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Effects of Smoking Abstinence, Smoking Cues and Nicotine Replacement in Smokers with Schizophrenia and Controls

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Abstract

The mechanisms underlying the low smoking cessation rates among smokers with schizophrenia (SS) are unknown. In this laboratory study, we compared the responses of 21 SS and 21 non-psychiatric controls (CS) to manipulations of 5-hour smoking abstinence, transdermal nicotine replacement (0, 21 and 42 mg), and *in vivo* smoking cues. Results indicate that SS were more sensitive than CS to the effects of acute abstinence on CO boost, but not more sensitive to the effects of abstinence on urge levels or withdrawal symptoms. SS and CS did not differ in urge response to in vivo smoking cues, but SS were less consistent in their reactions. These findings suggest that heightened sensitivity to the effects of abstinence on smoke intake may partially account for the low cessation rates experienced by SS, but other potential mechanisms should be explored using behavioral laboratory models.

Keywords

schizophrenia; smoking; nicotine dependence; comorbidity; craving; cue reactivity

Introduction

People with schizophrenia are three times more likely to initiate smoking and five times less likely to quit smoking than people in the general population (de Leon and Diaz, 2005). Cessation rates for smokers with schizophrenia (SS) appear limited even among those who are motivated to quit smoking and enroll in supportive treatment programs. For example, 0–19% of SS in smoking treatments that combined access to behavioral treatment with transdermal nicotine or bupropion were abstinent at the 6- or 12-month follow-up (Addington, el-Guebaly, Campbell, Hodgins, & Addington, 1998; Evins, Cather, et al., 2005; Evins et al., 2007; George

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et al., 2000; George et al., 2002; Ziedonis & George, 1997), compared to 21–35% of non-psychiatric heavy smokers enrolled in comparable or less-supportive programs (Richmond & Zwar, 2003; Shiffman et al., 2005; Transdermal Nicotine Study Group, 1991).

Both biological and environmental factors could contribute to a lower likelihood of smoking cessation in SS. Inadequate support for quitting and lack of interest in other reinforcing activities may reduce motivation or undermine quit attempts in these smokers (Lucksted, Dixon, & Sembly, 2000; Spring, Pingitore, & McChargue, 2003). In addition, SS may have more trouble quitting if they experience more severe effects of abstinence on affect due to illness-related abnormalities in dopaminergic transmission (Paterson & Markou, 2007). For example, nicotine withdrawal increases intracranial self-stimulation (ICSS) reward threshold, which is attenuated by bupropion (Epping-Jordan, Watkins, Koob, & Markou, 1998; Paterson, Balfour, & Markou, 2007). Heightened sensitivity to the effects of nicotine withdrawal on negative affect may reduce the abilities of SS to maintain smoking abstinence. Like other smokers, SS report that they smoke to reduce negative affect (Esterberg & Compton, 2005; Tidey & Rohsenow, 2007). However, there has been little research on the effects of abstinence on negative affect in these smokers (Tidey & Williams, 2007).

Smoking urge severity is a predictor of smoking cessation failure in smokers without psychiatric illness (e.g., Killen & Fortmann, 1997; Shiffman et al., 1997; West, Hajek, & Belcher, 1989), and the neurobiology of schizophrenia would suggest that SS may experience higher abstinence- or cue-elicited urge levels than other smokers. Nicotine and nicotine-associated stimuli (cues), increase mesolimbic DA release (Balfour, Wright, Benwell, & Birrell, 2000; Di Chiara, 2000; Di Chiara & Imperato, 1988). Repeated exposure to nicotine results in heightened neuronal DA release, produces locomotor sensitization, and may increase the motivational and appetitive effects of nicotine-associated stimuli (Balfour 2004; DiFranza & Wellman, 2005). Because schizophrenia is associated with intrinsically-enhanced mesolimbic DA function (Knable and Weinberger, 1997), people with schizophrenia may be particularly reactive to nicotine and smoking cues (Chambers, Krystal & Self, 2001).

In testing this hypothesis, one study that found that SS and equally-dependent smokers without psychiatric illness (CS) did not differ in urge response to smoking cue images (Fonder et al., 2005). However, images are generally less effective than *in vivo* cues at increasing urge levels (Shadel, Niaura, & Abrams, 2001), which may have reduced effect sizes in that study. Another study found that the effects of *in vivo* cues on smoking urge levels in SS appeared similar to those of non-psychiatric smokers, but lacked a concurrent matched control group (Tidey, Rohsenow, Kaplan, & Swift, 2005b). Therefore, one aim of this study was to directly compare reactivity to *in vivo* cues in SS and CS.

Controlled comparisons of the effects of abstinence, cues and nicotine replacement in SS and CS may help to clarify the degree to which these factors contribute to ongoing smoking in SS. Thus, the aims of the current study were: (1) to compare the effects of abstinence on unelicited smoking urges, nicotine withdrawal-related negative affect, and smoking behavior in SS and CS, (2) to compare the effects of transdermal nicotine on these measures, and (3) to compare reactivity to *in vivo* cues under non-abstinent, abstinent and nicotine replacement conditions in SS and CS.

Methods

Participants

Participants were recruited from the community. All were required to be 18 or older, to have smoked at least 20 cigarettes per day for at least the past year and to have a Fagerström Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker & Fagerstrom, 1991) score of at least 6. The FTND has good internal consistency and acceptable test-retest reliability in SS (Weinberger et al., 2006; Yang, McEvoy, Wilson, Levin, & Rose, 2003). The Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 1994) was used to confirm diagnoses of schizophrenia or schizoaffective disorder in SS and to rule out current Axis I disorders in CS. Participants were excluded for severe conceptual disorganization, disorientation or uncooperativeness, lack of competence to sign the informed consent, positive urine drug or pregnancy tests, positive breath alcohol at any visit, or use of medications that might affect smoking behavior or urges. Other medications were permitted as long as doses had been stable for at least 2 weeks. Procedures were approved by the institutional review boards involved. Twenty-seven SS and 24 CS were enrolled. Six SS and 3 CS withdrew before completing the study, leaving data from 21 SS and 21 CS.

Design overview

Participants underwent an initial visit for the collection of individual difference measures. Then, participants completed 8 sessions in which cue reactivity and smoking behavior measures were collected under 4 conditions: non-abstinent + 2 placebo transdermal patches, 5-h abstinent + 2 placebo patches, 5-h abstinent + 2 patches that delivered a total of 21 mg nicotine, and 5-h abstinent + 2 patches that delivered a total of 42 mg nicotine. Nicotine and matching placebo patches (GlaxoSmithKline, Parsippany, NJ) were applied under double-blind conditions. The non-abstinent sessions were presented first to facilitate acclimation to study procedures. Dose order in the remaining sessions was counter-balanced across participants. Sessions were separated by at least 48 hours. Two replications of each condition were performed and averaged to reduce variability. Participants received $400 for completing the study.

Individual Difference Measures

Information was collected on demographic variables, smoking histories, and current psychiatric symptoms (SS only). Readiness to change smoking was measured using the stages-of-change algorithm (DiClemente et al., 1991), with the modification suggested by Etter and Sutton (2002), to classify participants into the precontemplation stage, contemplation stage, or preparation stage. Psychiatric symptoms (SS only) were evaluated using the Positive and Negative Syndrome Scale (PANSS; Kay, Fizbein, & Opler, 1987). The FTND was used to assess nicotine dependence. During this visit, participants practiced completing urge and nicotine withdrawal symptom measures on the computer and practiced smoking using the topography equipment.

Laboratory Procedures

A schema depicting the laboratory sessions is shown in Figure 1. Participants provided breath samples for the assessment of carbon monoxide (CO) levels upon arrival for each session (Smokerlyzer, Bedfont Scientific Ltd., Kent, UK). At the first session, participants also provided saliva samples for cotinine analysis (Salimetrics, LLC, State College, PA). A trained interviewer used the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham, 1962) to assess psychiatric symptoms in SS before each session. Next, transdermal patches were applied to participants' upper arms (one per arm). Over the next 5 hours, participants were either permitted to smoke freely (non-abstinent + placebo condition) or were not permitted to smoke (abstinent + placebo, abstinent + 21 mg NRT, and abstinent + 42 mg NRT conditions). Participants were under continuous observation except for bathroom and lunch breaks, with CO monitoring to assure compliance with abstinence. Breath CO levels were measured at the end of this period.

Participants then underwent a smoking cue reactivity assessment as described previously (Tidey et al., 2005b). After a 10-min relaxation period, participants completed measures of smoking urge and nicotine withdrawal symptoms. Urge to smoke was assessed using the Questionnaire on Smoking Urges-brief form (QSU-brief; Cox, Tiffany, & Christen, 2001) and the item “How much is your urge to smoke right now?”, rated on a 100 mm visual analogue scale (VAS), with the anchors 0 = “no urge at all” and 100 = “strongest urge you’ve ever had”. Nicotine withdrawal symptoms were measured using the Minnesota Nicotine Withdrawal Scale (MNWS; Hughes and Hatsukami, 1986; 1998). The items included were depression, anxiety, anger/irritability/frustration, difficulty concentrating, restlessness, and increased appetite; the item “insomnia” was omitted as participants did not undergo overnight abstinence. Symptom were rated on 100-mm VAS with the anchors 0 = “not present” and 100 = “severe”. The score provided is the mean of ratings on the six items. Participants then underwent a neutral cues trial and a smoking cues trial similar to that described in detail previously (Tidey et al., 2005b). Neutral cues were a pencil, 25 mm × 65 mm eraser and a small pad of paper, which participants looked at and handled for 4 min. Smoking cues were a lit cigarette of the participant’s preferred brand, a lighter and an ashtray, which participants looked at and handled for 4 min. Participants completed the urge measures after each trial.

After a short break, CO levels were assessed and participants were instructed that they could smoke as little or as much as they wanted for the next 90 min. Cigarettes of the participants’ usual brands were provided by the experimenters, and were smoked using a smoking topography system (CReSS, Plowshare Technologies, Baltimore, Maryland). Smoking topography measures, recorded by the CReSS, included total number of puffs smoked, number of puffs smoked per cigarette, inter-puff interval, total session smoke volume, average puff volume, average puff duration, maximum puff velocity and latency to begin smoking. At the end of the smoking period, participants completed the urge measures, provided a breath sample for CO level assessment, completed the BPRS (SS only), and had their patches removed.

Data analysis

Dependent variables were examined for distributional assumptions and collinearity. Sphericity was intact. Smoke latency and inter-puff interval data were log-transformed to normalize the data. Number of puffs per cigarette and session smoke volumes were collinear with total number of puffs smoked per session (rs ≥ 0.80), so were removed from analyses. Average puff duration was collinear with average puff volume ($r = 0.84$) and was removed. QSU-brief and urge VAS scores were collinear (all rs > .60), so only the single-item urge scores were retained. Analyses used SPSS for Windows 11.5.0. Differences were considered significant when $p \leq .05$.

Group comparisons on demographic and smoking history measures were conducted using independent-samples *t*-tests for continuous variables and chi-square tests for categorical variables. Between-groups one-way analyses of variance tests (ANOVAS) were conducted to compare the groups on pre-session CO levels across sessions and on CO change during the 5-h satiation and abstinence periods (CO #2 minus CO #1 in Figure 1). A one-way ANOVA was used to analyze the effects of Condition on BPRS change scores (post-session total score minus pre-session total score) in SS only.

To compare the effects of abstinence and NRT in SS and CS, mixed-factor ANOVAs were conducted with the factors Group (SS, CS) and Condition (non-abstinent, abstinent + 0 mg NRT, abstinent + 21 mg NRT, abstinent + 42 mg NRT). Dependent variables were unelicited urge level (i.e., urge levels reported after the 10-min rest period), MNWS score, smoking topography measures and CO boost (CO #4 minus CO #3 in Figure 1). Topography data were missing for one CS participant and latency data were missing for 2 SS and 2 CS. Significant interactions were followed by simple effects tests. Effect sizes (η^2) are also provided when $p = .05 – .10$, with $\eta^2 \leq .05$ for small, $\eta^2 = .06 – .13$ for medium and $\eta^2 \geq .14$ for large effect sizes (Cohen, 1988). This study had 80% power to detect medium-sized effects.

To investigate aim 3, we first examined proportions of each group that reacted to cues. Participants were defined as "cue reactors" if their urge level during the smoking cues trial in the non-abstinent sessions exceeded their urge level during the neutral cues trial by at least one point (Fonder et al., 2005). Chi-square tests were conducted to determine whether the proportion of cue reactors differed within the SS and CS groups. T-tests and chi-square tests were used to examine differences between cue reactors and non-reactors within each group. We then conducted 3-factor ANOVAs to examine the effects of Group, Cues (Neutral, Smoke) and Condition on urge levels. These analyses were first performed within all SS and CS, consistent with analytic methods used in most smoking cue reactivity research (e.g., Hutchison et al., 1999; Sayette, Martin, Wertz, Shiffman, & Perrott, 2001; Tiffany, Cox, & Elash, 2000), and then with cue reactors only, to facilitate comparisons with Fonder et al. (2005).

Results

Individual difference measures

There were no significant differences between the groups on any demographic or smoking history measure (see Table 1). Psychiatric symptom levels for SS were similar to those reported previously by other studies in outpatients (e.g., Fonder et al., 2005;George et al., 2000). Pre-session breath CO levels, averaged across the 8 sessions, were significantly higher in SS than in CS (F (1, 40) = 10.39, $p < .01$; Table 1). The 5-hr satiation periods increased CO levels by 26% in SS and 20% in CS (NS). The 5-hr abstinence periods reduced CO levels by 49% in SS and 53% in CS (NS). Among SS, there was no significant effect of condition on BPRS change scores. Pre-session BPRS total scores were 28.13 ± 7.3 and post-session BPRS total scores were 27.09 ± 6.2.

Unelicited urge and nicotine withdrawal symptoms

There was a significant effect of Condition on unelicited urge level (F (3, 120) = 55.14, $p < .001$). Post-hoc tests indicated that urge levels were higher in all abstinent conditions compared to the non-abstinent condition (ps < .05), and that urge levels in the abstinent + 42 mg NRT condition were significantly lower than urge levels in the other abstinent conditions (ps < .05; Figure 2A). The effect of Group on unelicited urge level was not significant. The Group × Condition interaction on unelicited urge level approached significance (F (3, 120) = 2.23, $p = .09$; $\eta^2 = .05$), with abstinence tending to increase urge levels more in CS.

There was a significant effect of Condition on MNWS score (F (3, 120) = 7.90, $p < .001$). MNWS scores were significantly higher in the abstinent + 0 mg NRT and abstinent + 21 mg NRT conditions compared to the non-abstinent condition (ps < .05), and 42 mg NRT reduced MNWS scores to non-abstinent levels (Figure 2B). The effect of Group on MNWS score approached significance (F (1, 40) = 3.09, $p = .09$, $\eta^2 = .07$), with SS tending to have higher MNWS scores under all conditions. The Group × Condition interaction on MNWS score was not significant ($\eta^2 = .02$).

Smoking topography

Means and ANOVA results are shown in Table 2. Significant effects of Group were found on CO boost (Figure 2C), total puffs smoked, inter-puff interval, and puff velocity, with these variables consistently indicating that SS smoked more intensely than CS. There were effects of Condition on CO boost (Figure 2C), puff volume and latency to smoke, and a trend was found for total puffs ($p = .06$, $\eta^2 = .06$). Post-hoc tests indicated that abstinence increased CO boost and number of puffs smoked, and reduced puff volume and latency to smoke (ps < .05). The effect of abstinence on CO boost was significantly reduced by 42 mg NRT and the effect of abstinence on latency to smoke was significantly reversed by 21 mg NRT (ps < .05). There was also a significant Condition × Group interaction on CO boost (Table 2). Post-hoc tests indicated that abstinence increased CO boost to a greater extent in SS than CS (F (1, 40) = 5.01, $p < .05$), but effects of NRT were not significantly different for the two groups (Figure 2C).

Smoking cue reactivity

Twenty SS (95%) and 21 CS (100%) met the definition of "cue reactor" in at least one of the non-abstinent sessions. However, SS were less consistent than CS in their cue reactivity: 11 SS (52%) were cue reactors in both sessions, 9 (43%) were cue reactors in only one session, and one (5%) did not react to cues in either session. In contrast, 19 CS (91%) reacted in both sessions, two (10%) reacted in only one session, and there were no non-reactors. This pattern of response was significantly different for the two groups (X^2 (2, N = 42) = 7.59, $p < .05$). There was no indication that the consistent cue reactors differed from non-reactors within either group on any smoking or demographic variable (ps for all t-test and X^2 comparisons > 0.20).

In analyses that included all participants, there was a significant effect of Cues on urge levels (F (1, 40) = 23.53, $p < .001$), with means indicating that urge scores were higher during the smoking cues trial than during the neutral cues trial. There was a significant effect of Condition on urge (F (3, 120) = 19.61, $p < .001$). Post-hoc tests indicated that abstinence increased smoking urge levels and 42 mg NRT reduced urge levels relative to the abstinent + 0 mg NRT condition (ps < .05; Figure 3). There was also a significant Condition × Cues interaction on urge (F (3, 120) = 16.08; $p < .001$). Post-hoc simple effects tests indicated that effects of cues on urge were significant in the non-abstinent condition (F (1, 40) = 41.40, $p < .001$), were not significant in the abstinent + 0 mg NRT condition, and became significant again in the abstinent + 21 mg NRT and abstinent + 42 mg NRT conditions (F (1, 40) = 6.64, $p < .05$; F (1, 40) = 17.40, $p <.001$, respectively). As shown in Figure 3, NRT reduced urge levels in the neutral cues trial but not in the smoking cues trial.

The main effect of Group on urge level was not significant ($\eta^2 < .01$). The Condition × Group and Condition × Cues × Group interactions approached significance (F (3, 120) = 1.94, $p = .12$, $\eta^2 = .05$; F (3, 120) = 2.11, p = .10, $\eta^2 = .05$, respectively), with means indicating that NRT tended to reduce urge levels during neutral cues trials in CS but not in SS (Figure 3).

Analyses were repeated with the cue reactors only (11 SS, 19 CS). These analyses did not alter the outcomes of the ANOVAs. There were significant main effects of Cues and Condition on urge level (F (1, 28) = 17.95, $p < .001$, F (3, 84) = 34.25, $p < .001$, respectively). There was a significant Condition × Cues interaction (F (3, 84) = 29.26; $p < .001$) with effects of cues significant only in the non-abstinent and abstinent + 42 mg NRT conditions. There was no significant main effect of Group or significant interaction between Group and any other variable on urge level.

Discussion

The results of this study indicate that abstinence increased smoking urge, nicotine withdrawal symptoms and several smoking variables in SS and CS. NRT reduced nicotine withdrawal symptoms and smoking urges and increased latency to smoke in both groups. SS were more sensitive to the effects of abstinence on CO boost but not other variables, and SS were not less sensitive than CS to the effects of NRT. There are a number of points on which we would like to comment.

First, urge levels reported by SS and CS were strikingly similar under the various study conditions. Although few studies have systematically compared urge levels under non-abstinent and abstinent conditions in these groups, Weinberger et al. (2007) recently published a comparison under non-abstinent and overnight-abstinent conditions, with similar findings.

In contrast to their similar urge levels, MNWS scores tended to be higher in SS across conditions. This is not surprising as most of the items included in this measure are associated with schizophrenia (American Psychiatric Association [APA], 1994). However, the fact that abstinence increased, and NRT decreased, MNWS scores in both groups supports the validity of MNWS as a measure of nicotine withdrawal in SS. Group differences on smoking topography indicated that SS smoke more intensely according to several topography measures, consistent with findings that we and others have reported previously (Tidey, Rohsenow, Kaplan, & Swift, 2005a; Williams, Gandhi, Karavidas, & Foulds, 2006).

Abstinence increased urge levels, nicotine withdrawal symptoms and CO boost, and reduced smoking latency and puff volumes in both groups, with SS being particularly sensitive to the effects of abstinence on CO boost. The heightened sensitivity of the smokers with schizophrenia to the effects of abstinence on smoke intake is particularly interesting and it is noteworthy that this effect is greater than we would have predicted from looking at effects of abstinence on urge and MNWS scores in these smokers. Although this dissociation might suggest that the urge and MNWS measures are less valid for SS, the systematic manner in which SS altered their urge and MNWS reports in response to abstinence, cues and NRT argues against this interpretation. Another interpretation is that SS may experience exacerbations in another subjective state, not measured in this study, which in turn leads to increased smoking. For example, abstinence disrupts visuospatial working memory task performance in SS and resumption of smoking reverses this deficit (George et al., 2002; Sacco et al., 2005; but see Evins, Deckersbach, et al., 2005). Another possibility is that SS may be more sensitive to the effects of abstinence on sensorimotor factors associated with smoking (e.g., Brauer et al., 2001). Blood nicotine levels were not collected in this study; their inclusion would have indicated the proportion of nicotine replaced by NRT in these participants and helped to clarify this finding. It should also be noted that the effects of NRT were small in this study, which was powered to detect medium-sized effects. As recently noted by Perkins, Stitzer, & Lerman (2006), the fact that NRT often fails to reduce smoking cue-elicited urge levels in laboratory analogue studies, despite its proven efficacy on smoking cessation, may be related to the fact that many laboratory studies such as this one enroll participants who are not actively attempting to quit smoking during the study.

With regard to smoking cue reactivity, we found that SS were significantly less consistent than CS in their reactivity to cues, but there was no indication that the groups differed in the extent to which cues increased urge levels. Fonder et al. (2005) have also reported that baseline and image cue-elicited urge levels were closely similar in SS and CS. Together, the results of these studies do not support the idea that cues provoke higher urge levels in SS. Both SS and CS in this study were less sensitive to cues during abstinence. Similar findings have been reported in smokers with schizophrenia by Fonder et al. (2005) and in non-psychiatric smokers by others (e.g., Drobes and Tiffany, 1997; Maude-Griffin and Tiffany, 1996). It has been suggested that the endogenous effects of abstinence are more salient than the exogenous effects of cues in heavy smokers (Herman, 1974). Interestingly, NRT reduced urge levels during the neutral cue trials, but not the smoking cue trials. This is consistent with previous findings that NRT appears relatively ineffective against smoking cue-elicited urge levels in non-psychiatric smokers (Tiffany et al., 2000; Waters et al., 2004; Rohsenow et al., 2007).

An unexpected finding was that morning CO levels were higher in SS than CS, despite the groups' similarities in numbers of cigarettes smoked per day, salivary cotinine levels, FTND scores and minutes to their first cigarette after awakening. This difference could result from different diurnal patterning of smoking in these groups, i.e., the SS may have smoked more intensely in the early morning. The fact that group means on minutes to first cigarette of the day were highly similar in this study suggests that the SS were not restricted from smoking in their residences (Steinberg, Williams, Steinberg, Krejci, & Ziedonis, 2005).

Limitations of this study include its focus on acute effects of abstinence and NRT and its use of self-report measures of urge and withdrawal. Future studies could include a broader range of measures, including measures that do not rely on self report (e.g., Waters, Heishman, Lerman, & Pickworth, 2007). The generalizability concern raised by Perkins et al. (2006) could be addressed by incorporating a brief motivational intervention at study onset (e.g., Steinberg, Ziedonis, Krejci, & Brandon, 2004) or by offering modest monetary reinforcement for smoking reductions (e.g., Tidey, Higgins, Bickel & Steingard, 1999; Tidey, O'Neill, & Higgins, 2002). Nevertheless, this study contributes to the literature by demonstrating that SS are more sensitive than CS to the effects of acute abstinence on smoke intake, while not being more sensitive to effects of abstinence on urges and nicotine withdrawal symptoms. Future studies should compare other effects of abstinence in smokers with schizophrenia and controls to clarify this finding.

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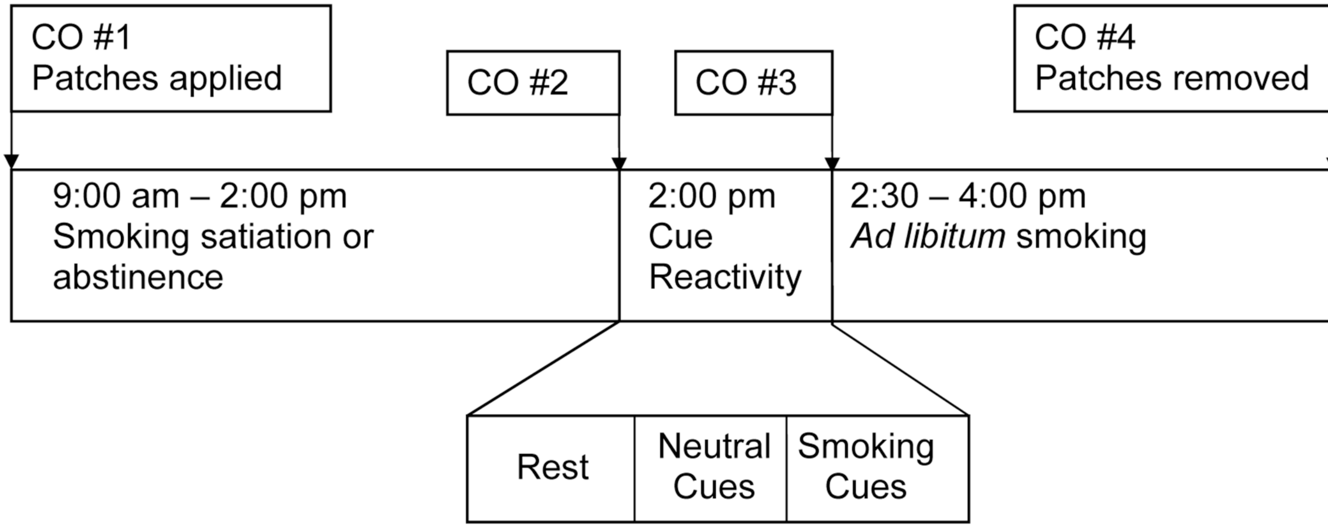

Figure 1.
Timeline of study sessions.

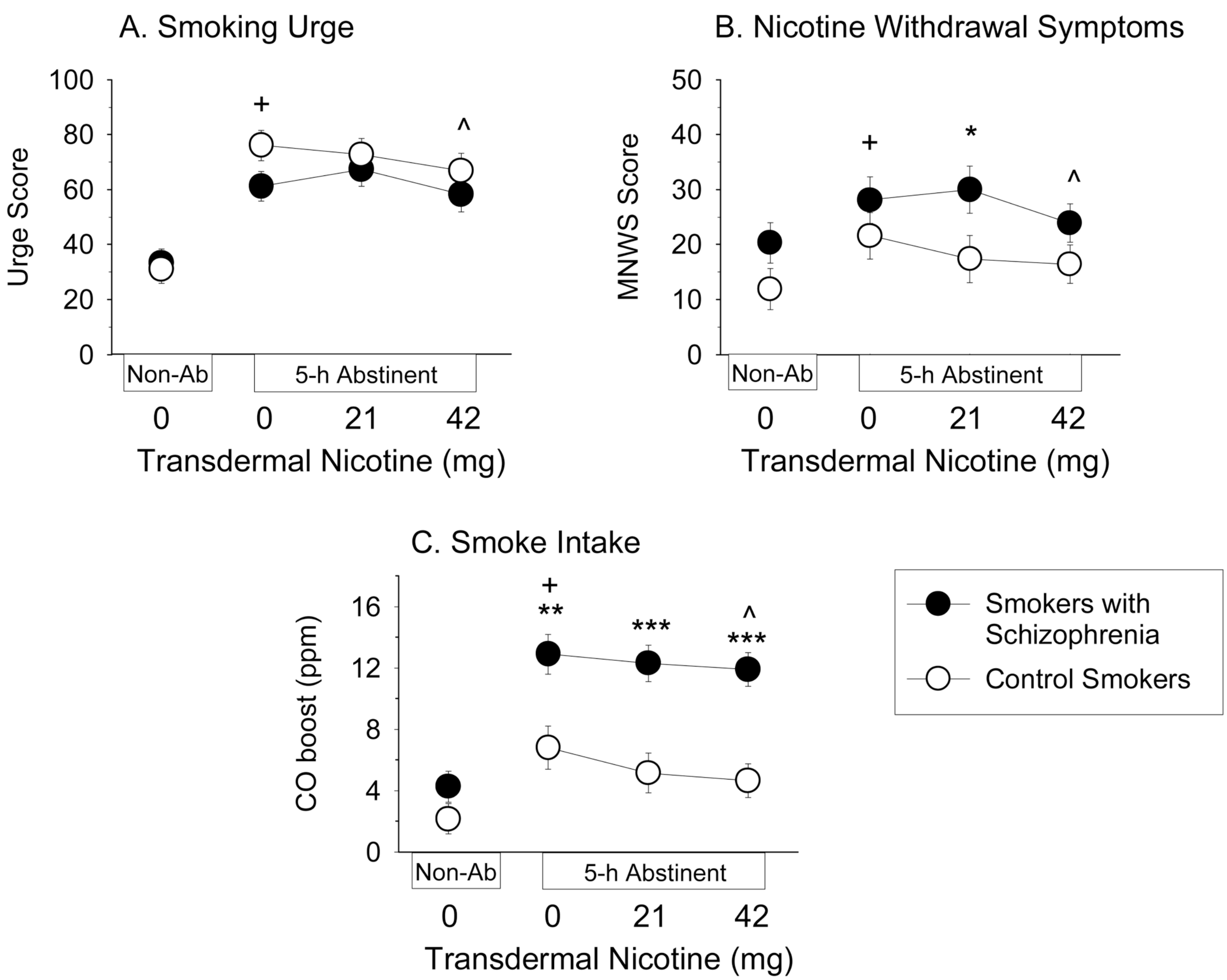

Figure 2.
Effects of 5-hr abstinence and 0, 21 and 42 mg transdermal nicotine (NRT) on (A) unelicited smoking urge levels, (B) nicotine withdrawal symptoms and (C) CO boost in smokers with schizophrenia (n = 21; solid symbols) and equally-heavy smokers without psychiatric illness (n = 21; open symbols). Data points represent *M* ± *SEM*. Plus signs indicate significant differences between the Non-abstinent + 0 mg NRT and Abstinent + 0 mg NRT conditions; carets indicate significant effects of NRT; asterisks indicate significant differences between groups (* p < .05; ** p < .01; *** p < .001).

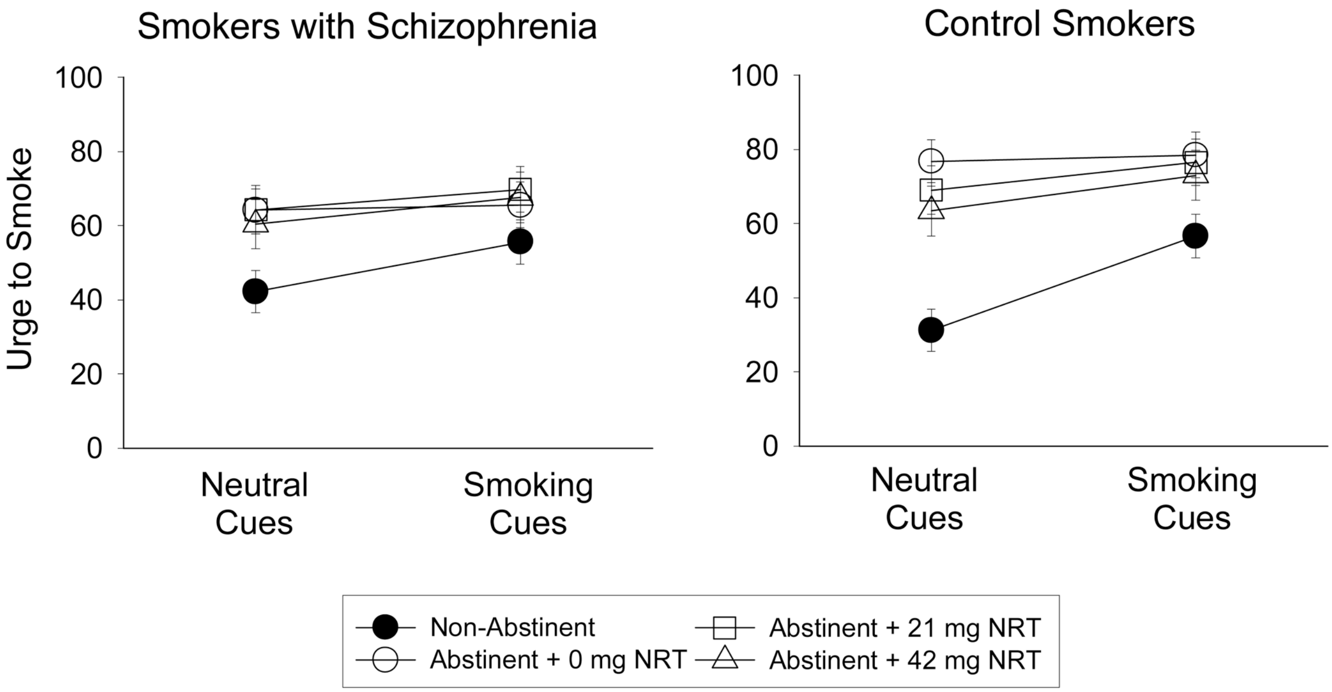

Figure 3.

Effects of 5-hr abstinence and transdermal nicotine (NRT) on urge levels following exposure to neutral cues and smoking cues in (left) smokers with schizophrenia (n = 21) and (right) equally-heavy smokers without psychiatric illness (n = 21). Data points represent *M* ± *SEM*.

Table 1

Demographic and Baseline Smoking Characteristics of Study Participants

	SS (*n* = 21)	CS (*n* = 21)
Age [*M* (*SD*)]	44.1 (7.0)	47.1 (10.4)
Male	14	11
Race	12 W / 2 AA / 7 0	16 W / 4 AA / 1 O
Hispanic ethnicity	2	2
Employed full- or part-time	2	5
Annual income above US$10,000	7	13
≥ 12 years of education	19	18
Cigarettes per day	32.6 (13.6)	31.0 (12.0)
Nicotine dependence (FTND score)	7.7 (1.4)	7.5 (1.4)
Min to first cigarette of the day	5.7 (7.5)	7.8 (9.4)
Years of daily smoking	26.4 (9.2)	31.8 (11.4)
Salivary cotinine level (ng/ml)	367.6 (147.4)	331.3 (167.1)
Pre-session CO level (ppm)	27.1 ± 8.6**	19.8 ± 6.3
Smoking stage of change	12 Pre/9 Con/0 Prep	11 Pre/7 Con/3
PANSS positive scale score	16.7 (4.4)	–
PANSS negative scale score	18.3 (6.8)	–
PANSS general scale score	33.6 (6.6)	–
PANSS total score	68.6 (16.5)	–
Antipsychotic drug class	6 Typ / 10 A / 5 O	–

Abbreviations: SS, smokers with schizophrenia; CS, control smokers; W, white; AA, African-American; O, other; FTND, Fagerström Test of Nicotine Dependence; CO, carbon monoxide; Pre, precontemplation; Con, Contemplation; Prep, preparation; PANSS, Positive and Negative Syndrome Scale; Typ, typical, A, atypical.

** $p < .01$

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Table 2

Smoking measures [*M*(*SD*)] during 90-minute smoking periods.

Measure		Non-Abstinent	Abstinent			Group	Cond	Group × Cond
		0 mg NRT	0 mg NRT	21 mg NRT	42 mg NRT	*F* (1, 39)	*F* (3, 117)	*F* (3, 117)
CO Boost (ppm)	SS	4.3 (4.9)	12.9 (7.5)	12.3 (6.8)	11.9 (5.7)	17.64**	27.69**	5.02**
	CS	2.2 (3.8)	6.6 (4.9)	5.0 (4.2)	4.7 (4.3)			
Total Puffs	SS	59.4 (44.2)	69.7 (58.6)	66.9 (51.7)	70.7 (65.1)	9.18**	2.46†	1.03
	CS	26.2 (22.1)	31.7 (26.9)	27.5 (18.6)	26.9 (18.9)			
Latency to Smoke[a]	SS	135.2 (2.5)	100.3 (3.3)	114.0 (3.2)	79.6 (3.2)	0.11	4.88**	0.79
	CS	158.9 (2.5)	104.2 (3.7)	111.8 (2.6)	92.2 (2.7)			
Puff Volume (ml)	SS	51.7 (16.4)	46.0 (14.5)	45.4 (14.6)	46.6 (14.1)	1.28	3.27*	2.26†
	CS	43.2 (14.6)	41.8 (14.4)	43.6 (16.3)	41.4 (13.9)			
Inter-Puff Interval (s)[a]	SS	21.4 (1.5)	20.4 (1.5)	20.4 (1.5)	20.5 (1.6)	15.14**	0.90	0.88
	CS	35.0 (1.7)	33.6 (1.5)	35.3 (1.6)	32.2 (1.5)			
Puff Velocity (ml/s)	SS	44.2 (9.0)	42.3 (10.0)	42.8 (11.4)	42.5 (10.7)	4.99*	1.24	1.35
	CS	36.7 (7.8)	36.4 (7.5)	36.5 (7.0)	37.4 (8.5)			

Abbreviations: Cond, condition; SS, smokers with schizophrenia; CS, control smokers.

[a] Data were log-transformed prior to analysis. Geometric means and standard deviations are reported.

** $p < .01$,

* $p < .05$,

† $p < .10$