Regional brain atlas for assessment of white matter hyperintensities

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Summary

This dataset contains a reference brain-extracted T1-weighted structural magnetic resonance image, representative of a normal brain from an individual in the first half of the 80th decade of life (70 to 75 years old), and the correspondent binary masks of the regions identified as relevant for studying white matter hyperintensities.

Background and rationale

White matter hyperintensites (WMH) are a common feature in structural MR scans of older people. Therefore, their presence, form and severity provide a valuable information for characterising aging and study the pathophysiology of geriatric disorders. Some methods, often considered as the best alternative, subdivide WMH into periventricular (PVWMH) and deep (DWMH), but this dichotomization itself is still in debate.

Previous studies (related in [1]) demonstrated that complementary rules were needed for classifying PVWMH and DWMH, because irregular PVWMH tend to coalesce with DWMH in advances stages and are more likely to be determined by chronic haemodynamic insufficiency, whereas DWMH are more likely determined by small vessel diseases. In addition, WMH sited close to the corticomedullary junction are thought to be related to a distinct pathological process, and may have different functional significance compared to WMH elsewhere due to predominantly being formed of U-fibres, rather than long fibres. Kim et al. [1] suggested a new sub-classification of WMH that might have better aetiological and functional relevance. We initially attempted to adopt the classification system proposed by Kim and colleagues, however it became clear that this would not be feasible for a number of reasons:

- it is not possible to segment the brain with the level of precision required using the software packages commonly used nowadays to draw regions of interests (e.g. Analyze™ 12.0, MRIcron, Mango),
- due to gyral folding and the complex nature of brain architecture it is very difficult to demarcate a zone of uniform thickness around the corticomedullary junction or around the ventricles
- in older brains the minimum distance from the ventricular surface to the corticomedullary junction required to accommodate the four regions described (20mm) is often not present

We, then, decided to modify the scheme to overcome these difficulties and make an atlas to apply the new sub-classification to segmented areas of WMH in scans of older people.

The representative brain

Sample that provided data

The Lothian Birth Cohort 1936 (LBC1936) [2] provided the sample for selecting the representative brain template. The LBC1936 is a large study of older community-dwelling adults, mostly living in the Edinburgh and Lothians area of Scotland, all of whom were born in 1936 and most of whom participated in the Scotland Mental Survey of 1947 at age 11 years. At ~70 years old, study participants (N = 1091) underwent an initial wave of cognitive and physical testing, from 2004-2007. Approximately three years later, 866 underwent a second wave of tests at mean age 72.8 years (SD = 0.7) which also involved a brain MRI scan [3]. The brain scan was undertaken by 700 individuals, but only 664 participants provided useable MRI data for the purpose of generating a cohort-specific age-relevant brain template. Of these, 664 individuals' scans, 147 were excluded due to (one or more of) the following reasons: old infarct lesions, cysts, bad quality of the scans, aneurisms, big meningeal calcifications or any anomaly in the dura matter and/or considerable mineral deposition, leaving a total of 517 image datasets. The Multi-Centre Research Ethics Committee for Scotland (MREC/01/0/56) and Lothian Research Ethics Committee (LREC/2003/2/29) approved use of the human subjects in this study, and all participants provided written informed consent.

Selection of the representative brain

For the 517 LBC1936 Study participants considered to have the features considered normal in this population, the volumetric measurements of the parameters that are more related with the brain shape, size and degree of abnormalities, were obtained as per [3]. These parameters were:

intracranial volume (ICV), cerebrospinal fluid (CSF), ventricular space, and white matter hyperintensities (WMH). For each individual, the atrophy measures were normalised by head size, and the WMHs were normalised by brain tissue volume. Then, the average and standard deviation of WMH and atrophy volumes for this cohort was calculated. These were used to calculate the Mahalanobis distance (Md) [4] and the scans were ordered in ascending Md value.

The Mahalanobis distance is a distance measure based on correlations between variables by which different patterns can be identified and analysed. It differs from the Euclidean distance in that it takes into account the correlations of the data set and is scale-invariant, having a multivariate effect size. The rationale of using Md was as follows: If each WMH and atrophy volumes are subtracted from the mean, we will know how far (or near) are these values from the one considered characteristic for this group. In modular terms and considering the variance of each parameter we will have that the normalised distance of the parameter x for any subject is equal to (mean-x)^2/variance. If we, now, add this normalised distance calculated for each parameter (e.g. % of WMH load in brain tissue, % of CSF in the ICV…), we will have a value that indicates how much, in general, a given scan differs from the hypothetic one that will have the characteristic values of these parameters for this cohort.

Mathematically, being:

X1 = % of WMH volume in Brain Tissue and m_{X1} and σ_{X1} the mean and standard deviation (respectively) of all X1 values

X2 = % of CSF volume in ICV and m_{X2} and σ_{X2} the mean and standard deviation of all X2 values

X3 = % of lateral right ventricle volume in ICV and m_{X3} and σ_{X3} the mean and standard deviation of all X3 values

X4 = % of lateral left ventricle volume in ICV and m_{X4} and σ_{X4} the mean and standard deviation of all X4 values

X5 = % of 3rd ventricle volume in ICV and m_{X5} and σ_{X5} the mean and standard deviation of all X5 values

X6 = % of 4th ventricle volume in ICV and m_{X6} and σ_{X6} the mean and standard deviation of all X6 values

$$Md^2 = \frac{(m_{X1} - X1)^2}{\sigma_{X1}^2} + \frac{(m_{X2} - X2)^2}{\sigma_{X2}^2} + \frac{(m_{X3} - X3)^2}{\sigma_{X3}^2} + \frac{(m_{X4} - X4)^2}{\sigma_{X4}^2} + \frac{(m_{X5} - X5)^2}{\sigma_{X5}^2} + \frac{(m_{X6} - X6)^2}{\sigma_{X6}^2}$$

Generalising the former equation:

$$Md^2 = \sum_{i=1}^{n} \frac{(m_{Xi} - Xi)^2}{\sigma_{Xi}^2}, \qquad (n=6)$$

The representative brain corresponded to the scan with lowest Md. The acquisition parameters of the T1-weighted sequence, and the process of extracting the volumes are described in detail in [3].

Generation of the white matter regional masks

The regional masks were generated manually using the Object Extractor Tool in Analyze™ 12.0 (visit http://analyzedirect.com/ for reference). The white matter of the representative brain was segmented in three zones:

Periventricular (PV) regions: range from 2-4 mm around the ventricular margin to 13 mm from the ventricular surface. The WMH in these regions are more likely to be haemodynamically determined as they would largely represent lesions related to cerebrospinal fluid leakage and hypoperfusion, but can be considered ischemic and associated with the disruption of long white matter tracts.

Deep (D) regions: are located contiguous to the periventricular areas and extended up to 6 mm from the corticomedullary junction. DWMH are associated with small vessel disease and considered ischemic lesions that cause disruption of the long white matter tracts.

Juxtacortical (JC) regions: are located within 3-6 mm adjacent to the corticomedullary junction. The juxtacortical WMLs are a subclassification from the commonly known DWMH that might have different vascular aetiologies because juxtacortical white matter regions have a dual blood supply and the majority of juxtacortical WM regions consist of U-fibers rather than long fibers.

Figure 1 shows a T1-weighted slice of the representative subject with the manual delineation of the white matter into these three areas. All image files are in Analyze 7.5 format. If these image data are converted to NIfTI-1, care must be taken on the orientation and origin.

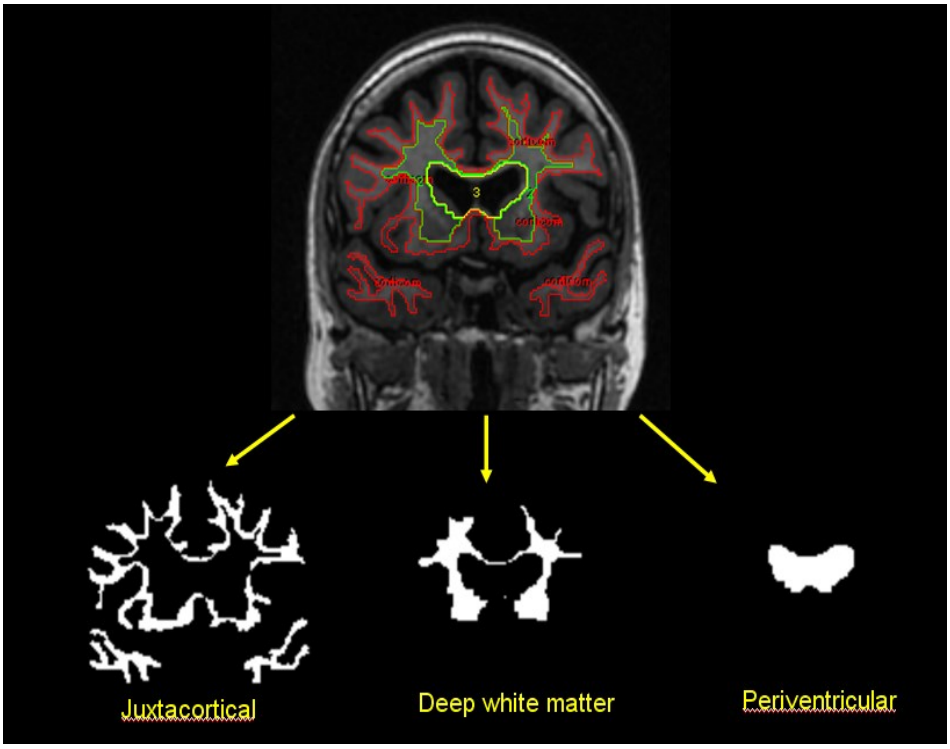

Figure 1. Mid-coronal view of the white matter regional atlas for studying WMH.

Dataset

In addition to this document, the present dataset contains the following files:

1) 13709_reference_brain.hdr/img : Brain-extracted T1-weighted image of the age-wise cohort-specific representative brain in Analyze 7.5 format
2) DeepWM_axial.hdr/img : Binary mask of the deep white matter region
3) PV_axial.hdr/img : Binary mask of the ventricular and periventricular region
4) Yuxtacortical_axial.hdr/img : Binary mask of the yuxtacortical region
5) WM_ROIs.obj : Analyze Object map of the three white matter regions

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