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Oral presentation

Dementia in the oldest-old: a limbic form?

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Several neuropathologic analyses postulate that Alzheimer's disease in the oldest-old is associated with substantial neurofibrillary tangle (NFT) formation in the CA fields of the hippocampus and neuronal loss confined to the entorhinal cortex. All of these studies have measured lesion densities, rather than absolute numbers, did not include an assessment of vascular components and, most importantly, do not take into account the potential interaction between neuropathological hallmarks in a global multivariate analysis. We present here a stereologic analysis of Alzheimer's disease -related pathology and microvascular structure in 12 oldest-old individuals including a complete assessment of total NFT, neuron numbers, amyloid volume as well as length and diameter of capillaries in entorhinal cortex, CA fields and dentate gyrus. The progression of NFT numbers and amyloid volume across the different Clinical Dementia Rating (CDR) groups was significantly slower in these cases compared to previously reported younger cases. Although patients with mild and moderate dementia showed significantly lower mean neuron numbers compared to CDR 0–0.5 cases, there was a marked overlap in individual values among CDR groups. A modest proportion of the variability in CDR scores was explained by NFT numbers in the CA2 field (18.1%) and the dentate gyrus (17.3%). In contrast, neither Nissl-stained neuron numbers nor total amyloid volume in the areas studied significantly predicted cognitive status. Importantly, the diameter of capillaries in CA1 field and entorhinal cortex was a strong and independent predictor of cognition in this group, explaining 34% and 40% of CR variability respectively. In contrast, total length of capillaries in the areas studied was not related to cognitive status. These data indicate that the occurrence and progression of Alzheimer's disease -related pathologic changes are not an unavoidable consequence of aging and that dementia in extreme aging depends on the damage of hippocampal subdivisions commonly less affected by NFT formation. The also suggest that structural parameters related to capillaries should be considered when establishing clinico-pathological correlations in this age group.