

improvement may also support the connection between the motor and sensory language areas.

P2-067 PIB BINDING IN ALZHEIMER'S DISEASE AND NONHUMAN PRIMATE BRAIN

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Background: The amyloid cascade hypothesis implicates the Abeta peptide as an upstream effector in Alzheimer's disease (AD) neurodegeneration. However, the deposition of Abeta in the human brain is not always associated with frank dementia, inasmuch as abundant Abeta lesions are sometimes found in the brains of aged humans without overt cognitive impairment. Furthermore, age-related accumulation of cerebral Abeta is commonly observed in nonhuman primates, yet no nonhuman species has been shown to exhibit the full behavioral or pathological characteristics of AD. Because of their close biological relationship to humans, nonhuman primates are a unique model of nonpathologic Abeta accumulation. We have extensively characterized cerebral Abeta populations in AD, aged chimpanzees, rhesus macaques, and squirrel monkeys. **Methods:** Using immunohistochemistry, ELISA, immunoprecipitation/ MALDI-TOF MS and in vivo Abeta-seeding assays, we found that Abeta populations are quantitatively and qualitatively similar in AD and nonhuman primate brain. To explain the pathological differences between humans and other primates, we hypothesized that higher-order structural features distinguish toxic Abeta in AD brain from the relatively benign Abeta in nonhuman primates. Recent reports show that Pittsburgh Compound B (PIB), a radioligand used for in vivo PET imaging of amyloid, binds with high affinity and stoichiometry to AD brain but with low stoichiometry to synthetic Abeta and to the Abeta deposits in transgenic mouse brain. We measured the binding of 3H-PIB to cortical homogenates from AD and nonhuman primate cases, all of which had been characterized for total soluble and insoluble Abeta levels. **Results:** We found that 3H-PIB binds with low stoichiometry to Abeta in nonhuman primate cortical homogenates, even in cases with levels of Abeta equal to those in AD. **Conclusions:** These data suggest that cerebral beta-amyloid deposits in aged nonhuman primates, which naturally develop cerebral beta-amyloidosis over the course of many years, are structurally distinct from those in humans with AD, and that high-affinity PIB binding may be relatively selective for pathogenic Abeta in the AD brain.

P2-068 AUTOMATIC DIAGNOSTIC CLASSIFICATION OF DEMENTIA WITH FDG-PET USING A SPATIAL DECISION TREE APPROACH

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Background: Alzheimer's disease (AD) and frontotemporal dementia (FTD) cause similar symptoms making accurate clinical diagnosis difficult. These disorders cause distinctive patterns of hypometabolism with positron emission tomography with [18F] fluorodeoxyglucose (FDG-PET). **Objective(s):** To develop an automated method to accurately classify FDG-PET scans in patients with AD and FTD. **Methods:** We used FDG-PET scans from 48 patients with pathologically confirmed AD (n=34) or FTD (n=14) to evaluate a novel automated method for diagnostic classification. Pixels representing peak values derived from stereotactic surface projection analysis, were grouped into empirically determined regions that best separated scans from patients with AD and FTD. These regions then were used as attributes in a decision tree learning algorithm using all 48 cases. Accuracy of this approach was evaluated with leave-one-out cross validation.

Results: Three decision nodes based upon hypometabolism in an arbitrarily shaped region were needed to correctly classify all 48 cases. The root node classified subjects as having AD if there was significant hypometabolism in a region of posterior temporoparietal cortex. The other two nodes of the tree corresponded to frontal and anterior temporal areas, which are hypometabolic in FTD. Leave-one-out cross validation demonstrated the diagnostic accuracy of this method was 94%. This method also had high AD sensitivity/FTD specificity (97%), AD specificity/FTD sensitivity (86%), positive likelihood ratio for AD (94%), and positive likelihood ratio for FTD (92%). **Conclusions:** The dynamic region selection of decision tree based on the information gain is a powerful, unbiased method for classifying brain scans, requiring no prior knowledge or assumptions. This method can locate areas of abnormality for specific dementias, not easily accomplished with other classification methods, such as neural networks and multivariate analysis. This method is feasible for clinical application to increase the accurate diagnosis of AD and FTD. Supported in part by the Center for Alzheimer's Care, Imaging and Research and NIH grants AG22394, AG16976, AG08671, and AG024904.

P2-069 BRAIN PERFUSION SPECT: CHARACTERIZATION AND PROGNOSTIC EVALUATION OF MILD COGNITIVE IMPAIRMENT

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Background: Mild Cognitive Impairment (MCI) is recognized as a clinical entity with a high risk to develop Alzheimer's disease (AD). There is actually a great interest in MCI characterization and the proposal of clinical variables that predict the conversion to AD. Our aim is to characterize MCI and to look for predictors of future development of AD, using regional cerebral blood flow (rCBF) as measured by single photon emission computed tomography (SPECT) and other AD diagnostic variables. **Methods:** Seventy-three subjects (38 MCI and 35 mild AD) matched for age, gender and education, were submitted to a clinical/neuropsychological comprehensive evaluation and Apolipoprotein E genotype was also obtained for both groups of patients. rCBF was measured using Tc-99m hexamethylpropyleneamine oxime (HMPAO) and quantitative analysis normalized to cerebellum were measured in 20 zones and 90 areas (Brodmann areas) using NeuroGam software. Elementary statistical analysis, t-Student test, and VisRed software, were used to analyze rCBF data. **Results:** MCI group presented a significant hypo-perfusion (more than 1.5 SD) comparatively to an internal-software control group, in posterior cingulate cortex (A23 e A24) and left entorhinal cortex (A28). As a group, mild AD subjects had more extensive areas of hypo-perfusion in neocortex comparatively to MCI, with significant differences (p<0,02) in internal temporal areas, Wernicke's area, parietal lobes, pre-frontal and cingulate cortex. However, cluster analysis using VisRed Software demonstrated that MCI and AD patients were incompletely segregated as two separated groups. Considering predictor variables, we observed that ApoE ε4 MCI carriers showed significant hypo-perfusion comparatively to MCI ApoE ε4 non-carriers (p<0,05) in frontal and pre frontal areas (A11, A25, A47). **Conclusions:** As a diagnostic tool, SPECT is not able to classify individual patients between MCI and mild AD. MCI-group and especially ApoE ε4 carriers present hypo-perfusion in cingulate cortex, medial temporal and pre-frontal regions, the typical profile of pre-clinical histological AD.

P2-070 INCREASED RANDOMNESS OF FUNCTIONAL BRAIN NETWORKS IN ALZHEIMER'S DISEASE: 'SMALL-WORLD' NETWORK ANALYSIS OF NON-LINEAR FUNCTIONAL CONNECTIVITY

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