Reduction in cerebellar grey matter in schizophrenia detected using the Spatially Unbiased Infratentorial (SUIT) toolbox

Florian Schubert[1], Simone Kühn[2], Alexander Romanowski[3], and Jürgen Gallinat[4]
[1]Physikalisch-Technische Bundesanstalt, Berlin, Germany, [2]Psychology and Educational Sciences, Ghent University, Ghent, Belgium, [3]Psychiatry and Psychotherapy, Charité University Medicine, Germany, [4]Psychiatry and Psychotherapy, Charité University Medicine

Introduction

Structural deficiencies within the cerebellum have been associated with schizophrenia, including the schizophrenic signs of thought disorders. Whereas several region-of-interest-based studies have shown deviations in cerebellum volume of schizophrenic patients [eg 1,2], meta-analyses on conventional whole brain voxel-based morphometry (VBM) studies do not show converging evidence for abnormalities in the cerebellum [3,4]. Inter-subject normalization being a crucial analysis step, the small size of the subdivisions in the cerebellum poses a particular challenge to conventional VBM methods. We therefore hypothesized that their lack of sensitivity to cerebellar structural deviations could be due to methodological problems in the cerebellum and tested this by using a cerebellum-optimized VBM procedure.

Subjects and Methods

MR examinations were performed on a 3T-scanner (MEDSPEC 30/100, Bruker Medical) using a circularly polarized head coil. T_1-weighted images (MDEFT, T_E = 3.8 ms, T_R = 20.53 ms; T_I = 550 ms, nominal flip angle 30 degrees) of the whole brain at a resolution of 1 x 1 x 1.5 mm^3 were acquired from 29 schizophrenic patients and 45 healthy controls. For image analysis we used a VBM approach utilizing the Spatially Unbiased Infratentorial (SUIT) toolbox [5] that ensures that infra-tentorial structures, namely cerebellum and brainstem, are isolated from the surrounding tissue to provide an optimized fine graded investigation of cerebellar structural alterations. To compare our results for cerebellum to those of common whole brain VBM analyses for cerebellum we computed the same analysis on grey matter (GM) maps based on the conventional optimized VBM procedure [6].

The severity of schizophrenia symptoms was assessed using the Brief Psychiatric Rating Scale (BPRS). Cognitive tests included the Trail Making test providing information on visual search, scanning, speed of processing, mental flexibility, and executive functions; the Stroop task; the two word fluency test; the continuous performance test; and a picture memory test. The correlation analysis for cerebellar volume deficit regions and clinical or cognitive parameters was performed using Pearson's one sided correlation test.

Results and Discussion

No cerebellar group differences were detected employing conventional optimized VBM. As analyzed using the SUIT toolbox, relative to healthy controls schizophrenic patients showed reductions of GM volume in the left cerebellum Crus I/II (corrected for multiple comparisons, $p < 0.001$, fig. 1). There were no regions where GM volume was significantly increased in schizophrenic patients compared to healthy controls. GM volume in left Crus I/II correlated negatively with thought disorder ($p < 0.05$; one sided) and positively with performance in the Trail Making Test B ($p < 0.05$) (fig 2), neither correlation surviving correction for multiple testing though.

The results derived from whole cerebellum analysis using the SUIT toolbox provide first evidence for distinct GM deficits in schizophrenia located in cerebellar Crus I/II. The association of this area with thought disorder score and Trail Making performance supports the previously suggested role of the cerebellum in schizophrenia for impaired coordination of mental processes including disordered thought. The failure of conventional VBM to detect such effects suggests that previous studies might have underestimated the importance of cerebellar structural deficits in schizophrenia.

References

1. Weinberger DR et al, Arch Gen Psychiatry 1982; 39:778
2. Keller, A et al, Am J Psychiatry 2003; 160:128
3. Cheung C et al, PLoSOne 2010; 5:e12233
4. Di, X et al, Prog Neuropsychopharmacol Biol Psychiatry 2009; 33:1390
5. Diedrichsen J, Neuroimage 2006; 33:127
6. Good, CD et al, Neuroimage 2001; 14:21

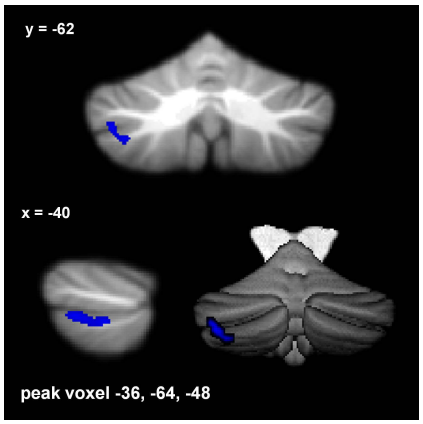

Fig. 1 (left): Significant cluster of cerebellar GM volume reduction in left Crus I/II (peak voxel: MNI -36, -64, -48) in schizophrenic patients compared to controls.
Top: coronal, bottom left: sagittal, right: 3D rendering of cerebellum.

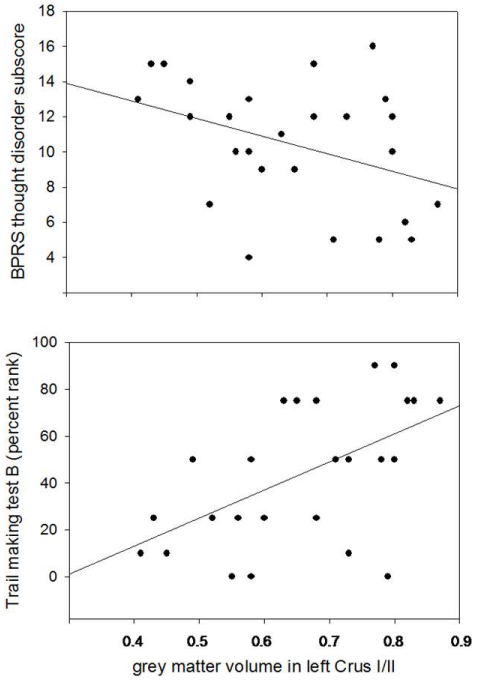

Fig. 2 (right): GM volume extracted from left Crus I/II of patients.
Top: *vs* BPRS thought disorder subscale (r = -0.383, $p < 0.05$, one-sided).
Bottom: *vs* Trail Making Test B (r = 0.394, $p < 0.05$).