

Oral presentation

## Tangles and neuron numbers but not amyloid load predict cognitive status in Alzheimer's disease

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### Objective

To examine the relationship between stereological estimates of Alzheimer disease-related pathology and severity of cognitive deficits in brain aging.

### Background

Previous studies reported substantial contributions of neurofibrillary tangles, amyloid deposits, and neuronal loss to the development of dementia. However, the prediction of cognitive status based on non-stereologic quantification of these parameters has led to conflicting results. Such studies have measured densities, rather than absolute numbers, and most do not take into account the potential interaction between the above pathological hallmarks in a global multivariate analysis.

### Methods

Clinicopathologic study in 22 elderly cases. Cognitive status assessed prospectively using the Mini Mental Score Examination (MMSE); stereologic assessment of neurofibrillary tangles (NFT), unaffected neurons and total amyloid volume in the CA1 field of the hippocampus, entorhinal cortex, and area 9. Statistical analysis was performed using both univariate and multivariate linear regression models.

### Results

High total NFT counts but not amyloid volume were strongly associated with a lower number of unaffected neurons in all areas studied. A very high proportion of the variability in MMSE scores was explained by NFT and neuronal counts in the CA1 field (83% and 85.4%), entorhinal cortex (87.8% and 83.7%) and area 9 (87% and 79%); amyloid volume in the entorhinal cortex, but not in the

CA1 field and area 9, accounted for 58.5% of MMSE variability. Multivariate analyses showed that total NFT counts in the entorhinal cortex and area 9 as well as neuron numbers in the CA1 field were the best predictors of MMSE score.

### Conclusions

These new stereological data indicate that neuronal pathology in hippocampal formation and frontal cortex closely reflects the progression of cognitive deficits in brain aging and Alzheimer's disease. They also demonstrate that amyloid volume has no additional predictive value, in terms of clinicopathological correlations, beyond its interaction with NFT