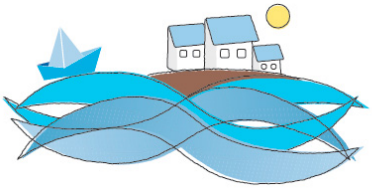

Mediterranean Thematic Workshops in Advanced Molecular Imaging

Contribution ID: **10** Type: **Oral**

SPM-guided PET analysis for the evaluation of non-lesional epilepsy.

Monday, May 2, 2016 5:00 PM (20 minutes)

Multi-modal preoperative evaluation with advanced structural, functional, and metabolic neuroimaging techniques is essential in the pre-surgical evaluation of refractory epilepsy for the delineation of the epileptogenic zone to be resected. In latter years, PET has gained a leading role in this evaluation since it has demonstrated to be simpler and more sensitive than ictal SPECT in certain situations. Furthermore, the availability of co-registered PET/MRI images has improved the interpretation of images of both modalities and enabled a more straightforward use of PET information on MRI-guided surgery. In this regard, MRI findings have demonstrated to be extremely useful for assisting PET analysis, since the location of anatomic anomalies related with epilepsy can focus the PET analysis on a reduced area, making possible to detect small focal hypometabolisms that might be dismissed on a simple visual inspection. Nevertheless, 35% of epilepsy patients show no lesions on the MRI, which are related with an earlier stage of the disease, and resective epilepsy surgery in non-lesional epilepsy is commonly associated with less favourable outcome. For these patients, PET is of particular importance, but its performance is reduced due to the lack of the aforementioned MRI guiding. In this context, the use of PET quantification techniques, such as Atlas-based Asymmetry Indices (AI) and especially Statistical Parametric Mapping (SPM) has improved the localization of the epileptogenic focus. In particular, SPM has potential for being a suitable substitute of MRI guiding the PET analysis when no anatomical lesions are found. On this work we evaluated the correlation between anatomical findings and SPM results on 24 patients with different types of epilepsy-related MRI lesions (12 cortical focal dysplasia, 12 mesial temporal sclerosis) and 5 patients with non-lesional MRI. PET images were processed with iSFS-RR resolution recovery algorithms and SPM maps were obtained by an unpaired t-test voxel-by-boxel comparison between the patient and the database of 97 healthy patients. Patients were evaluated by using PET, PET/MR and PET/SPM images, trying to reproduce a clinical scenario. On lesional epilepsy patients, SPM provided better sensitivity (91.6%) than PET only images (70.8%), and SPM findings showed high correlation with MRI anatomical findings. When applied to non-lesional epilepsy patients, PET/SPM also offered better sensitivity (80%) than simple PET visual analysis (40%). Thus, the purposed SPM-guided PET visual analysis demonstrated to be more effective than the routine visual inspection, showing potential for improving focus location on non-lesional epilepsy.

Summary

Introduction

Multi-modal preoperative evaluation with advanced structural, functional, and metabolic neuroimaging techniques is essential in the pre-surgical evaluation of refractory epilepsy for the delineation of the epileptogenic zone to be resected (Brázdil et al, Epileptic Disord 2006). In latter years, PET has gained a leading role in this evaluation since it has demonstrated to be simpler than ictal SPECT and more sensitive than MRI in certain scenarios (Ramey et al. Clin Neurol Neurosurg 2013). Furthermore, the availability of co-registered PET/MRI images has improved the interpretation of images of both modalities and enabled a more straightforward use of PET information on MRI-guided surgery (Shin et al, Neurology 2015). In this regard, MRI findings have demonstrated to be extremely useful for assisting PET analysis, since the location of anatomic anomalies related with epilepsy can focus the PET analysis on a reduced area, making possible to detect small focal hypometabolisms that might be dismissed on a simple visual inspection. Nevertheless, 35% of epilepsy patients show no lesions on the MRI, usually meaning that the lesion is so subtle that the scanner is not sensitive

enough to discriminate between the lesion and surrounding healthy brain tissue, which might be related with an earlier stage of the disease (Pardoe et al, Epilepsy Curr 2014). Resective epilepsy surgery in non-lesional epilepsy is commonly associated with less favourable outcome. For these patients, PET is of particular importance, but its performance is reduced due to the lack of the aforementioned MRI support (Hammers et al, Cambridge University Press 2015). On this context, the use of PET quantification techniques, such as Atlas-based Asymmetry Indices (AI) and especially Statistical Parametric Mapping (SPM) has improved the localization of the epileptogenic focus (Kyeong Kim et al, J Nucl Med 2016). In particular, SPM is an objective tool for the analysis of FDG-PET images and a useful complement for visual analysis (Archambaud et al, EJNMMI Res 2013). Due to this, it has potential for being a suitable substitute of MRI for the guidance of the PET analysis when no anatomical lesions are found. This combined with advanced resolution recovery techniques that help to increase PET image contrast and thus detect smaller pathological areas could severely increase PET performance for this particular application (Silva-Rodríguez et al, EJNMMI Physics 2015, Silva-Rodriguez et al, IEEE Trans Nucl Sci 2016, In press). On this work, we are aimed at evaluating the correlation between MRI anatomical findings and SPM results. Afterwards, we applied the evaluated methodology to non-lesional epilepsy patients.

Methods

Patients

This study was performed on 29 patients previously diagnosed and operated by the Refractory Epilepsy Surgery Unit at the University Hospital of Santiago de Compostela in the period 2012-2013. All patients underwent the presurgical evaluation by routine at our centre, which includes FDG-PET, SISCOM SPECT, 3T-MRI, video electro-encephalography and a wide range of neurological and neuropsychological tests. Positive epilepsy diagnosis and focus localization were obtained by evaluating the results coming from the whole group of tests included in our protocol. Patients were categorized between temporal lobe epilepsy (16 patients, 55.2%) and extra-temporal lobe epilepsy (13 patients, 44.8%). Along the temporal epilepsy group, most common MRI finding was hippocampal atrophy due to mesial temporal sclerosis (12 patients, 75.0%) followed by focal cortical dysplasia (2 patients, 12.5%) and non-lesional MRI (2 patients, 12.5%). On the extratemporal epilepsy group, most common MRI finding was focal cortical dysplasia of the frontal lobe (8 patients, 61.5%), followed by focal cortical dysplasia of the occipital lobe (2 patients, 15.4%) and non-lesional MRI (3 patients, 23.1%). Patients were also categorized in lesional (24 patients, 82.7%) and non-lesional (5 patients, 17.3%). A summary of this classification is shown in Table 1.

We also used images from 97 control subjects. These images were obtained from pre-treatment oncologic patients that underwent FDG-PET after signed consent. All of the control subjects were examined for ensuring that there are no signs of a neurologic or psychiatric disease and the obtained images were evaluated by two experienced nuclear medicine physicians and were considered normal. All the images were acquired following the protocols detailed below.

Imaging protocols

3T-MRI: structural imaging was performed with an Achieva 3.0T X-series MR imaging scanner (Philips Healthcare, Best, The Netherlands) using a head coil. The MRI protocol consisted of the acquisition of T1-weighted 3D TFE, FLAIR and T2-weighted sequences. The different sequences were visually evaluated for diagnosis following the protocols of the Refractory Epilepsy Surgery Unit.

FDG-PET: all patients underwent the routine neuroimaging protocol at our institution. Starting 45 min after after intravenous injection of 370 MBq of 18F-FDG, the patients were scanned during 30 min for emission data and 15 min for transmission data, required for attenuation correction. The imaging device was a GE Advance NXi PET scanner (General Electrics Healthcare, Little Chalfont, Buckinghamshire, United Kingdom). Following the default protocols of the GE Advance, scatter, randoms, attenuation and normalization corrections were applied before the reconstruction. PSF modeling and motion correction were not included. The images were reconstructed using 3D ordered subsets expectation maximization (3D-OSEM), with 4 subsets and 16 iterations. The size of the reconstructed image is 128x128x35, with a voxel size of 2×2×4.25 mm3. No smoothing was applied during or after the reconstruction. Prior to evaluation, PET images were corrected using Iterative Structural-Functional Sinergy Resolution Recovery (iSFS-RR) (Silva-Rodríguez et al, EJNMMI Physics 2015, Silva-Rodriguez et al, IEEE Trans Nucl Sci 2016, In press), an image-based PVC algorithm incorporating anatomical information provided by accurately co-registered and segmented T1-MRI into the PET image, thus enhancing resolution and image contrast.

Image Evaluation

MRI and PET images were co-registered for all patients by using SPM12 software package (Wellcome Trust Centre for Neuroimaging, University College London, United Kingdom). The co-registered PET has the same matrix and pixel size of the MRI image. Co-registered images were normalized to the MNI space using SPM12 via a segmentation routine. SPM voxel-by-voxel comparison was performed by an unpaired t-test between the patient and the database of 97 healthy patients. The results of this comparison were evaluated and only pixels with significant differences ($p<0.05$) were included in the final SPM map (Kyeong Kim et al, J Nucl Med

2016). The matrix obtained from the normalization process was inverted and applied to the SPM map, obtaining co-registered PET/MRI/SPM images on the patient space.
The sensitivity of the purposed PET/SPM methodology was assessed and compared with PET only and PET/MRI co-registered images trying to reproduce a clinical scenario:

Visual assessment of 18F-FDG PET: An experienced nuclear physician assessed the images looking for hypometabolisms compatible with the epileptogenic process. Prior information of the clinical findings from V-EGG and previous neurological tests was given to the physician.

Visual assessment of PET/MRI: An experienced nuclear physician evaluated the PET/MRI images looking for hypometabolisms related with the MRI findings. Aforementioned information, along with the findings report from an experienced radiologist about the MRI images was given to the physician.

Visual assessment of PET/SPM: An experienced nuclear physician assessed the co-registered PET/SPM images looking for hypometabolisms compatible with the epileptogenic process. Prior information of the clinical findings from V-EGG and previous neurological tests was given to the physician.

After the validation, the purposed protocol was applied to non-lesional epilepsy. The sensitivity was compared with PET only images. The final diagnosis based on the complete bunch of tests (MRI, PET, SPECT, V-EGG and neurological and neuropsychological tests) and the clinical outcome of the surgery after a year of follow-up (when possible) were used as gold standards along the experiment.

Results and discussion

Following the image evaluation procedures described in the previous, the sensitivity of a simple PET visual inspection, PET/MRI visual inspection and SPM-guided PET visual inspection were assessed for lesional patients in order to validate the methodology and the correlation of MRI and SPM findings. Figures 1 and 2 show examples of PET/SPM results correlation with MRI findings.

Table 2 shows the results obtained on the 24 positive-MRI patients. PET/MRI was more sensitive that PET alone (100% and 70.8%), in good agreement with previous studies (Yu-Shin Ding, Am J Nucl Med Mol Imaging 2014). SPM provided useful information for re-evaluating PET images in five patients, providing better sensitivity than PET only images (91.6% and 70.8%).

After this validation, the proposed PET/SPM methodology was applied on the 5 negative MRI patients and compared to PET visual analysis. On this group, PET visual analysis located lesions compatible with the epileptic process and in good agreement with V-EGG and neurological tests in 2 patients (40%), while PET/SPM located lesions in 4 patients (80%). In one case, PET/SPM helped the re-evaluation of the patient MRI (see Figure 3), locating a subtle lesion missed on the previous analysis.

Conclusions

SPM demonstrated to be a useful technique providing additional information to the physician in the evaluation of PET images in refractory epilepsy. In lesional patients, SPM findings showed high correlation with MRI anatomical findings, pointing to the fact that SPM could be used for guiding the visual interpretation of PET images. In a limited group of non-lesional epilepsy patients, SPM-guided PET analysis demonstrated to be more effective than the routine visual inspection, showing potential for improving focus location on non-lesional epilepsy.

*This is an on-going project. Work to be presented on MEDAMI 2016 shall include results of a bigger number of patients.

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