

Background: Alzheimer's disease (AD) affects an increasing number of individuals in our societies. It is characterized by accumulation of fibrillary amyloid plaques in the brain. Recently, several studies have emphasized the role of positron emission tomography (PET) using amyloid biomarkers which allow *in vivo* visualization of plaques to distinguish AD pathology from other forms of protein accumulations leading to dementia. However, very few studies have investigated the role of amyloid imaging in the differential diagnosis of atypical/unclear cases, that is complex dementia syndromes where even a comprehensive investigation yields no clear diagnosis. Moreover, no studies have investigated the impact of a correct diagnosis on caregivers and their perception of the process. **Methods:** Using a novel amyloid tracer (NAV4694), we scanned 20 patients with an atypical/unclear dementia syndrome as determined by an experienced behavioral neurologist from a tertiary care center. All patients had a full work-up (i.e., clinical, blood tests, neuropsychological evaluation, structural and functional imaging) yet no certain diagnosis. Amyloid-PETs were either positive or negative based on qualitative and quantitative reads by two independent readers. A questionnaire was given to the treating neurologist to determine whether amyloid imaging allowed a more accurate diagnosis and changed treatment plans. Caregivers were met one month after the revelation of the diagnosis and completed a questionnaire followed by a standardized interview designed to assess its impact. **Results:** A statistically significant increase in confidence levels amongst physicians who ordered amyloid imaging in such cases was found. Revelation of diagnosis to caregivers was associated with better acceptance of the disease as well as a clearer view of future challenges. **Conclusions:** This study suggests that amyloid imaging is useful in the differential diagnosis of atypical/unclear dementias, and has a positive impact on caregivers. Amyloid-PET is indicated in the investigation of complex, atypical/unclear dementing disorders.

IC-P-008 ANXIETY IS ASSOCIATED WITH BRAIN AMYLOIDOSIS IN COGNITIVELY NORMAL AND MILD COGNITIVE IMPAIRMENT SUBJECTS: A [¹⁸F]FLUTEMETAMOL PET STUDY

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Background: Neuropsychiatric behaviors are prominent features of Alzheimer's disease (AD) and mild cognitive impairment (MCI). Their association with brain amyloidosis is poorly understood. **Methods:** 65 subjects (27 NC and 38 MCI) who provided yearly neuropsychiatric inventory (NPI) data received [¹⁸F]Flutemetamol PET scan 4.6 (±1.0) year into the study. In our analyses neuropsychiatric symptoms were coded as present if present at one or more visits and absent if never reported by the caregiver. Mean standard uptake volume ratios (SUVR) using the whole cerebellum as the reference were calculated. Brain amyloidosis was defined as mean SUVR ≥ 1.27. We used Chi-square statistics to compare neuropsychiatric symptom prevalence between the amyloid positive and amyloid negative groups. Next we examined the association between amyloid status and neuropsychiatric symptoms using logistic regression with fixed effects for baseline diagnosis, amyloid status, their interaction and cognitive decline (defined as

transition from NC to MCI or dementia and transition to MCI or dementia in follow up). **Results:** There were no significant differences in baseline diagnosis, age, sex, education, follow-up duration or time to PET scan between the amyloid positive and amyloid negative groups. Amyloid positive individuals had significantly higher rates of pre-existing anxiety (46 vs. 10%, p=0.0009) and apathy (42 vs. 20%, p=0.05) relative to amyloid negative subjects. Presence of anxiety remained significantly associated with brain amyloidosis after adjusting for baseline diagnosis and longitudinal decline ($\beta=2.5$, p=0.05). NC who tested amyloid positive in follow-up were 12 times more likely to develop anxiety compared to amyloid negative NC. MCI who tested amyloid positive in follow-up were 4 times more likely to develop anxiety compared to amyloid negative MCI. **Conclusions:** We found a strong association between amyloid pathology and pre-existing anxiety in both our cognitively normal and MCI subjects. Our analyses suggest that NC subjects develop anxiety at a minimum at the time of but potentially even prior to reaching the threshold for amyloid positivity and suggest that anxiety might be one of the first clinical correlates of brain amyloidosis.

IC-P-009 LONGITUDINAL FOLLOW UP OF MCI PATIENTS WITH NEGATIVE PIB

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Background: The likelihood of progression from MCI to any form of dementia has been suggested to occur at a rate 3 to 5 times higher than those with normal cognition with an annual rate of progression of 12-20%. MCI patients with negative AD biomarkers are supposed to have a lower risk of dementia related to AD. However they still could suffer from other non-AD etiologies and convert to dementia. The aim is to assess the risk of progression to dementia of Mild Cognitive Impairment (MCI) patients with negative PET PIB for Alzheimer's Disease (AD). **Methods:** Thirty-two patients diagnosed with MCI and with negative PET PIB were selected. These patients underwent a complete Neuropsychological battery; brain MRI, PET FDG. Patients were classified into amnesic MCI, multiple domains MCI or non-amnesic MCI. They have been followed up with new neuropsychological testing after AD biomarkers were performed. We considered worsening of MCI status when patients presented worsening of global CDR (conversion to dementia), declination on neuropsychological testing or need to increase anti-dementia medication. **Results:** Fourteen patients were diagnosed with amnesic MCI, 6 with multiple domains MCI and 12 with non-amnesic MCI. All of them had negative PIB scan and were followed up for 1.6 years. The average age was 68 years old and the average educational level was 16 years. Eight of the 32 patients have worsened their clinical status and seven of them (21.8%) have converted to dementia (CDR 1). Only one of the patients that has converted to dementia was diagnosed with Dementia of Alzheimer type, this one had also PET FDG typical of AD. The rest who have converted to dementia were diagnosed with non-AD dementia (2 Frontotemporal Dementia, 2 vascular dementia, 1 suspected of encephalitis and 1 with psychiatric symptoms). **Conclusions:** We found in our MCI with negative PIB cohort the same conversion rate to dementia previously documented in MCI patients alone (12-20%). However, those patients who converted to dementia seemed to be due to non-AD dementia. Therefore,