participants (0.13; SD .20; Wilcoxon rank sum test p = 0.02). Participants exposed to antidepressants also had significantly lower rates of having a positive amyloid scan (5/52 vs 33/134;$?^2$ =5.19, p = 0.02). The cumulative duration of antidepressant use within the 5-year period preceding the PET Aß scan negatively correlated with MCBP (rho = -.16, p = 0.03), indicating that the greater the time exposed to antidepressants, the lower the Aß plaque deposition. **Conclusions:** A strength of the study's design is that participants with a history of antidepressant use did not differ in age, gender, MMSE and APOE4 status from participants with no antidepressant exposure. While this data is limited by being a sample of convenience, given the established safety profile of SSRIs and the accumulating evidence that serotonin signaling may regulate Aß production. It may be reasonable to explore this drug class as a therapeutic strategy to inhibit Aß production and block plaque formation.

O1-07-04 BLOOD-BRAIN BARRIER P-GLYCOPROTEIN FUNCTION IN ALZHEIMER'S DISEASE

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Background: Accumulation of amyloid-beta (Aß) in Alzheimer's disease (AD) may result from an imbalance between Aß production and Aß clearance. P-glycoprotein (Pgp) is an efflux pump at the blood-brain barrier (BBB) that is involved in Aß clearance. Pgp function can be quantified in vivo using (R)-[11C]verapamil and positron emission tomography (PET). The aim of this study was to assess BBB Pgp function in AD patients compared with age matched healthy controls (HC) using (R)-[11C] verapamil and PET. **Methods:** Successful dynamic (R)-[11C]verapamil PET scans with arterial blood sampling were performed in 10 AD patients and 12 HC. Using an automated template, regions of interest (ROIs) were placed on a co-registered MRI scan and transferred to the PET images. Data were analyzed using spectral analysis (SA), and a standard 2-tissue compartment model. Binding potential (BPND) of cerebellar, medial temporal, frontal (volume-weighted average of orbital frontal, medial inferior frontal, and superior frontal), parietal, temporal (volume-weighted average of superior temporal and medial inferior temporal) and occipital cortices and posterior and anterior cingulate were used. In addition, a global cortical region was defined consisting of the volume-weighted average of frontal, parietal, temporal, cingulate and occipital cortices. **Results:** Spectral analysis clearly showed the presence of two components in both AD patients and HC. In AD patients (age 66 ± 7 (mean ± SD), Mini-Mental State Examination (MMSE) 24 ± 3) global (R)-[11C] verapamil BPND values were significantly increased compared with HC (age 62 ± 4, MMSE 30 ± 1). (AD: BPND = 2.04 ± 0.16, HC: BPND = 1.55 ± 0.53, p = 0.012). For frontal, parietal, temporal, occipital and cingulate posterior ROIs, significant differences in BPND were found between AD and HC. There were no differences between the two groups for cingulate anterior, medial temporal lobe and cerebellum. **Conclusions:** These data show altered kinetics of (R)-[11C]verapamil in AD, indicating decreased Pgp function in AD patients. This is the first direct evidence that BBB dysfunction occurs in sporadic AD and suggests that decreased Pgp function may be involved in the pathogenesis of AD.

O1-07-05 INVESTIGATING ASTROCYTOSIS WITH 11C-DEUTERIUM-L-DEPRENYL IN MILD COGNITIVE IMPAIRMENT AND MILD ALZHEIMER'S DISEASE: A MULTI TRACER PET PARADIGM COMBINING 11C-PIB AND 18F-FDG

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Background: High amounts of astrocytes have been demonstrated to co-localise with fibrillar amyloid-beta (Aß) plaques in post-mortem Alzheimer's disease (AD) brain tissue. It is therefore crucial to investigate astrocytes in-vivo. A multi-tracer PET investigation was conducted in a group of patients with mild cognitive impairment (MCI), mild AD and healthy controls using ^{11}C-L-deuterium-deprenyl (DED) to measure astrocytosis. Along with DED-PET, ^{11}C-Pittsburgh compound-B (PIB), ^{18}F-FDG, T1 MRI, cerebrospinalfluid and neuropsychological data was acquired from the patients. **Methods:** DED-PET was performed in MCI (n = 8; age = 62.6 ± 7.5; MMSE = 27.5 ± 2.1), AD patients (n = 7; age = 65.1 ± 6.3; MMSE = 24.4 ± 5.7) and in healthy age matched controls (n = 14; age = 64.7 ± 3.6), A modified reference-Patlak model, with cerebellar grey matter as reference, was chosen for kinetic analysis of the DED data. Individual DED data from 20-60 min was analysed using a digital brain atlas. Mean regional FDG uptake and PIB retention were calculated for each patient with cerebellar grey matter as reference. **Results:** ANOVA analysis of the regional DED binding data revealed a significant group effect in the bilateral frontal and bilateral parietal cortices. All patients, except three MCI, showed high PIB retention (PIB+). Increased DED binding in most cortical and sub-cortical regions was observed in PIB+MCI patients relative to controls, PIB-MCI and AD patients respectively. Limited significant regional correlations were found between the three PET tracers particularly between DED and PIB. **Conclusions:** Increased DED binding throughout the brain of the PIB+MCI patients, who were also cognitively impaired, had low Aß42 and high tau in CSF relative to the PIB- patients, might suggest that astrocytosis is an early phenomenon in AD development.

O1-07-06 MILD DEMENTIA EVALUATED WITH [11C]DTBZ AND [11C]PIB POSITRON EMISSION TOMOGRAPHY

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Background: Neurodegenerative dementia develops commonly over age 65, and exponential increases in prevalence occur with further aging. Three clinicopathologic entities constitute the majority of neurodegenerative dementias: Alzheimer disease (AD); Frontotemporal dementias (FTD); and Dementia with Lewy Bodies (DLB). Clinical differentiation at an early stage is difficult. Molecular neurochemical imaging with positron emission tomography (PET) may be useful in differentiating dementia syndromes. We compared clinical with neurochemical imaging to predict diagnosis. **Methods:** 75 subjects with mild dementia were studied after IRB approval and informed consent were obtained. Subjects had MMSE scores =18 and cognitive symptoms for over 9 months, and were capable of completing neuropsychological testing and research neuroimaging. Clinical evaluations included history and neurologic examination, brain magnetic resonance imaging, laboratory evaluation, and a standardized neuropsychological evaluation. A panel of experienced clinicians blinded to the PET Neuroimaging reviewed the clinical data and classified each subject. Subjects underwent [^{11}C]PiB and [^{11}C]DTBZ PET imaging on the same half day, with at least 2 hours between scans to allow for radioactive decay of the first tracer prior to the second scan. **Results:** The mean age was 72 yr (range 54-90) and 40% of the subjects were female. 36 of the 75 subjects were classified clinically as AD, 14 as DLB, and 25 as FTD. With PET neurochemical imaging, 47 subjects were characterized as AD, 15 as DLB, and 13 as FTD. The overall kappa statistic for agreement between classifications was 0.39 (95% confidence interval: 0.27-0.58). With the molecular neuroimaging classification as the gold standard, clinical classifications of AD and FTD exhibited moderate specificities and sensitivities and clinical classification of DLB exhibited moderate sensitivity and good specificity. The most frequent discordance between the clinical and molecular imaging classifications occurred in subjects classified clinically as FTD. **Conclusions:** We found substantial differences between clinical and neurochemical imaging classifications of disease. Among the 3 diagnostic categories, we found the highest degree of concordance between neurochemical imaging and clinical classifications of DLB, and lower concordance between clinical

and neurochemical imaging classifications of AD and FTD. We will refine these results further by serial observation of these patients over time.

O1-07-07 PET AND TISSUE AUTORADIOGRAPHY EVIDENCE OF DECLINE OF METABOTROPIC GLUTAMATE RECEPTOR TYPE 5 (MGLUR5) IN THE PREFRONTAL CORTEX OF ALZHEIMER'S DISEASE

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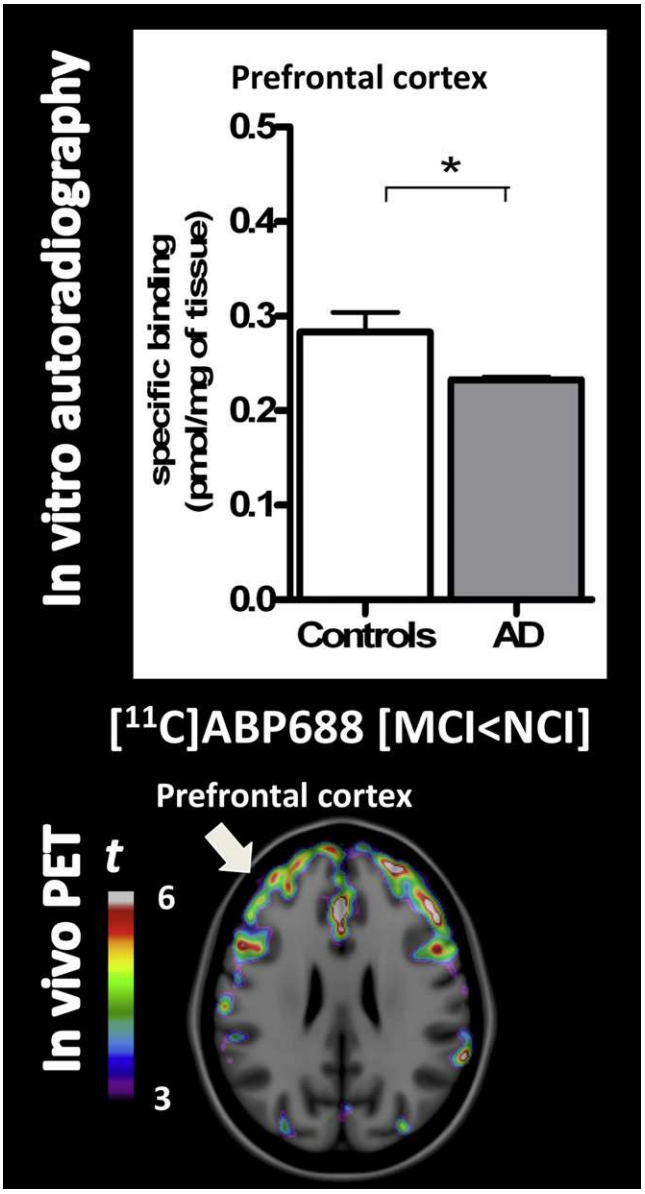
Background: Quantification of molecular processes directly affected by the presence of Alzheimer's disease (AD) pathology has potential applications for monitoring disease progression. Recent preclinical work has demonstrated that oligomeric forms of beta amyloid peptide directly impose deleterious effects on glutamatergic neurotransmission, particularly on the metabotropic glutamate receptor type 5 (mGluR5). However, it is not known whether mGluR5 concentrations are altered in patients with AD. Here we quantify mGluR5 binding in the prefrontal specimens of AD patients using autoradiography and in living individuals with mild cognitive impairment (aMCI) using Positron Emission Tomography (PET). Since the majority of aMCI harbors AD pathology, we hypothesized declines in mGLUR5 concentrations in aMCI and AD prefrontal cortex. **Methods:** We conducted two cross-sectional studies comparing mGLUR5 availability in (1) post-mortem brain tissue of AD patients using [3H]ABP688 autoradiography and (2) in living aMCI individuals using [11C]ABP688 PET. Brain specimens (Douglas Brain Bank, Canada) were cryosectioned (20 Âµm), incubated with 2 nM [3H]ABP688, washed, dried and exposed for five days to phosphor-imaging plates. Non-specific binding was determined with MPEP. In vivo studies were conducted using the brain-dedicated PET camera (Siemens; HRRT). All participants had a structural MRI and a 60 min [11C]ABP688 dynamic PET scan. The PET outcome measure was the binding potential calculated using the simplified reference tissue method and the cerebellum as reference region. Between-groups comparison were computed at the voxel level using RMINC. **Results:** AD (N = 5, age 72 ± 4.39) and controls specimens (N = 5, age 69.67 ± 5.61) did not differ in age, AD severity and post-mortem delay. Single concentration binding using [3H]ABP688 revealed lower binding in the patient group (Ctrl, 1.31 ± 0.06; AD 0.711 ± 0.03 pmol/mg tissue; $p < 0.001$; figure). aMCI (N = 9; age = 73 ± 8.6 y.o) and individuals with no cognitive impairment (NCI, N = 8; age = 67.5 ± 7.5 y) did not differ in age, gender. figure (bottom) shows average scans of NCI. Voxel-based analysis (figure, bottom) revealed that declines in mGLUR5 occur in the prefrontal cortices (right, t = 6.78; left, t = 6.14). No significant increases of [11C]ABP688 binding were observed in AD patients. **Conclusions:** We conclude that mGluR5 declines constitute an early neurodegenerative event possibly reflecting brain vulnerability to AD pathology.



O1-07-08 RESTING BRAIN METABOLIC CONNECTIVITY IN PRODROMAL ALZHEIMER'S DISEASE: EVIDENCE FOR EARLY FUNCTIONAL DISCONNECTION–AN EADC JOINT PROJECT.

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Background: Voxel-wise interregional correlation analysis of statistical parametric mapping (SPM) of [18F]FDG-PET has been proposed to study functional connectivity of brain networks. We were aimed at exploring resting-state metabolic connectivity in patients with prodromal AD (pAD) who later converted to AD dementia and in healthy controls. **Methods:** Thirty-six pAD patients converted to AD during the follow-up (18 males; mean age:72.1 ± 8.4 years; mean MMSEscore:27.5 ± 1.4; mean follow-up: 24.6 ± 18.5 months) and 36 healthy controls (CTR, 19 males; mean age:70.7 ± 6.5; mean MMSEscore:29.7 ± 0.8; mean follow-up 9.3 ± 3.8 months) underwent 18F-FDG PET at baseline. The two groups were compared with SPM8 ($p < 0.05$FDR-corrected at peak and cluster level; age and center as nuisance variables). The cluster