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The Impact of Menstrual Cycle Phase on Smoking Cessation-Related Variables

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Louisiana State University and
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in

The Department of Psychology

by

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ABSTRACT

Tobacco use remains the leading cause of preventable disease and death in the United States. Despite increased research and improved treatment modalities, rates of lapse and relapse remain high. Women in particular experience poorer smoking cessation outcomes (including more relapse), presumably due to unique considerations such as the hormonal milieu. Despite some conflicting results, researchers have speculated that timing cessation attempts to coincide with the luteal phase of the menstrual cycle, where levels of neuroprotective progesterone are at their peak, may decrease nicotine withdrawal and increase cessation success. Timing treatment onset with the luteal phase may positively impact smoking variables that influence cessation, such as withdrawal symptoms, tobacco craving, self-efficacy to quit, and motivation to quit among female smokers. The current study investigated if the luteal phase results in lower self-reported severity of withdrawal symptoms and tobacco cravings, as well as higher reported self-efficacy and motivation to quit, compared to study participants in the late follicular phase.

Female participants (n = 9; luteal phase n = 5, late follicular phase n = 4) completed online study measures. Menstrual cycle phase was determined based upon self-report (i.e., length of menses, length of cycle, last previous menses, next expected menses). Participants in the luteal and late follicular phases did not differ in smoking cessation-related variables (i.e., withdrawal severity, craving intensity, self-efficacy, motivation). Additionally, there was no evidence that the smoking cessation-related variables moderated the relationship between phase group and motivation to quit.
INTRODUCTION

Tobacco use is the leading cause of preventable death and disease in the United States. In 2010, the Surgeon General reported that more than 440,000 people die annually from smoking-related deaths (Centers for Disease Control and Prevention [CDC], 2012; United States Department of Health & Human Services [USDHHS], 2010). Tobacco use has been linked to a variety of medical conditions such as chronic bronchitis, emphysema, stroke, myocardial infarction, hypertension, and coronary heart disease. Smoking accounts for approximately one-third of all cancers and 90% of lung cancer (USDHHS, 2010). However, despite these health risks, approximately 46.6 million people in the United States over the age of 18 currently smoke cigarettes. Approximately 16.5% of all females in the United States smoke (Agaku, King, & Dube, 2012). Notably, females report longer durations of use compared to men. For example, the median cessation age for females is 37 years old compared to 33 years old for males (CDC, 2012; Cepeda-Benito, Reynoso, & Erath, 2004; Pierce & Gilpin, 1996).

Among current smokers, 68.8% report a desire to quit and millions attempt to quit every day; of those that do attempt to quit, only 3-5% maintain abstinence over 6-12 months (CDC, 2013; Hughes, Kelly & Naude, 2004). There are no consistent gender differences in the rates of smoking cessation or motivation to quit smoking (USDHHS, 2001). However, female smokers are particularly vulnerable to relapse (USDHHS, 2001). Across interventions, including pharmacotherapy (such as nicotine replacement therapy [NRT]) and psychotherapy techniques, women report lower abstinence rates and more severe withdrawal symptoms than men (Perkins, 2001; Pomerleau & Pomerleau, 1996). Data have indicated that levels of sex hormones associated with menstrual cycle phase at quit date may affect cessation outcomes, as well as nicotine craving, withdrawal, and relapse (Carpenter, Upadhya, LaRowe, Saladin, & Brady,
2006; Lynch & Sofuoglu, 2010; McVay & Copeland, 2011; Mello, 2010). That women have lower abstinence rates as compared to their male counterparts may be due to more distressing levels of withdrawal, which may fluctuate across the menstrual cycle. Thus addressing female factors related to smoking cessation attempts (e.g., withdrawal) may inform interventions designed to decrease the incidence of relapse among female smokers.

**Menstrual Cycle Phase**

The female menstrual cycle (or female sexual cycle) is a monthly rhythmic pattern characterized by changes in rates of female hormones and the releasing of an ovum (egg) for fertilization (Guyton & Hall, 2000). This process begins during puberty. The first cycle occurs at approximately 12 years of age. Puberty is marked hormonally by the increased production and release of gonadotropin releasing hormone (GNRH) by the hypothalamus, which leads to the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) by the pituitary gland. These pituitary hormones are responsible for follicular development and ovulation. The secretion of FSH and LH results in an increased ovarian secretion of estrogen. Elevated estrogen levels result in ovulation and the subsequent production of progesterone, marking menarche—the female’s first menses (Guyton & Hall, 2000). Following irregular menses for the first 12-18 months, a female’s average menstrual cycle lasts approximately 28 days, although 25-35 days is considered normal. Menstruation will temporarily cease during pregnancy (Jensvold, 1996; Sherwin, 1996). In some individuals, the cycle may range anywhere between 20-45 days; however, abnormal cycle length is often associated with decreased fertility (Guyton & Hall, 2000).

The conventional menstrual cycle is divided into the follicular (including menses and late follicular phases) and luteal phases, which are separated by a periovulatory phase, marked by a
mid-cycle LH surge (i.e., a rapid rise in LH), resulting in ovulation. The standardized 28-day menstrual cycle begins with the start of menses (days 1-4) and continues into the late follicular phase (days 5-11). During menses, both estrogen and progesterone levels are low until the beginning of the late follicular phase. Then estrogen levels begin to elevate, while progesterone levels remain low (Davidsen, Vistisen, & Astrup, 2007). The estrogen levels peak during the periovulatory phase (days 12-15), when ovulation occurs; these levels remain relatively elevated throughout the luteal phase (days 16-28; Hall, 2009; Davidsen et al., 2007). Conversely, progesterone levels continue to remain low during the periovulatory phase and do not peak until the luteal phase (Davidsen et al., 2007). If fertilization does not occur, estrogen and progesterone levels fall, marking the beginning of the next cycle (Guyton & Hall, 2000).

The length of the follicular phase can often fluctuate. These fluctuations are frequently identified as the cause of individual variability in overall cycle length, varying from 4 to 19 days (Hall, 2009). The late follicular phase is characterized by rising levels of estrogen, resulting in the growth of the lining of the uterus (Guyton & Hall, 2000; Hall, 2009; see Figure 1). Contrary to the late follicular phase, the length of the luteal phase remains fairly constant between cycles and typically lasts for 10 to 16 days (Jensvold, 1996). Also, combined hormonal contraceptives (i.e., oral, injectable, or implanted) typically inhibit this ovulation through various mechanisms of action; these differ from “low dose” progestin oral contraceptives that act locally on the cervix, uterus, or fallopian tubes (Jensvold, 1996b).

The monthly cycle will continue until menopause at age 51, on average (Jensvold, 1996). Menopause is a result of depletion of ovarian primordial follicles eventually leading to insufficient estrogen available to regulate cycling (Jensvold, 1996; Sherwin, 1996). According
to the World Health Organization (WHO), menopause occurs gradually over a 10-year period, and thus the process begins sometime after a female turns 40 years of age (Jensvold, 1996).

Figure 1. A representation of the typical 28-day menstrual cycle. FSH = follicular stimulating hormone. LH = luteinizing hormone. From “Food Cravings and Food Cue Responding Across the Menstrual Cycle,” (doctoral dissertation) by M. A. McVay, 2012, retrieved from http://etd.lsu.edu/cgi-bin/ETD-browse/browse.
Menstrual Cycle Phase and Smoking Cessation-Related Factors

It is well established by empirical research that female smokers experience unique challenges when attempting smoking cessation, due to a variety of influences such as negative affect, concerns about weight gain, available social support, and the hormonal milieu (Perkins, 2001; Mello, 2010). Although the mechanisms of these differences in smoking cessation are not fully understood, recent research has established that the ovarian hormones (estrogen and progesterone) may modulate nicotine withdrawal, craving, and relapse.

In a recent review, Lynch and Sofuoglu (2010) explain that progesterone may have therapeutic utility in female smoking cessation, whereas estrogen may augment vulnerability to cessation relapse. Progesterone acts as a neuroprotective substance through numerous short- and long-term mechanisms of action, such as its non-allosteric influence on GABA<sub>A</sub> receptors (Singh & Su, 2013). Progesterone has also been shown to negatively modulate α4β2 receptors (Bertrand, Valera, Bertrand, Ballivet, & Rungger, 1991; Lynch & Sofuoglu, 2010).

Conversely, there is evidence that the high levels of estrogen during the follicular phase of the menstrual cycle correlate with a more highly active reward circuitry in women (Dreher, Schmidt, Kohn, Furman, Rubinow, & Berman, 2007). This estrogenic effect may confound efforts for successful cessation attempts, whereas the role of progesterone in the negative signaling of the nicotinic receptor (i.e., α4β2 receptors) may assist in these attempts.

This theoretical background supports the relationship between estrogen, progesterone, and smoking cessation-related factors. In a randomized smoking cessation trial, Allen, Bade, Center, Finstad, and Hatsukami (2008) assigned 202 nicotine dependent women to begin psychotherapeutic smoking cessation treatment (30 minutes of behavioral counseling and self-
help manuals) in either the luteal or follicular phases of the menstrual cycle. Women who were randomized to quit during the luteal phase of their cycle (when progesterone levels were at their peak) demonstrated a longer period of time until relapse in comparison with those randomized to quit during the follicular phase (where estrogen levels are elevated). Additionally after 30 days, 86% of smokers who quit during the follicular phase relapsed compared to 66% of smokers who quit during the luteal phase (Allen et al., 2008). Furthermore, Sofuoglu and colleagues (2001) reported that administering progesterone during the follicular phase of the cycle decreased smoking behavior.

There is also evidence that selecting a smoking quit date during the luteal phase may yield better cessation outcomes. Allen, Allen, Lunos, and Hatsukami (2009) found that women (n = 138 female smokers) were more likely to relapse during the same menstrual phase in which they quit (i.e., if a participant quit during the luteal phase, she was also more likely to relapse during the luteal phase). The researchers attributed this to the fact that study participants relapsed quickly. However, 51% of those who self-selected a follicular phase quit date relapsed compared to 35% of women who self-selected a luteal phase date (Allen, Allen, Lunos, & Hatsukami, 2009). In another study, women who were given bupropion sustained release tablets and who self-selected quit dates in the luteal phase were more likely to have been nicotine abstinent at a 3-month follow-up compared to those who chose a follicular phase quit date (Mazure, Toll, McKee, Wu, & O’Malley, 2011). However, two weeks after the initial quit date, absence was higher in the follicular phase group than the luteal phase group; 32% compared to 19%, respectively (Carpenter, Saladin, Leinbach, LaRowe, & Upadhyaya, 2008). Additional research has reported better treatment outcomes for female smokers who schedule a quit attempt during the follicular phase compared to the luteal phase (Franklin et al., 2008).
Menstrual cycle and nicotine withdrawal. Together, these data provide further support for the contention that the follicular phase in and of itself may not be related to poorer cessation outcomes, but may be related to increases in relapse vulnerability factors that increase likelihood for relapse. In support of this hypothesis, Carpenter and colleagues (2008) collected pilot data to investigate the variability in cigarette craving and nicotine withdrawal across the menstrual cycle. The study randomized female smokers to quit in either the follicular or luteal phase, and over the course of the 6-week study the participants received two sessions (totaling 90 minutes) of smoking cessation counseling and the transdermal nicotine patch. Women in the follicular group reported greater withdrawal, craving, fatigue, and confusion when compared to the luteal group.

Franklin and Allen (2009) recently collaborated to develop a potential hypothesis about the role of withdrawal in cessation attempts in the follicular phase to attempt to explain the discordant results in research concerning menstrual cycle phase during smoking cessation attempts. The authors cited findings that quit attempts made during both the follicular phase and also the luteal phase have better cessation rates when compared to the opposite phase (Franklin et al., 2008; Allen et al., 2008). Franklin and colleagues (2008) demonstrated better outcomes in the follicular phase including both NRT, as well as a behavioral intervention. However the study by Allen and colleagues (2008) included only a behavioral component. Thus the authors propose that the inclusion of a pharmacotherapy may at least partially explain the varying results. Franklin and Allen (2009) suggested that the inclusion of NRT may protect against initial withdrawal symptoms in the follicular phase and therefore prevent increased reward.

Additionally, subjective appraisal views of past withdrawal symptoms have been hypothesized to be a powerful influence on motivation to quit, as well as one’s efforts to make future quit attempts (Weinberger, Maciejewski, McKee, Reutenauer, & Mazure, 2009). It has
been suggested that smokers who recall long and severe withdrawal symptoms may be less motivated and thus less likely to attempt cessation (Weinberger et al., 2009). Previous research has established that more severe withdrawal symptoms occur in the late follicular phase (Franklin & Allen, 2009; Weinberger et al., 2009). Anecdotal evidence suggests that female smokers experience higher levels of withdrawal symptoms than male smokers and that these symptoms may fluctuate as a function of hormone level changes across the menstrual cycle (Carpenter et al., 2006; Perkins, 2001).

Menstrual cycle and craving. There is also evidence that the hormone fluctuations of the female menstrual cycle augment nicotine cravings and thus it is important to consider how this may potentially impact an individual’s ability to resist a smoking lapse (Carpenter et al., 2006; Perkins, 2001). Sofuoglu, Babb & Hatsukami (2001) observed that administering 200mg of progesterone during the follicular phase attenuated nicotine subjective cravings more so than a placebo treatment. Additional research has also shown that women who quit during the follicular phase of the menstrual cycle show a trend toward greater subjective nicotine cravings than those who quit during the late luteal phase (Carpenter et al., 2006).

As mentioned above, a pilot study by Carpenter and colleagues (2008) randomized female participants to quit either in the follicular or luteal phases of the menstrual cycle. The participants received two sessions of smoking cessation counseling (totaling 90 minutes) and the transdermal nicotine patch. Women who quit during the follicular phase reported greater levels of subjective craving than their luteal phase counterparts. Additional research found that women using the transdermal nicotine patch during short-term smoking abstinence (5 days of abstinence) experienced greater reduced nicotine cravings during the luteal phase of the menstrual cycle compared to those in the follicular phase (Allen, Hatsukami, Christianson, & Brown, 2000).
This evidence suggests that nicotine cravings may be augmented during the follicular phase, thus increasing the smoking lapses.

Yet some evidence suggests craving may be higher in the luteal phase. During a 3-day period of abstinence, higher levels of subjective craving were reported during the luteal phase (Pomerleau et al., 2000). Higher levels of cue-induced craving were observed in female smokers during the luteal phase (Franklin, Napier, Ehrman, Gariti, O’Brien & Childress, 2004). Also, after a 24-hour period of smoking abstinence, females in the luteal phase showed a higher amount of craving than those in the follicular phase (Snively, Ahijevych, Bernhard, & Wewers, 2000).

Despite evidence of phase effects on craving, several studies have also observed no phase effects on tobacco craving (Allen, Hatsukami, Christianson, & Nelson, 1999; Perkins et al., 2000; Pomerleau, Mehringer, Marks, Downey, & Pomerleau, 2000). No phase effects were observed in the desire to smoke among women who were tobacco abstinent (Perkins et al., 2000). Additionally, stable craving ratings were observed across the menstrual cycle for women who were both nicotine abstinence and smoking ad lib (Allen et al., 1999). Further, during an ad lib smoking period, females with and without depression showed no phase differences in ratings of nicotine craving (Pomerleau et al., 2000). It should be noted that these discordant results may be the effect of methodological variations, small sample sizes, and inconsistent categorization of menstrual cycle phases (cf. Carpenter et al., 2006).

**Menstrual cycle and self-efficacy to quit smoking.** Self-efficacy is defined as one’s belief that he or she can successfully accomplish the goals that one sets for his or herself (Bandura, 1977). The importance of this concept within the context of substance use behaviors is demonstrated in Marlatt’s relapse prevention theory (Marlatt & Gordon, 1985). The theory
details that increases in self-efficacy predict positive cessation outcomes. Thus, those individuals with greater self-efficacy to quit are predicted to have a more successful cessation attempt.

In congruence with this theory, it has been established that self-efficacy to quit may predict smoking cessation treatment response. Schnoll and colleagues (2011) found that participants with greater self-efficacy to quit smoking were more likely to be abstinent throughout the course of treatment, as well as at a 6-month follow-up (Schnoll et al., 2011). Further, female smokers are less confident in their ability to successfully quit smoking compared to their male counterparts. This lower self-efficacy may make them vulnerable to more failed quit attempts (Blake et al., 1989).

Additionally, subjective appraisal views of past withdrawal symptoms have been hypothesized to be a powerful influence on self-efficacy to quit (Weinberger et al., 2009). Given that more severe withdrawal symptoms occur in the late follicular phase, this may greatly influence a female smokers’ self-efficacy in future cessation attempts (Franklin & Allen, 2009; Weinberger et al., 2009). In fact, females making quit attempts in the follicular phase of the menstrual cycle have reported lower levels of self-efficacy to quit compared to the luteal phase (Carpenter et al., 2008). Thus, the follicular phase may be characterized not only by greater nicotine withdrawal, but consequently, less self-efficacy to quit and thus, less motivation to quit.

**Summary**

Although there are many promising smoking cessation treatments (including psychotherapy techniques and NRT), rates of lapse and relapse remain very high (Fiore et al., 2000; Perkins, 2001). Female smokers have poorer cessation outcomes than males despite no difference in motivation to quit smoking (Perkins, 2001; USDHHS, 2001). The ovarian
hormones, progesterone and estrogen, may contribute to the gender differences in cessation attempts; research has provided evidence that progesterone’s neuroprotective component may contribute to successful cessation by protecting against relapse (Lynch & Sofuoglu, 2010). However, much of current research to date does not explicitly define the follicular phase in either number of days after the beginning of the cycle or by levels of hormones, such as estrogen. Thus, it is unclear as to whether or not previous studies included current menses, indicating low levels of progesterone and estrogen, within the follicular phase. This potentially confounds interpretation of prior studies’ results.

**Specific Aim 1**

The primary aim of this study was to evaluate if severity of withdrawal, self-efficacy to quit, and tobacco craving, fluctuate with phases of the menstrual cycle (i.e., luteal vs. late follicular phases), thus potentially impacting motivation to quit.

**Hypotheses 1-3.** The following hypotheses were made: (1) withdrawal severity would be higher in the late follicular phase of the menstrual cycle compared to the luteal phase; (2) self-efficacy to quit would be higher in the luteal phase compared to the late follicular phase; and (3) greater nicotine cravings would be observed in the late follicular phase compared to the luteal phase.

**Specific Aim 2**

The second aim of this study was to evaluate if the fluctuations of the menstrual cycle affect the level of motivation for smoking cessation. There is evidence that women who self-select a quit date in the luteal phase of the menstrual cycle experience higher rates of point prevalence abstinence (Mazure et al., 2011). It may be that motivation to quit smoking is greater
during the luteal phase, when withdrawal symptoms and urge to smoke are lower (Franklin & Allen, 2009; Sofuoglu et al., 2001).

**Hypotheses 4-5.** It was hypothesized that participants in the luteal phase would have higher levels of motivation to quit smoking than their counterparts in the late follicular phase. Additionally, it was hypothesized that smoking cessation variables (i.e., withdrawal severity, craving, and self-efficacy to quit) would moderate the relationship between menstrual cycle phase and the motivation to quit smoking.
METHOD AND MATERIALS

Participants

Participants included both undergraduate students and members of the Baton Rouge community who were recruited through on-line advertisements (e.g., Craigslist, laboratory and university-affiliated clinic websites), fliers posted on and around the campus of Louisiana State University (LSU), and through the LSU Psychology Department undergraduate research participant pool. All advertisement materials were tailored to recruit nicotine-dependent women interested in quitting smoking.

A total of 86 participants completed the online survey measures. Of those participants, 9 individuals met inclusion criteria (luteal phase, \( n = 5 \); late follicular phase, \( n = 4 \); other menstrual phases [i.e., periovulatory or early follicular phases] were excluded, \( n = 6 \)). If the participant was not between the ages of 18-40 years old \( (n = 3) \), was male \( (n = 1) \), or did not experience regular menses that occur every 25-35 days \( (n = 2) \) (Bakos, Lundkvist, Wide, & Bergh, 1994), they were excluded from the current study. Based upon the previous research for smoking cessation treatment (e.g., Zvolensky, Farris, Schmidt, & Smits, 2014; Zvolensky, Baker, Leen-Feldner, Bonn-Miller, Feldner & Brown, 2004), participants were required to smoke at least 8 cigarettes per day for at least the past year. Participants who did not smoke daily \( (n = 11) \) or did not smoke at least 8 cigarettes per day for at least the past year \( (n = 14) \) were excluded. Participants also had to endorse a motivation to quit smoking of at least 5 (“I often think about quitting smoking, but I have no plans to quit.”), but below a 9 (“I have quit smoking, but I still worry about slipping back, so I need to keep working on living smoke free.”) on a question to assess the participants’ current motivation to quit smoking (Appendix A). Participants who did
not report a motivation to quit within this range were excluded \((n = 5)\). Participants were also excluded if use of hormonal contraceptives that do not mimic the natural menstrual cycle was reported \((n = 32)\), if the individual did not finish the online surveys \((n = 1)\), or if the individual reported conflicting information in their menstrual cycle history and thus accurate menstrual cycle phase categorizations could not be determined \((n = 2)\). Additional exclusion criteria included the inability to give informed consent, any current use of smoking cessation products or treatment, or endorsement of symptoms of premenstrual dysphoric disorder (as measured by the Geiselman Menstrual Cycle Interview, P.J. Geiselman, personal communication, May 16, 2013), current lactation, pregnancy in the previous six months, plans to become pregnant within the next six months, and irregular menses that do not occur every 25-35 days were reported.

Of those participants in the late follicular phase and luteal phase at the time of completing the survey, the average age was 26.78 \((SD = 5.91, \text{range 22-39})\). Participants identified as 100% non-Hispanic White. Participants identified as 22.2% completing high school and 77.8% completing some college. Despite a large portion of participants completing some college, only one participant reported being a current LSU student. Approximately 22% of participants reported being single, 44.4% reported being in a relationship, and 33.3% identified as divorced. Participants reported an average of 15.22 cigarettes per day \((SD = 4.09, \text{range from 10-20})\) and an average of 9.67 years smoking \((SD = 7.97, \text{range from 2-25})\). Approximately 22% of participants reported smoking menthol brand cigarettes. Participants reported an average of 7.97 \((SD = 7.23, \text{range from 1-20})\) pack years. The average FTND score was 4.11 \((SD = 1.45, \text{range from 2-7})\), indicating a low to moderate level of dependence. Participants reported an average of 4.00 \((SD = 6.23, \text{range from 1-20})\) hours since the last cigarette smoked. The majority of
participants reported at least one past quit attempt (77.8%) and the mean number of quit attempts was 3.33 ($SD = 2.96$, range from 0-10).

**Measures and Materials**

**Independent variable**

**Menstrual cycle phase categorization.** The *Geiselman Menstrual Cycle Interview* (P.J. Geiselman, personal communication, May 16, 2013) assessed participants’ menstrual cycle characteristics, both recently and over the history of their cycle. Characteristics assessed include: typical length of menses, average length of cycle, and date of onset of most recent menses. Information was utilized to determine the participants’ current phase of the menstrual cycle.

**Dependent variables**

**Nicotine withdrawal severity.** The *Minnesota Nicotine Withdrawal Scale-Revised Self-Report Measure* (MNWS-R; Hughes & Hatsukami, 1986; Minnesota Nicotine Withdrawal Scale-Revised, 2007) is a 15-item questionnaire that utilizes a Likert-type scale from zero to four to assess the severity of the discomfort (such as irritability, depressed mood, and increased appetite) from nicotine withdrawal. The first nine items on the self-report measure are well-validated and when added together, calculate the total withdrawal discomfort score (Cappelleri, Bushmakin, Baker, Merikle, Olufade, & Gilbert, 2005). These nine items were used to calculate the total withdrawal discomfort score for the present study and they achieve an excellent internal consistency ($\alpha = 0.93$) in the current study.

**Self-efficacy to quit.** The *Smoking Self-Efficacy Questionnaire* (SEQ-12; Etter, Bergman, Humair, & Perneger, 2000) measures participants’ confidence to abstain from smoking when the individual encounters various internal and external stimuli. The questionnaire contains...
two, 6-item subscales. The first subscale measures the participants’ ability to refrain from smoking when facing internal stimuli and the second determines the ability when encountering external stimuli (Et et al., 2000). Internal consistency coefficients ("internal stimuli": $\alpha = 0.95$; "external stimuli": $\alpha = 0.94$) and test–retest intraclass correlation coefficients (0.95 and 0.93 for the two scales, respectively) are high within this measure (Etter et al., 2000). The present study observed an excellent internal consistency, $\alpha = 0.97$ for the SEQ-12 and similarly excellent internal consistency ($\alpha = 0.95$ and 0.96) was achieved for its internal and external subscales, respectively.

**Tobacco craving.** The *Tobacco Craving Questionnaire- Short form* (TCQ-SF; Heishman, Singleton, & Pickworth, 2008) is a shorted version of the 47-item Tobacco Craving Questionnaire (TCQ; Heishman, Singleton, & Moolchan, 2003). The TCQ-SF draws 3 items from each of the 4 factors of the original TCQ (emotionality, expectancy, compulsivity, and purposefulness). The revised questionnaire takes approximately four minutes to complete, and studies suggest that it has the same reliability and validity as the original measure (Heishman et al., 2008; Berlin, Singleton, Heishman, 2010). In the current sample, the measure had a good level of internal consistency, $\alpha = 0.89$. The emotionality, expectancy, and compulsivity subscales of the TCQ-SF, also achieved good levels of internal consistency in the current sample ($\alpha = 0.83$, $\alpha = 0.73$, and $\alpha = 0.82$, respectively). This is comparable to levels of internal consistency in a previous study ($\alpha = 0.82$, $\alpha = 0.70$, and $\alpha = 0.75$, respectively; Heishman et al., 2008). The subscale of purposefulness achieved a low level of internal consistency in the current sample ($\alpha = 0.46$), which was comparable to that observed in a previous study with a larger sample size ($\alpha = 0.48$; Heishman et al., 2008).
Motivation to quit. The Motivation to quit question (Zvolensky et al., 2014; Zvolensky et al., 2004) was included as part of the sample descriptive questionnaire (described below). The question asked participants to choose one of 10 statements that most accurately described the participants’ current thoughts regarding cessation. Choices ranged from 1 (“I enjoy smoking and have decided not to quit smoking for my lifetime.”) to 10 (“I have quit smoking and I will never smoke again.”). Because we were interested in examining the impact of menstrual phase on cessation-related factors among smokers interested in quitting smoking, participants were included in the current study if they endorsed a motivation to quit smoking of at least 5 (“I often think about quitting smoking, but I have no plans to quit.”), but below a 9 (“I have quit smoking, but I still worry about slipping back, so I need to keep working on living smoke free.”).

Sample descriptives. A questionnaire was designed to accommodate the specific inclusion and exclusion criteria for this study (based upon Vinci, Peltier, Shah, Kinsaul, Waldo, McVay, & Copeland, 2014). The measure consisted of 10 items that assessed age, gender, race and ethnicity, relationship status, level of education, current hormonal contraceptives and medications used, pregnancy and lactation status, daily smoking rate, years smoked, preferred brand of cigarettes, and previous quit attempts. Fagerström Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991) is a six-item questionnaire assessing for nicotine dependence. It evaluates the quantity of cigarette consumption, frequency of use, and craving to smoke. Possible scores range from 0-10, with a higher score suggesting greater dependence. FTND scores correlate with physiological measurements, such as cotinine and number of years smoked (Etter, Duc, & Perneger, 1999; Heatheron et al., 1991; Pomerleau, Carton, Lutzke, Flessland, & Pomerleau, 1994). Higher scores on the measure also correspond with more expected withdrawal symptoms and lower self-efficacy to quit (Dijkstra & Tromp,
2002; Etter, 2005; Etter, Ussher, & Hughes, 2013; Pomerleau et al., 1994). In the current study, the measure achieved lower internal consistency ($\alpha = 0.33$) than previously observed (e.g., $\alpha = 0.61$; Heatherton et al., 1991).

**Procedure**

The study was approved by the university’s Institutional Review Board prior to data collection. Interested participants provided informed consent and completed a series of measures via online survey using surveymonkey.com. If a prospective participant contacted the laboratory via email or telephone, she was provided the link to the online survey and invited to participate in the study.

Upon survey completion, all participants were thanked for their participation and received information on smoking cessation treatment at the Louisiana State University Psychological Services Center. Participants enrolled through the student participant pool received research credit for participating in the study and those enrolled via the community were entered into a lottery-style prize drawing ($50).

**Data Analytic Strategy**

Based upon prior research finding a large effect of menstrual cycle phase on smoking-related outcomes (Carpenter et al., 2008), a total of 52 participants (26 in each group) was the target goal to obtain an estimated large effect size (Cohen’s $f = 0.40$) with a power of .80 and alpha level of .05 (calculated with G*power; Faul, Erdfelder, Lang, & Buchner, 2007; based on Carpenter, et al., 2008). However, in congruence with previous research which recruited participants based upon cycle phase in a clinical setting, under similar time constraints (McVay, 2012), it was not possible to recruit and retain the total number of participants that were predicted to establish a significant effect. All foreseeable recruitment efforts were made to
achieve the proposed sample size; however since the needed 52 participants could not be recruited and retained through the study procedures, effect sizes and confidence intervals for all groups were also calculated.

To test for any between group differences (luteal vs. late follicular) on descriptive variables, one-way analyses of variance (ANOVAs) between the two groups were conducted for each of the continuous variables, including: age, daily smoking rate, number of years smoked, number of pack-years, severity of nicotine dependence, and number of previous quit attempts. Additionally, chi-square analyses were conducted to test for any between group differences in the categorical descriptive variables, including: race/ethnicity, education level, and referral status (psychology subject pool vs. community). Effect sizes for all ANOVA analyses were determined using $d$ (continuous variables) and Crammer’s $V$ (categorical variables; Cohen, 1988; Acock & Gordon, 1979). Effect sizes for $d$ are considered as small ($d = 0.20$), medium ($d = 0.50$), and large ($d = 0.80$; per Cohen, 1992). Additionally, effect sizes for Crammer’s $V$ are considered as small ($V = 0.10$), medium ($V = 0.30$), and large ($V = 0.50$; per Cohen, 1992).

To investigate whether the menstrual cycle phase affected the variables of withdrawal severity, self-efficacy to quit, tobacco craving, and motivation for smoking cessation, a series of one-way, between-subjects ANOVAs were conducted comparing menstrual cycle phase (luteal or late follicular phase) on these variables.

Finally, to determine if smoking-related variables (i.e., withdrawal severity, craving, and self-efficacy to quit) moderated the relationship between menstrual cycle phase and the motivation to quit smoking, moderation analyses were conducted using hierarchical linear regression as per guidelines set by Baron and Kenny (1986). Predictors were centered to address multicollinearity. Separate models were conducted for each moderator. In Step 1, the main
effects of the menstrual cycle phase (luteal phase and late follicular phase) and one of the proposed moderators (i.e., withdrawal severity, craving, self-efficacy to quit) were entered. The interaction between menstrual cycle and the smoking-related variable were entered in Step 2 of each model. Effect sizes were determined using $f^2$ (Cohen, 1988) and defined as small ($f^2 = 0.02$), medium ($f^2 = 0.15$), and large ($f^2 = 0.35$; Cohen, 1992).
RESULTS

Demographics

See Table 1 for sample descriptives by phase group. The groups did not significantly differ in age, number of cigarettes per day, or number of years smoking. Additionally, there were no differences between groups in number of pack years, FTND score, number of hours since last cigarette smoked, or number of quit attempts. Despite no significant differences between groups in demographic variables, there was a medium effect of the number of hours since last cigarette smoked, with a longer amount of abstinence observed in the luteal phase. Additionally, there was a large effect of the number of quit attempts, with a larger number of past quit attempts reported by participants in the luteal phase.

Chi-square analyses were conducted to assess differences between groups on the categorical variables of education level, relationship status, past quit attempts, and menthol cigarette brand. Results revealed no significant differences between groups on education level, relationship status, past quit attempts, or menthol cigarette brand. All effect sizes were small.

Nicotine withdrawal severity¹

See Table 2 for means, standard deviations, confidence intervals, and ANOVA results. There were no differences between groups regarding withdrawal severity; the effect size was very small.

¹ Analyses of covariance (ANCOVA) were conducted to control for length of time since last cigarette smoked and number of quit attempts. These analyses yielded non-significant differences between groups on smoking cessation-related variables and very small effect sizes.
Table 1. Differences between menstrual cycle phase groups demographic variables

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Luteal Phase</th>
<th>Late Follicular Phase</th>
<th>Luteal Phase 95% CI</th>
<th>Late Follicular Phase 95% CI</th>
<th>F or χ²</th>
<th>df</th>
<th>p</th>
<th>d or Cramer’s V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (SD)</td>
<td>27.40 (6.69)</td>
<td>26.00 (5.66)</td>
<td>[19.09, 35.71]</td>
<td>[17.00, 35.00]</td>
<td>0.11</td>
<td>1, 8</td>
<td>0.75</td>
<td>0.48</td>
</tr>
<tr>
<td>Cigarettes per day</td>
<td>15.40 (4.56)</td>
<td>15.00 (4.08)</td>
<td>[9.74, 21.06]</td>
<td>[8.50, 21.50]</td>
<td>0.02</td>
<td>1, 8</td>
<td>0.90</td>
<td>0.09</td>
</tr>
<tr>
<td>Years smoked</td>
<td>10.60 (8.56)</td>
<td>8.50 (8.27)</td>
<td>[0.03, 21.23]</td>
<td>[-4.65, 21.65]</td>
<td>0.14</td>
<td>1, 8</td>
<td>0.72</td>
<td>0.25</td>
</tr>
<tr>
<td>FTND score</td>
<td>4.20 (1.92)</td>
<td>4.00 (0.82)</td>
<td>[1.82, 6.59]</td>
<td>[2.70, 5.30]</td>
<td>0.37</td>
<td>1, 8</td>
<td>0.85</td>
<td>0.14</td>
</tr>
<tr>
<td>Pack years</td>
<td>9.35 (6.89)</td>
<td>7.50 (8.69)</td>
<td>[-0.21, 16.91]</td>
<td>[-6.33, 21.33]</td>
<td>0.27</td>
<td>1, 8</td>
<td>0.87</td>
<td>0.11</td>
</tr>
<tr>
<td>Hours since last cigarette</td>
<td>5.80 (8.23)</td>
<td>1.75 (0.96)</td>
<td>[-4.42, 16.02]</td>
<td>[0.23, 3.27]</td>
<td>0.93</td>
<td>1, 8</td>
<td>0.37</td>
<td>0.69</td>
</tr>
<tr>
<td>Number of quit attempts</td>
<td>4.60 (3.29)</td>
<td>1.75 (0.85)</td>
<td>[0.52, 8.68]</td>
<td>[-0.97, 4.47]</td>
<td>2.43</td>
<td>1, 8</td>
<td>0.16</td>
<td>1.09</td>
</tr>
<tr>
<td>Education (% some college)</td>
<td>55.56</td>
<td>22.22</td>
<td>-</td>
<td>-</td>
<td>3.21</td>
<td>1</td>
<td>0.07</td>
<td>0.15</td>
</tr>
<tr>
<td>Relationship status (% in relationship)</td>
<td>22.22</td>
<td>22.22</td>
<td>-</td>
<td>-</td>
<td>2.25</td>
<td>1</td>
<td>0.33</td>
<td>0.13</td>
</tr>
<tr>
<td>Made quit attempt (%)</td>
<td>55.56</td>
<td>22.22</td>
<td>-</td>
<td>-</td>
<td>3.21</td>
<td>1</td>
<td>0.73</td>
<td>0.15</td>
</tr>
<tr>
<td>Menthol cigarette (%)</td>
<td>22.22</td>
<td>11.11</td>
<td>-</td>
<td>-</td>
<td>0.23</td>
<td>1</td>
<td>0.64</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Note. CI = Confidence Interval
Tobacco craving\textsuperscript{1}

See Table 2 for means, standard deviations, confidence intervals, and ANOVA results. There were no significant differences regarding tobacco craving, and there was a small effect size. There were also no phase group differences on the following subscales of the TCQ-SF: emotionality, compulsivity, and purposefulness. There was a large effect of menstrual cycle phase on the expectancy subscale of the TCQ-SF, such that the luteal phase group was greater than the late follicular phase group.

Self-efficacy to quit\textsuperscript{1}

See Table 2 for means, standard deviations, confidence intervals, and ANOVA results. There were no differences between groups regarding self-efficacy to quit; there was a very small effect size. No group differences and small effect sizes were revealed on the internal and external subscales of the SEQ-12, $F(1,7) = 0.85$, $p = 0.78$, $d = 0.19$, and $F(1,7) = 0.01$, $p = 0.93$, $d = 0.06$, respectively.

Motivation\textsuperscript{1}

See Table 2 for means, standard deviations, confidence intervals and ANOVA results. There were no differences between phase groups on motivation to quit smoking.

Moderation analyses

See Table 3 for results of multiple linear regression analyses. Effect sizes for hierarchical multiple regression analyses were small and did not support any proposed moderators between participant menstrual cycle phase and motivation to quit smoking. After 2.2% variance was accounted for by the main effects of nicotine withdrawal and menstrual cycle phase group, the interaction of nicotine withdrawal and phase group accounted for 0.30% of the variance in the model. Additionally, after 34.7% variance was accounted for by the main effects of tobacco
Table 2.
Differences between menstrual cycle phase groups and smoking cessation-related variables

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Luteal Phase</th>
<th>Late Follicular Phase</th>
<th>Luteal Phase 95% CI</th>
<th>Late Follicular Phase 95% CI</th>
<th>F</th>
<th>df</th>
<th>p</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean MNWS-R (SD)</td>
<td>15.60 (8.50)</td>
<td>16.00 (16.33)</td>
<td>[5.04, 26.16]</td>
<td>[-9.98, 41.99]</td>
<td>0.002</td>
<td>1</td>
<td>0.96</td>
<td>0.03</td>
</tr>
<tr>
<td>TCQ-SF</td>
<td>67.20 (16.07)</td>
<td>61.50 (16.82)</td>
<td>[47.23, 87.15]</td>
<td>[34.73, 88.27]</td>
<td>0.27</td>
<td>1</td>
<td>0.62</td>
<td>0.35</td>
</tr>
<tr>
<td>TCQ-SF: emotionality</td>
<td>15.00 (5.10)</td>
<td>14.25 (7.27)</td>
<td>[8.67, 21.33]</td>
<td>[2.68, 25.83]</td>
<td>0.03</td>
<td>1</td>
<td>0.86</td>
<td>0.12</td>
</tr>
<tr>
<td>TCQ-SF: expectancy</td>
<td>19.40 (2.30)</td>
<td>16.00 (4.69)</td>
<td>[16.54, 22.26]</td>
<td>[8.54, 23.46]</td>
<td>2.06</td>
<td>1</td>
<td>0.19</td>
<td>0.92</td>
</tr>
<tr>
<td>TCQ-SF: compulsivity</td>
<td>15.40 (6.19)</td>
<td>13.75 (5.32)</td>
<td>[7.72, 23.08]</td>
<td>[5.29, 22.21]</td>
<td>0.18</td>
<td>1</td>
<td>0.69</td>
<td>0.28</td>
</tr>
<tr>
<td>TCQ-SF: purposefulness</td>
<td>17.40 (4.78)</td>
<td>17.50 (2.65)</td>
<td>[11.47, 23.33]</td>
<td>[13.29, 21.71]</td>
<td>0.02</td>
<td>1</td>
<td>0.97</td>
<td>0.03</td>
</tr>
<tr>
<td>SEQ</td>
<td>37.00 (19.17)</td>
<td>34.75 (22.94)</td>
<td>[13.20, 60.80]</td>
<td>[-0.75, 72.25]</td>
<td>0.01</td>
<td>1</td>
<td>0.93</td>
<td>0.06</td>
</tr>
<tr>
<td>SEQ: internal</td>
<td>19.40 (9.04)</td>
<td>17.50 (10.60)</td>
<td>[8.17, 30.63]</td>
<td>[0.64, 34.37]</td>
<td>0.85</td>
<td>1</td>
<td>0.78</td>
<td>0.19</td>
</tr>
<tr>
<td>SEQ: external</td>
<td>17.60 (10.36)</td>
<td>18.25 (12.42)</td>
<td>[4.74, 30.46]</td>
<td>[-1.51, 38.01]</td>
<td>0.01</td>
<td>1</td>
<td>0.93</td>
<td>0.06</td>
</tr>
<tr>
<td>Motivation</td>
<td>6.80 (1.01)</td>
<td>7.00 (0.82)</td>
<td>[5.44, 8.16]</td>
<td>[5.70, 8.30]</td>
<td>0.09</td>
<td>1</td>
<td>0.77</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Note. CI = Confidence Interval
craving and menstrual cycle phase group, the interaction of tobacco craving and menstrual cycle phase group accounted for 1.0% of the variance in the model. In regards to motivation to quit moderating self-efficacy to quit and participant menstrual cycle phase, after 6.2% variance was accounted for by the main effects of self-efficacy to quit and menstrual cycle phase group, the interaction of self-efficacy to quit and phase group accounted for 2.0% of the variance in the model.

Table 3. Hierarchical linear regression of potential moderators of menstrual cycle phase and Motivation to quit smoking

<table>
<thead>
<tr>
<th></th>
<th>ΔR²</th>
<th>ΔF</th>
<th>B</th>
<th>t</th>
<th>p</th>
<th>sr²</th>
<th>f²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine Withdrawal Severity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menstrual cycle phase group</td>
<td>0.02</td>
<td>0.07</td>
<td>0.94</td>
<td>0.94</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotine withdrawal severity</td>
<td></td>
<td></td>
<td>-0.12</td>
<td>-0.29</td>
<td>0.79</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menstrual cycle phase group X Nicotine withdrawal severity</td>
<td>0.003</td>
<td>0.02</td>
<td>0.90</td>
<td>0.90</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobacco Craving</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menstrual cycle phase group</td>
<td>0.35</td>
<td>1.60</td>
<td>0.28</td>
<td>0.28</td>
<td>1.16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobacco Craving</td>
<td></td>
<td></td>
<td>0.00</td>
<td>-0.00</td>
<td>0.99</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Step 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menstrual cycle phase group X Tobacco craving</td>
<td>0.01</td>
<td>0.07</td>
<td>0.71</td>
<td>0.71</td>
<td>0.03</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3 (cont.).

<table>
<thead>
<tr>
<th></th>
<th>Self-Efficacy to Quit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.06</td>
</tr>
<tr>
<td>Menstrual cycle phase group</td>
<td>-0.12</td>
</tr>
<tr>
<td>Self-efficacy to quit</td>
<td>0.22</td>
</tr>
<tr>
<td>Step 2</td>
<td>0.02</td>
</tr>
<tr>
<td>Menstrual cycle phase group X</td>
<td>0.20</td>
</tr>
<tr>
<td>Self-efficacy to quit</td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION

The present study examined the effects of the female hormonal milieu, specifically the effect of menstrual phase (luteal vs. late follicular) on smoking cessation-related variables (i.e., nicotine withdrawal, tobacco craving, level of self-efficacy to quit, and motivation), which can affect an individual’s cessation attempt. However, this study showed only small effect sizes and no significant differences between participants in the luteal and late follicular phases in regards to levels of nicotine withdrawal severity, tobacco craving, or self-efficacy to quit, as well as the level of motivation between participants in the luteal and late follicular phase. Additionally, there was no evidence that the smoking cessation-related variables moderated the relationship between phase group and motivation to quit.

There were no significant group differences between the phase groups (luteal vs. late follicular) in demographic variables; however, there was a medium effect of length of time since last cigarette (measured in hours), with the luteal phase group reporting longer periods of abstinence. Previous literature has suggested that the luteal phase may have therapeutic utility in smoking cessation, due to its high levels of the neuroprotective hormone, progesterone (Lynch & Sofuoglu, 2010). It has been shown that females making a quit attempt during the luteal phase report lower levels of nicotine withdrawal and craving (Carpenter et al., 2008), thus making it easier to abstain from smoking for a longer period of time. In the present study, a longer period of abstinence was observed in the luteal phase, as expected; however, there were no significant differences and only small effect sizes between groups in withdrawal and craving severities. Because of the lack of differences or compelling effect sizes observed in the present study between phase groups in regards to withdrawal and craving ratings, the medium effect of the amount of time since last cigarette could be explained by one participant in the luteal phase.
group who abstained from smoking for 20 hours. Others participants in the luteal phase abstained from smoking for an average of 2.50 ($SD = 2.25$) hours, which was similar to the late follicular phase group of 1.75 ($SD = 0.96$) hours. The average time participants abstained from smoking in the current study is consistent with previous literature, which identified female participants as smoking over 18 cigarettes per day (Carpenter et al., 2008), which when smoked over the course of a day yields a similar time of abstinence between cigarettes as observed in the luteal and late follicular groups of the present study.

Withdrawal severity was non-significantly lower during the luteal phase, in comparison to the late follicular phase and this was a very small effect. These results replicate previous research that shows no significant differences in nicotine withdrawal symptomatology between the luteal and follicular phases of the menstrual cycle (Allen et al., 1999; Snively et al., 2000). Allen and colleagues (1999) reported that nicotine withdrawal symptomatology remains stable throughout the menstrual cycle and no differences were observed between the follicular and late luteal phases in terms of smoking behavior and smoking cessation-related variables (i.e., nicotine withdrawal). However, recent pilot data suggest that females in the follicular phase report greater withdrawal, craving, fatigue, and confusion when compared to the luteal group during a quit attempt (Carpenter et al., 2008). The present study recruited a smaller sample size (luteal phase, $n = 5$; late follicular phase, $n = 4$) than Carpenter and colleagues’ (2008) pilot data set (follicular phase, $n = 25$; luteal phase, $n = 19$). Additionally, the pilot data did not distinguish between the early vs. late follicular menstrual cycle phases. The early follicular phase is typically characterized by the onset of menses, where both estrogen and progesterone levels are low until the beginning of the late follicular phase (Davidens et al., 2007). Estrogen levels begin to elevate during the late follicular phase, while progesterone levels remain low (Davidsen et al.,
Thus, combining the early and late follicular phases into one phase category potentially obscures any cessation-related effects, which may be related to the fluctuation of hormone levels across the menstrual cycle. Thus, not distinguishing between the early and late follicular phases potentially masks observable differences in craving, withdrawal, self-efficacy, and motivation between the two follicular phase categories. Additional research is needed to clarify if quitting during the luteal phase of the menstrual cycle as opposed to the late follicular phase significantly affects a premenopausal female’s quit attempt (especially withdrawal severity). Research also needs to further investigate the differences in smoking cessation-related variables between the early vs. late follicular phases of the menstrual cycle.

Although levels of tobacco craving were slightly higher during the luteal phase, the effect of phase on craving was small and not significant. This is consistent with previous research (Perkins et al., 2000) that found no differences between phase groups on craving. However, despite research establishing that there is no overall phase effect on craving, when using the transdermal nicotine path, women in the late luteal phase have shown lower craving ratings (Allen et al., 1999). Franklin & Allen (2009) theorize that the inclusion of a pharmacotherapy during a quit attempt may impact subjective craving ratings during the luteal phase. Thus the impact of the menstrual cycle phase on inclusion of pharmacotherapy (i.e., nicotine replacement therapy) in a quit attempt needs to be further clarified through future research. Although many studies to date have investigated the fluctuations of craving across the menstrual cycle (cf. Carpenter et al., 2006), the present study is the first to utilize the TCQ-SF and thus the first to look at components of tobacco craving (i.e., emotionality, expectancy, compulsivity, and purposefulness). The inclusion of these subscales is important, as they illustrate the complex processes that underlie craving in smoking behavior (Heishman et al., 2008). In the present
study, the subscales of the emotionality, compulsivity, and purposefulness demonstrated only non-significant differences and small effect sizes between groups.

Notably, there was a non-significant, but large effect of phase on the TCQ-SF subscale for tobacco expectancy, with the luteal phase group reporting higher expectancies. This subscale asks participants to rate items such as how much one would enjoy a cigarette right now or how “good” a cigarette would taste in the current moment. Thus, the scale evaluates anticipated positive effect of smoking a cigarette (Heishman et al., 2008). High levels of estrogen, as observed during the follicular phase of the menstrual cycle, correlate with a more highly active reward circuitry (Davidsen et al., 2007) and this reward circuitry is associated with encoding and evaluating expectancy of rewards, including drug rewards (Gardner, 2011). Recent research established that smokers have less menstrual phase variation of estrogen across the cycle (Dušková et al., 2012). The large effect size observed in the expectancy subscale of the TCQ-SF may be explained in part by these more stable levels of estrogen in female smokers. Given that the luteal phase is characterized by not only heightened levels of progesterone, but also to a lesser extent elevated levels of estrogen (Davidsen et al., 2007), more stable levels of estrogen may augment the activation of the reward circuitry during the luteal phase. Thus, this would contribute to females in the luteal phase more highly evaluating the expectancy of nicotine rewards.

There were no significant differences in levels of self-efficacy to quit smoking between the luteal and late follicular phase groups and the size of the effect of phase on self-efficacy was small. One study to date has explicitly explored the fluctuation of self-efficacy to quit across the menstrual cycle. This research demonstrated decreases in self-efficacy during the follicular phase (Carpenter et al., 2008). The present study had a smaller sample size when compared to
Carpenter and colleagues’ (2008) pilot data and our limited sample size may account for the present study’s lack of observable difference in self-efficacy to quit between the luteal phase and the late follicular phase. Additional research is needed to clarify whether or not self-efficacy to quit is stable across the menstrual cycle.

Similarly, there were not significant differences between phase groups in terms of motivation to quit smoking. Motivation was slightly lower during the luteal phase when compared to the late follicular phase; however this was also non-significant and a small effect size. Weinberger and colleagues (2009) theorized that smokers who remember or experience long and severe withdrawal symptomatology may be not only less motivated to quit, but also less confident in his or her ability to quit. Thus, in light of the lack of significant differences in withdrawal severity between phase groups, it is not surprising that no significant differences and only small effect sizes were observed in motivation.

Finally, smoking cessation-related variables (i.e., withdrawal severity, craving, and self-efficacy to quit) did not moderate the relationship between menstrual cycle phase and the motivation to quit smoking. This finding was not surprising in light of the finding that the smoking cessation-related variables did not differ between phases and it suggests that timing cessation attempts with the luteal phase may not dramatically improve treatment outcomes. To date, this is the first study to investigate if smoking cessation-related variables would moderate the relationship between menstrual cycle phase and the motivation to quit smoking. In the present study, the effect sizes for hierarchical multiple regression analyses were small and did not support any of the proposed moderators between participant cycle phase and motivation to quit smoking. Additionally, the interactions between the proposed moderators (i.e., withdrawal severity, craving, and self-efficacy to quit) and participant cycle phase did not account for a
substantial portion of the variance in their respective models. Due to the lack of prior research investigating the variables that potentially moderate the relationship between motivation to quit smoking and menstrual cycle phase, as well as the fluctuations of the underlying components of craving (i.e. emotionality, expectancy, compulsivity, and purposefulness) across the cycle, additional research should explore if specific components of craving moderate the relationship between motivation to quit and cycle phase.

The findings of the present study are consistent with a recent review, which detailed the results of five research studies suggesting that female premenopausal smokers who have higher levels of progesterone than their non-smoking counterparts, and thus higher levels of progesterone (as seen in the luteal phase) would not significantly alter smoking behaviors (Allen et al., 2014). This indicates that the luteal phase may not be an optimum time to make a quit attempt (Allen et al., 2014). However, the review makes note that there have been substantial difficulties in interpreting the literature surrounding ovarian hormones and smoking behavior/cessation, as there is a lack of consistency in methodology and continuously fluctuating endogenous hormone levels, among other concerns.

If future studies observe higher negative symptoms (i.e., higher tobacco craving and nicotine withdrawal) and simultaneous higher self-efficacy to quit during one phase of the menstrual cycle (i.e., luteal or late follicular), research should test if these variables interact to predict motivation. If so, it may prove to be an optimum time for health care providers to encourage female smokers to make a quit attempt. Health care providers are beginning to utilize motivational interviewing (MI) to encourage patients to make positive behavioral changes (Rubak, Sandbaek, Lauritzen, & Christensen, 2005). A fundamental goal of MI is to develop a discrepancy between the client’s current behavior and his or her desired behavior, thus
highlighting the importance of change. Developing discrepancy was originally framed as cognitive dissonance; however, MI has since described it as the discrepancy between the patient’s status quo and the desired change goal (Festinger, 1957; Miller & Rollnick, 2013). Through the use of specific questions and selective reflections, change will often occur when the patient perceives a discrepancy between problem behaviors and a broader set of values (Burke et al., 2003). Thus, as a female smoker experiences increased negative symptoms, such as craving, this may afford the opportunity for the client to view smoking as a problem behavior.

Timing this type of MI-based intervention with greater negative symptoms may make the female more committed to resolve the discrepancy and thus start making behavioral changes. Furthermore, prior research has established that MI interventions demonstrate some efficacy in both males and females, despite lower rates of confidence to quit in female smokers (Dunn et al., 2001; Whitlock et al., 1997). Heckman and colleagues (2010) report that patients (the majority of whom were females), who received an MI-based treatment reported an increase of 45% in abstinence rates at follow-up when compared to controls, indicating potential promise in utilizing brief motivational interview (BMI) in female cessation attempts. Timing the MI-based intervention with a patient’s menstrual cycle may improve psychosocial interventions with female smoking cessation patients.

This area of research is significant in that tobacco smoking results in nearly 1 million female deaths per year worldwide and is expected to increase to approximately 3 million deaths per year by 2020 (Peto, Lopez, Boreham et al., 1996). Despite no significant gender differences in rates of cessation attempts or motivation to stop smoking, female smokers have poorer cessation outcomes, making the increasing rates of smoking-related deaths an area of female health concern (USDHHS, 2001; Perkins, 2001). To increase successful female smoking
cessation attempts, more female-specific tailored cessation treatments may be needed. This is the first study to specifically examine whether the variables that affect cessation success (withdrawal, craving, self-efficacy, and motivation) differ across the luteal (when progesterone levels are at their peak) and late follicular (when estrogen levels are rising) phases of the menstrual cycle.

**Limitations and future directions**

The current study should be interpreted in light of its limitations. One major limitation is that it was underpowered. A posteriori power analysis determined that the present study obtained a power of .06 and an alpha of .05, with the current sample size of 9 participants (calculated with G*power; Faul et al., 2007). For the present study, a total of 43 more participants (22 in the late follicular group and 21 in the luteal group) would be needed to obtain an estimated large effect size (based on Cohen’s d), with a power of 0.08 and alpha level of .05 (calculated with G*power; Faul et al., 2007; based on Carpenter, et al., 2008), as determined by the a priori analyses. Thus, more participants are needed to achieve adequate power for the study. Additionally, this study characterized current menstrual cycle phase utilizing only participant self-report measures. Prior research has indicated that self-reported menstrual cycle history and calendar-based counting methods should not be used alone to categorize menstrual cycle phase events (Wideman, Montgomery, Levine, Beynnon, & Shultz, 2013). Thus in future research, it is suggested that ovulation testing and if possible, serum blood tests of progesterone and estrogen levels are utilized to determine current cycle phase.

Also, the present study did not control for a specific time of smoking abstinence (i.e., specific number of hours since last cigarette smoked). Other research groups monitored withdrawal and craving symptomatology within the context of a quit attempt (at least 24 hours of
abstinence; Allen et al., 2008). In the current sample, all of the participants had smoked within the past 24 hours, with participants ranging from 1 hour to 20 hours of smoking abstinence. A greater amount of time in which the participants abstained from smoking, as observed in previous studies may elevate the withdrawal and craving scores (Allen et al., 2008). This may highlight the differences between menstrual cycle phases observed in previous studies (Allen et al., 2008). Finally, the sample consisted of only non-Hispanic White females, which limits the generalizability of these results across females.

Regarding strengths of the present study, this was the first study to explicitly investigate the impact of female sex hormones in the luteal and late follicular phases of the menstrual cycle on withdrawal, craving, self-efficacy to quit, and motivation to quit. Previous studies (i.e., Carpenter et al., 2008; Allen et al., 2008) do not separate the early vs. late follicular phases and thus may confound previously established results. By not distinguishing between the early and late follicular phases, these studies have potentially obscured any cessation-related effects observed across the menstrual cycle. Additionally, this is the first study to date to consider the underlying constructs of tobacco craving and investigate these components’ fluctuation across the menstrual cycle. The present study was also the first to explore whether the smoking cessation-related variables would moderate the relationship between menstrual cycle phase and the motivation to quit smoking.

Although no significant differences were observed in the present study, possibly due to a small and underpowered sample size, future research should continue to investigate the role of menstrual cycle phase fluctuations in smoking cessation. In future research, if greater negative symptoms such as tobacco craving and nicotine withdrawal intensity, as well as greater self-efficacy to quit are observed in the luteal phase, it may be worthwhile to conduct additional
research to investigate whether or not a MI-based intervention for smoking cessation would be more effective if implemented in the luteal phase of the menstrual cycle.

Conclusions

Results of the current study did not show a difference between smoking cessation-related variables (i.e., withdrawal severity, craving intensity, and self-efficacy) and level of motivation between participants in luteal and late follicular phases. Additionally, these variables did not moderate the relationship between menstrual cycle phase and motivation to quit. Results should be interpreted with caution, however, in light of a small sample size. Further research is necessary to determine if there is a difference between smoking outcome variables and motivation to quit over the course of the menstrual cycle. If differences are present, MI-based interventions may be the most beneficial psychosocial interventions for female smoking cessation patients.
REFERENCES


Zvolensky, M.J., Farris, S.G., Schmidt, N.B., & Smits J.A. (2014). The role of smoking inflexibility/avoidance in the relation between anxiety sensitivity and tobacco use and

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APPENDIX A
Motivation to quit question for Survey Monkey

“Please pick the statement that most accurately describes your current thoughts about quitting.”

1) I enjoy smoking and have decided not to quit smoking for my lifetime.
2) I never think about quitting smoking, and I have no plans to quit.
3) I rarely think about quitting smoking, and I have no plans to quit.
4) I sometimes think about quitting smoking, but I have no plans to quit.
5) I often think about quitting smoking, but I have no plans to quit.
6) I definitely plan to quit smoking in the next 6 months.
7) I definitely plan to quit smoking in the next 30 days.
8) I still smoke, but I have begun to change, like cutting back on the number of cigarettes I smoke per day. I am ready to set a quit date.
9) I have quit smoking, but I still worry about slipping back, so I need to keep working on living smoke free.
10) I have quit smoking and I will never smoke again.
APPENDIX B

ACTION ON PROTOCOL APPROVAL REQUEST

TO: Julia Buckner
    Psychology

FROM: Robert C. Mathews
      Chair, Institutional Review Board

DATE: March 10, 2014
RE: IRB# 3461

TITLE: The Impact of Timing Menstrual Cycle Phase with Brief Motivational Interviewing on Smoking Lapse


Review type: Full _____ Expedited X _____ Review date: 3/11/2014

Risk Factor: Minimal X _____ Uncertain _______ Greater Than Minimal_______

Approved _____ X _____ Disapproved _______

Approval Date: 3/11/2014 Approval Expiration Date: 3/10/2015

Re-review frequency: (annual unless otherwise stated)

Number of subjects approved: 100

Protocol Matches Scope of Work in Grant proposal: (if applicable)

By: Robert C. Mathews, Chairman

PRINCIPAL INVESTIGATOR: PLEASE READ THE FOLLOWING – Continuing approval is CONDITIONAL on:

1. Adherence to the approved protocol, familiarity with, and adherence to the ethical standards of the Belmont Report, and LSU's Assurance of Compliance with DHHS regulations for the protection of human subjects*
2. Prior approval of a change in protocol, including revision of the consent documents or an increase in the number of subjects over that approved.
3. Obtaining renewed approval (or submittal of a termination report), prior to the approval expiration date, upon request by the IRB office (irrespective of when the project actually begins); notification of project termination
4. Retention of documentation of informed consent and study records for at least 3 years after the study ends.
5. Continuing attention to the physical and psychological well-being and informed consent of the individual participants, including notification of new information that might affect consent.
6. A prompt report to the IRB of any adverse event affecting a participant potentially arising from the study.
8. SPECIAL NOTE:

*All investigators and support staff have access to copies of the Belmont Report, LSU's Assurance with DHHS, DHHS (45 CFR 46) and FDA regulations governing use of human subjects, and other relevant documents in print in this office or on our World Wide Web site at http://www.lsu.edu/irb
Informed Consent Form

1. Study Title: The Impact of Timing Menstrual Cycle Phase with Brief Motivational Interviewing on Smoking Lapse

2. Performance Sites: This study will be conducted at the Louisiana State University Psychological Services Center (PSC), 33 Johnston Hall.

3. Investigators: The Principal Investigator, Julia D. Buckner, Ph.D., can be reached at 225-578-4096, Monday-Friday between 9:00 a.m. and 5:00 pm or at jbuckner@lsu.edu. Paula Geiselman, Ph.D, and MacKenzie R. Peltier, B.A. are co-investigators. Additional research staff can be contacted at 225-578-8626, M-Fr between 9:00 a.m. and 5:00 p.m or at lsusmokingresearch@gmail.com.

4. Purpose of the Study: The proposed study is designed to investigate the role of ovarian hormones (i.e. progesterone and estrogen) in smoking cessation treatment, mood states, and food cravings.

5. Study Inclusion: Female participants between the ages of 18-40 years old who experience regular menses that occur every 25-35 days. Participants must smoke at least 8 cigarettes/day for at least the past year. Additionally, participants must endorse a motivation to quit smoking; however, participants must not have quit yet. Exclusion criteria will include the following: inability to give informed consent, current use of smoking cessation products or treatment, use of hormonal contraceptives that do not mimic the natural menstrual cycle, symptoms of premenstrual dysphoric disorder (as measured by the Geiselman Menstrual Cycle Interview), current lactation, pregnancy in the previous six months, plans to become pregnant within the next six months, and irregular menses that do not occur every 25-35 days.

6. Number of Subjects: The maximum number of participants enrolled in this study will be 100.

7. Study Procedures: The study requires that you will complete a series of self-report assessments about your nicotine use patterns, smoking beliefs, mood states, and food cravings.

8. Benefits: You may derive benefit from participating in the self-assessment about your smoking, as participation may increase your awareness of your smoking behaviors. You may also develop a better understanding of research methodology. In addition, you will be contributing to the knowledge regarding how ovarian hormones may impact smoking processes and food cravings, which may help smokers successfully, quit in the future.
9. Risks/Discomforts: As with any study, there is a possible loss of confidentiality. You might feel uncomfortable disclosing and discussing personal information.

10. Injury/Illness: In the unlikely event of injury or medical illness resulting from study participation, participants are instructed to seek necessary medical care from their physician and contact the Principal Investigator, Julia Buckner, PhD (225-578-4096). The expense of medical treatment will be your responsibility. No compensation is available in case of study-related illness or injury.

11. Right to Refuse: Participation in this study is voluntary, and you may withdraw from the study at any time without any penalty at this present time or in the future at LSU. Choosing to not participate or withdraw at any time from the study will not jeopardize your academic standing at LSU or adversely affect your relationship with LSU or the research staff. The research staff reserves the right to drop participants from the study for the benefit and safety of the participant or research.

However, if you are an undergraduate psychology student and choose to not participate in this screening survey, as indicated by choosing the "I do not agree to participate at this time" option below, you will not receive SONA credit since you are not completing the survey, but you will also not be penalized for your decision to not participate. Instead you will be granted an excused no-show.

12. Privacy: Results of this study may be published, but no names or identifying information will be included in the publication. All personal information obtained in this study will be kept confidential unless release is legally compelled. Once all data have been collected, your name and telephone number will be destroyed. During the study, you will be assigned an identification number, and this number will be the only link between your name, phone number, and your responses. Your forms will be kept in a locked filing cabinet in a locked office. Only research staff members will have access to data files or other research-related information. The information collected in this research study will not be linked to your academic or judicial records at LSU.

13. Financial Information: Community participants will receive compensation via a lottery-style cash and prize drawing ($50) for completing study session. Participants who are recruited from the LSU Department of Psychology Undergraduate Student Research Participation Pool will earn class credit for completion of the study session.

All participants will be referred to the LSU PSC for smoking cessation treatment.

14. Signatures:

The study has been discussed with me and all my questions have been answered. I may direct additional questions regarding study specifics to the investigators. If I have questions about subjects’ rights or other concerns, I can contact Dennis Landin, Institutional Review
Board, (225) 578-8692, irb@lsu.edu, www.lsu.edu/irb. I agree to participate in the study described above and acknowledge the researchers’ obligation to provide me with a copy of this consent form if signed by me.

1.

I agree to participate in this survey, as described above and acknowledge the researchers’ obligation to provide me with a copy of this consent form if signed by me.

I agree to participate

I do not agree to participate at this time
VITA

MacKenzie Rae Peltier, a native of Boston, Massachusetts, received her bachelor’s degree in psychology and English communications at Emmanuel College (Boston, MA) in 2010. She has an interest in clinical psychology with particular emphasis on the role of gender in the etiology and treatment of substance abuse and eating disorders. She will receive her master’s degree in May 2015 and plans to continue working on her doctorate degree.