Assessment of brain tissue changes in the normal elderly: Insights from global and regional MTR analysis

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Introduction:

The normal aging brain is commonly characterized by atrophy and by the accumulation of so called white matter hyperintensities (WMH). Histopathological studies suggest that WMH may reflect a wide range of tissue damage which is also related to their size (1). A recent long-term follow-up study shows that more severe WMH may actually extend quite rapidly (2). Whether this progression develops from focal spreading of damage or is a result of "surfacing" of diffusely underlying white matter abnormality is still not resolved.

The magnetization transfer ratio (MTR) is known as a sensitive measure to probe tissue changes which are not detectable on conventional MRI. Previous MTR studies in the aging brain have used a histogram analysis to assess global tissue changes. However, as regional information gets lost in such type of analysis, the contribution of these studies to our understanding of WMH development is only limited. We therefore have performed a regional MTR study in normal elderly to address this issue in more detail. In addition, we have performed a histogram analysis to compare the findings with results from a global analysis.

Material and Methods:

This cross sectional study was performed in 198 elderly persons (136 f, 62 m, mean age 70 years) with normal neurological status and with no history of general or neuropsychiatric diseases. MRI was performed on a 1.5 Tesla scanner (Intera, Philips Medical Systems, Best) with a protocol that included a T2-weighted fast spin-echo sequence and a FLAIR sequence. MTI was performed with a spoiled 3D gradient echo sequence (TR=26ms, TE=4ms, FA=20°, THK = 3 mm, FOV=250 mm, matrix=256x256) that was performed with and without a binomial MT saturation pulse (1-2-1). Assessment of WMH and the definition of normal appearing white matter (NAWM) and grey matter (NAGM) were based on the FLAIR scans. First, WMH were specified and graded into absent, punctuate, early confluent, and confluent. Then, the volume of the WMH was measured semiautomatically on a workstation. For the regional MTR analysis, we used predefined templates to position the ROIs in similar locations of normal-appearing brain tissue. Great care was taken not to overlap with any of the outlined WMH. The ROIs were converted into WMH mask and the MTR was calculated for every WMH. MTR histogram analysis was performed both for the entire brain tissue and for the brain tissue after subtraction of the WMH masks. To reduce unwanted partial volume effects, the WMH masks were eroded by 1 pixel for the WMH analysis and dilated by 1 pixel for the whole brain histogram analysis. Non brain tissue was removed with a brain segmentation tool to obtain histogram representing brain tissue only. The following histogram parameters were used for further analysis: mean MTR, standard deviation, MTR peak position, and MTR peak height.

Results:

We found significant differences in the MTR throughout the NAWM. The individuals` age showed a modest but significant effect on the MTR of normal appearing brain tissue ($p<0.01$). The highest age dependency was found for the frontal and parieto-occipital cortex, where we observed a relative annual MTR decrease of 0.16% and 0.21%, respectively ($p<0.01$). In all white matter regions except the splenium of the corpus callosum we also observed significant increases of the standard deviation of the MTR with age ($p<0.01$).

The mean MTR of WMH was about 10% lower than that of average NAWM. We found a constant albeit weak decrease of the MTR with increasing WMH severity which was significant by one-way ANOVA ($p=0.02$). In parallel, univariate linear regression analysis also showed a significant negative association between the lesional MTR and the total volume (r=-0.24, $p=0.0016$) and number (r=-0.25, $p<0.001$) of WMH. Age had no effect on the MTR of WMH.

When comparing volunteers with different WMH grading, they did not differ significantly in the mean of all regional MTR values of normal appearing white matter (NAWM), i.e. in global NAWM MTR. Considered individually, however, the MTR of frontal white matter was decreasing ($p=0.044$) and the standard deviation in the corpus callosum ($p=0.041$) was increasing with greater WMH severity. In a linear regression model including age, WMH volume and WMH severity, WMH volume and age turned out as independent predictors of MTR changes in these regions. No association between WMH severity and regional MTR was seen in cortical and subcortical grey matter structures.

Whole brain histogram analysis revealed that the peak position was related to age and WMH volume ($p<0.0001$). After segmenting the WMH mask from the histogram, only the age effect remained, which became additionally significant for the relative peak height.

Conclusion:

This study shows that MTI is a valuable technique for the assessment of tissue damage associated with WMH and concurrent changes of the ageing brain. In contrast to other white matter disorders like MS, the severity of tissue destruction in WMH appears relatively mild but increases with lesion size. Our data also supports the concept of a focal origin of WMH. Distant effects of WMH are seen only in the frontal lobes and in the corpus callosum while the remaining white matter appears to alter with ageing per se. Although the MTR histogram is sensitive to age and WMH volume, these insights can not be derived directly from a histogram analysis because it can not differentiate between regional and diffuse effects. Nevertheless, the histogram analysis appears sensitive enough to detect WMH related changes and, in agreement with the regional analysis, the histogram of brain tissue without WMH also indicates that structural changes in normal appearing brain tissue are related to aging only.

References:

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