JOINT SOURCE BASED MORPHOMETRY TO IDENTIFY SOURCES OF GRAY MATTER AND WHITE MATTER RELATIVE DIFFERENCES IN SCHIZOPHRENIA VERSUS CONTROLS

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Introduction

In order to use the cross-voxel information in structural magnetic resonance imaging (sMRI) and identify the sources networks that are associated with the mental illness, we recently developed a method called source based morphometry (SBM) [1]. SBM is a multivariate alternative to voxel based morphometry (VBM) [2]. It requires three fundamental steps, preprocessing, independent component analysis and statistical analysis (See Fig. 1). SBM takes advantage of VBM by using its automatic preprocessing steps. SBM can be considered a multivariate version of VBM and can improve the estimate of the sources of interest while also enabling examination of their association with subject variables. Joint ICA is a data fusion method which can combine multiple types of data from the same participants and abstract their correlated information [3]. In this abstract we replace the normal ICA in the SBM by joint ICA, and hence SBM becomes joint SBM (jSBM). We propose to use jSBM to fuse gray matter and white matter images and hope to identify the joint sources networks that reflect the relative change of gray matter and white matter related to mental illness.

Figure 1

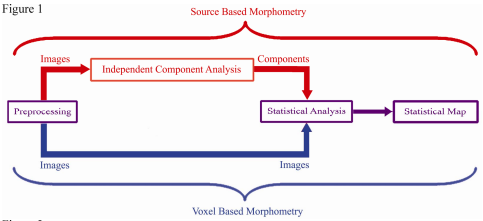
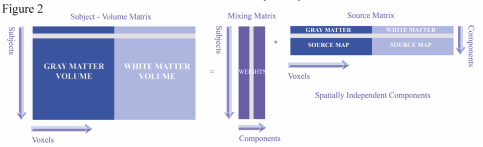


Figure 2



Methods

Preprocessing:

One hundred and twenty structural MRI images from schizophrenia patients and 120 images of healthy controls were scanned at Johns Hopkins University. The images were preprocessed using the preprocessing steps used for VBM [4] employing the Matlab program SPM5. Images were first spatially normalized to the T_1 MNI template, then interpolated to voxel dimensions of 1.5x1.5x1.5 mm and segmented into gray, white and cerebrospinal fluid (CSF) compartments. The gray matter images and white matter images were then smoothed with 12-mm full width at half-maximum (FWHM) Gaussian kernel.

Joint Independent Component Analysis (See Fig. 2):

Every gray matter or white matter image was converted to a one-dimensional vector. The 120 gray image vectors of schizophrenia patients and 120 gray images vectors of healthy controls were then arrayed into one 240 row subject-by-gray matter data matrix. The same was done to the 240 white matter images to get the subject-by-white matter data matrix. These two matrices stacked horizontally to get the subject-volume matrix. A modified Akaike's information criterion (AIC) [5, 6] was used to estimate the number of components, *k*, from the matrix [7]. The subject-volume matrix was decomposed into a mixing matrix and a source matrix using spatial ICA [7]. The mixing matrix expresses the relationship between subjects and *k* joint sources. The rows of the matrix are scores that indicate to what degree each of the *k* components contribute to a given subject. The columns of the matrix indicate how one component contributes to each of the 240 subjects. The source matrix expresses the relationship between the *k* joint sources and the voxels within the brain. Every row of the source matrix corresponding to a joint source can be separated into left part and right part according to gray matter source and white matter source. The gray matter source and white matter source have the same shared contribution to the subjects expressed by the mixing matrix. Therefore, the joint source indicates the coupled gray matter source and white matter source whose variances are the same within the subject.

Statistical Analysis:

A two sample t-test was used on each column of the mixing matrix, which tested the identical between healthy control and schizophrenia with respect to the k components. A corrected threshold of $p<0.05$ which controls for the false discovery rate (FDR) was used to determine the most significant sources [8]. The effects of age and sex on the sources can also be determined by regressing the columns of the mixing matrix separately on age and sex using a threshold of $p<0.05$.

Results

The number of components was estimated to be forty using the modified AIC approach. Seven joint sources whose loading scores differed significantly between controls and patients were identified. Here we list the two most interesting sources. Within source 1 (See Fig. 3, left), the patients have smaller gray matter than healthy controls in the bilateral superior temporal gyrus, inferior and medial frontal gyrus; the patients also show a relatively lesser white matter in the corpus callosum. Within source 2 (See Fig 3, right), the patients show more thalamus than healthy controls. The patients also have more relative gray matter on the white/gray boundary of inferior parietal lobule, postcentral gyrus and middle frontal gyrus (possibly due to overall atrophy). There was no significant effect of sex on the two sources, however the effect of age was significant. The correlation plots of age versus ICA weights are presented in Figure 4.

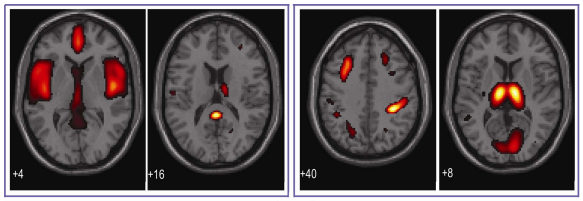


Figure 3

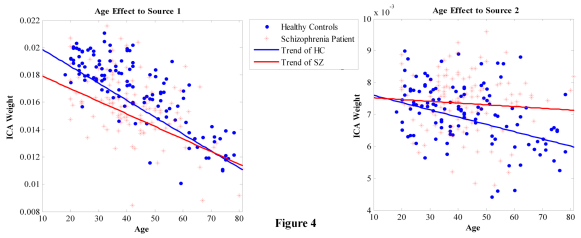


Figure 4

Discussion

We have presented joint SBM approach to identify natural joint sources networks of gray and white matter that were significantly different in schizophrenia patients. For source 1 the lesser gray matter in temporal and frontal gyrus and their intercorrelations are consistent with previous findings [9-11]. The smaller corpus callosum in white matter also agrees with previous reports [12]. The relatively less gray matter in temporal and frontal lobe with the lesser white matter in corpus callosum is interesting and may be related to the temporal lobe connections in the posterior corpus callosum [13]. For source 2, the larger thalamic white matter volumes in schizophrenia is consistent with previous work showing smaller thalamic gray matter volumes in schizophrenia [14, 15]. The gray larger matter in parietal and frontal lobe conjunct with white matter is consistent with earlier work, but may be related to complex shape changes and require computational anatomy to clarify [16]. Our findings also suggest gray matter difference in the parietal and frontal lobe are related to white matter difference in thalamus consistent with the relay station role of thalamus. We found significant age effects on both joint sources. For source 1, the source is slightly larger in controls at early age and decreases with age for both groups. Source 2 is similar for young patients and controls and decreases with age. The decrease in controls is slightly faster than that of the patients.

References

[1]. L.Xu, et al.,under review, Hum Brain Mapp; [2]. C.D. Good, et al., NeuroImage. 14(1 Pt 1): p. 21-36. 2001; [3]. V.D. Calhoun, et al.,Hum Brain Mapp. 2005; [4]. J. Ashburner and K.J. Friston, Neuroimage. 11(6 Pt 1): p. 805-21. 2000; [5]. H. Akaike. IEEE Trans Automatic Control. 19: p. 716-723. 1974; [6]. Y.-O. Li, et al., Hum Brain Mapp. 28(11): p. 1251-1266. 2007; [7]. V.D. Calhoun, et al.,Human Brain Mapping. 14(3): p. 140-51. 2001; [8]. R.C. Genovese, et al., NeuroImage. 15: p. 870-878. 2002; [9]. G.D. Pearlson, Progress in Neuro-Psychopharmacology & Biological Psychiatry. 21(8): p. 1203-29. 1997; [10]. R.E. Gur, et al., Archives of General Psychiatry. 57(8): p. 761-8. 2000; [11]. S.A. Mitelman, et al.,Schizophrenia Research. 76(2-3): p. 207-29. 2005; [12]. S. Bachmann, et al.,Psychol Med. 33(6): p. 1019-27. 2003; [13]. E. Downhill, Jr., et al.,Schizophr Res. 48(2-3): p. 187-99. 2001; [14]. J.G. Csernansky, et al.,Am J Psychiatry. 161(5): p. 896-902. 2004; [15]. C. Gaser, et al.,Am J Psychiatry. 161(1): p. 154-6. 2004; [16]. V.D. Calhoun, et al.,Hum Brain Mapp. 27(1): p. 47-62. 2006