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Short communication

Salivary cortisol concentrations are associated with acute nicotine withdrawal

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Abstract

Research has shown that smoking commercial cigarettes results in slight elevations in cortisol levels relative to smoking nicotine-free cigarettes. It is not clear however, whether cortisol concentrations are associated with nicotine withdrawal symptoms among regular cigarette smokers. Nicotine withdrawal symptoms resemble a stress response, and may therefore contribute to cortisol production. This preliminary study focuses on assessing the association between salivary cortisol levels and subsequent levels of self-reported withdrawal and craving symptoms. Twenty male smokers were studied during a 4-h deprivation period. All participants smoked an initial cigarette shortly after arrival and were informed that they would be unable to smoke for the remainder of the session. The session consisted of each participant watching a movie, and then waiting in the laboratory for two consecutive 30-min intervals. Self-reported nicotine withdrawal and craving were assessed four times and salivary cortisol, five times, during the session. Results show that baseline cortisol concentrations predicted subsequent withdrawal symptoms and craving measured using the Tobacco Withdrawal Symptom Checklist (WSC). This suggests that salivary cortisol may contribute to, or be a marker of, nicotine withdrawal symptoms.

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1. Introduction

Studies conducted in our laboratory have demonstrated that cortisol levels increase predictably in response to a number of stressors, including mental, social (al’Absi et al.,

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1997), physical (al'Absi, Petersen, & Wittmers, 2002), and situational challenges (al'Absi & Lovallo, 1993). It has also been shown that cortisol levels generally increase in proportion to the intensity of the stimulus and its emotional valence (Kuhn, 1989). Therefore, it would be expected, that the more intense the stressor, the greater the level of cortisol.

Nicotine has been shown to increase circulating levels of cortisol in male chronic smokers and there have been a number of studies that have documented the acute effects of cigarette smoking on the HPA axis (Wilkins et al., 1982; Winternitz & Quillen, 1977). This effect seems to be related to the dose of nicotine available in the cigarette, because high-yield cigarettes produce more reliable effects on cortisol production than low-yield cigarettes (see Pickworth & Fant, 1998).

Cortisol effects from acute nicotine withdrawal and craving are still unclear. We present in this study preliminary findings indicating an association between intensity of withdrawal symptoms and cortisol levels. These data were collected as part of a larger study. A portion of that data was previously published (Cohen, Britt, Collins, al'Absi, & McChargue, 2001), which focused on the usefulness of chewing gum to reduce nicotine withdrawal, craving, and salivary cortisol concentrations during temporary nicotine deprivation. Data presented in this study focus on the relationship between cortisol and nicotine withdrawal and craving symptoms.

2. Method

Participants for this study were 20 male undergraduate smokers who reported regularly smoking 16 or more cigarettes per day for at least 6 months. Female smokers were not included in the study because of the restricted time period (10 days during the follicular phase) needed for assessing cortisol activity (Chattoraj & Watts, 1987).

We used the Tobacco Withdrawal Symptom Checklist (WSC; Hughes & Hatsukami, 1986) to assess tobacco withdrawal symptoms. In this study, the total score on the WSC was calculated by taking the sum of all the items on the measure minus the craving and insomnia items. We wished to examine the craving item separately given that craving is one of the more common and reliable effects of nicotine abstinence (Hughes, Gust, & Skoog, 1991). We also omitted the insomnia item from the WSC given that we were measuring acute nicotine withdrawal over a 4-h time period where participants were not permitted to sleep.

Potential participants were instructed to visit the laboratory for a brief adaptation session where participants were exposed to the laboratory setting. During the experimental session, participants were asked to relax for approximately 20 min, provided a saliva sample (adaptation) and smoked a cigarette. From this point forward, there was no access to cigarettes until the completion of the protocol. Self-reported withdrawal and craving (using the WSC), and salivary samples were obtained four additional times: prior to watching a movie (baseline), after the movie (Time 1), and two consecutive 30-min intervals after the movie (Times 2 and 3).

Saliva samples were collected using a commercially available collection device (Salivette, Sarstedt, FRG). After each sample was collected, they were stored at -20°C with samples being assayed at a later date using a radioimmunoassay technique with a commercially available kit (Orion Diagnostica, Espoo, Finland).

3. Results

Means for the total score and “craving” item on the WSC as well as salivary cortisol levels were analyzed using three separate one-way repeated-measures analysis of variance (ANOVA). As anticipated, findings indicated significant changes across time on each of the dependent measures [WSC total: $F(1,19)=27.26$, $P<.001$; WSC craving item: $F(1,19)=117.52$, $P<.001$]. Additionally, there was a significant decrease across time in salivary cortisol concentrations [$F(1,19)=29.06$, $P<.001$].

Multiple regression analyses were conducted using baseline cortisol concentrations to predict subsequent withdrawal symptoms and craving obtained 2, 2.5, and 3 h later. Analyses

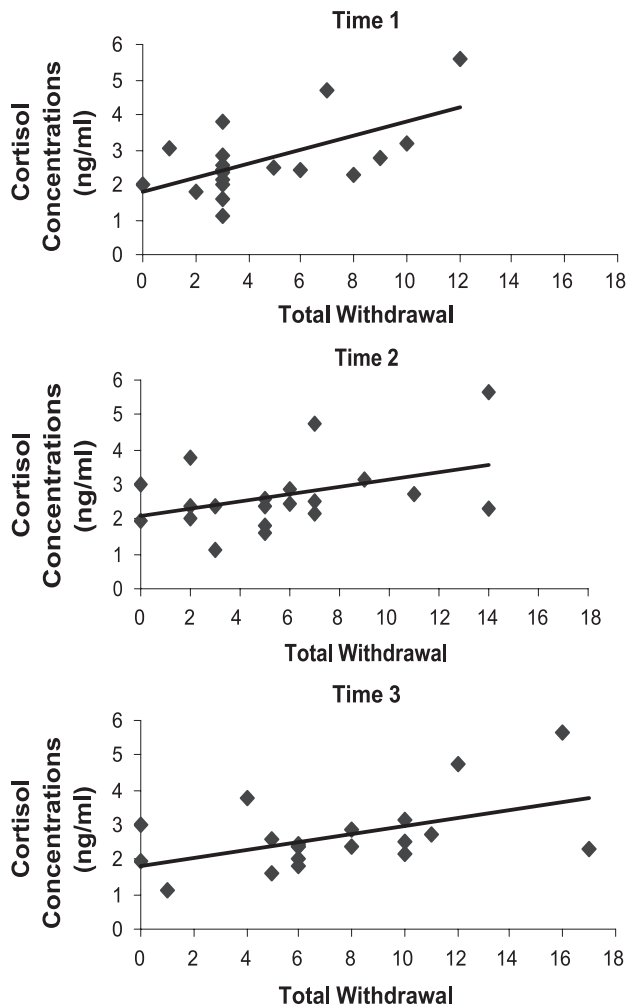


Fig. 1. Cortisol and total withdrawal plotted at Times 1, 2, and 3. r values=.61 ($P<.01$), .42 ($P=.07$), and .50 ($P<.05$), respectively.

revealed that cortisol concentrations predicted self-reported withdrawal at Times 1 ($R^2=.37$, $P<.01$) and 3 ($R^2=.25$, $P<.05$). A trend was observed at Time 2 ($R^2=.18$, $P=.07$). Fig. 1 presents cortisol concentrations and self-reported total withdrawal plotted for each participant across time. Cortisol concentrations also predicted self-reported craving for a cigarette at Times 1 ($R^2=.35$, $P<.01$), 2 ($R^2=.37$, $P<.01$), and 3 ($R^2=.29$, $P<.05$). Fig. 2 presents cortisol concentrations and self-reported craving plotted for each participant across time.

4. Discussion

This study provides preliminary data that cortisol concentrations may be associated with withdrawal symptoms and craving in minimally deprived habitual smokers. Cortisol is a

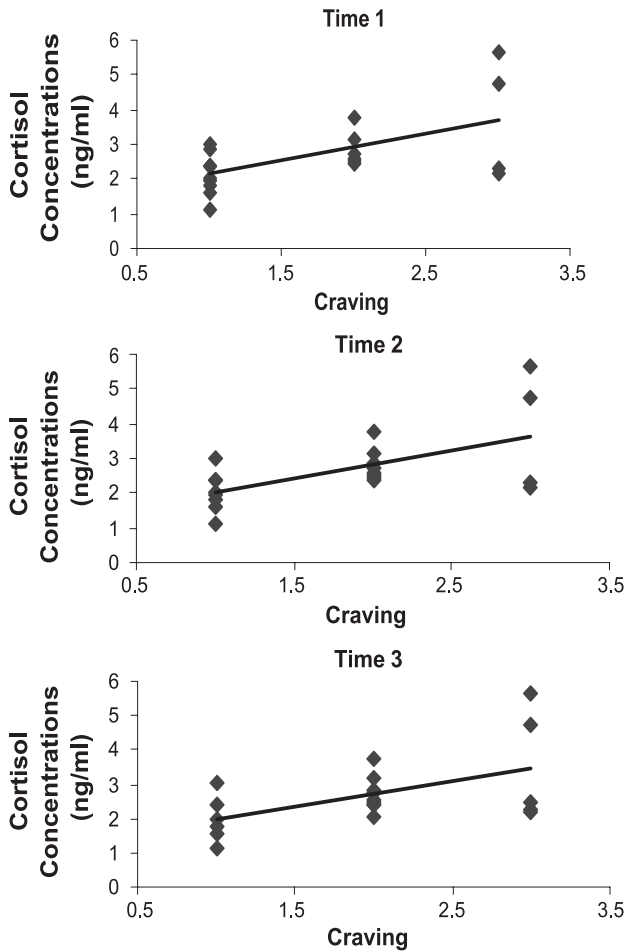


Fig. 2. Cortisol and craving plotted at Times 1, 2, and 3. r values=.59 ($P<.01$), .61 ($P<.01$), and .54 ($P<.05$), respectively.

primary stress hormone produced by the adrenal cortex. Because we propose that negative mood symptoms produced by nicotine withdrawal may lead to stress-like effects, we predicted that cortisol levels would be associated with the intensity of withdrawal symptoms. Our findings partially support this prediction, but need to be replicated in a larger and controlled study.

Alterations in the HPA function may result from chronic smoking (al'Absi, Wittmers, Erickson, Hatsukami, & Crouse, 2003) and it is possible that these alterations predispose smokers to significant rebound changes during abstinence (al'Absi et al., 2003). These changes may reflect long-term central nervous system (CNS) adaptation processes in response to nicotine, and may be mediated by cholinergic and dopaminergic effects. These systems influence the HPA axis through direct interactions with CRF-producing neurons in the hypothalamus. It is possible that abstinence from smoking produces CNS-based changes that lead to rebound increases in HPA hormonal output.

It is important that more detailed information about patterns of associations between cortisol production and nicotine abstinence be delineated. This study did not address effects of behavioral challenge and did not examine gender differences, leaving important questions about the presence and the significance of such changes open for future research. Nevertheless, the study provides important preliminary findings on the association between an important biological index of stress and nicotine withdrawal symptoms.

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