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Risky Decision-Making in Schizophrenia: Examination of Association Between Smoking, Substance Use and Performance on the Iowa Gambling Test: Pilot Study

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Abstract

There are two common hypotheses to explain such high comorbidity between nicotine dependence and Schizophrenia (SZ): Self-medication for decreasing psychiatric symptoms or common environmental risk factors can predispose to both nicotine dependence and other risky behaviors in SZ. Little is known about the influence of cigarette smoking comorbidities such Substance Use Disorder (SUD), criminal history, or risky decision among patients with SZ. The Iowa Gambling test (IGT) was administered to thirty-nine patients with SZ of whom 69% reporting cigarette smoking. Both groups were evaluated using a socio-demographic questionnaire and clinical assessment using PANSS and self-report questionnaire the Barratt Impulsiveness Scale (BIS-11). To evaluate decision making was evaluated with the Iowa Gambling Task (IGT). The full SZ sample performed worse on the IGT then normal population. Smokers with SZ performed significantly worse than nonsmokers on the IGT primarily because they preferred "disadvantageous" decks to a greater degree. The PANSS and impulsivity tendencies (BIS-11) did not predict overall performance on the IGT. Smokers with SZ had impaired affective decision-making. Behavior suggested preferential attention to the frequency amount of gain and inattention to amount of loss suggesting impairments in risk/reward decision-making. This study is the first to compare IGT in smokers and nonsmokers with SZ with adjustment of SUD, criminal history, and existing tattoo to further examine IGT performance. These results support the hypothesis that comorbidities between nicotine dependence and SZ can be linked to other common factor that is associated with other externalizing behaviors in SZ.

Keywords: Schizophrenia; Decision-making; Iowa gambling test; Nicotine; Substance use; Criminal history

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Introduction

Cigarette smoking is a common behavior and is responsible for roughly 20% of total U.S. mortality [1]. Tobacco use is not only related to negative health outcomes but also to increased risk for developing other addictive behaviors [2]. The motivation for smoking is still not clear. Some authors suggest that risky decisions may be a key factor in health-related behaviors like cigarette smoking [3]. However, Lejuez et al. [4] found no significant differences between smokers and nonsmokers in risky decisions. Tobacco is the most commonly abused substance in individuals with Schizophrenia (SZ) [5]. The prevalence of tobacco smoking in SZ is up to five times higher than other clinical and non-clinical groups [6]. The Iowa Gambling Test (IGT) is the most common tool used to measure risky decisions [7]. The IGT approximates the complexities of real-life decision-making based on uncertain approximations of future consequences rather than exact calculations [8]. Patients with SZ who smoked have more risky decisions than non-smoking SZ. SZ patients perform significantly worse on the IGT than healthy controls in both parts of the IGT: Under ambiguity and under risk Fond et al. [9,10]. Individuals with SZ were slow to come to a decision and made suboptimal choices [11,12]. However, studies of performance on the IGT individuals with SZ show conflicting results [13,14]. These findings could be related to multiple factors that affect IGT performance [15,16]. Several hypotheses can explain such high comorbidities between nicotine dependence and SZ: 1) SZ might cause the development of nicotine dependence as self-medication to treat the psychiatric symptoms [17,18]. The activation effects of nicotine can be a 'self-medication' for SZ-related cognitive deficits with a clear dose-response relationship [19,20]. Previously, cigarette

smoking was shown to partially improve performance deficits on cognitive tasks in individuals with SZ [21-24]. If nicotine does influence a wide range of cognitive performance, then it is possible that cigarette smoking may improve IGT performance. In a healthy population, comparisons between smokers and non-smokers have failed shown statistically significant differences in IGT performance [25,26]. Among SZ patients, the impact of regular smoking on decision-making is poorly understood [9]. Smoking SZ patients demonstrate better IGT performance than non-smoking patients with SZ [15]. Two overview studies concluded that not all types of Substance Use Disorders (SUD) manifest IGT impairments [27,28]. In addition, they found that comorbidity ranges from 40% to 70% between smoking and other Substance Use Disorders (SUD) in SZ. This supported the self-medication hypothesis [29]. In accordance with the self-treating theory, two recent meta-analyses demonstrated superior cognitive performance in cannabis-using patients with SZ *vs.* non-using counterparts [30,31]. In contrast, other studies reported worse cognitive performance or failed to demonstrate a difference in some cognitive tasks [32].

2) Other researchers hypothesized that the high comorbidity rate smoking and SUD in SZ has been due to common underlying environmental risk factors that predispose users to both nicotine dependence and other risky behaviors in SZ. Unfortunately, little is known about how smoking affects the decision-making process in individuals with SZ, which is often already comprised-especially with associations with different comorbidities such SUD, criminal history, and existing tattoo.

Study hypothesis

This study tested the hypothesis that smoking among patients with SZ is caused by risky decision-making. We compared the performance of individuals with SZ on the IGT according to smoking status. Our predictions were:

(1) SZ smokers would perform worse on the IGT than non-smoking SZ;

(2) SZ smokers would have a higher risk of SUD, criminality, and tattoos after controlling for demographics, psychopathological, and personality trait such as impulsiveness.

Materials and Methods

Subjects

Participants were recruited from the outpatient adult psychiatric clinic and the unit for dual diagnosis at Beer-Yaakov/Ness Ziona Hospital. We recruited 18 patients with a dual diagnosis of SZ (F20) and SUD (F19) as well as 21 patients diagnosed with SZ without SUD as the control group. Participation was voluntary and unpaid. After receiving a full explanation of the procedures (approved by the Institutional Review Board), all participants provided written informed consent indicating their willingness to participate. Data were collected through an individual session that included a psychiatric evaluation, a collection of extensive background information, a self-report questionnaire, and a computerized IGT assessment. The inclusion criteria were men aged 18 to 45 years diagnosed with SZ or SZ with SUD. They should be in a stable state of the disease with no underlying neurological disorders, mental retardation, history of head trauma, or organic brain syndrome. All participants were capable and provided informed consent. There were 39 participants aged 23 to 63 (M=34.5, SD=10); 69% (N=27) reporting the smoking.

Measures

Computerized risky decision-making: We applied a modified computerized animation version of the Iowa Gambling Test [33,7]. Participants were exposed to four decks of cards (A, B, C, and D) displayed next to each other on a computer screen. Participants were informed that each deck is capable of awarding them virtual money and that they have 100 choices with the ultimate goal of being awarded the highest possible amount of virtual money. Participants were required to keep selecting from decks of cards that had different proportions of gains or losses. Participants were instructed to choose one of the four decks in each trial by clicking the mouse on that deck to indicate their choice. Unbeknownst to the participants, of the four decks of cards, two disadvantageous decks (A and B) have high initial monetary rewards but lead to negative overall outcomes (meaning high losses). The other two decks (C and D) have lower initial monetary rewards but also lower losses over time making them advantageous in long-term performance. Over several trials in which participants receive feedback on their gains and loss, participants generally learn to avoid the risky decks and to develop a preference for the safe decks [7]. One hundred selections for each participant are divided into five blocks of 20 choices each. We calculated a net score for each block by subtracting the number of disadvantageous card selections from the number of advantageous card selections ([C+D] - [A+B]) for each block of 20 choices. A negative score implies that subjects adopted a disadvantageous strategy (more card selections in decks A and B) while a positive score implies an advantageous strategy (more card selections in decks C and D). The dependent measures are the net score of each block ([C+D] - [A+B]).

The positive and negative syndrome scale for schizophrenia: The Positive and Negative Syndrome Scale for Schizophrenia (PANSS) is a psychiatric evaluation and the most commonly-used tool for measuring the prevalence of positive and negative syndromes in schizophrenia [34].

The Barratt impulsiveness scale: The Barratt Impulsiveness Scale (BIS-11) is a 30-item self-reported instrument designed to assess the personality/behavioral construct of impulsiveness. Participants rated 30 statements on a 4-point Likert scale; the higher the total score, the higher the self-reported level of impulsivity (possible score range: 30 to 120). The BIS-11 is the most commonly administered self-report measure for assessing impulsiveness in both research and clinical settings [35].

Data analysis

Before testing for associations related to the main outcomes, we examined the difference between smokers and non-smokers on socio-demographics and clinical variables. We used t-tests for numerical variables, and chi-square tests or Fisher's exact test for categorical variables with cell counts higher or lower than five, respectively. For the study's main outcome, we used a mixed multiple linear regression model with each block's net score on the IGT as the dependent measure while controlling for socio-demographics differences by including them as predictors in the model. For the study's secondary outcomes, we used the same mixed multiple linear regression models as the main outcome adding PANSS scores or BIS scores as additional predictors. Data were analyzed using R version 4.0.1. All analyses used two-tailed levels of significance.

Results

Demographic and clinical characteristics

Univariate analysis found significant differences between the groups with regard to criminal history (p=0.009), whether they had tattoos (p=0.0009), personal history of substance use disorder (p<0.001), and family history of substance use (p=0.04). No other significant differences were detected (Table 1).

Between-group comparison of the IGT performance

A mixed multiple linear regression model was used to assess the effect of smoking *vs.* not smoking. The net score on the IGT was the dependent variable. Age and block number as well as characteristics found to be significantly different between the two groups - criminal history, substance use, having tattoos, and family history of substance use - were included as predictors in the model as well as an interaction effect of smoking in the X block number. Residuals of the model were normally distributed. To rule out inter-correlations between predictors, we calculated Variance Inflation Factors (VIF) for all predictors in the model showing that they all were below the acceptable threshold value. Results showed the IGT score on each block was predicted by the block number, cigarette smoking, and having tattoos as well as an interaction effect of "smoking X block number." The IGT score increased consecutively from block to block (β=1.02, p<0.001), and having tattoos was associated with a worse performance on average on the IGT (β= -1.92, p=0.04). Patients with SZ who smoked cigarettes performed better than non-smoking SZ patients on average (β=3.19, p=0.02), however the non-smoking group demonstrated a better learning curve. Non-smoking patients improved their IGT score from block to block, but such an improvement was not achieved in the smoking group (β= -0.92, p=0.04). This means that on each consecutive block of the IGT, the non-smoking group improved their average score by 0.92 points more than the smoking group (Figure 1). The overall model fit was marginal at R^2=0.143 (Table 2).

Table 1a: Demographic and clinical characteristics of smoking and non-smoking patients with schizophrenia.

Table 1a & 1b	nonsmoker (N = 12)	smoker (N=27)	p value
Demographics			
Age (mean (SD))	35.7 (12.13)	34.0 (9.22)	0.639
Marital status (nominal)			0.328
Single	11 (91.7)	22 (81.5)	1.0
Married	1 (8.3)	1 (3.7)	0.50
Divorced	0 (0.0)	4 (14.8)	0.50
High school diploma (N (%))	7 (58.3)	7 (25.9)	0.113
Currently employed (N (%))	7 (58.3)	12 (44.4)	0.65
Receiving disability benefits (N (%))	12 (100.0)	25 (92.6)	0.856
Ever been imprisoned (N (%))	1 (8.3)	9 (33.3)	0.131
Criminal history (N (%))	0 (0.0)	11 (40.7)	0.009**
Clinical history			
Currently hospitalized (N (%))	0 (0.0)	3 (11.1)	0.539
Ever hospitalized (N (%))	11 (91.7)	24 (88.9)	1
Ever involuntarily hospitalized (N (%))	5 (41.7)	18 (66.7)	0.266
Ever attempted suicide (N (%))	1 (8.3)	7 (25.9)	0.394
Currently medication adherent (N (%))	12 (100.0)	26 (96.3)	1
History of alcohol use disorder (N (%))	1 (8.3)	5 (18.5)	0.645
History of substance use disorder (N (%))	0 (0.0)	18 (66.7)	<0.001***
Tattooed (N (%))	0 (0.0)	11 (40.7)*	0.009**
Family history			
Family history of substance use (N (%))	0 (0.0)	8 (29.6)	0.042*
Family history of psychiatric illness (N (%))	4 (33.3)	14 (51.9)	0.322
PANSS			
Total PANSS score (mean-SD)	52.2 (12.65)	54.00 (17.45)	0.71
PANSS: positive score (mean-SD)	10.4 (3.19)	10.9 (4.68)	0.686
PANSS: negative score (mean-SD)	17.1 (5.45)	16.4 (6.95)	0.727
PANSS: general psychopathology score (mean-SD)	24.6 (5.56)	26.6 (8.33)	0.379

*p<0.05; **p<0.1; ***p<0.001

Table 1b: Demographic and clinical characteristics of smoking and non-smoking patients with schizophrenia.

BIS-11			
Total BIS score (mean-SD)	63.08 (9.82)	63.56 (11.53)	0.9
BIS: attention score (mean-SD)	15.50 (4.23)	16.67 (4.01)	0.42
BIS: Non-planning score (mean-SD)	26.08 (4.40)	23.63 (5.62)	0.19
BIS: Motor score (mean-SD)	21.50 (3.63)	23.26 (4.47)	0.24

* While group numbers are identical, participants in the criminal history and tattoos groups differed

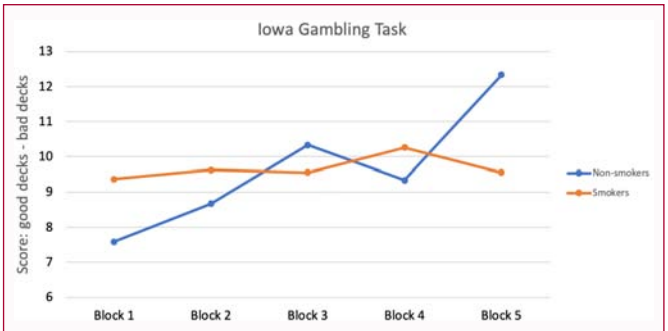

Figure1: Mean Iowa Gambling Task net scores on each of the five blocks in both schizophrenia groups: smokers *vs.* non-smokers.
In performance on IGT, the differences between groups became significant in block 5. The positive net score of the non-smoked SZ group on block 5 can be explained by their fast learning in contrast to the smoked individuals with SZ who did not improve during the task and exhibited non-optimal outcomes because they failed to correct disadvantageous choices.

Secondary outcome: Effect of PANSS scores on the IGT performance

To assess the effect of PANSS scores on IGT performance, we utilized the same model as our primary outcome adding PANSS scores as predictors. To avoid multi-collinearity due to the use of subscale and total scores in the same model, we performed separate analyses for each score. We assessed the effect of total PANSS, positive symptoms, negative symptoms, and general psychopathology scores. None of the PANSS scores significantly predicted performance on the IGT (all p values >0.483, before applying correction for multiple testing).

Secondary outcome: Effect of BIS scores on the IGT performance

To assess the effect of BIS scores on IGT performance, we utilized the same models as before again performing separate analysis to avoid multi-collinearity: total BIS, attentional impulsiveness, motor impulsiveness, and non-planning impulsiveness scores. None of the BIS scores significantly predicted performance on the IGT (all p

Table 2: Results of the mixed linear regression model.

	Dependent variable: IGT score		
Predictors	Estimate (b)	Confidence interval	p
Interaction: block number X smoking	-0.92	-1.79 – -0.05	0.04*
Block number	1.02	0.29 – 1.74	0.006**
Smoking	3.19	0.60 – 5.77	0.02*
Age	0	-0.07 – 0.08	0.98
Tattooed	-1.92	-3.79 – -0.05	0.04*
Substance use	1.38	-0.63 – 3.39	0.18
Criminal history	-1.35	-3.21 – 0.52	0.16
(Intercept)	6.57	3.36 – 9.79	<0.001
Marginal R^2	0.143		

*p<0.05; **p<0.01; ***p<0.001

values >0.31 before applying correction for multiple testing).

Discussion

This study investigated the relationship between smoking status and decision-making process among patients with SZ. To the best of our knowledge, this is the first study to attempt an evaluation of association between smoking, substance use, and criminal history in patients with SZ. Patients with SZ were impaired on the IGT performance, but smokers had a worse decision-making strategy with lower net scores than non-smoking counterparts. Furthermore, decisions in the initial phase of the IGT (conditions of maximal uncertainty without awareness to the probabilities of reward or loss) did not differ between smoking and non-smoking patients with SZ. The second part of the IGT performance constitutes "decision-making under risk", in which subjects become more knowledgeable on the risks associated with each deck. Non-smoking SZ was significantly better at the end of this stage than the smoker with SZ (Figure 1). Risky decision-making by the smoking patient with SZ results from impaired ability to adapt to short- *vs*. long-term gains, and suboptimal selection of choices based on probability [28]. Smokers with SZ show more selection of the disadvantageous decks with big gains albeit with maximal losses during performance on the IGT relative to non-smoking with SZ. Smokers seem to be more reward-sensitive than non-smokers. These findings may suggest that smokers are generally risk insensitive [36]. Even though we expected two distinct groups, participants in both groups presented similar characteristics in most clinical parameters as reflected by their scores on the PANSS. Correlational analyses were conducted to explore the relationship between clinical (PANSS) scores and IGT performance. Among patients with SZ, none of the PANSS scores significantly predicted performance on the IGT in accordance with previous work; these were not concordant with others [10,14,37]. Although impulsiveness (as measured by the BIS-11) may play an important role in the loss of behavioral control over substance use, our patients did not show impacts on IGT performance in accordance with previous study [38]. Our findings confirmed previous studies regarding on the increased comorbidity of a smoking with SUD and criminal history among patients with SZ [39]. A history of SUD, history of criminal behavior, and having a tattoo have been found to influence IGT performance among the non-schizophrenic population [40-42]. Thus, variations in study population and confounding variables might have contributed to the discordant findings. In contrast to our expectation, a hierarchical logistic regression analysis showed that the association between smoking and SZ is lost after adjustment for getting tattoo. It is possible that smoking and tattooing is linked to other common factor that can be associated with a wide range of externalizing behaviors. In a healthy population, smokers are more likely to be involved in risky behaviors such as traffic accidents, risky sexual behavior, and reduce likelihood of wearing seatbelts relative to non-smokers [43-45]. In this line, prior investigations in a healthy population show that persons who have tattoos have a higher rate of current tobacco smoking, alcohol and drug use, traffic accidents, and risky sexual behavior [42,46-48]. These findings hint at associations between smoking and tattooing. Thus, the higher rate of tattoos in smokers with SZ can cause more severe impairments of IGT performance.

Limitations

This study has several limitations that should be noted. The first limitation is the small sample size-only 39 participants in total. Second, the generalizability of our findings is limited because our study sample represented a specific subtype of SZ patients: Those with partially preserve insight reflected by their consensual adherence to the outpatient clinic. Third, this real-life sample of patients only shows partial information regarding the extent and type of substance use. Fourth, due to the higher-than-average prevalence of cigarette smoking in SZ, relatively few SZ non-smokers participated [39,21].

Conclusion

We examined the influence of smoking on risky decisions in a group of outpatients with SZ. In general, patients with SZ demonstrated impaired affective- decision-making, but smokers had a worse IGT performance than non-smokers. The impaired performance on IGT in smoker with SZ may be related to confounding factors such criminality and SUD and getting tattoos. However, tattooing was the strongest factor associated with smoking status among patients with SZ. Impairment on the IGT among smokers with SZ can be a potential marker for wide range of externalizing behaviors. The fact that we can detect differences between the small groups in terms of SUD, criminal history, and getting a tattoo suggests that the groups are distinct from each other. Future research is needed to establish the relationship between risky decision-making and cigarette smoking during categorization of smoking and non-smoking patients with SZ based on regency, volume, and type of comorbid substance and number of tattoos.

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