Alzheimer's Disease: a comparative study using Statistical Parametric Mapping and Principal Component Analysis

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Objective: Principal Component Analysis (PCA) has recently been proposed to explore functional connectivity in human brain. The aim of the study was to compare PCA and Statistical Parametric Mapping (SPM), in identifying regional cerebral blood flow (rCBF) distribution differences between Alzheimer's disease patients (AD) and controls.
Methods: Thirty-seven healthy volunteers (CTR; 14/23=M/F; age: 63.8±7.6), 30 mild AD (mildAD; 12/18=M/F; age: 71.7±6.9; MMSE score: 23.7±2.3) and 27 moderate AD (modAD; 8/19=M/F; age: 72.3±7.4; MMSE score: 14.6±3.5) patients were investigated with 99mTc-HMPAO SPECT with a high-resolution, brain-dedicated camera (CERASPECT). rCBF differences were compared by SPM (height threshold p=0.001), Volumes of Interest (VOIs) analysis and PCA. A computerized brain atlas (CBA) was used in the analysis of brain images obtained by patients and normal controls. The atlas, when registered to the image data, defines volumes of interest (VOIs), corresponding to anatomical and functional areas of the brain (Brodmann areas and central structures). ANCOVA was performed on 27 VOIs in each hemisphere and then on 10 factors identified after submitting all 54 VOIs to PCA.
Results & Discussion: SPM identified at CTR versus mildAD clusters with lower rCBF distribution bilaterally in nc.caudatus and in the left temporal-occipital cortex (Fig. 1). At CTR versus modAD lower rCBF distribution was found by SPM bilaterally in the nc.caudatus, parietal, posterior frontal and posterior cingulate cortex and in the left insula and inferior-medial temporal lobe. VOIs analysis highlighted 9 regions in the CTR versus mildAD and 8 regions in the CTR versus modAD in the bilateral parietal-temporal-limbic cortex and central structures. PCA showed decreases in 3 factors at CTR versus mildAD and in 4 factors at CTR versus modAD in bilateral parietal-temporal-limbic cortex. Such factors covered in CTR versus mildAD areas larger than SPM especially in inferior parietal cortex and posterior cingulate (Fig. 2a,b=lateral view, c-d= medial view), regions typically affected early in the disease.
Conclusions: CBF pattern in AD is likely to be the result of a combination of pathological lesions having effects on distant parts of the brain. Such networking cannot be revealed by univariate analysis, as that implemented by SPM, since it considers voxels and brain functions in a segregated way, that is, taking into account only the brain connections occurring in patches or clusters. An advantage with a VOI based approach is that it allows for the investigation of the rCBF relationships between anatomically distributed but physiologically correlated brain regions using principal component analysis (PCA). Applying PCA to the VOIs permits a reduction of the number of variables through the grouping of VOIs into factors. This latter characteristic of PCA might be of utmost importance in analysing pathological conditions in which functionally integrated pathways are involved in the disease process. In this study, the presence of regional differences at PCA not detectable with SPM emphasised the value of taking into account the relationships among brain regions for rCBF investigations.
References & Acknowledgements:

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