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Iowa Gambling Task in Schizophrenia: A Review and New Data in Patients with Schizophrenia and Co-Occurring Cannabis Use Disorders

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Abstract

Background: We reviewed previous studies comparing schizophrenia patients and healthy subjects for performance on the Iowa Gambling Task (IGT) (a laboratory task designed to measure emotion-based decision-making), and found mixed results. We hypothesize that deficits in IGT performance in schizophrenia may be more specifically related to concurrent substance use disorders. To test this hypothesis, we compared schizophrenia patients with (SCZ⁽⁺⁾) or without (SCZ⁽⁻⁾) cannabis use disorders, to healthy subjects, on measures of cognition and IGT performance.

Methods: A comprehensive battery of cognitive tests and the IGT were administered to three groups of subjects: (1) 13 subjects with DSM-IV diagnosis of schizophrenia and no concurrent substance use disorders (mean age: 28 ± 12 (SD); 54% males); (2) 14 subjects with schizophrenia and concurrent cannabis use disorders (mean age: 29 ± 9 (SD); 71% males); and (3) 20 healthy subjects (mean age 33 ± 10 (SD); 60% males).

Results: Compared to the healthy group, both schizophrenia groups were cognitively more impaired, and did worse on IGT performance. There were no differences between SCZ⁽⁺⁾ and SCZ⁽⁻⁾ patients on most of the cognitive tests, and IGT performance.

Conclusions: Schizophrenia patients show widespread impairments in several cognitive domains and emotion-based decision-making. These results are consistent with the evidence that schizophrenia reflects a dorsolateral and orbitofrontal/ventromedial prefrontal cortex dysfunction. More intriguing, it appears that the concurrent abuse of cannabis has no compounding effects on cognition, as well as emotion/affect-based decision-making.

Keywords

Schizophrenia; Cannabis; Decision-making; Iowa Gambling Task; Cognition

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1. Introduction

Schizophrenia is a chronic illness with deficits in emotional processing (for a review, see e.g., Treméau, 2006). It has been proposed that emotions play a key role in decision-making (Bechara et al., 1997; Bechara, 2005). Several studies have looked at emotion-based decision-making in schizophrenia using the Iowa Gambling Task (IGT), a laboratory task specifically developed to measure decision-making in patients with lesions of the orbito-/ventromedial prefrontal cortex and with compromised emotions (Bechara et al., 1994).

Table 1 summarizes the studies comparing IGT performance between patients with schizophrenia and healthy subjects.

In several studies, patients with schizophrenia showed poor IGT performance compared to healthy subjects. Beninger et al. (2003) compared 36 patients with schizophrenia and 18 healthy controls and found that patients on atypical, but not typical, antipsychotics performed worse on the IGT compared to healthy controls. Ritter et al. (2004) compared 20 patients with schizophrenia or schizoaffective disorder with 15 healthy subjects, and found that patients chose more cards from the disadvantageous decks than the advantageous deck compared to healthy subjects. Shurman et al. (2005) compared 39 patients with schizophrenia and 10 healthy controls and found worse performance on the IGT in schizophrenia patients. In a recent study of our group, Kester et al. (2006) found worse IGT performance in 15 adolescents with schizophrenia compared to 25 normal controls. In contrast, several other studies did not find poor IGT performance in schizophrenia patients compared to healthy subjects. Wilder et al. (1998) compared 11 patients with schizophrenia and 20 healthy controls and found no significant differences between groups for IGT performance. Cavallaro et al. (2003) found no differences in IGT performance between 110 patients and 56 normal controls. Evans et al. (2005) did not find differences in IGT performance between 19 patients and 19 age- and level of education-matched normal controls. Rodríguez-Sánchez et al. (2005) compared 80 first-episode patients with schizophrenia spectrum disorders (schizophrenia, schizoaffective disorder and schizophreniform disorder) with 22 healthy subjects. There were no differences between groups in IGT performance although healthy subjects had a preference for “low frequency–high punishment” decks compared to patients. Thus, IGT performance is impaired in some (Beninger et al., 2003; Ritter et al., 2004; Shurman et al., 2005; Kester et al., 2006), but not all (Wilder et al., 1998; Rodríguez-Sánchez et al., 2005; Evans et al., 2005) studies.

Deficits in IGT performance in schizophrenia may be related to deficits of other areas of the prefrontal cortex. In contrast to the orbitofrontal region, which has been associated with the emotional aspects of behavior and inhibition of inappropriate behavior, the dorsolateral region is involved in working memory, language production, and executive functioning. Previous studies in schizophrenia have found cognitive deficits associated with the dorsolateral region including attention, working and declarative memory, verbal fluency, and executive function (for a review, see Williamson, 2006). The IGT may involve several dorsolateral cognitive functions such as working memory, attention, and executive function that may explain the observed deficits in schizophrenia. Some of the reviewed studies examined correlations between the IGT and tests that index parcellated aspects of dorsolateral prefrontal function. Compared to patients on typical antipsychotics, Beninger et al. (2003) found that patients on atypical antipsychotics had worse performance at the IGT but better performance on the Wisconsin Card Sorting Test (WCST — a test involving attention, working memory, and executive function). Ritter et al. (2004) found decreased performances on the IGT and WCST in schizophrenia but did not find a correlation between the two tests. Similarly, Shurman et al. (2005) reported worse performance on the IGT, WCST, and Delayed Match to Sample Task (a test assessing spatial working memory) in schizophrenia patients compared to healthy subjects but did not report a correlation between the two tests. Kester et al. (2006) reported

deficits on the IGT and WCST in adolescents with schizophrenia compared to healthy adolescents, but did not find a correlation between the two tests. Thus, these studies suggest widespread deficits of prefrontal cortical functions in schizophrenia but no direct relationship between deficits of the orbitofrontal and dorsolateral prefrontal cortex.

Deficits in IGT performance in schizophrenia may be more specifically related to the co-occurrence of substance use disorders. Rates of concurrent substance use disorders are high in schizophrenia, and several studies have associated poor IGT performance with alcohol (Mazas et al., 2000; Bechara et al., 2001), psychostimulants (Bechara et al., 2001; Bolla et al., 2003), opiates (Petry et al., 1998; Mintzer and Stitzer, 2002), and marijuana (Whitlow et al., 2004; Bolla et al., 2005) abuse, as well as polysubstance abuse (Grant et al., 2000). Most drugs of abuse increase dopaminergic activity, and converging evidence from animal and human studies suggests that addiction is associated with dopaminergic dysfunction (Kalivas and Volkow, 2005). It has been suggested that individuals with addictive behaviors have reduced dopamine (D2) receptor density and dopamine release resulting in a decreased sensitivity of reward circuits to stimulation by natural rewards (Volkow et al., 2004). Further, there is evidence that emotion-based decision-making is sensitive to changes in dopaminergic activity. Czernecki et al. (2002) reported that patients with Parkinson's disease have deficits on both a reversal task and the IGT, neither of which was sensitive to L-dopa. Recently, we found that the acute administration of a branched-chain amino acid mixture (BCAA) valine, leucine, and isoleucine in healthy subjects increases prolactin levels and impairs IGT performance (Sevy et al., 2006). The acute administration of a BCAA mixture has been demonstrated to lower the plasma ratio of tyrosine + phenylalanine to BCAA and to increase prolactin levels secondary to a decrease in dopaminergic activity (Harmer et al., 2001; Gijssman et al., 2002).

As described in Table 1, several studies excluded subjects with recent use of substances (Wilder et al., 1998; Beninger et al., 2003; Ritter et al., 2004), but it was not clear whether subjects with a lifetime history of substance use disorders were excluded. Some studies did not provide information regarding the inclusion of subjects with substance use disorders (Cavallaro et al., 2003; Evans et al., 2005; Thurnbull et al., 2006). One study included patients with cocaine and alcohol use disorders, but the "healthy" subject group also included individuals using cocaine and alcohol (Ritter et al., 2004). However, the authors reported that alcohol abuse/dependence as a covariate did not significantly change the results. To date, there have been no studies that directly compared IGT performance between schizophrenia patients with and without substance use disorders. In contrast, several studies have compared schizophrenia patients with and without substance use disorders with regard to cognitive functions dependent on the dorsolateral prefrontocortical region. Studies have reported some cognitive deficits in cocaine (Sevy et al., 1990; Serper et al., 2000) and alcohol (Allen et al., 1999; Bowie et al., 2005) abusers compared to non-substance users, but other studies did not find cognitive differences between substance abusers and non-substance users (Cleghorn et al., 1991; Nixon et al., 1996; Addington and Addington, 1997; Pencer and Addington, 2003). Discrepancies between studies in schizophrenia patients abusing alcohol may be age related, with cognitive deficits becoming more apparent in older patients abusing alcohol (Allen et al., 1999; Bowie et al., 2005).

Thus, we postulated that (1) schizophrenia patients have widespread cognitive deficits associated with the orbitofrontal prefrontal cortex (OFPFC) and dorsolateral prefrontal cortex (DLPFC) compared to healthy subjects; (2) deficits of the OFPFC are more specifically associated with a history of cannabis use disorders; and (3) deficits of the OFPFC are not associated with deficits of the DLPFC or other areas of the cortex. The latter hypothesis is also based on previous findings in individuals with substance use disorders showing no association between IGT deficits and cognitive deficits related to other areas of brain function (Grant et al., 2000).

To test the first hypothesis, we compared schizophrenia patients and healthy subjects on a battery of cognitive tests, which tap into DLPFC function, and with the IGT, which assays OFPFC function. We applied a computational model, the Expectancy-Valence model (Busemeyer and Stout, 2002; Yechiam et al., 2005) to identify the relative contributions of distinct components (attention to past outcomes, relative weight of wins and losses, choice strategies) to decisions made during performance of the IGT.

To examine the second hypothesis, we compared schizophrenia patients with and without cannabis use disorders on the same measures. We focused on cannabis because it is the most commonly used illicit drug in schizophrenia (Murray et al., 2003).

Finally, we tested the third hypothesis by examining correlations between performance on the IGT and performance on cognitive tests indexing parcellated aspects of the DLPFC.

2. Materials and methods

2.1. Subjects

2.1.1. Patients with schizophrenia—Twenty-seven patients were recruited from various inpatient and outpatient programs at the North Shore-Long Island Jewish Health System through referrals from clinicians and fliers that were posted in these programs. Inclusion criteria were: (1) current diagnosis of schizophrenia or schizoaffective disorder confirmed by a structured clinical interview for DSM-IV Axis I disorders (SCID-IV/Patient edition; First et al., 1998); (2) no DSM-IV criteria for a current substance-induced psychotic disorder or a psychotic disorder due to a general medical condition.

Thirteen patients with schizophrenia and no substance use disorders (SCZ⁽⁻⁾) had no past or current DSM-IV diagnosis for substance or alcohol use disorders.

Fourteen patient with schizophrenia and cannabis use disorders (SCZ⁽⁺⁾) had the additional following inclusion criteria: (1) current DSM-IV diagnosis for cannabis abuse or dependence; (2) having cannabis as a main drug of choice; (3) being in a supervised program (inpatient, residential, or intensive day program) in order for the staff to monitor substance use and accurately determine the duration of sobriety; and (3) being sober for at least 1 week.

2.1.2. Healthy subjects—Twenty normal controls were recruited at the Zucker Hillside Hospital for other studies on cognition in schizophrenia. Consenting subjects were assessed with the SCID-IV/non Patient edition (First et al., 2001) and were excluded if they had any history of psychiatric and/or substance use disorders. Six healthy subjects (30%) had a history of occasional use of marijuana and smoked marijuana 10 times or less during their lifetime. All the healthy subjects were sober for more than 3 months prior to testing.

The study was conducted according to the guidelines of the Institutional Review Board of the North Shore — Long Island Jewish Health System (Lake Success, NY). All subjects were paid for their participation in the study.

2.2. Experimental design and procedures

2.2.1. Assessments of cognition

1. Premorbid intelligence was estimated with the Wide Range Achievement Test—Third Edition, Reading subtest (WRAT-3R) (Spreen and Strauss, 1998).
2. Visual attention and working memory was assessed with the CPT Identical Pairs test (CPT-IP) (Cornblatt et al., 1988,1989).

3. Auditory attention and verbal working memory was measured with the Wechsler Adult Intelligence Scale—Revised, Digit Span Subtest (WAIS-R Digit Span).
4. Verbal learning and memory was assessed with the California Verbal Learning Test (CVLT) (Delis et al., 1987).
5. Verbal fluency was measured with the Controlled Oral Word Association Test (COWAT) (Spreen and Strauss, 1998).
6. Processing speed and executive function was assessed with the Trail Making Test Parts A and B is drawn from the Halstead-Reitan Neuropsychological Battery (Reitan, 1979).

Cognitive tests are described in the Supplemental materials.

2.2.2. Assessment of emotion-based decision-making—Emotion-based decision-making was assessed with the computerized version of the IGT (Bechara, 2005). The IGT is described in the Supplemental materials section.

2.3. Data analysis

Groups were compared using either a Chi-square test or Fisher's exact test, as appropriate, for categorical variables, and analysis of variance (ANOVA) for Continuous variables. Correlations were analyzed using Spearman rank correlation coefficients. A result was considered statistically significant at the 0.05 level of significance. Repeated measures analysis of covariance (RM ANCOVA) was used to analyze net scores, where the model contained one repeated (within) factor (net scores), two covariates of “years of education” and “WRAT-3 Reading Subtest”, and a between factor (grouping) of patient group: schizophrenia patients vs. healthy subjects or SCZ⁽⁻⁾ vs. SCZ⁽⁺⁾. Power calculation is described in Supplemental materials.

3. Results

3.1. Schizophrenia patients vs. healthy subjects

3.1.1. Demographics (Table 2)—Groups did not differ for age or sex. Schizophrenia patients had less years of education than healthy subjects ($F=24.5$; $df=2,45$; $p<0.0011$). There was a higher proportion of tobacco users in the schizophrenia group compared to the healthy subject group (48% vs. 5%, $p<0.01$).

3.1.2. Cognition and emotion-based decision-making (Table 2)—There was a significant difference between the two groups for scores at the WRAT-3R ($F=10.05$; $df=1,41$; $p<0.0029$), CPT-IP fndprime ($F=16.85$; $df=1,37$; $p<0.0002$), Digit Span Forward ($F=6.53$; $df=1,40$; $p<0.0145$), Digit Span Backward ($F=11.28$; $df=1,40$; $p<0.0017$), CVLT ($F=26.89$; $df=1,40$; $p<0.0001$), COWAT Phonemic ($F=4.43$; $df=1,31$; $p<0.0435$) and Semantic ($F=26.91$; $df=1,33$; $p<0.0001$) Fluency, Trail Making A ($F=4.31$; $df=1,40$; $p<0.0443$) and B ($F=13.53$; $df=1,40$; $p<0.0007$). There were no differences between these two groups for any of the IGT variables (Fig. 1).

Mean net scores for trials 61–100 suggest that healthy subjects had a learning curve in the positive direction, whereas schizophrenia patients had a negative learning curve. Lack of findings may have been due to the large variance of net scores. Hence, net scores were categorized into two groups: if the sum of the net scores was greater than or equal to 0 vs. the sum of the net scores being less than 0 for both trials 1–60 and trials 61–100. There was no difference between these two groups for the categorized net scores for trials 1–60. However, for trials 61–100 there was a lower proportion of schizophrenia patients whose sum of the net

scores was greater than or equal to 0 compared to the healthy controls (Chi-square=6.031; $df=1$; $p<0.02$).

3.2. Schizophrenia patients without substance use disorders (SCZ⁽⁻⁾) and with cannabis use disorders (SCZ⁽⁺⁾)

3.2.1. Clinical characteristics (Table 3)—14 schizophrenia patients out of 27 had a concurrent cannabis use disorder (abuse or dependence) and had a history of smoking one “joint” (about 0.5 g of cannabis) or more per day, 4 days or more per week (Table 3).

Seven of them had also concurrent alcohol use disorders, and among those patients with alcohol use disorders, three had cocaine use disorders and one had opioid use disorders. Ten subjects were abstinent for more than 1 year, 3 subjects were abstinent for 2 months or more, and one subject was abstinent for 2 weeks. Hence, the period of sobriety was long enough in our sample to rule out an acute effect of cannabis on cognition. Eleven patients were on atypical antipsychotics (including four patients on clozapine), one patient on typical antipsychotics, and two patients on a combination of atypical and typical antipsychotics. Two patients were on anticholinergic medications. The onset of cannabis use preceded the onset of psychosis in 11 patients (79%), occurred at the same time as the onset of psychosis in 2 patients (14%), and started 1 year after the onset of psychosis in one patient (7%). Among SCZ⁽⁻⁾ patients, 11 patients were on atypical medications (including two patients on clozapine), and two patients were on a combinations of typical and atypical antipsychotic medications. One patient was taking anticholinergic medication.

There were no significant differences between these two groups for age, sex, and marital status. SCZ⁽⁻⁾ patients had on average 2 more years of education compared to SCZ⁽⁺⁾ patients ($p<0.0243$). Age at onset of psychosis, duration of psychotic illness, BPRS and SANS total scores, and SANS subscores for flat affects, alogia, and anhedonia did not differ between groups. However, SCZ⁽⁺⁾ patients had higher mean SANS subscore for avolition than SCZ⁽⁻⁾ patients ($F=5.18$; $df=1,25$; $p<0.0317$). There was a higher proportion of tobacco users in the SCZ⁽⁺⁾ group compared to the SCZ⁽⁻⁾ group (79% vs. 15%, $p<0.01$).

3.2.2. Cognition and emotion-based decision-making (Table 3)—There were no differences between patients with and without cannabis use disorders for scores at the WRAT-3R, CPT-IP fndprime, CVLT, Phonemic and Semantic Fluency, Trail Making A and B, or for any of the IGT variables. SCZ⁽⁺⁾ patients had higher digit span forward scores ($t=2$; $df=1,23$; $p<0.05$) compared to SCZ⁽⁻⁾ patients. There were no differences between SCZ⁽⁺⁾ patients with ($n=7$) and without ($n=7$) alcohol use disorders. However, sample size may be too small to detect differences between patients with ($n=7$) and without ($n=7$) alcohol use disorders.

3.3. Associations between IGT and cognitive test performances

In the schizophrenia group ($n=27$) there were no statistically significant correlations between total net scores and any of the cognitive scores.

4. Discussion

Similar to previous studies (for a review, see Nuechterlein et al., 2004) and in support of our first hypothesis, we found that patients with schizophrenia had cognitive deficits for attention, working memory and executive functioning compared to normal controls. In agreement with some but not all of the reviewed studies, we found differences between schizophrenia patients and normal controls for IGT performance. These findings suggest that patients with schizophrenia have impaired cognitive functioning, thought to be more linked to the

dorsolateral prefrontal cortex, and impaired emotion-based decision-making more linked to the ventromedial/orbital prefrontal cortex.

There are multiple possible reasons for discrepancies between studies looking at IGT performance in schizophrenia. First, most of the studies (including ours) included small sample size and negative findings may be due to the large variance of net scores. Second, as suggested by Rodríguez-Sánchez et al. (2005), there is a wide disparity in performance by healthy subjects across studies. Third, IQ and education may be correlated with IGT performance (Rodríguez-Sánchez et al., 2005), which may explain IGT performance differences in studies that did not control for educational or IQ level (Shurman et al., 2005). Finally, discrepancies between studies may be related to the heterogeneity of diagnostic groups. Many of the negative studies included schizophrenia and schizoaffective disorder (Wilder et al., 1998; Ritter et al., 2004; Rodríguez-Sánchez et al., 2005). Positive studies have generally included only patients with schizophrenia (Beninger et al., 2003; Shurman et al., 2005; Kester et al., 2006), although some studies that included only patients with schizophrenia failed to find differences between groups (Cavallaro et al., 2003; Evans et al., 2005; Thurnbull et al., 2006).

We did not find significant differences between SCZ⁽⁻⁾ and SCZ⁽⁺⁾ patients for many of the cognitive tests administered, with the exception of Digit Span Forward. Our results are in agreement with a previous study showing no differences between schizophrenia patients with ($n=38$) and without ($n=25$) a history of cannabis abuse for performance at tests assessing intelligence, memory, learning, fluency, and problem solving (Cleghorn et al., 1991). However, in a study comparing schizophrenia patients with ($n=26$) and without ($n=37$) cannabis use 10–12 years after the admission for a first-episode of psychosis, Stirling et al. (2005) reported that cannabis users had better cognitive functioning than patients without cannabis use in several domains including design memory, verbal fluency, object assembly, block design, picture completion, picture arrangement, and face recognition memory. Contrary to our expectations, there were no differences between SCZ⁽⁻⁾ and SCZ⁽⁺⁾ patients for IGT performance. Other factors such as better premorbid functioning and socialization (Arndt et al., 1992; Sevy et al., 2001) may be more critical than impaired emotion-based decision-making for increasing the risk of substance use disorders in patients with schizophrenia.

In support of our third hypothesis, we did not find any statistically significant correlations between IGT total scores and cognitive scores. Our results suggest that deficits of the DLPFC and OPFC are not directly related to one another.

Our study has some limitations. There was a higher proportion of tobacco users in the schizophrenia group compared to the healthy subject group (48% vs. 5%) and in the SCZ⁽⁺⁾ group compared to the SCZ⁽⁻⁾ group (79% vs. 15%). It has been suggested that nicotine may help schizophrenia patients to be more vigilant, focused, and improve their working memory (Lee et al., 1997; George et al., 2002). Although all subjects were asked not to smoke before testing, nicotine levels were not assessed in this study. Hence, there is a possibility that some patients had improved cognitive performance following nicotine use. Since most of the schizophrenia smokers were cannabis abusers, nicotine may have improved cognition of SCZ⁽⁺⁾ patients to a level similar to SCZ⁽⁻⁾ patients, which may have resulted in differences between groups being too small to detect. Our negative results may also be due to small sample sizes. The reported confidence intervals for the difference between the means raise the possibility that the statistical power was too low to detect small differences between SCZ⁽⁺⁾ and SCZ⁽⁻⁾ groups for cognition and emotion-based decision-making. Future studies will have to include larger sample sizes in order to confirm our preliminary findings.

In summary, findings on IGT performance in schizophrenia have been mixed. Similar to several previous studies, we found deficits in cognitive functioning and emotion-based decision-

making in schizophrenia. However, concurrent abuse of cannabis had no compounding effects on cognition, as well as emotion-/affect-based decision-making. Future studies will be needed to determine if the neurobiological mechanisms underlying addiction differ between individuals with and without schizophrenia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi: 10.1016/j.schres.2007.01.005.

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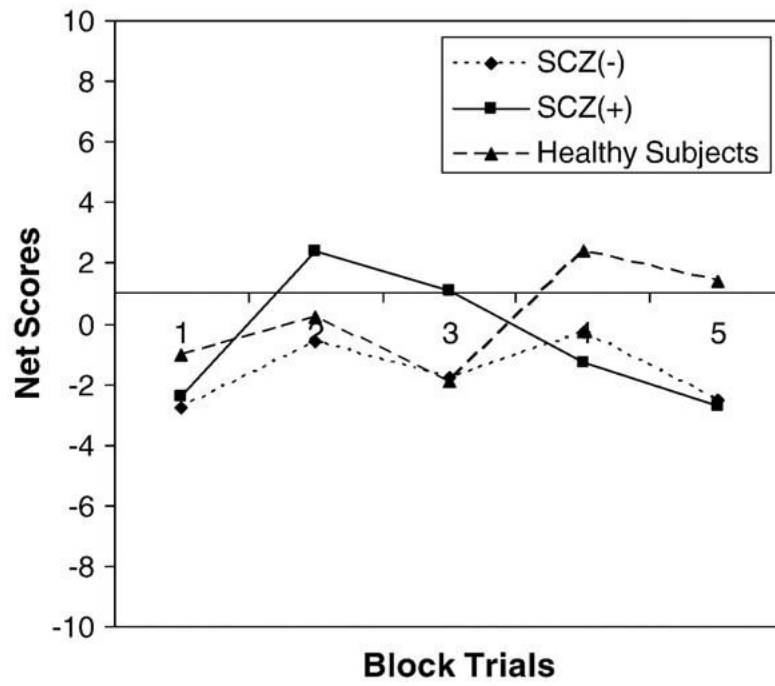


Fig 1.
Iowa Gambling Task in SCZ(+), SCZ(-) and healthy subjects.

Table 1

Studies comparing patients with schizophrenia or schizoaffective disorders and normal controls for the performance at the Iowa Gambling Task (IGT)

Authors	Subjects	Assessments	Results	Comments
<i>Studies showing differences in IGT performance between groups</i>				
Beninger et al. (2003)	36 patients (half on typical (67% male; age: 46 (mean)±1 (SD)) and half (67% male; age 42±12) on atypical anti-psychotics) and 18 controls (67% male; age: 45±3). Exclusion of patients with substance abuse in the past month.	IGT (real card version), MMSE, BPRS, WCST, declarative memory questionnaire	IGT: patients on atypicals had fewer choices from advantageous decks compared to patients on typicals or controls ^a . Patient groups differ from controls for declarative memory and MMSE. Patients on typicals perform worse at the WCST than patients on atypicals and controls	No information about substance use disorders in controls. No information about past history of substance use disorders in patients
Ritter et al. (2004)	20 chronic patients (100% male, age: 48±6) and 15 controls (100% male, age: 47±10). Exclusion of subjects with substance use disorders for the past 3 months	IGT (computerized version) North American Adult Reading Test, WCST, BPRS, SANS	IGT: Patients had a larger differential between disadvantageous and advantageous cards and lost more money than controls. There were no differences between groups across blocks ^a . A history of alcohol use disorder as a covariate did not change results. Both groups perform poorly at the WCST.	No correlations between IGT variables and WCST or symptoms.
Shurman et al. (2005)	39 patients (72% male, age: 33±10) and 10 controls (50% male, age: 32±4). Exclusion of subjects with a history of substance use disorders	IGT (computerized version) WCST, DMST, PANSS, SANS, SAPS	IGT: Patients had smaller total net scores and earned less money than controls. Group differences for IGT performance across blocks ^a was significant at $p=0.08$. Patients had a preference for decks with low frequency and high punishments. Patients had worse WCST and DMST performances than controls. Total money amount earned at IGT was negatively correlated with SANS score.	
Kester et al. (2006)	15 adolescents with schizophrenia (60% male, age: 16±3) and 25 controls (56% male, age: 17±2). Exclusion of subjects with substance use disorders	IGT (computerized version), WRAT-3, BPRS, SANS, PAS, GAS, and WCST	Patients are doing worse than controls for IGT ^a and WCST	
<i>Studies showing no differences in IGT performance between groups</i>				
Wilder et al. (1998)	12 patients (91% male, age: 33±6) and 30 controls (41% male; age: 30±10). Exclusion of subjects with substance use disorders for the past 6 months ^b	IGT (real card version) ^b , CVLT, LNSP, WCST WAIS-R, and WRAT-R reading test	No differences between groups for number of choices made from each deck and overall money lost at the IGT. Patients had a preference for decks with low frequency and high magnitude punishments. No correlations between IGT and cognitive variables	No analysis of substance use disorder data
Cavallaro et al. (2003)	110 patients with chronic schizophrenia (60% male; age: 33±9), 67 patients with OCD ^c (49% male; age: 30±9) and 56 controls (40% male; age: 31±6). Exclusion of patients with "multiple diagnoses"	IGT (real card version), WCST (real card version), Tower of Hanoi	Number of choices for disadvantageous decks did not differ between schizophrenia and control. Schizophrenia performed worse at the WCST and tower of Hanoi compared of controls	Unclear if subjects with substance use disorders were excluded from the study
Evans et al. (2005)	19 patients (gender not reported; age: 38±10) and 19 controls	IGT (real card version) WCST, COWAT, SANS,	No differences between groups for IGT performance and subjective experience across blocks ^a .	No information on substance

Authors	Subjects	Assessments	Results	Comments
<i>Studies showing differences in IGT performance between groups</i>				
	case-matched for age and level of education	SAPS	Correlation between behavioral performance and subjective ratings No correlations between IGT outcomes and severity of symptoms	use disorders. No comparison of groups for WCST and COWAT performances No information on history of substance abuse in patients
Rodríguez-Sánchez et al. (2005)	80 first-episode (FE) patients (69% male, age: 26±7) and 22 controls 55% male, age: 26±6). Exclusion of patients with substance dependence	IGT (computerized version) WAIS-III backward digits, FAS, TMT, SANS, SAPS	No differences between groups for IGT (net scores, total net score, choices per Deck). Patients had worse cognition than controls	No information on substance use disorders. Not specified if same sample as Evans et al. (2005)
Thurnbull et al. (2006) ^d	21 chronic patients (61% male, age: 13±1) and 21 controls matched for age and education. No exclusion of substance use disorders	IGT (real card version), COWAT, WCST, tests of set-shifting abilities, SANS, SAPS	No differences between groups for IGT ^a . High levels of negative symptoms were associated with difficulties of reversal contingencies	No information on substance use disorders. Not specified if same sample as Evans et al. (2005)

CVLT = California Verbal Learning Test; WCST = Wisconsin Card Sorting Test; LNSP = Letter Number Span; WAIS-R = Wechsler Adult Intelligence Scale—Revised; WRAT-3 = Wide Range Achievement Test—Third Edition; BPRS = Brief Psychiatric Rating Scale; SANS = Scale for the Assessment of Negative Symptoms; DMST = Delayed match to Sample Task; PANSS = Positive and Negative Syndrome Scale; SAPS = Scale for the Assessment of Positive Symptoms; FAS = verbal fluency test; TMT = Trail Making Test; COWAT = Controlled Oral Word Association; PAS = Premorbid Adjustment Scale; GAS = Global Assessment Scale.

^aTwo-way analysis of variance (ANOVA; groups by net scores interaction effects).

^bPersonal communication from Dr. T. Goldberg.

^cResults for OCD patients are not reviewed.

^dIncludes same patients as Evans et al. (2005).

Table 2
Demographics, cognition, and emotion-based decision-making in patients with schizophrenia and healthy subjects

	Patients with schizophrenia (n=27)	Healthy subjects (n=20)	<i>p</i> ^a	Confidence intervals
<i>Demographics</i>				
Age, in years	30±9 (18–46) ^b	33±10 (19–50)	ns	(–8.61, 2.61)
Gender (male/female)	17 m/10 f	12 m/8 f	ns ^c	
Years of education	12±2 (9–15)	15±2 (12–18)	<0.0011	(–4.19, –1.81)
<i>Cognitive testing</i> ^d :				
WRAT-3 reading subtest	89±15 (60–111)	101±11 (76–117)	<0.0029	(–20.00, –4.00)
CPT-IP, fndprime	1±0.7 (–0.3–2.6)	2±0.9 (0.7–4.0)	<0.0002	(–1.47, –0.53)
Digit Span Forward	6±1 (4–9)	7±2 (4–11)	<0.0145	(–1.90, –0.11)
Digit Span Backward	4±0.9 (2–6)	6 ±2 (2–11)	<0.0017	(–2.87, –1.13)
CVLT	35±12 (11–60)	54±11 (34–76)	<0.0001	(–25.89, –12.11)
COWAT, Phonemic Fluency	32±11 (14–62)	40±13 (18–65)	<0.0435	(–15.06, –0.94)
COWAT, Semantic Fluency	14±5 (6–23)	24±4 (19–31)	<0.0001	(–12.74, –7.26)
Trail Making A	41±24 (14–132)	29±10 (17–50)	<0.0443	(0.49, 23.51)
Trail Making B	130±65 (39–300)	67±32 (36–125)	<0.0007	(31.15, 94.85)
<i>Iowa Gambling Task:</i>				
Total amount of money won/lost (\$)	–1296±862 (–3015–500)	–981±945 (–2640–830)	ns	(–848.55, 218.55)
Total number of cards chosen from:				
Deck A'	20±7 (2–36)	18±5 (12–27)	ns	(–1.70, 5.70)
Deck B'	32±11 (16–56)	31±8 (19–56)	ns	(–4.85, 6.85)
Deck C'	23±6 (13–41)	23±6 (8–33)	ns	(–3.57, 3.57)
Deck D'	24±8 (11–43)	27±6 (12–38)	ns	(–7.29, 1.29)
Net scores: ^e				
Trials 1–20	–2.6±4 (–16–4)	–1.0±5 (–8–14)	ns	(–4.24, 1.04)
Trials 21–40	1.0±6 (–16–14)	0.2±4 (–10–8)	ns	(–2.32, 3.92)
Trials 41–60	–0.3±7 (–14–18)	–1.9±7 (–14–14)	ns	(–2.56, 5.76)
Trials 61–80	–0.8±6 (–16–10)	2.4±8 (–12–20)	ns	(–7.31, 0.91)
Trials 81–100	–2.6±8 (–18–12)	1.4±9 (–20–20)	ns	(–9.01, 1.01)
Total net score (sum of Net scores)	–5.0±18 (–46–22)	1.2±17 (–40–32)	ns	(–16.65, 4.25)
Categorical scores				
Trials 1–60 (0/1) ^f	14/13	13/7	ns ^c	
Trials 61–100 (0/1)	15/12	4/16	<0.02 ^c	
Expectancy-Valence Model				
Recency parameter	0.24±0.32 (0–1)	0.37±0.42 (0–1)	ns	(–0.35, 0.09)
Attention to Wins/Losses parameter	0.42±0.43 (0–1)	0.40±0.37 (0–1)	ns	(–0.22, 0.26)
Choice consistency parameter	0.48±2.9 (–5–5)	–1.04±3.17 (–5–5)	ns	(–0.27, 3.31)

^a *T*-test except when indicated.

^b Mean±standard deviation (range).

^c Chi-square test.

^d On all tests except Trails A and Trails B, higher scores represent better performance. Trails A and B are time to completion, thus higher scores reflect worse performance.

^e Net score: number of cards chosen from advantageous decks (C' or D') minus number of cards chosen from disadvantageous decks (A' or B') during 20 trials.

^f Categorical scores = 1 if \sum net scores for trials 1–60 or trials 61–100 ≥ 0 , and = 0 if \sum net scores for trials 1–60 or trials 61–100 < 0 .

Table 3
Demographics, cognition and clinical characteristics of schizophrenia patients with (SCZ⁽⁺⁾) and without (SCZ⁽⁻⁾) cannabis use disorders and healthy subjects

	Patients with schizophrenia		<i>p</i>	Confidence intervals
	SCZ ⁽⁻⁾ (<i>n</i> = 13)	SCZ ⁽⁺⁾ (<i>n</i> = 14)		
Age, in years	31±9 (18–46) ^a	29±9 (18–45)	ns	(-5.14, 9.14)
Gender (male/female)	7/6	10/4	ns ^b	
Years of education	13±1 (11–15)	11±1 (9–14)	<0.0005	(1.21, 2.79)
Age at onset of psychosis, in years	21±5 (12–29)	20±4 (15–32)	ns	(-2.58, 4.58)
Age at onset of cannabis use, in years		16±1 (14–18)		
Duration of psychotic illness, in years	10±9 (0–28)	9±9 (1–27)	ns	(-6.14, 8.14)
<i>Symptoms:</i>				
Brief Psychiatric Rating Scale (BPRS) Total Score	28±8 (19–47)	29±7 (19–46)	ns	(-6.95, 4.95)
Scale for the Assessment of Negative Symptoms (SANS) Total Score	5.8±4.7 (0–13)	8.0±3.9 (2–16)	ns	(-5.61, 1.21)
<i>Subscales:</i>				
Flat affect	1.8±1.5 (0–4)	2.0±1.3 (0–4)	ns	(-1.31, 0.91)
Alogia	1.0±1.2 (0–3)	1.1±1.2 (0–3)	ns	(-1.05, 0.85)
Avolition	1.3±1.4 (0–3)	2.5±1.3 (0–5)	<0.0317	(-2.27, -0.13)
Anhedonia	1.7±1.4 (0–4)	2.3±1.4 (0–4)	ns	(-1.71, 0.51)
<i>Cognitive testing^c:</i>				
WRAT-3 reading subtest	85±15 (61–107)	92±14 (60–111)	ns	(-18.50, 4.50)
CPT-IP, fndprime	0.9±0.7 (-0.3–2.1)	1±0.8 (0.0–2.6)	ns	(-0.70, 0.50)
Digit Span Forward	6±1 (4–7)	7±1 (5–9)	<0.0485	(-1.79, -0.21)
Digit Span Backward	4±1 (2–5)	4±1 (3–6)	ns	(-0.79, 0.79)
CVLT	33±10 (11–48)	36±14 (18–60)	ns	(-12.71, 6.72)
COWAT, Phonemic Fluency	32±7 (19–42)	31±14 (14–62)	ns	(-7.89, 9.89)
COWAT, Semantic Fluency	14±6 (6–23)	14±5 (8–23)	ns	(-4.37, 4.37)
Trail Making A	49±28 (29–132)	34±18 (14–87)	ns	(-3.52, 33.52)
Trail Making B	151±72 (61–300)	110±53 (39–213)	ns	(-8.86, 90.86)
<i>Iowa Gambling Task:</i>				
Total amount of money won/lost (\$)	-1157±807 (-2400–460)	-1424±921 (-3015–500)	ns	(-421.82, 955.82)
Total number of cards chosen from:				
Deck A'	21±8 (2–36)	20±6 (10–29)	ns	(-4.58, 6.58)
Deck B'	33±11 (21–56)	32±11 (16–51)	ns	(-7.73, 9.73)
Deck C'	24±7 (13–41)	22±5 (14–34)	ns	(-2.80, 6.80)
Deck D'	22±6 (11–33)	26±8 (14–43)	ns	(-9.64, 1.64)
Net scores ^d				
Trials 1–20	-2.8±5 (-16–4)	-2.4±4 (-10–2)	ns	(-3.98, 3.18)
Trials 21–40	-0.6±7 (-16–14)	2.4±6 (-6–14)	ns	(-8.16, 2.16)
Trials 41–60	-1.8±5 (-10–6)	1.1±9 (-14–18)	ns	(-8.74, 2.94)
Trials 61–80	-0.3±4 (-8–8)	-1.3±7 (-16–10)	ns	(-3.57, 5.57)
Trials 81–100	-2.5±8 (-18–12)	-2.7±8 (-18–8)	ns	(-6.15, 6.55)
Total Net score (sum of Net scores)	-8.0±17 (-46–14)	-2.9±18 (-30–22)	ns	(-19.00, 8.81)
Categorical scores				
Trials 1–60 (0/1) ^e	9/4	5/9	ns ^b	
Trials 61–100 (0/1)	7/6	8/6	ns ^b	
Expectancy-Valence Model				
Recency parameter	0.16±0.17 (0–0.50)	0.31±0.41 (0–1)	ns	(-0.40, 0.10)
Attention to Wins/Losses parameter	0.41±0.42 (0–1)	0.44±0.44 (0–1)	ns	(-0.37, 0.31)
Choice consistency parameter	0.11±3.2 (-5–5)	0.81±2.79 (-5–5)	ns	(-3.08, 1.68)

^a Mean ± standard deviation (range).

^b Chi-square or Fisher's Exact (when *n* < 5 in one of the cells) test.

^c On all tests except Trails A and Trails B, higher scores represent better performance. Trails A and B are time to completion, thus higher scores reflect worse performance.

^d Net score: number of cards chosen from advantageous decks (C' or D') minus number of cards chosen from disadvantageous decks (A' or B') during 20 trials.

^e Categorical scores = 1 if \sum net scores for trials 1–60 or trials 61–100 ≥ 0 , and = 0 if \sum net scores for trials 1–60 or trials 61–100 < 0.