

Relative contributions of subcortical cerebrovascular disease, hippocampal sclerosis, and Alzheimer disease to cognitive impairment

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Background: Subcortical cerebrovascular disease (SCVD) may contribute to cognitive impairment, either alone or in combination with Alzheimer disease (AD).

Purpose: To assess the relative contributions of SCVD- and AD-pathology to cognitive impairment (CI) and dementia (D).

Methods: We report clinical-pathological correlations from 79 autopsy cases derived from prospective longitudinal study (IVD Program Project: P01AG12435). SCVD was defined by hyperintensities on proton density MRI. At last clinical examination, 13 subjects were cognitively normal (CN), 13 had cognitive impairment (5 CI-AD, 8 CI-SCVD) and 53 had dementia (20 AD, 11 SCVD, 22 Mixed AD/SCVD).

Results: 39% of cases had significant CVD-pathology (CVD-path score ≥ 3), 68% had significant AD-pathology (Braak Stage \geq III), and 18% had significant hippocampal sclerosis (HS score ≥ 2). In a logistic regression analysis, each of the 3 pathology variables contributed independently to cognitive status (CN, CI, or D): CVD-path score odds ratio (OR) = 1.1 [1.00 to 1.30], Braak & Braak Stage OR = 2.75 [1.78 to 4.24], HS OR = 2.4 [1.01 to 5.81]. No significant interactions were found among the 3 pathology variables. Cases were further stratified by the status of the hippocampus: 59 "involved" (HS ≥ 2 or Braak \geq III) vs. 20 "spared" (HS ≤ 1 and Braak \leq II). Significant associations between CVD-path score and cognitive status were found only when the hippocampus was spared (Fisher exact test, $p < 0.01$).

Conclusions: SCVD, AD, and HS contribute independently to cognitive impairment. We found no evidence for interaction, suggesting that the contribution of each type of pathology is additive rather than multiplicative. A significant deleterious effect of CVD-path score on cognitive status was observed only when the hippocampus was spared. In this convenience sample, AD or HS appeared to overwhelm the adverse effects of SCVD on cognitive status.