

Cortex morphology and subcortical brain grey matter deficits in schizophrenia and unaffected relatives and neurological soft signs

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Objectives

In this study we hypothesized that cerebello-thalamo-prefrontal structural abnormalities and neurological soft signs (NSS) can be detected in individuals with schizophrenia and in unaffected first-degree relatives, using optimized voxel-based morphometry and a validated comprehensive neurological examination scale.

Methods

We recruited a group of 28 patients diagnosed with schizophrenia, with an illness duration range from 5 to 15 years, treated with atypical antipsychotic and clinical stable in the last 6 months. Patients who had received electroconvulsive therapy or clozapine were excluded. We also recruited a group of 22 unaffected siblings of patients with schizophrenia not included in the study, without history of other mental, neurological or somatic diseases, and a group of 31 healthy volunteers. None of the three groups met criteria for substance use disorder or history of other mental disorder.

In this cross-sectional morphometry study we compared volume of grey matter using high-resolution 3D-anatomical MRI imaging data and using Voxel-Based Morphometry (VBM) with SPM8. We used an absolute threshold masking of 0.1 and implicit but no explicit masking. The resulting statistical maps indicate all voxels of the brain that show a significant group difference at a minimum cluster size = 100mm³, p-value thresholded at p>0.05. In the post-hoc tests, owing to the three comparisons (patients, relatives, controls), the significance level was adjusted to p>0.05. The three groups were clinically evaluated, and the exploration of minor neurological signs assessed using a standardized neurological examination on the Neurological Evaluation Scale (NES)².

Table 1. Demographic characteristics

	Healthy Controls n=31	Unaffected Siblings n=22	Patients n=28	p
Mean Age (years) ± SD	36.78 ± 7.61	40.92±10.32	37.97±7.13	0.165a
Gender (M/F)	14/17	10/12	15/13	0.713b
School Level (years) ± SD	12.89±1.76	11.50±2.65	10.00±2.80	0.033*a
PANSS Positive			10.13±1.43	
PANSS Negative			13.29±2.21	
GAF			68.5±5.67	

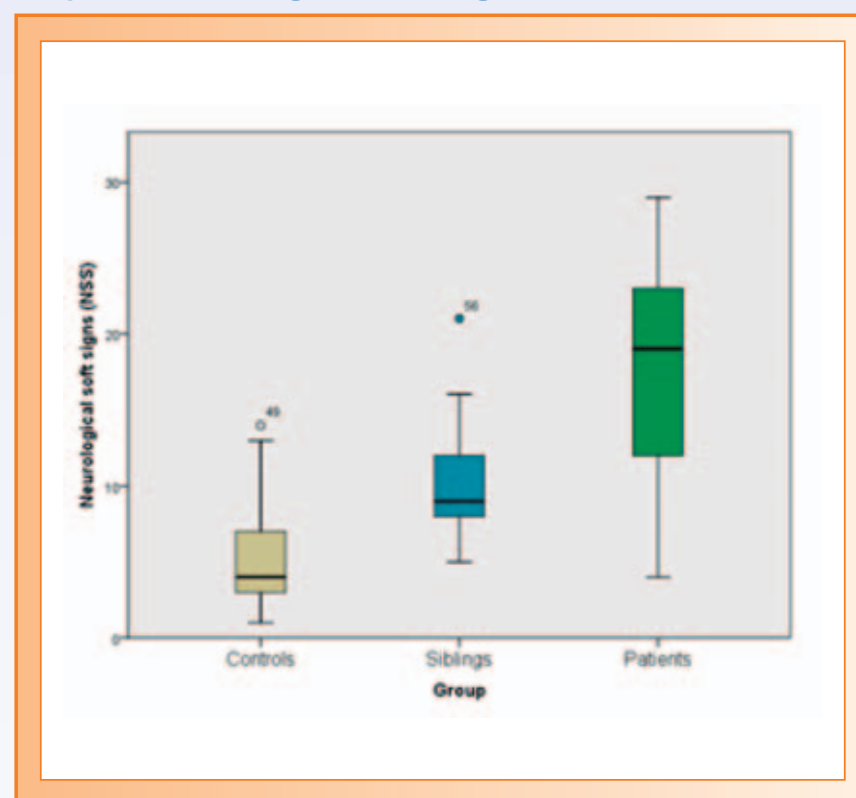
SD:Standard Deviation a:Anova M:Male F:Female b:Chi- square tests *:Significant Differences

Results

Table 2. GM volumes differences across all groups

Structure	Coordinates	P-value (FWE corrected)	Post-hoc t-test Cluster _{KE} t-value
Left inferior frontal	-50, 18, 2	0.029	CON>PAT (1350): t=4.43
	-45, 42, 5	0.027	CON>REL (1885): t=3.11
Right inferior frontal	54, 20, 4	0.002	CON>PAT (2224): t=4.10
Left parietal superior	-24, 52, 50	0.976	REL>CON(211):t=3.18
	-24, 54, 50	0.978	REL>PAT(558):t=2.76
Right temporal middle	52, -46, -2	0.978	REL>CON(453): t=.278
	50, -34, 2	0.258	REL>PAT(558):t=2.76
Right cerebellum	44, -68, 54	0.999	CON>REL(266): t=3.35
	34, 36, 38	0.967	REL>PAT(148): t=3.39
Right cingulum ant	4, 48, 10	0.005	CON>PAT(1923): t=3.08
Right paracentral	8, -26, 76	0.999	CON>PAT (128): t=3.54
	6, 22, 74	0.956	CON>REL (1409): t=3.10
Right postcentral	-12, 20, 78	0.999	REL>PAT (7563): t=3.40
	34, 22, 50	0.956	CON>REL(1409): t=3.10
	-18, -28, 74	0.999	REL>PAT(113): t=3.27

Graphic 1. Neurological softs signs-Anova



Conclusions

- The patients with schizophrenia and the unaffected relatives present more NSS. We found in cerebellum significantly lower volumes in patients and relatives in comparison with control, which represents a structural alteration in the cerebello-thalamo-prefrontal network involved in the pathophysiology of the NSS¹.
- The post-hoc single contrasts revealed a continuum of control, relatives and patients in the right paracentral area. The left superior parietal and the right middle temporal showed significantly lower volumes in patients and controls in comparison with relatives.

References

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Key Words: Brain imaging, Schizophrenia: clinical, Neuroimaging: functional