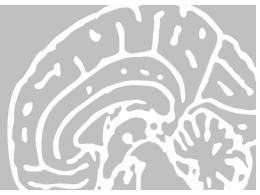
White matter hyperintense lesions in ageing and degenerative parkinsonism



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Changes of white matter in ageing brain are common findings as shown as hyperintense signals in conventional MRI. Those are generally resulted from ischemic insults and associated with vascular risk factors. There are also evidences about widespread and ongoing white matter pathology, which may impact on ageing process and degenerative disorders. Findings about the white matter hyperintense lesions in the elderly and degenerative parkinsonism will be briefly reviewed.

Key Words: White matter, Ageing, Parkinsonism

Introduction

White matter hyperintensities (WMHs) on T2 and FLAIR images are very common findings in the elderly. Those can influence on the normal ageing process and also on pathogenesis of degenerative disease mainly affecting elderly population. The impacts and pathology of WMHs in the general population will be briefly reviewed, and then the findings of the degenerative parkinsonian disorders and the WMHs will be discussed.

White matter hyperintensities in general elderly population

Increasing age is one of the most important risk factors for WMHs, showed prevalence of about 15% at the age of 60, and around 80 % at the age of 80.[1,2] A variety of vascular risk factors, such as hypertension, diabetes and smoking, are also associated.[3,4]

Generally, these are associated with an increased risk of cognitive decline and dementia, stroke and even death.[2,5] Large studies consistently showed associations between WMHs and cognitive impairment.[6,7] WMHs are also associated with longitudinal change in cognitive performance.[8,9] And WMHs are related to balance impairment and mobility in otherwise healthy elderly individuals and showed association with gait abnormalities—specifically, slower gait speed, reduced stride length, and increased stride width.[10-12] The severity of WMHs was correlated with depression, particularly in elderly population.[13,14]

WMHs are primarily related to small vessel ischemic pathology or more general vascular processes.[15] Pathological studies suggested that WMHs appear brighter on FLAIR due to increased water content and molecular degeneration in damaged white matter, and that the underlying nonspecific pathology of WMH includes demyelination, gliosis, and axonal atrophy.[16,17] In addition to those findings, altered functions of astrocytes, oligodendroglia and microglia have emerged.[18] So these findings suggest that WMHs are not simply the markers of an episode of ischemia, but reflect an active and complex pathogenesis, as also shown by the active pathologic process in surrounding normal-appearing white matter.[18]

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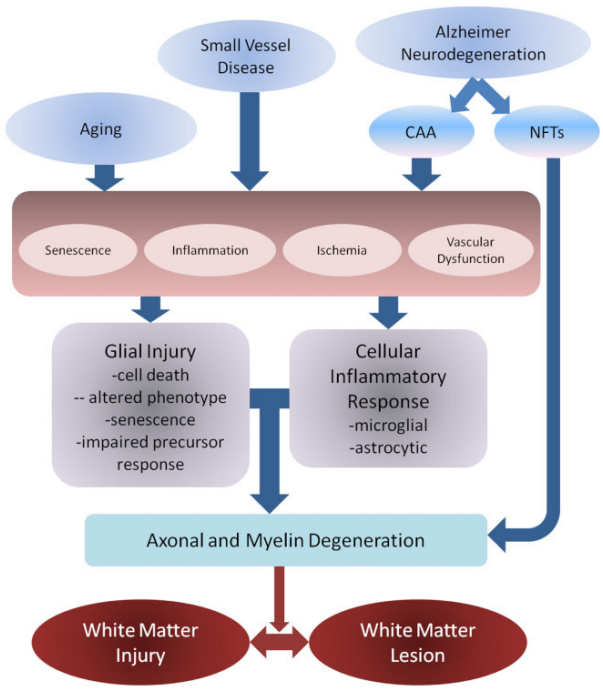

Figure 1. Pathogenesis of white matter pathologies in ageing brain. (Adopted from Wharton et al.[18])

White matter hyperintensities in Parkinson's disease

Imaging studies show WMHs to be present in 30–55% of patients with PD.[19-22] The impacts of WMHs on motor symptoms of PD can be summarized as severe gait problems, postural instability, balance impairment, rapid progression, and correlation with the severity of axial symptoms. And PD phenotype with postural instability gait difficulty demonstrated significantly increased WMHs burden.[20] As shown in elderly population, cognitive impacts of WMHs are also shown in PD. Although there were conflicting results in earlier studies, convincing evidences are increasing in recent studies with prospective design.[23-26] WMHs was associated with progression from PD-MCI to PDD and with ongoing decline in general cognitive status in PD-MCI, more sensitively in WMHs of the cholinergic pathway.[25] Low hippocampal volume was shown to be a significant predictive factor for the progression from PD-NCI to PD-MCI and also from PD-MCI to PDD, and WMH also shown to be an additional factor determining the progression.[26] There also studies for the associations between WMHs and other non-motor symptoms of PD. PD patients with depression showed more frequent periventricular and BG regions WMHs and the severity of depression significantly correlated with periventricular WMHs total score.[27] PD with nocturnal hypertension showed increased burden of WMHs.[28] The studies for the correlation of orthostatic hypotension were inconclusive.[29,30]

White matter hyperintensities in other degenerative parkinsonism

WMHs were shown to be increased in patients with multiple system atrophy (MSA) than patients with PD or control subjects.[31] There was no difference in WMH between patients with MSA-C and MSA-P in the study. Age, supine systolic blood pressure, and blood pressure drop were identified to be correlated with WMH, and the use of pressor agent did not associated with the incidence of supine hypertension.[31,32]

In studies of dementia with Lewy body (DLB), the results of association with WMHs are conflicting. One study found that the DLB group had a higher prevalence of frontal WMHs compared to AD.[33] In contrast, WMH volume was significantly higher for AD versus controls, but not significantly different between LBD and controls.[34] Another study found that similar levels of WMH between AD and LBD, and WMH load was associated with cognition in AD, but not in LBD.[35]

Fronto-temporal WMHs are reported as one of imaging features of corticobasal degeneration (CBD) along with asymmetric cerebral atrophy.[36] Those are localized in the subcortical areas of precentral or superior frontal gyrus contralateral to the more clinically affected side.[37,38]

Though the pathology of white matter in progressive nuclear palsy (PSP) is well-known, it is hard to find the changes in white matter with conventional MRI and most of the studies report that the changes of white matter using morphometry or diffusion tenor imaging.[39-41]

Conclusion

There are convincing evidences about the impacts of WMHs on ageing population and recent studies suggest active nature of white matter pathology, involving not only the ischemia or hypoperfusion but also a lot of other factors (Figure 1). These findings implicate the importance of WMHs as a potentially modifiable risk factor in a general population. Although there are limited studies regarding the atypical parkinsonism, cumulating evidences of the association between WMHs and motor/non-motor features of PD warrant the aggressive primary or secondary treatment of vascular or metabolic risk factors, which may contribute to the progression of WMHs, in other words, which may affect the severity and progression of the disease.[42]

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