IV. 8. Clinical Application of SPM and PET to Localize Epileptogenic Foci in Temporal Lobe Epilepsy

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Introduction

Positron emission tomography using $^{18}$F-fluoro-deoxyglucose (FDG) has been widely applied to epileptic patients to localize epileptogenic foci for presurgical evaluation, and to investigate the pathophysiology around the lesion. Numerous studies have confirmed a 60 to 90% incidence of interictal hypometabolism in patients of temporal lobe epilepsy[1]. Because PET images have been analyzed usually by visual inspection or semi-quantitative method applying regions of interest (ROIs) on the suspected areas, these methods are likely to be affected by the operator bias.

The Statistical Parametric Mapping (The Wellcome Department of Cognitive Neurology, London, SPM 99) has recently established as a tool for detection of regional brain activations or physiological abnormalities in the analysis of brain images obtained by PET, SPECT or fMRI2-3). In this article we report the reliability of SPM and PET to localize functional brain abnormalities in epileptic patients.

Method

Subjects and method

Nine patients with temporal lobe epilepsy and 24 healthy normal volunteers participated in this study. PET scan was carried out using Shimadzu HEADTOME-V scanner in 3-D data acquisition mode at 45 minutes after intravenous injection of 37 MBq in average of FDG. The subjects lay comfortably in the scanner bed and all studies were performed with their eyes close in a dim room and minimal auditory stimulation. The studies of epileptic patients were undergone in interictal condition. PET images were analyzed with SPM 99 implemented on Matlab (Mathworks, Natick, Mass., USA)2-3). At first PET images obtained from subjects were anatomically normalized to the standard template brain in the standard stereotaxic space defined by Talairach and Tournoux[4]. This process was undergone using linear and non-linear transformation algorithm. The transformed PET images were smoothed with a Gaussian filter kernel of $15 * 15 * 13$ mm
FWHM. PET images were compared between from one patient and from 24 healthy volunteers using the 'compare group' statistics with the threshold at p<0.001, uncorrected for the multiple comparisons and p<0.05, with voxel-based correction. Subsequently, the regions with decreased relative glucose consumption were displayed as the MIP images (glass brain) and over the T1-weighted MR template images included in SPM99. The precision and reliability of this method was assessed both by visual inspection of the original PET images and SPM analysis.

Results

In eight of nine patients, decreased glucose metabolism was detected by visual inspection only in the temporal lobe. Statistical analysis using SPM99 with a threshold at p<0.001, uncorrected for the multiple comparisons, localized the lesions also, which matched the region detected by visual inspection. On the other hand, the lesion was much smaller than visual inspected area with a threshold set at P<0.05, with voxel-based correction.

All the normalized images of 8 patients were checked visually. Normalization using linear and nonlinear algorithm could transform all the PET images to a standard image adequately in spite of focal abnormalities. In one patient SPM analysis successfully revealed focal lesion in lateral portion of the temporal lobe, which was not detected by visual inspection.

Case presentation

In case 1 magnetic resonance (MR) imaging showed the left hippocampal atrophy. Electrocorticography (ECoG) indicated the epileptogenic spikes in the left temporal and frontal lobes. FDG PET image demonstrated evident glucose hypometabolism spreading over the whole left temporal and parietal lobes (fig. 1A). The normalization process transformed the raw PET image to almost adequate brain image (fig. 1B). SPM analysis also revealed the glucose hypometabolism in the left temporal and parietal lobes (fig. 1C).

In case 2 the scalp EEG suggested that epileptic focus is located in the mesial temporal lobe. However, FDG PET image scanned at interictal condition did not reveal apparent focal lesion (fig. 2A). The normalization was successful (fig. 2B) and SPM analysis could localize a focal lesion in the lateral portion of the temporal lobe (fig. 2C).

Discussion

Functional neuroimaging to measure cerebral blood flow and metabolism is reported to be most effective non-invasive technique for localization of epileptogenic foci. Previous studies have shown a 60 - 90 % incidence of glucose hypometabolism by FDG PET in the epileptogenic area suspected by EEG study. These metabolic disturbances are often larger than areas proved pathologically by surgical procedures or than the lesions detected by 11C-
flumazenil (FMZ) PET, uptake of which was though to be correlated with regional neuronal loss. These findings implied functional disturbances around the focus, which was the source of epileptic discharge\(^5\). Visual inspection and ROI method have been often applied to detect hypometabolic regions on PET images. However, these methods are subjective and not sufficient to be used for small or subtle lesions. In this study we applied a statistical imaging analysis and compared its validity with the conventional methods.

The results revealed that In 8 of 9 temporal lobe epilepsy cases, the SPM analyses clearly delineated hypometabolic regions of glucose which was comparable with the visual inspection. However, In 1 case, SPM disclosed a significant hypometabolic region in the lateral portion of the temporal lobe, which was not picked up by visual inspection.

Although the number of cases in this study is still small, the SPM analysis proved to be potentially useful for detection of abnormal regions, which might be missed or not conclusive by visual inspection due to its subtlety. We stress the robust and objectiveness of this SPM analysis which is essential for presurgical examinations of epilepsy treatment.

It is reported that some temporal lobe epilepsy patients with suspected foci in mesial portion of the temporal lobe showed marked hypometabolism in the lateral portion of the temporal lobe\(^6\). This phenomenon was explained by either trans-synaptic effects by disturbed efferent pathways due to reduced viable cells in the focus in mesial temporal lobe or due to a reduced number of efferent fibers to the temporal neocortex from the hippocampal formation\(^6\). In case 2 SPM analysis demonstrated this pathophysiological abnormality as a spotty hypometabolic area in the lateral temporal lobe.

The anatomical normalization in SPM basically employs linear (affine) transformation which assumes regional similarity between the target and the template images. Substantial caution is required to apply this technique to the images where regional abnormality is expected. Previous studies indicated that only linear transformation without nonlinear algorithm should be applied to this situation. Some authors suggested that the anatomical transformation should be first applied to MR images (patient's to the template) and the obtained transformation matrices could be used for PET images afterward, with MRI and PET images co-registered beforehand. However, normalization of PET images only was found almost adequate in this study with relatively mild functional abnormalities. Technical simplicity is important for clinical evaluation.

References


Fig. 1A. (A) FDG PET images delineated apparent hypometabolism spreading over the temporal and parietal lobes. (B) The normalized image generated by SPM reveals almost adequate brain shape. (C) The regions with decreased relative glucose consumption detected by SPM analysis are displayed over the T1-weighted MR template images (left) and as the MIP images (glass brain) included in SPM99 (right). The regions almost correspond to the area identified by visual inspection of the original PET image.
Fig. 2. Case 2. (A) FDG PET images scanned at interictal condition does not reveal apparent hypometabolic region. (B) The normalized image generated by SPM shows adequate brain shape. (C) The focal hypometabolic lesion in the lateral portion of the right temporal lobe detected by SPM is displayed over the T1-weighted MR template images (left) and as the MIP images (right).