Analysis of Functional Connectivity in Human Working Memory using Positron Emission Tomography and Principal Component Analysis

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Abstract

To reveal the interconnected brain regions involved in human working memory, their functional connectivity was analyzed using principal component analysis (PCA). rCBF PET scans were performed on 5 normal volunteers during the verbal and visual working memory tasks and PCA was applied. PCA produced the first principal components related with the increase of the difficulty and the second one which demonstrate the dissociation of verbal and visual memory system.

Introduction

Measurement of rCBF using $H_2{}^{15}O$ PET has been proved as a useful tool for the functional mapping of human brain. We have previously reported the result of a study on human working memory (Lee *et al.*, 1998) using the rCBF PET and statistical parametric mapping method. These results indicated that the laterality and dissociation of verbal and visual working memory system and the pivotal role of frontal cortex and cingulate gyrus in working memory. To understand the relationship among the activated regions in our previous study, we measured their functional connectivity.

Theory

Let's consider the hemo-dynamic change at the *i*th voxel across different conditions as random variable X_i (i=1, 2, ⋯, p).

Principal components, particular linear combinations of these random variables represent geometrically the selection of a new coordinate system obtained by rotating the original one as the coordinate axes. The new axes represent the directions with maximum variability and provide a simpler and more parsimonious description of the covariance structure. In terms of functional connectivity, a principal component represents a truly distributed brain system within which there are high intercorrelations.

If $\boldsymbol{\Sigma}$ is the $p \times p$ covariance matrix of the random vector $\mathbf{X}'=[X_1, X_2, \cdots, X_p]$ and has eigenvalue-eigenvector pairs $(\lambda_1, \mathbf{e}_1)$, $(\lambda_2, \mathbf{e}_2)$, ⋯, $(\lambda_p, \mathbf{e}_p)$, the principal components are given by the uncorrelated linear combinations PC_1, PC_2, ⋯, PC_p as belows.

$$
\begin{aligned}
PC_1 &= \mathbf{e}_1'\mathbf{X} = e_{11}X_1 + e_{21}X_2 + \cdots + e_{p1}X_p \\
PC_2 &= \mathbf{e}_2'\mathbf{X} = e_{12}X_1 + e_{22}X_2 + \cdots + e_{p2}X_p \\
&\vdots \\
PC_p &= \mathbf{e}_p'\mathbf{X} = e_{1p}X_1 + e_{2p}X_2 + \cdots + e_{pp}X_p
\end{aligned}
$$

X_i : time series vector at each voxel (n×1)
PC_i : principal component vector (n×1)
n : number of scan
p : number of voxel

The weighting factors e_{ij} reflect the cross correlation between each voxel and the corresponding principal component. Eigenimage composed of them shows the interconnected regions whose blood flow values are positively or negatively correlated with the principal component.

Method

Subjects were 5 normal volunteers. All were male, right-handed, and free of neurologic, psychiatric, or medical disorders.

Procedure of activation study and data acquisition was previously described (Lee *et al.*, 1998). The procedure is summarized below.

Repeated $H_2{}^{15}O$ PET (ECAT EXACT 47, Siemens-CTI, Knoxville, USA) scans with one control and three different activation tasks were performed on each subject.

Each activation task was composed of 13 matching trials. On each trial, four targets, a fixation dot and a probe were presented sequentially and subject's task was to press a response button to indicate whether or not the probe was one of the previous targets.

Short meaningful Korean words, simple drawings and monochromic pictures of human faces were used as matching objects for verbal or visual memory. One control task was performed before the activation tasks to remove the effect of visual stimulation and activation due to the movement of finger to push the button.

All the images were spatially normalized and statistically analyzed (ANCOVA) using SPM96 (Statistical Parametric Mapping 96). We applied PCA on those voxels significant at $p<0.01$ (uncorrected) using the omnibus F ratio.

Results

Figure 1 shows the first principal component account for 83.0% of the variance and its positive and negative eigenimages (upper). Anterior cingulate included in negative eigenimage which represented the brain areas whose blood flow value increased along the tasks seems to be related with the increase of the difficulty of the tasks.

Second principal component shown in figure 2 indicated the difference between verbal (observation 2 and 3) and visual (observation 4) memory tasks. Dominance of left hemisphere in verbal working memory and that of right in visual memory are clearly demonstrated.

Conclusion

We conclude that functionally connected brain areas involved in verbal and visual working memory could be lateralized and discriminated by the PCA.

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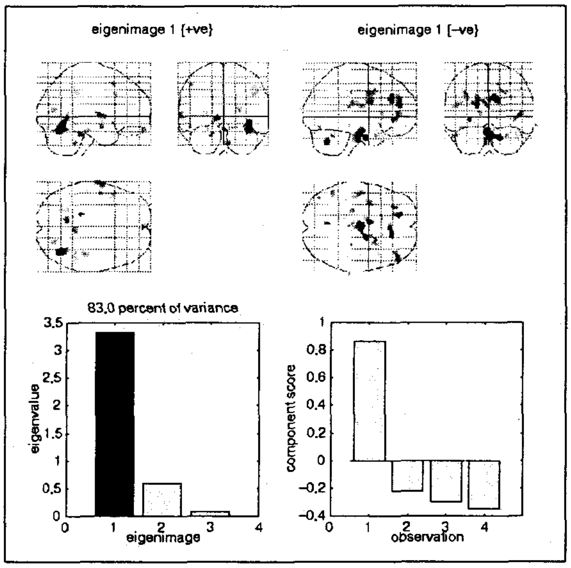

Fig. 1. First principal component eigenimages across the four conditions: 83.0% of the variance was contributed by the first component. Positive and negative eigenimages (upper) represented respectively the brain areas whose blood flow decreased or increased along the tasks.

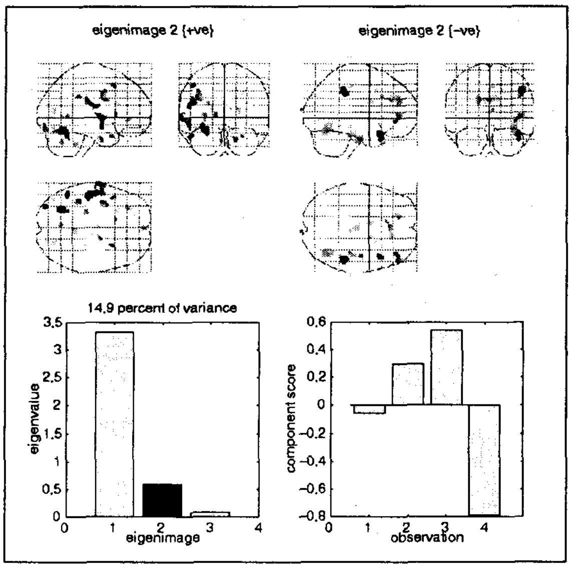

Fig. 2. Second principal component eigenimages across the four conditions: 14.9% of the variance was contributed by the second component. Both eigenimages represented respectively the brain areas those are involved in verbal (left) and visual (right) working memory system.