

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

Scan for preprint and author affiliations



Michelle G Jansen^{1,2}, Ludovica Griffanti^{3,4}, Clare E Mackay^{3,4}, Melis Anatürk^{3,5}, Luca Melazzini^{4,6}, Ann-Marie G de Lange^{3,7}, Nicola Filippini⁸, Enikő Zsoldos^{3,4}, Kim Wiegertjes², Frank-Erik de Leeuw², Archana Singh-Manoux^{9,10}, Mika Kivimäki⁹, Klaus P Ebmeier³, Sana Suri^{3,4}

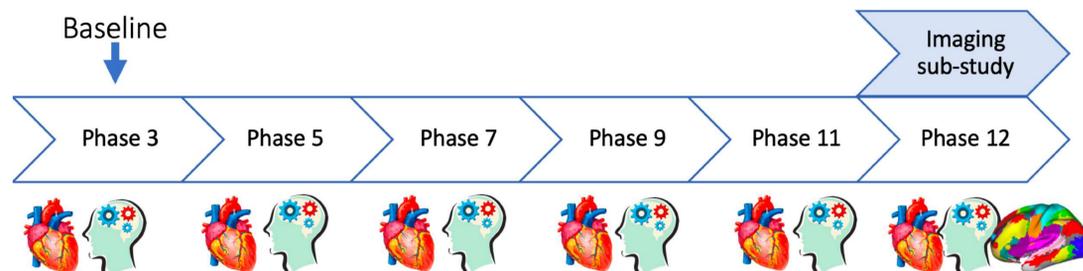
BACKGROUND

- 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)

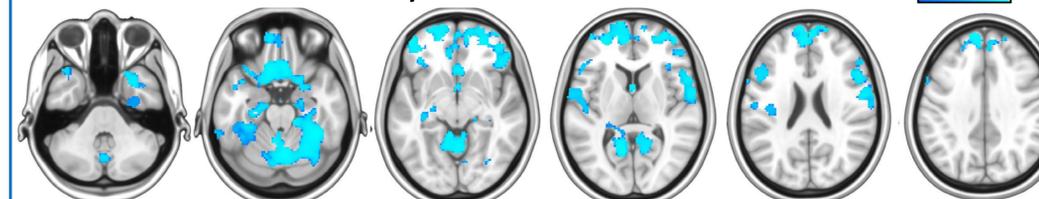


- Total SVD scores were calculated based on STRIVE criteria
- Imaging data was processed using FSL to acquire measures of grey matter (GM) density and white matter (WM) microstructure
- GLM was used to investigate concurrent associations of SVD burden with GM density and WM microstructure; and whether 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

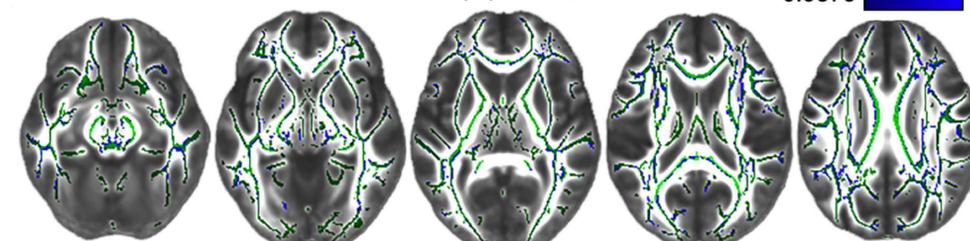
RESULTS

Higher SVD burden was associated with:

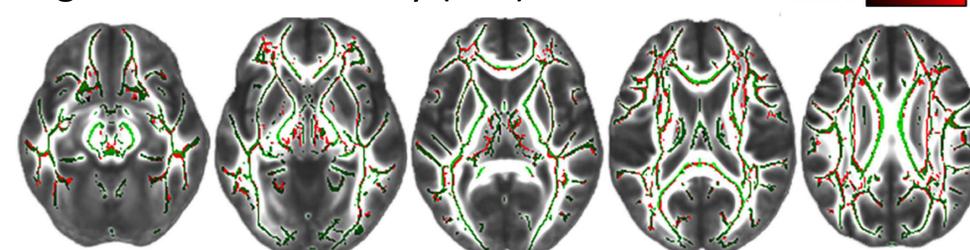
- Reduced GM density



- 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 ($\beta=3.36$, 95% CI [0.42-6.30])
- Faster 25-year cognitive decline in letter fluency ($\beta=-0.07$, 95% CI [-0.13--0.01]), and verbal reasoning ($\beta=-0.05$, 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.**

