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Associations of Attention-Deficit Hyperactivity Disorder Symptom Dimensions with Smoking Deprivation Effects in Adult Smokers

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Abstract

Identifying relations of Attention-Deficit Hyperactivity Disorder (ADHD) symptom dimensions to individual facets of the tobacco withdrawal syndrome could elucidate the mechanisms linking ADHD and regular smoking. This study examined the unique relations of inattention (IN) and hyperactivity-impulsivity (HI) symptom dimensions of ADHD to a variety of tobacco withdrawal symptoms. 132 community-dwelling adult smokers recruited without regard to ADHD status completed a self-report measure of ADHD symptoms experienced over the past 6 months at a baseline visit. At two subsequent experimental sessions (one following overnight tobacco deprivation and one nondeprived; order counterbalanced), participants completed measures of tobacco withdrawal symptoms, mood, and desire to smoke. Preliminary analyses showed that higher levels of IN and HI symptoms were both associated with higher levels of negative affect and concentration difficulties during nondeprived (“baseline”) states (P s < .01). Over and above nondeprived ratings, higher levels of HI symptoms were associated with larger deprivation-induced increases in negative affect, concentration problems, and desire to smoke, particularly for negative affect relief, during deprived states (P s < .01). ADHD symptoms, particularly HI symptoms, are associated with more severe exacerbations in abstinence-induced withdrawal symptoms, which could be an important mechanism of ADHD-smoking comorbidity. These findings suggest the need for clinical studies examining the role of these unique and potentially more severe withdrawal profiles experienced by smokers with high-levels of ADHD symptoms in smoking reinstatement and cessation outcomes.

Keywords

inattention; hyperactivity-impulsivity; withdrawal; relapse prevention; comorbidity

Introduction

Clinical samples of adults with Attention Deficit Hyperactivity Disorder (ADHD) smoke at rates significantly higher than the general population and/or non-diagnosed controls (41 – 42% vs. 26% for ADHD and non-ADHD, respectively) (Lambert & Hartsough, 1998; Pomerleau, Downey, Stelson, & Pomerleau, 1995). In addition, in population-based studies, the level of ADHD symptoms experienced in adults, irrespective of clinical ADHD diagnosis, is an independent risk factor for tobacco use and regular smoking over and above common ADHD comorbidities such as conduct disorder (Fuemmeler, Kollins, & McClernon, 2007; Tercyak, Lerman, & Audrain, 2002). For example, retrospectively-reported ADHD symptoms were significantly associated with the likelihood of lifetime regular smoking, the progression from experimentation to regular smoking, and the level of nicotine dependence in a large, population-based sample of young adults (Fuemmeler et al., 2007; Kollins, McClernon, & Fuemmeler, 2005).

One potential mechanism underlying the association between ADHD symptoms and regular and persistent forms of tobacco use is that individuals with ADHD symptoms experience more severe nicotine withdrawal symptoms during abstinence (McClernon & Kollins, 2008). As a result, smokers with higher levels of ADHD symptoms may be more motivated to resume smoking following abstinence to suppress withdrawal symptoms, which could ultimately lead to more regular, heavy, and persistent patterns of smoking. Effects from tobacco deprivation onset within hours following the discontinuation of smoking (Hendricks, Ditte, Drobes, & Brandon, 2006; Hughes & Hatsukami, 1986) and include a variety of withdrawal symptoms such as depressed mood, anxiety, difficulty concentrating, sleep and appetite disturbance, irritability, reduced heart rate, restlessness, general negative affect, cigarette craving, and decreases in positive affect, (APA, 2000). These symptoms are particularly pronounced during the acute stages (12 to 24 hr) of smoking abstinence (Hatsukami, Hughes, Pickens, & Svikis, 1984; Leventhal, Waters, Moolchan, Heishman, & Pickworth, 2010; Shiffman, Ferguson, Gwaltney, Balabanis, & Shadel, 2006) when relapse back to smoking is particularly prominent and can interfere with the ability to maintain 24 hours of continuous abstinence following a quit attempt (Japuntich et al., 2011).

Prior research offers support for an association between ADHD and withdrawal. In one study, retrospective smoking withdrawal symptoms were evaluated in adult smokers with current ADHD, adult smokers with a history of childhood but not current ADHD, and adult smokers without a history of or current ADHD. Individuals in the ADHD groups reported experiencing greater irritability and difficulty concentrating during prior quit attempts compared to smokers without a history of or current ADHD (Pomerleau et al., 2003). In a separate study, adult smokers with current ADHD exhibited significantly greater disruptions in response inhibition following overnight abstinence compared to non-ADHD smokers, even after controlling for baseline differences (McClernon et al., 2008). This study was followed up with a contingency-managed 12 day abstinence trial of 21 smokers with ADHD and 19 non-ADHD smokers. In this study, particularly during the first five days of abstinence, smokers with ADHD experienced greater craving, negative affect, physical symptoms, and habit withdrawal compared to smokers without ADHD and these abstinence effects were independent of changes in ADHD symptoms (McClernon et al., 2011). Finally,

recent reports have demonstrated that higher levels of withdrawal and craving were associated with ADHD symptom level in laboratory (Ashare & Hawk, 2012; Kollins et al., 2013) and population-based (Ameringer & Leventhal, 2012) studies of smokers and in a clinical trial of those making a cessation attempt particularly after (vs. before) quit day (Berlin, Hu, Covey, & Winhusen, 2012). While extant findings provide support the ADHD-tobacco withdrawal relation, several features of this association require further attention.

Method factors in prior ADHD-tobacco withdrawal research can influence interpretation of extant results. ADHD has pathognomonic and comorbid symptoms irrespective of smoking that resemble the tobacco withdrawal syndrome, such as depression, anxiety, irritability, concentration problems, and restlessness. Hence, ADHD symptoms may be associated with certain smoking withdrawal symptoms (e.g., concentration problems) during regular smoking, which reflect baseline disturbances associated with the ADHD syndrome rather than withdrawal effects per se. Indeed, preliminary laboratory work using small samples has suggested certain aspects of withdrawal may be elevated in ADHD smokers regardless of abstinence status, but suggest that there may not be further increases during abstinence states (Kollins et al., 2013). Further, studies that do not contrast abstinent and non-abstinent states (Pomerleau et al., 2003) leave unclear whether withdrawal symptoms reported in smokers with elevated ADHD symptoms are true abstinence effects or simply reflect baseline levels of psychological disturbance. Finally, studies that examine ADHD-withdrawal associations in the context of an actual cessation attempt are useful for generalizing to real-world conditions (Berlin et al., 2012; McClernon et al., 2011). However, these investigations are vulnerable to potential confounding or bias due to non-abstinent status, as the most severely dependent smokers may relapse back to smoking and be excluded from withdrawal analyses. Thus, controlled laboratory studies that include larger sample sizes and manipulate tobacco deprivation are critical to determining whether ADHD symptoms moderate the casual influence of tobacco abstinence on withdrawal symptom exacerbation.

Further, extant tobacco withdrawal studies may not have modeled ADHD symptomatology in the most optimal fashion (Berlin et al., 2012; Kollins et al., 2013; McClernon et al., 2011; Pomerleau et al., 2003). Prior work has typically used a categorical diagnosis of ADHD. Given that there is strong evidence to suggest that ADHD may exist on the extreme end of a continuum of behavior (Levy, Hay, McStephen, Wood, & Waldman, 1997), many researchers have advocated for the analysis of continuous measures of ADHD symptoms rather than categorical diagnoses. Fittingly, prior research in non-clinical samples suggests a linear relationship between increasing levels of current ADHD symptoms and smoking variables in adults (Kollins et al., 2005; Whalen, Jamner, Henker, Delfino, & Lozano, 2002). In addition, factor analytic work consistently supports the distinction between inattention (IN) and hyperactivity-impulsivity (HI) symptom facets of ADHD (DuPaul et al., 1997). Of note, previous research suggests that there may be some differential associations between IN and HI in the prediction of smoking trajectories (Fuemmeler et al., 2007). Thus, it is important to examine whether continuous measures of ADHD symptoms linearly associate with withdrawal effects during tobacco abstinence and, further, whether there are differential associations with IN and HI symptom dimensions.

Additionally, the specific facets of the tobacco withdrawal syndrome that may be prominent in smokers with ADHD symptoms are not entirely clear. Preliminary evidence suggests that ADHD may be more strongly associated with some withdrawal experiences than others (Kollins et al., 2013; McClernon et al., 2011; Pomerleau et al., 2003); yet, it is important to expand investigations to include a broad array of well-established measures of subjective withdrawal experiences (Hughes, 2007b). Such information can tell us about the typology and qualitative aspects of the withdrawal syndrome expressed in those with high levels of ADHD symptoms. Given that there is evidence that different components of withdrawal have differential relations to cessation outcomes and may require different treatments (Piper et al., 2011; Strong et al., 2009; Strong et al., 2011), elucidating the specific manifestations of tobacco withdrawal that are exacerbated in smokers with ADHD symptoms can shed light on tailoring smoking cessation treatments for this population.

This study examined the extent to which gradations in inattention (IN) and hyperactivity-impulsivity (HI) symptom dimensions of ADHD predicted exacerbations in a variety of withdrawal symptoms during both nondeprived tobacco states and during experimentally-manipulated tobacco deprivation in adult non-treatment-seeking smokers. Previous research suggests that individuals with high trait impulsivity experience stronger cigarette craving (Doran, Cook, McChargue, & Spring, 2009) and may be more likely to smoke for negative affect relief (Doran et al., 2006), whereas high inattention may be associated with smoking to improve concentration problems and desire to smoke for stimulation (Lerman et al., 2001). Therefore, we hypothesize that HI symptoms will predict greater deprivation-induced negative affect, craving, and desire to smoke for negative affect relief. We expect that IN symptoms will predict greater deprivation-induced increases in concentration problems and fatigue.

Method

Participants

Participants were 198 smokers from the community recruited via advertisements (e.g., flier postings, website announcements [e.g., craigslist.com, facebook.com]) announcing opportunities to take part in a study on personality and smoking. Inclusion criteria were: (1) 18 years old; (2) report regular cigarette smoking for ≥ 2 years; (3) report currently smoking ≥ 10 cig/day; (4) and fluent in English. Exclusion criteria were: (1) current *DSM-IV* non-nicotine substance dependence; (2) current *DSM-IV* mood disorder or psychotic symptoms; (3) breath carbon monoxide (CO) levels < 10ppm at intake; (4) use of non-cigarette forms of tobacco or nicotine products; (5) current use of psychiatric or psychoactive medications; and (6) currently pregnant. Participants were compensated \$200 for completing the study. Those who were ineligible ($n = 49$), dropped out ($n = 15$), or twice failed to meet abstinence criteria at the deprived session ($n = 2$; see below) were excluded from analyses, leaving a final sample of 132. The University of Southern California Internal Review Board approved the protocol.

Procedure

After a telephone screen that assessed general inclusion and exclusion criteria (e.g., number of daily cigarettes, use of non-cigarette forms of tobacco or nicotine products), participants attended an in-person baseline session involving informed consent, breath CO analysis, psychiatric interview (performed by a trained research assistant who was supervised by a licensed clinical psychologist), and self-report measures of ADHD and smoking, and, in order to further characterize the clinical characteristics of the sample, self-report measures of mood, anxiety, and alcohol and drug use.

Participants then attended two experimental sessions (one deprived and one nondeprived; order counterbalanced) that commenced at 12pm. For deprived visits, participants were instructed not to smoke after 8pm the night before the session. For nondeprived visits, they were instructed to smoke normally. The procedures were identical across the two visits except that participants smoked a cigarette of their preferred brand in the laboratory in order to standardize deprivation level at the beginning of the nondeprived session prior to providing an exhaled CO whereas the deprived session began with the CO assessment. Following published recommendations indicating a CO of 10ppm or greater indicates recent smoking and prior laboratory tobacco withdrawal research (Leventhal et al., 2010; SRNT, 2002), participants' with CO indicating non-abstinence (> 9 ppm) at their deprived session could return later that week for a second attempt to complete their deprived session ($n = 8$). Those with CO > 9 ppm on their second attempt were discontinued from further participation ($n = 2$). Also at the outset of each session, participants completed a breath alcohol analysis. If the reading was positive (i.e., BrAC > 0.00 g/dl), the session was stopped and rescheduled for a different day. Following all breath analysis procedures, participants completed a single administration of measures of nicotine withdrawal, affect, and smoking urges (listed below). Following the subjective measures reported here, participants completed a series of behavioral tasks assessing emotional processing and smoking motivation which are not the focus of the current report.

Measures

Baseline Session—Structured Clinical Interview for DSM-IV Non Patient Edition (First, Spitzer, Gibbon, & Williams, 2002) mood disorder, psychotic screen, and substance use disorder modules were used to assess psychiatric diagnoses for eligibility purposes.

Demographic and Smoking History Questionnaire: An author-constructed questionnaire was used to assess demographic and smoking characteristics (e.g. cigarettes smoked per day, age of smoking onset, etc.).

Fagerström Test of Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991). The FTND is a well-validated six-item measure of nicotine dependence severity.

Adult ADHD Self-Report Scale (ASRS; Kessler et al., 2005) is a well-established self-report rating scale for assessing ADHD in individuals 18 years or older that shows a high internal consistency (Cronbach's $\alpha=0.88$) and high concurrent validity (Intra-class

correlation coefficient = .84) with clinician administered interviews (Adler et al., 2006). The ASRS includes 18 items that correspond directly to *DSM-IV* ADHD symptoms rated over the previous 6 months on a 1-5 scale ranging from *Never* to *Very Often*. ASRS ratings were summed into two subscales: 9 items reflecting *DSM-IV* inattentive symptoms and 9 items reflecting *DSM-IV* Hyperactivity/Impulsivity Items.

Alcohol Use Disorders Identification Test (AUDIT; Saunders, Aasland, Babor, de la Fuente, & Grant, 1993). The AUDIT is a well-validated 10-item screening survey designed to measure degree of alcohol problems.

Drug Abuse Screening Test (DAST; Gavin, Ross, & Skinner, 1989). The DAST is a well-validated 20-item screening survey designed to measure degree of drug problems.

Mood and Anxiety Symptom Questionnaire – Short Form (MASQ; Clark & Watson, 1991). The MASQ is a 62-item self-report measure of anxiety and depressive symptoms based upon the tripartite model of emotional disorder. Participants rate how much they experienced each symptom in the previous week (1=not at all to 5=extremely). The Anxious Arousal (MASC-AA) scale measures anxiety specific symptoms (17 items; e.g., “Was trembling or shaking,” “felt dizzy or lightheaded”), and the Anhedonic Depression (MASC-AD) scale measures symptoms specific to depression (22 items; e.g., “Felt like there wasn't anything interesting or fun to do,” “Felt like nothing was very enjoyable”). Each subscale is computed by taking the sum across the respective items.

Experimental Sessions—Each of the following questionnaires has shown sufficient sensitivity to tobacco deprivation effects and adequate psychometric properties (Hughes, 2007a; Leventhal et al., 2010).

The Minnesota Nicotine Withdrawal Scale (MNWS; Hughes & Hatsukami, 1986) is a widely used and well-validated measure of tobacco withdrawal. The 11-item MNWS variant used in this study assessed symptoms of craving, angry/irritable, anxious/tense, difficulty concentrating, restlessness, impatient, excess hunger, physical symptoms, increased eating, drowsiness, and headache experienced “so far today” on 6-point Likert scales (Leventhal et al., 2010). The total mean score across the 11 symptoms is reported (range 0 – 5).

The Wisconsin Smoking Withdrawal Scale (WSWS; Welsch et al., 1999) is a multi-dimensional tobacco withdrawal scale. The WSWS contains 23 items that comprise six subscales of tobacco withdrawal (i.e., anxiety, anger, hunger, concentration problems, craving, sadness). As in Leventhal et al (2010), we excluded the items that assess sleep problems because most participants would not have been abstinent for a long period before going to sleep to result in sleep disruption and instructed participants to respond based on how they were feeling “so far today.” The WSWS was added midway into the study; thus the N for analyses of WSWS measures is 89. The WSWS was included as an alternative measure of withdrawal because it provides multiple-item symptom indexes, which may have higher reliability.

The Brief Questionnaire of Smoking Urges (QSU; Cox, Tiffany, & Christen, 2001). The QSU is a measure of cigarette urges experienced “right now.” It includes two subscales that

assess desire for the positive effects of smoking and intention to smoke (Factor 1; 5 items) and desire for relief of negative affect and an urgent need to smoke (Factor 2; 5 items). Items are rated on 6-point Likert scales (range 0 – 5) and average scores per subscale are reported.

The Profile of Mood States; (POMS; McNair, Lorr, & Droppleman, 1971). The POMS is multidimensional questionnaire assessing affect. This study used a 72-item version in which participants rated affect adjectives on a 5-item Likert scale based on how they were feeling “right now” (0-not at all; 4-extremely). The measure yielded 7 affect scales (anxiety, vigor, depression, fatigue, confusion, anger, and elation).

Data Analysis

For preliminary analyses, we calculated correlations between ADHD IN symptoms and ADHD HI symptoms, and Cronbach's alpha coefficients for each of the symptom indexes. To test the main effects of deprivation on CO (manipulation check) and our primary outcomes, we calculated deprivation-induced change scores (Deprived – Nondeprived) for each outcome and then conducted single sample t-tests to test for significant departure from zero.

In two-way factorial experimental designs, it is customary to test the main effects of both factors as well as the interaction. However, in the current quasi-experimental study, reporting the relation of ADHD to withdrawal symptoms averaged across nondeprived and deprive conditions (i.e., “main effects” of ADHD symptom level) could conceptually and empirically obscure the relative influence of deprivation making these results difficult to interpret. For instance, showing that ADHD has a main effect on concentration problems measured on the tobacco withdrawal scales averaged across the two conditions could be a result of: (1) the expression of the ADHD syndrome while non-abstinent; (2) the expression of withdrawal phenomena while abstinent; or (3) some combination of these two processes. Thus, we take the approach of testing the effects of ADHD on nondeprived states and (separately) testing associations among ADHD symptom dimensions on deprivation-induced changes while including nondeprived states as a covariate. This an approach that has been taken in prior studies examining psychopathology as a predictor of deprivation effects on tobacco withdrawal symptoms (e.g., Leventhal, Ameringer, Zvolensky, & Langdon, 2013) and is mathematically equivalent to the ADHD $\times$ deprivation interaction, with the exception of additionally adjusting for non-abstinent states. This adjustment is a critical analytic addition because the quasi-experimental nature of this study generates systematic relations between ADHD levels and nondeprived withdrawal symptom levels, before the introduction of the deprivation manipulation, that can be statistically controlled.

Thus, the relation of ADHD to levels of withdrawal measured during the nondeprived condition (i.e., “baseline”) was tested using linear regressions where ADHD IN and HI symptoms predicted non-deprived ratings of withdrawal, mood, and smoking urges outcome measures. For each outcome, three types of models were calculated: 1) a univariate model that included IN symptoms as the sole predictor, 2) a univariate model that included HI symptoms as the sole predictor, and 3) a combined model that included IN and HI symptoms

as simultaneous predictors to examine their unique associations with outcomes after controlling for their covariance.

For the primary analyses, we used similarly structured linear regression models to test associations of IN and HI symptoms to abstinence-induced changes in withdrawal, mood, and smoking urges outcome measures. Again, for each outcome, an IN univariate model, an HI univariate model, and one combined model were calculated. In order to control for nondeprived ratings, the corresponding nondeprived outcome measure was included as a predictor in each model.

Because prior literature has suggested that females with ADHD may experience greater withdrawal severity (McClernon et al., 2011), we also explored gender by ADHD symptom interactions by testing models that included a main effect of gender and a gender by ADHD symptom dimension (IN or HI) interaction term.

We used an empirical approach to covariate selection and tested age, gender, race, number of daily cigarettes, and FTND for association with ADHD symptoms. Of the demographic and smoking characteristics, only age and FTND were significantly associated with either symptom dimension and were both included as covariates in all regression models.

Finally, in order to decrease the probability of Type 1 errors associated with multiple comparisons, we adjusted our p -value based on Benjamini and Hochberg's (1995) methods for controlling for false discovery rates (FDR), which adjusts the α level post hoc by using the generated p values and examining the proportion of potential false discoveries among the total number of independent tests.

All analyses were executed in SPSS (SPSS Statistics 19.0). Prior to fitting regression models, the ADHD and outcome data were initially examined for outliers and distribution normality and no transformations were required. Primary results of the regression models are reported as standardized β and standard errors.

Results

Preliminary analyses of descriptive characteristics and deprivation effects

Demographic, smoking, and other substance use variables—Information on the age, gender, ethnic representation, psychiatric comorbidities, smoking characteristics, and alcohol and other drug use for the sample is reported in Table 1. MASQ-AA and MASQ-AD ratings are consistent with those reported in other samples of smokers (e.g. Johnson, Stewart, Zvolensky, & Steeves, 2009). In addition, the sample falls in the very low risk range for both the DAST and AUDIT. ADHD symptoms were correlated with anxiety, mood, alcohol, and drug use as follows: ADHD IN: MASQ-AA = 0.42 ($p < .0001$), MASQ-AD = 0.40 ($p < .0001$), AUDIT = 0.18 ($p = .09$), DAST = 0.11 ($p = .30$); ADHD HI: MASQ-AA = 0.46 ($p < .0001$), MASQ-AD = 0.31 ($p = .0002$), AUDIT = 0.21 ($p = .04$), DAST = 0.25 ($p = .02$).

ADHD characteristics— $M \pm SD$ of ADHD IN and HI symptom indexes are reported in Table 1. 7.4% of the sample endorsed 9 or more ASRS items, a cut point that results in the strongest concordance with a clinical diagnosis of ADHD (Kessler et al., 2005).

Correlations between ADHD symptom variables

IN and HI indexes evidenced high internal consistency (Cronbach's $\alpha = .90$ and $.87$, respectively). IN and HI had 55% overlapping variance with one another, which is consistent with prior studies and indicates that the two indexes assess related, but separable constructs (Lahey & Willcutt, 2002).

Main effects of deprivation—The mean deprivation-induced change scores for each outcome measure, the effect sizes, and p -values for single sample t -tests for significant departure from zero are reported in Table 2. For CO, the deprived-non deprived change score significantly differed from zero (Cohen's $D = -1.4$, $p < .001$) indicating that participants were adherent to the deprivation manipulation. There was a significant effect of deprivation on all but three of the measures: POMS Depressed, POMS Fatigue, and POMS Arousal.

Relations of ADHD on nondeprived ratings—The results for the single and combined models testing the relations of ADHD IN and HI symptom dimensions on nondeprived withdrawal ratings are reported in Table 3. Significant associations of ADHD symptoms to nondeprived ratings of various withdrawal outcomes were found, as follows. In the individual models, IN was associated with higher nondeprived ratings on each of the negative affect and concentration difficulties subscales and total withdrawal on the MNWS. HI was associated with these same measures, as well as lower ratings on POMS Vigor. In the combined models, IN was independently associated with two negative affect subscales (POMS Anger and Depressed) and the two concentration difficulties subscales and HI was independently associated with three negative affect scales (WSWS Anger, WSWS Anxiety, and POMS Fatigue).¹

Primary Analysis

The results for the single and combined models testing associations with ADHD symptoms dimensions and deprived-induced changes in withdrawal measures including negative affect, positive affect, concentration, and craving/smoking urges, and other withdrawal (as measured by the MNWS, POMS, QSU, and WSWS) are reported in Table 4.

Individual models—In the individual models, IN was significantly associated with greater deprivation-induced changes on the following measures: WSWS Anger; and POMS Confusion. HI was significantly associated with greater deprivation-induced changes on the following measures: Negative Affect (WSWS: Anger, Anxiety, Sadness; POMS: Anger, Anxious, Depressed, Fatigue); Concentration Difficulties (WSWS Difficulties Concentrating

¹The main effects of ADHD on withdrawal effects averaged across deprived and non-deprived states are available upon request from the corresponding author (LCB)

and POMS Confusion); Craving/Urges: WSWs Craving, QSU Factor 2 (Withdrawal relief); and overall withdrawal as measured by the MNWS Total score.

Combined models—In the combined models, HI was associated with greater deprivation-induced changes on nearly all same outcomes as found in the single models. However, the significant associations with IN and greater deprivation-induced changes reduced below significance after accounting for HI-IN covariation.²

Gender by ADHD symptom interactions—Neither the main effect of gender nor the gender by ADHD symptom dimension (IN or HI) interaction effect reached significance in any of the models.

Controlling for false discovery rates—We controlled for FDR using the methods outlined in Benjamini & Hochberg (1995). Based on the 96 independent tests included in the primary analyses (single and combined models testing associations with IN and HI symptoms and deprivation-induced change scores), 9 tests with a *p* value of .01 or less met significance criteria (See Table 4).

Discussion

Results from the current study indicate that ADHD symptoms and tobacco withdrawal are associated in a community sample of smokers and extend previous clinical and retrospective research on this topic (Ameringer & Leventhal, 2012; Berlin et al., 2012; McClernon et al., 2011; Pomerleau et al., 2003). The quantitative analysis, experimental design, and comprehensive assessment of tobacco withdrawal in this study support several novel conclusions regarding the ADHD-withdrawal relation. First, gradations in ADHD symptom level that may not meet diagnostic thresholds associate with quantitative variation in withdrawal symptom severity during both deprived and nondeprived states. Thus, diagnostic indicators of ADHD may perhaps obscure subtle variation below and above the diagnostic threshold that may confer risk for more severe tobacco withdrawal. Second, the relation between ADHD and withdrawal symptoms may not solely reflect criterion contamination in which withdrawal measures are simply tapping aspects of the ADHD syndrome. Rather, the current findings indicate that, while ADHD symptoms were associated with greater levels of negative affect and concentration difficulties during nondeprived smoking states, smokers with higher levels of ADHD symptoms experience more severe exacerbations in these tobacco withdrawal symptoms upon abstinence irrespective of their baseline withdrawal disturbance. Third, ADHD symptoms associate with a deprivation-induced changes in a variety of withdrawal phenomena spanning negative affect, cognitive disturbance, and cigarette craving/urges. Thus, the risk of withdrawal conferred by ADHD symptoms may not be limited to those pathognomonic with ADHD (i.e. difficulty with concentration).

While our findings are consistent with the broader literature on ADHD and withdrawal, they are in contrast to some recent laboratory work. Two recent studies using relatively smaller

²Item level analyses examining individual ADHD symptoms and withdrawal effects are available upon request from the corresponding author (LCB).

samples have found an association of ADHD symptoms with generally more severe withdrawal symptoms, but not a specific effect of ADHD on abstinence-induced changes in withdrawal measures, including constructs tapped in our study such as negative affect (Ashare & Hawk, 2012; Kollins et al., 2013). Importantly, each study used a different definition of ADHD (subthreshold symptoms vs. clinical diagnosis, respectively) and neither of these prior studies examined ADHD on an IN/HI dimensional level. These contrasting findings underscore the need for future, large laboratory-controlled studies that not only include continuous measures of ADHD IN and HI symptomatology, but a broad array of subjective and objective withdrawal measures.³

With regard to the two symptom dimensions of ADHD, based on prior work (Doran et al., 2009; Lerman et al., 2001) we predicted that IN would be associated with abstinence-provoked increases in concentration problems and fatigue, whereas HI would be related to abstinence-related increases in negative affect, craving, and desire to smoke to attenuate negative affect. Results were partially consistent with our predictions. IN symptoms were associated with only increased anxiety and elevations in anger, whereas HI symptoms were associated with a broader range of withdrawal symptoms, including cognitive disturbance, craving, various manifestations of negative affect (e.g., anger, anxiety, sadness, depression), and desire to smoke to alleviate negative affect. When accounting for the covariation among IN and HI symptoms, only HI predicted increased ratings on these same withdrawal symptoms, whereas IN did not have incremental predictive value over and above HI.

The finding that the HI symptom index is a more consistent predictor of deprivation effects than IN is in line with prior epidemiological work showing that while both IN and HI were associated with nicotine dependence, only HI was associated with progression from non-smoking to regular smoking and progression from experimentation to regular smoking (Fuemmeler et al., 2007). Whether HI in this context more strictly reflects subthreshold ADHD symptoms or also taps a more general latent impulsivity construct, is not clear. However, these findings also add to a literature linking impulsivity and smoking abstinence (Harrison, Coppola, & McKee, 2009; Mitchell, 2004) and suggesting that smokers with impulsive traits are prone to smoke for negative affect relief and experience strong cigarette cravings (Doran et al., 2009). Also, it is important to note that we did not test whether the strength of relations of ADHD symptoms to withdrawal significantly differed across IN and HI. Such tests of differential strength of relations would require substantial sample size to provide sufficient power. Rather, we tested whether the strength of each relation significantly departed from zero. Thus, we can safely conclude that HI significantly predicts higher withdrawal effects over and above covariance with IN, but cannot conclude that HI has stronger relations to withdrawal relative to IN. Such predictions about differential strength of relations could be addressed in future work employing larger samples that yield more precise effect size estimates allowing for refined empirical comparisons across effects.

Our finding that IN symptoms had less consistent associations with abstinence-provoked concentrating difficulties is counter-intuitive because the link with ADHD and smoking has

³Results of analyses examining ADHD symptoms as a predictor of objective behavioral and cognitive laboratory measures will be presented in future publications.

commonly been attributed to the effects of nicotine on ADHD-related deficits in concentration and attentional control (Lerman et al., 2001; McClernon et al., 2008). Given that we used a subjective measure of concentration problems, individuals with high levels of IN may be less subjectively aware of any deficits in cognition induced by tobacco abstinence. Future studies should seek to differentiate the role of IN and HI symptom dimensions in withdrawal-related concentration difficulties using objective measures of cognitive and attentional control. In addition, IN symptoms were not significantly associated with fatigue. Given that no main effect of deprivation on fatigue emerged in the present study, it is not surprising that an association with ADHD symptoms was also not present. Similarly, in a previous study of deprivation effects in 202 daily smokers (Leventhal et al., 2010), a similar measure to the POMS fatigue scale (i.e., Minnesota Nicotine Withdrawal Scale “Drowsiness” item) showed very modest abstinence effects (Cohen's $d = .17$). Thus, it is possible that the failure to find effects on fatigue may reflect a type-II error given that the current sample ($n=132$) may not provide adequate power to detect small effects.

With regard to associations with ADHD symptoms and “baseline” withdrawal ratings, both IN and HI were associated with increases in particular aspects of negative affect and concentration difficulties during nondeprived states. These findings are partially consistent with results among ADHD symptom dimensions and retrospective withdrawal symptoms in a prior population-based study (Ameringer & Leventhal, 2012). Both the current study and Ameringer and Leventhal (2012) illustrated that gradations in ADHD symptom levels were associated with higher withdrawal symptoms in smokers not recruited with regard to ADHD diagnostic status. However, there were some differences in findings across the current study and Ameringer and Leventhal regarding to the independent relations of HI versus IN to withdrawal symptoms. In Ameringer and Leventhal, item level analysis of DSM-IV withdrawal symptoms indicated associations between IN and all tobacco withdrawal symptoms; similarly, HI associated with nearly all withdrawal symptoms, except for feeling depressed and concentration difficulties. Ameringer and Leventhal also reported results from a combined model accounting for the covariance between HI and IN, which showed that nearly all HI-withdrawal associations reduced below significance whereas most IN-withdrawal associations remained significant. A critical difference between our current study and Ameringer and Leventhal (2012) is that the prior study examines withdrawal ratings collected via retrospective report of previous experiences during prior abstinence periods and does not directly compare experimentally controlled abstinence vs. nonabstinence states. It is possible that IN might associate more consistently with the retrospective withdrawal ratings measured in the prior study because of memory biases attributing symptoms associated with the ADHD syndrome and baseline functioning to withdrawal. The current study parses that limitation using a robust experimental design to manipulate deprivation states. Further, the prior study examines these associations in a population-based sample of all U.S. adults who had smoked at least 100 cigarettes in their lifetime, whereas the current sample includes smokers not interested in quitting who smoke at least 10 cigarettes per day for at least two years. Thus, these differences in smoking level may also impact the extent to which different dimensions of ADHD symptoms are associated with smoking withdrawal symptoms across the two samples.

In the current study gender did not significantly interact with IN or HI to significantly predict deprivation effects on any of the withdrawal measures. This is in contrast to prior work showing more severe withdrawal experiences in females with ADHD (e.g. McClernon et al., 2011). It is possible that the gender effects on withdrawal characteristics found in the prior study were partially attributable to higher levels of smoking severity and immediate post-quit increases negative affect in female participants. Although gender $\times$ ADHD symptom interactions were not found in our study after covarying out level of nicotine dependence, future work should continue to examine the potential influence of gender on the relationship with ADHD symptoms and withdrawal experiences.

Limitations and Future Directions

These findings should be interpreted in the context of the study's limitations. First, ADHD symptoms were assessed using self-report in adulthood. While this approach to characterizing adult ADHD symptoms has been shown to generate data with adequate reliability and validity (Adler et al., 2006) and may be more generalizable to the broader population of smokers (Kollins et al., 2005), these deprivation effects should also be examined in concert with clinical ratings and diagnoses of ADHD which include information on childhood history. Second, this is a laboratory study with individuals who are not necessarily interested in quitting. While previous studies have shown that ADHD status moderated cessation outcomes (Covey, Manubay, Jiang, Nortick, & Palumbo, 2008; Humfleet et al., 2005), these laboratory assessments may not directly translate to the real-world experience of motivated quitters making a quit attempt. While the current study maximizes internal validity of the effects studied herein, naturalistic designs (i.e. the use of ecological momentary assessment of withdrawal effects) will be important for future research to broaden the external validity of these findings. Third, our study did not assess quality of sleep during the night prior to the deprived and non-deprived laboratory sessions, which could potentially have influenced deprivation effects. While it is unlikely that sleep was significantly disrupted during the relatively short period of overnight abstinence, future studies can directly test this with a measure of sleep quality. Fourth, the current design cannot disentangle the effects of abstinence from nicotine specifically versus withdrawal from the behavioral and psychological effects of smoking abstinence more generally. Our findings should be followed up with studies that include additional comparison conditions that decouple the effects of the smoking ritual and nicotine per se. Finally, though the withdrawal assessment battery was comprehensive, it was restricted to subjective measures, which have limitations. Given that abstinence has been shown to impact a variety of behavioral, cognitive, and physiological indices (Leventhal et al., 2010), it would be useful to examine IN/HI-withdrawal relations on such measures.

Summary

Despite these limitations, findings reported here reflect consistent unique associations of self-reported HI symptoms to smoking deprivation effects, suggesting the HI may be an important phenotypic marker of the ADHD syndrome that is relevant to tobacco withdrawal. Therefore, researchers and clinicians predicting severity of withdrawal symptoms during abstinence should consider measuring ADHD at the individual symptom dimension level. In addition, these results from a community sample of adults extend to individuals who may

not cross the threshold for ADHD diagnosis. Indeed, only 7% of our sample reported clinically-significant levels of ADHD symptoms that may concord with an ADHD diagnosis. Thus, relying solely on categorical diagnostic thresholds may overlook subclinical variation across the ADHD continuum that could be important to smoking etiology and cessation. Given that subthreshold ADHD symptoms are likely to be present at higher rates in smokers, our findings potentially generalize to a broader population of smokers beyond those with a clinical diagnosis of ADHD. Finally, our findings suggest that only particular withdrawal symptoms are related to ADHD symptoms and point to cognitive factors, negative affect, and negative reinforcement processes as potentially the most salient withdrawal mechanisms linking ADHD symptoms and smoking. Other factors such as pleasure enhancement may be less important and suggest that interventions for smokers with high levels of ADHD symptoms should be designed to specifically target critically-involved processes. Future research should seek to determine which aspects of withdrawal are associated with risk for relapse and seek to develop more targeted interventions for smoking cessation in individuals with high levels of ADHD symptoms.

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Table 1

Demographics, smoking and other substance use characteristics, ADHD symptoms, and other psychiatric variables.

<i>Demographics</i>		
Gender, <i>N</i> (%)		
Male	88	(66.7%)
Female	44	(33.3%)
Ethnicity, <i>N</i> (%)		
White	50	(37.9%)
Black	63	(47.7%)
Multi-racial	5	(3.8%)
Other	6	(4.5%)
Unknown	8	(6.1%)
Age, <i>M</i> (<i>SD</i>)	43.5	(10.3)
<i>Smoking and Substance Use Characteristics</i>		
FTND, <i>M</i> (<i>SD</i>)	5.4	(2.0)
CO level in ppm, <i>M</i> (<i>SD</i>)	20.5	(9.5)
Number of cigarettes per day, <i>M</i> (<i>SD</i>)	16.7	(6.0)
Age of smoking onset (at least 1 cigarette/day), <i>M</i> (<i>SD</i>)	16.3	(4.5)
Alcohol Use Disorders Identification Test (AUDIT), <i>M</i> (<i>SD</i>)	3.2	5.3
Drug Abuse Screening Test (DAST), <i>M</i> (<i>SD</i>)	1.4	3.2
<i>Psychiatric Variables</i>		
Adult ADHD Self Report Scale (ASRS) Ratings		
Inattention, <i>M</i> (<i>SD</i>)	20.1	(6.4)
Hyperactivity/Impulsive, <i>M</i> (<i>SD</i>)	19.1	(6.3)
Mood and Anxiety Symptom Questionnaire (MASQ)		
Anhedonic Depression, <i>M</i> (<i>SD</i>)	53.1	14.5
Anxious Arousal, <i>M</i> (<i>SD</i>)	20.7	6.4

Note. FTND = Fagerström Test of Nicotine Dependence; CO = Carbon Monoxide.

Table 2

Main effects of deprivation on CO level and primary outcomes

	M(SD) Non-deprived	M(SD) Deprived	M(SD) Deprived-Non Deprived	Cohen's <i>D</i>
<i>Manipulation Check</i>				
CO level	28.1 (14.8)	5.5 (2.0)	-22.9 (11.5)	-2.0 **
<i>MNWS</i>				
MNWS Total	1.1 (1.0)	1.9 (1.1)	0.9 (1.06)	0.80 **
<i>WSWS Scales</i>				
Anger	1.1 (1.1)	1.7 (1.3)	0.6 (1.2)	0.51 **
Anxiety	1.7 (0.9)	2.2 (0.9)	0.5 (0.9)	0.55 **
Difficulty Concentrating	1.2 (0.9)	1.6 (1.0)	0.4 (1.0)	0.44 **
Craving	1.7 (0.9)	2.9 (0.9)	1.1 (1.1)	1.08 **
Hunger	1.7 (0.9)	2.0 (0.9)	0.3 (1.1)	0.31 *
Sadness	1.2 (0.8)	1.5 (0.8)	0.3 (0.8)	0.37 *
<i>POMS Scales</i>				
Anxious	0.7 (0.8)	1.2 (1.0)	0.5 (0.9)	0.50 **
Vigor	2.3 (1.0)	1.8 (1.0)	-0.4 (0.8)	-0.53 **
Depressed	0.4 (0.7)	0.5 (0.7)	0.1 (0.6)	0.14
Fatigue	0.9 (0.9)	0.9 (0.9)	0.0 (0.9)	0.01
Confusion	0.8 (0.7)	1.0 (0.8)	0.2 (0.8)	0.20 *
Anger	0.4 (0.7)	0.7 (0.8)	0.3 (0.8)	0.36 **
Elation	1.9 (0.8)	1.5 (0.8)	-0.4 (0.7)	-0.58 **
<i>QSU</i>				
Factor 1	1.2 (1.3)	4.2 (1.0)	2.9 (1.5)	2.00 **
Factor 2	0.7 (1.1)	2.5 (1.4)	1.8 (1.3)	1.32 **

Note.

1Effect sizes (Cohen's *D*) and *p*-values for single sample t-tests of deprived-nondeprived change score for significant departure from zero; MNWS = Minnesota Nicotine Withdrawal Scale; WSWS = Wisconsin Withdrawal Scale; POMS = Profile of Mood States; QSU= Questionnaire of Smoking Urges

*
p<.01

**
p<.001.

Table 3

Results of regression models for single and combined models for association between IN and HI symptom dimensions and nondeprived subjective withdrawal ratings

	IN		HI		Combined		HI	
	Beta	se	Beta	se	Beta	se	Beta	se
<u>Negative Affect</u>								
WSWS Anger	0.40**	0.02	0.51**	0.02	0.18	0.02	0.38*	0.03
WSWS Anxiety	0.40**	0.01	0.52**	0.01	0.06	0.02	0.48***	0.02
WSWS Sadness	0.37**	0.01	0.38**	0.01	0.18	0.02	0.25	0.02
POMS Anger	0.39**	0.01	0.34**	0.01	0.32**	0.01	0.10	0.02
POMS Anxious	0.38**	0.01	0.42**	0.01	0.17	0.01	0.30	0.02
POMS Depressed	0.45**	0.01	0.36**	0.01	0.42**	0.01	0.05	0.01
POMS Fatigue	0.37**	0.01	0.47**	0.01	0.06	0.02	0.42**	0.02
<u>Positive Affect</u>								
POMS Vigor	-0.21	0.01	-0.27*	0.01	-0.04	0.02	-0.24	0.02
POMS Elation	-0.16	0.01	-0.16	0.01	-0.11	0.02	-0.07	0.02
<u>Concentration</u>								
WSWS Difficulty Concentrating	0.50**	0.01	0.48**	0.01	0.35*	0.02	0.22	0.02
POMS Confusion	0.42**	0.01	0.43**	0.01	0.39*	0.01	0.13	0.02
<u>Craving/Urges</u>								
WSWS Craving	0.23	0.01	0.18	0.02	0.21	0.02	0.03	0.02
QSU Factor 1	-0.12	0.02	-0.19	0.02	0.00	0.02	-0.20	0.03
QSU Factor 2	0.04	0.01	-0.03	0.01	0.11	0.02	-0.11	0.02
<u>Other Withdrawal</u>								
MNWS Total	0.40**	0.01	0.38**	0.01	0.27	0.02	0.18	0.02
WSWS Hunger	0.23	0.01	0.18	0.02	0.25	0.02	-0.01	0.02

Note. IN=inattentive; HI=hyperactive-impulsive; MNWS = Minnesota Nicotine Withdrawal Scale; WSWS = Wisconsin Withdrawal Scale; POMS = Profile of Mood States; QSU= Questionnaire of Smoking Urges; Models were constructed to include Age and FTND as covariates

* p<.01
** p<.001
/ Standardized Beta.

Table 4

Results of regression models for single and combined models for association between ADHD IN and HI symptom dimensions and deprivation-induced changes in subjective withdrawal ratings

	IN		HI		Combined IN		HI	
	Beta	se	Beta	se	Beta	se	Beta	se
<u>Negative Affect</u>								
WSWS Anger	0.30 [*]	0.02	0.36 ^{***}	0.02	0.16	0.02	0.24	0.03
WSWS Anxiety	0.18	0.01	0.31 [*]	0.01	-0.03	0.02	0.33 ^{*2}	0.02
WSWS Sadness	0.18	0.01	0.23	0.01	0.08	0.01	0.18	0.02
POMS Anxious	0.19	0.01	0.39 ^{***}	0.01	-0.15	0.02	0.50 ^{**2}	0.02
POMS Depressed	0.18	0.01	0.32 ^{***}	0.01	-0.11	0.01	0.40 ^{**2}	0.01
POMS Fatigue	0.13	0.01	0.19	0.01	0.02	0.02	0.18	0.02
POMS Anger	0.18	0.01	0.30 ^{***}	0.01	-0.07	0.02	0.35 ^{*2}	0.02
<u>Positive Affect</u>								
POMS Vigor	0.03	0.01	0.11	0.01	-0.13	0.01	0.21	0.02
POMS Elation	-0.08	0.01	-0.06	0.01	-0.13	0.01	0.04	0.01
<u>Concentration</u>								
WSWS Difficulty Concentrating	0.17	0.02	0.32 [*]	0.02	-0.08	0.02	0.37 ^{*2}	0.02
POMS Confusion	0.24 [*]	0.01	0.36 ^{***}	0.01	-0.03	0.01	0.38 ^{**2}	0.02
<u>Craving/Urges</u>								
WSWS Craving	0.11	0.01	0.27 [*]	0.01	-0.19	0.02	0.40 ^{*2}	0.02
QSU Factor 1	0.10	0.01	0.15	0.01	-0.05	0.02	0.19	0.02
QSU Factor 2	0.16	0.02	0.31 ^{***}	0.02	-0.16	0.02	0.43 ^{**2}	0.02
<u>Other Withdrawal</u>								
MNWS Total	0.19	0.01	0.31 ^{***}	0.02	-0.05	0.02	0.34 ^{*2}	0.02
WSWS Hunger	0.10	0.01	0.20	0.02	-0.09	-0.01	0.26	0.02

Note. IN=inattentive; HI=hyperactive-impulsive; MNWS = Minnesota Nicotine Withdrawal Scale; WSWS = Wisconsin Withdrawal Scale; POMS = Profile of Mood States; QSU= Questionnaire of Smoking Urges; Models were constructed to include Age, FTND, and corresponding nondeprived ratings as covariates

* p<.01
** p<.001

/ Standardized Beta

²Test remained significant after Benjamini and Hochberg's (1995) False Discovery Rate correction.