Identifying neuropsychological profiles associated with white matter hyperintensities

Jana Kynast, Leonie Lampe, Tobias Luck, Katrin Arelin, Dominik Fritzsch, Karl-Titus Hoffmann, Steffi G Riedel-Heller, Arno Villringer and Matthias L Schroeter
Max Planck Institute for Human Cognitive and Brain Sciences, Germany

Background: White matter hyperintensities (WMH) feature as a marker of long-term white matter (WM) degeneration, caused by a broad range of pathologies. WMH can be detected on T2-weighted fluid attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI) scans and progressively increase with age. Age-related WMH are strongly associated with vascular risk factors and are assumed to cause a global decline in cognitive performance. The progression of WMH majorly affects attention and executive functioning. However, a comprehensive, domain-specific characterization of the neuropsychological features associated with WMH is needed to validate recent findings and to further identify cognitive patterns associated with WMH.

Aim: Here, we aim at the identification of neuropsychological characteristics associated with WMH in a large, non-clinical sample.

Methods: We included 850 persons participating in the study of the Leipzig Research Centre for Civilization Diseases at the University of Leipzig, Germany (M = 60 years, SD = 13.1 years, range: 21-79 years). MRI was acquired for every participant with a 3 Tesla MRI-scanner. The amount of WMH on the individual FLAIR sequences was quantified on the 4-stage Fazekas scale (Fazekas, 1987) by experienced neuroradiologists. The sample was categorized in 4 Fazekas groups. Age, sex and education were identified as confounding factors.

The neuropsychological test battery included the Trail Making Test (parts A and B), the Stroop Test, the Consortium to Establish a Registry of Alzheimer’s Disease (CERAD) test battery and the 20-item Dysexecutive Questionnaire (DEX) of the Behavioral Assessment of the Dysexecutive Syndrome (BADS). Neuropsychological subtests were assigned to the cognitive domains attention, executive function, memory, learning, language, verbal fluency and perceptual-motor abilities, under well-established theoretical considerations and with respect to the clinical diagnostic criteria for mild and major neurocognitive disorder.

Individual test results were age-standardized (M = 0, SD = 1) to the mean of the corresponding age group (<65 y, 66-69 y, 70-74 y, 75+ y). Age-standardized scores corresponding to the same cognitive domain were averaged to seven cognitive domain scores indicative of objective cognitive performance. A content based categorization of DEX items to five cognitive domains (attention, executive function, memory, language and social cognition) was applied. The sum score for every domain was age-standardized to the mean of the corresponding age group. Differences between the four Fazekas groups in (1) objective measures of cognitive performance (7 measures) and (2) subjective cognitive complaint (5 measures) were analyzed with the nonparametric rank-sum test with data-alignment (critical alpha level: p < .05. Data was aligned for the effects of sex and education and their interaction with Fazekas score. Data was corrected for identical ranks. Group differences were examined using the single comparison algorithm proposed by Schaich&Hamerle. For single comparisons, the alpha level was adjusted due to multiple comparisons.

Results: A general decline in cognitive performance is associated with a higher Fazekas score. The decline in cognition becomes evident with higher lesion load (starting at Fazekas score 2). Fazekas groups significantly differed in performance measures of attention ($\chi^2(3,846) = 13.77$, p < .01) and executive functions ($\chi^2(3,846) = 12.84$, p < .01). Analyses yielded marginally significant group differences in objective measures of memory ($\chi^2(3,438) = 7.74$, p = .05) and visuo constructive abilities ($\chi^2(3,434) = 7.73$, p = .05). In all four cognitive domains, performance significantly declines with larger WM lesion load (Fazekas score 2), while low lesion load (Fazekas score 1) was not associated with a decline in cognitive performance.

Fazekas groups significantly differed in measures of memory complaint ($\chi^2(3,796) = 18.8$, p < .001) and complaint on executive function ($\chi^2(3,796) = 39.88$, p < .001). For both measures, persons with low lesion load (Fazekas score 1) worried significantly less than healthy persons (Fazekas 0) and persons with larger lesion load (Fazekas score 2, 3).