Association of cerebral small vessel disease burden with brain structure and cognitive and vascular risk trajectories in mid-to-late life

Michelle G Jansen1,2, Ludovica Griffanti3,4, Clare E Mackay3,4, Melis Anatürk1,5, Luca Melazzini3,6, Ann-Marie G de Lange3,7, Nicola Filippini8, Enikő Zsoldos3,4, Kim Wiegertjes2, Frank-Erik de Leeuw2, Archana Singh-Manoux3,10, Mika Kivimäki9, Klaus P Ebmeier9, Sana Suri3,4

BACKGROUND

- Cerebral small vessel disease (SVD) is a major cause of cognitive impairment
- Controlling vascular risk factors earlier in the lifespan may preserve structural brain health in older ages
- However, little is known about how longitudinal trajectories of risk factors throughout mid-to-old-age associate with later-life SVD burden

We aimed to characterize the associations of total cerebral small vessel disease (SVD) burden with brain structure, trajectories of vascular risk factors, and cognitive functions in mid-to-late life.

METHODS

- 623 subjects from the Whitehall II Imaging Sub-Study with multi-modal MRI (mean age 69.96 SD=5.18, 79% men)
- Imaging data was processed using FSL to acquire measures of grey matter (GM) density and white matter (WM) microstructure
- GLM was used to investigate concurrent associations of SVD burden with GM density and WM microstructure; and whether these associations were modified by cognitive status (Montreal Cognitive Assessment, MoCA)
- Linear mixed effect models in R to investigate associations of SVD burden with up to 25-year retrospective trajectories with vascular risk factors and cognitive performance

RESULTS

Higher SVD burden was associated with:

- Reduced GM density
- Lower fractional anisotropy (FA)
- Higher mean diffusivity (MD)*

FWE corrections were applied, threshold-free cluster enhancement (TFCE) statistics are reported.

*similar results obtained for radial (RD) and axial diffusivity (AD)

- Associations of SVD burden with MD, AD, and RD were more pronounced in individuals with cognitive impairments (MoCA < 26)

Severe SVD burden in older age was associated with:

- Higher mean arterial pressure throughout midlife (β=3.36, 95% CI [0.42–6.30])
- Faster 25-year cognitive decline in letter fluency (β=–0.07, 95% CI [-0.13—–0.01]), and verbal reasoning (β=–0.05, 95% CI [-0.11—–0.001]).

CONCLUSION

- Higher SVD burden related to more pronounced and widespread alterations in GM and WM measures
- Midlife blood pressure (mean age of 48) may contribute to SVD burden 20 years later (mean age 70)
- Individuals with high SVD burden demonstrated slightly steeper rates of cognitive decline
- Together, our findings further emphasize the importance of midlife vascular health to maintain brain structure and function.