What Do White Matter Hyperintensities Really Represent?

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See related article, pages 600–606.

White matter hyperintensities and small, incidentally found brain infarcts are common findings on MRI, especially in old people, usually regarded as surrogates of small vessel disease. Debette and colleagues have studied the significance of such changes in upper middle-aged persons using the Framingham Offspring cohort. Volumetric brain MRI and neuropsychological testing were performed in 2229 participants with a mean age of 62 years that were prospectively controlled for incident stroke, dementia, and mortality. The incidence of mild cognitive impairment was assessed in 1694 persons who underwent a second neuropsychological evaluation. Outcomes were subsequently related to the MRI findings.

The prospective setting in a large and slightly younger population is an obvious strength of this study as is the quantitative measurement of the white matter changes. On the other hand, the MRI-defined brain infarcts are not stratified according to number and size, which may be envisioned as a weakness. Lacunar infarcts have recently been shown to be dynamic in that they increase in both prevalence and size with aging and it is likely that many large lacunes in an individual of a certain age have a more significant impact as compared with 1 single, small lacune in an age-matched control subject. Regarding the imaging material, the authors have unfortunately chosen to show segmented, heavily postprocessed images instead of original T2-weighted images. This makes it difficult for the reader to fully appreciate especially the described white matter alterations and relate them to what can be seen in daily practice.

The finding that brain infarcts and white matter hyperintensities may predict incident stroke, mild cognitive impairment, and dementia as well as increasing the risk of mortality is highly expected both based on previously published articles and on what is commonly believed.

Although convincingly shown, it can be questioned how newsworthy these findings are for the neurological and neuroradiological communities. Conversely, it is very interesting that the association of white matter hyperintensities with cognition impairment was independent of vascular risk factors, interim stroke, and brain infarcts and that it was found only in individuals > 60 years of age. In addition, the association of white matter hyperintensities, but not brain infarcts, with mortality was also independent of vascular risk factors although it became weaker after adjustments for interim dementia and stroke. So, it might be concluded that an elderly person with no vascular risk factors or disease may still have white matter hyperintensities associated with cognitive deficits and be at a slightly higher risk for mortality also from other causes than dementia and stroke.

White matter hyperintensities and lacunar infarcts are usually thought to be concomitant expressions of arteriosclerotic disease. These results indicate that white matter hyperintensities in certain individuals may also represent something else besides the generally accepted concept of small vessel disease or be the very initial phase of such sclerosis that in combination with some other mechanism can affect cognition and to some extent mortality. For instance, no major study has so far in this context investigated the possibility of vascular pathology also on the venous side, and, indeed, the effect of white matter hyperintensities on cognition has been shown to vary substantially between individuals indicating a diversified level of tolerance. I hope that the authors will continue their efforts in trying to elucidate what such white matter abnormalities really represent and how they can be used for diagnostic and therapeutic purposes.

Disclosures

None.

References


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