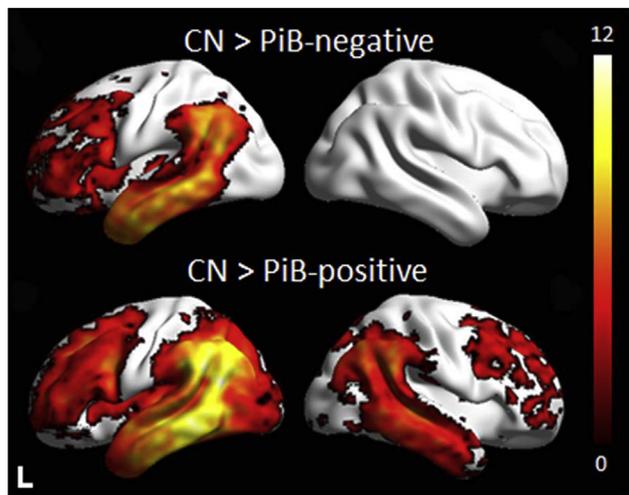


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Background: Patients with Alzheimer's disease (AD) can present with early and prominent deficits in language, characterized by anomia, difficulty repeating sentences and phonological errors. Our aims were to determine what proportion of patients presenting with these signs and symptoms have beta-amyloid (A β) deposition, and whether clinical or neuroimaging features differ between those with and without A β deposition. **Methods:** Fifty patients that presented with at least two of the following three language features (anomia, difficulty repeating sentences and phonological errors), underwent speech/language, neurological, and neuropsychological assessments, MRI, diffusion tensor imaging, 18-F-fluorodeoxyglucose and Pittsburgh Compound B (PiB) PET. A β positivity was determined by a cortical-to-cerebellar ratio >1.5. PiB-negative subjects were screened for mutations in progranulin, tau, C9ORF72 and TARDBP. Patterns of atrophy, hypometabolism, and white matter integrity were assessed. **Results:** Forty-four patients (88%) were PiB-positive. Three of the six PiB-negative patients (50%) harbored progranulin gene mutations. PiB-positive patients performed better on action fluency and worse on spatial perception tasks, and showed greater atrophy and hypometabolism in right temporoparietal and frontal lobes than PiB-negative patients (Figure). Strikingly more asymmetric left-sided patterns, with greater involvement of left anteromedial temporal lobe, medial prefrontal cortex, inferior longitudinal fasciculus, uncinate fasciculus and forceps minor, were observed in the PiB-negative group. **Conclusions:** Alzheimer's disease pathology accounts for a high proportion of patients presenting with anomia, difficulty repeating sentences and phonological errors. Highly asymmetric MRI findings and preserved spatial perceptual skills, suggest that AD pathology is absent. In such instances, a progranulin gene mutation should be suspected.



IC-P-031

A COMPARISON OF THE REGIONAL DISTRIBUTION OF MICROBLEEDS IN ATYPICAL AND TYPICAL PRESENTATIONS OF ALZHEIMER'S DISEASE

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Background: Alzheimer's disease (AD) can often be associated with the presence of small hemosiderin deposits, or microbleeds, in the brain. Sub-

jects with AD typically present with episodic memory deficits, although a large proportion present with other cognitive complaints, including difficulty with language or visuospatial/perceptual function. It is unknown whether the proportion of subjects affected by microbleeds, or the regional distribution of microbleeds, differs between subjects with typical and atypical presentations of AD. **Methods:** A cohort of 45 subjects that had amyloid deposition on Pittsburgh compound B (PiB) PET and presented with predominant language (n=31) or visuospatial/perceptual (n=14) deficits were prospectively recruited and underwent a T2* weighted MRI. These subjects were compared to a cohort of 40 subjects with typical dementia of the Alzheimer's type from the Alzheimer's Disease Neuroimaging Initiative (ADNI). Each microbleed was identified by an expert rater and assigned a lobar location. **Results:** Prevalence of microbleeds was 40% in atypical AD and 32% in typical AD. Within the subjects with microbleeds, the mean (SD) number of microbleeds per subject was 14.2 (35.3) in atypical AD and 3.2 (4.6) in typical AD. The topographic density of microbleeds was highest in the frontal and temporal lobes in atypical AD. In contrast, density in typical AD was highest in the temporal and occipital lobes, with lowest density observed in frontal lobes. Subjects with atypical AD had a higher proportion of deep grey and white matter microbleeds than typical AD (13% vs. 0%, p=0.02), with similar proportions of microbleeds observed in infratentorial regions (7% vs. 5%, p=0.74). The total number of microbleeds was associated with age (p=0.07), but not PiB-PET burden, in atypical AD. Within atypical AD, the prevalence of microbleeds was higher in subjects with language (52%) versus visuospatial/perceptual deficits (14%, p=0.02). **Conclusions:** Microbleeds affect a large proportion of subjects with atypical clinical presentations of AD, particularly those with language deficits. The topographic distribution of microbleeds differs from typical AD, with greater burden in the frontal lobes and deep brain regions suggesting possible differences in underlying etiology.

IC-P-032

COMPARATIVE ANALYSIS OF PIB *IN VIVO* WITH 6-CN-PIB AND A β -IMMUNOHISTOCHEMISTRY POSTMORTEM IN FAMILIAL ALZHEIMER DISEASE ASSOCIATED WITH THE PSEN1 I229F MUTATION

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Background: In AD, a correlation of in vivo [C-11]Pittsburgh Compound B (PiB) retention with postmortem measures of fibrillar A β pathology is essential for interpretation of PET imaging results. **Methods:** Structural magnetic resonance imaging (MRI) and Positron emission tomography (PET) with [C-11]PiB images of a familial AD (FAD) patient were acquired 12 months ante-mortem, using a standardized protocol to assess amyloid pathology in vivo. MRI and PET images were visually compared with those obtained postmortem using histopathology. The entire left cerebral hemisphere, sliced into 22 coronal slabs, and left cerebellar hemisphere, sliced into parasagittal sections, were processed postmortem and embedded in paraffin. Serial sections were stained for histology and A β 1-42 immunohistochemistry (IHC). Sections were also incubated in 10 μ M 6-CN-PiB (a highly fluorescent derivative of PiB). High resolution low magnification images of complete coronal (cerebrum) or sagittal (cerebellum) sections were created and analyzed. **Results:** A 39 year old woman developed memory