Should We Distinguish Between Periventricular and Deep White Matter Hyperintensities?

To the Editor:

The recent article by DeCarli et al1 addresses a somewhat neglected aspect of white matter hyperintensities (WMH), the significance of their anatomical location. The authors argue that the commonly accepted categorization into deep (DWMH) and periventricular (PVWMH) WMH is arbitrary, because the two are very highly correlated, and a spatial analysis does not reveal distinct populations. We think that this conclusion is premature, because the categorization depends on a number of factors. The first limitation of their analysis is that they examined individuals in their 70s who presented to a specialty clinic, suggesting that the white matter lesions in their sample were at an advanced stage. If an analogy is drawn from cerebral atrophy in dementia, regional differences in atrophy that are present in the different subtypes of dementia become less prominent in the later stages. In our study of WMH in middle age (60 to 64 years), the correlation of DWMH and PVWMH was much lower ($r=0.621$; $P<0.001$; $n=477$), accounting for $<40\%$ of the variance.2 It is possible that the two subtypes of WMH have different but converging trajectories, possibly because of overlapping but not identical risk factors and pathogenesis. Neuropathological differences between DWMH and PVWMH have been reported,3 which suggest that whereas cerebral ischemia is a common etiological factor, other mechanisms may be differentially involved. In our study, hypertension was a risk factor for both, but diastolic blood pressure (BP) correlated significantly with DWMH, whereas both systolic and diastolic BP were correlated with PVWMH.4 Homocysteine was a determinant of DWMH but not PVWMH,5 but lung capacity was more strongly related to PVWMH.6

The functional significance of the two subtypes is also likely to be different. In an earlier study involving stroke patients,7 we showed that although DWMH accounted for only one third of the total WMH volume, with the other two thirds being PVWMH, it had a stronger relationship with cortical perfusion. Our recent analysis of data from 397 community-based middle-aged individuals suggests that DWMH have a significant relationship with cortical atrophy ($r=0.15$; $P=0.003$) and ventricular dilatation ($r=0.18$, $P<0.0005$), but PVWMH do not ($r=0.06$, $P=0.21$; $r=-0.03$, $P=0.56$ respectively).8 There are also demonstrated differences in the effect of DWMH or PVWMH on cognitive function, motor function,9 and emotions.10

Therefore, we support the continuing distinction between DWMH and PVWMH, at least for research. In fact, additional anatomical categorization into lobar and arterial territorial regions may be relevant for some purposes. To lump all of the WMH into one category will hamper our understanding of their pathogenesis and functional relevance.

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