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## **Neuroanatomical markers of early Alzheimer's disease** John Csernansky\*

Address: Department of Psychiatry, Washington University School of Medicine, St. Louis, MO, USA \* Corresponding author

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Structural deformities of the hippocampus and other structures of the limbic system are characteristic of individuals with very mild and mild forms of dementia of the Alzheimer type (DAT). Recent studies from our laboratory suggest that similar neuroanatomical deformities may predict the onset of dementia in nondemented elders. Using high dimensional diffeomorphic transformations of a neuroanatomical template, we quantified hippocampal volumes and surfaces in nondemented elder subjects, including a partitioning of the hippocampal surface into three zones (i.e., lateral, superior and inferior-medial) that were proximal to specific underlying cellular subfields. Annual clinical assessments using the Clinical Dementia Rating scale (CDR), were then performed for a mean of 4.9 years (range 0.9-7.1 years), to monitor subjects who converted from having no dementia to having very mild dementia. Smaller left hippocampal volumes and inward deformation of the zone of the left hippocampal surface corresponding to the CA subfield significantly predicted time to conversion. The pattern of hippocampal surface deformation observed in the nondemented subjects who later converted to having very mild dementia was similar to the pattern of hippocampal surface deformation that we had previously observed to discriminate subjects with very mild DAT and nondemented subjects. These results suggest that inward deformation of the left hippocampal surface in a zone corresponding to the CA1 subfield is an early predictor of the onset of DAT in nondemented elderly subjects.