Voxel Based Morphometry and Statistical Parametric Mapping of Positron Emission Tomography (SPM-PET) in Patients with Frontal Lobe Epilepsy Compared to Normal Controls

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Purpose

It has been known that patients with Juvenile Myoclonic Epilepsy (JME) and Frontal Lobe Epilepsy (FLE) subjects have deficits in working memory [1]. High resolution MRI has found increasing number of neuronal dysplastic regions in the so-called "cryptogenic" (unknown) origin group in FLE subjects. The subjects with FLE show neuro-cognitive deficits in the frontal domain, whether or not a clear structural lesion is seen, leading to the hypothesis that it is the seizures, not the structure abnormalities that cause the cognitive dysfunction. Many neuroimaging studies have been performed for JME, and the findings include a lack of increased prefrontal glucose uptake during an activation paradigm [2], increased gray matter in the medial frontal region [3], possible decreased NAA in the cingulate [4], increased myoinositol in the prefrontal cortex [1], and abnormal texture of the thalamus [5]. Fewer studies were available for FLE, but NAA is decreased on the epileptogenic side. Voxel-Based Morphometry and SPM-PET of FLE subjects have not been reported and the stability of any the above changes are unknown. In this study, the voxel-based morphometry (VBM) analysis was performed to assess the differences across the whole brain between FLE and normal age-matched controls. The VBM findings were compared to PET activity differences between patients with FLE and normal age-matched controls analyzed using the SPM2 package.

Methods

Twenty eight subjects, 14 FLE (34±11 years old, 7 M, 7 F) and 14 controls (31 ± 10 years old, 7M, 7F) were included in this study. Diagnosis of epilepsy was confirmed by findings of myoclonic jerks, generalized tonic clonic seizures, and generalized fast polyspike wave complexes on EEG. MRI was performed on a 1.5 T Philips Eclipse scanner. The seizure focus was localized on the left in all FLE subjects. The 3D high resolution T1 weighted images were acquired using TR=20 ms, TE=4.47 ms, flip angle=20º, slice thickness= 1.5 mm, FOV=25.6 cm, matrix= 256x256. PET scan was acquired on the GE Advance PET scanner using number of time slices= 1, slick thickness =4.25 mm, number of slice=35, FOV=30 cm, matrix=128x128. Glucose levels were performed prior to scanning and subjects with serum glucose > 110mg cc^{-1} were not scanned. For subjects who were scanned, 10± 0.1 mCi of F^{18}-FDG was injected intravenously, and the subjects rested in a quiet environment for 45 minutes before scan. For Voxel-based Morphometry (VBM) analysis, all individual scans were used to create the template and the GM, WM, and CSF probability maps using the technique describe in [6]. The template and the probability maps were smoothed with 8 mm FWHM Gaussian kernel. Next, all original scans were normalized to this template then segmented. The resultant GM and WM maps were smoothed with 12 mm FWHM Gaussian kernel. Statistical inferences were made using an analysis of covariance ($p < 0.001$) with TBV, age, and gender as nuisance variables. The differences in GM volume between FLE and Control were investigated further using the small volume correction (S.V.C) procedure. For SPM-PET analysis, all individual PET scans were normalized to the PET template provide in the SPM2 package, the normalized PET scans were smooth with 10 mm FWHM Gaussian kernel. Statistical inferences were done using an analysis of covariance ($p < 0.001$) with age and gender as nuisance variables. The differences in PET activity between FLE and Control were investigated using the S.V.C procedure.

Results

Results from Voxel-based Morphometry (VBM) analysis showed Control had more gray matter (GM) in the left thalamus region than FLE group. Interestingly, the FLE group had more GM than the Control in the inferior frontal gyrus (F3), the right Parahippocampus (PaH) and the right Postcentral gyrus (POG). Results from SPM-PET analysis showed Control had more PET activity than FLE in the superior frontal gyrus (F1), in the middle frontal gyrus (F2) and the left inferior frontal gyrus (F3). In contrast, FLE had more PET activity than Control in the right precentral gyrus (PRG).

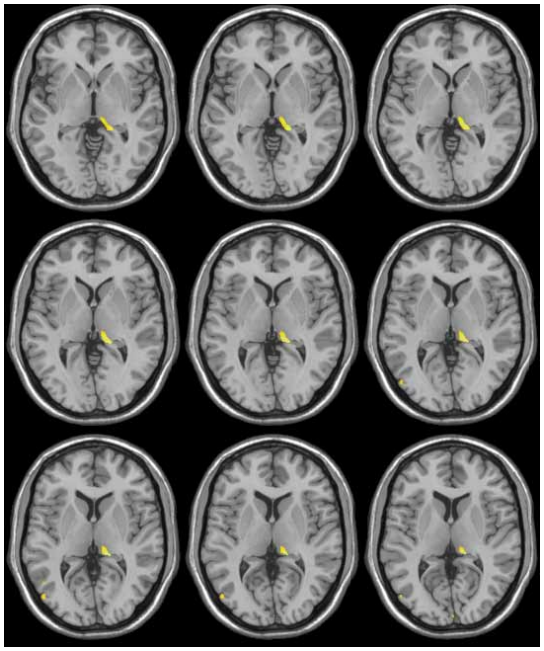

Figure1. VBM analysis of regions where the FLE group have less gray matter in the thalamus than the control group, summarized in Table 1.

Table 1: Regions showing differences between FLE and Control in VBM

Region	Cluster size k	Voxel T	Z score
Left Thalamus	560	4.39	3.89
Right Parahippocampus	175	4.84	4.21
Left Inferior Frontal Gyrus	289	4.21	3.76
Right Inferior Frontal Gyrus	135	4.25	3.79

Discussion

Our VBM analysis supports the hypothesis that the control group has more GM than FLE group in the thalamus region. Our results indicate that VBM can be applied to investigate thalamus atrophy without performing manual analysis, which may be in part due to that the thalamus is a relatively large and anatomically well-defined region. Unlike the findings in JME [3], our VBM analysis shows that FLE has more GM than Control in the inferior frontal gyrus (F3), the parahipppocamus (PaH) and the right postcentral gyrus (POG). However, SPM-PET analysis does not show FLE has any increasing in glucose uptake in these regions except the precentral gyrus (PRG). Likewise, SPM-PET analysis supports our hypothesis that Control has more glucose uptake than FLE in the F1, F2 and F3 regions, but our VBM analysis does not show any decreasing in gray matters in these regions of FLE subjects. Taken together, these findings might suggest that in the FLE group, decreasing in glucose uptake in one region does not imply a decreasing in gray matter in that region, and vice versa. Therefore the structural changes and functional changes may provide complementary information for further understanding of the manifestation of FLE. If these results are validated in more subjects, they may be used with EEG to differentiate between JME and FLE subjects.

References [1] Swartz et al. J Epilepsy 1994, 7(3): 232-241. [2] Swartz et al. Neurology 1996, 47(5): 1203-1212. [3] Woehrmann et al. Brain 1999: 2101-8. [4] Savic et al. Epilepsia 2000, 41(3): 290-296. [5] Betting et al. Neurology 64(S1): A152; 2005. [6] Good et al. NeuroImage 2000, 14(1): 21-36.

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