DETECTION OF RAT BRAIN ACTIVATION USING STATISTICAL PARAMETRIC MAPPING ANALYSIS IN FDG-PET STUDIES

J.J. Vaquero, M. L. Soto, J.D. Gispert, J. Pascau, P. Garcia-Barreno, M. Desco
Medicina y Cirugia Experimental, Hospital GU Gregorio Marañón

Introduction: Statistical parametric mapping (SPM) is an analysis technique long been used in clinical research to detect subtle activity changes in brain; it is an excellent exploratory tool as it does not require a priori assumptions about the expected brain region activations.
Research in animal imaging may also take benefit from this technique, if properly adapted to the new scenario. This is the case of brain activation studies in murine models using PET tracers and dedicated imaging devices. This work proposes the use of an SPM methodology adapted to the analysis of 2-deoxy-2-[18F] fluoro-D-Glucose (FDG) positron emission tomography (PET) scans of rat brains. Advantages over conventional region of interest (ROI) based analysis were assessed in an experiment addressing the detection of brain activation in of rats which underwent three different visual stimulation paradigms.

Materials and Methods: A total of 23 female Wistar rats, weighting between 280 and 300 g, were intraperitoneally injected with FDG (2.3 ± 0.8 mCi). The animals were exposed to a visual stimulus paradigm: Group A (N=10) ambient light condition; Group B (N=6) confined in a dark environment; Group C (N=7) positioned in front of a stroboscopic light pulsed at 5 Hz. After being stimulated for 60 minutes the animals were imaged with a dedicated small animal PET. Datasets were reconstructed
using a 3D-OSEM algorithm (1.8 mm FWHM). To perform SPM analysis, the reconstructed image sets were realigned with respect a FDG-PET template by means of a rigid registration algorithm based on the maximization of mutual information. The template image was generated by co-registering and averaging selected images from the control group; a brain mask was manually segmented on the template and applied to all registered scans prior to perform an intensity normalization.
The resulting images were smoothed with a gaussian kernel (1.5 x 1.5 x 3.0 mm. FWHM), and analyzed with the SPM2b software, using an ANOVA design to detect differences between groups. Statistical significance threshold was set to uncorrected $p < 0.01$.

Results: Visual assessment of the results did not manifest differences among the different groups, making it impossible to define ROIs to be quantified. The SPM result, however, showed a statistically significant higher metabolism in Group C with respect Groups A & B apparently located

in bilateral auditory area (Figure 1). Furthermore, an statistically significant lower metabolism was also found on the bilateral amygdale in Group C with respect to Groups A & B.

Discussion: Unexpected results were obtained after the SPM analysis: visual cortex activation was expected; however significant changes appeared in the visual-auditory cortex and amygdale. A possible explanation is that visual stimulus was inadequate (some animals fell asleep), while the rhythmic sound produced by the stroboscopic device actuated during all the uptake period. Although the amygdale hypoactivation could speculatively be related to a different degree of stress, we do not have a confirmed explanation yet.

Conclusions: The small differences detected by means of SPM in our setting prevented from using classical ROI-based analysis. This work demonstrates the feasibility of using adapted SPM techniques for the statistical analysis of FDG-PET scans of small animals and suggests it may present advantages over ROI-based quantitative analysis for exploratory analysis and when subtle differences are involved.

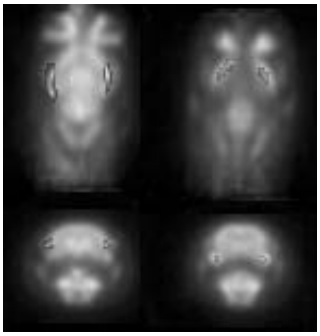

Figure1. *Resulting images of the SPM analysis highlighting activated areas. Coronal (upper) and axial (lower) views of the template. Left panel: Statistical parametric map ($p<0.01$) revealing stimulation of the rat brain on the visual-auditory area. Right panel: SPM map showing amygdale hypoactivation.*