Mapping CSF Changes in First Episode Schizophrenia

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Introduction

Increases in cortical and subcortical CSF are widely documented in schizophrenia. The regional specificity of CSF enlargements near the time of disease onset, however, is less well characterized. In this study, we used computational image analysis methods to map regional changes in lateral ventricular volume and sulcal and subarachnoid CSF between first episode schizophrenia patients and healthy comparison subjects.

Methods

High-resolution MR images were obtained from 72 (51m/21f) first episode patients and 78 (37m/41f) demographically similar healthy subjects. Scans were corrected for RF inhomogeneities, resliced into a standard orientation using rigid-body transformations and classified into tissue types after editing scalp, meninges and bone from the data. Computational cortical pattern matching methods were used to spatially relate the same cortical regions between subjects. The proportion of CSF voxels in the sulcal and subarachnoid space were then measured within a sphere of fixed radius at thousands of homologous surface locations. Principal Components Analyses (PCA) reduced local CSF proportion measures into component scores allowing the examination of global extra-cortical CSF effects. Comparing CSF proportion measures at each cortical location across the entire cortex in 3D identified regional effects. Total lateral ventricular volumes and volumes of each ventricular horn volumes were obtained after subcortical regions were traced on coronal brain slices at sub-voxel resolution while simultaneously viewing orthogonal planes. Anatomical mesh modeling methods were used to obtain ventricular surface averages within groups. For statistical comparisons, diagnosis was included as between subjects factor, and when appropriate, hemisphere as a within subjects factor. Sex and age were included as covariates and analyses were performed both with and without correcting for intracranial size.

Results

Intracranial gray matter volume was significantly reduced in first episode patients, while intracranial CSF was significantly greater only after correcting for overall intracranial size. Sex and Age effects were present for all intracranial tissue compartments, although Sex effects were no longer significant after accounting for intracranial size. No significant diagnostic group differences were observed for total or subdivided lateral ventricular volumes. Ventricular volumes, however, were shown to increase with age and were larger in the left hemisphere, and in males before correction for intracranial size. Alternatively, extra-cortical CSF factor scores

from the first two principle components, accounting for 51 and 7.2 percent of the total variance respectively, showed main effects of Diagnosis irrespective intracranial size correction. For all analyses, the covariates were not shown to interact with diagnosis. Statistical mapping of local extra-cortical CSF proportion measures revealed significant regional sulcal and subarachnoid CSF increases surrounding temporal and perisylvian cortices bilaterally in first episode patients compared to healthy subjects.

Conclusion

First episode patients, who had received little to no prior medication exposure, failed to exhibit overall or regional increases in lateral ventricular volumes. Global and regional increases in sulcal and subarachnoid CSF, however, were observed in first episode schizophrenia. CSF increases in the extra-cortical space appear more characteristic of first onset patients than enlargements in lateral ventricular volumes and may index regional reductions in gray matter volume surrounding temporal cortices.