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Neuroimaging / differential diagnosis

Regional white matter hyperintensities predict Alzheimer's-like neurodegeneration

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Abstract

Background: Small vessel cerebrovascular disease, best visualized as white matter hyperintensities (WMH) on T2-weighted MRI scanning, is associated with cognitive decline and increases risk for clinical Alzheimer's disease (AD), particularly when it is distributed in posterior brain regions. There is much debate, however, about whether cerebrovascular disease represents a comorbidity or whether it is more fundamental to the pathogenesis of AD. The purpose of this study was to examine whether regional WMH volume predicts neurodegeneration, operationally-defined as longitudinal decline in cortical thickness, among community-dwelling older adults.

Method: Two hundred thirty-eight participants(73.18±5.23 years old, 60% women, 35% APOE-ε4 carriers, 30% non-Hispanic White/32% Hispanic/38% Black, 14% with MCI) from the Washington Heights Inwood Columbia Aging Project (WHICAP) received high-resolution structural 3T MRI scans at baseline and 4.09±1.57 years later. Regional WMH volume was derived with in house developed software and the FreeSurfer (v6.0) longitudinal processing stream was used to calculate change in cortical thickness. Using QDEC, we examined the relationship of total and regional WMH volume with annualized rate of decline in cortical thickness (symmetrized across the two visits) with vertex-wise general linear models adjusted for age, sex, and APOE status. We additionally adjusted for a baseline marker of AD-related atrophy (entorhinal cortex thickness).

Result: Baseline total WMH volume predicted widespread cortical atrophy in a pattern consistent with AD-associated atrophy, which included parahippocampal, temporal, and parietal regions. When examined regionally, the effects were most prominent for parietal lobe WMH, which predicted entorhinal cortex atrophy predominantly. Adjusting for baseline entorhinal cortical thickness did not alter the findings. In stratified analyses, the effects were strongest among Hispanic and Black participants compared with White participants, and similar across APOE groups.

Conclusion: White matter hyperintensity volume, especially in the parietal lobes, predicts Alzheimer's-like neurodegeneration, suggesting that small vessel cerebrovascular disease contributes to the 'N' aspect of the 'A/T/N' pathogenic models of AD. The results were independent of and stronger than baseline atrophy measures, suggesting that WMH are not simply a *result* of neurodegeneration. These effects may manifest differently across racial/ethnic groups, with small vessel cerebrovascular disease playing a more prominent role in future neurodegeneration among racial/ethnic minorities.