Original Investigation

Smoking Withdrawal Symptoms Are More Severe Among Smokers With ADHD and Independent of ADHD Symptom Change: Results From a 12-Day Contingency-Managed Abstinence Trial

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Abstract

Introduction: Smokers with attention deficit hyperactivity disorder (ADHD) have greater difficulty quitting than those without ADHD, but preliminary data (McClernon, Kollins, Lutz, Fitzgerald, Murray, Redman, et al., 2008) suggest equivalent severity of withdrawal symptoms following brief abstinence. The objective of this study was to characterize the differential effects of intermediate term smoking abstinence on self-reported withdrawal and ADHD symptoms in adult smokers with and without ADHD.

Methods: Forty adult (50% female), nontreatment seeking moderate-to-heavy smokers with and without ADHD were enrolled in a 12-day quit study in which monetary incentives were provided for maintaining biologically verified abstinence. Self-reported withdrawal, mood, and ADHD symptoms were measured pre- and post-quitting.

Results: ADHD and controls did not vary on smoking or demographic variables. Significant Group $\times$ Session interactions were observed across a broad range of withdrawal symptoms and were generally characterized by greater withdrawal severity among ADHD smokers, particularly during the first 5 days of abstinence. In addition, Group $\times$ Sex $\times$ Session interactions were observed for craving, somatic symptoms, negative affect, and habit withdrawal; these interactions were driven by greater withdrawal severity among females with ADHD. Group $\times$ Session interactions were not observed for ADHD symptom scales.

Conclusions: The results of this study suggest that smokers with ADHD, and ADHD females in particular, experience greater

withdrawal severity during early abstinence—independent of effects on ADHD symptoms. Whereas additional research is needed to pinpoint mechanisms, our findings suggest that smoking cessation interventions targeted at smokers with ADHD should address their more severe withdrawal symptoms following quitting.

Introduction

Attention deficit hyperactivity disorder (ADHD) is characterized by developmentally inappropriate levels of inattention, hyperactivity, and impulsivity (American Psychological Association, 2000). Individuals with ADHD smoke at higher rates than the general population and/or nondiagnosed controls among adults and adolescents (Lambert & Hartsough, 1998; Milberger, Biederman, Faraone, Wilens, & Chu, 1997; Molina & Pelham, 2003; O. F. Pomerleau, Downey, Stelson, & Pomerleau, 1995). Individuals with ADHD also start smoking at an earlier age (Milberger, Biederman, Faraone, Chen, & Jones, 1997) and have a higher level of nicotine dependence (O. F. Pomerleau et al., 1995).

Smokers with ADHD also have greater difficulty quitting. Among adults with ADHD, the proportion of ever-smokers who became ex-smokers was lower (0.29) than that observed in the general population (0.49), suggesting that individuals with ADHD less frequently attempt or succeed at quitting (O. F. Pomerleau et al., 1995). A history of childhood ADHD also increases risk of relapse, even after controlling for demographic and smoking-related variables (Humfleet et al., 2005). Finally, the association between ADHD and relapse risk extends to individuals not diagnosed with the disorder. In a post-hoc

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analysis of clinical trial data, smokers high in ADHD symptoms (but without formal diagnosis) achieved lower abstinence rates than those with lower ADHD symptoms (Covey, Manubay, Jiang, Nortick, & Palumbo, 2008).

Several factors could account for increased relapse risk among ADHD smokers. First, individuals with ADHD exhibit increased impulsivity (Barkley, 1997) and reward sensitivity (Luman, Tripp, & Scheres, 2010), which may make resisting smoking urges more difficult. Second, nicotine can improve attention in nicotine naïve individuals with (Conners et al., 1996; Levin et al., 1996) and without (Froeliger, Gilbert, & McClernon, 2009; Heishman, Kleykamp, & Singleton, 2010; Levin et al., 1998) ADHD. Also, nicotine and nicotinic agonists reduce ADHD symptom severity (Gehricke, Hong, Whalen, Steinhoff, & Wigal, 2009; Shytle, Silver, Wilkinson, & Sanberg, 2002; Wilens et al., 1999). These findings have led to the hypothesis that ADHD individuals smoke to alleviate inherent cognitive deficits and/or ADHD symptoms (McClernon & Kollins, 2008). As such, the exacerbation of such deficits and symptoms upon quitting smoking may negatively reinforce continued smoking behavior (i.e., relapse). Consistent with this hypothesis, we showed in a previous study that overnight abstinence amplified attention and inhibitory control deficits among ADHD smokers (McClernon et al., 2008).

Smokers with ADHD might also experience greater severity of withdrawal symptoms and craving following quitting. Adult smokers with ADHD retrospectively reported greater withdrawal symptoms than smokers without ADHD (C. S. Pomerleau et al., 2003). However, a prospective study observed equivalent effects of overnight abstinence on severity of withdrawal symptoms (McClernon et al., 2008). Prospective assessment of the effects of longer term abstinence on withdrawal symptoms in ADHD smokers has not been conducted.

The goal of this study was to prospectively evaluate the effects of 12-day smoking abstinence on smoking withdrawal symptoms in smokers with and without ADHD. Smokers were provided monetary incentives for maintaining abstinence in order to retain them throughout the study. We hypothesized that compared with controls, ADHD smokers would report greater intensity of withdrawal symptoms and greater disruption of affect. Since previous work has reported that smoking withdrawal among those with ADHD may simply represent an exacerbation of ADHD symptomatology (Gray, Baker, Carpenter, Lewis, & Upadhyaya, 2010), we also assessed whether smoking abstinence also impacted self-reported ADHD symptoms. Finally, our previous work (McClernon et al., 2008) has suggested that females with ADHD may exhibit more profound effects of smoking abstinence than males. Thus, sex was included as a factor in all analyses.

Materials and Methods

Participants and Screening

Participants were 47 male and female adult smokers between the ages of 18 and 50 years. Twenty-four participants were diagnosed with ADHD; 23 controls had no psychiatric diagnosis (except for nicotine dependence). Three participants (2 ADHD and 1 control) dropped from the study or were lost to contact prior to the quit date (QD). An additional four participants (1 ADHD and 3 control) were not abstinent at the first postquit assessment and were excluded from analysis. Thus, the final sample consisted of 21 ADHD and 19 control participants. There were no significant group (ADHD vs. control) differences for any demographic or smoking-related variables (Table 1). All procedures were approved by the local institutional review board.

Participants were recruited from the community via print advertisements. A telephone prescreen was conducted, and

Table 1. Sample Characteristics

	Full sample		ADHD (<i>n</i> = 21)		Control (<i>n</i> = 19)		<i>T</i> or χ^2_{a}	<i>p</i> Value
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%		
Sex								
Female	20	50.0	9	42.9	11	57.9	0.90	.34
Male	20	50.0	12	57.1	8	42.1		
Race								
Caucasian	30	75.0	16	76.2	14	73.7	1.15	.56
Black	9	22.5	5	23.8	4	21.1		
Hispanic	1	2.5	0	0.0	1	5.3		
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>		
Age	31.7	9.1	29.5	9.2	34.1	8.7	1.60	.12
K-BIT composite ^a	107.1	10.1	104.3	9.9	110.2	9.7	1.86	.07
Years smoked	14.0	9.9	12.4	9.2	15.8	10.6	1.08	.29
Age started	17.3	3.3	16.5	2.7	18.1	3.8	1.59	.12
Cigarettes/day	16.4	4.7	16.7	5.5	16.1	3.7	0.37	.71
FTND	4.5	2.1	4.7	2.3	4.3	2.0	0.67	.51
Screening CO	22.2	8.8	23.2	10.2	21.1	7.1	0.76	.45

Note. ADHD = attention deficit hyperactivity disorder; FTND = Fagerström Test for Nicotine Dependence; K-BIT = Kaufmann Brief Intelligence Test.

^aK-BIT scores were unavailable for one ADHD and one control participants.

potential participants were invited to the clinic for a screening visit. Since this was not a controlled intervention trial, individuals who explicitly expressed interest in cessation treatment were excluded and referred elsewhere.

During screening, participants read and signed a consent form and completed a medical and smoking history. Smoking was assessed via self-report and expired carbon monoxide (CO) concentration. To be included, participants were required to report smoking ≥ 10 cigarettes/day and have an afternoon CO concentration of ≥ 10 ppm.

All participants underwent a psychiatric evaluation. The Conners' Adult ADHD Rating Scale (CAARS)—Self-Report Version (Conners, Erhardt, Sparrow, & staff, 1998), the Structured Clinical Interview for the DSM-IV (SCID; First, Gibbon, Williams, & Spitzer, 1997), and the Conners' Adult Diagnostic Interview for DSM-IV (CAADID; Epstein, Johnson, & Conners, 2000) were administered and reviewed by a Ph.D.-level clinical psychologist along with a follow-up interview. Individuals in both groups were excluded if they met diagnostic criteria for any DSM-IV Axis I or II disorder other than ADHD or nicotine dependence. For the ADHD group, individuals were included if they met DSM-IV criteria for any subtype (Combined, Inattentive, Hyperactive-Impulsive). Participants were excluded for significant medical problems, current pregnancy, or positive urine drug screen. Estimates of intellectual functioning were obtained with the Kaufmann Brief Intelligence Test (Kaufman & Kaufman, 2004).

Participants in the ADHD group taking medication for ADHD were allowed to participate provided they had been on a stable dose and product for ≥ 3 weeks prior to baseline and agreed not to alter their regimen during the study. Six ADHD participants were on methylphenidate or amphetamine-based stimulant medication during the study. There were no significant differences between the medicated and unmedicated ADHD participants with respect to baseline CO, cigarettes per day, age started smoking, years smoking, or number of clinician-rated ADHD symptoms (all $ps > .10$). However, a significantly greater proportion of females with ADHD were medicated compared with males (56% vs. 9%, respectively, $p = .05$, two-tailed Fisher's exact test). Controls taking psychoactive medications were excluded. Comprehensive feedback and treatment referrals (when necessary) were provided to ADHD participants.

Study Design and Procedures

Participants completed two baseline sessions during which a battery of self-report and cognitive performance measures (reported elsewhere) were completed. At the second baseline, a QD was established after which participants were instructed to abstain from smoking for 12 days. QDs were scheduled for Sunday evenings, so that the first postquit visit was the following day (Monday). During the 12 days following quitting, participants visited the laboratory at a set time each day Monday to Friday. No visits were scheduled on Saturday and Sunday. During each visit, participants provided an expired-air sample, and the Shiffman-Jarvik Withdrawal Questionnaire (SJWQ) and Positive and Negative Affect Schedule (PANAS) were completed. Participants also kept a daily smoking diary, which was reviewed at each visit.

Monetary Incentive Procedures

Participants were instructed that, starting on the first day following the QD, they would earn money contingent on CO

samples that met the criterion of ≤ 4 ppm. An escalating schedule was used in which participants earned \$4 for the first day and an additional \$4 each day thereafter. An escalating bonus was also made every two days that participants remained abstinent such that on the second day postquit, participants earned \$10 for meeting the abstinence requirement, on the fourth day postquit \$20, and so on. Participants could earn up to \$370 for abstinence across 10 sessions. Participants were discontinued if they provided CO samples of > 4 ppm at any visit, failed to attend a scheduled visit, or self-reported smoking.

Dependent Measures

CO Levels

Expired-air CO concentrations were measured using a handheld monitor (Vitalograph) and calculated by subtracting ambient from peak CO.

Shiffman-Jarvik Withdrawal Questionnaire

A version of the SJWQ (Shiffman & Jarvik, 1976) modified by Rose et al. (1990) was used. This is a 32-item measure of craving (e.g., Are you thinking of cigarettes?), arousal (e.g., Do you feel wide awake?), negative affect (e.g., Do you feel irritable?), somatic symptoms (e.g., Is your heart beating faster than usual?), habit withdrawal (e.g., Do you miss having something to do with your hands?), and appetite disturbance/hunger (e.g., Do you feel hungrier than usual?).

The Positive and Negative Affect Schedule

The PANAS is a 20-item measure of positive and negative affective states (Watson, Clark, & Tellegen, 1988). The PANAS consists of adjectives (e.g., excited, guilty, jittery), and participants rate their current state on a scale from 1 = *very slightly* or *not at all* to 4 = *extremely*. Scale scores were calculated separately for positive and negative affect.

Conners' Adult ADHD Rating Scale

The CAARS was used to assess self-reported ADHD symptomatology over the course of the study (Conners et al., 1998). The Self-Report Short Version of the scale was used, which is a 26-item scale that assesses ADHD-related symptoms on a 4-point scale and yields separate empirically supported factor scores for Inattention symptoms, Hyperactivity symptoms, and Impulsivity symptoms. The CAARS was only administered at the two baseline visits and at postquit days 1, 3, 5, 8, and 12.

Statistical Analysis

Group differences on demographic and smoking variables were assessed using independent sample t tests or chi-square analyses. Questionnaire data were submitted to repeated measures general estimating equation models in SPSS 17.0 (using the GENLIN command) with Group (ADHD and control) and Sex (male and female) as between-subjects factors and Session as a within-subjects factor. Measures were assumed to be correlated between sessions (AR1). Post-hoc analyses were evaluated at $p = .05$; magnitude of effects is presented in SD units.

Results

Sample Characteristics

The ADHD and control groups did not differ on smoking or demographic variables (Table 1).

Abstinence and Abstinence Verification

Details regarding the efficacy of the monetary incentive procedures are reported elsewhere (Kollins, McClernon, & Van Voorhees, 2010). Briefly, 64% of ADHD and 50% of controls maintained abstinence throughout the 12-day abstinence phase (Fisher's exact p value = .54). There was a main effect of session on CO (Wald = 318.05, $p < .001$) due to lower levels on all postquit days relative to the second baseline (all $ps < .001$). Mean CO levels (in parts per million) for baseline Sessions 1 and 2 were 21.0 ($SD = 8.6$) and 22.3 ($SD = 10.0$), respectively. Mean CO on the first day postquit was 7.3 ($SD = 4.4$) and less than 3 ppm postquit days 2–12. There was also a Sex $\times$ Session interaction (Wald = 32.5, $p = .001$), and follow-up analyses revealed higher CO levels in males compared with females at postquit days 2, 3, 5, and 11 ($ps < .05$).

Shiffman–Jarvik Withdrawal Questionnaire

Across all sessions, ADHD smokers were higher than controls in negative affect (Wald = 7.68, $p = .006$) and habit withdrawal (Wald = 13.16, $p < .001$) and lower in arousal (Wald = 18.44, $p < .001$). Sex differences were also observed. Across all sessions, females reported higher craving (Wald = 4.78, $p = .029$), negative affect (Wald = 7.14, $p = .008$), and habit withdrawal (Wald = 4.56, $p = .033$) and lower arousal (Wald = 4.61, $p = .032$). Main effects and interactions involving Session are described below and in Figure 1.

Craving

Craving for cigarettes varied significantly across the trial (main effect of Session, Wald = 158.9; $p < .001$). Post-hoc analyses indicated that craving increased significantly following smoking abstinence ($p < .001$) but returned to baseline levels by Day 8 postquit ($p = .27$). A Group $\times$ Session interaction was observed (Wald = 21.55, $p = .028$). Compared with Controls, ADHD smokers reported higher craving at baseline sessions ($p = .015$ and $.006$) and through Day 4 postquit (all $ps < .05$). Finally, a Group $\times$ Sex $\times$ Session interaction was observed (Wald = 26.6, $p = .005$). This effect was largely driven by ADHD females who exhibited increased craving relative to baseline and to the other groups (Figure 1). ADHD females reported significantly greater craving at the second baseline than male and female Controls ($p = .003$ and $.008$, respectively) and greater craving than all other groups on postquit days 2–4 (all $ps < .005$). On Day 7 postquit, craving severity reported by ADHD females was not significantly higher than any other group.

In order to characterize this interaction, we calculated the magnitude in SD units of the change in craving severity from baseline for each group (ADHD males, ADHD females, control males, and control females) 1, 3, and 5 days following quitting ($[\text{mean Day } \# - \text{mean second baseline}] / \text{average } [SD \text{ Day } \#, SD \text{ second baseline}]$). Among ADHD females, craving was 2.3, 2.2, and 0.7 SD units greater at 1, 3, and 5 days postquit relative to the second baseline. These values were higher than those observed for ADHD males (0.5, 0.1, and 0.1) and control females (1.6, 1.1, and .7) and males (1.9, 1.5, and 0.2). This pattern suggests that ADHD females experienced greater craving following abstinence, even when accounting for higher baseline levels.

Negative Affect

Negative affect also varied across sessions (Wald = 103.586, $p < .001$) increasing significantly following quitting ($p < .001$) but

returning to baseline levels by Day 8 postquit ($p = .24$). A Group $\times$ Session interaction was observed (Wald = 21.926; $p = .025$). Compared with controls, ADHD smokers reported higher negative affect at baseline sessions ($p = .015$ and $.006$) and through Day 2 postquit (all $ps < .05$). In addition, a Sex $\times$ Session interaction was observed (Wald = 36.16, $p < .001$); females had higher negative affect at Days 1, 2, 3 (all $ps < .01$), and 5 ($p < .05$). Finally, a Group $\times$ Sex $\times$ Session interaction was observed (Wald = 25.18, $p < .009$). This interaction was driven largely by data from ADHD females who reported significantly higher levels of negative affect than male and female controls at baseline (all $ps < .05$) and higher negative affect than all groups at postquit days 1 (all $ps < .001$), 2 ($ps < .01$), and 3 ($ps < .05$). In addition, ADHD females were higher in negative affect than control males at postquit days 4 and 11 ($ps < .05$).

Again, examination of the magnitude of change from baseline helped characterize the interaction. Among females with ADHD, negative affect was 2.2, 2.0, and 0.7 SD units greater at 1, 3, and 5 days postquit relative to the second baseline. These values were higher than those observed for ADHD males (0.2, 0, and -0.2) and control males (0.9, 1.1, and 0.5) but comparable to those of control females (1.8, 2.2, and 2.6). By 12 days postquit, negative affect levels fully resolved among ADHD ($-.5 SD$ units) but not among control females (0.9 SD units).

Appetite Disturbance

Appetite was disrupted by abstinence (Wald = 59.14, $p < .001$) with smokers reporting greater appetite disturbance at all post quit days compared with the second baseline ($ps < .01$). In addition, a Sex $\times$ Session interaction (Wald = 20.12, $p < .044$) was observed. Across sessions, males reported greater appetite disturbance than females but only significantly so on the first post quit day ($p = .003$). No effects involving Group were observed.

Arousal

Self-report arousal was significantly modulated by smoking abstinence (Wald = 56.61, $p < .001$) with lower arousal reported at postquit days 1 through 5 ($ps < .01$) and 8 ($p = .03$). A Group $\times$ Session interaction was observed (Wald = 21.34, $p = .03$) with ADHD smokers reporting lower arousal at both baseline sessions ($p \leq .001$) and postquit days 1, 3–5, and 11 ($ps < .01$). A Sex $\times$ Session interaction was also observed (Wald = 82.20, $p < .001$), but sex differences did not emerge until postquit days 10 and 11 at which males reported greater arousal than females ($ps < .001$).

Somatic Symptoms

Somatic symptom severity varied across sessions (Wald = 25.57, $p = .008$). Relative to the second baseline, somatic symptoms were greater at postquit days 1 ($p < .01$) and 2 ($p < .05$) but significantly lower at Days 10–12 ($ps < .05$). A Group $\times$ Session interaction was observed (Wald = 30.16; $p = .001$). ADHD smokers reported higher somatic symptoms at Days 3 and 4 postquit ($ps < .05$). A Sex $\times$ Session interaction was observed (Wald = 44.68, $p < .001$). This interaction was characterized by higher somatic symptoms in females at 1–3 days postquit but lower symptom severity at Days 4–12. However sex differences were not significant at any session. Finally, a Group $\times$ Sex $\times$ Session interaction was observed (Wald = 41.8, $p < .001$). While similar in nature to the interactions for craving and negative affect, the effect for somatic symptoms was less striking: ADHD

Figure 1. Mean $\pm$ SD Shiffman-Jarvik Withdrawal Questionnaire scale scores in male and female smokers with and without attention deficit hyperactivity disorder (ADHD). See text for statistical results.

females were only higher in somatic symptoms than control females at postquit day 2 ($p < .05$) and all groups at postquit day 3 ($ps < .05$). The magnitude of difference from the second baseline at Day 3 (in *SD* units) was 0.8 for ADHD females, 0 for ADHD males, and -0.1 and 0.0 female and male controls, respectively.

Habit Withdrawal

Overall, the pattern observed for habit withdrawal was similar to craving and negative affect. A main effect of Session (Wald = 143.73, $p < .001$) was characterized by greater postquit habit withdrawal on all postquit days ($p \leq .01$) relative to the second baseline. In addition, a Group $\times$ Session interaction was observed (Wald = 49.00, $p < .001$). ADHD smokers reported greater habit withdrawal at both baseline sessions ($ps < .01$), postquit days 1 and 2 ($ps < .001$), 3–5 ($ps < .01$), 10 ($p < .05$), and 12 ($p < .01$). Finally, a Group $\times$ Sex $\times$ Session interaction was observed (Wald = 49.00, $p < .001$). Similar to other symptoms, the interaction for habit withdrawal was driven primarily by ADHD females who reported greater symptom severity than male and female controls at baseline ($ps < .05$) and all groups at postquit days 1 and 2 ($ps < .001$), 3 ($ps < .01$), and 4 and 8 ($ps < .05$).

Among females with ADHD, habit withdrawal was 2.3, 1.7, and 1.3 *SD* units greater at 1, 3, and 5 days postquit relative to the second baseline. These values were higher than those observed for ADHD males (0.8, 0.7, and 0.8) but approached values observed for non-ADHD females (1.2, 1.5, and 1.3) and non-ADHD males (1.5, 1.9, and 1.2). Habit withdrawal did not fully resolve for any of the groups, with Day 12 *SD* units ranging from 0.6 to 0.8.

Self-Report Mood (PANAS)

PANAS negative affect was higher in the ADHD compared with control group (Wald = 14.22, $p < .001$). In addition, negative affect varied across sessions (Wald = 39.21, $p < .001$) and was greater at postquit days 1 ($p < .001$) and 3 ($p < .05$) relative to the second baseline. A Sex $\times$ Session interaction was observed (Wald = 32.66, $p = .001$). Self-report negative affect was higher in female smokers at postquit days 1 ($p < .001$) and 2 ($p < .05$).

PANAS positive affect varied across sessions (Wald = 52.97, $p < .001$). Relative to the second baseline, positive affect was lower postquit day 1 ($p < .05$) but higher on Days 10–12 ($ps < .05$). No effects or interactions involving Group were observed.

Self-reported ADHD Symptoms—CAARS

Self-reported CAARS scores were significantly higher in the ADHD group compared with control group across all sessions for Inattention symptoms (Wald = 132.43, $p < .0001$), Hyperactivity symptoms (Wald = 158.32, $p < .0001$), and Impulsivity symptoms (Wald = 41.06, $p < .0001$). There were also main effects of session for the Inattention (Wald = 20.04, $p < .005$) and Impulsivity (Wald = 13.78, $p < .05$) subscales. For both, symptom levels peaked at postquit day 3 but returned to baseline levels by postquit day 12. Inattention symptoms were lower at postquit day 1 compared with the first baseline and postquit day 3 ($ps < .05$); Impulsivity symptoms were lower at postquit day 12 than at second baseline and postquit day 3. There were no main effects of Sex.

There was a significant Group $\times$ Sex interaction for Inattention symptoms (Wald = 5.28, $p < 0.05$). Females with ADHD reported marginally greater Inattention symptoms than ADHD males ($p = .078$); the opposite, though nonsignificant, pattern was observed among non-ADHD participants. A Sex $\times$ Session interaction for Impulsivity symptoms (Wald = 24.22, $p < .0001$) was also observed: Females reported greater Impulsivity symptoms than males at postquit day 3 ($p < .05$). In contrast to withdrawal symptoms, there were no significant Group $\times$ Session interactions or Group $\times$ Sex $\times$ Session interactions.

Discussion

The present study evaluated the effects of smoking abstinence on the time course and severity of self-reported withdrawal symptoms and affect in smokers with and without ADHD. There were three main findings. First, smokers with ADHD exhibited greater craving, negative affect, somatic symptoms, and habit withdrawal and lower arousal than smokers without ADHD. These group differences were most pronounced during the first days of abstinence. Second, increased withdrawal severity for some symptoms observed in the ADHD smokers was driven by ADHD females, who exhibited greater symptom severity relative to males with ADHD and controls regardless of sex. Finally, the relatively greater smoking withdrawal symptoms observed in the ADHD group occurred independently from changes in ADHD symptoms, suggesting a dissociable pattern of effects. Our findings provide prospective support for previous findings (C. S. Pomerleau et al., 2003) and extend earlier work from our laboratory (McClernon et al., 2008) that examined the effects of brief abstinence (12 hr) in smokers with and without ADHD.

ADHD and Smoking Withdrawal

The results of this prospective study provide novel evidence that smokers with ADHD experience more severe smoking withdrawal symptoms, particularly during early abstinence. These findings were observed in the absence of any group differences in smoking history. Specifically, Group $\times$ Session interactions reflected higher symptom severity among these individuals for all SJWQ scales except appetite disturbance. These findings are consistent with a previous study in which adult smokers with ADHD provided retrospective reports of greater withdrawal symptom severity, specifically in the domains of depressed mood, insomnia, irritability, and difficulty concentrating (C. S. Pomerleau et al., 2003).

In the present study, group differences were most pronounced early in abstinence. This stands in contrast with the results of a previous study in our laboratory also using the SJWQ in which we observed no group differences in symptom severity following overnight abstinence (McClernon et al., 2008). Several factors may account for these differences in findings. First, participants in the earlier study were heavier smokers owing to an inclusion criterion of smoking ≥ 15 cigarettes/day and exhibited greater increases in craving and negative affect following overnight abstinence (2.4 and 1.2 *SD* unit increases in craving and negative affect compared with 1.2 and 0.8 *SD* unit increases in the present study). As such, group differences in the earlier study may have been obscured by ceiling effects. Other study characteristics (e.g., abstinence

duration, provision of contingencies) may also account for differences.

A previous study argued that ADHD symptoms confound the measurement of smoking withdrawal symptoms since there is some overlap between the two constellations of symptoms (e.g., Gray et al., 2010). That study, however, did not measure either smoking withdrawal or ADHD symptoms in the context of experimentally manipulated abstinence. Results from the present study in which Session did not interact with ADHD group status suggest that withdrawal symptoms in individuals with ADHD are increased independently of increases in ADHD symptoms and across a wider range of withdrawal symptoms. As such, it does not appear that smoking withdrawal is confounded simply by exacerbation of ADHD symptoms.

What is the clinical significance of greater withdrawal severity among smokers with ADHD? Though the literature is sparse, data suggest that individuals with a childhood history of ADHD (Humfleet et al., 2005) or with elevated ADHD symptoms (Covey et al., 2008) have worse cessation outcomes. Greater withdrawal severity may negatively reinforce smoking behavior to a greater extent among individuals with ADHD, which in turn may increase relapse probability. Future studies that examine associations between withdrawal symptoms and outcomes can address this question. In addition, if greater withdrawal severity does indeed mediate maintenance of smoking abstinence, this may be a valid target for interventions designed to treat ADHD smokers.

Sex Differences

ADHD versus control differences in the present study were largely moderated by sex. Significant Group $\times$ Sex $\times$ Session interactions were observed on four of six SJWQ scales: craving, negative affect, somatic symptoms, and habit withdrawal, and these interactions were driven by greater symptom severity among ADHD females. These findings are consistent with our previous findings that following overnight abstinence, female ADHD smokers performed significantly worse on laboratory measures of attention and motor impulsivity than did ADHD males and control males and females (McClernon et al., 2008).

To our knowledge, this is the first study to demonstrate that female smokers with ADHD exhibit greater withdrawal symptoms during early abstinence. Our findings are consistent, however, with a growing body of research suggesting gender differences in cigarette craving and withdrawal (for a review, see Carpenter, Upadhyaya, LaRowe, Saladin, & Brady, 2006). Xu et al. (2008), for instance, observed greater abstinence-induced negative affect and craving, following overnight abstinence among female smokers and greater relief from these effects after smoking. These findings are consistent with our observation that negative affect among female smokers, irrespective of group, was elevated compared with males during early abstinence.

The finding of greater withdrawal symptoms among females with ADHD in the present study is tempered somewhat by the fact that ADHD females were more likely to be medicated than ADHD males. One possible explanation for greater withdrawal symptoms among females with ADHD is that females taking ADHD medication had more severe baseline ADHD

symptoms and/or were more dependent on smoking, which led them to experience more severe withdrawal. Follow-up analyses among ADHD females (medicated $n = 5$ vs. unmedicated $n = 4$) indicate no differences in nicotine dependence, smoking history, or ADHD symptoms (all $ps > .1$). We also conducted analyses directly comparing withdrawal severity by medication status for those measures in which we identified significant Group $\times$ Sex $\times$ Session interactions. In general, differences were modest and likely unreliable, given the small sample sizes. Future studies recruiting equivalent numbers of males and females with ADHD who are and are not medicated will be necessary to fully address this question. We also did not assess menstrual status in our female participants, which could have impacted the effects on craving and withdrawal. Ongoing work in our laboratory is systematically controlling for hormonal status in similar follow-up studies.

Limitations and Future Directions

These results of this study are limited by the following factors. First, the duration of abstinence, though longer than our previous study, was still relatively short, and some group differences persisted through the end of the study. Second, abstinence in this study was reinforced with monetary incentives. Although these incentives increased the likelihood of subjects complying with abstinence requirements and should have served to decrease problems associated with differential attrition, their use may limit generalizability to group differences in withdrawal symptoms under conditions where no immediate incentives are provided. Third, given the known rates of psychiatric comorbidity in adults with ADHD (Kessler et al., 2006), it is unclear how the results from this study with ADHD-only smokers would generalize to the broader population of smokers with ADHD. Given that our current understanding of smoking in any psychiatric conditions is fairly limited, this initial study is a necessary step to begin to gain an unconfounded understanding of the factors that may place individuals with ADHD at risk for smoking. Certainly future studies would be well served to systematically assess the additive effects of additional psychiatric comorbidity on smoking-related outcomes. Finally, subjects in this study were not interested in treatment. It is unclear whether motivation to quit smoking might have altered results. In previous studies that have shown ADHD status moderating outcomes (e.g., Covey et al., 2008; Humfleet et al., 2005), participants were enrolled in clinical trials for smoking cessation. As such, our findings may not generalize as well to these populations, and future studies should examine the role of motivation for change on withdrawal in ADHD and control smokers.

Summary

In spite of the limitations above, the present study provides evidence that smokers with ADHD experience relatively greater withdrawal symptoms, particularly during the first 1–5 days of abstinence and that these symptoms occur independently of ADHD symptoms. This study also adds to the small database of studies examining differences in withdrawal as a function of psychiatric comorbidity (C. S. Pomerleau, Mehringer, Marks, Downey, & Pomerleau, 2000; Tidey, Rohsenow, Kaplan, Swift, & Adolfo, 2008). The effects in this study were observed in the absence of any group differences in smoking history or behavior. Since the risk for regular smoking as well as relapse following a quit attempt has been shown to be related to the ADHD

symptoms independent of diagnosis (Covey et al., 2008; Kollins, McClernon, & Fuemmeler, 2005), these findings may have implications for smokers in the general population. Finally, these findings should give rise to additional research seeking to (a) better characterize the role of ADHD diagnosis and symptoms in withdrawal symptom severity, (b) assess the extent to which increases in withdrawal symptoms are associated with risk for relapse, and (c) develop more targeted interventions for smoking cessation.

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