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Brief report

Correlations between executive function, decision-making and impulsivity are disrupted in schizophrenia versus controls

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ABSTRACT

Schizophrenia ($n=68$) and control ($n=62$) participants matched on cigarette smoking history were assessed on executive function, decision-making and impulsivity tasks. In controls, executive function and decision-making correlated positively with each other and negatively with impulsivity. There were no inter-task correlations in schizophrenia participants. The significance of these findings is discussed.

1. Introduction

Cognitive dysfunction is a core feature of schizophrenia (SZ) linked to functional outcome (Green, 1996). Executive function, decision-making and impulsivity deficits have been associated with poor prognosis (Green et al., 2000), social maladjustment (Kim et al., 2007), and propensity toward addictive disorders in SZ (Dervaux et al., 2001).

Cognitive fragmentation, disconnection between brain regions and subsequent lack of integration of information, may be responsible for the cognitive impairment in SZ (Cole et al., 2011; Schmitt et al., 2011; Stephan et al., 2009). However, few studies have explored the relationship between higher-order cognitive functions such as executive function, decision-making and impulsivity in both control and SZ populations.

Studies examining the relationship between executive function and decision-making, assessed by the Wisconsin Card Sorting Task (WCST) and Iowa Gambling Task (IGT) respectively, have yielded mixed results (Toplak et al., 2010), some reporting associations in controls (Brand et al., 2007; Yip et al., 2009) and in SZ (Lee et al., 2009; Yip et al., 2009), and others not (Denburg et al., 2005; Kester et al., 2006; Kim et al., 2009; Nakamura et al., 2008; Ritter et al., 2004; Shurman et al., 2005). Only one study examined the relationship between such tasks and delay discounting (a form of impulsivity); rapid delay discounting (i.e., high impulsivity) was associated with poor performance on the IGT in controls (Sweitzer et al., 2008). It is of note that with the exception of Yip et al. (2009), none of the aforementioned studies considered cigarette-smoking in their analyses. Given that nicotine can markedly affect cognition depending on psychiatric diagnosis (Barr et al., 2008; Jubelt et al., 2008; Wing et al., 2011, 2012), controlling for cigarette smoking is essential.

The present study investigated the relationship between executive function, decision-making and impulsivity in SZ and non-psychiatric controls, while controlling for cigarette smoking history.

2. Methods

2.1. Participants

One hundred and thirty participants were recruited into two cross-sectional studies of the effects of cigarette smoking on cognitive function in SZ: 68 outpatients with a diagnosis of SZ or schizoaffective disorder and 62 healthy controls. Participants were divided into current ($n=33$ and $n=23$), former ($n=12$ and $n=11$) and never smokers ($n=23$ and $n=28$); biochemically verified by expired carbon monoxide levels. Smokers were studied under satiated conditions, as ensured by hourly smoke breaks (Sacco et al., 2005).

Participants were 18–65 years old, evaluated using the Structured Clinical Interview for DSM-IV (SCID-IV; (First et al., 1996)), had no illicit drugs or alcohol abuse in the past 6 months (confirmed by urine toxicology Medtox®; Wilmington, NC) and an estimated full-scale IQ ≥ 80. Participants with SZ or schizoaffective disorder were psychiatrically stable, had a Positive and Negative Syndrome Scale

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(PANSS; (Kay et al., 1987)) score <70 and stable antipsychotic medication (≥ 1 month). Controls did not meet criteria for current Axis I disorders. For further details see Wing et al. (2012).

2.2. Neuropsychological testing

2.2.1. Executive function

A computerized version of the WCST was administered (for detailed description, see Heaton et al., 1993). This task relies heavily on dorsolateral prefrontal cortex (DLPFC) functioning (Berman et al., 1995; Nagahama et al., 1996). Categories completed, % total errors, % perseverative errors and % non-perseverative errors were analyzed.

2.2.2. Decision-making

A computerized version of the IGT was administered (for detailed description of task, see Bechara et al., 1994). Performance in this task provides a measure of risk-reward decision-making (Bechara et al., 1994) and is associated with ventromedial PFC (vmPFC) function (Bechara et al., 2000). Total money and total net score were analyzed.

2.2.3. Delay discounting

The Kirby Delay Discounting Task (KDDT) requires participants to make a series of choices between hypothetical monetary rewards which vary as a function of magnitude and length of delay to obtain the reward (Kirby et al., 1999). While deliberative processes of DD involve the DLPFC, limbic areas and interconnected regions, particularly the orbito-frontal cortex (OFC), preferentially respond toward immediate rewards (McClure et al., 2004). Discounting rates [Ln(k)] at the small, medium and large reward size were analyzed.

2.3. Statistical analysis

Statistical analysis was conducted using SPSS (v.15.0; Chicago, IL), significance level; $p<0.05$. Demographic and clinical characteristics were analyzed by Chi-square and analyses of variance (ANOVA). Participants that had outlying WCST, IGT or DD measures on box plots produced in SPSS (>1.5 times greater than the inter-quartile range), were removed from subsequent analysis of that task. The relationships between task outcome measures in CON and SZ groups (whole group and divided by smoking history) were examined using Pearson correlation coefficients and partial correlation analyses to control for demographic variables. Fisher r-to-z transformations were conducted to assess the statistical significance of the difference between group correlation coefficients (http://faculty.vassar.edu/lowry/rdiff.html). A principal component analysis was conducted in each sample to determine the variance accounted for in the first component and hence how much of the correlational variance of the variables are truly shared.

3. Results

3.1. Demographic and clinical characteristics

The demographic and clinical characteristics of the sample have been presented previously (Wing et al., 2012). IQ, education and gender differed between groups. All correlations analyses were therefore repeated using partial correlation analyses that controlled for these factors. Although some tests no longer reached statistically significance under these conditions, trends in the same direction remained.

3.2. Task performance

Compared to controls, SZ patients were significantly impaired on the IGT and WCST (see Supplementary materials) but not the KDDT (Wing et al., 2012). Outcome measures within the same task were highly intra-correlated in both control and SZ participants (data not shown).

3.3. Inter-task correlations

Analyses show that IGT measures were significantly correlated with WCST measures in controls; the lower the IGT scores and money (i.e., poor decision-making), the more errors on the WCST (i.e., poor executive function) (Table 1). Furthermore, in controls, IGT and WCST measures significantly correlated with DD; poor performance on the IGT (i.e., low scores) and WCST (i.e., high errors) were associated with increased DD (i.e., increased preference for small immediate rewards over larger delayed rewards) (Table 1). Correlations in the control current, former and never smoking subgroups (see Supplementary materials) were of the same nature but did not always reach statistical significance. However, no significant correlations were identified between any WCST, IGT and KDDT measures in the SZ sample, neither when collapsed across smoking subgroups (Table 1) nor when controlling for smoking history. The levels of statistical significance of the difference between the inter-task correlations (r) identified in the SZ and control groups are shown in Table 1. Principal component analyses of the variables reported in Table 1 confirmed that the variance accounted for in the first component was higher in the control sample compared to the schizophrenia sample (45.7% vs. 33.1%), thus indicating that more of the correlational variance of these variables is shared in the control group.

4. Discussion

This was the first study to assess the relationship between IGT, WCST and KDDT within SZ and control populations. Controls demonstrated robust relationships between WCST, IGT, and KDDT performance. Specifically, poor executive function was associated with risky decision-making, both of which were associated with high levels of impulsivity (i.e., DD). Analyses by these subgroups revealed similar but less robust correlations. However, interpretation of these findings was limited by the small subgroup sizes. In contrast, no correlations between task performances were observed in the SZ group as a whole or by smoking history subgroups.

While WCST, IGT and DD are distinct tasks, the inter-task correlations identified in controls suggest that overlapping brain regions and common neurocircuitry facilitate their execution. Convergent evidence highlights the overlapping contributions of the DLPFC, OFC and vmPFC in the service of these processes (Kaladjian et al., 2010; O'Doherty et al., 2001; Weinberger et al., 1986). For example, these subregions interact in the maintenance of 'nonrisky' decision-making (Manes et al., 2002; McClure et al., 2004), DLPFC damage can indirectly impair vmPFC functioning (Verdejo-García and Bechara, 2009), and patients with OFC damage, which is associated with inhibitory deficits, make more perseverative errors on the WCST despite this task being thought to represent DLPFC function (Demakis, 2003). Therefore, intact OFC, vmPFC, and DLPFC functioning may each be necessary for effective executive function and rational, non-impulsive, decision-making .

The lack of inter-task correlations found in SZ may be due to the heterogeneous nature of the disorder (Joyce and Roiser, 2007). While cognitive impairment presents itself in $\sim$80% of patients (Keefe et al., 2005), patients vary along a severity continuum (Kremen et al., 2000) and can be classified into distinct cognitive profiles (Chan et al., 2006; Kremen et al., 2004; Nuechterlein et al., 2004). Thus, cognitive performance may be deficient in some domains but not others, thereby leading to lack of inter-task correlations. Our findings may also be the result of cognitive fragmentation. Cognitive fragmentation in SZ may result from aberrant dopamine (DA) signaling (Howes and Kapur, 2009), which is hypothesized to affect functional connectivity within the cortex (Nagano-Saito et al., 2008). If the integrity of the PFC circuitry regulating higher-order cognitive processes is compromised in SZ (Goldman-Rakic, 1999; Seamans and Yang, 2004), subregions may be rendered functionally independent of one another (Friston and Frith, 1995), thus explaining lack of association between cognitive domains. As the present study solely included medicated SZ patients, the effects of DA D2 receptor blockade