Schizophrenia Research 113 (2009) 167–175

Contents lists available at ScienceDirect

Schizophrenia Research

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

A comparison of neuropsychological dysfunction in first-episode psychosis patients with unipolar depression, bipolar disorder, and schizophrenia

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ARTICLE INFO

Article history:
Received 17 December 2008
Received in revised form 6 April 2009
Accepted 9 April 2009
Available online 17 May 2009

Keywords:
Schizophrenia
Bipolar disorder
Psychotic depression
Psychosis
Neuropsychology

ABSTRACT

The severity and profile of cognitive dysfunction in first episode schizophrenia and psychotic affective disorders were compared before and after antipsychotic treatment. Parallel recruitment of consecutively admitted study-eligible first-episode psychotic patients (30 schizophrenia, 22 bipolar with psychosis, and 21 psychotic depression) reduced confounds of acute and chronic disease/medication effects as well as differential treatment and course. Patient groups completed a neuropsychological battery and were demographically similar to healthy controls ($n=41$) studied in parallel. Prior to treatment, schizophrenia patients displayed significant deficits in all cognitive domains. The two psychotic affective groups were also impaired overall, generally performing intermediate between the schizophrenia and healthy comparison groups. No profile differences in neuropsychological deficits were observed across patient groups. Following 6 weeks of treatment, no patient group improved more than practice effects seen in healthy individuals, and level of performance improvement was similar for affective psychosis and schizophrenia groups. Although less severe in psychotic affective disorders, similar profiles of generalized neuropsychological deficits were observed across patient groups. Recovery of cognitive function after clinical stabilization was similar in mood disorders and schizophrenia. To the extent that these findings are generalizable, neuropsychological deficits in psychotic affective disorders, like schizophrenia, may be trait-like deficits with persistent functional implications.

A growing body of literature describes shared aspects of psychopathology, genetics, neurobiology and treatment efficacy among schizophrenia and psychotic affective disorders (Berrettini, 2000; Ivleva et al., 2008; Murray et al., 2004). Cognitive similarities across these disorders have also been identified and may result from overlapping alterations to functional brain systems and related genetic risk factors (Berrettini, 2000; Bramon and Sham, 2001; Pearlson et al., 1997). However, cognitive dysfunction in psychotic affective disorders has been reported predominantly in chronic patients during acute episodes (Quraishi and Frangou, 2002) and it remains unclear whether neuropsychological impairments are present at illness onset, vary with clinical symptomatology, and respond differentially to pharmacological treatment.

In the schizophrenia literature, there is considerable interest in neuropsychological deficits as a major cause of functional disability (Green, 2006), a treatment target (Harvey and Cornblatt, 2008), and a phenotype marking familial risk (Berrettini, 2000; Cannon and Keller, 2006). Overlapping neuropsychological deficits have been reported in schizophrenia and affective psychoses (Daban et al., 2006; Hill et al., 2004a; Krabbendam et al., 2005; Reichenberg et al., 2008; Schretlen et al., 2007) and in their unaffected relatives (McIntosh et al., 2005; Pirkola et al., 2005). These overlapping cognitive deficits as well as persistent cognitive and functional impairments observed in psychotic bipolar disorder

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doi:10.1016/j.schres.2009.04.020

(Dickerson et al., 2004; Martinez-Aran et al., 2004; Tabares-Seisdedos et al., 2008) raise questions about the classic Kraepelinian model by suggesting more similarities regarding persistent functional deficits across the disorders.

A related line of work has compared neurocognitive function in psychotic and nonpsychotic patients with affective disorders. Psychosis in affective disorders has been associated with more severe neuropsychological dysfunction compared to nonpsychotic variants. For example, more severe impairments in executive function (Glahn et al., 2007) and spatial working memory (Glahn et al., 2006) have been observed in bipolar disorder with than without a history of psychosis. More severe cognitive dysfunction has also been reported in psychotic vs. nonpsychotic unipolar depression (Grant et al., 2001; Hill et al., 2004a; Jeste et al., 1996).

Few investigations have directly compared affective psychoses and schizophrenia in studies with parallel recruitment of all eligible patients and a broadly focused neuropsychological battery. Such strategies are needed to assess for neuropsychological profile differences, which may indicate differentially affected functional brain systems. Some studies directly comparing schizophrenia and psychotic affective disorders have reported select areas of more severe neuropsychological impairments in schizophrenia (Badcock et al., 2005; Mojtabai et al., 2000; Reichenberg et al., 2008). However, the preponderance of available evidence suggests either comparable neurocognitive deficits (Albus et al., 1996; Hill et al., 2004a; Jeste et al., 1996; Rossi et al., 2000) or somewhat greater global dysfunction in schizophrenia compared to psychotic affective disorders (Goldberg et al., 1993; McClellan et al., 2004; Mojtabai et al., 2000; Schretlen et al., 2007).

Given the numerous confounds potentially associated with different course of illness and medications used to treat schizophrenia and affective disorders, comparing disorder-associated neuropsychological function in the early course of illness may provide important insight regarding neuropsychological similarities and differences across these disorders. In addition, studies comparing cognitive abilities during acute episodes of illness to performance after treatment initiation and clinical stabilization may shed light on the impact of acute illness on cognition and deficit persistence across disorders. To our knowledge, no previous investigation has longitudinally compared neuropsychological performance in unipolar depression with psychosis, bipolar disorder with psychosis, and schizophrenia in a parallel recruitment study of first-episode patients. A diverse battery of neuropsychological tests was administered at baseline while antipsychotic-naïve or after a brief treatment discontinuation. Patients who completed 6 weeks of treatment (primarily with risperidone monotherapy) were retested to compare cognitive change at follow-up across the disorders.

1. Method

1.1. Participants

Consecutive admissions who presented with a recent onset psychotic disorder were recruited at the University of Illinois Medical Center. Because diagnosis is often unclear during acute episodes, particularly in first episode psychosis patients, patients were followed clinically for several months before a consensus diagnosis could be reached. Diagnosis was determined during multi-disciplinary consensus conferences

Table 1
Demographic and clinical data for each group.

Demographics	Healthy comparison (HC)	Schizophrenia (SZ)	Bipolar w/ psychosis (BP)	Psychotic depression (PsyDep)	F/χ^2 (df)	Significant post-hoc comparisons
	$n=41$	$n=30$	$n=22$	$n=21$		
Age (years)	24.90(8.79)	23.03(7.32)	22.68(6.35)	24.38(7.70)	0.56 (3,110) [ns]	
Range	12–41	13–50	12–45	14–43		
Sex					$\chi^2=5.24$ (3) [ns]	
Male	58.5%	80.0%	59.1%	52.4%		
Female	41.5%	20.0%	40.9%	47.6%		
Race					$\chi^2=3.82$ (6) [ns]	
Caucasian	32.6%	26.7%	22.7%	25.0%		
African-American	51.2%	46.6%	63.6%	45.0%		
Asian/Latino/Other	16.3%	26.7%	13.6%	30.0%		
Annett Handedness scale	8.66(6.35)	8.20(5.04)	8.23(5.87)	5.24(9.24)	1.36 (3,110) [ns]	
Education	12.59(2.78)	12.13(2.53)	13.24(3.25)	12.24(2.28)	0.77 (3,109) [ns]	
Parental SES	2.48(0.85)	2.93(1.02)	2.70(1.08)	3.06(1.00)	2.01 (3,102) [ns]	
WRAT-III Reading	99.35(7.51)	93.00(11.69)	94.77(14.36)	96.71(10.80)	2.14 (3,109) [ns]	
Clinical variables						
Median DUP (mos)		5.5	3.0	6.0		
PANSS total		81.18(13.33)	73.14(8.83)	72.45(17.45)	3.18 (2,66) [*]	SZ>BP, PsyDep
PANSS Pos		23.61(3.88)	23.48(4.96)	17.60(4.28)	13.32 (2,66) [§]	PsyDep<SZ, BP
PANSS Neg		18.93(4.65)	12.62(5.41)	16.60(6.08)	8.46 (2,66) [§]	BP<SZ, PsyDep
HDRS		25.86(9.52)	29.14(8.62)	35.25(8.78)	6.33 (2,66) [†]	PsyDep>SZ
Simpson–Angus		0.25(0.65)	0.10(0.30)	0.85(2.72)	1.42 (2,66) [ns]	
GAF		37.31(7.05)	44.05(4.90)	43.94(7.94)	8.22 (2,64) [§]	SZ<BP, PsyDep

[ns] $p>0.05$.
[*] $p<0.05$.
[†] $p\leq 0.01$.
[§] $p\leq 0.001$.