oral contraceptives did not take the ovulation test. Participants were taking orth-tricyclin lo (norgestimate/ethinyl estradiol) resulting in a 28 day menstrual cycle. Participants took ImPACT during day 1 to 4 for follicular phase, day 15 to 19 for luteal phase and day 22 to 26 for menses phase.

Testing Session

This study was performed in the computer lab in IM Sports Circle, on the Michigan State University campus during pre-arranged times convenient for the participants and researchers. There was a total of three testing sessions. For naturally cycling females (no oral contraceptive) the first testing session was determined by the start of their first day of bleeding of their last menses cycle. Their current menstrual cycle phase was determined by counting the days from the last menstrual cycle which determined if they are in the follicular phase which occurs 15 to 22 days before onset of new menstrual cycle, luteal phase which

occurs 3 to 9 days before the onset of a new menstrual cycle, or menses the second to fourth day of bleeding. The participant then took the ImPACT neurocognitive test battery. After the participants completed the ImPACT test battery the remaining two testing sessions were determined and scheduled.

Participants taking oral contraceptives were all on a 28 day menstrual cycle, and taking ortho tri-cyclen lo (norgestimate/ethinyl estradiol). All phase cycles were approximated because the participants had a set menstrual cycle. Participants took ImPACT during day 1 to 4 of the start of a new oral contraception pill pack for follicular phase, day 15 to 19 for luteal phase and day 22 to 26 for menses phase.

Data Management

Data was recorded through the ImPACT software. The data were then transferred into a Microsoft Excel spreadsheet and imported into an SPSS data file for statistical analysis. All data files were kept on a password protected personal computer in a locked office. A backup of the data was kept on a USB travel drive that was kept in a locked desk in a locked office. All consent forms and results of the ovulation test were also kept in a locked office and only authorized researchers had access to the consent forms and data files. Participant privacy was assured by issuing a participant number to each person to ensure that their names are not linked to their data after the testing procedure is complete.

Data Analyses

The ImPACT yields composite scores for verbal memory, visual memory, visual processing speed, and reaction time. A higher score by the participant on verbal and visual memory, and processing speed indicates better performance. Verbal and visual memory scores are presented as a percentage of 100 and processing speed as a number composite score. A lower score on reaction time indicates a better performance. The ImPACT also yields individual scores for concussion symptoms. A 2 group (oral contraceptive, no oral contraceptive) X 3 time (menses, follicular, luteal) multivariable analysis of variance (MANCOVA) controlling for history of concussion was performed on the ImPACT composite scores. The statistical significance level was set at $p < 0.05$. All analyses were conducted using SPSS version 15.1 (SPSS Inc, Chicago, IL).

Threats to Internal Validity

There are many threats to internal validity in this study; however, maximum efforts will be taken to minimize the effects of these threats. Reverse causation was a threat because a decreased ImPACT score could have several possible explanations. This was controlled for by have the participants take ImPACT during every phase of the menstrual cycle.

There are numerous time threats that occurred in this study. History was a threat in this study because the participants took ImPACT on three different days within the menstrual cycle. History was controlled for by having each participant take ImPACT during each phase, therefore, acting as their own control. Maturation was also a threat to this study because the participants had

approximately a week and half in between testing sessions. This was controlled for by having the participant take the test as soon as possible during the menstrual cycle phase. Instrumentation is a threat because ImPACT could malfunction at any point therefore tainting the data. The computers used for ImPACT were piloted to make sure the program is working before each testing session. Reactivity to testing is controlled by ImPACT itself, the computer test has been tested to minimize learning affects.

Researcher expectancy could have had a negative effect because the researcher might expect a change in ImPACT scores through the different menstrual cycle phases. This was controlled for by the researcher not being in the room when the participant was taking the test. On-stage effects could pose a threat if the researcher was watching the participant take the ImPACT test, or other participants are taking the test at the same time. This was controlled for by having the researcher not in the room when the test is being taken and by having each participant take the test in a separate room. Group threats could pose a problem because there will not be random assignment of groups. This was minimized because the participants served as their own control.

Threats to External Validity

Threats to external validity were identified and efforts were made to minimize the effects of these threats. Due to the repetitive testing procedures there may be reactive/interactive effects of testing. This was controlled by the nature of the ImPACT test. There should not be an interaction of selection bias and treatment in the current study. In an effort to minimize the threat of a

reaction to experimental setting, the test was done in a computer lab where it is very quiet and free of any distractions. Multiple treatment interference is not a threat because there were no actual treatment.

CHAPTER 4

RESULTS

The results section is separated into demographic information, baseline data, and evaluation of the research questions. Overall there were no significant differences with ImPACT during the three menstrual phases between participants in the oral contraceptive and no oral contraceptive groups.

Demographic Information

A total of 32 collegiate females from a Mid-Western Division I-A university participated in the current study. All demographic information was collected by ImPACT and a short questionnaire. Nineteen participants (age= 21.05 ± 2.25 years, height= 65.65 ± 2.681 inches, weight= 149.40 ± 24.96 lbs.) comprised the no oral contraceptive group and 13 participants (age= 21.34 ± 2.10 years, height= 65.46 ± 2.22 inches, weight= 138.77 ± 23.08 lbs.) were on the ortho tri-cyclen lo (norgestimate/ethinyl estradiol) birth control pill.

Baseline Data

A MANCOVA controlling for concussion history was used to examine differences in baseline ImPACT composite scores between the oral contraceptive and no oral contraceptive groups. Baseline ImPACT composite scores and normative data are presented in Table 4-1. In general, the baseline ImPACT composite scores for this sample were average compared to established normative data for this population.

Table 4-1 Descriptive Baseline ImPACT Composite and Symptom Scores for the Total Sample (N=32)

ImPACT	Mean	SD	ImPACT Norms
Module			University Women†
Verbal Memory			
No OC	.88	.07	0.92
OC	.91	.06	
Visual Memory			
No OC	.78	.09	0.79
OC	.81	.11	
Motor Speed			
No OC	38.67	9.85	38.25
OC	41.85	7.91	
Reaction			
No OC	.55	.05	0.55
OC	.51	.05	

†Median values of women's ImPACT scores
Oral Contraceptive (OC)

A comparison of oral contraceptive and no oral contraceptive participants indicated no significant differences on baseline ImPACT composite scores between groups (*Wilk's* $\lambda = 0.696$, $F_{[5, 25]} = 2.18$, $p = 0.088$, $\eta^2 = 0.504$). Similarly, a comparison of all participants and normative data revealed no significant differences on baseline ImPACT composite scores. The data suggests that participants were similar in regard to baseline ImPACT composite scores regardless of these potential confounding factors. Hence, any differences between ImPACT composite scores would likely be due to menstrual cycle phases and/or oral contraceptives.

Evaluation of Hypothesis

Hypothesis: There will be no difference in cognitive function during the three different phases of the menstrual cycle for females who do not take oral contraceptives and females who take oral contraceptives.

A 2 group (oral contraceptive, no oral contraceptive) x 3 time (menses, follicular, luteal) repeated measures MANCOVA controlling for concussion history was used to assess within and between group differences on ImPACT composite scores and total symptoms during the three phases of the menstrual cycle. Descriptive statistics of each ImPACT composite score and symptom totals can be found in Table 4-2.

Table 4-2 Descriptive Statistics for No Oral Contraceptives and Oral Contraceptives Groups on ImPACT Composite Scores and Total Symptoms.

	Menses		Follicular		Luteal	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Verbal Memory						
No OC*	0.88	0.08	0.89	0.08	0.92	0.06
OC	0.91	0.07	0.92	0.07	0.90	0.05
Visual Memory						
No OC	0.78	0.09	0.76	0.12	0.73	0.13
OC	0.80	0.12	0.73	0.10	0.77	0.13
Processing Speed						
No OC	38.67	9.85	41.29	8.15	40.84	8.73
OC	41.86	7.91	41.54	7.41	42.81	4.90
Reaction Time						
No OC	0.55	0.05	0.54	0.05	0.53	0.04
OC	0.51	0.05	0.51	0.05	0.52	0.06
Total Symptoms						
No OC	4.42	5.49	6.42	9.20	3.95	7.02
OC	9.85	13.38	7.54	11.19	7.08	12.22

*Oral Contraceptive (OC)

Box's M test of equality of covariance matrices (see Table 4.3) and Levene's test of equality of error variances (see Table 4.4) were both upheld. Therefore, both the oral contraceptive and no oral contraceptive groups had an equal distribution. The MANCOVA results indicated no significant differences for within subject effects for time (*Wilk's* $\lambda = 0.68$, $F_{[5, 18]} = .91$, $p = 0.54$, $\eta^2 = 0.32$), and the interaction between group and time (*Wilk's* $\lambda = 0.56$, $F_{[5, 18]} = 1.09$, $p = 0.42$, $\eta^2 = 0.35$) (see Table 4.5). The MANCOVA results also indicated a no significant differences between the oral contraceptive and no oral contraceptive groups (*Wilk's* $\lambda = 0.80$, $F_{[5, 18]} = 1.25$, $p = 0.32$, $\eta^2 = 0.20$) (see Table 4.6).

Table 4.3 *Box's Test of Equality of Covariance Matrices(a)*

Box's M	144.86
F	0.98
Df1	78
Df2	2112.12
Significance	0.54

Table 4.4 Levene's Test of Equality of Error Variances(a)

	F	df1	df2	Sig.
Verbal Memory				
Menses	0.32	1	30	0.58
Follicular	0.17	1	30	0.68
Luteal	0.10	1	30	0.76
Visual Memory				
Menses	0.21	1	30	0.65
Follicular	1.25	1	30	0.27
Luteal	0.02	1	30	0.90
Processing Speed				
Menses	0.10	1	30	0.76
Follicular	0.03	1	30	0.87
Luteal	1.50	1	30	0.23
Reaction Time				
Menses	0.66	1	30	0.42
Follicular	0.03	1	30	0.87
Luteal	2.07	1	30	0.16

Table 4.5. MANCOVA within Subjects Effect for Time and Group X Time

	Effect	Value	F	Hypothesis df	Error df	Sig
Time+	Pillai's Trace	.315	.919	10.00	20.00	.535
	Wilks' Lambda	.685	.919	10.00	20.00	.535
	Hotelling's	.460	.919	10.00	20.00	.535
	Trace	.460	.919	10.00	20.00	.535
	Roy's Largest Root					
Group++ X Time	Pillai's Trace	.354	1.094	10.00	20.00	.412
	Wilks' Lambda	.646	1.094	10.00	20.00	.412
	Hotelling's	.547	1.094	10.00	20.00	.412
	Trace	.547	1.094	10.00	20.00	.412
	Roy's Largest Root					

* $p \leq 0.05$

+Time: All Participants

++Group: Menstrual Cycle Phases

Table 4.6. MANCOVA between Oral Contraceptive and No Oral Contraceptive Groups

	Effect	Value	F	Hypothesis df	Error df	Sig
Group	Pillai's Trace	.200	1.249	5.00	25.00	.317
	Wilks' Lambda	.800	1.249	5.00	25.00	.317
	Hotelling's	.250	1.249	5.00	25.00	.317
	Trace	.250	1.249	5.00	25.00	.317
	Roy's Largest Root					

** $p \leq 0.05$*

CHAPTER 5

DISCUSSION

Previous research has demonstrated numerous discrepancies on the effects menstrual cycle has on cognitive function (Maki & Resnick, 2001, Dietrich et al., 2000, Keenan et al., 1995). The current study adds to the present body of literature that states that the menstrual cycle phases have no impact on cognitive function.

Discussion of ImPACT Composite Scores

The findings of this study found no differences on cognitive function during the three phases of the menstrual cycle. These results were similar to other studies that found no significance differences on cognitive function and menstrual cycle phases (Collins et al., 1985, Sommer, 1972, & Owens et al., 2002). For example, Owen et al. (2002) found no significant differences in verbal learning when ovarian hormone levels were changed. The authors suggest no changes were found because the participants that were tested were healthy, intelligent young females, similar to the participants in this study. Although Owen et al. (2002) chemically altered ovarian hormone levels the results can be applied to this study because hormone levels naturally change throughout the different menstrual cycle changes.

Comparable to the present study and others, Collins et al. (1985) found no difference in cognitive function when using neuropsychological tests such as cognitive-conflict, mental arithmetic and a computer game, all similar to the ImPACT test used in this study. Collins et al. (1985) attributed no significant

change in test results to the sample selection. All participants were well educated college aged females that had no history of menstrual cycle problems. Similarly this study also found no differences in cognitive function across the phases of the menstrual cycle.

Contrary to the findings of this study there have been a few studies that have found changes in brain function during the different phases of the menstrual cycle (Maki & Resnik, 2001, Dietrich et al., 2000, & Schoning et al., 2007). For example, Schoning et al. (2007) used mental rotation of 3-D objects which tested participants' visuo-spatial memory. This study used functional MRI (fMRI), and found an increase in cortical activation across the phases of the menstrual cycle. The luteal phase of the menstrual cycle demonstrated the greatest increase in cortical activation. However, this study did not use mental rotation testing techniques or an fMRI. Hence, the different findings between Schoning et al. (2007) and this study could be attributed to different methodologies used. Schoning et al. (2007) used fMRI which measures brain activation while this study examined a behavioral cognitive task measure by ImPACT.

There have been very few studies that have evaluated cognitive function during phases of the menstrual cycle on females taking oral contraceptives. According to our findings there were no significant differences between the oral contraceptive and the no oral contraceptive groups. In contrast with this study, Wright and Badia (1999) found that oral contraceptive users had higher alertness and performance in skills such as switching task, two column addition, digit recall, reaction time task, dual task, continuous recognition, memory recall and

dual task when compared to females who did not take oral contraceptives during sleep deprivation. Wright and Badia (1999) contributed the higher scores to the participants on oral contraceptives having significantly higher body temperature than participants not taking oral contraceptives. Wright and Badia (1999) suggest that temperature level strongly relates to nocturnal waking neurobehavioral function. The contrary in findings could be attributed to the small sample size and sample selection. The participants in this study were healthy and fully rested, whereas in Wright and Badia's (1999) study the participants were sleep deprived.

Clinical Interpretation of Results

It appears that when testing verbal and visual memory, reaction time and processing speed across the menstrual cycle phases there are no difference in cognitive function. A possible reason may be because ImPACT is not sensitive enough to detect any changes through the three different phases. The ImPACT neurocognitive test was originally developed to evaluate the neurocognitive impairments that can occur after a concussion. The participants in this study did not have any injury therefore; the ImPACT test might not have been sensitive enough to pick up on any minor changes in cognitive function that possibly could occur during the different phases of the menstrual cycle.

It could be possible that when testing normal females that the hormonal fluctuations are not great enough to detect. Another possible explanation may be due to verbal and visual memory, reaction time and processing speed are not affected by the hormonal changes in females. Estrogen and progesterone are

the two main hormones involved in the menstrual cycle. This study demonstrates that females have the same thought process regardless of progesterone or estrogen levels. It can be stated that although some women do report an impairment of their mental capacity before or during menstruation, when objective measures of performance were employed this study failed to demonstrate significant menstrual cycle phase-related changes.

Limitations

There were several limitations in this study. One limitation to the current study was the sample population and size. Only females from one Division I-A Institution participated in this study. Recruiting females from various institutions and from multiple regions of the country would aid in providing a more diverse sample. In addition the current study had a small sample size which may have contributed to the findings.

Another limitation was the use of only one type of oral contraceptive, ortho tri-cyclen lo. Although it was necessary to control oral contraceptives for this study, ortho tri-cyclen lo (norgestimate/ethinyl estradiol) is not the only oral contraceptive on the market. Other forms of oral contraceptives might effect the results due to different doses and combinations used. Other forms of birth control were also not used in this study. Evaluating other forms of birth control such as the patch or intra-uterus devices might affect the results of this study.

Other limitations that occurred in this study were the estimation of menstrual cycle phases. Blood samples were not taken to confirm blood hormone levels throughout the menstrual cycle phases. Although an ovulation

test was done to confirm ovulation and resulting in changes from the follicular phase to the luteal phase not all participants displayed a positive test.

Performing blood samples would ensure that all participants were in the correct menstrual phase.

Future Research Considerations

Future research considerations should include differentiations in sample population to include NCAA athletes and other physically active populations. There have been many documented studies that illustrate differences in females who exercise and females who do not exercise.

Future research needs to test concussed females during the different phases of the menstrual cycle. The ImPACT test is more commonly used for post-concussion testing. Incorporating menstrual cycle phases in concussion testing would be beneficial. Involving females who have abnormal menstrual cycles would also be beneficial to researchers.

Conclusion

The menstrual cycle is a complex process that all females experience. Most females have attributed pain, mood disorders, and decreased mental function to the menstrual cycle at least once. However, this study along with many others has shown that there is no evidence to support that the menstrual cycle is responsible for any differences in cognitive function. The information presented in this study provides more insight into the cognitive function of females menstrual cycle. Overall this study failed to demonstrate any significant changes in cognitive function across the different phases of the menstrual cycle.

APPENDIX A
Human Subjects Consent Form

**Relationship between Menstrual Cycle Phases and Cognitive Function in Females
who Use and Do Not Use Oral Contraceptives**

Informed Consent

***For questions regarding this study,
Please contact:***

Tracey Covassin Ph.D, ATC
Department of Kinesiology
Programs
Michigan State University
Phone: (517) 353-2010
E-mail: covassin@msu.edu or

***For questions regarding your rights
as a research participant, please contact:***

Peter Vasilenko, Ph.D.
Director of MSU's Human Research Protection

Michigan State University
202 Olds Hall
East Lansing, MI 48824
irb@msu.edu
Phone: (517) 355-2180
Fax: (517) 432-4503

1. Purpose of Research:

You are being asked to participate in a research study to determine if phases of the menstrual cycle affect your cognitive function. You have been selected as a possible participant in this study because you are a female either taking oral contraceptive or are naturally cycling. From this study, the researchers hope to learn if neurocognitive function changes during the different phases of the menstrual cycle. Your participation in this study will take about 90 minutes to complete (3 sessions for 30 minutes each). You must be 18 years or older to participate in this research study.

2. WHAT YOU WILL DO:

The study will use the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) computer program as an assessment tool. In this study, ImPACT will be used to test your short and long term memory, concentration level, processing speed, and reaction time during the different phases of the menstrual cycle. Screening is neither intelligence, nor achievement testing. Non-oral contraceptive users will be required to take a urine test to confirm ovulation. No invasive procedures are performed.

3. POTENTIAL BENEFITS:

You will directly benefit from participation in this study. You will receive test scores from all phases of the menstrual cycle. You will benefit from determining if the phase of the menstrual cycle affects neurocognitive dysfunction.

4. POTENTIAL RISKS:

You are aware that your participation in the above stated study involves little or no discomfort or harm to you. Please be assured that you may choose to not answer certain questions and still continue to participate in this study. All answers are strictly confidential and will not be released to anyone.

5. PRIVACY AND CONFIDENTIALITY:

The researcher and one graduate student will have access to your data and will be able to link data to you. This data will be destroyed in seven years. Participation in this study is completely voluntary. You have the right to say no. You may change your mind at any time and withdraw. Confidentiality will be protected by; (a) results will be presented in aggregate form in any presentations and publications; and (b) all data will be stored in a computer that has a password necessary to see confidential data. Your privacy will be protected to the maximum extent allowable by law. You may also discontinue participation at any time without penalty. Your participation in this research project will not involve any additional costs to you or your health care insurer. The results of this study may be published or presented at professional meetings, but the identities of all research participants will remain anonymous.

6. COSTS AND COMPENSATION FOR BEING IN THE STUDY:

Procedures being performed for research purposes only will be provided free of charge by Dr. Covassin and her research assistant. You will not receive money or any other form of compensation for participating in this study.

7. CONTACT INFORMATION FOR QUESTIONS AND CONCERNS

If you have any questions about this study, such as scientific issues, how to do any part of it, or to report an injury, please contact the researcher Dr. Tracey Covassin at 517-353-2010 or e-mail her at covassin@msu.edu (105 IM Sport Circle, Department of Kinesiology, East Lansing, MI 48824).

If you have any questions about your role and rights as a research participant, or would like to register a complaint about this study, you may contact, anonymously if you wish, the Director of MSU's Human Research Protection Programs, Dr. Peter Vasilenko, at 517-355-2180, FAX 517-432-4503, or e-mail irb@msu.edu, or regular mail at: 202 Olds Hall, MSU, East Lansing, MI 48824.

8. DOCUMENTATION OF INFORMED CONSENT.

Your signature below indicates your voluntary agreement to participate in this study.

I, _____ have read and agree to participate in this study as
(Please Print Your Name) described above.

(Please Sign Your Name)

_____/_____/_____
(Date)

APPENDIX B
Health History Questionnaire

Relationship between Menstrual Cycle Phases and Cognitive Function in
Females who Use and Do Not Use Oral Contraceptives

MICHIGAN STATE UNIVERSITY
HEALTH HISTORY QUESTIONNAIRE

Name _____

Age _____

E-mail Address _____

Phone Number _____

How much exercise do you do a week? _____

Do you have any learning disabilities? _____

Have you had any concussions within the last 6 months? _____

Do you take oral contraceptives? _____

If so, when did you start taking the oral contraceptive and what kind are
you taking? _____

Do you have any documented menstrual cycle problems? _____

When was the start of your last menstrual cycle? _____

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