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

L. Vu[1], B. Swartz[2], M. Mandelkern[3], O. Nalcioglu[1], and M-Y. Su[1]

[1]Tu & Yuen Center for Functional Onco Imaging, University of California, Irvine, CA, 92697, United States, [2]Epilepsy Center, Hoag Hospital, Newport Beach, CA, 92663, United States, [3]Deparment of Physics, University of California, Irvine, CA, 92697, United States

Purpose

It has been known that patients with Juvenile Myoclonic Epilepsy (JME) and Frontal Lobe Epilepsy (FLE) have deficits in working memory [1]. JME is a syndrome of idiopathic generalized epilepsy with an age-related onset of seizures; it is characterized by myoclonic jerks, tonic-closure seizures and less frequently by typical absences. There are no neuro-radiological signs, and very often visual inspection of high-resolution MRI is normal in the JME patients. Some 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]. Voxel-Based Morphometry and SPM-PET can evaluate the global changes in the brain, and may provide additional supporting evidence to verify the above-mentioned findings. In this study, the voxel-based morphometry (VBM) analysis was performed to assess the difference of gray matter density across the whole brain between JME and normal age-matched controls. We also analyzed the PET activity in these patients to compare the metabolic differences with structural differences.

Methods

Thirty four subjects, 16 JME (34±11 years old, 6 M, 10 F) and 18 controls (31 ± 10 years old, 8M, 10F) 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 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 with slick thickness =4.25 mm, number of slice=35, FOV=30 cm, matrix=128x128. Glucose levels were checked prior to scanning and subjects with serum glucose > 110mg cc^{-1} were not scanned. Approximately 10 mCi of $F^{18}DG$ 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 a study specific 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 JME 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, then 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 JME and Control were also investigated using the S.V.C procedure.

Results

VBM analysis showed that normal controls had more gray matter (GM) in the left thalamus (Th), left superior temporal gyrus (T1), left middle temporal gyrus (T2), and left parahippocampus (PaH) regions than JME group. Interestingly, JME group had more GM than Control in the left inferior frontal gyrus (F3), right superior temporal gyrus (T1), left caudate (Ca) and right posterior cingulate (Cing) regions. Results from SPM-PET analysis showed normal controls had a higher PET activity than JME in the superior frontal gyrus (F1) and in the middle frontal gyrus (F2). In contrast, JME had a higher PET activity than normal controls in the right precentral gyrus (PRG).

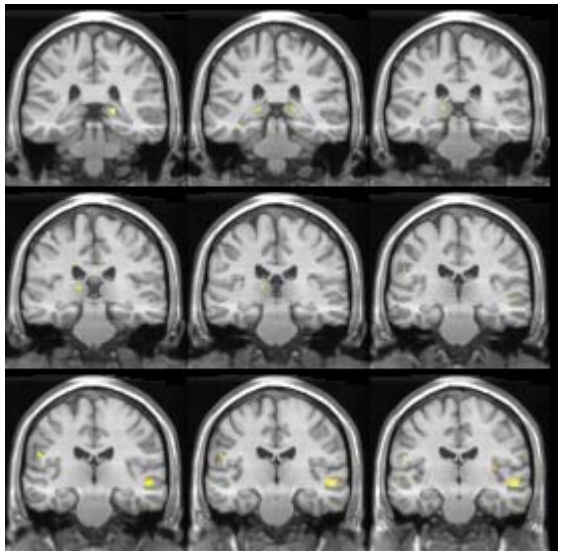

Figure1. VBM analysis of regions where the JME group has less gray matter in the Parahippocampus and Superior Temporal gyrus regions than the normal control (NC) group, summarized in Table 1.

Table 1: Regions showing decreased gray matter in JME compared to NC

Region	Cluster size k	Voxel T	Z score
Left Thalamus	115	3.22	2.99
Left Parahippocampus	209	4.01	3.62
Left Superior Temporal Gyrus	969	3.70	3.37
Left Middle Temporal Gyrus	676	3.27	3.03

Discussion

The results that JME had less gray matter in the thalamus region support the hypothesis that JME might have sustained some tissue damage leading to compromised thalamus structure [5]. This finding also agrees with the MRS study of the same subjects reported by Baek et al [7]. Our results indicate that VBM can be applied to investigate thalamus atrophy without performing manual analysis, which is known to be difficult due to that the thalamus is a relatively large and not anatomically well-defined region. In addition, our VBM analysis showed that JME had more GM than Controls in the left F3, the right superior temporal gyrus (T1), the left Caudate and the right posterior cingulate regions. However, SPM-PET analysis did not show increased glucose uptake in these regions in JME, except in the right precentral gyrus (PRG). SPM-PET analysis showed that Controls had more glucose uptake than JME in the F1 and F2 regions, but the VBM did not show increased gray matter density in these regions. Thus, these findings might suggest that in the JME group, decrease in glucose uptake in one region does not imply a decreased gray matter in that region and vice versa, therefore, they may provide complementary structural and functional information. If our results are validated in larger subject population, they can be used with EEG to differentiate between JME and FLE subjects.

References [1] Swartz et al. J Epilepsy 1994; 7:232-241. [2] Swartz et al. Neurology 1996; 47:1203-1212. [3] Woehrmann et al. Brain 1999; 122:2101-2108. [4] Savic et al. Epilepsia 2000; 41:290-296. [5] Betting et al. Neurology 2005; 64(S1): A152. [6] Good et al. NeuroImage 2000; 14:21-36. [7] Baek et al, ISMRM 2007, #3573.

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