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Smoking cessation and inattention or hyperactivity/impulsivity: a post hoc analysis

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Abstract

Tobacco use is more prevalent and smoking cessation less likely among persons with attention deficit hyperactivity disorder (ADHD) than the general population. Evidence that tobacco use and nicotine hold divergent relationships with inattention (IN) and hyperactivity/impulsivity (HI), the core symptoms of ADHD, prompted this post hoc investigation of abstinence patterns by type of ADHD symptoms. Subjects were 583 adult smokers treated openly with bupropion and nicotine patch during the initial eight-week phase of a maintenance treatment study. Using the ADHD Current Symptom Scale, clinically significant ADHD symptom subtypes, i.e., predominantly inattention (ADHD-IN) and predominantly hyperactivity/impulsivity with or without inattention (ADHD-HI+/-IN), were identified. The study outcome was abstinence status, verified by expired carbon monoxide <8 parts per million, at five clinic visits from Week 1 through the end of treatment at Week 8. The distribution by ADHD symptom status was: No ADHD=540; ADHD-IN=20; ADHD-HI+/-IN=23. The study groups did not differ on demographic or smoking variables. The frequency of past major depression was highest with ADHD-IN and the frequency of past alcohol dependence was highest with ADHD-HI+/-IN. Compared to smokers with no ADHD, smokers of both ADHD subtypes combined showed lower abstinence rates throughout the study (OR=0.54, 95% CI: 0.32-0.99). Disaggregation by symptom subtype and separate comparisons against smokers with no ADHD showed that lower odds of quitting occurred mainly with ADHD-HI+/-IN (OR=0.40, 95% CI=0.19-0.82), not with ADHD-IN (OR=0.74, 95% CI=p=0.36-1.51). Combined bupropion and nicotine patch treatment appears to be helpful for smokers with IN but not smokers with HI symptoms. The reasons for this divergent treatment response warrant further investigation.

The remarkable decline in the prevalence of cigarette smoking in the United States, from 44% in 1965 to 24% in 1997, subsided in the next decade, with the smoking rate reaching only about 21% in 2006 (Centers for Disease Control, 2007). This slowing down, despite

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extensive anti-smoking public health efforts and the growing stigmatization of cigarette smoking, is said to reflect “hardening” or the increased resistance to smoking cessation among later-day smokers (Irvin and Brandon, 2000). Although other forces are acknowledged, the greater propensity to smoke and difficulty quitting among persons with mental illness is thought to play a role in the “hardening” phenomenon (Hughes and Brandon, 2003). Indeed, much empirical data, including findings from two large nationally representative samples (Grant, Hasin, Chou, Stinson, Dawson, 2004; Lasser, Boyd, Woolhandler, Himmelstein, McCormick, Bor, 2000) have demonstrated linkages of smoking and nicotine dependence with the most common psychiatric disorders, notably depression, anxiety, and substance abuse/dependence. Although Attention Deficit Hyperactivity Disorder (ADHD) is also a common psychiatric condition in the U.S., estimated to affect up to 18% of children and adolescents (Faraone, Sergeant, Gillberg, Biederman, 2003) and 4.4% of adults (Kessler, Adler, Barkley, Biederman, Conners, et al, 2006), less attention has been paid to the association between tobacco use and ADHD. Nevertheless, available evidence indicates that tobacco use is a significant problem among persons with ADHD (Spencer, Biederman, Mick, 2007; Sullivan and Levin, 2001),

ADHD

ADHD is a neuropsychiatric condition that begins during childhood and, in most cases, persists to adolescence and adulthood (American Psychiatric Association, 1994). Worldwide, the prevalence of ADHD is about 5% (Polanczyk, de Lima, Horta, Biederman, Rohde, 2007). Persons with ADHD experience functional impairment in multiple settings throughout the lifespan. The core symptom domains in ADHD are inattention (IN) and hyperactivity/impulsivity (HI). The Diagnostic Statistical Manual-Fourth Edition (DSM-IV) sub-classifies ADHD into three subtypes: predominantly inattention, predominantly hyperactivity/impulsivity, and combined inattention and hyperactivity/impulsivity. Observed differences among the ADHD subtypes in patterns of psychiatric comorbidity (Murphy, Barkley, Rush, 2002; Sprafkin J, Gadow KD, Weiss MD, Schneier J, Nolan EE, 2007) and etiological factors such as genetic influence (Larsson, Lichtenstein, Larsson, 2006) and familial psychopathology (Stawicki, Nigg, von Eye, 2006), are thought to suggest that the symptom subtypes represent distinct disorders.

ADHD and tobacco use

Studies of adolescents and young adults have found higher levels of various smoking behaviors among persons with the diagnosis or symptoms of ADHD in comparisons with non-affected individuals, i.e., higher lifetime prevalence, (Pomerleau, Downey, Mehringer, Marks, Pomerleau, 2003; Tercyak, Lerman, Audrain, 2002), greater amount smoked, (Kollins, McClernon, Fuemmeler, 2005; Lambert and Hartsough, 2000), and earlier age of smoking onset (Kollins et al, 2005; Lambert and Hartsough, 2000). Much evidence that nicotine improves attentiveness and performance deficits among persons with ADHD (Bekker, Bocker, VanHunsel, vandenBerg, Kenemans, 2005; Conners, Levin, Sparrow, Hinton, Erhardt, Meck, Rose, March, 1996; Poltavski and Petros, 2006; Potter and Newhouse, 2004) provides a “self-medicating” rationale for greater tobacco use among persons with ADHD. Pre-clinical data showing that dopamine, a neurotransmitter relevant to attentional processes (Volkow, Wang, Newcorn, Telang, Solanto, et al, 2007) and impulse control (Diergaarde, Pattij, Poortvliet Hogenboom, de Vries et al, 2008), is released upon smoking (Levin et al, 1998) is consistent with the self-medication hypothesis. .

ADHD subtypes and tobacco use

Divergent relationships of the symptom subtypes with nicotine or smoking outcomes have been observed. Among studies that examined nicotine effects on both symptoms in the same

study, most found that nicotine exerted positive effects on attention, but no or adverse effects on hyperactivity and impulsivity (Bekker, Bocker, VanHunsel, vandenBerg, Kenemans, 2005; Blondel, Simon, Sanger, Moser, 1999; Burke, Loeber, White, Stouthamer-Loeber, Pardini, 2007; Decamp and Schneider, 2006; Lerman, Audrain, Tercyak, Hawk, Bush et al, 2002). In studies that examined the effect of symptoms on smoking outcome, prediction of various tobacco use measures, such as initiation, progression to regular smoking or nicotine dependence, and increased tendency to relapse, was more apparent for hyperactivity/impulsivity, than inattention (Elkins, McGue, Iacono, 2007; Fuemeller, Kollins, McClernon, 2007; Kollins et al, 2005; Molina, Smith, Pelham, 1999). These opposing relationships of the subtypes with smoking outcomes have implications on response to smoking cessation treatment.

Smoking cessation and ADHD

Tobacco use is the major risk factor for mortality in the United States and many other countries worldwide (National Cancer Institute, 1997; World Health Organization, 1997). Tobacco cessation reduces that risk (Peto, Darby, Deo, Sillocks, Whitley, Doll, 2000). In this context, that divergent associations exist between the symptom subtypes and efforts to stop smoking has important public health consequences. The effect of ADHD by itself on smoking cessation, however, has rarely been examined; the effects of the individual ADHD symptom subtypes on smoking cessation, even less so. Two studies that considered ADHD as a single entity found lower cessation rates when ADHD symptoms are currently present (Pomerleau, Downey, Stelson, Pomerleau CS, 1995) or when childhood symptoms were retrospectively reported (Humfleet, Prochaska, Mengis, Cullen, Muñoz, et al, 2005). One study that examined ADHD symptoms by subtype found that increased HI, but not increased IN, immediately following quitting predicted eventual treatment failure (Rukstalis, Jenson, Patterson, Lerman, 2005); the effects of ADHD symptoms at baseline were not reported in that investigation. Studies that examined impulsivity, without regard to ADHD, found that a high level of this trait predicts more relapse to smoking (Doran, Spring, McChargue, Pergadia, Richmond, 2004; Krishnan-Sarin, Reynolds B, Duhib AM, Smith A, Liss T et al, 2007). To our knowledge, the effects of IN or HI assessed at baseline as separate domains of ADHD symptomology on cessation treatment outcome have not been examined.

Hypotheses

The present study investigated separate effects of the ADHD symptom subtypes, inattention (IN) and hyperactivity/impulsivity (HI) at baseline when compared to the absence of these symptoms on smoking cessation treatment response. Data collected during the run-in phase of a maintenance treatment study for preventing smoking relapse (Covey, Glassman, Jiang, Fried, Masmela et al, 2007) were analyzed. To obtain an adequate sample of abstainers for the four-arm placebo-controlled maintenance treatment phase, bupropion and nicotine patch (B/NP) were co-administered openly in an eight-week treatment study. A multi-site trial had demonstrated the superior efficacy of B/NP treatment compared to either medication delivered alone for achieving smoking cessation at the end of nine weeks (Jorenby, Leischow, Nides, Rennard, Johnston et al, 1999).

Based on the expectation that smokers with ADHD as a group would have greater difficulties when they attempt cessation (Sullivan and Levin, 2001), we first hypothesized that smokers with predominantly IN symptoms would benefit from treatment with B/NP. They would manifest this effect through a similarity in their abstinence rates when compared to smokers without ADHD symptoms. Support for this prediction comes from evidence that nicotine (Conners et al, 1996; Levin, et al, 1998; Levin, et al, 1996) and bupropion (Wilens, Spencer, Biederman, Girard, Doyle et al, 2001) reduce symptoms of IN. Our second

hypothesis was that smokers with elevated symptoms of HI, when compared to smokers with no ADHD symptoms, will experience lower abstinence rates in response to the same treatment. Although evidence on the effects of bupropion alone or of combined B/NP on HI symptoms is lacking, we based this second prediction on earlier findings of adverse effects of nicotine on HI (Bekker, et al, 2005; Blondel, Simon, Sanger, Moser, 1999), along with evidence that trait-impulsivity reduces ability to maintain abstinence from smoking (Doran, et al, 2004; Krishnan-Sarin, et al, 2007). Findings from this study could lead to treatment guidelines appropriate to smokers with problems of IN and HI.

Methods

Participants

Participants were recruited from the community through various media outlets in the New York metropolitan area. Of 1,859 smokers screened by telephone, 588 met eligibility criteria; data from five persons who did not complete the ADHD symptom rating scale were excluded. Inclusion criteria were: aged 21 years or more, a previous quit attempt, and smoking at least 10 cigarettes daily during the past month. Exclusion criteria were: medical history contraindicating use of bupropion or nicotine patch; unstable or uncontrolled medical condition; major depressive disorder or alcohol/drug dependence within the past six months; lifetime history of bipolar disorder or any psychotic illness; current treatment for tobacco dependence; current use of psychoactive medication; and among women, lactation, pregnancy or intention to become pregnant during the study. Participants provided written informed consent after an investigator's full description of the study protocol. The Institutional Review Board of the New York State Psychiatric Institute approved and monitored this study.

Clinical procedures

Participants were initially screened for eligibility by telephone. They were screened further at a baseline clinic visit; if deemed eligible, they received the study medications and planned a quit date. They were to use bupropion SR 150 mg. for eight weeks beginning at 150 mg once daily for three days then twice daily beginning on day 4 throughout the study. Quit day (complete nonsmoking) was the seventh day after starting bupropion upon which nicotine patch use was begun following a regimen of 21 mg, 14 mg, and 7 mg for 4, 2, and 1 week, respectively. Participants returned to the clinic at Week 1 (the day after quit day), at the end of Week 2, and at the end of Weeks 4, 6, and 8. At the clinic visits, they received individual cessation counseling from trained counselors with a minimum of a bachelor's degree. The counseling program covered topics on the addictive nature of smoking, selection and preparation for Quit Day, and coping with withdrawal symptoms and urges to smoke.

ADHD symptoms and subtypes

At the screening visit, participants completed the ADHD Current Symptoms Scale (Barkley and Murphy, 1998), a self-administered questionnaire consisting of 18 items representing the DSM-IV ADHD symptoms as experienced during the past six months. Nine items measure IN and nine items measure HI symptoms. Responses to each item range from 0 (never or rarely), 1 (sometimes), 2 (often), and 3 (very often). A response of 2 or 3 on each item indicated that the symptom was met. In the present sample, IN scores ranged from 0 to 8; HI scores ranged from 0 to 9. Tests of internal reliability produced alpha coefficients of 0.87 for the 9 IN items, 0.78 for the 9 HI items, and 0.89 for the total 18 items. The continuous measures of IN and HI were correlated at $r=0.60$ ($p<0.001$), indicating substantial but not overwhelming overlap.

Categorical subtypes by ADHD symptom status were obtained based on procedures and normative data provided by the authors. For each subject, a clinically significant threshold for IN or HI symptomatology was indicated when the sum of endorsed symptoms was equal to or greater than one standard deviation above the mean score for IN or HI in samples categorized by age (17-25 years, 26-35 years, 36 + years). Of 583 study participants, 43 (7.4%) received a score indicating clinically significant levels of IN or HI symptoms; of these, 20 received ratings indicating IN only, 12 of HI only, 11 had significant levels of both HI and IN (HI+IN). Because of small numbers, we combined the subgroups with HI and HI +IN into a single group, and constructed a categorical variable, i.e., ADHD status, consisting of three subgroups: No ADHD (n=540), ADHD-inattention only (ADHD-IN) (n=20) and ADHD-hyperactivity with or without inattention (ADHD-HI+/-IN) (n=23). Comparisons of IN and HI mean scores by ADHD status supported the validity of our trichotomous ADHD variable, i.e., both IN and HI mean scores were lowest in the No ADHD subgroup, IN mean scores were highest in the ADHD-IN subgroup and HI mean scores were highest among the HI+/-IN subgroup;

Covariates

At the screening visit, participants completed an intake form that elicited demographic (age, gender, marital status, education, and occupation) and smoking history information (age first smoked a cigarette, age began smoking daily, number of cigarette smoked daily during the past week, number of past quit attempts, confidence in ability to quit smoking), and the Fagerstrom Test for Nicotine Dependence (FTND), a 6-item self-administered instrument with acceptable reliability and validity (Heatherton, Kozlowski, Becker, Frecker, Fagerstrom, 1991). Trained raters administered the Schedule for Clinical Interviews (First, Spitzer, Williams, Gibbon, 1995) a semi-structured interview based on the DSM-IV to assess lifetime major depressive disorder and alcohol dependence.

Abstinence outcome

The primary outcome consisted of the abstinence rates (number abstinent/583 enrollees) at Weeks 1, 2, 4, 6, and 8 after quit day. Abstinence status during the interval between visits was indicated when both conditions of self-reported continuous abstinence and expired carbon monoxide (CO) level <8 ppm (Jarvis, Tunstall-Pedoe, Feyerabend, Vesey, Salojee, 1987) at the completed clinic visit were met. The Bedfont Scientific Smokerlyzer (Medford, NJ) was used to measure CO level. Abstinence at Week 1 indicated not smoking since quit day; abstinence at each study week indicated continuous abstinence during the interval between the previous and the current visit. Following the practice of many smoking cessation investigators (Hughes, Keely, Niaura, Ossip-Klein, Richmond, Swan, 2003), participants who withdrew from the study and did not provide data at subsequent visits were considered non-abstainers.

Statistical analysis

Comparisons of baseline characteristics by ADHD status were performed using the χ^2 -test for categorical variables and analysis of variance for continuous variables. To test the effect of ADHD status on abstinence rates during the study, we used a mixed effects model for longitudinal data analysis where participants' smoking or abstinence status at each visit was modeled as a function of ADHD status, time (in study weeks), and ADHD status $\times$ time. Baseline participant characteristics associated ($p < 0.10$) with ADHD status were entered in the model as covariates. Interactions among the predictor and covariates were tested; if interaction terms were not significant, a model without the interaction term was used to fit the data and inferences were based on the final model. Odds ratios (OR) and 95% confidence intervals (CI) for abstinence were calculated to estimate the likelihood of abstinence of the two ADHD symptom subtypes using smokers with No ADHD as the referent group.

In further analyses, we again applied the mixed effects model where symptom scores for IN and HI were entered as continuous variables. Odds ratios and 95% confidence intervals associated with the covariates in each of the models tested were obtained. PROC GENMOD in SAS (SAS 9.1.3) was used to estimate and test the model.

Results

Participant characteristics

Overall, 52% of the sample was male; the proportions of males varied by ADHD status; males were fewest in the No ADHD group and highest among those with HI+/-IN (linear trend $p=0.06$); no significant differences were observed on age, race/ethnicity, marital status, education, or occupation. On the smoking variables, no significant differences by ADHD status were observed on age of smoking onset, age of smoking regularly, frequency of past quit attempts, number of cigarettes smoked, confidence in ability to quit smoking, nor on the biological indicators of tobacco use, i.e., expired carbon monoxide, and serum cotinine. The mean FTND score overall was 5.22 (s.d.=2.04); it varied by ADHD status at borderline significance ($p<0.10$) but not in pair-wise comparisons ($ps<0.10$). For history of major depression, the proportions with positive histories were similar in smokers with no ADHD and HI+/-IN and highest among the IN subgroup (19.7%, 21.7%, 55.4%, respectively, $p=0.005$), and the difference between the ADHD-IN and the ADHD-HI+/-IN subgroups was significant ($p=0.02$). For past alcohol dependence, smokers with no ADHD and the ADHD-IN subgroup showed similar proportions, whereas the subgroup with HI+/-IN reported the highest prevalence (13.7%, 10%, 30.4%, respectively, $p=0.07$); the difference between the two ADHD subtypes was borderline significant ($p=0.10$).

Abstinence rates

Quit rates during the eight-week treatment were consistently lower among smokers with ADHD symptoms compared to those without ADHD symptoms (Figure 1A). Based on the mixed effects model, the odds of abstinence from smoking in the total ADHD group (ADHD-IN and ADHD-HI+/-IN combined) was significantly lower (OR=0.54, 95% CI=0.32-0.99) than that in No ADHD group.

Breakdown of the ADHD group by subtype revealed a more complicated picture (Figure 1B). ADHD-IN smokers showed similar abstinence rates immediately after quit day (Week 1) compared to the group without ADHD; a drop in quit rates one week later; and, uniquely among the study groups, stability in quit rates through the end of treatment (EOT), producing abstinence rates during Weeks 4 to 8 that increasingly converged with those of smokers without ADHD. At the EOT, the proportion of abstainers among ADHD-IN smokers was virtually identical to those with ADHD (55% vs. 54%, respectively). The ADHD-HI+/-IN subgroup, on the other hand, showed lower quit rates throughout the treatment period compared to smokers without ADHD; in effect, the differences observed between smokers with or without ADHD symptoms (see Figure 1) had occurred only in the presence of HI.

To test for statistical significance, the mixed effects analysis model comparing the longitudinal trend in abstinence rates throughout the eight-week study was applied. The main predictor variable was ADHD status, with the No ADHD subgroup as the reference, and the baseline variables that were associated with ADHD status ($p<0.10$, see Table 1) entered as covariates. This analysis supported our hypotheses: 1) abstinence rates of smokers with IN were not significantly different from abstinence rates among smokers with No ADHD (OR=0.74, 95% CI=0.36-1.51); and 2) abstinence rates among smokers with HI+/-IN were significantly lower compared to smokers with no ADHD (OR=0.40, 95%

CI=0.19-0.82). The analysis showed a significant effect of time (weeks in study) ($f_2=97.56$, $df=1$, $p<0.001$), and a significant main effect of gender ($f_2=4.68$, $df=1$, $p=0.03$) indicating a lower probability of smoking abstinence among females than males (OR=0.74, 95% CI=0.57-0.97). No significant main effect of FTND, history of major depression, past alcohol dependence, nor of interaction among the predictors, was observed. We also tested the study hypotheses without assuming that dropouts were non-abstainers, in effect, assuming that dropping out occurred randomly. The data analysis showed similar trends as the categorical analysis of ADHD status, although the difference in abstinence rates among the HI+/- subgroup and those with no ADHD was smaller and not statistically significant (OR=0.60, 95% CI=0.25-1.29). This statistical outcome is not surprising given the reduced samples when dropouts are excluded in the analysis.

Analysis wherein IN and HI were entered as continuous variables failed to show a significant effect of either variable on the trend in weekly abstinence rates ($p=0.23$ and $p=0.26$, respectively). Juxtaposed against results from the analysis of ADHD status as a categorical variable, the latter finding could be suggesting that the adverse influence on abstinence of HI occurs only at high levels of those symptoms and/or that a threshold level exists for detecting the adverse effect of HI.

Retention, medication compliance, and adverse events

The number of clinic visits attended (equivalent to the number of counseling sessions), amount of study medications used, and the occurrence of side effects did not vary by ADHD status. The proportion of participants who completed all clinic visits during the eight-week study was 60.7% (354/583). The median survival time in all the study groups was six weeks. The mean number of weeks of remaining in the study were 4.93, 4.50 and 3.96 for the No ADHD group, ADHD-IN group, and ADHD-HI+/-IN group, respectively ($p>0.10$). Among 504 participants who returned to the study through the first two weeks, the mean number of bupropion pills (22.9 s.d.=3.5) and the mean number of nicotine patches (8.0, s.d.=1.9) used did not vary among the three comparison groups (both $ps>0.35$); further analysis based on study completers only did not indicate differences by baseline ADHD symptom type. The most commonly reported adverse events were: sleep disturbance (37.9%), dizziness (36.5%), agitation (27.1%), skin rash (22.5%), headache (20.9%), and nausea (19.4%). The mean number of adverse events per participant was 2.95 (s.d.=2.3) and did not differ by ADHD status (all $ps>0.50$).

Discussion

Smokers with significant levels of ADHD symptoms showed lower weekly abstinence rates when compared to smokers without ADHD symptoms. Disaggregating the ADHD-affected smokers by ADHD-IN and ADHD-HI+/-IN subtype revealed that the pattern of lower abstinence rates occurred mainly when HI symptoms were present. These findings must be interpreted in light of the fact that all participants were treated with bupropion and nicotine patch. The subgroup with HI symptoms was least able to achieve abstinence during the study. Perhaps the treatments failed to adequately protect these smokers against the exacerbation of HI symptoms as they tried to stop smoking. In a study that examined effects of overnight smoking abstinence, response inhibition and attentional control were disrupted in smokers with ADHD but not among smokers unaffected by ADHD; interestingly, craving and withdrawal symptoms did not differ between smokers with or without ADHD (McClernon, Kollins, Lutz, Fitzgerald, Murray et al, in press). Alternatively, following observations of nicotine-induced increases in response inhibition and impulsivity (Bekker et al, 2005; Blondel et al, 1999; Olausson, Ericson, Löf, Engel, Söderpalm, 2001), perhaps the study medications either alone or in combination exacerbated or heightened sensations that disproportionately decreased resistance to smoking cues among highly impulsive smokers.

The favorable treatment response among smokers with IN symptoms is compatible with known benefits of nicotine on attention, noted above, and has neurobiological plausibility. Both nicotine and bupropion enhance levels of dopamine and epinephrine (Benowitz, 1988; Stahl, Pradko, Haight, Modell, Rockett et al, 2004) which are implicated in problems of inattentiveness (Volkow, et al, 2007). Of additional interest, the pattern of abstinence rates among smokers with IN symptoms --- initially lower quit rates followed by persistent abstinence through the EOT (Figure 1B), is analogous to the finding of symptom improvements only after four weeks of bupropion treatment in patients with ADHD (Wilens et al, 2001). The delayed response could be a signal that longer pre-cessation bupropion treatment than the standard one week duration is indicated for smokers with IN symptoms.

No difference by ADHD status (Table 1) was observed on demographic or smoking parameters; however, past major depression was most frequent among smokers with IN and past alcohol dependence was most frequent among smokers with HI symptoms. A greater responsiveness to the anti-depressant properties of nicotine and bupropion among those with past major depression might have helped to increase abstinence among smokers with IN. The higher frequency of past alcohol dependence among smokers with HI symptoms is consistent with the observation that HI but not IN symptoms predicted future alcohol use in a sample of adolescent boys (Burke, Loeber, Lahey, 2001) and the related findings that: 1) HI but not IN accounted for an observed comorbidity between ADHD and cocaine dependence (Saules, Pomerleau, Schubiner, 2003) and, 2) impulsivity is frequently associated with substance use (as reviewed in Doran, McChargue Spring, VanderVeen, Cook JW, Richmond M. 2006). The convergence of HI, nicotine dependence, and alcohol/drug dependence may be pointing to a particularly vulnerable subgroup deserving of increased clinical research attention.

We acknowledge several limitations of our study. First, because we administered two medications and did not have an un-medicated comparison group, the natural trends in abstinence rates by ADHD status, as well as the precise effects of one or the other medication, or both together, on abstinence rates and on potential mediators such as withdrawal symptoms and post-quit changes in levels of IN or HI, according to baseline ADHD symptoms states remain to be known. Second, we did not obtain information regarding childhood onset of symptoms and impairment in multiple life settings, which are essential features of the diagnosis. We also did not obtain confirmatory information from significant others or other “witnesses” to participants’ self-reports, a standard method for determining reliability of externalized behaviors indicative of HI. These limitations prevent us from assuming that we had identified clinically diagnosable cases of ADHD. Third, although the total sample for this study was large, the number of persons with significant ADHD symptomatology was small, diminishing the study's power to investigate other differences. A larger sample might also have revealed interaction effects involving the covariates, such as gender, since ADHD is more common among males, or major depression, which was more common among smokers with IN symptoms. Fourth, our analysis lacked information on long-term abstinence; because a high risk of relapse characterizes most smoking cessation attempts, information on longer-term outcome, at the minimum six months after quit day, is more reliable (Hughes, Keely, Niaura, Ossip-Klein, Richmond, Swan, 2003). Although one-year information was available from the abstainers in this study, the number of participants who provided such data and the complexity of the protocol (randomized assignment to four treatment conditions) did not yield an adequate sample for long-term analysis by ADHD status. Finally, multiple exclusion criteria required by the ethics of research and the high level of motivation implied by willingness to enter a long-term study, do not permit generalization of study findings to smokers who do not meet those characteristics. More research with adequate and controlled samples, generalizable measures of ADHD, and the appropriate longitudinal design is desirable.

Conclusion

In an open treatment study with combined bupropion and nicotine patch, smokers with elevated HI symptoms at baseline achieved abstinence rates that were significantly lower compared to smokers with no ADHD symptoms. By contrast, smokers with IN symptoms seemed to derive treatment benefit, achieving abstinence rates similar to smokers with no ADHD symptoms. To increase smoking cessation rates among smokers with symptoms of ADHD, treatments matched to the predominance of inattention or hyperactivity/impulsivity may be required. The suggestion of different treatment response by ADHD symptom subtype supports speculations that the subtypes represent distinct processes and implies the need for specific treatment approaches. That both nicotine dependence and ADHD are early onset disorders adds significance to further elucidation of how the conditions are related; the knowledge gained could be useful for early prevention of either one or both conditions.

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Figure 1. Abstinence rates (abstainers/all participants) during Weeks 1 to 8 by Attention Deficit Hyperactivity Disorder (ADHD) symptom status

A) Inattention and Hyperactivity/Impulsivity Combined (ADHD) versus No ADHD ($p < 0.01$); B) ADHD-Inattention only (IN) versus No ADHD ($p = 0.41$); ADHD-Hyperactivity (HI) with or without Inattention (HI+/-IN) versus No ADHD ($p = 0.01$).

Table 1

Comparison of smokers by Attention Deficit Hyperactivity Disorder (ADHD) symptom status

Variable	ADHD Symptom Status			P
	(a) No ADHD (N=540)	(c)(b) Hyperactivity/Impulsivity with(N = 20) (N=11) or without Inattention (N=12)		
	Mean (S.D.) or %	Mean (S.D.) or %	Mean (S.D.) or %	
Age, in years	41.4 (10.7)	40.0 (9.0)	41.9 (12.0)	n.s.
Gender (% male)	50.9	60.0	69.6	0.06 ¹
Race/ethnicity				
White	61.1	60.0	52.2	n.s.
Black	20.0	30.0	21.7	
Hispanic	12.2	10.0	21.7	
Asian + other	6.7	0.0	4.3	
Marital Status				
Never	40.7	45.0	30.4	n.s.
Former	21.1	15.0	26.1	
Married	38.1	40.0	43.5	
Education				
College or more	77.8	80.0	91.3	n.s.
High School or less	22.2	20.0	8.7	
Confidence in ability to quit smoking	7.9 (1.9)	6.9 (2.2)	7.0 (2.2)	n.s.
Number of cigarettes smoked daily	22.1(14.5)	20.1 (9.9)	19.1 (6.1)	n.s.
Carbon monoxide at baseline	16.4(8.7)	15.3 (7.2)	15.4 (6.6)	n.s.
Age first smoked a cigarette	15.4(3.6)	16.2 (3.5)	14.7 (4.1)	n.s.
Age began smoking daily	17.4(3.8)	18.2 (4.1)	17.7 (4.7)	n.s.
Fagerstrom Test Nicotine Dependence	5.2(2.0)	5.6 (2.1)	6.0 (2.0)	.10 ² a=b=c
Past Major Depression				
Absent	80.4	45.0	78.3	.005 ³
Present	19.6	55.0	12.7	
Alcohol Dependence history				
Absent	86.3	90.0	69.6	0.07 ⁴
Present	13.7	10.0	30.4	

¹ fi linear=3.60, df=1, p=0.06² F=2.32, df=2/580; p=0.10³ 22 fi =14.59, df=2, p=0.005; b vs c fi =5.07, df=1, p=0.02⁴ 22 fi =5.36, df=2, p=0.07; bvs. c fi =2.70, df=1, p=0.10