The relationship between reward-based learning and nicotine dependence in smokers with schizophrenia

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Abstract

Cigarette smoking rates remain remarkably high in schizophrenia relative to smoking in other psychiatric groups. Impairments in the reward system may be related to elevated rates of nicotine dependence and lower cessation rates in this psychiatric group. Smokers with schizophrenia and schizoaffective disorder (SWS; n = 15; M_age = 54.87, SD = 6.51, 100% male) and a non-psychiatric control group of smokers (NCL; n = 16; M_age = 50.38, SD = 11.52; 93.8% male) were administered a computerized signal detection task to measure reward-based learning. Performance on the signal detection task was assessed by response bias, discriminability, reaction time, and hit rate. Clinician-assessed and self-reported measures of smoking and psychiatric symptoms were completed. SWS exhibited similar patterns of reward-based learning compared to control smokers. However, decreased reward-based learning was associated with increased levels of nicotine dependence in SWS, but not among control smokers. Nicotine withdrawal and urge to smoke were correlated withanhedonia within the SWS group. Among SWS, reduced reward responsiveness and increased anhedonia were associated with and may contribute to greater co-occurring nicotine dependence. These findings emphasize the importance of targeting reward system functioning in smoking cessation treatment for individuals with schizophrenia.

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All other authors declare no conflicts of interest.

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Keywords

Cigarette smoking; Anhedonia; Reward responsiveness

1. Introduction

Estimates indicate that 70 - 85% of individuals with schizophrenia are cigarette smokers (de Leon and Diaz, 2005; Lasser et al., 2000; Workgroup on Substance Use Disorders, 2006). These psychiatric smokers remain difficult to treat (McChargue et al., 2002; Williams and Ziedonis, 2004), with quit rates consistently lower in smokers with schizophrenia than in non-psychiatric control smokers (Fagerström and Aubin, 2009; George et al., 2008). However, it is unclear what etiological mechanisms may underlie the common co-occurrence of nicotine dependence and schizophrenia. Anhedonia, defined as decreased reactivity to pleasurable stimuli or diminished pleasure in daily activities, has been linked to cigarette smoking. Increased levels of anhedonia are reported among cigarette smokers and are considered to be a risk factor for smoking relapse among psychiatric patients (Cook et al., 2010; Leventhal et al., 2008, 2009). In fact, smokers with increased rates of anhedonia and low positive affect report increased craving to smoke and are a high priority group for smoking cessation interventions (Ameringer and Leventhal, 2010).

In schizophrenia, anhedonia is a well-established clinical phenomenon that has been described throughout historical conceptualizations of the illness (Chapman et al., 1976; Wolf, 2006). Over the last twenty years, research has advanced our understanding of the nature of anhedonia and blunted positive emotional reactivity among individuals with schizophrenia (Kring, 2011; Kring and Caponigro, 2011). Findings in this area suggest that individuals with schizophrenia are impaired in their expression of positive emotion, but report normative subjective experience of emotion in response to pleasurable stimuli (e.g., Kring, 2011).

More recent research has highlighted differences between expected versus experienced pleasure in our understanding of anhedonia in schizophrenia. Cumulatively, findings support decreased anticipation of pleasure (i.e., anticipatory pleasure) and normative experience of positive emotion during exposure to pleasurable stimuli (i.e., consummatory pleasure; Cohen and Minor, 2010; Gard et al., 2007). However, one recent study suggested that consummatory pleasure may also be compromised in this population (Strauss et al., 2011). Unique neurobiological processes are thought to underlie anticipatory and consummatory pleasure, with nucleus accumbens activation linked to anticipatory, but not consummatory, processes in nonpsychiatric groups (Berridge and Robinson, 2003; Knutson et al., 2001). Impairments in anticipatory pleasure have been specifically associated with anhedonia and functional impairment in schizophrenia (Gard et al., 2007). Related research also has highlighted an inability to maintain positive emotion and failure to translate this emotion into adaptive behavior as key features of anhedonia in this disorder (e.g., Heerey et al., 2008; Kring and Werner, 2004).

Building on findings characterizing the nature of anhedonia in schizophrenia, recent research suggests that reward system dysfunction contributes to reduced hedonic capacity in this population (e.g., Dillon et al., 2008; Gold et al., 2008; Pizzagalli et al., 2005). Behavioral and biological indices of reward system dysfunction have been associated with anhedonic symptoms in schizophrenia and related disorders (Simon et al., 2010). A critical component of reward system functioning is the ability to engage in reward-based learning (e.g., the ability to learn associations between neutral and unconditioned rewarding stimuli and to produce behavioral change via positive reinforcement). Recent research examining

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the acquisition of reward-based learning in schizophrenia has generated debate about the presence and nature of acquisition deficits (e.g., Heerey et al., 2008; Waltz et al., 2007). Within this limited literature, several studies show impairments in acquisition of reinforcement learning in this group (Gold et al., 2008; Murray et al., 2008; Waltz et al., 2007; Weiler et al., 2009). However, two recent investigations have found no differences in the acquisition of reward-based learning in schizophrenia as compared to non-psychiatric controls (Heerey et al., 2008; Herbener, 2009). Preliminary research examining reward learning in schizophrenia has also shown deficits in reversal learning (Murray et al., 2008; Weiler et al., 2009) and more rapid decay of reward-based memory (Herbener, 2009). Impairments in reward-based learning may be an important etiological mechanism contributing to the experience of anhedonia in schizophrenia. However, the form and function of these deficits in schizophrenia remain unclear, and little is known about the relationship between reward-based learning and nicotine use in this population.

Preclinical and clinical research has established nicotine as a pharmacological agent that directly affects reward-based learning (Barr et al., 2008; Kenny and Markou, 2006). Acute administration of nicotine has been associated with increased responsiveness to non-drug reward, whereas withdrawal has been associated with insensitivity to reward (Epping-Jordan et al., 1998; Kenny and Markou, 2006). For example, among healthy nonsmokers, a single dose of nicotine was found to enhance the acquisition of reward-based learning (Barr et al., 2008). This study used a computerized signal-detection task assessing change in behavior in response to differential monetary reward. Despite this established relationship between reward responsivity and nicotine use, no research has formally examined the potential role of reward-based learning deficits in smoking behavior in schizophrenia.

The aim of the current study was to examine the characteristics of reward-based learning among smokers with schizophrenia (SWS) using an established probabilistic reward-based learning task rooted within signal detection theory (Pizzagalli et al., 2005). We hypothesized that SWS participants will demonstrate poorer performance on the signal detection task (indexed by response bias and hit rate) as compared to a non-psychiatric control group (NCL). Furthermore, nicotine dependence was expected to be negatively correlated with reward-based learning in SWS smokers. The goal of this study was to extend reward-based learning research to understand possible behavioral mechanisms that contribute to the high rates of tobacco use amongst individuals with schizophrenia.

2. Methods

2.1 Participants

Smokers with schizophrenia and schizoaffective disorder (SWS; n = 23) and non-psychiatric controls (NCL; n = 18) were recruited from a large VA Healthcare System in the Northeastern United States (Table 1). Eligible participants were 18-65 years old and smoked more than 10 cigarettes/day. SWS participants met DSM-IV criteria for schizophrenia or schizoaffective disorder as determined by study personnel (JL, VK, KLG). NCL participants had no current or past diagnosis of schizophrenia or bipolar disorder, no current diagnosis of major depressive disorder, alcohol or substance abuse or dependence, or post-traumatic stress disorder. Exclusion criteria across both groups included unstable medical problems (past 6 months), other tobacco product use, breath alcohol level >0.005 g/l, other substance abuse or dependence (past month), current smoking cessation treatment, or unstable psychiatric symptoms (e.g., severe psychosis).
2.2 Materials and Procedure

Study participation included two days in the laboratory. During the first study day, participants completed assessments of medical history, psychiatric symptoms using the Structured Clinical Interview for DSM-IV (First et al., 2002), Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987), Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962), and Beck Depression Inventory-II (BDI-II) (Beck et al., 1996), nicotine dependence using the Fagerström Test for Nicotine Dependence (FTND) (Heatherton et al., 1991), smoking urges using the Questionnaire on Smoking Urges-Brief Form (QSU-Brief) (Cox et al., 2001), and nicotine withdrawal using the Minnesota Nicotine Withdrawal Scale (MNWS) (Hughes and Hatsukami, 1986). The following baseline biological assessments were performed: a breath test for recent alcohol use (AlcoMate Prestige AL6000) and for expired breath carbon monoxide (CO) level (Micro 4 Smokerlyzer).

On the second day, participants completed a 30-minute computerized signal detection task on a Dell Optiplex 760 computer using E-Prime software (version 2.0; see Pizzagalli et al., 2005 for a full description of the task). This signal detection task provides an objective characterization of reward responsiveness and is designed to measure shift in responding toward a differentially (more frequently) rewarded stimulus. Participants are instructed to win as much money as possible by identifying, in each trial, which of two stimuli (short or long mouth) is presented on a cartoon face. To allow for the emergence of a response bias, the short (11.5 mm) and long (13 mm) mouth were perceptually similar and presented very briefly (100 ms); more critically, correct identification of one stimulus was rewarded three times more frequently (n = 30/block) than correct identification of the other stimulus (n = 10/block). The stimulus reinforced more frequently was defined as the “rich” stimulus, whereas the less reinforced stimulus was referred to as the “lean” stimulus. The stimulus (short or long mouth) selected for the “rich” stimulus was counterbalanced within participant groups. After two practice trials designed to ensure task comprehension, a total of 200 trials across two 100-trial blocks (Block 1, Block 2) were completed. All participants were told they could earn up to $6 for completion of this task, depending on performance. Participants were permitted to smoke ad lib during circumscribed time periods throughout the two study visits. Breath tests for recent alcohol use and for expired breath carbon monoxide (CO) level were performed prior to the signal detection task.

2.3 Data Collection and Reduction

Behavioral data derived from the signal detection task include three primary variables: response bias (RB), discriminability, and reaction time (RT; see Pizzagalli et al., 2005). RB assesses preference for the more frequently rewarded stimulus (i.e., short or long mouth). Calculation of response bias is as follows:

\[ \log b = \frac{1}{2} \log \left[ \frac{(\text{Rich}_{\text{correct}} \times \text{Lean}_{\text{incorrect}})}{(\text{Rich}_{\text{incorrect}} \times \text{Lean}_{\text{correct}})} \right] \]

The rich and lean stimuli in the study varied according to counterbalancing of rewarded stimulus type (Pizzagalli et al., 2005). Greater response bias is associated with more correct identifications of the rich stimulus and fewer correct identifications of the lean stimulus. Discriminability refers to participants’ ability to differentiate between the short and long mouth stimuli and is an overall measure of task difficulty. Calculation of discriminability is as follows:
For both response bias and discriminability quotients, each variable (e.g., Long_correct) refers to the number of correct or incorrect responses for that stimulus. For both variables, 0.5 was added to each cell in the formula, following prior recommendations (Hautus, 1995). Hit rate (% correct) and reward learning (Block 2 RB - Block 1 RB) were examined as secondary task performance measures. Reward learning is defined as the change in RB during the course of the task (Santesso et al., 2008) and is thought to capture participants’ propensity to modulate behavior as a function of the reinforcement schedule.

Consistent with established procedures (Pizzagalli et al., 2005), data screening was performed to identify outlying data points within Blocks and across participants. The following criteria were used for exclusion. Individual trials with RT < 150 ms or > 2500 ms were considered outliers and removed. Data were excluded from statistical analyses for participants who had: 1) < 80% valid trials within a Block; 2) < 25 rich rewarded trials per block; 3) > 30 outliers trials across the entire task; and 4) < 60% accuracy (i.e., chance performance) for each Block. Eight (34.8%) SWS participants were identified as outliers and their data were excluded from subsequent analyses. Of these, five were excluded due to task non-compliance, and three were excluded due to performance at chance level. Two (11.1%) NCL participants were identified as outliers. Of these, one was excluded due to non-compliance with the task and one was excluded due to performance at a chance level. These rates of invalid task administrations are similar to other studies using this task in samples of individuals with severe psychopathology (e.g., Bipolar Disorder; Pizzagalli et al., 2008).

2.4 Statistical Analyses

One-way ANOVA and chi-square tests were performed on demographic data. Initial data screening showed that response bias (Block 1, Block 2, total) and cigarettes per day were non-normally distributed in the SWS group. Thus, Spearman’s rho was used to examine bivariate correlations that included response bias or cigarettes per day variables within SWS. Pearson product-moment correlations were used to examine relationships among the remaining normally distributed variables (e.g., signal detection, smoking, and anhedonia measures). A Mann-Whitney U test was performed to examine between group differences in cigarettes per day. Mixed-model repeated measures ANOVAs with two within-subject factors of Stimulus (rich, lean) and Block (Block 1, Block 2) and one between-subject factor of Group (SWS, NCL) were performed on measures of accuracy and reaction time. For response bias and discriminability, mixed-model repeated measures ANOVAs with Block and Group as factors were performed. ANOVA was utilized to examine group differences in response bias across blocks as this statistical test is considered to be robust to violations of normality (Hays, 1994; Kirk, 1995; Winer et al., 1991). A one-way ANOVA test was performed to examine group differences on reward learning.

3. Results

3.1 Demographic and Smoking Variables

In the final sample (N=31), SWS (n = 15) and NCL (n = 16) groups were matched with respect to demographics, with the exception of employment (SWS were more likely to be unemployed; see Table 1). Consistent with the literature (e.g., Williams et al., 2007), SWS exhibited differences in smoking variables. Although the SWS group did not differ from the NCL group on a standard measure of nicotine dependence (FTND), SWS demonstrated...
higher baseline CO and reported smoking greater numbers of cigarettes per day compared with NCLs. In addition, SWS exhibited greater nonabstinent urge to smoke (OSU-brief) and withdrawal symptoms (MNWS) compared with NCL participants (p's < 0.05).

### 3.2 Signal Detection Task Manipulation

#### 3.2.1 Response bias—
There were no significant main effects of Block or Group on response bias ($F's < 1.4, p's > .25$); similarly, the interaction was not significant ($F(1, 29) = 0.01, p > .97$). Mean response bias (averaged across blocks) did not differ between SWS ($M = 0.16, SD = 0.19$) and NCL ($M = 0.08, SD = 0.20$) groups (all $p > 0.10$).

#### 3.2.2 Discriminability—
There were no significant main effects of Block or Group or the interaction between variables on discriminability, indicating no difference in the ability of the SWS ($M = 0.50, SD = 0.29$) and NCL ($M = 0.57, SD = 0.29$) groups to differentiate between the rich and lean stimuli (all $p > 0.10$).

#### 3.2.3 Reaction time—
Across SWS and NCL groups, a trend main effect of Block indicated faster RT on trials in Block 2 ($M = 607.76$ ms, $SD = 162.91$) compared with Block 1 ($M = 640.91$ ms, $SD = 182.52$), $F(1, 29) = 4.01, p = 0.06$. A main effect of Stimulus indicated that RT was significantly faster to rich ($M = 606.83$ ms, $SD = 165.38$), versus lean, stimuli ($M = 641.85$ ms, $SD = 173.30$), $F(1, 29) = 10.71, p = 0.003$. No differences were found between groups or for interactions amongst variables. Differences in RT during the task in the SWS ($M = 676.13$ ms, $SD = 239.59$) and NCL ($M = 572.55$ ms, $SD = 231.98$) groups were also not statistically significant ($p = 0.09$).

#### 3.2.4 Hit rate—
The main effect of Stimulus was significant, $F(1, 29) = 18.85, p < 0.001$, due to the fact that, as expected, rich stimuli were more correctly identified (79.9%) compared with lean stimuli (69.4%). A trend interaction of Group x Block emerged ($F(1, 29) = 2.91, p = 0.10$), due to a decline in hit rate between Block 1 and 2 within the SWS group (75.3% vs. 72.0%), but an increase in hit rates in the NCL group (74.6% vs. 76.6%). There were no significant main effects of Block, Group or other interactions. SWS (73.6%) and NCL (75.6%) groups were similar in their mean accuracy rates averaged across the two blocks ($p = 0.62$).

#### 3.2.5 Reward learning—
SWS ($M = 0.03, SD = 0.10$) and NCL ($M = -0.02, SD = 0.21$) groups demonstrated similar patterns of change in response bias between Block 1 and Block 2 ($p = 0.42$).

### 3.3 Reward-based Learning and Cigarette Smoking

As mentioned above, initial data screening showed that response bias (Block 1, Block 2 and total) was significantly positively skewed and leptokurttic within the SWS group. As a result, nonparametric statistics (Spearman rank-order correlations) were calculated for all relationships between response bias (Block 1, Block 2, and total) and variables of interest within this sample. In the SWS group, increased nicotine dependence (FTND score) was correlated with decreased response bias toward the reinforced stimulus (rich stimulus) during Block 1, $r(12) = -0.66, p = 0.02$, and for total response bias across the task (Block 1 + 2; see Figure 1A), $r(12) = -0.59, p = 0.05$, with a trend noted for the relationship between nicotine dependence and response bias during Block 2, $r(12) = -0.50, p = 0.10$. This relationship was not evident in the NCL sample (all $p$ values $> 0.54$). Average number of cigarettes smoked per day was not significantly correlated with response bias indices in either the SWS or NCL groups. In addition, reward learning was negatively associated with CO level in SWS (see Figure 1B), $r(15) = -0.54, p = 0.04$, but not NCL ($p = 0.47$).
3.4 Anhedonia and Cigarette Smoking

Clinician-administered and self-report measures of anhedonia/affective blunting were related to increased smoking behavior among SWS, but not control, subjects. Specifically, in SWS, baseline nicotine withdrawal (as assessed by the MNWS) was positively correlated with blunted affect as measured by the PANSS, $r(13) = 0.60, p = 0.03$. Similarly, SWS urge to smoke was positively associated with loss of pleasure/anhedonia on the BDI-II, $r(15) = 0.60, p = 0.02$. These relationships were not demonstrated in the NCL group.

4. Discussion

Results from this study identified a pattern of reward-based learning that was directly linked to biochemical and behavioral measures of cigarette smoking among SWS. Using a laboratory-based probabilistic reward task, we found that reduced acquisition of reward-based learning in SWS was related to increased levels of nicotine dependence, as assessed by the FTND. The relationship between nicotine dependence and reward-based learning was evident within Block 1 and across the total task, with a trend suggesting a similar relationship in Block 2. In addition, SWS smokers’ impaired learning (i.e., poorer reward learning throughout the course of the task) was related to increased levels of expired CO. Finally, self-report and clinician-rated measures of anhedonia (e.g., BDI-II loss of pleasure, PANSS blunted affect) were significantly associated with proxy measures of increased nicotine dependence (e.g., QSU-brief, MNWS) in SWS. These results emerge from multimodal assessments of anhedonia/reward-based learning and smoking behavior. Findings support the presence of a relationship between anhedonia/reward-based learning impairments and nicotine use in schizophrenia. Importantly, these relationships among smoking variables, performance on the signal detection task, and anhedonia were absent in NCL smokers. Such findings indicate that impairments in reward learning may not be similarly related to cigarette smoking in smokers within the general population.

The current findings suggest that anhedonia and deficits in the acquisition of reward-based learning may contribute to the severity of nicotine dependence in SWS. Of note, these results were found using a well-validated measure of nicotine dependence, the FTND (Heatherton et al., 1991). However, data did not demonstrate similar relationships between self-report of average number of cigarettes smoked per day and reward-based learning in SWS. Importantly, our significant findings were based on the FTND which is a stronger assessment tool with established psychometric validity and broader-based measurement of nicotine dependence.

Significant associations between related measures of nicotine dependence and anhedonic symptoms support the presence of a relationship between reward system impairment and nicotine use in schizophrenia. Specifically, greater reported withdrawal symptoms and urge to smoke were related to increased severity of clinician-assessed blunted affect and self-reported anhedonia in SWS. Our findings are consistent with literature indicating that cigarette smoking and relapse to smoking may be more directly associated with blunted hedonic responses and reward system dysfunction in psychiatric smokers (Cook et al., 2010; Leventhal et al., 2008, 2009). This study extends these findings to individuals with schizophrenia.

The empirical evidence emerging from this study supports the conceptualization that SWS who are heavier smokers may utilize nicotine within cigarettes to ameliorate existing deficits in reward-based learning and responsivity. The degree of heavy smoking in schizophrenia patients may represent a marker of illness severity, particularly in terms of reward processing and negative symptoms (i.e., blunted affect as measured by the PANSS and loss of pleasure/anhedonia as measured on the BDI-II). Given the demonstrated pharmacological...
properties of nicotine among animal and nonpsychiatric human subjects (i.e., nicotine functions to increase the reinforcing properties of environmental stimuli; Barr et al., 2008; Kenny and Markou, 2006), SWS may engage in this drug-use behavior as a means of improving reward-based learning. Consistent with this idea, SWS who are less dependent on nicotine demonstrate increased hedonic capacity (based on multimodal assessments of anhedonia and nicotine dependency) and thus may be less reliant on nicotine for enhancement of reward system functioning. However, future studies are needed to replicate findings from the existing study and further evaluate this interpretation, including examination of how nicotine withdrawal may affect reward-based learning in SWS.

Contrary to our initial hypothesis, no significant differences emerged between groups on measures of acquisition of reward-based learning (i.e., response bias). The absence of significant group differences could be the result of the small sample size and restricted power in this pilot study. Alternatively, the use of two smoking groups and the potentially powerful effects of nicotine use on reward-based learning may mask the presence of any reward-based learning deficits intrinsic to the disorder of schizophrenia (e.g., Barr et al., 2008). Lastly, individuals with schizophrenia, irrespective of their nicotine use, may not have deficits in the acquisition of reward-based learning (e.g., Heerey et al., 2008). Findings from the current study are consistent with two other studies that found no differences in the acquisition of reward-based learning between individuals with schizophrenia and non-psychiatric control participants (Heerey et al., 2008; Herbener, 2009). However, other studies support the presence of acquisition deficits in schizophrenia (Gold et al., 2008; Murray et al., 2008; Waltz et al., 2007; Weiler et al., 2009). Importantly, few of these studies have assessed and controlled for co-occurring nicotine dependence in their examination of reward-based learning in schizophrenia (e.g., Heerey et al., 2008; Weiler et al., 2009). Rates of smoking are extremely high among individuals with schizophrenia (e.g., 70-85%; de Leon and Diaz, 2005; Workgroup on Substance Use Disorders, 2006), and failure to evaluate the role of co-occurring nicotine use in research examining reward-based learning in schizophrenia may be central to the conflicting debate about these deficits. Thus, the current investigation is among the first to attempt to elucidate the relationship between reward learning and co-occurring nicotine dependence in this group.

A number of methodological limitations of this study should be noted. First, the sample size is limited, and replication of these results is needed with larger samples. In addition, although consistent with smoking rates in this population, SWS smokers exhibited differences when compared to NCL smokers in various smoking and clinical characteristics (e.g., cigarettes/day, baseline CO level, withdrawal and depressed mood). Due to sample size restrictions, we were unable to control for depression in analyses examining relationships between reward learning and nicotine dependence. Thus, co-occurring depression cannot be eliminated as a potential third variable that could account for observed relationships between reward learning and smoking behavior in SWS. Despite these limitations, this study is among the first to investigate the relationships among reward system functioning, anhedonia, and smoking in individuals with schizophrenia. Findings indicate unique associations between nicotine dependence and reward-based learning deficits in SWS smokers that were not evident in NCL smokers. Future studies are needed to replicate and extend these findings in SWS and to continue to determine the mechanisms that might explain high rates of smoking among these psychiatrically ill individuals. Future development of a conceptual model to more clearly delineate causal relations among reward-based learning, anhedonia, and nicotine dependence in smokers with schizophrenia will improve current and future smoking cessation treatments in this population.
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Dr. Pizzagalli is the inventor of the software program used in this study. In the past three years, Dr. Pizzagalli received research support and consulting fees from Advanced Neuro Technology (ANT) and honoraria and consulting fees from AstraZeneca for studies unrelated to the current project.

References


Figure 1.
Response bias toward a more frequently rewarded stimulus was negatively associated with nicotine dependence, as measured by the FTND, in SWS (Panel A); Reward Learning on the task (as calculated by change in response bias from Block 1 to Block 2) was negatively associated with CO level in SWS smokers (Panel B).
# Table 1
Demographic, Smoking and Clinical Variables of Smokers with Schizophrenia (SWS) and Control Smokers (NCL)

<table>
<thead>
<tr>
<th></th>
<th>SWS (n = 15)</th>
<th>NCL (n = 16)</th>
<th>SWS vs. NCL</th>
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<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
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<tr>
<td>Age</td>
<td>54.87</td>
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<td>Gender (% male)</td>
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<td>Marital Status (% never married)</td>
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<td>37.5%</td>
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<tr>
<td>Employment (% unemployed)</td>
<td>80.0%</td>
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<tr>
<td>FTND</td>
<td>4.67</td>
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</tr>
<tr>
<td>Number of cigarettes/day</td>
<td>28.67</td>
<td>16.98</td>
<td>15.81</td>
</tr>
<tr>
<td>QSU-Brief Total (baseline)</td>
<td>3.25</td>
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<td>MNWS Total (baseline)</td>
<td>10.08</td>
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<td>BPRS Total</td>
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</table>

Note: SWS = Smokers with schizophrenia; NCL = Non-psychiatric controls; FTND = Fagerström Test for Nicotine Dependence (Heatherton et al., 1991); QSU = Questionnaire on Smoking Urges – Brief Form (Cox et al., 2001); MNWS = Minnesota Nicotine Withdrawal Scale (Hughes and Hatsukami, 1986); CO = Carbon Monoxide; BDI-II = Beck Depression Inventory-II (Beck et al., 1996); PANSS = Positive and Negative Syndrome Scale (Kay et al., 1987); BPRS = Brief Psychiatric Rating Scale (Overall and Gorham, 1962).