CA1 specific loss in Patients with Alzheimer's Disease and Mild Cognitive Impairment

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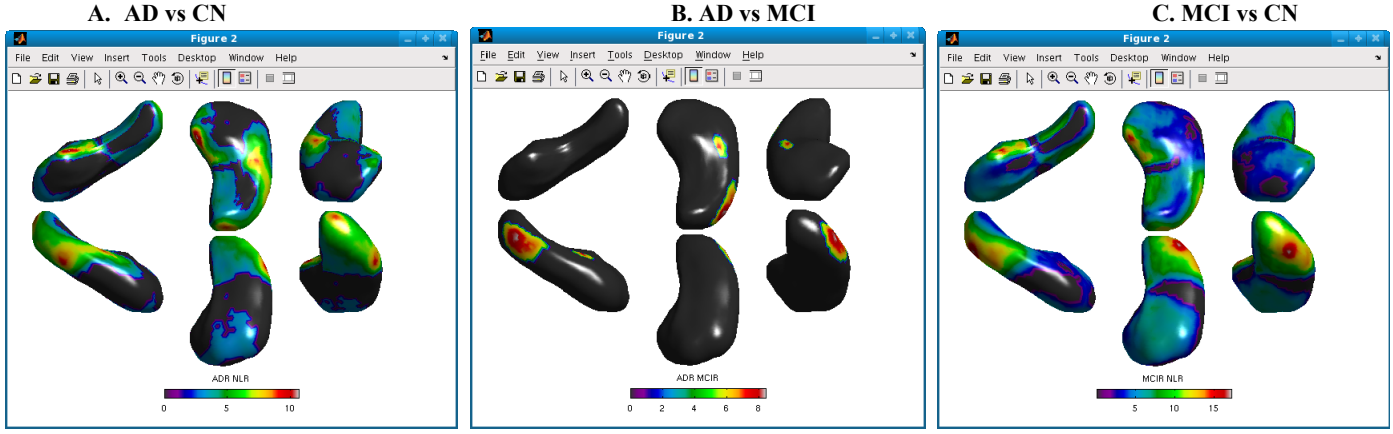
Introduction: Alzheimer's disease (AD) is a neurodegenerative disease that is the most frequent type of dementia in the elderly and amnestic mild cognitive impairment (MCI) has been considered as an intermediate cognitive state between healthy aging and AD. Atrophy of the hippocampus is a well-described feature of AD, or the risk of AD. Magnetic resonance imaging (MRI)-based volumetric assessment of brain structure has been widely employed in the study of AD, MCI, and healthy aging and the consistent findings are volume loss in the hippocampus and entorhinal cortex. However, it is not a unique finding of MCI and AD, which could be also seen in healthy aging. The emerging tools of computational neuroanatomy have increased the ability to detect subtle abnormalities of brain structure (Gutman B, et al. , Qiu A, et al , Li S, et al. , Scher AI, et al. , Wang L, et al.) . In this study, we assessed regional shape differences of hippocampus through automated hippocampal segmentation in healthy aging (CN), MCI and AD.

Materials and Methods: Amnestic MCI patients (n=26) were included if the scores for immediate recall in Seoul Verbal Learning Test and/or Rey complex figure test were below 1 SD of the normative database, but there was no impairment of activity of daily living. We included same numbers of patients with probable AD according to NINCDS/ADRDA criteria (n=26). Also healthy control subjects (n=26) were included proved by normal results of detailed neuropsychological tests and brain MRI. A three-dimensional T1-weighted imaging (i.e. MPRAGE) sequence was run to obtain whole brain using a 3T MRI system (Philips, Acheiva). A fully automated hippocampal segmentation method was used for reconstructing three dimensional hippocampal shapes in each subject. To validate accuracy of the automated methods, one reader manually outlined the left and right hippocampus using published criteria and the results were compared to those of automated methods for percent volume overlap. In each subject, the locations of the hippocampal surface were registered on age-matched neuroanatomical template and the variations in hippocampal diameter were calculated.

Results: The automated hippocampal segmentation method was well-correlated to hand tracing it. Fig 1 shows the results of comparisons of the right hippocampus shapes between CN and AD or MCI. Automated hippocampal shape analysis showed a regional pattern of shape difference between normal control and amnestic MCI, more evident for inward deviation of lateral zone of the hippocampus, which intersects the area of the hippocampus containing the CA1 region. However, a comparison of amnestic MCI and AD showed less significant differences.

Fig1. Results of comparisons of the right hippocampus shapes between CN and AD or MCI



Discussions: In AD, pathological changes appear in hippocampus, but it is not a unique pathological finding of AD without specifying specific sub-regions and also seen in other types of dementia, MCI, and healthy aging. In this study, hippocampal surface deformation was most pronounced in the lateral zone covering CA1 subfield in amnestic MCI compared to normal control, but the difference was not found between amnestic MCI and AD. These results suggest that degeneration of CA1 and adjacent regions develops in early course of AD. Also, the automated surface analysis methods used in this study can display early structural changes of hippocampus in AD, which could be a useful tool for group-level studies.

Conclusion: We analyzed regional shape differences as means of distinguishing the MCI and AD hippocampus from the changes associated with normal aging. The CA1 area damaged mostly in AD or MCI compared with HC.

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