Fusion of Structural-Functional Brain Images Reveals Differences in Schizophrenia in a Multi Site Study

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Introduction

It is a common practice to acquire multi-modal information in brain imaging studies. For example structural MRI (sMRI) is collected with functional MRI (fMRI). Each modality provides information about different aspects of the brain. The brain is a vastly interconnected organ and it is reasonable to expect local changes to result in modulations of brain activity in distant regions. The disconnection hypothesis of schizophrenia [2] states that the neural mechanisms of schizophrenia are not circumscribed and that schizophrenia may be characterized by a deficit of interconnections between different brain regions. In this study we introduce techniques to measure how gray matter concentration, measured using sMRI, is correlated with functional activity, measured using fMRI, while performing a sensorimotor (SM) task. Our results show that correlation between structure and function is stronger in healthy controls (HC) than in patients with schizophrenia (SZ).

Methods

94 HC and 85 SZs were imaged as part of a large study (Mind Clinical Imaging Consortium) at four different sites and each participant had given written, informed and IRB approved consent at their respective sites. After removing outliers based on fMRI data and selecting subjects to match demographics we reduced the data set to 70 subjects in each group. The SM task was designed to robustly activate the auditory cortex. It is an on/off block design and during the on-block, 200ms tones were presented. There were eight tones at different pitches along a scale and were presented in ascending and descending cycles. After each tone the subject was required to press a button with the right thumb. Scans were acquired with either a GE or Siemens scanner with field strength of 1.5 or 3.0T. Scanning parameters varied slightly between sites. Structural and functional images were down sampled to voxel sizes 3.4x3.4x4mm

Preprocessing steps included motion correction, spatial normalization and smoothing. sMRI images were segmented to obtain gray matter maps and fMRI data were reduced to activation maps

Comprehensive Spatial Correlation Analysis

The 3 dimensional brain images contained about 60,000 (N) voxels. Images of subjects belonging to a certain group were used to compute sMRI and fMRI matrices where voxels were placed along the columns and subjects along the rows. Let x and y be the column vectors across all subjects for the jth voxel from sMRI and the ith voxel from fMRI respectively. Our interest was in finding the correlation between x and y, where i and j varied independently from 1 to N. An analysis of this nature requires a large structural-functional cross correlation matrix (Rsf) of size N x N. Computing Rsf is not easy due to limitations in computer memory and the interpretation of Rsf will be based on reduced statistics. We introduce efficient techniques to obtain three statistics of Rsf without fully computing it. Method1: Find the histogram of its elements. This is a modification of a technique we introduced in [1] to fuse multiple fMRI images. Method2: Find the mean of Rsf along its rows. Method3: Segment Rsf into AAL atlas regions and find the inter-regional mean. In Method1 we compute a row of Rsf, find its histogram, repeat the procedure for all rows of Rsf and finally add the individual histograms. Method1 gives a general sense of the degree of structural-functional correlation. Method2 gives a map of how a structural voxel is correlated to all functional voxels. Method3 reduces the number of Rsf to 116 x 116 structural-functional inter-regional correlations (there are 116 anatomical regions specified in the AAL atlas). All three methods are applied to data from HC and SZ separately and differences between the means are detected.

Results

Method1: The difference between HC and SZ histograms (Fig 1) showed that HC had a higher number of correlations near +0.2 and -0.2 than SZ, and SZ had higher number of correlations at zero correlation than HC. Correlation value of 0.2 has a significance of P<0.05 for 70 subjects. Method2: From the difference (HC-SZ) map (Fig 2) of how a structural voxel is correlated to all functional voxels, it is seen that HC shows significant positive correlations in the cerebellum and in the same region SZ showed mostly negative correlations. Method3: While investigating significant (P<0.01) inter-regional correlation differences between HC and SZ (Fig 3) we found that HC showed positive correlations between AAL atlas structural regions of cerebellar vermis with functional regions of Rolandic oper, calcarine, fusiform and heschl. In SZ there were negative interregional correlations between structural regions of cingulum and paracentral_lobule and functional regions of putamen, pallidum and temporal_pole.

Discussion

Method1: Results indicate that the inter-relationship between structure and function is stronger in HC than in SZ for the SM task. This may arise as a result of a compromised connectivity in SZ. This interpretation supports the disconnection hypothesis of schizophrenia [2]. Results from Methods 2 and 3 again support the disconnection hypothesis as well as the theory of cognitive dysmetria [3] where schizophrenia is modeled as a dysfunction in cortical-subcortical-cerebellar circuitry. Method3 did not show high correlation between structure and function in healthy controls. Our results show that the correlation between structure and function is stronger in healthy controls (HC) than in patients with schizophrenia (SZ).

References


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