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Effects of Contingency Management and Bupropion on Cigarette Smoking in Smokers with Schizophrenia

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Abstract

Rationale—Individuals with schizophrenia have high smoking-related morbidity and mortality rates and need powerful and innovative smoking cessation interventions.

Objectives—This proof-of-concept study investigated the feasibility and initial efficacy of combining a contingency management intervention with bupropion to reduce smoking in people with schizophrenia.

Methods—Using a double-blind, placebo-controlled, between-groups design, 57 non-treatment seeking participants were randomized to receive 300 mg/day bupropion or placebo. One week later, participants were randomized to a contingency management (CM) intervention in which reductions in urinary cotinine levels were reinforced, or a non-contingent reinforcement (NR) condition in which session attendance was reinforced, regardless of cotinine level. Over the 22-day study period, participants visited the laboratory approximately three times per week to provide urine samples for analysis of cotinine levels, to give breath samples for analysis of carbon monoxide (CO) levels, and to report number of cigarettes smoked per day, nicotine withdrawal symptoms, cigarette craving and psychiatric symptoms.

Results—Cotinine and CO levels significantly decreased during the study period in participants randomized to the CM condition, but not the NR condition. Bupropion did not reduce cotinine levels or increase the efficacy of CM. Cigarette craving and psychiatric symptom levels significantly decreased during the study in all groups.

Conclusions—The results of this study indicate the efficacy and feasibility of this CM intervention for reducing smoking in individuals with schizophrenia.

Keywords

tobacco dependence; nicotine; psychiatric comorbidity; dual diagnosis; smoking cessation; incentives; craving

Introduction

People with schizophrenia are more than three times as likely to smoke as people without psychiatric illness (de Leon and Diaz 2005), are less likely to attempt and achieve smoking

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cessation than other smokers (Kalman et al. 2005; Ziedonis et al. 2008), and have smoking-related morbidity and mortality rates that are two- to three-times higher than those of the general population, resulting in a 25-year shorter lifespan (Brown et al. 2010; Hennekens et al. 2005; Parks et al. 2006; Saha et al., 2007). Among smokers with schizophrenia (SWS) who enroll in pharmacological and psychosocial smoking cessation treatment programs, abstinence rates are about 30% at the end of treatment, declining to about 12% within 6 months post-treatment (e.g., Addington et al. 1998; Chou et al. 2004; Evins et al. 2001; 2005; 2007; George et al. 2000; 2002; 2008). Clearly, powerful and innovative treatment approaches are needed to reduce smoking in this population.

Contingency management (CM) interventions for substance use disorders, which involve providing a tangible reinforcer upon objective confirmation of drug abstinence or another target behavior (Higgins et al. 1994), have long been recognized as effective methods of reducing smoking (e.g., Stitzer and Bigelow 1982; 1985; Tevyaw et al. 2009). Several short-term studies have found that CM interventions reduce cigarette smoking in SWS (Roll et al. 1998; Tidey et al. 1999; 2002). These studies used breath carbon monoxide (CO) levels to monitor smoking behavior, which necessitates frequent breath testing to confirm continuous abstinence due to the short half-life of CO (SRNT 2002). More recently, CM interventions for non-psychiatric smokers have used on-site quantitative analysis of the nicotine metabolite, cotinine, in urine or saliva samples to confirm smoking abstinence or reduction (Heil et al. 2008; Higgins et al. 2004; 2007). This is an important methodological advance because the longer half-life of cotinine (16 h in the general population; SRNT 2002) enables treatment providers to confirm continuous smoking abstinence with considerably less frequent testing than does breath CO, which increases the feasibility of incorporating these interventions into clinical practice.

CM interventions are particularly effective when combined with other treatments for substance use disorders, perhaps because the interventions have complementary effects across individuals, across behavioral mediators of relapse, or on treatment adherence (Budney and Higgins 1998; Carroll and Rounsaville 2007). For example, CM combined with desipramine or bupropion reduces cocaine use more effectively than either treatment alone (Kosten et al. 2003; Poling et al. 2006). Similarly, CM combined with bupropion may reduce cigarette smoking in adolescents more effectively than either treatment alone (Gray et al. 2011). Two studies have examined the combined effects of CM with a pharmacological intervention for smoking in SWS. One short-term study found that CM was highly effective for reducing smoking in SWS, but transdermal nicotine did not increase the efficacy of CM (Tidey et al. 2002). A longer smoking cessation treatment study found that neither CM alone nor CM combined with transdermal nicotine increased biochemically-confirmed quit rates relative to a self-quit control group (Gallagher et al. 2007); however, in that study, CO levels were measured only once per week, which is too infrequent to confirm continuous abstinence. To our knowledge, no previous study has investigated the efficacy of bupropion in combination with a CM intervention for SWS, but previous double-blind, placebo-controlled studies have found that bupropion significantly reduces smoking and is well tolerated by SWS (Evins et al. 2001; 2005; George et al. 2002).

This study evaluated the separate and combined effects of bupropion and a contingency management procedure for reducing smoking behavior in SWS. Smoking reductions were reinforced in addition to abstinence because reinforcing successive approximations of the goal behavior has been found to increase the effectiveness of CM interventions for smoking, particularly in heavy smokers (Lamb et al. 2005; 2010). A 3-week study period was selected because abstinence within the first two weeks of a smoking intervention has been repeatedly found to predict longer-term response (e.g., Dale et al. 2001). Participants were not required to be seeking treatment for smoking but only to have some interest in quitting, because this

motivation level is typical of this population (e.g., Steinberg et al. 2004; Tidey & Rohsenow 2009b). We hypothesized that the combined bupropion + CM intervention would reduce smoking more than either the placebo + CM or bupropion + non-contingent reinforcement (NR) interventions, and that all three active interventions would reduce smoking more than the placebo + NR intervention.

Methods

Participants

Participants were recruited using advertisements posted in the surrounding community and at an outpatient clinic at a local VA medical center. Participants were eligible if they had a diagnosis of schizophrenia or schizoaffective disorder as confirmed by the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I; First et al. 1997), were at least 18 years of age, smoked at least 20 cigarettes per day, had scores of 6 or more on the Fagerström Test for Nicotine Dependence (FTND; Heatherton et al. 1991), had been clinically stable on psychoactive medications for at least 2 months prior to enrollment, and had scores of 4 or more on the Contemplation Ladder (Biener and Abrams 1991), indicating some interest in quitting smoking. Exclusionary criteria included pregnancy, positive breath alcohol level or urine drug toxicity test, medication or medical condition contraindicating the use of bupropion, and very high psychiatric symptom severity that would preclude the completion of study procedures (ratings of 6 or higher on the excitement, uncooperativeness, conceptual disorganization, tension, posturing, disorientation or emotional withdrawal items from the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham 1962). All participants provided written informed consent to participate and passed a quiz that assessed their understanding of critical elements of informed consent.

Procedures

This study used a double-blind, placebo-controlled, between-groups design, in which individuals were randomized into 1 of 4 treatment conditions: CM plus bupropion (BUP), CM plus placebo (PLA), NR + BUP or NR + PLA. Participation required 9 study visits over a 22-day period. At the first visit, baseline socio-demographic, psychiatric symptom and smoking history information were collected, baseline urinary cotinine and breath CO levels were measured, and participants completed baseline measures of craving and nicotine withdrawal symptoms (all measures are described below). At the end of the first visit (Week 1), participants were randomized by coin toss to medication condition and received a one-week supply of BUP or PLA, under double-blind conditions, in 7-day morning/evening divided medication organizers. One week later, at the second study visit (Week 2), participants were asked about their past-week medication compliance, medication side effects and number of cigarettes smoked per day. Participants provided urine and breath samples for cotinine and CO analysis and completed the measures of cigarette craving and nicotine withdrawal symptoms. Participants were then randomized by coin toss into either the CM or NR condition (described below).

Participants returned to the laboratory three times per week for the next 2 weeks (Weeks 3 and 4). At each visit, urine and CO samples were analyzed, the measures of cigarette craving and nicotine withdrawal symptoms were completed, medication compliance and side effects were assessed and medication organizers were refilled. Once per week, psychiatric symptoms, movement disorders and number of cigarettes smoked per day in the past week were assessed. On the last day of participation, the Contemplation Ladder was re-administered to determine whether study participation had altered participants' interest in smoking cessation. Participants who expressed interest in smoking cessation were referred to local agencies and given self-help resources from the American Lung Association.

Measures

Schizophrenia symptom levels were assessed using the Positive and Negative Syndrome Scale (PANSS; Kay et al 1987). Movement disorders associated with antipsychotic medication use were assessed using the Motor Examination section of the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn & Elton, 1987) and the Abnormal Involuntary Movements Scale (AIMS; NIMH 1976). The primary measure of smoking was level of the nicotine metabolite, cotinine, which was analyzed on-site using enzyme immunoassay tests (EMIT; Microgenics Corporation, Fremont, CA, USA), run on a Roche Cobas Mira Plus chemistry analyzer (distributed by High Technology, Inc., Walpole, MA, USA). Two secondary measures of smoking were also obtained: breath carbon monoxide (CO) levels, analyzed using a Smokerlyzer ED50 CO monitor (Bedfont Scientific Ltd., Kent, UK), and number of cigarettes smoked per day (CPD) during the past week, collected using a TimeLine Follow-Back (TLFB) interview (Sobell and Sobell, 1992; DeMarce et al., 2007).

Cigarette craving was measured using the Questionnaire on Smoking Urges-brief form (QSU-brief; Cox et al., 2001), on which items are rated on scales from 1 (strongly disagree) to 7 (strongly agree). Nicotine withdrawal symptoms were measured using the Minnesota Nicotine Withdrawal Scale (MNWS; Hughes and Hatsukami, 1986), on which 7 withdrawal-related mood symptoms (depression, insomnia, irritability/frustration/anger, anxiety, difficulty concentrating, restlessness and increased appetite) are rated on scales from 0 (not present) to 4 (severe). The QSU and MNWS are valid and sensitive to smoking abstinence in SWS (Tidey et al. 2002; 2008; Weinberger et al., 2006).

Medication and CM Interventions

Twice-a-day medication organizers were filled with bupropion-SR 150 mg (Zyban, GlaxoSmithKline, Research Triangle Park, North Carolina, USA) or matched placebo tablets (University of Pennsylvania Investigational Drug Service, Philadelphia, PA, US), by an investigator who did not have contact with study participants, and were dispensed to participants under double-blind conditions. The medication organizers held one 150-mg bupropion or placebo tablet per day on days 1–3 and two 150-mg bupropion or placebo tablets per day starting on day 4 until day 22, when medication was discontinued. Participants were asked to bring their medication organizers to every study visit and to keep any missed or skipped doses in the tray for the research assistant to record. Medication was initiated a week prior to the CM procedure so that levels would reach steady-state by the time the CM procedure was implemented.

Those randomized to the NR condition received a \$25 store gift card for attending study sessions and providing urine samples at each visit, regardless of cotinine analysis results. Those randomized to the CM condition received a \$25 gift card payment for attendance, and could also earn cash bonuses for reducing their urinary cotinine levels by 25% compared to the previous sample, or for maintaining cotinine levels below an abstinence threshold of 80 ng/mL (Higgins et al., 2004; 2007). The contingent payments for smoking reductions began at \$25 per sample and increased by \$5 for each consecutively reduced or abstinent sample. Non-reduced cotinine results or missed visits resulted in no payment for that visit and reset the value of the contingent payment for the next reduced or abstinent sample to \$25, but two consecutive reduced or abstinent samples restored the value to the pre-reset level (Heil et al., 2008).

Data analysis

Baseline characteristics of the study groups were compared using 2×2 (Medication condition x Contingency condition) analysis of variance tests (ANOVAs) for continuous

variables and chi-square tests for categorical variables. Frequencies of adverse events were compared in the BUP and PLA groups using chi-square tests. Mixed factor $2 \times 2 \times 4$ ANOVAs were used to test the effects of Medication condition (BUP vs. PLA), Contingency condition (CM vs. NR), and Week (study weeks 1–4) on cotinine levels, breath CO levels, CPD, QSU, MNWS, PANSS, AIMS and UPSDRS scores. For these analyses, measures collected multiple times per week (cotinine, CO, QSU and MNWS) were averaged to provide a weekly measure for each. Week 1 data comprised baseline data collected at Session 1 (i.e., prior to either intervention), Week 2 data comprised those collected at Session 2 (i.e., after one week of medication only), Week 3 data comprised those averaged across Sessions 3, 4, 5 and 6 (i.e., the first week of the combined interventions) and Week 4 data comprised those averaged across Sessions 7, 8 and 9 (the second week of the combined interventions). Following intent-to-treat principles, all participants who were randomized to both interventions were included in analyses, with baseline values imputed for missing values. In addition, 2×2 ANOVAs were used to analyze the effects of Contingency condition and Medication condition on total number of cotinine samples meeting the smoking reduction criterion. Contemplation Ladder scores collected at enrollment and the last session were compared using $2 \times 2 \times 2$ (Medication condition $\times$ Contingency condition $\times$ Pre-Post) mixed-factor ANOVAs. Significant interactions were followed by simple effects tests. Differences were considered significant when $p \leq .05$. Given the exploratory nature of this study, Bonferroni adjustments on confidence intervals were not conducted and effect sizes (η^2) are provided, with $\eta^2 \leq .05$ for small, $\eta^2 = .06 - .13$ for medium and $\eta^2 \geq .14$ for large effect sizes (Cohen, 1988). Analyses were conducted using PASW Statistics 17.0 for Windows (SPSS, Inc.).

Results

Baseline participant characteristics

A total of 159 potential participants were screened for this study, 64 were eligible to enroll, 57 enrolled and were randomized to medication condition and 52 were randomized to both the medication and contingency conditions. Of the 5 individuals who were randomized to medication condition but discontinued study participation prior to randomization to contingency condition, 4 had been randomized to BUP and all 4 of these individuals reported that they discontinued study participation due to medication side effects or another concern about the medication. The reason for study discontinuation in the participant who was randomized to PLA is unknown because that participant was lost to contact.

Demographic and baseline characteristics of study participants are shown in Table 1. Participants were on average 45.1 ± 8.2 years of age, 71% male, 75% White, smoked 27 ± 12 cigarettes per day and had Contemplation Ladder scores of 6.5 ± 2.6 , indicating that they planned to quit smoking within the next 6 months. Participants were taking a variety of antipsychotic medications, including quetiapine (37%), olanzapine (21%), risperidone (19%), aripiprazole (10%), clozapine (8%), fluphenazine (8%), and haloperidol (6%), and the groups did not differ on antipsychotic medication type. Psychiatric symptom levels were generally mild and similar to those reported by other smoking treatment studies in SWS (e.g., Evins et al., 2007; George et al., 2002; Williams et al. 2010). There were significant differences among groups on PANSS positive and negative symptom scores, with lower PANSS positive symptom scores in those randomized to the NR + PLA group than the CM + PLA or NR + BUP groups and higher PANSS negative symptom scores in the two NR groups relative to the CM + BUP group (Table 1). There were no other differences among the groups on baseline characteristics. Medication compliance was very high, with participants taking $97.4 \pm 5.8\%$ of assigned pills, and there were no differences among groups on rates of medication compliance. Study completion rates were high overall, with 99% of visits completed in the CM + BUP group, 99% in the CM + PLA group, 95% in the

NR + BUP group and 94% in the NR + PLA group. Rates of missing samples were not significantly different among groups.

Smoking Behavior

Analyses of the smoking outcome measures indicated significant main effects of Week on all measures, such that cotinine, CO and CPD levels were significantly lower in weeks 3 and 4 than in weeks 1 and 2 ($F(3, 144) = 10.70, p < .001$; $F(3, 144) = 5.42, p < .01$; $F(3, 144) = 19.06, p < .001$, respectively). Moreover, significant Contingency x Week interactions indicated that those in the CM conditions had lower cotinine, CO, and CPD in weeks 3 and 4 compared to baseline ($F(3, 144) = 6.40, p < .001$; $F(3, 144) = 5.02, p < .01$; $F(3, 144) = 4.63, p < .01$, respectively). Those in the NR conditions reported smoking fewer CPD in weeks 3 and 4 compared to baseline but did not have correspondingly significantly lower cotinine or CO levels (Figure 1). Because the groups differed on PANSS negative symptom scores (Table 1), post-hoc Contingency x Medication x Week analyses were conducted while covarying these scores. The Contingency x Week interaction effects remained significant for cotinine and CO levels ($F(3, 141) = 4.58, p < .01$; $F(3, 141) = 2.92, p < .05$, respectively) but the Contingency x Week interaction effect was no longer significant for CPD ($\eta^2 = 0.04$). There were no significant Medication x Week interactions on any smoking measure (η^2 's $< .04$) and no significant Medication x Contingency x Week interactions on any smoking measure (η^2 's $< .04$).

Those randomized to CM submitted more samples that met the cotinine reduction or abstinence criterion than those randomized to NR ($F(1, 48) = 12.52, p < 0.01$). The main effect of Medication and the Medication x Contingency interaction effect on total number of samples meeting the criterion were not significant (η^2 's < 0.03). The total number of samples meeting the criterion was 3.23 ± 1.7 ($M \pm SD$) in the CM + BUP group, 2.40 ± 1.5 in the CM + PLA group, 1.36 ± 1.03 in the NR + BUP group and 1.54 ± 0.97 in the NR + PLA group.

Urge to Smoke, Nicotine Withdrawal Symptoms and Motivation to Quit

Across groups, QSU scores were significantly higher in week 1 than in subsequent weeks ($F(3, 144) = 8.96, p < .001$). There were no significant Contingency x Week, Medication x Week or Contingency x Medication x Week interactions on QSU score (η^2 's $< .01$). Averaged across groups, in Weeks 1–4, respectively, QSU scores ($M \pm SD$) were 3.6 ± 1.8 , 2.9 ± 1.6 , 2.9 ± 1.5 and 2.8 ± 1.5 . There were no significant main or interaction effects on MNWS score (η^2 's $< .03$). Averaged across groups, in Weeks 1–4, respectively, MNWS scores ($M \pm SD$) were 0.4 ± 0.4 , 0.5 ± 0.5 , 0.4 ± 0.5 and 0.4 ± 0.4 .

There were no significant main or interaction effects on Contemplation Ladder score (η^2 ranging from 0.004 – 0.016). Contemplation Ladder scores at baseline are shown in Table 1. Contemplation Ladder scores at visit 9 were 7.1 ± 2.3 in the CM + BUP group, 7.2 ± 2.2 in the CM + PLA group, 6.7 ± 3.0 in the NR + BUP group and 6.2 ± 2.4 in the NR + PLA group.

Safety and Tolerability Measures

Significant main effects of Week indicated that, across groups, PANSS and UPDRC scores were significantly higher in Week 1 than in Weeks 2–4 and AIMS scores were significantly higher in Week 1 than in Weeks 3–4 ($F(3, 144) = 12.92, p < .001$; $F(3, 144) = 7.15, p < .001$; $F(3, 144) = 8.29, p < .001$, respectively). There were no significant Contingency x Week, Medication x Week or Contingency x Medication x Week interactions on PANSS, UPDRC and AIMS scores. Averaged across groups, in Weeks 1–4, respectively, PANSS scores ($M \pm SD$) were 54.0 ± 13.5 , 47.1 ± 10.0 , 47.0 ± 9.6 and 48.2 ± 11.5 , UPDRC scores

were 9.1 ± 10.4 , 5.9 ± 6.4 , 5.8 ± 6.0 and 5.9 ± 6.4 , and AIMS scores were 3.2 ± 4.2 , 1.9 ± 3.0 , 1.5 ± 2.3 and 1.3 ± 2.1 .

There were no differences between medication groups on the number of participants reporting adverse events. The following events were reported at least once by participants during the study: insomnia, reported at least once by 41% of those in the BUP group and 57% of those in the PLA group; restlessness (50% of BUP, 46% of PLA); dry mouth (54% of BUP, 38% of PLA); anxiety (36% of BUP, 54% of PLA); headache (41% of BUP, 38% of PLA); nausea (41% of BUP, 31% of PLA); diarrhea (23% of BUP, 39% of PLA); chest pain (27% of BUP, 19% of PLA); blurred vision (18% of BUP, 15% of PLA); memory problems or confusion (19% of BUP, 12% of PLA); and racing heartbeat (9% of BUP, 12% of PLA). The incidence of other events was < 5%. No seizures or suicidal behaviors were reported. Levels of adverse events were largely mild to moderate, with the following exceptions: in the PLA condition there was one report of severe diarrhea in week 3 and in the BUP condition there was one report of severe insomnia in week 3, one report of severe nausea in week 3 and one report of severe chest pain in week 2. The latter participant was discontinued from the study and the symptom resolved promptly without further incident.

Discussion

To our knowledge, this is the first study to evaluate the combination of bupropion and CM for smoking reductions in SWS. The results of this study indicate that the CM intervention reduced cotinine and CO levels by approximately 30% relative to pre-study levels. The magnitude of this effect is comparable to those observed in previous CM-smoking studies in SWS (Roll et al. 1998; Tidey et al. 2002), but a notable advantage of the current CM intervention over those in these previous studies was the use of cotinine rather than CO levels to verify smoking abstinence. This procedure, developed by Higgins and colleagues (2004), substantially reduces participant burden by reducing the frequency of study visits necessary to biologically verify continuous smoking abstinence from 2–3 times per day to 3 times per week. Furthermore, the present study used a novel reinforcement contingency in which systematic reductions in urinary cotinine concentration were reinforced in order to increase the likelihood that participants would contact the reinforcer. Overall, the results of this study indicate the feasibility and initial efficacy of integrating CM into smoking cessation treatments for smokers with schizophrenia.

The results of the current study also indicate that 300 mg/day sustained-release bupropion did not reduce smoking by itself or increase the efficacy of the CM intervention. This finding is in contrast with previous smoking treatment studies in SWS, which found that bupropion reduced breath CO levels by about 30–40% (Evins et al., 2001; 2005; George et al., 2002). However unlike the Evins et al (2001; 2005) and George et al. (2002) studies, the present study enrolled participants who were not actively seeking smoking cessation treatment; rather, participants indicated that they were interested in undergoing smoking cessation within the next 6 months. As intention to quit has been found to moderate the effects of bupropion and other smoking cessation medications (Perkins et al. 2008; 2010; Tidey & Rohsenow 2009), it is possible that the lower motivation levels of participants in the current study may have reduced the efficacy of the medication. Other factors that may have contributed to the failure to detect significant effects of bupropion include the short treatment period and small sample size, which reduced the study's power to detect statistically significant effects, and the study's reliance on self-report and pill count measures of medication compliance, which may overestimate true medication compliance.

Bupropion did not increase psychiatric symptoms or movement disorders in the current study, consistent with the findings of others (Evins et al., 2001; 2005; George et al., 2002).

The bupropion and placebo groups did not differ in the frequency of medication side effects, and almost all side effects were reported to be of mild or moderate severity. However, of the 5 individuals who dropped out of the study in the week between randomization to medication and randomization to contingency condition, 4 were randomized to BUP and all 4 reported that they discontinued study participation due to medication side effects or another medication-related concern. Furthermore, some potential participants were excluded from this study due to neuropsychiatric symptoms that may be exacerbated by bupropion or medications that are contraindicated with bupropion (GlaxoSmithKline 2010). These limitations highlight the need for the development of additional pharmacological and non-pharmacological interventions for smoking cessation that can be used with this population.

A number of supplementary findings also support the use of the CM interventions for reducing smoking in SWS. Psychiatric symptoms and smoking urge levels were highest at Session 1 and decreased in all groups thereafter. As these measures were administered in Session 1 under non-abstinent conditions and before randomization to study condition, the higher symptom and urge levels observed in Session 1 may be due to a non-study-specific factor such as the stress of the novel environment (e.g., Finlay and Zigmond, 1997). Nicotine withdrawal symptoms remained low in all groups throughout the study, indicating that the subjective distress from smoking deprivation that participants experienced was mild. The comparison of Contemplation Ladder scores measured before and at the end of the trial indicate that the CM intervention neither increased nor eroded motivation to quit smoking.

The findings from the current study are promising, but it is clear that an important next step for this research is to increase the efficacy of the CM intervention, as smoking reductions alone do not result in significant health benefits (Tverdal and Bjartveit 2006). The CM intervention used in this study might be strengthened by raising the value of the reinforcer (Stitzer and Bigelow, 1984), or by combining it with varenicline, which appears to be highly effective at reducing smoking in smokers with schizophrenia (Nino-Gomez et al., 2010). This CM intervention could also be used to reduce smoking rates prior to introducing another smoking treatment. Smoking reductions have been found to increase the likelihood of future smoking cessation in smokers who are not ready to quit, perhaps by reducing physical dependence levels (Hughes and Carpenter, 2006).

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Figure 1.

Urinary cotinine levels (top), breath carbon monoxide levels (middle) and self-reported number of cigarettes smoked per day (bottom) in participants randomized to CM + BUP (solid circles), CM + PLA (open circles), NR + BUP (solid triangles) and NR + PLA (open triangles) conditions across study weeks. Error bars indicate SEM. Asterisks indicate significant differences from Week 1 ($p < .05$).

Table 1

Participants' Demographic and Smoking Characteristics at Enrollment [M (SD) or %].

	CM + BUP (n = 12)	CM + PLA (n = 16)	NR + BUP (n = 11)	NR + PLA (n = 13)
Age	42.9 (11.9)	46.3 (6.7)	43.7 (7.3)	46.9 (6.8)
Male	67%	63%	73%	85%
Race				
White	58%	88%	73%	77%
African-American	25%	6%	9%	23%
Other	17%	6%	18%	0%
Hispanic ethnicity	0%	12%	9%	8%
Employed full- or part-time	17%	19%	0%	31%
Years of education	11.7 (1.4)	12.5 (1.9)	11.5 (1.8)	11.9 (2.6)
Cigarettes per day	28.8 (12.6)	26.3 (10.9)	23.0 (10.7)	29.9 (14.0)
FTND score	7.3 (1.7)	7.0 (1.4)	7.1 (1.6)	7.0 (1.5)
Years of daily smoking	24.6 (13.6)	28.4 (7.7)	23.1 (8.6)	29.6 (7.6)
Breath CO level (ppm)	26.8 (14.5)	26.6 (9.5)	31.7 (19.1)	26.0 (14.7)
Salivary cotinine (ng/ml)	1532 (544)	1334 (606)	1583 (447)	1493 (434)
Contemplation Ladder score	6.8 (2.8)	6.5 (2.4)	7.3 (2.4)	5.7 (2.7)
PANSS positive scale score *	11.5 (3.3)	14.3 (5.4) ^a	14.4 (1.9) ^a	10.9 (2.1) ^b
PANSS negative scale score *	11.4 (3.9) ^a	13.4 (3.9)	18.9 (3.0) ^b	15.8 (7.1) ^b
PANSS general scale score	24.4 (4.8)	26.8 (8.8)	31.4 (5.1)	26.0 (5.9)
Typical antipsychotic	8%	6%	9%	0%
Atypical antipsychotic	75%	81%	64%	85%
Both types	8%	6%	18%	15%
Other psychiatric medication	33% SSRI, 8% AD, 25% AM, 33% AA	37% SSRI; 31% AD, 25% AM, 25% AA	27% SSRI; 35% AD, 18% AM, 46% AA	31% SSRI, 23% AD, 31% AM, 0% AA

Abbreviations: CM, Contingency Management; NR, Non-Contingent Reinforcement; BUP, bupropion; PLA, placebo; FTND, Fagerström Test of Nicotine Dependence; CO, carbon monoxide; PANSS, Positive and Negative Syndrome Scale; SSRI, selective serotonin reuptake inhibitors; AD, non-SSRI antidepressant; AM, antimanic; AA, antianxiety.

* $p < .05$;

^{a,b} superscripts within a row indicate significant differences among groups.