

Oral presentation

Towards a new definition of mixed dementia

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Although microscopic cortical infarcts, thalamic and basal ganglia lacunes as well as periventricular and deep white matter demyelination represent the main determinants of cognitive decline in pure vascular cases, their exact role in cases with substantial AD pathology remains unclear. To explore the pathological substrates of mixed dementia, we performed a detailed analysis of lacunar and microvascular pathology in 156 prospectively studied elderly individuals with various degrees of AD pathology. Cognitive status was assessed prospectively using the Clinical Dementia Rating (CDR) scale; neuropathological evaluation included Braak NFT and A β -protein deposition staging and bilateral semiquantitative assessment of microvascular ischemic pathology and lacunes; statistical analysis included univariate and multivariate regression models controlling for age. Four independent variables were significantly related to CDR scores. These included Braak NFT staging, A β deposition staging, cortical microinfarct as well as thalamic and basal ganglia lacune scores. The concomitant assessment of these neuropathological variables predicted 27% of the CDR variability. In contrast, white matter lacunes, periventricular and diffuse white matter demyelination as well as focal and diffuse cortical gliosis were not significantly related to CDR scores. In a stepwise approach, the vascular scores explained 15% of the variability of the presence of dementia, Braak NFT staging 30.4% and A β deposition staging 3.5%. These findings indicate that the clinical expression of the vascular component in mixed cases is highly dependent on lesion type and location as well as severity of concomitant AD-related pathology. In particular, they reveal that the progressive development of CMIs may have a stronger cognitive impact than white matter changes or lacunes visualized by structural neuroimaging in mixed dementia.