Schizophrenia Research 170 (2016) 80–86

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Impulsivity across the psychosis spectrum: Correlates of cortical volume, suicidal history, and social and global function

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ARTICLE INFO

Article history:
Received 7 August 2015
Received in revised form 24 November 2015
Accepted 30 November 2015
Available online 23 December 2015

Keywords:
Impulsivity
Psychosis spectrum
Orbitofrontal cortex
Cortical volume
Psychotic disorders

ABSTRACT

Patients with psychotic disorders appear to exhibit greater impulsivity-related behaviors relative to healthy controls. However, the neural underpinning of this impulsivity remains uncertain. Furthermore, it remains unclear how impulsivity might differ or be conserved between psychotic disorder diagnoses in mechanism and manifestation. In this study, self-reported impulsivity, measured by Barratt Impulsiveness Scale (BIS), was compared between 305 controls (HC), 139 patients with schizophrenia (SZ), 100 with schizoaffective disorder (SZA), and 125 with psychotic bipolar disorder (PBP). In each proband group, impulsivity was associated with regional cortical volumes (using FreeSurfer analysis of T1 MRI scans), suicide attempt history, Global Assessment of Functioning (GAF), and Social Functioning Scale (SFS). BIS scores were found to differ significantly between participant groups, with SZA and PBP exhibiting significantly higher impulsivity than SZ, which exhibited significantly higher impulsivity than HC. BIS scores were significantly related to suicide attempt history, and they were inversely associated with GAF, SFS, and bilateral orbitofrontal cortex (OFC) volume in both SZA and PBP, but not SZ. These findings indicate that psychotic disorders, particularly those with prominent affective symptoms, are characterized by elevated self-reported impulsivity measures. Impulsivity's correlations with suicide attempt history, GAF, and SFS suggest that impulsivity may be a mediator of clinical outcome. The observed impulsivity-OFC correlations corroborate the importance of OFC deficits in impulsivity. These correlations' presence in SZA and PBP but not in SZ suggests that impulsivity may have different underlying mechanisms in affective and non-affective psychotic disorders.

1. Introduction

Impulsivity is a multidimensional construct broadly described as a tendency towards reacting rapidly to internal or external stimuli without planning or concern for possible consequences (Moeller et al., 2001). Impulsivity-related behaviors can be measured in multiple ways including self-report inventories, measures of delay-discounting, and computer-tasks (Meda et al., 2009). Various forms of impulsivity have been found to be elevated in disorders across the psychosis spectrum, including bipolar disorder (Peluso et al., 2007; Strakowski et al., 2010; Swann et al., 2001), schizoaffective disorder, and schizophrenia (Enticott et al., 2008; Nolan et al., 2011; Premkumar et al., 2008). It appears to exacerbate morbidity in these disorders, as impulsivity has been associated with increases in the risks for violence (Quanbeck et al., 2007; Volavka and Citrome, 2008), substance abuse (Dervaux et al., 2001; Schiffer et al., 2010), more intensive hospital course (Bigelow et al., 1988; Bowers et al., 2008; Greenfield et al., 1989), and suicide attempts (Gut-Fayand et al., 2001; Swann et al., 2005, 2009). Impulsivity has also been used to guide treatment and it is an important factor to consider when selecting appropriate medication regimens (Chengappa et al., 2002; Dursun et al., 2000; Krakowski et al., 2006; Spivak et al., 2003; Volavka and Citrome, 2008).

Despite evidence indicating that impulsivity differentiates psychotic patients from healthy controls, it remains unclear how impulsivity might differ across psychotic disorders. In a relatively small-scale

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http://dx.doi.org/10.1016/j.schres.2015.11.030
0920-9964/

study comparing bipolar disorder (independent of psychosis) to schizophrenia, self-reported impulsivity was elevated in the bipolar group and risk averse behavior was elevated in the schizophrenia group (Reddy et al., 2014). However, to our knowledge, impulsivity-related measures have never been compared specifically across the psychosis spectrum. Inter-disorder comparisons are of interest as the nosology of psychotic disorders remains an open and active area of research given the heterogeneity within and overlap between diagnoses (Keshavan et al., 2013). Given that forms of impulsivity have been demonstrated to be heritable traits (Niv et al., 2012; Seroczynski et al., 1999) occurring in psychotic disorders, it may be a useful measure for addressing these nosological questions, as it may help clarify differences or similarities inherent to diagnoses.

Impulsivity's neural underpinnings are imperfectly understood. A series of fMRI studies to assess neural correlates of impulsivity in schizophrenia has yielded divergent findings, identifying association with dysfunction in a variety of brain regions including ventrolateral prefrontal cortex (Kaladjian et al., 2011), dorsolateral prefrontal cortex (Arce et al., 2006), anterior cingulate cortex (Rubia et al., 2001), posterior cingulate cortex (Laurens et al., 2003), caudate nucleus, and thalamus (Barkataki et al., 2008). Similarly, structural studies in bipolar disorder have pointed to several brain regions of impulsivity-associated abnormality, including anterior medial frontal regions (Matsuo et al., 2010) and anterior cingulate cortex (Matsuo et al., 2009). Moreover, neural correlates of impulsivity in different psychotic diagnoses have only been investigated in separate studies. Direct comparison within a single study is required to evaluate whether the neural correlates of impulsivity differ or are conserved between psychotic disorders.

In this study, we aimed to compare total level of impulsivity, its subdimensions, and its clinical and neural associations across the psychosis spectrum. We measured self-reported impulsivity-related behavior and correlated it with social and global functioning, suicidal history, and regional cortical volumes in healthy controls and in probands across the psychosis spectrum recruited as part of the six-site Bipolar-Schizophrenia Network for Intermediate Phenotypes (B-SNIP) research program.

2. Methods

2.1. Study participants

The study included 305 healthy controls (HC), 139 patients with schizophrenia (SZ), 100 with schizoaffective disorder (SZA), and 125 with bipolar disorder type I who endorsed psychotic symptoms (PBP) from the B-SNIP database (Table 1). Study participants underwent diagnostic interview using the Structured Clinical Interview for DSM-IV-TR (SCID-IV) (Spitzer et al., 1997) and were categorized by diagnosis. Diagnoses were made by a consensus process led by a senior clinician at each site involving reviews of results from clinical interviews, psychiatric and medical histories, and medical records. Inclusion criteria, diagnostic techniques, and recruitment strategies were identical across all sites, as described in previous B-SNIP studies, and institutional review boards at each site approved the project (Tamminga et al., 2013).

2.2. Procedures

Participants' impulsivity was assessed using Barratt Impulsiveness Scale (BIS) version 11, a 30-item self-report measure designed to assess the personality trait of impulsivity composed of three subscales: attentional (intolerance of complexity), motor (impetuous action), and nonplanning (lack of future orientation) impulsivity (Patton et al., 1995). Patient functioning was measured by Social Functioning Scale (SFS) (Birchwood et al., 1990) and Global Assessment of Functioning (GAF) (Jones et al., 1995). Patient symptomatology was quantified using Positive And Negative Syndrome Scale (PANSS) (Kay et al., 1987) and cognition was evaluated using Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe, 2004). Patient histories of suicide attempts were also recorded based on clinical interview and recorded by Beck Lethality Scale (Beck et al., 1979). Patients were also rated on Schizo-Bipolar Scale (SBS) (Keshavan et al., 2011), a descriptive measure capturing the type and relative proportions of psychotic and affective symptoms in psychotic disorder patients and thereby placing these patients on a spectrum of psychopathology. SBS is scored on a 10-point scale where 0 represents the most bipolar-like and 9 represents the most schizophrenia-like disorder.

Table 1
Demographics of included participants.

	Controls	Schizophrenia	Schizoaffective	Psychotic bipolar
n	305	139	100	125
Mean age (SD)	37.7 (12.2)	36.7 (13.0)	36.6 (11.4)	36.0 (13.0)
Race distribution	AA 81 (27%) CA 196 (64%) OT 28 (9%)	AA 67 (48%) CA 64 (46%) OT 8 (6%)	AA 45 (45%) CA 49 (49%) OT 6 (6%)	AA 30 (24%) CA 88 (70%) OT 7 (6%)
Gender distribution	F 159 (52%) M 146 (48%)	F 43 (31%) M 96 (69%)	F 56 (56%) M 44 (44%)	F 88 (65%) M 37 (27%)
GAF (SD)	N/A	42.5 (12.2)	40.7 (10.9)	51.3 (11.7)
SFS (SD)	N/A	107.8 (21.9)	104.3 (23.4)	115.9 (21.7)
SBS (SD)	N/A	7.9 (1.2)	5.1 (1.5)	1.1 (1.1)
CPZ equivalents (SD)	0.0 (0.0)	351.6 (376.1)	344.7 (472.9)	194.0 (337.0)

SD — standard deviation; AA — African American; CA — Caucasian; OT — other; F — female; M — male; GAF — Global Assessment of Functioning; SFS — Social Functioning Scale; SBS — Schizo-Bipolar Scale.

Structural data were acquired and underwent rigorous data quality control as described in previous work (Giakoumatos et al., 2015). Total cortical volume values were calculated in 64 anatomically defined cortical parcellations that covered the entire cortex (Desikan et al., 2006).

Outliers in impulsivity, clinical measures, and structure were handled by winsorizing all values to a level of three standard deviations from the mean.

2.3. Statistical analysis

Impulsivity measures were compared between participant groups (HC, SZ, SZA, and PBP) by performing analyses of covariance (ANCOVAs) and then Tukey's honest significant difference (HSD) tests on BIS total score and subscale scores for pairwise comparisons, controlling for age, sex, site, race, and chlorpromazine equivalents of antipsychotic dosages, which were included as covariates in all statistical analyses. Impulsivity was also directly compared across the psychosis spectrum by performing Pearson's correlations between BIS total score and SBS score. The relationships between impulsivity and clinical measures of functioning for each patient group were evaluated by conducting Pearson's correlations between BIS total score and both SFS and GAF scores, with Benjamini–Hochberg adjustment for the number of functioning scales. For scales with a trending association with BIS total score ($p < 0.10$), correlations with each of the impulsivity subscales were calculated, with Benjamini–Hochberg adjustment for the number of subscales. The normality of impulsivity distributions was evaluated by performing Shapiro–Wilk tests of normality on BIS total scores within each patient group.

The relationship between impulsivity and suicidality was assessed by performing a logistic regression associating a history of suicide attempt with BIS total score. Logistic regressions were also performed associating history of suicide attempt with each of the impulsivity