

# Differential brain changes in males with early-onset psychotic disorders by diagnosis

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## Introduction

Progressive loss of cortical grey matter and increase of ventricular volumes have been reported not only in adult patients with first-episode schizophrenia but also in children and adolescents with early-onset psychoses [1]. However, it is still unclear if those changes are comparable between different psychotic disorders.

To address this gap in knowledge we used a multicenter sample of children and adolescents with a first episode of early-onset psychosis to examine longitudinal differences in progression of brain changes by diagnostic group at two-year follow-up.

## Methods

•We used data from the Child and Adolescent First-Episode Psychosis Study (CAFEPS) [2], a Spanish multicenter follow-up longitudinal study which followed early-onset psychosis patients and matched healthy controls for 2 years (mean = 25 months). We had valid clinical and MRI data for 61 patients (20 females) and 70 controls (23 females).

•DSM-IV diagnoses were established with the K-SADS-PL

•An anatomical brain MRI was performed at baseline and at the two-year follow-up visit. Total volumes of grey matter (GM) and cerebrospinal fluid (CSF) were obtained using an automated method based on the Talairach atlas.

•Repeated measures ANCOVA was used to test for differences in longitudinal change among diagnostic groups and controls, and paired t-tests to test for longitudinal change in volume variables within each group.

## Results

■37.7% of patients had schizophrenia, 26.2% had bipolar disorder, and 36.1% had other psychotic disorder at two-year follow-up.

■Patients and controls were not significantly different in terms of age, sex, SES, years of education, race, or handedness or between-scan follow-up period.

■Duration of illness (time between the onset of the first positive symptom and recruitment) was  $2.1 \pm 1.7$  months (range 1 - 6 months).

■Duration of treatment at baseline was 4.2 weeks (range 0 -16 weeks).

■Following, we report image data from males

**Table 1. Volume measurements (in cc) of male patients with psychotic disorders and controls at baseline and 2-year follow-up**

	Controls (n=47)					Patients (n=41)					baseline (b)	longitudinal (c)
	baseline		follow-up		%Ch(a)	baseline		follow-up		%Ch(a)		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD			
Intracranial	1527	121.5	1521	119	-0.4	1557	132.1	1542	123.9	-1.0		
Total Grey Matter	875.5	71.4	858.1	68.5	-1.6***	869.3	75.4	834.1	69.2	-3.0***	**	*
Total White Matter	397.8	38.0	409.4	40.7	3.3***	406.5	37.1	420.6	40.1	4.5***		
Total CSF	253.2	35.7	253.1	35.9	0.5	281.1	50.3	286.9	53.5	3.8	***	
<b>Grey Matter</b>												
Frontal Left	83.2	8.2	82.4	7.8	-0.3	79.9	7.5	76.7	9.0	-2.9**	***	*
Frontal Right	86.2	8.1	85.4	7.9	-0.3	82.3	8.1	79.0	8.7	-2.9**	***	
Parietal Left	67.5	7.3	64.9	7.0	-3.3***	67.0	8.2	62.5	8.6	-5.6***		*
Parietal Right	67.7	7.3	65.2	6.6	-3.0***	67.2	7.6	63.2	7.5	-4.9***	*	
Temporal Left	84.5	6.9	82.1	7.1	-2.4***	85.7	9.5	82.4	8.5	-2.7***		
Temporal Right	83.5	7.1	80.8	6.9	-2.9***	85.4	8.7	81.1	8.8	-3.9***		
<b>CSF</b>												
Frontal Left	25.1	5.0	27.4	6.4	10.4***	28.1	7.4	34.6	9.4	26.6***	*	*
Frontal Right	26.8	4.8	27.4	5.9	2.8	29.8	7.6	31.5	8.4	7.7*	*	
Parietal Left	22.2	4.4	23.8	5.0	8.4**	24.4	4.7	27.1	6.7	14.1**	*	
Parietal Right	21.0	4.4	21.5	4.4	3.8	23.7	5.5	24.1	5.2	6.5	**	
Temporal Left	21.1	4.1	21.0	4.0	0.2	23.5	4.7	23.7	4.8	2.9	***	
Temporal Right	19.9	4.7	18.5	4.3	-5.5**	22.5	5.4	20.3	5.8	-8.6***	***	

(a): Volume change (%Ch) between baseline and follow-up for each group (Paired t-test).  
 (b): Baseline differences between patients with psychotic disorders and controls (ANCOVA)  
 (c): Differences in 2-year longitudinal change between patients with psychotic disorders and controls (Repeated measures ANCOVA; Time\*Diagnosis interaction)  
 \*: P< 0.05; \*\*: P< 0.01; \*\*\*: P< 0.001

**Table 2. Volume measurements (in cc) of males with schizophrenia, bipolar disorder, and other psychotic disorders at baseline and 2-year follow-up**

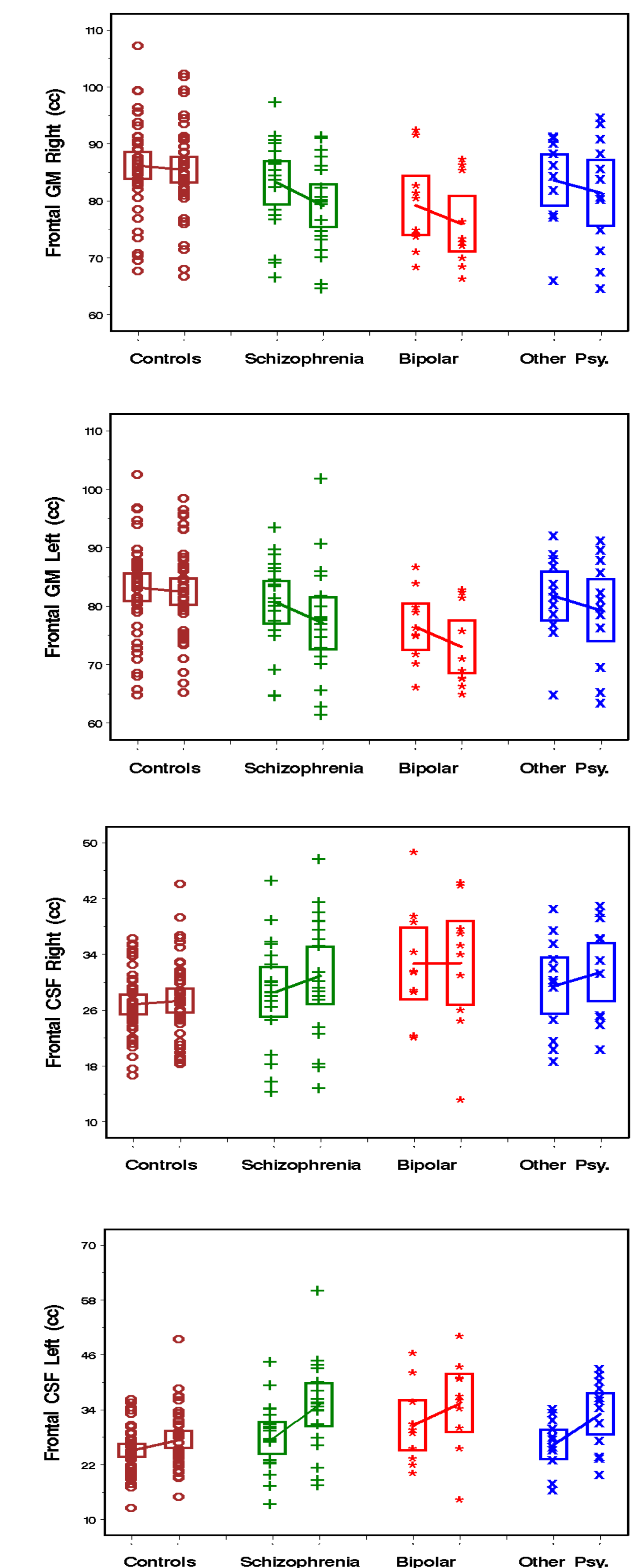
	Schizophrenia (n=19)					Bipolar (n=10)					Others (n=12)					Baseline (b)		Longitudinal (c)				
	baseline		follow-up		%Ch(a)	baseline		follow-up		%Ch(a)	baseline		follow-up		%Ch(a)	SZ	B	O	SZ	B	O	
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		Mean	SD	Mean	SD								Mean
Intracranial	1578.4	134.8	1561.5	138.2	-1.0	1497.5	99.5	1483.0	123.7	-1.0	1572.0	146.1	1559.0	149.6	-1.0							
Total Grey Matter	886.7	76.3	845.1	61.6	-3.6***	827.2	52.8	800.8	64.3	-2.2	876.7	81.6	844.6	80.6	-2.8*	**			**			
Total White Matter	408.3	33.4	423.2	30.3	4.8***	395.9	29.7	400.3	33.4	2.1	412.5	48.0	433.3	53.5	5.9***							
Total CSF	283.4	55.7	293.3	58.9	5.0	274.4	56.2	282.0	59.0	5.6	283.1	38.8	281.1	42.0	0.3	**	**	***				
<b>Grey Matter</b>																						
Frontal Left	80.6	8.0	77.1	9.6	-3.4	76.5	6.2	73.0	7.1	-3.1	81.7	7.3	79.3	9.2	-2.0	**	*	*	**	**		
Frontal Right	83.1	8.2	79.1	8.1	-3.7*	79.2	8.2	76.0	7.7	-2.6	83.6	7.8	81.4	10.0	-1.8	***	**	**	*	*		
Parietal Left	67.8	7.1	63.6	10.1	-5.4*	63.1	6.8	59.3	6.8	-4.8	68.9	10.1	63.4	7.1	-6.6**				*			
Parietal Right	67.9	7.5	64.3	8.4	-4.4*	63.7	6.4	60.9	7.7	-3.5	68.9	8.3	63.4	5.9	-6.8**							
Temporal Left	89.0	9.9	84.5	8.4	-3.8**	80.4	5.0	78.4	6.0	-1.4	84.9	10.0	82.5	9.7	-2.0							
Temporal Right	87.8	8.4	82.6	10.1	-4.6	80.1	5.3	77.3	5.6	-2.5	86.0	10.0	81.8	8.6	-3.9**	*						
<b>CSF</b>																						
Frontal Left	27.8	7.6	35.1	10.2	29.9***	30.6	8.7	35.4	10.1	18.4	26.4	5.6	33.0	7.8	28.4**	***		*	**			
Frontal Right	28.6	7.8	31.0	8.9	9.9**	32.7	8.1	32.8	9.5	2.3	29.5	6.9	31.4	7.2	8.6	***						
Parietal Left	25.7	5.2	28.9	8.4	14.8	22.5	4.6	25.8	5.2	20.8	23.8	3.5	25.3	4.0	7.5*	*	*					
Parietal Right	23.1	5.3	24.2	5.6	7.9	22.5	5.9	23.2	5.1	13.8	25.5	5.4	24.6	5.0	-1.8			**		*		
Temporal Left	24.5	5.1	25.3	5.3	5.5	22.2	4.6	22.3	4.7	2.9	23.0	4.1	22.3	3.6	-1.2	***	*					
Temporal Right	23.1	6.0	20.8	6.3	-8.9*	21.5	5.0	20.4	4.8	-3.7	22.4	4.8	19.4	4.0	-12.3**	**	**					

Abbreviations: SZ= schizophrenia; B= bipolar disorder; O= other psychotic disorders  
 (a): Volume change (%Ch) between baseline and follow-up for each diagnostic group (Paired t-test).  
 (b): Baseline differences between each diagnostic subgroup and controls (ANCOVA)  
 (c): Differences in 2-year longitudinal change between each diagnostic subgroup and controls (Repeated measures ANCOVA; Time\*Diagnosis interaction)  
 \*: P< 0.05; \*\*: P< 0.01; \*\*\*: P< 0.001

## REFERENCES:

- Arango C, Moreno C, Martínez S, Parellada M, Desco M, Moreno D, et al. Longitudinal Brain Changes in Early-Onset Psychosis. Schizophr Bull. 2008; 34(2):341-53
- Castro-Fornieles J, Parellada M, González-Pinto A, Moreno D, Graell M, Baeza I, et al. The child and adolescent first-episode psychosis study (CAFEPS): design and baseline results. Schizophr Res. 2007;91(1-3):226-37.

**Figure 1. ANCOVA for differences between males with schizophrenia, bipolar disorder, and other psychotic disorders and controls using age and scanner as cofactors of no interest**



## Conclusions

All diagnostic groups presented baseline differences from controls in some GM lobes and CSF volumes. Volume differences between patients with schizophrenia and controls increased over the two-year follow-up. Volume deficits in this population are not static, suggesting that at least one group of patients, mainly those eventually diagnosed with schizophrenia, experience greater progressive brain changes than expected.