Regional Quantification of White Matter Hyperintense Lesions and Its Association with Age and Cognitive Impairment

Y-F. Chen[1,2], H. Wang[1], Y. Chu[1], O. Nalcioglu[1], M-Y. Su[1]

[1]Tu & Yuen Center for Functional Onco-Imaging, University of Califonia, Irvine, Irvine, CA, United States, [2]Dept. of Medical Imaging, National Taiwan University Hospital, Taipei, Taiwan, Taiwan

Purpose

Studies of the relationship between white mater hyperintensities (WMH) and cognitive impairment have found conflicting results [1-2]. In most prior studies the severity of WMH was assessed qualitatively (for periventricular and subcortical WMH) or semiquantitatively (for subcortical WMH). In cases with severe WMH, the hyperintensity may diffuse from periventricular into subcortical regions without differentiable boundary. In this study, we developed a quantitative method to measure the volume of total WMH based on signal intensity histogram. The analysis was performed separately in different brain lobes. The obtained regional WMH volumes were correlated with age as well as cognitive function in subjects with Alzheimer's disease (AD), mild cognitive impairment (MCI), and healthy normal controls (NC).

Methods

Subjects were identified from the demented cohort and the successful aging program in the Alzheimer's Disease Research Center at our institute, including 27 AD patients (76 ± 6 years), 15 MCI subjects (74 ± 7 years) and 14 NC (75 ± 4 years). All patients had undergone an MRI scanning and a neuropsychological test battery. MRI studies were performed on a Phillips Eclipse 1.5 Tesla scanner. The axial fluid-attenuated inversion recovery (FLAIR) images were used for analysis. The acquisition parameters were TR=6000ms, TE=96ms, TI=1800 ms, field of view=22cm, slice thickness= 6mm, gap= 1mm, and matrix=256x192. An in-house Matlab-based program (ROITOOL) was developed for the quantitative analysis. The original axial images along with the reconstructed sagittal and coronal images were displayed together. According to the major landmarks identified on all 3 planes, the frontal, temporal, and parieto-occipital lobes could be easily separated. In each lobe, an ROI containing all WMH was roughly outlined, and the program generated a signal intensity histogram based on all pixels included in that ROI. The threshold was adjusted to automatically define the border of WMH (examples shown in Fig.1). The pencil thin hyperintensity around the ventricles was normal, and excluded in the manual ROI.

The age among three groups was compared using ANOVA, and the gender distribution was compared using the Kruskal-Wallis test. The group difference in the WMH was assessed with ANOVA and Bonferroni correction. For cognitive performance, the scores of Mini-Mental State Examination (MMSE), Boston Naming Test (BNT) and CERAD Category Fluency Test (CCFT) were used in the correlation analysis. To adjust the age effect, partial Pearson's correlation analysis was used to examine the relationship between neuropsychological performances with each regional and the total WMH volumes. All statistical tests were regarded as significant at $p < 0.05$.

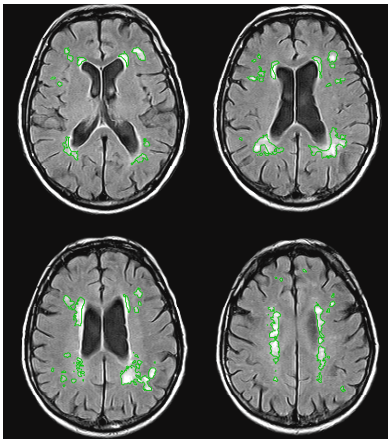

Fig 1. Illustration of total WMH on FLAIR images of one 83 years old normal control.

Results

Age and gender distributions were comparable among three groups. The AD patients had the greatest total WMH volume, followed by MCI, and the NC had the lowest lesion volume; however, after Bonferroni correction the difference did not reach a significant level. Taking all 3 groups together, there is a positive correlation between the frontal WMH volume and age (r = .034, p = .01). The correlation with cognitive scores was performed separately in each group, adjusting for the age effect. Figure 2 shows the partial linear correlation analysis between the performance score of BNT with the total WMH volume in the AD group. The higher WMH was correlated with lower BNT scores (significant, r = - .57, p = .03). In normal controls, a negative relationship was also found between the BNT score and the total WMH (r = - .67, p = .03), and also the frontal WMH volume (r = - .73, p = .01). The correlation analysis results are summarized in Table 1, and those reaching a significance level are highlighted.

Table 1. Partial correlation coefficients between cognitive scores and regional and total WMH volumes after controlling for age in AD, MCI and HC groups

		AD (n = 27)			MCI (n = 15)			NC (n = 14)		
WMH volume		MMSE	BNT	CCFT	MMSE	BNT	CCFT	MMSE	BNT	CCFT
Temporal lobe	*r*	- .005	- .45	- .33	--	--	--	.18	- .15	- .01
	p	.98	.11	.23				.59	.67	.97
Frontal lobe	*r*	- .03	- .36	- .17	.25	.00	- .08	.46	**- .73**	- .14
	p	.90	.20	.54	.41	.99	.79	.15	**.01**	.69
Parietal lobe	*r*	- .13	- .5	- .35	.33	.12	- .05	.43	- .26	.49
	p	.43	.07	.20	.27	.70	.88	.18	.44	.13
Total	*r*	- .06	**- .57**	- .34	.30	.07	- .06	.49	**- .67**	.01
	p	.78	**.03**	.22	.32	.82	.84	.12	**.03**	.97

Discussion

The significance of WMH in normal aging and the development of dementia is unclear [1-2]. In this study, we found that age was positively associated with frontal WMH volume, which was consistent with prior studies [3], suggesting that age is a major risk factor of WMH and that the frontal lobe is predominantly involved. The negative correlation between the frontal WMH volume and BNT score among healthy elderly supports the role of frontal lobe in naming task. The white matter lesions in the frontal lobe might deteriorate the naming ability in healthy elderly. However, no significant relationship was observed between the frontal WMH volume and BNT score in either AD or MCI group. This might be due to the damage of neural circuit originating from the frontal lobe during the neurodegenerative processes, and the naming disability might be attributed to pathological conditions in multiple brain regions rather than confining within the frontal lobe. Another interesting finding is that the total WMH volume is associated with the BNT score among healthy elderly and AD patients, but not among MCI individuals. The reasons for such dissociative patterns during the continuum from normal aging to AD via MCI are not clear. One possible explanation is the wide variation of possible pathological conditions which may lead to MCI, and the relative small case number in our MCI group. As some MCI would go on to develop AD and some would remain stable, it is possible that the WMH might play a role in predicting disease progression. In summary, we have developed a user-friendly analysis tool for regional quantification of WMH. It may facilitate investigation of the role of regional WMH during the development of early AD.

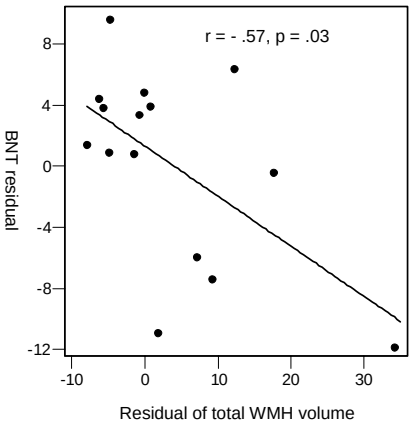

Fig 2. Partial regression plots depict the negative correlation between the total WMH volume and the BNT score in AD patients.

References:

[1] Barber et al. J Neurol Neurosurg Psychiatry. 1999; 67:66-72. [2] De Groot et al. Ann Neurol. 2002; 52:335-341. [3] Breteler et al. Neurology 1994; 44:1246-1252.