VOXEL-BASED ANALYSES OF PITTSBURGH COMPOUND-B AND FDG IN AD

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Background: Region-of-interest (ROI) results for the PET amyloid-beta imaging agent Pittsburgh Compound-B (PIB) were previously reported and showed significantly greater PIB retention in Alzheimer’s disease (AD) subjects (relative to controls) in posterior cingulate/precuneus, frontal, parietal, and temporal cortices (Wilcoxon, 1-sided, p<0.05). Objectives: The present study was undertaken to evaluate voxel-based statistical methods for the assessment of PIB retention and to compare these results to FDG studies of glucose metabolism performed in the same subjects on the same day. Methods: PET studies were performed (ECAT HR+/+ in 10 mild AD subjects (age: 69±8 years; MMSE: 25±3) and 11 control subjects (age: 74±6 years; MMSE: 29±1). Parametric images of PIB retention were generated using the Logan graphical analysis with cerebellar (reference region) data as input. The final measure of PIB retention was the distribution volume ratio (DVR). FDG standardized uptake value (SUV) images were generated by summing the activity from 40-60 min post-injection and then normalizing this to the cerebellar SUV value. Data were compared using statistical parametric mapping (SPM) with the false discovery rate correction (FDR) for multiple comparisons. Results: The voxel-based PIB results were consistent with previous ROI results, as AD subjects showed marked retention in primary cortical areas (relative to controls), with the most significant results in: frontal cortex p=1.19e-10; parietal/temporal cortex p=1.19e-10; and posterior cingulate/precuneus p=1.20e-10. No group differences were evident for white matter or cerebellum. AD subjects showed marginally significant decreases in FDG uptake in the same cortical areas (corrected p-values: parietal/temporal p=0.098; frontal p=0.098; posterior cingulate/precuneus p=0.098). Conclusions: The SPM DVR results were more robust than the FDG results in distinguishing AD and control subjects, as the former reached greater significance and detected differences with a larger spatial extent. These results indicate that voxel-based methods will be useful for future larger longitudinal studies of amyloid-beta deposition that could improve AD diagnosis and anti-amyloid therapy assessment.

DIFFUSION TENSOR MRI CORRELATES WITH EXECUTIVE DYSFUNCTION IN PATIENTS WITH DEMENTIA

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Background: Recently, diffusion-tensor imaging (DTI), which provides noninvasive maps of microscopic structural information of oriented tissue in vivo, is finding utility in studies of cognition in the normal and abnormal aging population. Objective(s): To determine whether DTI measures are correlated with frontal dysfunction in the dementia subjects. Methods: 29 dementia patients, including mild cognitive impairment, Alzheimer and vascular types, underwent DTI and neuropsychological assessments specific for frontal lobe function. Results: For all the subjects with a mild to moderate degree of dementia, the severity of impairment in WAIS-III IQ test is associated with reductions of fractional anisotropy (FA) in splenium area (p<0.05). The mean diffusivity in bilateral periventricular areas and FA in the right subcortical and periventricular areas is associated with the performance of Trail-making test (P < 0.05). Conclusions: These data confirm that white matter changes in frontal lobe are related to impairment of executive function in dementia subjects.

THE DIAGNOSTIC UTILITY OF REGIONAL ATROPHY IN FRONTOTEMPORAL DEGENERATION

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Background: The neuropathology of frontotemporal degeneration (FTD) is centered on changes to frontal and temporal lobes. Neuroimaging findings during life, when present, are focused in frontal and temporal regions but are not required within the core consensus clinical criteria for FTD. Objective(s): We investigated the potential diagnostic utility of atrophy in frontotemporal regions as detected on magnetic resonance imaging (MRI). Methods: We conducted a prospective cohort study on a sample consisting of MRI data from 21 subjects with FTD and 21 age-matched controls to compare frontotemporal volumes delineated with reproducible semi-automatic brain region extraction methods. We used logistic regression to identify those regions most helpful for distinguishing FTD from controls. Linear regression tested the correlation of duration of illness to atrophy severity. Conclusions: Most of the frontal and temporal volumes of interest (VOIs) were significantly smaller in the FTD group than controls (p values ranging from .00001 to .035), but atrophy focused in the left anterior cingulate and medial Brodmann area 10 (medial middle frontal VOI), as well as right anterior temporal parenchyma, can distinguish 90% of the subjects with FTD from controls. The grey matter of the left medial middle frontal and the white matter of the right anterior temporal VOI accounted for the reduced volumes in these VOIs. Further logistic regression revealed that while no VOIs distinguished between the language variant of FTD and controls, the left medial middle frontal, right anterior temporal, and right superior parietal VOIs could be used to separate behavioral FTD and controls with 88% accuracy. Relative absence of atrophy in the right superior parietal area ruled out global atrophy in two subjects who would otherwise have been misclassified as controls. Among the 13 subjects with behavioral FTD, duration of illness was significantly associated with atrophy in the left orbitofrontal VOI. Atrophy on structural MRI due to FTD involves both grey and white matter compartments. Global atrophy is not supportive of the diagnosis of FTD.