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The predictive value of FDG-PET with 3D-SSP for surgical outcomes in patients with temporal lobe epilepsy

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ABSTRACT

Purpose: We retrospectively evaluated the diagnostic value of ^{18}F-2-fluorodeoxy-D-glucose positron emission tomography (FDG-PET) with statistical analysis for the foci detection and predictive utility for postsurgical seizure outcome of patients with mesial temporal lobe epilepsy (mTLE).
Method: We evaluated 40 patients who were diagnosed mTLE and underwent selective amygdalo-hippocampectomy (SAH) or anterior temporal lobectomy (ATL) in our institute. Preoperative interictal FDG-PET with statistical analysis using three-dimensional stereotactic surface projection (3D-SSP) was detected with several clinical data including seizure semiology, MRI, scalp electroencephalography, surgical procedure with SAH or ATL and postsurgical outcome. The region of interest (ROI) was defined on 'Hippocampus & Amygdala', 'Parahippocampal gyrus & Uncus', 'T1 & T2', and 'T3 & Fusiform gyrus'. We obtained the ratio of hypometabolism difference (RHD) by 3D-SSP, and evaluated the relation among hypometabolic extent, surgical outcome and surgical procedure.
Result: The RHD in each ROIs ipsilateral to operative side was significantly higher than that of contralateral side in good outcome group. Hypometabolism of 'Hippocampus & Amygdala' was most reliable prognostic factor. Patients of discordant with presurgical examinations hardly showed obvious lateralized hypometabolism. Nevertheless, when they have significantly high RHD in mesial temporal lobe, good surgical outcome was expected. There was not significant difference of RHD distribution between SAH and ATL in good outcome group.
Conclusion: Significant hypometabolism in mesial temporal lobe on FDG-PET with 3D-SSP is useful to predict good surgical outcome for patients with mTLE, particularly in discordant patients with hypometabolism in mesial temporal structure. However, FDG-PET is not indicative of surgical procedure.

1. Introduction

The conventional diagnosis of an epileptic focus location is based on seizure semiology, electroencephalography (EEG), and magnetic resonance imaging (MRI). ^{18}F-2-fluorodeoxy-D-glucose positron emission tomography (FDG-PET) can provide additional information to determine the focus localization by representing foci as hypometabolic areas of glucose [1,13,34]. Visual assessment of FDG-PET images has been routinely used for clinical evaluation. However, its interpretation is subjective and depends on observer's experience [4]. Hypometabolic areas tend to extend further than actual epileptic foci [32], and often patients with mesial temporal lobe epilepsy (mTLE) show hypometabolic areas spreading across extratemporal or contralateral to the epileptic area.

Recently, objective statistical approaches have been proposed to improve the diagnostic accuracy of epileptic focus localization [22,28]. They evaluate focus lateralization by an asymmetry index of a specific region of interest (ROI). *Z*-Score mapping that is indicating differences between normal and actual value for each voxel with an asymmetry index using statistical parametric mapping (SPM) improved regional glucose hypometabolism detection [28].

In this study, we investigated the diagnostic value of FDG-PET with a three-dimensional stereotactic surface projection (3D-SSP) as a statistical method for patients with TLE. We evaluated the following: (1) comparison of the diagnostic value of FDG-PET with

Abbreviations: FDG-PET, ^{18}F-2-fluorodeoxy-D-glucose positron emission tomography; mTLE, mesial temporal lobe epilepsy; 3D-SSP, three-dimensional stereotactic surface projection; HS, hippocampal sclerosis; SAH, selective amygdalohippocampectomy; ATL, anterior temporal lobectomy; RHD, ratio of hypometabolic difference.

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3D-SSP to visual inspection for focus detection during pre-operative diagnostic work-up. (2) Detection of a diagnostically significant region leading to good surgical outcome after using 3D-SSP. (3) Evaluation of differences in FDG-PET findings between patients with or without concordant data from non-invasive presurgical studies. (4) Evaluation of the potential contribution of FDG-PET findings to decide the extent of surgical resection for patients with TLE (selective amygdalohippocampectomy (SAH) vs. anterior temporal lobe resection (ATL)).

2. Materials and methods

Patients with pathologically proven hippocampal sclerosis (HS) who presented at our facility from 2006 to 2013 with complex partial seizures (CPS) that were presumed to originate from the temporal lobe were enrolled in this study. Pre-surgical evaluations of seizure semiology, MRI, scalp video EEG and neuropsychological examinations were performed in all patients. Patients who had a typical CPS and a unilateral HS on MRI with ipsilateral ictal and interictal epileptic discharges (IEDs) from ipsilateral temporal leads on a scalp video EEG belonged to the concordant group. Having concordant data satisfied our indications for an epileptic focus resection without invasive EEG recordings. When the findings were discordant (discordant group), we implanted bilaterally subdural electrodes over the mesial and lateral temporal lobes to record habitual seizures and epileptic discharge patterns for several days [27].

We performed a trans-sylvian selective amygdalohippocampectomy (SAH) with recording of intraoperative electrocorticography (ECoG) from the hippocampus, amygdala and lateral temporal cortex under 2.5% sevoflurane anaesthesia [7]. After resecting the mesial temporal lobe structures, we again recorded the ECoG from the lateral temporal cortex. When some persisting epileptic discharges were recorded from the lateral temporal lobe, we carried out an additional lateral temporal resection.

The postsurgical seizure outcomes were evaluated using the classification of the international league against epilepsy (ILAE) committee [33] at 1-year and 2-years after surgery. Class 1 and 2 ILAE classifications were regarded as good surgical outcomes, and class 3–6 were considered to be poor.

2.1. Data acquisition for the ^{18}F-FDG-PET with 3D-SSP analysis

The ^{18}F-FDG PET scans were performed using a Discovery ST scanner (General Electric Healthcare, Fairfield, Connecticut, USA). The trans-axial spatial resolutions (full width at half maximum) at 1- and 10-cm off-axes were 6.2 and 6.7 mm, respectively. The subjects fasted for at least 4 h before the scan. After an intravenous administration of 185 MBq/2 ml ^{18}F-FDG, the subjects were kept in a dimly illuminated isolation room and instructed to remain still with their eyes open and to avoid falling asleep. A set of trans-axial images was obtained in a standard 3D emission scan mode starting 40 minutes after the injection with scan duration of 15 min. The images were reconstructed using 3-dimensional iterative reconstruction, including a correction for attenuation measured by a transmission scan. The matrix size, each voxel size, slice thickness, and number of images were 128 × 128 mm, 2.25 mm, 3.3 mm, and 47 slices, respectively.

We analysed the FDG-PET images using 3D-SSP in NEUROSTAT developed by Minoshima et al. [17–19], in which the cerebral metabolic rate of glucose (CMRglc) was projected over a standardized anatomical brain. For anatomic standardization, first, the midsagittal plane of the brain is determined from the PET image set, and the bicommisural (anterior commissure to posterior commissure) (AC-PC) line is defined on the midsagittal plane. In this way, the AC-PC line is matched to the center of the co-ordinate system of the atlas's brain. Next, individual brain size is corrected linearly to the standard dimension of the atlas brain. The anteroposterior length was measured as the distance between the most anterior edge of frontal cortex and the most posterior edge of the occipital cortex. The brain width was measured as the distance between the midsagittal plane and the most lateral edge of the parietotemporal cortex. The brain height was measured by matching midsagittal plane derived and fitted to the brain contour in the atlas varying the vertical scale linearly.

To extract metabolic data after anatomic standardization for cortical metabolic activity, pixels located on the outer and medial surface of both hemispheres are predetermined along with three-dimensional vectors perpendicular to the surface at each pixel. For each predetermined pixel, the techniques each for the highest pixel value in a direction inward along the vector to a six-pixel depth (13.5 mm) into the cortex on the individual's anatomically standardized PET image set and assigned the maximum value to the surface pixel.

The CMRglc images were normalized to the mean whole brain CMRglc activity. A normal database was acquired from 26 Japanese volunteers (13 males and 13 females) ranging from 40- to 64-year-olds from the Juntendo Tokyo Koto geriatric medical centreusing the same PET scanning technique [8]. The number of volunteers under 50 years old was 10 (5 male, 5 female. average 44.2 yeas old), 50–60 was 10 (6 male, 4 female. average 54.5 years old), and 61–64 was 5 (2 male, 4 female. Average 61.8 years old). The 3D-SSP was performed using normal data with the decade of age matched. When a patient's age was below 40, we used the data from the 40-year decade as the normal. The region of interests (ROIs) to evaluate the CMRglc in this study were the following: "Hippocampus & Amygdala", "Parahippocampal & Uncus", "T1 & T2 gyri", and "T3 & Fusiform gyri". Individual anatomical information was converted to standardized brain mapping using the Talairach Daemon brain atlas. The template of standardized brain was obtained by Talairach Client 2.4 program [14]. To demonstrate the regional patterns of CMRglc, a two-sample *t*-test was performed to obtain *Z*-scores on a voxel-by-voxel basis between each patient and the normal database using the stereotactic extraction estimation [12] program developed by Mizumura and Kumita [20]. The 1.96 value of the *Z*-scores was automatically defined and values less than 1.96 were rejected by definition. To illustrate the extent of hypometabolism in each ROI, we defined the ratio of hypometabolism difference (RHD) in each ROI by dividing the number of voxels established for each patient by the number of voxels as a control.

2.2. Comparing the 3D-SSP and Visual analysis of FDG-PET

To evaluate the 3D-SSP method in relation to the existing conventional approach, we compared the two methods. On visual assessment, the FDG-PET images were evaluated by an expert neurosurgeon and a neuroradiologist who were blinded for the patients' background and surgical results. The decision was only for the existence of laterality within the temporal lobe, not the localization or extent of the hypometabolic area. If it was difficult to decide on certain case, it was considered to be 'unknown'. When the two examiners had different decisions, the case was also considered to be "unknown". Cohen's kappa score was 0.75, which was regarded as a good agreement.

2.3. Evaluation of the diagnostic value of 3D-SSP

We evaluated the potential diagnostic value of the 3D-SSP (RHD) by validating it in the good outcome group. We compared the following: (1) *The significance of RHD values to predict good surgical outcome and identify correctly the epileptic focus location.*