HHS Public Access

Author manuscript

Addict Behav. Author manuscript; available in PMC 2016 November 01.

Published in final edited form as:

Addict Behav. 2015 November ; 50: 135–139. doi:10.1016/j.addbeh.2015.06.026.

Associations between adrenocortical activity and nicotine response in female smokers by menstrual phase

Eileen A. Huttlin[1], **Alicia M. Allen**[1], **Nicole L. Tosun**[1], **Sharon S. Allen**[1], and **Mustafa al'Absi**[2]

[1]University of Minnesota Medical School, Department of Family Medicine and Community Health, 20 Delaware St. SE, MMC 381, Minneapolis, MN 55414, United States

[2]University of Minnesota Medical School, 1035 University Drive, Room 236 D601, Duluth, MN, United States

Abstract

Previous research suggests menstrual phase may influence smoking-related symptomatology. The present study analyzes the relationship between menstrual phase and salivary cortisol with subjective responses to nicotine among female smokers during ad libitum smoking. We hypothesize higher cortisol levels would be associated with increased positive and decreased negative subjective responses to nicotine. We also expected that these associations would vary by menstrual phase. Females aged 18-40 who smoke at least five cigarettes/day, reported regular menstrual cycles and did not use exogenous hormones or psychotropic medications were enrolled into a controlled cross-over trial. Participants completed identical data collection procedures during follicular (F) and luteal (L) phases; including self-collected salivary cortisol samples and completion of a nicotine response lab session involving administration of nicotine nasal spray and monitoring of subjective response to nicotine via the Subjective State Scale and Visual Analog Scale. Participants (n=116) were 29.1±6.9 years old and smoked an average of 12.3±5.5 cigarettes daily. During F phase, higher morning cortisol was associated with decreased negative affect ($r=-0.21$, $p=0.03$), withdrawal ($r=-0.30$, $p<0.01$) and increased relaxation ($r=0.24$, $p=0.02$) after administration of nicotine nasal spray. Conversely, during L phase, higher morning cortisol was associated with a decrease in head rush ($r=-0.26$, $p=0.01$) and urge to smoke ($r=-0.21$, $p=0.04$) after administration of nicotine nasal spray. Similar associations between greater diurnal cortisol variation and response to nicotine were seen. These observations indicate cortisol may have a phase-specific association with some subjective responses to nicotine in female smokers. Additional research should explore how these relationships may influence smoking cessation efforts.

Corresponding Author: Alicia Allen, PhD, MPH Department of Family Medicine & Community Health Medical School, University of Minnesota 717 Delaware Street SE, Mail Code: 1932 Minneapolis, MN 55414 Phone: 612-624-0896 Fax: 612-624-4610 alle0299@umn.edu.

The authors disclose no conflicts of interest.

Keywords

Cortisol; Menstrual Phase; Nicotine; Smoking; Subjective Response

1.0 INTRODUCTION

Smoking is the leading cause of preventable death and disability in the United States, with a prevalence of 20% in adults, and 15% in women specifically (Centers for Disease Control, 2011). Though almost 70% of current smokers express a desire to quit, less than 7% reported success in quitting in the past year (Centers for Disease Control, 2011). Therefore, it is important to understand more about the factors that may influence nicotine usage/ cigarette smoking in order to develop more comprehensive and effective cessation programs. Investigation of potential barriers to smoking cessation is especially important for female smokers, as women may experience less success in quitting than their male counterparts (Perkins et al, 2002; Royce et al, 1997; Scharf and Shiffman, 2004). This suggests that current cessation strategies may not be optimized for female smokers.

The stress hormone cortisol is associated with hypothalamic-pituitary-adrenal (HPA) axis activity, and alterations in its secretion pattern have been associated with chronic stress, anxiety and distress (Vedhara et al, 2003; Miller, Chen & Zhou, 2007). Additional research suggests that cortisol may also be involved in modulating responses to nicotine (Cohen, al'Absi & Collins, 2004; McKee et al, 2010). Cohen and colleagues (2004) assessed the relationship between salivary cortisol and nicotine withdrawal/craving during acute smoking abstinence; the authors reported that, among 20 male participants, higher cortisol levels correlated with a greater experience of withdrawal symptoms and greater craving two and three hours following cessation of smoking. Another study we encountered investigated the relationship between cortisol and smoking satisfaction (McKee et al 2010). They reported that following a night of smoking abstinence, 37 male and female participants were presented with a stressful story. Blood cortisol concentrations were then measured and positively correlated with smoking satisfaction, suggesting a relationship between cortisol and response to smoking. Further, research has shown that cortisol blocking agents decrease both cigarette craving and smoking satisfaction among male smokers (Reuter et al, 2002). Together, these results indicate that cortisol levels may be related to certain aspects of smoking satisfaction and withdrawal.

Sex hormones have also been postulated to influence smoking behaviors, cravings and withdrawal (Carpenter et al, 2006). These hormones fluctuate during the menstrual cycle, which consists of the follicular (F) phase and the luteal (L) phase. The follicular phase begins during menses and is associated with rising levels of estrogen secreted by the ovaries. The L phase follows ovulation and is associated with rising levels of progesterone secreted by the corpus luteum (Boron & Boulpaep, 2012).

Studies addressing the relationship between menstrual phase and symptoms of craving and withdrawal during smoking cessation attempts have shown mixed results. Women using nicotine replacement therapy (NRT) had more favorable outcomes if their quit date occurred during the follicular phase (Carpenter et al, 2008; Franklin et al, 2008), whereas women

utilizing pharmacotherapy including buproprion or behavioral counseling, were more likely to remain abstinent if they quit in the luteal phase (Allen et al, 2008; Mazure et al, 2011). Taken together, these findings suggest that menstrual phase might influence withdrawal and craving, and ultimately modulate cessation attempts. Therefore, additional work is needed to determine the specific mechanisms of action involved in these observations.

We have investigated the combined influence of cortisol and menstrual phase on cigarette cravings and the success of quit attempts (Allen et al, 2009). Among the 38 female smokers studied, lower morning cortisol levels were associated with greater cigarette craving in the L phase only. These data suggest that cortisol levels and menstrual phase might be associated to influence cigarette craving. The goal of the present study was to expand upon our previous work, determine if salivary cortisol levels are associated with an increased response to nicotine administration among female smokers and to explore this relationship by menstrual phase. The specific aims are to assess the relationship between salivary cortisol levels (measured by absolute cortisol values at waking and by diurnal changes in cortisol values) and nicotine response among female smokers during the F and L phases of the menstrual cycle. We hypothesized that a positive relationship would exist between cortisol levels and favorable response to nicotine, and that this relationship would vary by menstrual phase.

2.0 METHODS & MATERIALS

2.1 Participants

Participants in this study were recruited for participation in a larger study (Allen et al, 2014) using television, internet and radio advertisements, printed flyers and brochures, and physician referrals. To be eligible for this study, participants had to be between the ages of 18 and 40, in stable physical/mental health, have regular menstrual cycles and have smoked at least five cigarettes a day for the past year. Participants were excluded if they were pregnant or breastfeeding, had current or a recent history (defined as <6 months) of Major Depressive Disorder or a lifetime history of Premenstrual Dysphoric Disorder as determined by Composite International Diagnostic Interview (World Health Organization, 1993), used illicit drugs or products with nicotine other than cigarettes (e.g. nicotine replacement therapy, other types of tobacco) or use of hormonal medication (including contraception medication).

2.2 Procedures

In this controlled cross-over trial, participants were randomly assigned to complete the first week of testing during either the F phase or the L phase of the menstrual cycle, followed by the alternate menstrual phase. F phase was operationally defined as days 2-7 of the menstrual cycle (with day one defined as the onset of menses), while L phase was considered days 2-7 after luteinizing hormone surge (which heralds ovulation within 24-48 hours). Cycle phase status was determined using menstrual cycle calendars and urine ovulation test results, with respective confirmation of blood hormone levels (progesterone and estradiol).

A full outline of the testing protocol is outlined elsewhere (Allen et al, 2014). Briefly, testing weeks consisted of two days of ad libitum smoking followed by four days of abstinence. Data analyzed in this report came from the second day of ad libitum smoking. Salivary cortisol samples were collected by participants at five specific times during the testing day; waking in the morning, 30 minutes after the first collection, two hours after first collection, approximately 8 pm and at bedtime. Samples were collected with swabs and stored in plastic containers at room temperature until returned to study staff. Samples were then stored at −20° C until they were processed in batches by the lab. This analysis utilized a time-resolved immunoassay with fluorometric end point detection with a sensitivity of 0.4 nmol/L (Dressendorfer et al, 1992) at the Behavioral Medicine Laboratories at the University of Minnesota Medical School, Duluth.

On the same day, participants also completed a nicotine response lab session. During this 2.5-hour session, nicotine response was measured following administration of a nicotine nasal spray (Nicotrol; 2mg dose total, two nasal sprays in each nostril) using several subjective reactivity indicators. All measures were completed 30 minutes prior to delivery of the nicotine nasal spray (baseline) and five minutes following the nicotine nasal spray. Following the completion of the testing week, participants resumed ad libitum smoking and returned to the lab (approximately six weeks later) to complete the second week of testing, which took place during the opposite menstrual phase

All study procedures were approved by the Institutional Review Board at the University of Minnesota and participants were provided informed consent prior to study enrollment.

2.3 Measures

Salivary cortisol levels are reported in two different ways: (1) absolute value in ng/mL at the morning wake-up time point; and (2) diurnal change over the day (first morning sample value minus expected nadir level at 8pm).

Subjective responses to nicotine were measured using two different instruments. The Subjective State Scale (SSS; al Absi et al, 2004; al Absi, Hatsukami & Davis, 2005) includes 24-items assessed by a seven-point Likert-type scale. The SSS consists of subscales on positive affect, distress and nicotine withdrawal. The second instrument is the Visual Analog Scale (VAS; Jones, Garrett & Griffiths, 1999) which allows participants to describe their experience of certain nicotine effects (alert, dizzy, head rush, jittery, pleasant, relaxed, stimulated, and urge to smoke) on a 100-mm line ranging from “not at all” to “very much.”

2.4 Statistical Analysis

Descriptive statistics were used to describe the baseline characteristics of the study sample. The diurnal cortisol value is a change score that was computed by subtracting the 8pm (nadir) value from the waking value. Change scores for the SSS and VAS were calculated by subtracting the ‘post nicotine nasal spray’ value from the ‘baseline’ value (e.g. +5 minute value - −30 minute value). Pearson correlations were calculated between the independent variables (e.g. morning cortisol and diurnal cortisol values) and dependent variables (e.g. baseline and change scores for SSS and VAS) within each menstrual phase (F vs L) separately. A within subject analyses using a mixed linear regression model was done to

assess an interaction between menstrual phase and cortisol value on nicotine response outcome. All analyses were conducted using SAS 9.3 software.

3.0 RESULTS

3.1 Study Participants

A total of 116 participants completed both testing weeks, and thus were included in this analysis (Table 1). The average age of participants was 29.1 ± 6.9 (SD) years. Of the participants, 75.1% were never married, 63.2% had an income of $20,000 or less, and 56.5% were non-Hispanic White. Participants smoked an average of 12.5 ± 5.5 cigarettes per day and had a Fagerström Test for Nicotine Dependence (FTND; Heatherton et al, 1991) score of 3.8 ±2.1.

3.2 Morning Cortisol and Subjective Response to Nicotine

No significant differences in the absolute morning cortisol values were found between the F and L phases (Table 1). During the F phase, higher morning cortisol levels were correlated with greater declines in both negative affect and withdrawal after nicotine administration ($r=-0.21$, $p=0.03$; $r=-0.30$, $p<0.01$ respectively; Table 2), as well as an increase in relaxation ($r=0.24$, $p=0.02$). Conversely, during the L phase, higher morning cortisol levels were correlated with a greater decline in head rush ($r=-0.26$, $p=0.01$) and urge to smoke ($r=-0.21$, $p=0.04$). Additionally, during the L phase, higher morning cortisol values were associated with feeling less pleasant prior to the administration of nicotine nasal spray ($r=-0.24$, $p=0.02$). Finally, four trends were noted suggesting a difference by menstrual phase. The follicular (F) phase may be associated with a stronger positive effect of cortisol on withdrawal both by absolute withdrawal score ($p=0.06$) and change in withdrawal score ($p=0.07$). Conversely, the luteal (L) phase may be associated with a stronger negative effect of cortisol on the change in head rush ($p=0.09$) and the absolute value of pleasant ($p=0.07$). No other significant associations were observed.

3.3 Diurnal Change in Cortisol and Subjective Response to Nicotine

No significant differences in diurnal cortisol change values were observed between the F and L phases (Table 1). Greater diurnal cortisol variation during the F phase was significantly associated with a lower urge to smoke prior to nicotine administration ($r=-0.28$, $p<0.01$). Additionally, during the F phase, greater diurnal cortisol variation was significantly correlated with a greater increase in negative affect and withdrawal after nicotine administration ($r=0.29$, $p<0.01$, $r=0.31$, $p<0.01$, respectively). Finally, during the L phase, greater diurnal variation in cortisol was significantly associated with greater pleasantness prior to nicotine administration ($r=0.27$, $p=0.02$). There were no significant menstrual phase differences.

4.0 DISCUSSION

The results of this study indicate that the associations between cortisol levels and subjective response to nicotine vary by menstrual phase. Specifically, during the follicular (F) phase, higher morning cortisol levels, as well as a greater diurnal variation in cortisol, were

associated with a stronger subjective response to nicotine, as measured by negative affect and withdrawal. On the other hand, during the luteal (L) phase, higher morning cortisol levels and greater diurnal variation in cortisol were significantly associated with pleasantness prior to the administration of nicotine. This suggests that there are menstrual phase differences in how HPA hormones modulate the subjective experience of nicotine.

The nature of the proposed synergistic relationship between cortisol and menstrual phase on nicotine response is unclear. It is well established that cortisol levels do not differ significantly between F and L phases of the menstrual cycle (Kudielka & Kirschbaum, 2003; Wolfam, Bellingrath & Kudielka, 2011), and our data was consistent with this finding as neither the morning cortisol levels nor diurnal change in cortisol differed by menstrual phase. Therefore, the variable relationship between cortisol and nicotine response seen in each menstrual phase is not likely due to menstrual hormones modulating cortisol secretion. Additionally, it is unclear from this study what aspect of the menstrual cycle is involved. Many hormones, including estrogen, progesterone, lutenizing hormone and follicular stimulating hormone, fluctuate during the menstrual cycle, and any one of these hormones or their ratio could be implicated in the proposed interaction. Further research measuring these hormone concentrations is needed to establish which hormones, if any, are implicated.

The observed correlation between cortisol concentrations, both absolute and diurnal variation, and nicotine response observed during the F phase may help reconcile conflicting reports regarding menstrual phase and success in smoking cessation. Specifically, we observed that the associations between cortisol and subjective response during the F phase were, primarily, observed after the administration of nicotine. Studies utilizing buproprion therapy or behavioral approaches for smoking cessation observed more favorable outcomes for smokers quitting in the L phase (Allen et al, 2008; Mazure et al, 2011). In contrast, other studies using nicotine replacement therapies for smoking cessation reported better outcomes for smokers who quit during the F phase (Carpenter et al, 2008; Franklin et al, 2008). This suggests that women during the F phase may be especially receptive to the effects of nicotine and have more difficulty quitting during that time without the aid of NRT, and that cortisol may play a role. A complex interaction between cortisol and the hormones of F phase may lead to potentiating the pleasant effects of nicotine.

The results from this analysis are complicated by the fact that smoking acutely stimulates the HPA axis (Rohleder & Kirschbaum et al, 2006) and smoking more cigarettes alters salivary cortisol concentrations in a somewhat dose-dependent manner (del Arbol et al, 2000). It is possible that the cortisol levels are higher among people who respond more positively to nicotine because they smoke more cigarettes. A causal relationship cannot be established based on the correlational data reported in this study, and further investigation into this phenomenon is warranted.

Our previously published study (Allen et al, 2009), which examined the relationship between menstrual phase, cortisol and smoking behaviors, suggested lower cortisol levels at waking were associated with greater cigarette cravings among women smokers in the L phase only. In the present study, we observed an inverse association between morning cortisol and urge to smoke prior to nicotine administration (F phase only) and diurnal

change in cortisol and change in urge to smoke after nicotine administration (L phase only). While craving and urge to smoke are slightly different variables, together both studies indicate that cortisol is involved with the desire to smoke, and that this association may vary by menstrual phase. Therefore, further investigations are warranted.

Although there were several strengths to this study including a within subjects design and detailed identification of menstrual cycle, other aspects limit the interpretation of the results. The saliva samples were collect by the participants and the exact time of sample collection cannot be verified. Also, this study focused on smokers currently engaging in ad libitum smoking, and the findings may be different among smokers attempting to quit. It is possible that individual differences in stress reactivity during menstrual phase account for the observed association, however this hypothesis should be better addressed in a future study examining stress reactivity directly.

The results from this study indicate that there may be menstrual phase variations in the association between salivary cortisol and response to nicotine. Additional research is necessary to confirm these results, further characterize this complex association and explore their effect on smoking cessation efforts.

ACKNOWLEDGEMENTS

We would like to thank our research staff – Jennifer Churma, Lindsay Jarvis, Sara Paradise, Kathryn Resner, Jennifer Widenmier, and Danielle Young – for their dedication to participant recruitment and follow-up, as well as data collection, entry, cleaning and management, as well as Scott Bischoff and Elizabeth Greene for their editorial assistance. Funding for this study was provided by NIH/NIDA R01DA08075 and NIH/NIDA/OWHR P50-DA033942. Huttlin was supported by a grant from the Minnesota Medical Foundation. A. Allen was supported by the University of Minnesota's Masonic Cancer Center and the Building Interdisciplinary Research Careers in Women's Health Grant (# K12HD055887) from the Eunice Kennedy Shriver National Institutes of Child Health and Human Development (NICHD), the Office of Research on Women's Health, and the National Institute on Aging, NIH, administered by the University of Minnesota Deborah E. Powell Center for Women's Health. This publication was also supported by the National Center for Advancing Translational Sciences of the National Institutes of Health Award Number UL1TR000114. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. These funding sources had no role in the study design, collection, analysis or interpretation of data, writing the manuscript or the decision to submit the paper for publication.

Funding: NIH/NIDA R01-DA008075

NIH/NIDA/OWHR P50-DA033942

NIH/NCRR M01RR00400

NIH/NCRR 1UL1RR033183

NIH/NCATS 8UL1TR00011

NIH/NICHD K12HD055887

Minnesota Medical Foundation Student Research Grant

REFERENCES

al'Absi M, Hatsukami D, Davis G. Attenuated adrenocorticotropic responses to psychological stress are associated with early smoking relapse. Psychopharmacology. 2005; 181(1):107–117. doi: 10.1007/s00213-005-2225-3. [PubMed: 15834539]

al'Absi M, Hatsukami D, Davis GL, Wittmers LE. Prospective examination of effects of smoking abstinence on cortisol and withdrawal symptoms as predictors of early smoking relapse. Drug Alcohol Depen. 2004; 73(3):267–278. doi: 10.1016/j.drugalcdep.2003.10.014.

Allen AM, Allen SS, Widenmier J, al'Absi M. Patterns of cortisol and craving by menstrual phase in women attempting to quit smoking. Addict Behav. 2009; 34:632–635. doi: 10.1016/j.addbeh.2009.03.024. [PubMed: 19409710]

Allen SS, Bade T, Center B, Finstad D, Hatsukami D. Menstrual phase effects on smoking relapse. Addiction. 2008; 103:809–821. doi:10.1111/j.1360.0443.2008.02146.x. [PubMed: 18412759]

Allen SS, Allen AM, Tosun N, Lunos S, al'Absi M, Hatsukami D. Smoking- and menstrual-related symptomatology during short-term smoking abstienece by menstrual phase and depressive symptoms. Addictive Behaviors. 2014; 39:901–906. dio: 10.1016/j.addbeh.2014.01.029. [PubMed: 24594903]

Boron, WF.; Boulpaep, EL. Medical Physiology, Updated Second Edition. Saunders; 2012. The female reproductive system.; p. 1146-1169.

Carpenter M, Upadhyaya H, LaRowe S, Saladin M, Brady K. Menstrual cycle phase effects on nicotine withdrawal and cigarette craving: A review. Nicotine Tobacco Res 2006. 2006; 8:627.

Carpenter MJ, Saladin ME, Leinbach AS, Larowe SD, Upadhyaya HP. Menstrual phase effects on smoking cessation: A pilot feasibility study. J Womens Health. 2008; 17(2):293–301. doi: 10.1089/jwh.2007.041s.

Centers for Disease Control. Vital signs: Cigarette smoking among adults aged ≥ 18 years-United States, 2005-2010. Morbidity and Mortality Weekly Report. 2011; 60:1207–1212. Retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6035a5.htm?s_cid=%20mm6035a5.htm. [PubMed: 21900875]

Cohen LM, al'Absi M, Collins FL Jr. Salivary cortisol concentrations are associated with acute nicotine withdrawal. Addict Behav. 2004; 29:1673–1678. doi: 10.1016/j.addbeh.2004.02.059. [PubMed: 15451136]

del Arbol JL, Muñoz JR, Ojeda L, López Cascales A, Rico Irles J, Miranda MT, Ruiz Requena ME, Aguirre JC. Plasma concentrations of beta-endorphin in smokers who consume different numbers of cigarettes per day. Pharmacol Biochem Be. 2000; 67:25–28.

Dressendorfer RA, Kirschbaum C, Rohde W, Stahl F, Strausburger CJ. Synthesis of a cortisol-biotin conjugate and evaluation as a tracer in an immunoassay for salivary cortisol measurement. J Steroid Biochem. 1992; 43:683–692. doi: 10.1016/0960-0760(92)90294-s.

Franklin TR, Ehrman R, Lynch KG, Harper D, Sciortino N, O'Brien CP, Childress AR. Menstrual cycle phase at quit date predicts smoking status in an NRT treatment trial: A retrospective analysis. J Womens Health. 2008; 17(2):287–292. doi:10.1089/jwh.2007.0423.

Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. British Journal Addiction. 1991; 86:1119–1127.

Jones HE, Garrett BE, Griffiths RR. Subjective and physiological effects of intravenous nicotine and cocaine in cigarette smoking cocaine abusers. J Pharmacol Exp Ther. 1999; 288(1):188–197. [PubMed: 9862770]

Kudielka BM, Kirschbaum C. Awakening cortisol responses are influenced by health status and awakening time but not by menstrual cycle phase. Psychoneuroendocrinology. 2003; 28:35–47. [PubMed: 12445835]

Mazure CM, Toll B, McKee SA, Wu R, O'Malley SS. Menstural cycle phase at quit date and smoking abstinence at six weeks in an open label trial of bupropion. Drug Alcohol Depend. 2011; 114(1):68–72. doi: 10.1016/j.drugalcdep.2010.07.024. [PubMed: 20832955]

McKee SA, Sinha R, Weinberger AH, Sofuoglu M, Harrison ELR, Lavery M, Wanzer J. Stress decreases the ability to resist smoking and potentiates smoking intensity and reward. J Psychopharmacol. 2010; 25(4):490–502. doi: 10.1177/0269881110376694. [PubMed: 20817750]

Miller G, Chen E, Zhou ES. If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. Psychological Bulletin. 2007; 133(1):25–45. doi: 10.1037/0033-2909.133.1.25. [PubMed: 17201569]

Perkins KA, Jacobs L, Sanders M, Caggiula AR. Sex differences in the subjective and reinforcing effects of cigarette nicotine dose. Psychopharmacology. 2002; 163:194–201. doi:10.1007/s00213-002-1168-1. [PubMed: 12202966]

Reuter M, Netter P, Rogausch A, Sander P, Kaltschmidt M, Dörr A, Hennig J. The role of cortisol suppression on craving for and satisfaction from nicotine in high and low impulsive subjects. Hum Psychopharm Clin. 2002; 17:213–224. doi: 10.1002.hup.402.

Rohleder N, Kirschbaum C. Hypothalamic-pituitary-adrenal (HPA) axis in habitual smokers. Int J Psychophysiol. 2006; 59:236–243. doi: 10.1016/j.ijpsycho.2005.10.012. [PubMed: 16325948]

Royce JM, Corbett K, Sorensen G, Ockene J. Gender, social pressure, and smoking cessations: The community intervention trial for smoking cessation (COMMIT) at baseline. Soc Sci & Med. 1997; 44:359–370. doi: 10.1016/S0277-9536(96)00149-9. [PubMed: 9004370]

Scharf D, Shiffman S. Are there gender differences in smoking cessation, with and without bupropion? Pooled- and meta-analyses of clinical trials of Bupropion SR. Addiction. 2004; 99:1462–1469. doi:10.1111/j.1360-0443.2004.00845.x. [PubMed: 15500599]

Vedhara K, Miles J, Bennet P, Plummer S, Tallon D, Brooks E, Gale L, Farndon J. An investigation into the relationship between salivary cortisol, stress, anxiety and depression. Biol Psychol. 2003; 62:89–96. doi: 10.1016/D0301-0511(02)00128-x. [PubMed: 12581685]

Wolfram M, Bellingrath S, Kudielka BM. The cortisol awakening response (CAR) across the female menstrual cycle. Psychoneuroendocrinology. 2011; 36:905–912. Doi: 10.1016/j.psyneuen.2010.12.006. [PubMed: 21237574]

World Health Organization. Composite International Diagnostic Interview, version 1.1. Geneva: 1993.

HIGHLIGHTS

- Women smokers completed labs in the follicular (F) and luteal (L) phases.
- The correlation between cortisol and nicotine response was assessed.
- During the F phase, cortisol was associated with negative affect and withdrawal.
- During the L phase, cortisol was associated with heard rush and urge to smoke.
- The relationship between cortisol and nicotine response varied by menstrual phase.

Table 1

Baseline Characteristics (n=116)

Demographics	
Age (years; mean ± standard deviation)	29.1 ± 6.9
Marital Status (% Never Married)	75.1%
Education (% ≤ Some College)	33.9%
Income (% ≤ $20,000)	63.2%
Race (% white)	56.5%
Smoking Behavior	
Cigarettes per Day (mean ± standard deviation)	12.3 ± 5.5
Smoking within 30 minutes of waking (%)	35.3%
FTND Score(mean ± standard deviation)[1]	3.8 ± 2.1
Cortisol Values	
Follicular Phase – Waking Value (mean ± standard deviation)	28.32 ±13.45 ng/mL*
Follicular Phase – Diurnal Change[2] (mean ± standard deviation)	15.02 ± 15.05 ng/mL**
Luteal Phase – Waking Value (mean ± standard deviation)	29.02 ± 16.48 ng/mL*
Luteal Phase – Diurnal Change[2] (mean ± standard deviation)	14.38 ± 17.15 ng/mL**

[1] Fagerstrom Test for Nicotine Dependence (Heatherton et al, 1991)

[2] Calculated by subtracting waking value from nadir (8pm) value.

* Paired t-test: p=0.907

** Paired t-test: p=0.142

Addict Behav. Author manuscript; available in PMC 2016 November 01.

Table 2

Pearson Correlations between Cortisol Concentrations and Subjective Response to Nicotine by Menstrual Phase in Women during Ad Libitum Smoking (n=116)

	F Phase				L Phase			
	Absolute Value		Change Score*		Absolute Value		Change Score*	
	r	p-value	r	p-value	r	p-value	r	p-value
Correlates with AM Cortisol Concentration								
Positive Affect[1]	−0.07	0.51	0.18	0.07	0.00	0.97	0.14	0.16
Negative Affect[1]	0.04	0.73	−0.21	0.03	−0.02	0.86	−0.10	0.31
Withdrawal[1]	0.15	0.13	−0.30	<0.01	−0.08	0.38	0.00	0.97
Craving[1]	0.14	0.17	−0.15	0.13	0.00	0.98	−0.11	0.29
Stimulated[2]	0.00	0.97	0.09	0.34	0.08	0.46	0.02	0.83
Jittery[2]	0.18	0.08	−0.13	0.21	0.12	0.24	−0.02	0.86
Head Rush[2]	0.05	0.61	0.06	0.51	0.00	0.97	−0.26	0.01
Relaxed[2]	0.00	0.99	0.24	0.02	−0.19	0.06	0.15	0.14
Pleasant[2]	0.01	0.89	0.18	0.09	−0.24	0.02	0.13	0.21
Dizzy[2]	0.00	0.97	0.06	0.57	−0.03	0.80	−0.07	0.45
Alert[2]	−0.05	0.58	0.03	0.71	−0.03	0.76	0.06	0.53
Urge to Smoke[2]	0.19	0.07	−0.07	0.45	0.08	0.41	−0.21	0.04
Correlates with Diurnal Change in Cortisol Concentration**								
Positive Affect[1]	0.09	0.35	0.01	0.90	0.00	0.93	−0.03	0.77
Negative Affect[1]	−0.08	0.42	0.29	<0.01	−0.02	0.83	0.02	0.83
Withdrawal[1]	−0.16	0.14	0.31	<0.01	0.08	0.39	−0.03	0.83
Craving[1]	−0.15	0.14	0.14	0.18	0.11	0.27	0.05	0.59

	F Phase				L Phase			
	Absolute Value		Change Score*		Absolute Value		Change Score*	
	r	p-value	r	p-value	r	p-value	r	p-value
Stimulated[2]	0.06	0.58	−0.05	0.62	0.03	0.77	0.01	0.96
Jittery[2]	−0.15	0.15	0.15	0.16	0.01	0.89	0.01	0.92
Head Rush[2]	0.02	0.87	−0.14	0.17	0.17	0.10	0.09	0.41
Relaxed[2]	0.03	0.75	−0.17	0.10	0.19	0.06	−0.09	0.40
Pleasant[2]	0.11	0.29	−0.12	0.25	0.27	0.02	−0.09	0.39
Dizzy[2]	0.00	1.00	0.02	0.83	0.16	0.12	0.06	0.57
Alert[2]	0.11	0.32	0.03	0.75	0.12	0.25	−0.08	0.43
Urge to Smoke[2]	−0.28	<0.01	0.16	0.13	−0.03	0.74	0.16	0.10

[1] Item from Subjective State Scale (al Absi et al, 2004; al Absi, Hatsukami & Davis, 2005)

[2] Item from Visual Analog Scale (Jones, Garrett & Griffiths, 1999)

* Calculated by subtracting the baseline value (e.g. 30 minutes prior to nicotine nasal spray administration) from the post nasal spray value (e.g. 5 minutes post nicotine nasal spray administration).

** Calculated by subtracting waking value from nadir (8pm) value.