THE ASSOCIATION BETWEEN COGNITIVE FUNCTION AND WHITE MATTER LESION LOCATION IN OLDER ADULTS: A SYSTEMATIC REVIEW

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Background: Maintaining cognitive function is essential for healthy aging and to function autonomously within society. White matter lesions (WMLs) are associated with reduced cognitive function in older adults. However, whether their anatomical location moderates these associations is not well-established. This review systematically evaluates peer-reviewed evidence on the role of anatomical location in the association between WMLs and cognitive function.

Methods: In accordance with the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement, databases of EMBASE, PUBMED, MEDLINE, and CINAHL, supplemented by reference lists were searched. We limited our search results to adults aged 60 years and older, and studies published in the English language from 2000 to 2011. Studies that investigated the association between cognitive function and WML location were included. Two independent reviewers extracted: 1) study characteristics; 2) WML outcomes; and 3) cognitive function outcomes.

Results: Of the 14 studies included, seven compared the association of subcortical versus periventricular WMLs with cognitive function. Seven other studies investigated the association between WMLs in specific brain regions (e.g., frontal, parietal lobes) and cognitive function. Overall, the results suggest that periventricular WMLs may have a greater impact on executive function/processing speed than subcortical WMLs. Only two of the 14 studies compared the association of subcortical versus periventricular WMLs with cognitive function among older adults with different levels of cognitive function. Therefore, no conclusions could be drawn as to whether the association of subcortical versus periventricular WMLs with cognitive function is different across cognitive states. Also, whether WMLs in different brain regions have a differential effect on cognitive function remains unclear.

Conclusions: Evidence suggests that periventricular WMLs have a significant negative impact on cognitive abilities of older adults. This finding may be influenced by study heterogeneity in: 1) different MRI sequences, WML quantification methods, and neuropsychological batteries; 2) underlying pathologies for WMLs; and 3) statistical analysis and sample size. To better understand the role of anatomical location in the association between WML and cognitive function, future studies should examine the spatial distribution of WMLs on the whole brain, or specific brain regions identified in this review as being highly associated with cognitive dysfunction.

Table 4
Association between the structural location of white matter lesion (i.e., subcortical, periventricular, or regional) with two domains of cognitive function (i.e., memory and executive function/processing speed). (Continued)

| Reference | Association |
|-----------|-------------|
| Tullberg et al. | In non-demented individuals, increased volumes of frontal (specifically prefrontal and dorsolateral), parietal, and occipital WML were separately associated with lower executive function/processing speed scores. Frontal WMLs were also associated with reduced memory function in non-demented group. No association was found for individuals with dementia. |

Abbreviations: WML = White Matter Lesion; CDR = Clinical Dementia Rating Scale.