Effects of Spatial Normalization on Onset Localization of Prerhinal Cortex Activation in Individual Subjects Using fMRI

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Abstract

Pursuing sensitive fMRI probes for detecting functional alterations in preclinical Alzheimer’s Disease (AD), parahippocampal and perirhinal cortices (PHC) have received considerable attention [1, 2]. As PHC activity decreases, so may the sensitivity of functional MRI (fMRI) to detect disease. The use of spatial normalization for defining a test region for AD research is widely used for defining a test region for AD research; however, Vandenbroucke et al. [3] showed that temporal lobe regions (MTL) are poorly registered across individuals with such methods. We compared the relationship between fMRI activations as visualized in native space and after spatial normalization.

Background

In pursuit of sensitive fMRI probes for detecting functional alterations in preclinical Alzheimer’s Disease (AD), paradigms have been developed for evoking activity increases in regions known to be affected early in the course of the disease [4]. Based on evidence for early impairment in perirhinal cortex (PHC) [5], and on previous studies of PHC in monkeys [2] and humans [3-5], we used a simple object encoding task to produce reliable PHC activation in intact subjects [6]. In adapting such an fMRI paradigm for clinical use, however, it is necessary to define a priori for each individual the region within which the evoked activation should occur. Spatial normalization (and template matching) is widely used for this purpose; however, Vandenbroucke et al. [7] showed that MTL regions are poorly registered across individuals with such methods. We compared the relationship between PHC activations as visualized in native space and after spatial normalization.

Methods

MTL regions of 12 healthy subjects (9 female; mean age 28.0, range 23-31) were included in the selection. The MTL regions of interest were defined using a corner-cube visualization technique [10, 11]. Use of current spatial normalization techniques to define specific MTL regions for evaluation of fMRI probes may lead to significant loss of sensitivity.

Objective

To assess the reliability with which PHC activation could be detected in individual subjects with and without the use of spatial normalization and template-based ROI definition.

Results

The data analysis was performed at both the individual level in native space and at the group level using a random effects analysis (in MNI space). For each individual subject the coordinate of the peak activation in PHC in native space was transformed into standard space, using the deformation toolbox in SPM2, and visualized using corner-cube visualization [10, 11] as implemented in the “Brede Toolbox” [12].

Discussion and Conclusion

As in pursuit of significant activation occurred in PHC (using q<0.05, FDRcorr). Here we show a) that individuals exhibited different patterns of PHC activity; and b) spatial normalization resulted in the displacement of some activations into other regions in the normalized space. The group-derived activation peak was distant from activation sites observed in many individuals. Spatial variability of individual activations is displayed using corner-cube visualization [10, 11]. Use of current spatial normalization techniques to define specific MTL regions for evaluation with fMRI probes may lead to significant loss of sensitivity.

References


Figure 1: The behavioral paradigm. Note that the stimuli in the encoding phase are identical, and that the only varying aspect is the forthcoming instruction.

Figure 2: Left: Group peak of OE > PE, located in the left posterior PrC (MNI space). Right: Individual activations of all 12 subjects (native space). All images are FDR corrected with a voxel threshold of 5. Statistical thresholds: yellow: q<0.05, red: q<0.1, green (for illustrative purposes): q<0.5.

Figure 3: Corner cube visualisation using the “Brede Toolbox”. Note how several of the individually normalised activation maps end up outside the MTL. The group activation (Grp.) is the PHC activation marked with the crosshair in Figure 2.