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Changes in Circulating Leptin Levels During Acute Stress and Associations with Craving in Abstinent Smokers: A Preliminary Investigation

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Abstract

Recent research suggests a role for the appetite hormone leptin in cigarette smoking. This study examined patterns of change in leptin in response to stress and associations with craving during the initial phase of a quit attempt. Thirty-six smokers (average age $\pm$ SEM, 33.4 ± 2.4) interested in smoking cessation set a quit day and were required to be abstinent for 24 hours. After, they completed a laboratory session including public speaking and cognitive challenges, and attended 4 weekly post-cessation assessments. Blood samples and self-report measures were collected throughout the laboratory session. The results indicated that leptin levels significantly increased following exposure to acute stress. We also found positive correlations between leptin and craving for cigarettes. No differences were observed in leptin levels between smokers who maintained abstinence for 4 weeks and those who relapsed during this period. These findings suggest that leptin levels may change in response to stress and that leptin could be a useful marker of craving for smoking.

Keywords

Leptin; Stress; Craving; Tobacco; Relapse

1. Introduction

Research has shown that psychosocial stressors increase smoking as well as the risk for smoking relapse (Cohen and Lichtenstein, 1990; Shiffman et al., 1996). Smokers whose

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Conflict of Interest

All authors report no financial interests or potential conflicts of interest.

Contributors

Dr. Mustafa al'Absi designed the research protocol, as well as was involved in data collection, data analysis and revision of the manuscript. Dr. Motohiro Nakajima was involved in data analysis and manuscript revision. Tiffany Cragin was involved in data management and the assaying of leptin. Sheena Potretzke performed the literature search, data analysis and composition of the manuscript.

lapse is elicited by stress progress more rapidly into full relapse than those for whom lapses are elicited by eating or drinking (Shiffman et al., 1996). Smokers unsuccessful in their quit attempts, either failing to quit or relapsing after a short period, report high stress levels preceding initial abstinence, or at 1, 3, and 6 months post cessation (Cohen and Lichtenstein, 1990). These observations suggest an important role for stress in cessation outcomes. Stress may increase craving for cigarettes (Shiffman et al., 1997). Craving embodies a potent motivational factor for smoking (West et al., 2007). Subjective craving is the most commonly experienced symptom during withdrawal from nicotine, as well as the aspect of quitting expected to be most difficult (von der Goltz et al., 2010). Intensity of smoking cravings within the first few days of abstinence has been shown to predict those who will relapse (al'Absi et al., 2004, 2007), suggesting that craving may mediate the relationships between stress and tobacco use.

Recent evidence indicates the role of appetite hormones in craving for drugs of abuse. For example, leptin concentrations have been demonstrated to predict craving and relapse in alcoholics under treatment (Kiefer et al., 2005; Hillemacher et al., 2007). Plasma leptin levels have been shown to be associated with craving for alcohol (Kiefer et al., 2001, 2002); significantly increasing at onset of withdrawal, and correlating highly with self-reported alcohol craving ratings. Leptin is a product of the *ob* gene found mainly in adipocytes, known primarily for its function as an endocrine signal quintessential in the regulation of appetite and energy expenditure (Pellemounter et al., 1995). Leptin functions to regulate the hypothalamic centers involved in energy homeostasis, body weight, and gene expression of corticotrophin-releasing hormone and pro-opiomelanocortin (Cheung et al., 1997; Mantzoros, 1999).

Previous studies examining leptin levels in smokers have demonstrated an association between the hormone and smoking status; however, these results were not consistent (Reseland et al., 2005; Koc et al., 2009). Others studies found positive correlations between levels of circulating leptin and cigarette craving in smokers who were minimally deprived of nicotine (von der Goltz et al., 2010) as well as in those after 24 h of abstinence (al'Absi et al. 2011). However, the findings of these studies were limited due to the use of only a single hormonal sample and limited assessment of craving and withdrawal symptoms. The current study aimed to expand previous findings by collecting multiple biological samples and subjective craving measures to examine patterns of changes in those indices in response to laboratory stress among habitual smokers who were at the initial phase of smoking cessation. We also tested the extent to which leptin responses to stress were associated with smoking relapse. In addition, the relationship between leptin and craving was assessed at each period of the study (e.g., baseline, immediately after stress) to evaluate whether the linkages vary across period.

2. Methods

2.1 Participants

Cigarette smokers were recruited using newspaper advertisements and posters displayed throughout the university community. Prospective participants completed a preliminary telephone screening interview including questions regarding any current or recent history of

medical and/or psychiatric disorders, medication(s), and satisfaction of designated smoking criteria (e.g. habitual smoking of an average of 10 cigarettes or more per day for a minimum of 2 years, with a strong motivation to quit). Those participants who met preliminary screening criteria were invited to an on-site screening session.

At this session, participants were screened and enrolled if they met the following study criteria: no history of major illness or psychiatric disorder, weight within $\pm 30\%$ of Metropolitan Life Insurance norms, consumption of two or fewer alcoholic drinks per day, and no routine prescription medication use (with exception of oral contraceptives). They then provided a breath sample for assessment of expired carbon monoxide (CO), and completed forms assessing medical and smoking history (e.g. previous quit attempts), demographics and psychosocial measures (described below). Female participants answered additional questions regarding the regularity of their menstrual cycle and use of contraceptive medications. Based on self-reports of regularity and prior menstrual cycle, quit dates for menstruating women were arranged during the follicular phase (day 3 to day 10) of the menstrual cycle. Participants reviewed and signed a written consent form approved by the Institutional Review Board of the University of Minnesota and were compensated monetarily for participation.

The current study was part of a larger project examining psychobiological stress response and smoking relapse (al'Absi et al., 2005). The present report comprises data from assays pertaining to leptin measurement from available plasma samples. Therefore, the final sample consisted of 36 (women= 14) habitual smokers between the ages of 18 and 68 (average age $\pm$ SEM, 33.39 ± 2.41).

2.2 Measures

Blood samples were collected throughout the laboratory session using an indwelling catheter. Plasma leptin was assayed using a direct sandwich ELISA (Linco, Missouri); with inter- and intra-assay coefficients of variance for the assays below 8%. Plasma cortisol was assayed in duplicate using enzyme immunoassay (EIA ; DSL, Sinsheim, Germany) with a lower sensitivity of 0.1 $\mu\text{g/dL}$ and inter-/intra-assay coefficients of variance below 10%. Saliva samples were collected and assayed for cotinine levels using EIA (DRG Diagnostics, Marburg, Germany); with inter- and intra-assay variations for cotinine measurements below 12%. MicroCOTM monitors (Micro Direct Inc., Auburn, Maine) were used to measure expired CO. Cardiovascular measures including: systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were measured using a Dinamap oscillometric monitor system (Critikon, Tampa, FL).

Participants completed a modified version of the Minnesota Nicotine Withdrawal Scale (MNWS; Hughes and Hatsukami, 1998) and a brief version of the Questionnaire of Smoking Urges (QSU-Brief; Cox et al., 2001) multiple times during the laboratory session (described below). Included in the MNWS were items assessing: irritability, anger, anxiety, difficulty concentrating, restlessness, depressed or sad mood, and hunger; the item "desire to smoke", or craving was analyzed separately from other items as it has been shown that craving is different from withdrawal symptoms (Hughes and Hatsukami, 1998). Two factor measurements were included in the QSU-Brief: appetitive urges to smoke (Factor 1), and

urges associated with relief of the aversive experience of withdrawal (Factor 2). Factor 1 incorporates items that signify a strong want and intention to smoke, while Factor 2 incorporates items signifying anticipation of alleviation of negative affect (aversive urges).

Positive affect and distress were also assessed throughout the laboratory session, using the Revised Subjective States Questionnaire (SSQ; Lundberg and Frankenhaeuser, 1980). Positive affect assessment included items of: cheerfulness, content, calmness, controllability, and interest. Distress assessment included items of: anxiety, irritability, impatience, and restlessness. The scale has been shown to reliably track laboratory stress-related changes in mood (al'Absi et al., 1994, 1998). Reliability as assessed by Cronbach's alphas were 0.85 and 0.82 for positive affect and distress, respectively (al'Absi et al., 2003). Physical symptoms which have been shown to be associated with smoking abstinence, including: headache, stomachache, drowsiness, sweating, tremor, fatigue and coughing (American Psychiatric Association, 1994) were also included.

During the screening session, participants completed the following forms: the Fagerström Test of Nicotine Dependence (FTND; Heatherton et al., 1991), the Center for Epidemiologic Studies-Depression scale (CES-D; Radloff, 1977), the Anxiety Sensitivity Index (ASI; Reiss et al., 1986), the State-Trait Anxiety Inventory (Trait-Form; STAI; Spielberger et al., 1983), the 10-item version of the Perceived Stress Scale (PSS; Cohen et al., 1983), and the Profile of Mood State questionnaire (POMS; McNair et al., 1992).

2.3 Stress Protocol

The public speaking challenge entailed participants composing and delivering three 4-min speeches focusing on three scenarios. The three scenarios were presented in a counterbalanced order. In one scenario, participants were presented with a controversial social issue and were asked to introduce their positions and defend them. In another scenario, participants were given an article about an issue of general interest and were asked to construct a presentation based on this article. In a third scenario, participants were asked to imagine a hypothetical situation where they were being accused of shoplifting (see al'Absi et al., 1997). Participants were given 4 min to prepare prior to delivery of each presentation and were informed their speech would be both videotaped and evaluated at a later date by members of the research team. The cognitive challenges consisted of a mental arithmetic task and the Paced Auditory Serial Addition Task (PASAT). Order of administration of the tasks was counterbalanced. In the mental arithmetic task participants were required to consecutively add the digits composing a three digit number to the three digit number (al'Absi et al., 1997). The PASAT (Gronwall, 1977) required the participant to add successive numbers as they were presented from an auditory tape and answer with the correct sum. Each number was summed with the digit presented immediately before it. Four trials of the PASAT were employed, with varying inter-stimulus interval lengths progressing from 2.4, 2.0, 1.6, and 1.2 s (Sherman et al., 1997). Both tasks were performed for 8 min each.

2.4 Procedures

After the medical screening, participants were asked to set a quit day. On the quit day, participants attended a brief assessment session before beginning abstinence. No pharmacological or systematic behavioral interventions were employed in this study; due to the purpose of this particular study being to examine determinants of smoking relapse (al'Absi et al., 2005). All participants were required to abstain from smoking for at least the 24 hours until the following laboratory session. Participants were instructed to eat a light lunch at least 2 h prior to the session.

All laboratory sessions took place at approximately noon. At the beginning of the laboratory session, breath samples were collected for assessment of expired CO and an intravenous catheter was inserted. Participants then viewed a neutral nature documentary for 30 min- this was the baseline rest period. Participants then performed the public speaking task, lasting 24 min. This was followed by a 30 min recovery period. Participants then performed the mental arithmetic task and the PASAT for 16 min, followed by a final 30 min recovery period. Blood samples for measurement of plasma leptin levels, as well as mood, craving, withdrawal and physical symptoms ratings were collected: (1) before the onset of the baseline rest period (i.e., pre-baseline), (2) at the end of the baseline rest period (i.e., pre-stress), (3) immediately after the completion of a speech task (i.e., speech task), (4) at the end of the rest period (i.e., rest), (5) immediately after the completion of the mental arithmetic and PASAT tasks (i.e., cognitive tasks), and (6) after conclusion of the final recovery period (i.e., recovery). BPs and HR were taken every 3 min during the baseline and recovery periods and every 2 min during the acute stressors.

Weekly assessment sessions were conducted for 4 weeks following the quit date. Biochemical measures were collected to examine smoking status, along with self-report measures pertaining to smoking behavior (not reported here). Brief support sessions were also provided to embolden the participant's efforts to maintain abstinence or reduce smoking rate if they had returned to smoking.

2.5 Data Analysis

Leptin and Factor 2 of the QSU-B are reported as log transformed values to correct for divergence from normal distribution and/or violation of the assumption of homogeneity of variance. A series of multivariate analyses of variance (MANOVA) using Pillai's trace tests were employed to examine leptin concentrations, cardiovascular measures, measures of withdrawal symptoms, craving, positive affect, distress, and physical symptoms, in a 2 (relapse status: relapser vs. abstainer) $\times$ 6 (sampling period: pre-baseline, pre-stress, speech task, rest, cognitive tasks, recovery) model. Due to the small sample size, sex was included as a covariate. Bonferroni correction was applied for post-hoc multiple comparison tests. Correlational analysis was conducted to examine relationships between leptin levels collected throughout the lab period and withdrawal symptoms, craving, mood and cortisol. Area under the curve was calculated for leptin levels at successive time periods and similarly used in correlational analysis. Variables related to participant characteristics (i.e., demographics, smoking data, and trait measures) were analyzed using analysis of variance (ANOVA) to examine differences between relapsers and abstainers. Welch's F is reported

when the assumption of homogeneity of variance was violated as indicated by a significant Levene's test. A chi-square test was used to examine alcohol intake in relapsers and abstainers. Due to the relatively small sample size and expected counts under 5, the likelihood ratio will be reported. A lapse was defined as smoking at least one cigarette following the 24 h abstinence period. Over the course of the 4 week follow-up, 27 participants relapsed (women = 11), while 9 participants were able to successfully abstain (women = 3).

3. Results

3.1 Participant characteristics

Participants who relapsed within the 4 week follow-up period (relapsers) were comparable to those who were able to successfully abstain (abstainers) in: age, body mass index (BMI), years of education, caffeine intake, physical activity, and average hours of sleep per night ($ps > 0.05$), as well as CES-D, STAI, ASI, and PSS ($ps > 0.09$; Table 1). There was no significant association between relapse status and alcohol intake, $L\chi^2(3) = 2.08, p > 0.05$. However, relapsers displayed significantly lower levels of vigor than abstainers ($F(1, 34) = 4.40, p < 0.05$). Relapsers did not differ significantly from abstainers in smoking history variables: average number of cigarettes smoked per day, number of years smoking at current rate, age of first smoke, ratings of desire to quit smoking cigarettes, number of previous quit attempts, FTND scores, and pre-quit expired CO levels ($ps > 0.41$; Table 1). Relapsers did, however, have significantly higher cotinine levels after the 24 hour abstinence period than abstainers, $F(1, 32) = 4.78, p < .03$; Table 1).

3.2 Cardiovascular Measures

All cardiovascular measures significantly varied across sampling time: SBP, $F(6, 28) = 11.46, p < 0.001$; DPB, $F(6, 28) = 12.67, p < 0.001$; HR, $F(6, 28) = 16.33, p < 0.001$. Post-hoc analysis displayed an increase in all measures throughout the course of pre-baseline, pre-stress and the speech task ($ps < 0.001$), then decreasing during the rest period ($ps < 0.001$), increasing during the mental arithmetic ($ps < 0.001$), remaining stable during the PASAT task ($ps > 0.59$), and finally decreasing during the recovery period ($ps < 0.001$). Relapsers and abstainers did not differ in SBP, DBP or HR ($F(1, 33) > 0.14, ps > 0.14$, see Table 2).

3.3 Withdrawal symptoms and mood

Withdrawal symptoms, as measured by the MNWS, significantly varied across time of sampling, $F(5, 27) = 4.00, p < 0.01$ (see Table 2). Post-hoc analysis found that levels immediately following the cognitive tasks were greater than those of pre-stress and rest periods ($ps < .02$). Reports of craving as assessed by the item on the MNWS varied significantly across time, $F(5, 27) = 3.03, p < 0.05$. Levels immediately following the speech and cognitive tasks were greater than those in the rest period between these tasks ($ps < .05$). Although relapsers consistently reported greater levels of withdrawal symptoms and craving throughout the lab session, these difference were not significant (withdrawal symptoms: $F(1, 31) = 3.48, p > 0.07$; craving: $F(1, 31) = 1.28, p > 0.27$). Smoking urges as assessed by QSU-B (factor 1 and 2) did not vary over time or by relapse status ($ps > .06$).

A significant effect of time in reported distress ($F(5, 27) = 3.40, p < 0.05$) indicated greater levels after the cognitive tasks than the pre-stress period ($p < 0.02$). There was also a significant time effect in positive affect ($F(5, 27) = 4.55, p < 0.01$), reflecting lower levels after the speech and cognitive tasks than the rest period between these tasks ($ps < .01$), and lower levels after the speech task relative to the final recovery ($p < .005$). A significant time effect in physical symptoms ($F(5, 27) = 2.71, p < 0.05$) indicated lower levels after cognitive tasks than after pre-stress and rest periods ($ps < 0.05$). Relapsers reported lower positive affect than abstainers as indicated by a main effect of group ($F(1, 31) = 6.97, p < 0.05$). Relapsers and abstainers did not differ in distress or physical symptoms, $ps > 0.07$.

3.4 Leptin Concentrations

A significant effect of time was found in leptin concentrations ($F(5, 25) = 25.07, p < 0.001$; see Figure 1). For post hoc multiple comparison tests, p value was adjusted ($p = .05/3$ [number of tests] = 0.167). Leptin levels during rest (after the speech task), cognitive tasks, and final recovery were significantly higher than the levels during the speech task (the lowest of all periods; $ps < 0.001$). Relapsers and abstainers displayed comparable leptin levels throughout the lab session, $F(1, 29) = 0.57, p > 0.46$.

3.5 Correlation analyses

Pre-stress leptin levels (period 2) were positively correlated with Factor 1 of the QSU-B (all periods: $rs > .34, ps < .05$) and craving (all periods except recovery: $rs > .35, ps < 0.5$). Leptin levels following the completion of the speech task (period 3) were associated with craving during the pre-stress period ($r = .38, p < .05$). Leptin levels collected during the rest period (period 4) were related to craving (the first 3 periods: $rs > .34, ps < .05$), physical symptoms at the same period ($r = .37, p < .05$), and QSU-B F1 at the pre-baseline period ($r = .34, p < .05$). Leptin levels following the completion of the cognitive stress tasks (period 5) were linked with pre-stress craving ($r = .35; p < 0.05$). Lastly, leptin levels following the final recovery period (period 6) were correlated with craving during pre-stress ($r > .35, p < .05$), and physical symptoms and distress following the speech task ($rs > .34, ps < .05$). Plasma leptin and cortisol levels during periods where a stress response was indicated in leptin levels (periods 4, 5, and 6) were not correlated, $rs > -.24, ps > .05$.

When area under the curve, is calculated between each successive time period and used as a composite score in correlation analysis, results are similar. Leptin levels from the pre-baseline period throughout pre-stress (periods 1 to 2) was positively correlated with craving throughout the laboratory, void of the rest and recovery periods ($ps < 0.05, rs > 0.34$, period 2: $p < 0.001, r = 0.43$), as well as Factor 1 of the QSU-B during the speech task (period 3: $p < 0.05, r = 0.33$). Likewise, leptin levels from baseline throughout the speech task (periods 2 to 3) were positively correlated with craving in all periods void of the rest and recovery periods ($ps < 0.05, rs > 0.34$, period 2: $p < 0.001, r = 0.44$) and Factor 1 throughout pre-baseline, pre-stress, speech task and rest (periods 1 through 4: $ps < 0.05, rs > 0.33$). Leptin levels from the speech task through the rest period (period 3 to 4) were positively correlated with craving during pre-baseline and pre-stress ($ps < 0.05, rs > 0.34$) and Factor 1 during the pre-stress period ($p < 0.05, r = 0.33$). Leptin levels from rest through the cognitive tasks were positively correlated with craving at pre-stress ($p > 0.05, r = 0.38$). Finally, leptin

levels from the cognitive tasks through recovery were correlated with pre-stress craving ($p < 0.05$, $r = 0.35$).

4. Discussion

The main finding of this study was the significant increases in leptin concentrations following exposure to acute stress. Leptin levels declined between baseline and the first stress period and then increased during the following periods. These observations suggest a delayed pattern of leptin release in response to the speech task. That is, initial decline may have been due to pre-stress rest and the subsequent increase may have reflected the response to the acute stressors. This delayed response pattern has been shown in cortisol release pattern (al'Absi et al., 1997). While the lack of a control rest day condition or a nonsmoking control group call for cautious interpretation of the results, the present study is among the first to examine patterns of leptin release across time before and after exposure to acute stress among habitual smokers.

The current study found significant changes in circulating leptin levels following exposure to acute stress. These increases in leptin levels are possibly related to increased sympathetic activation typically observed in response to acute stressful challenges. Increased sympathetic activity may increase activation of white adipose tissues leading to increased leptin concentrations. The study also showed linkages between leptin and self-reports of craving for cigarettes. Greater leptin during the pre-stress baseline period was associated with greater craving and urges to smoke throughout the session. Also, craving during the pre-stress period was positively associated with leptin during all period except the first sample. These findings are consistent with previous studies on tobacco use (al'Absi et al., 2011; von der Goltz et al., 2010), further supporting the potential usefulness of leptin as a biological correlate of craving during smoking abstinence. Moreover, these results are compatible with results from alcohol-based studies which demonstrate leptin levels to predict craving and relapse, in alcoholics receiving treatment (Kiefer et al., 2005; Hillemacher et al., 2007). These findings suggest the mediating role of leptin in craving for drugs of abuse.

Although specific mechanisms for the relationship between leptin and craving for cigarettes are yet to be elucidated, there is evidence to suggest a role for appetite-regulating peptides, including leptin, in the modulation of reward pathways beyond their function in the hypothalamic regulation of energy homeostasis (Palmiter, 2007). A possible mechanism for increased craving during nicotine withdrawal is a leptin-moderated reward deficit (von der Goltz et al., 2010), which suggests that leptin may obstruct the dopaminergic relay during withdrawal from nicotine in a bidirectional manner, and modulate craving. Given the interaction of leptin with reward processing during food consumption, as well as dopamine transmission in the nucleus accumbens (NAcc), leptin could also influence the subjective reward value and reinforcing properties of nicotine (and other drugs of abuse), and so the motivation to smoke (von der Goltz et al., 2010). Leptin has been demonstrated to directly modulate mesocorticolimbic reward pathways activity (Leininger et al., 2009). Nicotine works to modulate the mesolimbic system by binding to nicotinic acetylcholine receptors positioned on neurons which facilitate γ -aminobutyric acid (GABA) and dopaminergic transmission in various brain regions, including the ventral tegmental area (VTA), the

nucleus accumbens (NAcc), and prefrontal areas (PFC) (Laviolette & van der Kooy, 2004). Leptin binds to specific dopaminergic receptors positioned on neurons within the VTA, inhibiting dopamine signaling to the NAcc (Laviolette and van der Kooy, 2004; Palmiter, 2007). Moreover, the striatum of smokers exhibits diminished dopamine D1 (Dagher et al., 2001) and D2 receptors, as compared to nonsmokers (Fehr et al., 2008). A down-regulated dopaminergic mesolimbic system appears to be involved in the maintenance of addictive behaviors in both nicotine and alcohol dependent individuals (Tan et al., 2009).

Leptin levels as well as self-report measures of craving and distress were not related to smoking relapse. While the finding on leptin was consistent with our previous observation (al'Absi et al., 2011), we note our results should be considered preliminary due to small sample size. No study has directly examined stress-related changes in leptin and smoking cessation outcomes. Studies have reported attenuated cortisol stress response in chronic smokers and such alteration predicted early smoking relapse (al'Absi et al 2005). While leptin is suggested to be involved in central stress regulatory systems (Heiman et al., 1997), no relationship was found between leptin and cortisol and cardiovascular measures among dependent smokers (al'Absi et al., 2011). It is possible that the association between leptin in response to stress and smoking relapse is mediated by multiple mechanisms such as other appetite hormones. More research is needed to identify mediators of the association between leptin, craving, and cessation outcomes.

The findings of the present study are limited by the small sample size, lack of control group and careful examination of sex differences in leptin response to stress. Inclusion of a larger sample size with an equal number of men and women, as well as nonsmokers should improve the results. Sex differences appear particularly promising as previous research supports a difference in circulating leptin levels and cardiovascular responses to acute stress in men and women independent of smoking status, with women exhibiting higher circulating leptin levels and greater cardiovascular responses to stress than men (Brydon et al., 2008). Furthermore, the effect of different types of acute stress on leptin levels may differ between men and women; as illustrated by Häfner et al. (2011) who showed that social isolation, and the interaction between social isolation and depressed mood are associated with increased leptin levels in men, but not in women. To clarify the effects of stress on leptin, future research should include a rest day where no stress tasks are introduced, and compare changes in leptin during that day with those measured in the stress day. The results of leptin and self-report measures were correlational; it is not clear whether changes in leptin caused an increase in craving, enhanced craving lead to elevated leptin, or third variable(s) were responsible for the observed relationships. It should be noted, however, that our study was among the first to collect multiple samples to examine patterns of changes in leptin in response to acute laboratory stress, and their associations with craving among habitual smokers who were going through smoking withdrawal.

In conclusion, the current study showed that the appetite hormone leptin changed across a short laboratory session in habitual smokers. Leptin levels were positively associated with reported craving, withdrawal symptoms, and distress throughout the study. These findings provide initial support for the potential usefulness of leptin in examining psychobiological mechanisms of stress and cigarette craving in smokers.

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Figure 1.

Changes in circulating leptin in response to laboratory stress.

Entries show mean and line bars indicate standard error of the mean. * There was a significant time effect indicating that lower leptin levels after the speech task relative to other periods ($p < 0.001$). Changes in leptin did not differ between abstainers and relapsers.

Table 1

Participant characteristics and averaged smoking, psychological and craving measures.

	<i>Relapse Status</i>	
	Abstainers (N = 9)	Relapsers (N = 27)
<i>Participant Characteristics</i>		
Age (years)	39.11 (19.78)	31.48 (12.12)
BMI (kg/m²)	25.63 (3.37)	24.21 (4.61)
Education (years)	12.50 (4.07)	14.21 (2.40)
Caffeine intake (servings/day)	6.33 (4.06)	3.84 (2.95)
Physical activity (hours/week)	3.14 (2.19)	4.21 (2.94)
Average sleep (hours/night)	6.88 (1.55)	7.00 (1.18)
Alcohol consumption	Abstainers (N = 9)	Relapsers (N = 26)
<i>Never</i>	1	4
<i>Rarely (1-2/day)</i>	8	19
<i>Approx. 2/day</i>	0	2
<i>>2/day</i>	0	1
<i>Smoking Variables</i>		
Cigarettes per day	17.78 (2.64)	20.26 (8.89)
Duration of smoking (years)	11.71 (10.37)	11.67 (12.10)
Age of first smoke (years)	15.89 (2.93)	15.70 (4.29)
Motivation to quit (rating)	6.00 (1.12)	6.04 (0.81)
Previous quit attempts	3.89 (2.67)	3.56 (2.29)
FTND	5.33 (1.32)	5.52 (2.24)
<i>Psychological and Craving Measures</i>		
CES-D	8.00 (7.78)	14.56 (10.43)
ASI	20.11 (11.30)	17.32 (9.84)
STAI	34.56 (5.46)	39.15 (10.59)
PSS1 (medical screen)	13.44 (5.94)	16.63 (6.91)
PSS2 (quit lab)	12.33 (6.12)	16.48 (5.44)
POMS		
	Abstainers	Relapsers
<i>Tension</i>	10.56 (6.02)	10.52 (6.68)
<i>Depression</i>	4.78 (6.00)	9.52 (8.31)
<i>Anger</i>	5.22 (6.26)	10.52 (8.72)
<i>Vigor</i> *	20.11 (5.65)	16.22 (4.54)
<i>Fatigue</i>	7.78 (5.02)	8.78 (6.18)
<i>Confusion</i>	6.67 (5.83)	7.96 (3.94)
<i>Physiological Measures</i>		
CO (ppm)	25.89 (16.94)	22.63 (8.58)
Salivary cotinine (ng/mL) *	27.16 (75.08)	117.20 (114.38)

**p < 0.01

***p < 0.001.

Means (standard deviation of the mean); BMI = body mass index; FTND = Fagerström Test of Nicotine Dependence; CES-D = Center for Epidemiologic Studies Depression Scale; ASI = Anxiety Sensitivity Index; STAI = State Trait Anxiety Inventory, PSS = Perceived Stress Scale; CO = carbon monoxide.

*
 $p < 0.05$

Table 2

Changes in self-report mood and withdrawal symptoms.

		Abstainers (n=9)	Relapsers (n=27)
Craving^a			
	Pre-baseline	2.7 (0.9)	4.0 (0.5)
	Pre-stress	2.8 (0.9)	3.5 (0.5)
	Speech task	3.0 (0.8)	4.0 (0.5)
	Rest	2.0 (0.8)	3.5 (0.5)
	Cognitive tasks	3.0 (0.9)	4.0 (0.5)
	Recovery	2.7 (0.8)	3.5 (0.5)
Withdrawal symptoms^a			
	Pre-baseline	6.3 (3.0)	11.9 (1.8)
	Pre-stress	3.9 (2.9)	10.0 (1.8)
	Speech task	5.0 (3.2)	12.3 (1.9)
	Rest	4.7 (3.1)	10.7 (1.9)
	Cognitive tasks	7.1 (3.3)	14.8 (2.0)
	Recovery	5.7 (3.3)	11.2 (2.0)
Distress^a			
	Pre-baseline	5.2 (2.5)	9.4 (1.5)
	Pre-stress	2.8 (2.3)	8.0 (1.4)
	Speech task	4.2 (2.5)	9.9 (1.5)
	Rest	3.8 (2.5)	8.2 (1.5)
	Cognitive tasks	4.9 (2.6)	11.2 (1.6)
	Recovery	4.3 (2.7)	9.3 (1.6)
Positive affect^{ab}			
	Pre-baseline	25.9 (3.2)	18.4 (1.9)
	Pre-stress	27.9 (3.1)	18.2 (1.8)
	Speech task	24.8 (3.2)	15.9 (1.9)
	Rest	28.7 (3.2)	18.3 (1.9)
	Cognitive tasks	23.6 (3.4)	15.9 (2.1)
	Recovery	28.9 (3.0)	18.1 (1.8)
Physical symptoms^a			
	Pre-baseline	3.1 (1.4)	5.1 (0.9)
	Pre-stress	4.6 (1.6)	5.6 (0.9)
	Speech task	3.8 (1.7)	5.4 (1.0)
	Rest	4.7 (1.6)	5.9 (1.0)
	Cognitive tasks	2.8 (1.3)	4.1 (0.8)
	Recovery	3.6 (1.3)	4.4 (0.8)
QSU-B Factor 1			
	Pre-baseline	21.1 (4.4)	25.5 (2.5)
	Pre-stress	19.1 (4.5)	23.5 (2.6)

		Abstainers (n=9)	Relapsers (n=27)
	Speech task	19.7 (4.4)	26.1 (2.5)
	Rest	18.9 (4.5)	23.7 (2.6)
	Cognitive tasks	19.1 (4.6)	26.2 (2.7)
	Recovery	18.1 (4.5)	23.3 (2.6)
QSU-B Factor 2			
	Pre-baseline	13.6 (4.1)	17.7 (2.4)
	Pre-stress	10.5 (4.1)	16.4 (2.4)
	Speech task	11.8 (4.5)	20.0 (2.6)
	Rest	9.6 (4.1)	16.7 (2.4)
	Cognitive tasks	10.4 (4.8)	19.8 (2.8)
	Recovery	9.4 (4.3)	16.2 (2.5)
	Pre-baseline	118.0 (23.5)	113.0 (12.2)
	Pre-stress	127.7 (25.7)	126.3 (18.8)
	Speech task	140.7 (38.2)	134.1 (23.7)
	Rest	118.9 (19.0)	117.6 (15.8)
SBP	Cognitive tasks		
	<i>Mental Arithmetic</i>	128.9 (18.8)	128.9 (22.9)
	<i>PASAT</i>	128.9 (20.2)	128.3 (20.4)
	Recovery	117.9 (18.4)	117.0 (15.0)
	Pre-baseline	70.9 (10.9)	63.0 (7.5)
	Pre-stress	74.9 (9.7)	70.0 (10.1)
	Speech task	81.5 (11.3)	76.8 (12.0)
	Rest	71.5 (8.9)	63.9 (8.6)
	Cognitive tasks		
	<i>Mental Arithmetic</i>	77.1 (8.8)	74.0 (13.0)
DBP	<i>PASAT</i>	78.5 (9.6)	73.4 (11.0)
	Recovery	72.3 (8.1)	66.9 (9.6)
	Pre-baseline	58.3 (10.8)	60.5 (8.0)
	Pre-stress	63.1 (12.4)	68.5 (10.5)
	Speech task	69.1 (13.1)	73.1 (9.8)
	Rest	58.0 (9.0)	60.7 (8.2)
	Cognitive tasks		
	<i>Mental Arithmetic</i>	65.6 (9.9)	67.5 (8.3)
	<i>PASAT</i>	64.9 (11.6)	68.8 (8.6)
	Recovery	57.0 (10.5)	59.2 (7.8)
HR			

Entries show mean and standard error of the mean. Scores for QSU-B Factor 2 were log-transformed in data analysis. *Mental Arithmetic + PASAT* = period 5.

^aTime effect was significant.

^bGroup effect was significant.