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Cortical morphology of adolescents with bipolar disorder and with schizophrenia

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ABSTRACT

Introduction: Recent evidence points to overlapping decreases in cortical thickness and gyrification in the frontal lobe of patients with adult-onset schizophrenia and bipolar disorder with psychotic symptoms, but it is not clear if these findings generalize to patients with a disease onset during adolescence and what may be the mechanisms underlying a decrease in gyrification.
Method: This study analyzed cortical morphology using surface-based morphometry in 92 subjects (age range 11–18 years, 52 healthy controls and 40 adolescents with early-onset first-episode psychosis diagnosed with schizophrenia (n = 20) or bipolar disorder with psychotic symptoms (n = 20) based on a two year clinical follow up). Average lobar cortical thickness, surface area, gyrification index (GI) and sulcal width were compared between groups, and the relationship between the GI and sulcal width was assessed in the patient group.
Results: Both patients groups showed decreased cortical thickness and increased sulcal width in the frontal cortex when compared to healthy controls. The schizophrenia subgroup also had increased sulcal width in all other lobes. In the frontal cortex of the combined patient group sulcal width was negatively correlated ($r = -0.58$, $p < 0.001$) with the GI.
Conclusions: In adolescents with schizophrenia and bipolar disorder with psychotic symptoms there is cortical thinning, decreased GI and increased sulcal width of the frontal cortex present at the time of the first psychotic episode. Decreased frontal GI is associated with the widening of the frontal sulci which may reduce sulcal surface area. These results suggest that abnormal growth (or more pronounced shrinkage during adolescence) of the frontal cortex represents a shared endophenotype for psychosis.

1. Introduction

Patients with early-onset first-episode psychosis (EOP), defined as the presence of psychotic symptoms within a psychiatric disorder appearing before the age of 18 years, may eventually develop schizophrenia, bipolar disorder or other psychotic disorders. By assessing cortical structural brain abnormalities in adolescent EOP patients (classified into schizophrenia or bipolar disorder with psychotic symptoms based on a two-year clinical follow-up diagnosis), we set out to elucidate whether both groups of subjects share cortical structural abnormalities at an early point in the development of the disease.

Surface-based morphometry studies are able to separately measure cortical thickness, surface area and gyrification-related metrics such as the width of the sulci (Aleman-Gomez et al., 2013). Recent surface-based morphometry studies showed that, when compared to healthy

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controls, adult patients with schizophrenia and those with bipolar I disorder have decreased cortical thickness in lateral and medial frontal and superior temporal regions (Rimol et al., 2010). Reduced thickness and surface area extended to parietal and occipital regions in patients with schizophrenia only (Rimol et al., 2010). Rimol et al. reported no regions with cortical thinning that were uniquely affected in bipolar I disorder and overlapping regions in the frontal cortex such as the medial and middle superior frontal gyrus showed greater thinning in schizophrenia when compared to bipolar I disorder (Rimol et al., 2010). Decreased gyrification has also been demonstrated in the frontal cortex in both disorders and, as with cortical thickness, seems more pronounced in schizophrenia (Palaniyappan and Liddle, 2013). A reduction in gyrification, i.e. a reduction in cortical surface complexity, may be partly due to increased sulcal width (Kochunov et al., 2005; Hogstrom et al., 2012; Liu et al., 2012; Zilles et al., 2013). However, a direct relationship between sulcal width and gyrification has not yet been assessed in psychotic populations. Taken together, it is unclear if the cortical surface-based findings from studies in adults can be extrapolated to adolescent-onset schizophrenia and bipolar disorder, as no previous surface-based morphometry study has compared adolescent-onset schizophrenia, bipolar disorder with psychotic symptoms and healthy controls.

This study simultaneously examines lobar cortical thickness, surface area, the gyrification index (GI) and sulcal width in healthy controls, EOP-schizophrenia and EOP-bipolar disorder with psychotic symptoms subgroups. Based on studies in adults we hypothesized, first, that both patient subgroups would show decreased cortical thickness and GI and increased sulcal width in the frontal lobe with respect to controls. Second, we hypothesized that an increased sulcal width would be associated with a decreased GI in patients with EOP.

2. Materials and methods

2.1. Sample

The sample was selected out of a larger group of EOP patients and controls belonging to two studies (Moreno et al., 2005; Castro-Fornieles et al., 2007) of which one multicenter study (Castro-Fornieles et al., 2007). Inclusion criteria for patients were: 1) age between 7 and 17 years, 2) presenting with a first psychotic episode following a DSM-IV disorder of less than six months duration, and 3) absence of concomitant Axis I disorder at the time of evaluation (APA, 1994). Control subjects were recruited from the same schools and residential areas as the patients. The inclusion criteria for healthy controls were:

Table 1
Sociodemographic and clinical characteristics at baseline of healthy controls, early-onset psychosis (EOP) patients with a two-year follow-up diagnosis of schizophrenia and EOP patients with a 2-year follow-up diagnosis of bipolar disorder with psychotic symptoms.

	Healthy controls	Schizophrenia	Bipolar disorder	Statistics		
	N = 52	N = 20	N = 20	ANOVA/Chi square/Student's *t*	p	Post hoc[a]
				$F/X^2/t$		
Age (years)[b]	15.4 (1.5)	15.8 (1.8)	16.4 (1.6)	$F = 2.5$	0.9	
Sex, n (% male)	32 (61.5)	18 (90)	13 (65)	$X^2 = 5.6$	0.06	
Handedness, n (% right)	44 (84.6)	18 (90)	17 (85)	$X^2 = 5.6$	0.86	
Parental education (years)	14.12 (4.1)	11.16 (3.1)	11.18 (2.8)	$F = 6.8$	<0.01	1 > 2, 1 > 3
Parental socioeconomic status[c]	3 (1.3)	2.8 (1.1)	2.9 (1.2)	$F = 0.3$	0.71	
Estimated intelligence quotient	108 (17.6)	81 (16.0)	82 (21.5)	$F = 20.8$	<0.01	1 > 2, 1 > 3
Age at onset of psychotic episode (years)[d]		15.5 (1.8)	16.1 (1.5)	$t = -1.2$	0.22	
Duration of psychotic episode (months)[e]		3.9 (3.2)	2.5 (2.3)	$t = 1.6$	0.12	
Symptoms at baseline						
PANSS positive		26.1 (4.4)	26.0 (5.3)	$t = 0.3$	0.97	
PANSS negative		21.9 (8.4)	19.1 (10.2)	$t = 1.0$	0.34	
PANSS general		43.9 (8.3)	48.1 (10.8)	$t = -1.4$	0.17	
YMRS		15.5 (8.1)	23.6 (16.6)	$t = -2.0$	0.06	
HDRS		13.8 (5.7)	16.3 (8.6)	$t = -1.1$	0.29	
c-GAF	91.6 (4.5)	35.1 (16.0)	35.4 (15.9)	$F = 309.8$	<0.01	1 > 2, 1 > 3
Medication after enrollment:						
Antipsychotic medication CPZ[f]		282.39	256.56	$t = 0.3$	0.77	
First/second/combined generation (number of patients)		0/15/5	0/11/9			
Olanzapine		4	5			
Quetiapine		5	6			
Risperidone		9	12			
Not antipsychotic medication						
Antidepressant			2			
Lithium			4			
Medication before enrollment:						
Antipsychotic medication		11	9			
Not antipsychotic medication						
Benzodiazepine		1	6			
Antidepressant		4	4			
Lithium		0	1			
Other mood stabilizers		2	2			
Stimulants		0	1			

PANSS, Positive and Negative Symptoms Scale; YMRS, Young Mania Rating Scale; HDRS, Hamilton Depression Rating Scale; c-GAF, Children's Global Assessment of Functioning scale; CPZ, chlorpromazine equivalents.

[a] 1: Controls; 2: Schizophrenia; 3: Bipolar disorder.

[b] All measures are mean (SD) unless indicated otherwise.

[c] Parental socioeconomic status, assessed with the Hollingshead–Redlich Scale (ranging from 1 to 5). A rating of 1 corresponds to the highest socioeconomic status and a rating of 5 to the lowest socioeconomic status.

[d] Age at onset of psychotic episode was defined as the age at which positive symptoms appeared for the first time.

[e] Duration of psychotic episode was defined as the time between date of onset of first positive symptom and date of scan acquisition.

[f] CPZ, cumulative antipsychotic medication intake in chlorpromazine equivalents.