Grey matter abnormalities before the onset of psychosis: An automated MR image analysis

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Background

Structural neuroimaging studies have established that there are abnormalities in the brain structure of patients with established schizophrenia [1,2] and recent evidence suggests that part of the abnormalities that are found in the temporal and frontal structures occur before the onset of psychosis[3,4] suggestive of a neurodevelopmental origin [5-7].

Hypothesis

We predicted that prodromal subjects who are at ultra high risk of developing a psychosis would show volumetric abnormalities compared to normal controls and that these would be qualitatively similar to those seen in patients with established schizophrenia.

Method

Our recent research investigated people at ultra high-risk (UHR) of developing psychosis looking at two comparisons, cross sectional and longitudinal [3]. The present study extends this work by comparing this group to a control group with a new method. 102 people with prodromal signs of psychosis (UHR) and 40 normal controls were scanned with a 1.5 Tesla GE Signa scanner acquiring a SPGR sequence with 124 contiguous, 1.5 mm coronal slices. After at least 12 months, 28 UHR (27%) had developed psychosis (UHR_psych) and 64 (63%) had not (UHR_nonpsych). The MR images were pre-processed using tools from FSL Library (Image Analysis Group, Cambridge University, UK) and statistical analysis were conducted using BAMM (Brain Mapping Unit, Oxford University, UK). Between-group differences in grey matter volume at the baseline MRI scan were estimated by fitting an analysis of covariance (ANCOVA) model at each intracerebral voxel in standard space, with age at scan and intracranial volume as covariates. Analysis design was split into three analyses: 1: All UHR compared to controls, 2: UHR_psych compared to controls and 3: UHR_nonpsych compared to controls.

Results

Analysis 1) Comparing all of the UHR people (n=102) with controls (n=40) we identified deficits in grey matter in the left parahippocampal gyrus (Brodmann's area: BA28), superior temporal gyrus (BA22), post central gyrus (BA40) and bilaterally in the posterior cingulate (BA31). Excesses in grey matter were found in the left orbital gyrus (BA11&47).
Analysis 2) The UHR_psych (n=28) when compared to controls had a deficit in grey matter in the left middle frontal gyrus and superior frontal gyrus (both BA11). There were not excesses in the UHR_psych group.
Analysis 3) The UHR people who did not go on to develop a psychosis (UHR_nonpsych) (n=64) compared to controls have the same deficits as all of the UHR plus deficits in the left middle temporal gyrus (BA21), lingual gyrus (BA18), anterior cingulate (BA32) and bilaterally in the middle frontal gyrus (BA25) and superior frontal gyrus (BA10). There was also the same excess in grey matter found in the left orbital gyrus (BA11&47).

Conclusions

Comparing prodromal people (UHR) who may or may not develop a psychosis to a group of normal controls using automated MR image analysis methods we found that grey matter abnormalities were apparent before the transition to psychosis and that they were similar to differences found in people at their first expression and in established schizophrenia. The UHR-psychotic group had reduced frontal regions, consistent with our previous imaging findings [3] and neuropsychological findings of impaired working memory [8] and smell identification ability [9]; the other differences in cingulate and MTL regions are consistent with our previous ROI and morphological analyses [10,11]. These results are consistent with early neurodevelopmental insults. The findings will be considered in light of other recent cross-sectional and longitudinal work in high-risk populations [3,12].

References

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