

structures, i.e. hippocampus (Hip) and amygdala (Amy), and in the whole brain (WB), as predictors and correlates of clinical status, and their incremental accuracy over the parieto-temporal and posterior cingulate cortices. **Results:** At baseline, reductions in Hip, Amy, and WB MRglc were found for NL-MCI, MCI and AD as compared to NL-NL ($p < .05$). The NL-MCI had Hip (17%, $p < .05$), WB (14%) and Amy (8%, $p < .05$) MRglc reductions that were comparable to those observed in clinical MCI patients (19%, 16% and 11%, respectively). These MRglc measures predicted decline from NL to MCI with accuracies of 81% (Hip), 67% (WB), and 65% (Amy). No differences in baseline cortical MRglc were found between NL-MCI and NL-NL, whereas the MCI group showed reduced temporal cortex MRglc, and the AD group showed the typical parietal, temporal, and posterior cingulate cortex hypometabolism ($p < .05$, corrected). Longitudinally, Hip MRglc highly correlated with clinical progression with greater rates of annual reductions in the following order: AD (3.7%) > MCI (2.9%) > NL-MCI (2.1%) > NL-NL (1.2%). **Conclusions:** Years prior to clinical change, NL subjects destined to decline to MCI show a PET profile intermediate between normal aging and MCI, characterized by early WB and MTL MRglc reductions. These findings show that PET MRglc measures are predictors and correlates of cognitive impairment, and may help identify subjects at risk for future AD.

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SEROTONIN RECEPTOR BINDING IN MILD COGNITIVE IMPAIRMENT STUDIED BY PET AND [18F]-ALTANSERIN

Steen G. Hasselbalch^{1,2}, Karine Madsen², Claus Svarer², Lars Pinborg², Jette Stokholm¹, Soeren Holm³, Olaf B. Paulson⁴, Gunhild Waldemar¹, Gitte M. Knudsen², ¹Memory Disorders Research Unit 6702, Copenhagen, Denmark; ²Neurobiology Research Unit, Rigshospitalet, Copenhagen, Denmark; ³PET Centre, Rigshospitalet, Copenhagen, Denmark; ⁴Danish Research Center for Magnetic Resonance, Hvidovre Hospital, Copenhagen, Denmark. Contact e-mail: sgh@pc.dk

Background: In post mortem studies of patients with Alzheimer's disease (AD) reduced serotonin (5-HT) receptor density has been described. Using positron emission tomography (PET) in patients with AD with and without depression, reduced binding to the 5-HT_{2A} receptor subtype in cortical areas was found in two studies (1;2). These reductions may reflect early and specific changes in the serotonergic transmitter system in AD. **Objective:** To evaluate possible changes in cerebral 5-HT_{2A} receptor binding in patients with mild cognitive impairment (MCI) and correlate these to cognitive function and neuropsychiatric symptoms. **Methods:** Seventeen patients with MCI of the amnesic type (7 females, 10 males, mean age 72, range 59-82, mean MMSE 26.2, range 23-30) and 17 age and sex matched control subjects were studied with PET and MRI. The distribution volumes of specific tracer binding (BP₁) were calculated for 17 brain regions using cerebellum as a reference region and individual plasma-curves corrected for radiolabelled metabolites. Volumes of interest were applied by an automated MRI-based template approach (3). PET data was corrected for partial volume effects due to atrophy (4). All subjects underwent an extensive neuropsychological and neuropsychiatric evaluation. **Results:** BP₁ was reduced globally by 20-30% in limbic and neocortical areas (p-values ranging from <0.002 to <0.05, Student t-Test). Reduced 5-HT_{2A} binding correlated significantly with lower MMSE score in caudate nuclei and putamen bilaterally (Pearson $r=0.54$, $p=0.009$; and Pearson $r=0.53$, $p=0.017$, respectively), and with poorer performance on Trail B Test in frontal and temporal neocortical areas (Pearson $r=0.47-0.57$, $p=0.026-0.047$). Reduced 5-HT_{2A} binding correlated significantly with NPI depression and anxiety subscores in the right caudate nucleus (Pearson $r=0.60$, $p=0.006$). **Conclusion:** Widespread reductions in 5-HT_{2A} receptor binding were found in amnesic MCI, suggesting a specific dysfunction of the serotonergic system in prodromal AD because atrophy could not explain the reduced tracer activity. Further, the correlation between reduced 5-HT_{2A} receptor binding in fronto-striatal regions and cognitive dysfunction (both global and executive) may suggest that re-

duced serotonergic modulation of these areas plays a role in the cognitive dysfunction found in early AD.

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IMAGING BIOMARKERS TO MONITOR TREATMENT EFFECTS FOR ALZHEIMER'S DISEASE TRIALS: THE ALZHEIMER'S DISEASE IMAGING INITIATIVE

Michael W. Weiner¹, Leon J. Thal², Ronald C. Petersen³, Clifford R. Jack, Jr³, **William Jagust**⁴, John Q. Trojanowski⁵, Laurel A. Beckett⁶, ¹SFVAMC/UCSF, San Francisco, CA, USA; ²UCSD, San Diego, CA, USA; ³Mayo Clinic, Rochester, MN, USA; ⁴UC Berkeley, Berkeley, CA, USA; ⁵University of Pennsylvania, Philadelphia, PA, USA; ⁶UC Davis, Davis, CA, USA. Contact e-mail: jagust@berkeley.edu

Background: Improved information concerning the pathogenesis of Alzheimer's disease (AD) now raises the possibility that treatments which modify the rate of neurodegeneration will be available for human testing and clinical trials. Validated biomarkers, which have increased statistical power when compared to clinical/cognitive tests, are needed to detect response to treatments. To assess and compare possible biomarkers, the National Institute of Aging and the pharmaceutical industry have funded the Alzheimer's Disease Neuroimaging Initiative. **Objectives:** 1) Develop improved methods, which will lead to uniform standards for acquiring longitudinal multisite MRI, PET, blood and CSF biomarker data in patients with Alzheimer's disease (AD), mild cognitive impairment (MCI), and elderly controls. 2) Create a generally accessible data repository, which describes longitudinal changes in brain structure and metabolism. In parallel, acquire clinical, cognitive and biomarker data for validation of imaging surrogates. 3) Determine those methods, which provide maximum power to distinguish treatment effects in trials involving AD and MCI patients. **Methods:** To date uniform MRI and PET acquisition techniques have been implemented at 36 participating sites and subject recruitment has begun. Subjects with AD (n=200), MCI (n=400) and 200 controls will have clinical/cognitive assessments and 1.5 T structural MRI every 6 months for 2-3 years; 50% of subjects will also have FDG PET scans and 25% of subjects will have 3T MRI at each time interval. All scans are rapidly, electronically, transferred to the Laboratory of Neuroimaging (LONI) at UCLA, and will be available for image processing. All clinical data is collected by the ADCS at UCSD. Blood, urine and CSF samples for biomarker analysis are sent to the University of Pennsylvania, and stored for later analysis. Importantly, all ADNI data will be accessible to any qualified scientist through the Internet. In February 2006, 36 sites had screened 207 subjects and enrolled 74 subjects. **Conclusion:** An update of this project, including preliminary results, will be presented.

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DO ATROPHY RATES ACCELERATE IN MCI AND NORMAL AGING?

Maria M. Shiung, Stephen D. Weigand, Ronald C. Petersen, Scott A. Przybelski, Peter C. O'Brien, Jeffery L. Gunter, Bradley F. Boeve, David S. Knopman, Glenn E. Smith, Robert J. Ivnik, Eric G. Tangalos, Clifford R. Jack, Jr, Mayo Clinic, Rochester, MN, USA. Contact e-mail: shiung.maria@mayo.edu

Background: The brain atrophies among the healthy elderly but atrophies at a faster rate among those with mild cognitive impairment (MCI). It is unclear whether atrophy rates are relatively constant or accelerate in these groups. This can be assessed by measuring brain volume at 3 or more points in time. **Objective(s):** To evaluate whether rates of brain atrophy accelerate in 3 groups of subjects: cognitively normal elderly; patients with MCI who convert to probable Alzheimer's disease (AD); and MCI patients who remain stable. **Methods:** 42 cognitively normal elderly controls were age and gender matched to 42 MCI subjects who converted to AD. 28 MCI subjects who did not convert to AD were individually matched to 28 patients from the larger MCI converter cohort. All subjects had 3 or more serial MRI scans. The scan acquired at conversion from MCI to AD was