

Potential (BP). In addition, SPM analysis of Ichise BP images was performed. **Results:** Increased [11C](R)-PK11195 binding in AD was found in medial inferior frontal lobe, medial inferior temporal lobe, entorhinal cortex, posterior cingulate cortex and occipital lobe. In MCI the medial temporal lobe and, more specifically, the entorhinal cortex showed increased binding. However, BP did not allow for differentiation between converters or non-converters. SPM analysis showed increased binding in lateral temporal and occipital lobes in both MCI and AD. **Discussion:** The distribution of increased [11C](R)-PK11195 binding in MCI and AD agrees with areas known to be affected pathologically in AD and supports the theory that inflammation might be an early phenomenon in the etiology of AD. Although this ligand might lack sensitivity for diagnostic purposes in individual patients, it could be useful for addressing changes in [11C](R)-PK11195 binding (e.g., due to therapy) at a group level.

O1-03-02 **IN VIVO TARGETING OF ANTIBODY FRAGMENTS TO THE NERVOUS SYSTEM FOR ALZHEIMER'S DISEASE IMMUNOTHERAPY AND MOLECULAR IMAGING OF AMYLOID PLAQUES**

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The ability to target therapeutic or diagnostic proteins to the nervous system is limited by the presence of the blood-brain/nerve barriers. We report that a monoclonal anti-fibrillar human A β 42 immunoglobulin (IgG4.1) or its F(ab')₂ fragment (F(ab')₂4.1) that are polyamine modified have increased permeability at the blood-brain barrier. Both the native and modified F(ab')₂4.1 also showed increased binding to the antigen compared to the whole IgG as determined by ELISA. The F(ab')₂4.1 and polyamine modified F(ab')₂4.1 showed comparable *in vitro* binding to amyloid plaques in Alzheimer's disease (AD) transgenic mouse brain sections. Furthermore, intravenous injection in the AD transgenic mouse demonstrated efficient targeting to amyloid plaques throughout the brain. High-resolution emulsion autoradiography also demonstrated targeting of the radioiodinated polyamine-modified F(ab')₂4.1 to cerebrovascular amyloid deposits. Polyamine modification of this antibody derivative may have increased therapeutic potential for treating AD since exclusion of the Fc portion of the antibody should minimize the inflammatory response and cerebral hemorrhaging associated with passive immunization. Coupling contrast agents or appropriate radioisotopes to the polyamine-modified F(ab')₂4.1 might facilitate the molecular imaging of amyloid plaques using MRI or micro PET. While this approach has direct applications to AD, the efficient delivery of IgG fragments to the nervous system may have important applications to other neurodegenerative disorders or for the generalized targeting of nervous system antigens.

O1-03-03 **FROM MILD COGNITIVE IMPAIRMENT TO ALZHEIMER'S DISEASE: PRELIMINARY RESULTS OF A ¹H-MRS LONGITUDINAL STUDY**

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Background: Mild Cognitive Impairment (MCI) is a possible prodromal state of Alzheimer's disease (AD). Therefore it is necessary to analyze the metabolic evolution of MCI, especially of the subjects that subsequently develop Alzheimer's disease, in order to better understand the pathogenesis of this type of dementia. **Objective(s):** The aim of our study is to compare the changing, in twelve months, of the brain metabolite levels in two different subgroups of MCI subjects: one of those remained stable (sMCI) and one of those evolved into AD (pMCI). **Methods:** 18 MCI (14 sMCI and 4 pMCI) subjects were enrolled; they underwent a comprehensive clinical and instrumental assess-

ment, a cerebral ¹H MRS scan to measure N-acetyl aspartate (NAA), choline (Cho), myo-inositol (mI) and creatine (Cr) in the paratrigonal white matter, bilaterally. After 1 year all the subjects were again assessed in the same way. Then we compared the metabolites measured at the enrollment and after twelve months in the two different subgroups. **Results:** We found that in pMCI subjects the NAA level of the left hemisphere was significantly different after one year (T₀ 1.572; T₁₂ 1.625; p 0.046). No significant differences were measured in the other metabolites in pMCI and in sMCI. **Conclusions:** The fact that NAA is significantly different after 12 months and that this is associated with the clinical onset of dementia can be related to a metabolic impairment of the pMCI that can be the leading cause of AD.

O1-03-04 **RELEVANCE OF TEMPORO-PARIETAL ATROPHY IN MCI CONVERSION TO ALZHEIMER'S DISEASE: A VOXEL-BASED MORPHOMETRY STUDY**

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Background: Patients with mild cognitive impairment (MCI) have an increased chance of converting to Alzheimer's disease (AD). It is known that patients with AD have more medial temporal lobe atrophy (MTA) and temporo-parietal atrophy compared to patients with MCI and that patients with MCI have more MTA compared to healthy elderly controls. **Objective(s):** We used voxel-based morphometry (VBM) to find out whether there are structural differences in baseline MRI of the brain between amnesic MCI converters and non-converters, with conversion defined at three years follow-up. **Methods:** Twenty-four amnesic MCI patients (diagnosed according to the Petersen criteria) were included. After three years 46% had converted to AD, n=11, age 72.7+/-4.8 sex F/M 8/3. For 13 patients age 72.4+/-8.6 sex F/M 10/3 the diagnosis remained MCI. Baseline MRI was performed on a 1.5T scanner and included a coronal 3DT1 [160 slices, TR 2700, TE 4, TI 950, ST 1.5]. Localized grey matter differences were sought for with VBM. Total grey matter volume was assessed with the automated method SIENAX. **Results:** The converters had more atrophic left medial (including the hippocampus) and lateral temporal lobe structures, left parietal lobe structures and right lateral temporal lobe structures. After correction for age, gender, total grey matter volume (SIENAX) and NYU paragraph recall test, only the left-sided atrophy remained statistically significant. Specifically, converters had more parietal atrophy (angular gyrus and inferior parietal lobule) and lateral temporal lobe atrophy (superior and middle temporal gyrus). Hippocampal atrophy was not significantly different between groups after correction for the above variables. **Conclusions:** In this VBM study of a patient population followed up for three years and with a conversion rate of 46%, converters exhibited more atrophy than non-converters in the lateral temporal lobe and parietal lobe, rather than in the medial temporal lobe region (which probably has become quite atrophic in an earlier disease phase).

O1-03-05 **IMPROVED CLASSIFICATION OF MCI AND ALZHEIMER'S DISEASE USING DIFFUSION TENSOR IMAGING OF CINGULUM WHITE MATTER**

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Background: Hippocampal volumes do not completely separate MCI and AD from normal aging. The goal was to determine if DTI improved identification of MCI and AD from normal aging. **Objectives:** We hypothesized: 1) MCI and AD are associated with reduced fractional anisotropy (FA) in the cingulum fibers; 2) DTI improves classification of AD and MCI from healthy aging when used with hippocampal volume. **Methods:** 17 AD patients (age: 77.1 ± 8.8 yrs; MMSE: 22.1 ± 4.0), 17 MCI (age: 73.1 ± 7.4 yrs; MMSE: 27.9 ± 2.0), and 16 cognitive normal (CN) subjects (age: 69.9 ± 8.3 yrs; MMSE: 29.8 ± 0.4) had MRI and DTI. Hippocampal volumes (HV) were measured using semi-automated software. DTI data were processed by tracing cingulum fibers connecting the hippocampus and posterior cingulate cortex and computing fractional anisotropy (FA). Diagnostic values of HV and FA were compared by logistic regression and a receiver operator characteristics analysis (ROC), including cross-validation of the area under the ROC curve (AUC). **Results:** HV was markedly reduced in AD ($p < 0.05$) compared to CN. In contrast to HV, FA of the cingulum fibers was reduced ($p < 0.01$) in MCI and even more in AD ($p < 0.001$). Furthermore, the reductions were more prominent on the left side than on the right side ($p = 0.08$) in MCI. HV alone could not reliably separate MCI from CN subjects ($p = 0.07$), but the addition of FA in the posterior cingulate improved classification ($p = 0.007$). HV reliably separated AD patients from CN subjects ($p = 0.01$), as expected; the addition of FA improved the classification further ($p = 0.007$). See table for summary; AUC is listed including 95% confidence intervals. **Conclusion:** Measuring FA of the cingulum fibers improves identification of MCI and may be a sensitive indicator of early AD pathology. Prospective studies are underway to determine if DTI predicts cognitive decline and conversion to AD.

Table
Group Classifications Using Hippocampal Volume and Fractional Anisotropy of Posterior Cingulated

Factors in the Logistic Regression	Group Classifications and AUC				P - value
	Sens. (%)	Spec. (%)	Acc. (%)	AUC	
MCI vs. CN					
Total HV	65	62	63	0.71 (0.58 - 0.85)	$p = 0.07$
+ FA	71	69	70	0.81 (0.68 - 0.85)	$p = 0.007$
AD vs. CN					
Total HV	76	83	80	0.88 (0.77 - 0.96)	$p = 0.01$
+ FA	94	94	94	0.99 (0.97 - 1.00)	$p = 0.007$

* Area under the curve (AUC) of a receiver operator characteristics analysis, mean values and 95% confidence intervals in brackets.

O1-03-06 CONSISTENCY OF RESTING STATE NETWORKS ACROSS HEALTHY SUBJECTS MEASURED WITH FMRI

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Background: FMRI can be applied to study networks of connectivity during a resting-state, termed Resting State Networks (RSNs). Fluctuations in the BOLD-signal during rest reflect the neuronal baseline activity of the brain, representing the state the human brain is in when deliberate neuronal action and external input are absent. Several studies have described 'similar' RSNs. The spatial consistency, however, has not been evaluated yet. To investigate this a model-free analysis technique that does proper group analyses, is needed. **Objective:** In this study we applied Tensor-PICA to resting-state FMRI data to find grey matter RSNs that are consistent across

subjects and sessions. **Methods:** 10 healthy subjects (age 28.1 ± 6 , 5 male) were scanned twice at 'rest'; lying awake with eyes closed. The two group data sets were de-composed separately into the spatial, frequency and subject domains, using tensor-PICA. Maps were thresholded at alternative hypothesis probability of $p > 0.5$. In order to characterize the consistency, we followed a bootstrapping approach and estimated mean RSNs out of 100 surrogate data sets. **Results:** Data analysis resulted in 10 functionally relevant networks, consisting of regions involved in motor function, visual processing, executive functioning, auditory processing, memory and the 'default' network (figure). The percentage BOLD signal change was calculated showing values reaching up to 3%. In general, areas with a high mean percentage BOLD signal change are also the areas showing the least variation around this mean, i.e., are the most consistent. **Conclusion:** Our findings show that the baseline activity of the brain is very consistent and dynamic, with percentages signal change comparable to those found in task related experiments. It is of great interest to investigate whether these RSNs are present to the same extent under different conditions. An advantage of using resting-state FMRI to investigate the influence of disease on the brain is that no complicated setup is required and no task needs to be practiced beforehand. This is a major benefit especially when studying patients who may have difficulties performing a task, like patients with Alzheimer's disease. **Acknowledgements:** This study was supported by ISOA grant number: 231002 and NWO grant number: 916.36.117.

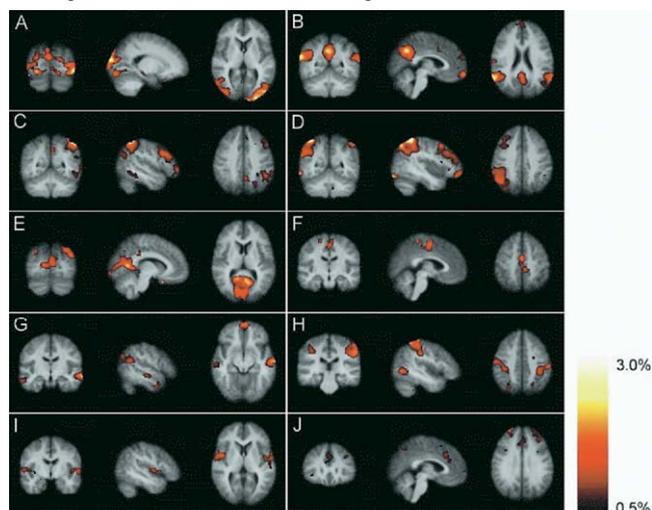


Figure: Mean Tensor PICA estimated resting patterns, coronal, sagittal and axial view of spatial map per RSN. Images are percentage BOLD signal change, overlaid on the average high-resolution scan transformed into standard (MNI152) space. Black to yellow is percentage signal change, ranging from 0.5%-3.0%. The left hemisphere of the brain corresponds to the right side of the image.

SUNDAY, JULY 16, 2006
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O1-04-01 VISUAL HALLUCINATIONS AND LEWY BODY PATHOLOGY: A COMMUNITY-BASED AUTOPSY CASE SERIES

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Background: Visual hallucinations (VH) commonly occur in patients with dementia with Lewy bodies (DLB). It is unclear if these symptoms are associated with a specific pathological subtype of Lewy body pathology (LBP). Furthermore, some have previously demonstrated that limbic subtypes of DLB are associated with the presence of VH, while others have