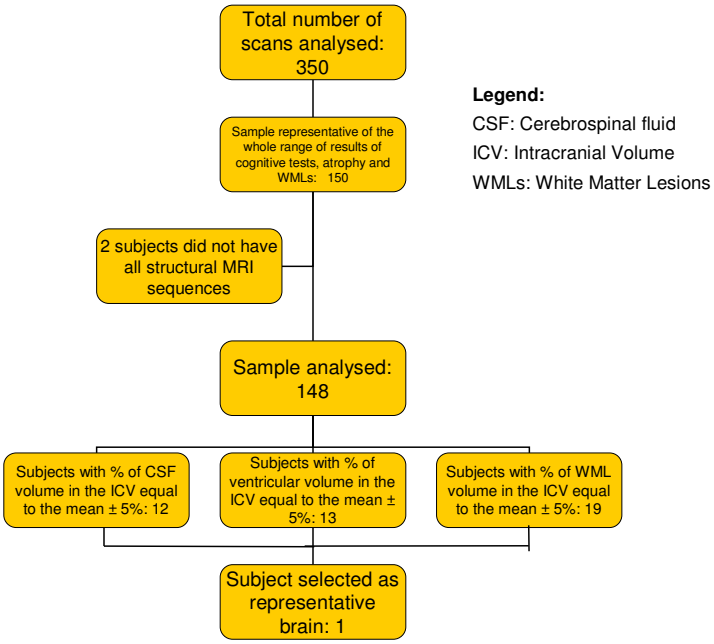
Pilot study to classify white matter lesions by their location in the brain on MRI

The aim of this work is to explore the sub-classifications of white matter lesions by their location in the brain to facilitate the study of their causalities and reduce heterogeneity of findings in future research.

Subjects:

The study was conducted using brain MRI data from the first 350 older subjects of the Lothian Birth Cohort 1936 participants in The Disconnected Mind Study who undertook cognitive testing at age 11 and again at age 70 [1]. None showed signs of dementia, all had MMSE scores above 23.



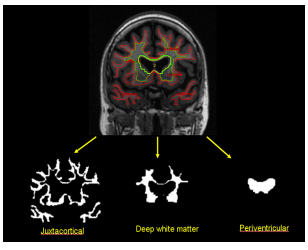
Legend:
CSF: Cerebrospinal fluid
ICV: Intracranial Volume
WMLs: White Matter Lesions

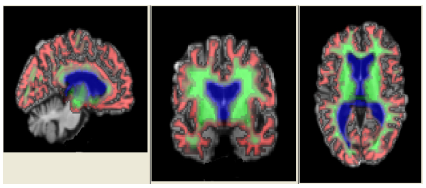
Methods:

After reviewing the distinctions between periventricular (PV) WMLs and deep (D) WMLs in terms of etiology, histopathology, functional correlates and imaging methodologies, we developed a brain atlas to classify WMLs.
In the representative brain we manually delineated three zones:

- PVWMLs: range from 2-4 mm around the ventricular margin to 13 mm from the ventricular surface,
- DWMLs: contiguous to the periventricular areas and extended up to 6 mm from the corticomedullary junction,
- Juxtacortical (JC) WMLs: located within 3-6 mm adjacent to the corticomedullary junction predominantly formed of U-fibres, rather than long fibres.

We used ANALYZE Object Extraction Tool followed by manual editing for brain extraction, and the FMRIB software library algorithms FLIRT and FNIRT [2] for linear and non-linear registration respectively.

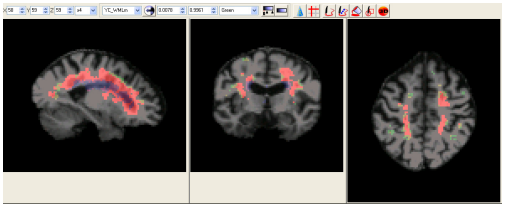




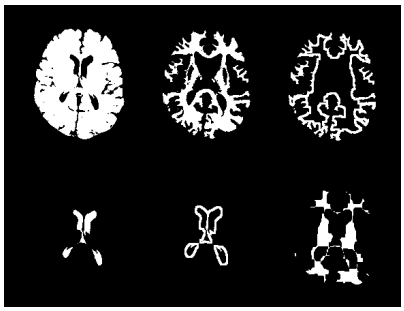
Juxtacortical, Deep and ventricular/Periventricular boundaries manually delineated in our representative brain (left) and sagittal, coronal and axial central slices of the representative brain, linearly registered to the MNI152 standard brain, showing these areas mapped on it after the registration (right).

We applied this classification to WML masks obtained from 20 elderly subjects and evaluated the results.
We also segmented the WMLs in the sample following the same criteria using an in-house software developed in MATLAB which uses morphological (erosion and dilation) and binary operations to derive masks of the PV, D and JC areas for each subject out from the masks of the brain tissue and white matter.

Results:



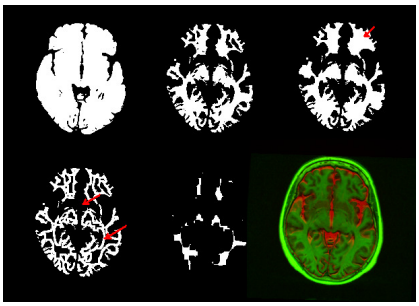
Result of mapping the manually delineated areas of our representative brain to the WMLs segmented in one of the 20 subjects used to test the atlas-based approach.



From top-left to bottom-right, axial masks of:
Brain tissue, white matter, juxtacortical areas, ventricles, periventricular areas and deep white matter areas obtained automatically using the in-house developed software.

Similar sequential morphological operations can not be applied automatically in lower axial slices. Red arrows show misclassified areas. Manual editing is required.

The fused T1-T2 weighted image mapped in green and red respectively helps visualising the errors.



Discussion:

These subdivisions will allow us to explore whether there might indeed, be different mechanisms for causing WMLs in different locations in the brain or if they all arise from the same mechanism, and hopefully it will contribute to reduce the heterogeneity of WML findings in future research.

Masks obtained semi-automatically deliver the best results. More reliable automatic non-linear registration methods are worth exploring if a fully automated atlas-based approach is going to be used as some overlap in the subdivided masks was observed.

Summary:

We have developed an atlas of the human brain that will help to classify the lesions commonly seen in the white matter (the wiring) of the brain of older people. The brain atlas was divided according to the type of white matter and its location so that we can study the biological causes of the lesions. This classification was applied to the brains of 20 elderly subjects to evaluate the results. We hope that this new analysis will help us understand the discrepancies in previous studies of white matter lesions.

References:

[1] Deary IJ, et al. BMC Geriatr 2007;7:28. [2] FMRIB, Oxford, UK; http://www.fmrib.ox.ac.uk.

SFC Brain Imaging Research Centre

M.C. Valdés Hernández[1,2,3], M.R. Jackson[1,4], S. Muñoz Maniega[1,2,3], N.A. Royle[1,2,3], I.J. Deary[2,3], M.E. Bastin[2,3,5] and J.M. Wardlaw[1,2,3]
[1] SFC Brain Imaging Research Centre. Department of Clinical Neurosciences, University of Edinburgh, Edinburgh, UK.
[2] Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, UK
[3] SINAPSE collaboration, UK
[4] NHS Scotland, UK
[5] Department of Medical and Radiological Sciences, University of Edinburgh, Edinburgh, UK