Combining FMRI data in cases of diffuse and focal brain abnormality

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ABSTRACT

In clinical samples, individual variability in anatomical MRI data due to brain abnormalities leads to difficulties in combining functional MRI data. This issue may be relevant across a variety of samples including multiple sclerosis, schizophrenia, traumatic brain injury and even aging, yet it is widely ignored. Specifically, spatial normalization algorithms based upon comparing signal intensity or a voxelwise statistic between the source and template brain may result in poor spatial normalization in the abnormal brain. In order to make comparisons between participants and between groups of participants, it is necessary to determine the exact brain structure containing the activation. The current findings indicate that the chosen normalization procedure does influence not only the magnitude of the activation, but also the magnitude of the fMRI signal in both TBI and HC cases of TBI, however, there often exist both focal and diffuse brain changes, therefore increasing the complexity of the analysis. During Normalization: the source brain (for patient brain) is moved into normal brain space through the use of software using linear and nonlinear transformations. Key Normalizations:

1. Provides a normalized brain for between subject and group comparisons
2. For brain activation, there is an assignment of three dimensional coordinates which allows for determination of the exact brain structure containing the activation

Non-Normalization works:

Several studies have shown that without normalization, it is impossible to compare findings in an individual with and without a lesion. The data from the same brain cannot be compared if the brain has been moved in space. To avoid this problem, it is possible to use an algorithm that is able to move the brain into the template template space (Talaraich space) through the use of both linear and nonlinear transformations.

Linear:

An affine transformation of 3-space represented as a 4x4 affine transformation matrix parameterized by 12 parameters to optimize a function which measures goodness of fit. See Figure 1.

Non-Linear:

Non-affine normalization can result in over-fitting, excessive warping of space to produce small reductions in the cost measures, whereas the warping is quantified and controlled. Regulation is the process of incorporating the amount of warping into the cost measure. Regulation of the warping is very sensitive to differences in intensity in the brain at local sites and in the case of nonlinear, these algorithms work to match the source and template brain in intensities at the expense of the remainder of the brain, through the use of sum of least squares.

METHOD

In order to make comparisons between participants and between groups of participants, it is necessary to map or transform images from several subjects into a space that is the same standardized brain space as the template image. This procedure is known as spatial normalization and typically occurs following registration of the functional and structural images. An advantage of using spatially normalized images is that activation data can then be registered to the Talairach coordinate system to allow for comparison across studies. However, there often exist both focal and diffuse brain changes, therefore increasing the number of variables in the analysis.

We analyzed Blood-Oxygenation Level-Dependent (BOLD) Functional Magnetic Resonance Imaging (FMRI) data from participants with moderate to severe Traumatic Brain Injury (TBI) and healthy adults (HCs) collected on a 1.5 GE MRI scanner. A fundamental problem in testing the results of spatial normalization methods is the lack of a `true` gold standard for comparison. In order to examine the influence of brain abnormalities on spatial normalization, we compared the registration fit between 2 and 4 polynomial models. We compared these strategies for spatial normalization of nonlinear data by subjecting the data to using the degree of fit required for the structural image of both TBI and HCs. The results indicated that both location and magnitude of brain activation in cases of TBI may be influenced by the normalization procedure chosen. In addition, we compared separate polynomial models, procedures are differentially influenced by the presence of brain abnormalities. The implications for these findings are discussed as well as suggestions for appropriate pre-processing of FMRI data in clinical samples.

RESULTS

Comparison of SPM99 default normalization procedure and affine only transformation

FMRI has the potential to dramatically influence the nature of TBI research. In TBI rehabilitation, FMRI provides researchers with an important opportunity to examine the changes at the level of the cerebral substrate that coincide with behavioral changes that have been linked to therapeutic intervention.

However, before fMRI is to be clinically useful, it will be important to establish reliable and valid research protocols and consistent approaches to data interpretation.

The current findings indicate that the chosen normalization procedure does influence not only the location of the resultant brain activation, but also the magnitude of the activation. This was particularly evident in the case presented in Figure 2, where the statistical parametric maps were dependent upon the type of normalization employed (i.e., affine only versus the SPM99 default).

Non-affine normalization using high numbers of parameters without regularization resulted in over-fitting in both TBI and control cases. The degree of over-fitting was not substantially greater in TBI data than it was in the controls.

Future investigations should work to further characterize the influence of diffuse and focal brain lesions on pre-processing procedures.

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