Cerebral Microbleeds and Cognition

The Epidemiology of Dementia in Singapore Study

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Abstract: Cerebral microbleeds (CMBs) are considered to be a novel marker of cerebral small vessel disease. However, the link with cognitive impairment remains unclear. We investigated whether CMBs—independent of other traditional markers of cerebral small vessel disease—are related to cognition. Chinese subjects from the population-based Singapore Chinese Eye Study, who failed an initial cognitive screening and were recruited into the ongoing Epidemiology of Dementia in Singapore Study, underwent neuropsychological testing and 3 T brain magnetic resonance imaging. The presence and number of CMBs were graded using Brain Observer Microbleed Scale on susceptibility-weighted images. Other magnetic resonance imaging lesions that were graded included presence of lacunes, white matter lesion, and total brain volumes. A comprehensive neuropsychological battery was administered and cognitive function was summarized as composite and domain-specific Z-scores. Among 282 subjects, 91 had any CMBs (32.3%), of whom 36 (12.8%) had multiple CMBs. CMBs were independent of cardiovascular risk factors and other markers of cerebral small vessel disease—significantly associated with poorer cognitive function as reflected by composite Z-score (mean difference per CMB increase: −0.06; 95% confidence interval: −0.11, −0.01) and with domain-specific Z-scores including executive function, attention, and visuoconstruction. Among Chinese subjects CMBs were, independent of other concomitant markers of cerebral small vessel disease, associated with poorer cognitive function.

Key Words: cerebral microbleeds, cognition, magnetic resonance imaging, cerebral small vessel disease

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Cerebral microbleeds (CMB) are radiologically defined lesions on magnetic resonance imaging (MRI) sequences, most commonly on gradient-echo T2* or susceptibility-weighted images (SWI), which correspond pathologically to hemosiderin deposits surrounding small vessels.1–2 In healthy populations the reported prevalence of CMBs ranges from 3.8% to 38.3%, whereas in patients with stroke the corresponding figures may be as high as 50% to 70%.3–6 Histopathologic studies have shown that CMBs are associated with surrounding tissue damage.7,8 Although a direct impact of CMBs on cognitive function has been hypothesized, results from studies have varied.9–12 CMBs are associated with both a higher amyloid burden and are also known to occur in patients with Alzheimer disease. Furthermore, previous studies showed that CMBs occur concomitantly with white matter lesions (WMLs) and lacunar stroke.13–14 Thus, an independent effect of CMBs on cognition may be implicated only if other associated pathologies are accounted for.15

With respect to Asian populations, studies from Japan reported that the presence of CMBs is related to a poorer cognitive function.16,17 However, in these studies cognitive function was assessed solely by the mini-mental status examination (MMSE), and 1.5 T MRI was utilized for assessment of CMBs. As yet, there are no data from Chinese populations on the association with cognitive impairment as assessed by an extensive neuropsychological test battery. Therefore, in the present study, we investigated the association of CMBs with cognition, as assessed by a comprehensive neuropsychological evaluation among Chinese subjects from the population-based Singapore Chinese Eye Study (SCES), who failed an initial cognitive screening and were recruited into the ongoing Epidemiology of Dementia in Singapore (EDIS) Study. Furthermore, when examining this association we took into account the presence of other MRI features, as reflected by markers of cerebral small vessel disease and neurodegeneration on MRI.

METHODS

Study Population

The ongoing EDIS study drew subjects from the population-based study among Chinese aged 40 to 85 years, who participated in the SCES. To use the limited resources in an efficient way, it was decided to focus on those subjects who were most likely to have some cognitive problems. Hence, in the first phase of the EDIS Study, Chinese