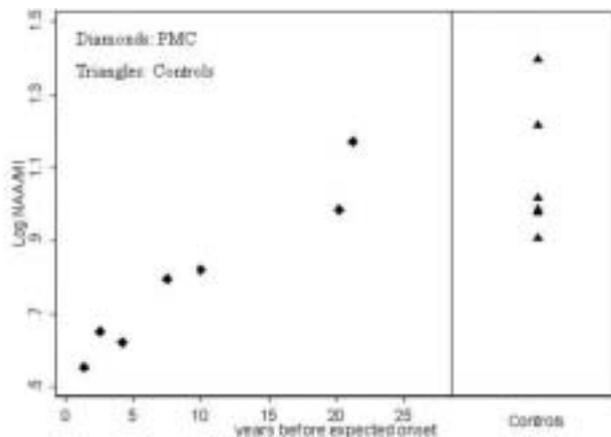


before expected onset of AD and are related to proximity of expected disease onset age.



P-134 BINDING CHARACTERISTICS OF NOVEL MRI CONTRAST AGENTS FOR THE DETECTION OF ALZHEIMER'S DISEASE

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Background: Recently "smart" MRI contrast agents (CAs) prepared from a gadolinium complex linked to a A β [1-40] was shown to bind to SPs in the brain of an AD mouse model and aid in the visualization of brain lesions associated with AD. However, the high cost of preparing this complex CA suggests that its potential clinical use may be limited. **Objective:** The objective of the present study was to develop relatively simple MRI CAs permeable to the blood-brain barrier and able to target either senile plaque (SP) deposits or neurofibrillary tangles (NFT) or both. In general, these MRI CAs consist of a neutral lanthanide-containing macrocycle (Gd⁺³-DOTA) conjugated to a targeting agent able to bind to A β in SPs or aggregated tau in the NFTs. **Methods:** We prepared these novel agents and studied their binding to A β [1-40] and recombinant full-length tau (htau40) using a fluorescence depolarization assay. **Conclusions:** We found that one hexapeptide derivative and an amino stilbene derivative bound very strongly to these targets. We believe that these agents will be good candidates for "smart" MRI CAs.

P-135 MEASUREMENT OF HIPPOCAMPAL SUBFIELDS AND AGE-RELATED CHANGES WITH HIGH RESOLUTION MRI AT 4TESLA

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Background: Normal aging and Alzheimer's disease (AD) are both associated with loss of hippocampal neurons. However, histological studies suggest that hippocampal neuronal loss is different in normal aging and AD. While in AD neuron loss is most pronounced in CA1, normal aging is thought to predominantly impact the hilus and subiculum, although this is controversial. **Objective:** The aims of this study were: 1. To test if hippocampal subfields can be identified and reliably traced using anatomical landmarks on MR images with submillimeter resolution. 2. To test if age-related volume changes of subfields can be detected. **Methods:** 14 subjects (12 healthy controls mean age 47.3, range: 24-77 years were

studied on a 4T system with using a T2 weighted high resolution turbo-spin-echo sequence (TR/TE: 3500/19 ms, turbofactor 15, 18.6 ms echo spacing, 160° flip angle, FOV 200, 512x384 matrix, 2 mm slice thickness, 24, interleaved slices without gap). Using anatomical landmarks, entorhinal cortex (ERC), subiculum, CA1, CA2 and CA3/dentate compound (CA3, CA4, dentate gyrus) on both sides were traced twice by two raters. Intra-class correlation coefficients (ICC) were calculated to assess reliability of markings within and between raters. The mean ICC for rater 1 was 0.96 (range 0.83- 0.99) and for rater 2 the mean ICC was 0.87 (range 0.66- 0.98). The between rater ICC for the different subfields ranged between 0.67 and 0.93 and was above 0.87 for the CA1 sectors. In the group of healthy subjects, there was a significant correlation between age and the left and right CA1 (left: $r = -0.63$, $p = 0.02$; right: $r = -0.53$, $p = 0.04$). **Conclusions:** These preliminary results suggest that it is possible to reliably identify and mark hippocampal subfields on high resolution MRIs of the hippocampus. The major finding was a significant correlation between age and the CA1 but not other subfields. This contrasts with some histological data suggesting that age is primarily associated with atrophy of the hilus and subiculum. Further studies on a larger group of subjects are needed to assess the changes in hippocampal subfields in normal aging and AD and to determine the value of these measurements for the early detection of AD.

P-136 HIPPOCAMPAL SHAPE ABNORMALITIES IN EARLY AD: A REPLICATION STUDY

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Background: In previous MR studies of very mild dementia of the Alzheimer type (DAT), we reported deformities of the hippocampal surface proximal to the CA1 subfield and subiculum. To assess variation in the hippocampal surface, bilateral template hippocampal surfaces, including three zones corresponding to underlying subfields (lateral, inferior-medial, and superior) were created by our expert consensus. **Objective(s):** We hypothesized that significant hippocampal deformities could be found in the lateral and inferior-medial zones, but not the superior zone, and that this shape information could be used to distinguish subjects with early DAT from nondemented comparison subjects. **Methods:** MR scans of 66 nondemented subjects (CDR 0) and 49 subjects with very mild DAT (CDR 0.5) were included in this study. In addition, scans of 20 age-matched healthy control subjects from a schizophrenia study were also included (table). Large-deformation high-dimensional brain mapping was applied to all scans to generate hippocampal surfaces from the template in each subject scan. An average hippocampal surface was constructed from the 86 comparison subjects. For each subject in the study, displacements from this average were computed for all surface points. A mean surface displacement for each zone was computed for each subject as a shape measure. **Conclusions:** Shape measures for the DAT subjects are summarized in the table below. After adjusting for multiple comparisons, highly significant group differences were found in the lateral and inferior-medial zones, but not the superior zone. When the displacements across all zones and hemispheres were modeled as repeated measurements, there was a significant group effect ($F = 83.5$, $df = 1, 133$, $p < .0001$). Further, while all surface displacements in the comparison subjects were inversely correlated with age (r ranging -0.27 to -0.51), similar correlations were not observed in the DAT subjects. There were no statistical differences between the slopes for the two subject groups when each shape measure was regressed against age. These results suggest that irregularities of hippocampal shape can be used to distinguish subjects with early DAT from nondemented subjects, but that these irregularities may have