

# White matter microstructure and cortical thickness in individuals at familial risk for affective disorders and schizophrenia

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## Background and Aims:

The analysis of neuroanatomical brain profile in the familial risk subjects is a highly informative approach to the study of endophenotypes of the disease. The aim of the **exploratory preliminary** study was to determine the brain structural characteristics in unaffected first degree relatives of patients with affective disorders and schizophrenia.

## Methods:

Mentally healthy right-handed first degree relatives of patients with affective disorders (F31-33) and those of patients with schizophrenia (F20) as well as two corresponding age and sex matched control groups (without family loading of mental disorders) (Table 1) were examined.

Table 1. Demographic data

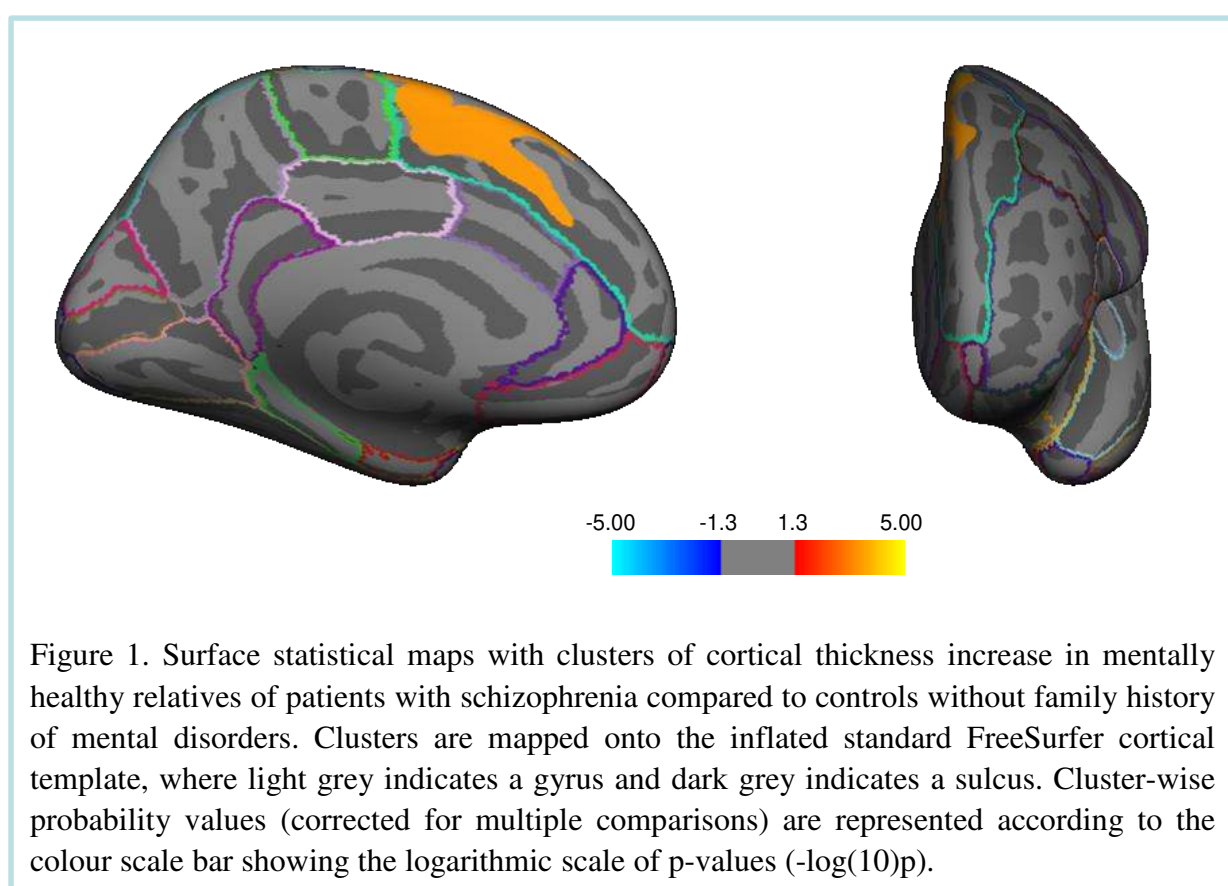
	FDR A N=13	Ctr 1 N=15	FDR S N=13	Ctr 2 N=16
Age, years	19.4-31.8 25.6±3.9	19.3-30.0 25.3±3.0	19.0-34.1 26.7±5.0	19.5-30.0 25.3±2.9
Gender (M/F)	10/3	11/4	4/9	5/11
Handedness: right-handed (%)	100	100	100	100

FDR A, FDR S – mentally healthy first degree relatives of patients with affective disorders and schizophrenia, correspondingly, Ctr 1, Ctr 2 – mentally healthy controls without family loading of mental disorder, correspondingly

The study conformed to the Code of Ethics of Medical Association (Helsinki Declaration of 1975, as revised in 2008), all participants signed informed consent.

T1-weighted (TFE, TR = 8 ms, TE = 4 ms, flip angle = 8°, field of view = 240 mm, voxel size of 0.98×0.98×1 mm, no gap) and diffusion-weighted (EPI, TR = 3.6 s; TE = 91 ms, flip angle = 90°, voxel size of 1.75×1.75×2.5 mm, no gap; b = 0 s/mm<sup>2</sup> and 1000 s/mm<sup>2</sup>, 32 noncollinear directions) images were acquired at 3T Ingenia scanner (Philips, The Netherlands).

The participants underwent MRI scanning at 3T Ingenia scanner (Philips, The Netherlands).



The surface-based morphometry for cortical thickness was performed in FreeSurfer 5.3.0 (Fischl, 2012), the results were corrected for multiple comparisons using a Monte-Carlo cluster-based simulation (Hagler et al., 2006) with 10,000 repeats. In addition, cluster-wise p-values were corrected for the number of hemispheres using the Bonferroni method.

DW-MRI data were analysed using TRACULA package (Yendiki et al., 2011) with reconstruction of 16 tracts and obtaining of FA, MD, RD, and AD values for each tract. Intergroup comparisons were performed using R 3.1.3 with correction for multiple comparisons by Holm method (Holm, 1979).

## Results:

Neuroanatomical alterations have been found only in the relatives of patients with schizophrenia. The group was characterized by increased radial diffusion (anterior thalamic radiation and uncinate fascicles of both hemispheres; right superior longitudinal fascicle), decreased fractional anisotropy (right anterior thalamic radiation, uncinate fascicles of both hemispheres, right superior longitudinal fascicle) (Table 2) and increased grey matter thickness in a medial part of the left superior frontal gyrus (Figure 1).

## Conclusions:

The findings suggest that the familial high risk of schizophrenia might be associated with an altered trajectory of brain development. However whether it is pathological or compensatory processes remains to be elucidated via further longitudinal research.

Table 2. Results of intergroup comparison of DW data

Tracts, Diffusion parameters	FDR S (M ± std)	Ctr 2 (M ± std)	Statistics	
			F	P (uncorr)
Anterior thalamic radiation, left				
RD (10 <sup>-3</sup> mm <sup>2</sup> /s)	0.566 ± 0.021	0.539 ± 0.021	10.0	0.004*
FA	0.429 ± 0.018	0.452 ± 0.026	6.5	0.017
Anterior thalamic radiation, right				
RD (10 <sup>-3</sup> mm <sup>2</sup> /s)	0.584 ± 0.019	0.554 ± 0.026	12.0	0.002*
FA	0.410 ± 0.017	0.442 ± 0.024	16.0	0.0005*
Uncinate fascicles, left				
RD (10 <sup>-3</sup> mm <sup>2</sup> /s)	0.610 ± 0.029	0.576 ± 0.022	11.9	0.002*
FA	0.399 ± 0.026	0.437 ± 0.024	17.3	0.0003*
Uncinate fascicles, right				
RD (10 <sup>-3</sup> mm <sup>2</sup> /s)	0.612 ± 0.025	0.582 ± 0.025	10.8	0.003*
FA	0.400 ± 0.024	0.429 ± 0.023	11.0	0.003*
Superior longitudinal fasciculus – temporal bundle, right				
RD (10 <sup>-3</sup> mm <sup>2</sup> /s)	0.543 ± 0.028	0.509 ± 0.021	12.7	0.001*
FA	0.411 ± 0.030	0.450 ± 0.028	11.9	0.002*
Superior longitudinal fasciculus – parietal bundle, right				
RD (10 <sup>-3</sup> mm <sup>2</sup> /s)	0.538 ± 0.028	0.507 ± 0.019	11.0	0.003*
FA	0.424 ± 0.033	0.459 ± 0.026	8.8	0.007

\*significant after correction for multiple comparisons

FDR S - relatives of patients with schizophrenia, Ctr 2 - controls without family loading of mental disorders