Distribution and Progression of Cerebral White Matter Hyper-intensities per Flow Territories in a Large Population of Elderly Subjects

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Introduction

Cerebral white matter hyperintensities (WMHs) are commonly seen in normal aging, dementia and late-onset depression. The presence of WMHs in middle aged to old individuals is abundant and lacks discriminating power for the identification of disease. It is now known that, besides increasing age, cerebrovascular diseases are associated with the presence and severity of WMH in the brain. The purpose of this work was to investigate the spatial density and the progression of the WMH in respect to flow territories (FTs) in a large scale longitudinal study on elderly subject with or at risk for vascular disease.

Material and Methods

Subjects were recruited for a multicenter study the PROspective Study Of Pravastatin in the Elderly at Risk (PROSPER) [1].The sample included 527 non-demented Dutch elderly aged between 70-83 years with preexisting vascular disease or at risk of developing this condition. Subjects have been followed for a period of approximately 3 years. MRI was performed on a clinical MR-system operating at a 1.5 Tesla field strength (Philips Medical Systems, Best, The Netherlands). Dual fast spin-echo images (TE 27/120ms, TR 3000 ms, echo train length factor 10, 48 contiguous 3 mm slices, matrix 256x256, FOV 220, acquisition percentage 80% scanning time 6.09 min) were obtained in all patients at baseline and follow-up (mean interval: 2,5 years). The WMH were semi-automatically segmented using in-house software as described in [2].

A standardized high resolution T1 weighted image (resized and co-registered to the Montreal Neurological Institute brain template space) was used to delineate manually FTs of the anterior (ACA), posterior (PCA) and medial (MCA) cerebral artery following the Tatu atlas [3]. This delineation was performed by an a trained operator and was done only once in the template image. Because the Tatu's flow territories description covers mainly the cerebral cortex and not the white matter, we generated 3D distance maps to each FT region in order to extend the FT territories to cover the whole brain. Each brain voxel was assigned to the closest (3D distance) FT region. Using automatic affine-12 parameters image registration, the FT template was thereafter automatically mapped for every subject, on previously identified WMHs in both base-line and follow-up scans. After visual quality control of the registration outcome we excluded all the subjects for which the template match was not found satisfactory enough (See Table 1 for the number of remaining subjects). We considered peri-ventricular lesions and sub-cortical lesions separately.

Table 1: WMH volumes in FT

All volumes are given in ml. mean (SD). BL=base line; FU=follow-up Δ=FU - BL ; *: Significant results (P<0.05) Mann-Whitney U test

WMH		subcortical				Periventricular			
mean volumes	**nr. of subjects**	**TOT**	**ACA**	**MCA**	**PCA**	**TOT**	**ACA**	**MCA**	**PCA**
male (BL)	259	0.922 (1.601)	0.140 (0.364)	0.328 (0.543)	0.020 (0.050)	4.792 (10.670)	0.681 (1.473)	0.748 (2.788)	0.232 (0.645)
male (FU)	224	1.117 (1.684)	0.157 (0.377)	0.405 (0.597)	0.030 (0.063)	6.082 (10.903)	0.719 (1.343)	0.989 (2.829)	0.340 (0.732)
female (BL)	198	1.362 (1.947)	0.185 (0.368)	0.493 (0.719)	0.034 (0.093)	5.029 (10.940)	0.687 (1.455)	0.793 (2.847)	0.303 (0.848)
female (FU)	161	1.913 (2.878)	0.267 (0.526)	0.672 (1.046)	0.037 (0.087)	7.470 (11.789)	1.063 (1.821)	1.184 (3.214)	0.463 (0.916)
Δ male	191	0.263 (0.930)	0.026 (0.207)	0.096 (0.379)	0.016 (0.071)	2.277 (4.325)	0.161 (0.618)	0.388 (1.346)	0.151 (0.430)
Δ female	137	0.638 (1.712)	0.107 (0.333)	0.190 (0.531)	0.009 (0.085)	2.221 (4.468)	0.325 (0.757)	0.442 (1.999)	0.140 (0.380)
Male vs. female comparison *(p-values)*									
BL	457	P=0.007*	P=0.027*	P=0.010*	P=0.646	P=0.327	P=0.061	P=0.558	P=0.111
FU	385	P=0.001*	P=0.000*	P=0.008*	P=0.142	P=0.019*	P=0.011*	P=0.248	P=0.017*
Δ	328	P=0.050	P=0.014*	P=0.737	P=0.960	P=0.553	P=0.017*	P=0.493	P=0.951

We assessed the volume and progression of periventricular and subcortical WMH volume between baseline (BL) and follow up data(FU) for each FT and investigated possible differences between males and females using Mann-Whitney tests.

Results and Conclusion

The outcome of our volumetric analysis in FTs is summarized in Table 1. Our comparison of WMH volume in male and female revealed that women had significantly higher lesion volume, both subcortical and periventricular, in the ACA, compared to men, in both baseline and follow up data. Subcortical lesion volume in MCA was also significantly higher in female participants. Furthermore, in females, the periventricular WMH load of the ACA and PCA was significantly higher in the follow up data, compared to baseline.

In a direct gender comparison of the WMH volume progression between baseline and follow up, females had a significantly higher progression of subcortical and peri-ventricular WMH volume load in the ACA, compared to men.

We conclude that in females, compared to males, the ACA plays an important role in the etiology and progression of WMHs. In future studies, the clinical relevance of the ACA for aging and WMH progression in females has to be explored further. The associations of these volumetric findings with the clinical data are under investigation.

References

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