cortices, and to a lesser degree in the left superior parietal- and frontal cortices. Conclusion: Our findings suggest that a six-months stage-specific cognitive intervention program imparted cognitive benefits, which could be linked for the first time to a delayed decline of cortical glucose metabolism in brain regions typically affected by AD. Moreover, our results underscore the potential of FDG-PET to detect progression of AD-related cerebral changes over short time intervals such as 6 months. Based on these results, we are initiating an investigation in a larger population and over a longer observation period.

OP049

MCI patients declining and not declining at mid-term follow-up: FDG-PET findings

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Patients with Mild Cognitive Impairment (MCI) not converted to dementia at one to three years follow-up represent a heterogeneous group across studies, by including 'late converters' but also patients without any neurodegenerative disease. We tested the hypothesis that the combination of memory and brain metabolic assessment could identify subgroups of memory decliners (MCI/Decl) and non-decliners (MCI/noDecl) before a long follow-up time is available. From twenty-seven patients with amnestic MCI (aMCI) at baseline, three groups were identified at follow-up: 10 patients who converted to AD (MCI/AD); 10 patients showing episodic memory worsening (MCI/Decl) and 7 patients showing no memory worsening or even improvement (MCI/noDecl). They were compared at base-line with a group of fourteen elderly controls (CTR) by FDG-PET performed by means of voxel-based analysis (SPM2), accepting an uncorrected $p<0.001$ height threshold at voxel level and a corrected $p<0.05$ threshold at cluster level. Two hypometabolic clusters were found in MCI/AD versus CTR, including the bilateral posterior cingulate cortex and the parietal precuneus, fusiform and inferior temporal gyri in the left hemisphere. The MCI/Decl showed a hypometabolic region in the left medial temporal lobe versus both CTR (hippocampus) and MCI/noDecl (fusiform gyrus). No significant difference was found in the comparison between CTR and MCI/noDecl, neither in the comparison between MCI/Decl and MCI/AD. Thus, non converter MCI patients comprised a sub-group of 'decliners' with AD-like metabolic and cognitive patterns, likely including 'late converters', and a sub-group lacking this pattern, with stable or improving memory function and a brain metabolic picture similar to that in healthy controls. Combining neuropsychological and FDG-PET information could be used for prognostic purposes in aMCI patients at medium-term follow-up.

OP050

Kinetics of FDG brain uptake in Mild Cognitive Impairment population in PET imaging

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Aim: Cerebrospinal fluid (CSF), produced by the choroid plexus (CP), plays a fundamental role in brain pathophysiology. Recent research has underlined the CSF's involvement in neurodegenerative processes. We present a new imaging processing to study CSF and CP with [18F]fluorodeoxy-D-glucose (^{18}F-FDG) positron emission tomography (PET) and evaluate them in Mild Cognitive Impairment (MCI) population. **Materials & Methods:** The control population is constituted of 10 subjects (age range 67-79 y) with a malignant pathology not affecting the brain and without any neurological pathology. A second population is constituted of 8 subjects (age range 71-85 y) identified as MCI. A 45 minutes dynamic PET acquisition on Biograph 6^{TM} PET/CT (Siemens Medical Solutions) was scheduled in 34 time frames with FORE+AW-OSEM reconstruction (256 x 256 matrices with a zoom of 2 (i.e. voxel volume: 1.33 x 1.33 x 2 mm^3), 6 iterations and 16 ordered subsets, 3D Gaussian post-filtering (FWHM = 2 mm), scatter and attenuation corrections).^{18}F-FDG was injected on the scanner bed after starting PET aquisition. For every voxel, the analysis consisted in calculating 3 parameters (R,G and B) of a fitting function, using the Levenberg-Marquardt algorithm, for the 34 time frames (t). This function is, where *i* correspond to the voxel *i*. Finally, the ^{18}F-FDG dynamic uptake of each voxel was displayed as a RGB-map colour. Regions of interest (ROI) were drawn on the RGB-map and applied to the initial volume to generate mean raw uptake curves of the ^{18}F-FDG in these regions. **Results:** For all patients, two different kinds of structure inside the ventricles were found in RGB-maps, corresponding respectively to the CP and CSF. These structures could not be distinguished on the conventional CT and static PET images. The ^{18}F-FDG kinetics in the CP differs significantly from those seen in the CSF ($p < 0.002$ with Wilcoxon test between CSF and CP for means and standard deviations, for the R, G and B fitting parameters). Moreover, CSF and CP ^{18}F-FDG fixations were significantly decreased in MCI population in comparison with control population. **Conclusion:** The results show that it is possible to monitor the kinetics of ^{18}F-FDG uptake by the CP and the CSF during a PET acquisition. This work is an initial step towards using PET to evaluate CSF production alteration in MCI population.

OP051

SPECT and PET changes in those receiving Alzheimer's disease (AD) Tau therapy rember™ (Methythioninium chloride)

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Neurofibrillary tangles are a hallmark pathology of AD and consists of aggregated tau protein in an insoluble form. rember™ (Methythioninium chloride) is known to dissolve these tangles in vitro and in mouse models. This study recruited a sub-sample of a larger clinical trial testing the effects of rember™. Of the 322 patient randomized in the main study 154 patients were imaged twice using rCBF HMPAO-SPECT (N=133) or FDG PET (N=21) imaging at 11 sites. Patients were imaged prior to the start of therapy and ar approximately 24 weeks. The patients were split into 4 dose groups (30, 60, 100 mg and placebo). AD diagnosis was confirmed using DSM-IV criteria and NINCDS-ADRDA criteria for probable AD. Both ROI and SPM image analyses were performed. Using HMPAO SPECT both forms of analysis showed that those receiving placebo had significant reduction in rCBF. Those receiving rember™ showed no significant reduction in rCBF. Comparing the groups indicated that rember™ significantly reduced the rate of rCBF loss particularly in the temporal and parietal regions. The PET images showed a significant increase in FDG uptake in the medial temporal lobes in the treated group when compared to the placebo group. In conclusion, rember™ affects the trajectory of rCBF and FDG decline in AD patients and SPECT and PET provides complimentary evidence that rember™ is an effective therapy in AD.

OP052

Brain perfusion SPECT correlates with CSF biomarkers in Alzheimer's disease

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Objectives. Cerebrospinal fluid (CSF) biological markers of Alzheimer's disease (AD), such as β-amyloid 42 (Aβ42), total and phosphorylated tau-protein (t-tau and p-tau) have been shown to be useful instruments for the diagnosis of AD and for the prognosis of MCI conversion to dementia. One of the major shortcomings in their evaluation is the lack of data on correlations with neuroimaging markers of the disease. Our aim was to study the correlations between CSF biomarkers levels and brain perfusion SPECT in AD, with a voxel-based methodology. Patients and Methods. 31 patients with clinical features of AD (n = 25) according to NINCDS-ADRDA criteria, or amnestic mild cognitive impairment (aMCI) (n=6) according to Petersen's criteria (1999) were retrospectively included. All subjects underwent the same clinical, neuropsychological and neuroimaging tests. They had a lumbar punction for CSF biomarkers measurements and a brain perfusion SPECT scan (99mTc-ECD) within a time interval of 10 (±26) days. After spatial normalization to the SPECT template provided with SPM2 software, reconstructed volumes were smoothed using a Gaussian kernel (FWHM=12 mm). Correlations between CSF biomarkers concentrations (i.e. Aβ42, t-tau and p-tau) and perfusion were studied, with gender and age as nuisible variables. Individual adjusted normalized regional activities values were extracted from the eligible clusters for calculation of correlation coefficients. Results. No significant correlation was found between Aβ42 concentrations and brain perfusion. A significant correlation ($p<0.01$, corrected for multiple comparisons) was found between perfusion and t-tau concentrations in left parietal (angular and inferior parietal) and mid-cingulum ($r=-0.645$), and p-tau concentrations in left mid-cingulum and precuneus ($r=-O.690$). Conclusion. Our results suggest a strong correlation between t-tau and p-tau levels and perfusion decrease in regions typically affected by neuropathological changes in AD.

OP053

Agreement assessment between brain-SPECT, CSF biomarkers and neurological evaluation in MCI patients

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Background Mild Cognitive Impairment (MCI) could be a very early stage of Alzheimer's disease (AD). Evaluation of cerebral perfusion by [^{99m}Tc]-HMPAO-SPECT, cerebrospinal fluid (CSF) biomarkers and neuropsychological workup (NW) may enable early identification of AD-converter patients. Our study aimed at assessing the agreement between SPECT, CSF and NW to early detect AD-converters among MCI patients. Patients and methods We included 29 consecutive MCI patients in a longitudinal study. At baseline, all underwent [^{99m}Tc]-HMPAO-SPECT and NW, and 24 also had a titration of the T-tau, P-tau and Aβ1-42 proteins in the CSF. A dichotomy criterion of at risk or not at risk for AD was used to differentiate patients according to SPECT, CSF and NW evaluation. Two senior physicians read SPECT images and classified patients into 2 groups: at risk for AD if parieto-temporo-occipital hypoperfusion was present in at least one hemisphere; not at risk for AD in all other cases. CSF profile was considered at risk for AD if i) increase of T-tau, increase of P-tau, decrease of Aβ1-42 or ii) P-tau > 60 pg/ml and the IATI index < 0.8. In the NW, patients with neuropsychological cut-off scores of free recall score > 17 or total recall score > 40 at the Free and Cued Selective Recall Reminding Test were considered at risk for AD. Results Mean age and median MMSE of the 29 patients (19 men, 10 women) were respectively 69.2 ± 7.7yrs and 27±3. Inter-reader agreement for SPECT evaluation was 27/29; the 2 discordant cases were read again and total agreement was reached. SPECT analyses were at risk for AD in 24/29 MCI patients, CSF analyses in 9/24 , and NW evaluation in 8/29 . Agreement between SPECT and CSF was 13/24 (at risk for AD n=9; not at risk n=4). Agreement between SPECT and NW was 9/29 (at risk for AD n=6; not at risk n=3). Agreement between NW and CSF was 17/24 (at risk for AD n=5; not at risk n=12). Conclusion In this MCI cohort, agreements between SPECT, CSF and NW are pretty variable. Of the three methodologies, SPECT detected the most abnormalities in MCI patients. To better define the role of each evaluation method in the early detection of AD-converter patients, patient-follow up is currently undergoing.

OP054

BAY 94-9172 - A promising ^{18}F-labeled β-amyloid plaque PET tracer for *in vivo* diagnosis of Alzheimer's disease

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