AMYLOID-IMAGING IN DEMENTIAS OF UNCERTAIN ETIOLOGY WITH PITTSBURGH COMPOUND B

David A. Wolk, William E. Klunk, Julie C. Price, Judy A. Saxton, Beth E. Snitz, Oscar L. Lopez, Brian J. Lopresti, Chester A. Mathis, Steven T. DeKosky, University of Pittsburgh, Pittsburgh, PA, USA. Contact e-mail: wolkda2@upmc.edu

Background: The PET ligand 11C-PiB visualizes the amyloid-beta (Ab) plaques and cerebrovascular amyloid of Alzheimer’s Disease (AD). The presence or absence of Ab pathology could help to clarify the diagnosis in cases in which the etiology of the symptoms remains unclear after clinical evaluation. Further, recent studies have reported AD pathology (Ab plaques and neurofibrillary tangles) as the primary etiology in a significant proportion of patients presenting with atypical “focal” dementias (e.g. Primary Progressive Aphasia).

Methods: We performed PiB scans on 23 patients in whom, following extensive neurological and neuropsychological assessments, the etiology remained unknown. In addition to AD, the differential diagnoses included Posterior Cortical Atrophy, Frontotemporal Dementia, and Primary Progressive Aphasia. DUE studies were compared to reference results in 44 Ab plaque-negative controls and 22 typical AD cases. MRI was used for image co-registration, ROI determination, and atrophy correction. PiB retention was assessed using Logan distribution volume ratios (DVR = $V_R/V_{AD}$) that were determined using the cerebellum as reference for each ROI. The 44 Ab plaque-negative controls were identified based on PiB binding with an iterative process of outlier removal from a total of 60 cognitively normal controls. Relative to PiB binding in this control group, objective criteria were applied to categorize DUE and AD cases as Ab plaque-positive, Ab plaque-negative, or Ab plaque-intermediate. Results: Using the same criteria that defined the 44 controls as AB plaque-negative, all AD patients were AB plaque-positive; 6 DUE cases were clearly AB plaque-positive while 14 DUE cases were AB plaque-negative. Three DUE cases fell into the intermediate range. Conclusions: In ~90% of cases, PiB-PET appeared to unequivocally indicate the presence or absence of AB plaque pathology and therefore may be able to rule-in or rule-out AD from the differential diagnosis of DUE. This may be especially helpful in unusual cases, those with an atypical history, or when the differential diagnosis includes AD. Since we found ~25% of DUE cases to be AB plaque-positive, determining the presence of such pathology in these cases has great potential clinical significance with the emergence of AB targeted therapeutics.

COMPARISON OF DIAGNOSTICS VALUES OF CEREBROSPINAL FLUID TAU AND STRUCTURAL MAGNETIC RESONANCE IMAGING IN CLASSIFYING PATIENTS WITH ALZHEIMER’S DISEASE VERSUS NORMAL SUBJECTS

Sharon X. Xie, Christos Davatzikos, Jesse Chittams, Xiaoying Wu, Susan Leight, Virginia M.-Y. Lee, John Q. Trojanowski, Christopher M. Clark, University of Pennsylvania, Philadelphia, PA, USA. Contact e-mail: sxie@mail.med.upenn.edu

Background: Identification of the prodromal phase of Alzheimer’s disease (AD) is challenging because of the difficulty in distinguishing age-related changes from those caused by pathology. There is a need for reliable, inexpensive, minimally invasive biomarkers of AD. The objective of this study is to determine and compare the diagnostic values for cerebrospinal fluid (CSF) tau and structural magnetic resonance imaging (MRI) in classifying patients with Alzheimer’s disease versus normal subjects. Methods: The study cohort includes 27 AD patients and 17 normal subjects over the age of 65. Clinical and CSF tau measurements were obtained via spinal taps, and measurements of regional atrophy were obtained via atlas-based segmentation approaches that parcellated the brain into 28 regions. Logistic regression was used to select the optimum combination of MRI regions to predict AD versus control. Standard diagnostic statistics were computed. Results: The average Mini Mental State exam score was 29 in normal subjects and 19 in AD subjects. The area under the receiver operating characteristic curves (AUC) for CSF tau in classifying AD versus control was 0.80 (95% confidence interval [CI]: 0.66-0.94). MRI-derived volumes for the lateral ventricle, medial temporal lobe, and temporal lobe white matter were significantly associated with predicting AD versus control (p < 0.05). The corresponding AUC for MRI was 0.93 (95% CI: 0.87-1.0). There was no significant difference between the AUCs for CSF tau and MRI (p = 0.09). Conclusions: Both MRI and CSF tau have good diagnostic values in identifying AD versus control. MRI is less invasive and thus can be a potentially useful biomarker to apply in community health care settings.

HEMODYNAMIC CORRELATES OF VASCULAR RISK FACTORS IN ALZHEIMER’S DISEASE

Takashi Yamazaki1, Ken Nagata1, Hirono Utsumi2, Research Institute for Brain and Blood Vessels, Akita, Japan; 2Tokyo Medical University, Tokyo, Japan. Contact e-mail: yamazaki@akita-noken.go.jp

Background: Mounting evidence from a variety of research fields draw attention to the participation of vascular factors in the pathophysiology underlying Alzheimer’s disease (AD). To clarify the influence from the vascular and genetic risk factors, we investigated the relationship between the cerebral blood flow images provided by single photon emission CT (SPECT) and blood pressure, brain natriuretic peptide (BNP), ApoE4 phenotyping and white matter lesions on magnetic resonance imaging (MRI). Methods: The present study was based on 197 patients (66 men and 131 women) who were diagnosed as having a probable AD according to the NINCDS-ADRDA criteria. Their mean age was 76.6 ± 6.7 years old. All patients underwent biochemistry tests, neuropsychological evaluation including Mini-mental state exam (MMSE), MRI and 99mTc ECD SPECT. Results: The mean MMSE score was 13.2 ± 4.3, and the mean BNP was 70.8 ± 82.3 mg/dL. The MMSE scores correlated with the diastolic blood pressure positively (p < 0.05), and with BNP negatively (p < 0.05). Then BNP correlated positively with age positively (p < 0.01). Statistical parametric mapping (SPM) of the SPECT images revealed a significant hypoperfusion in the posterior cingulate gyri, precuneus, and parito-temporal region in those having ApoE4 as compared with those without ApoE4. As compared with those without white matter hypointensity (WMH) on MRI, those with mild WHM showed a significant hypoperfusion in the anterior cingulate gyri, right superior, middle and inferior temporal gyri, and left inferior frontal gyrus, and those with marked WHM showed more expansive hypoperfusion areas on SPM. The subjects were classified into two groups according to the level of BNP: those with greater BNP showed a significant hypoperfusion in the anterior cingulate gyri and superior frontal gyri as compared with those with smaller BNP. Conclusions: The posterior hypoperfusion as related to the presence of ApoE4 may imply a degenerative process of AD, whereas the anterior hypoperfusion as related to the increase of BNP may indicate a possible participation of vascular factors in AD.

ALTERED FUNCTIONAL CONNECTIVITY OF TEMPORAL AND FRONTAL LOBE IN THE ALZHEIMER’S DISEASE PATIENTS WITH PARANOID DELUSIONS

Jong-Chul Youn1, Dong Young Lee2, Il Han Choo2, Ki Woong Kim3, Jin Hyeong Jho2, Jong In Woo2, Kyunggi Provincial Hospital for the Elderly, Yongin, Republic of Korea; 2Seoul National University Hospital, Seoul, Republic of Korea; 3Seoul National University Bundang Hospital, Sungnam, Republic of Korea; 4Kangwon National University Hospital, Chuncheon, Republic of Korea. Contact e-mail: sjyc0811@snu.ac.kr

Background: To date, pathophysiological mechanism of paranoid delusion in Alzheimer’s disease is not well understood. This study aimed to investigate the changes of functional connectivity in the Alzheimer’s dis-