Using Ultra-High Field Quantitative MRI and Inflammatory Biomarkers to Improve the Characterization, Diagnosis, and Treatment of Cerebral Small Vessel Disease

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Introduction

Cerebral small vessel diseases (CSVD) are common and potentially severely disabling disorders. They are typically associated with deterioration in gait and balance, mood disorders, and both ischaemic and haemorrhagic strokes. Furthermore, CSVD plays a significant role in vascular cognitive impairment and dementia. However, signs of CSVD are often detected in individuals with no apparent neurological history.

CSVD neuroimaging features are revealed by brain MRI as small subcortical infarcts, white matter hyperintensities of presumed vascular origin, enlarged perivascular spaces, lacunes of presumed vascular origin, cerebral microbleeds, cortical superficial siderosis, brain atrophy and cortical cerebral microinfarcts.

CSVD result from two main processes: arteriolosclerosis and cerebral amyloid angiopathy (CAA). These processes are not easily distinguishable using conventional MRI techniques.

This ongoing study aims to use ultra-high field (7 Tesla) quantitative MRI (qMRI) to measure microstructural abnormalities within CSVD macroscopic lesions and in normal-appearing brain tissue (NABT). The characterization of these CSVD features will be associated with the measurement of inflammation markers in the blood.

Materials and methods

Adult patients admitted or followed at the Department of Neurology of the CHU Liège whose routine MRI scan shows signs of CSVD will be considered. A sample of healthy controls (HCs) will be recruited in a ratio of one HC to three patients. The aim is to recruit approximately 100 participants. A clinical and cognitive assessment will be conducted during a medical consultation.

A single brain scan session will be conducted using a 7T Tesla MRI scanner located at the Cyclotron Research Centre in Liège. The acquisition protocol will consist of T1, FLAIR and MP2RAGE sequences, as well as a multiparameter mapping protocol from which quantitative maps will be extracted. Neurite orientation dispersion and density imaging (NODDI) will also be used. Parenchymal lesions of CSVD will be separated from NABT using an automatic segmentation process, and quantitative values (R1, R2*, proton density, magnetization transfer, magnetic susceptibility, and NODDI) will be extracted from each tissue type.

On the scanning day, a blood sample will be taken for the measurement of the following inflammation biomarkers: GFAP, galectin-3, UCH-L1, S100B, S100A8/A9, CXCL4-PF4, serpin E1, MMP-2, D-dimers, H3cit (NUQ), IL-6, hs-CRP, MPO and NE. These analyses will be conducted at the GIGA cardiovascular laboratory.

Objectives

The aim of this project is to characterize microstructural changes in CSVD parenchymal lesions and NABT in comparison to age-matched controls. We expect to find a correlation between advanced MRI data and blood biomarkers of inflammation to identify potential new biomarkers that could enhance the distinction between CAA and arteriolosclerosis and CSVD severity (in terms of clinical manifestation and MRI lesion load), as well as potentially identifying new targets for future treatment.

Conclusion

This project will use advanced MRI tools and blood biomarker dosages to enhance our understanding of CSVD and potentially find new biomarkers to improve CSVD characterization and treatment. Currently, the project is still in the recruitment and MRI protocol development phase.