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Hypertrophy of Hippocampal CA1 Neurons in Asymptomatic Alzheimer's Disease in the Oldest Old 90+ Study

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Autopsy data from longitudinal studies of aging indicate that the brain of some cognitively normal older adults bears substantial amyloid neuritic plaques (nP) and neurofibrillary tangles (NFT) characteristic of Alzheimer_s disease (AD), a clinical pathological state we call asymptomatic AD (ASYMAD). In two previous studies of subjects in their 80s, we observed significant hypertrophy of CA1 neurons in ASYMAD subjects. Here we ask whether neuronal hypertrophy occurs in subjects a decade older. We examined the CA1 region of hippocampus in 19 oldest-old subjects from The 90+ Study divided into three groups based on their clinical and pathological findings: controls (n=7, age 96.7 years), ASYMAD (n= 6, 99.0 years), and AD (n= 6, 97.8 years). Controls had normal cognition and no significant AD pathology (nP CERAD 0, NFT Braak 0-III), ASYMAD subjects had normal cognition and AD pathology (nP CERAD B-C, NFT Braak IV-V), and AD patients were demented with AD pathology (nP CERAD B-C, NFT Braak IV-VI). Dementia and AD diagnoses were made (using DSM-IV and NINCDS-ADRDA criteria) by consensus conference using all available information including neuropsychological testing, neurological examination and medical records. Using the stereological Nucleator probe, we measured the volumes of CA1 neuronal soma, nuclei, and nucleoli. The mean vol-ume of CA1 soma was 3561 Km3 in controls, 4670 Km3 in ASYMAD, and 3758 Km3 in AD. One Yway ANOVA yielded a p =0.025. The mean volume of CA1 neurons in ASYMAD was 31% larger than controls (pG0.02) and 24% larger than AD (pG0.05). There was no difference in the volumes of nuclei or nucleoli.These observations suggest that even in the 10th decade, the brain has enough plasticity that allows hippocampal neurons to become larger in the asymptomatic stages of AD. This neuronal change may con-tribute to the preservation of cognitive performance in ASYMAD.