Blood Volume of White Matter Hyperintensities in the Elderly Brain

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Introduction

Hyperintense white matter (WM) lesions are frequently found in the elderly brain on T2-weighted MRI and may contribute to age-related cognitive decline. In the early stages, two types of lesions are generally recognized: small, focal hyperintensites in the deep WM (dWMHs) and lesions adjacent to the ventricles (pWMHs). The goal of this study is to quantify the blood volume (vb) in pWMHs and dWMHs in the elderly brain using dynamic contrast enhanced (DCE) MRI. We hypothesize that ischemic small vessel injury may play an important role in dWMH formation, while demyelinating/gliotic processes may contribute more to pWMHs.

Methods

20 elderly subjects (12 male, 8 female; 71 ± 6 yrs) with no history of diabetes, uncontrolled hypertension or vascular disease were enrolled (Table I). MR data were obtained on a 7T Siemens MAGNETOM instrument. High resolution T1-weighted (IR-MPRAGE) and T2-weighted fluid-attenuated IR (FLAIR) images were acquired. Five full-volume R1 (= 1/T1) maps centered on the lateral ventricles were prepared before and 12, 31, 45 and 57 min after contrast reagent (CR) injection using variable inversion time MPRAGE acquisitions. R1 maps and FLAIR images were coregistered to the high resolution IR-MPRAGE image (FSL).

vb maps were prepared by voxelwise fitting of R1 values in tissue and blood to an equation for two-site (transendothelial) water exchange. Binary masks of dWMHs and pWMHs were prepared by segmentation of FLAIR images (Seg3D), which provide excellent conspicuity of lesions. Statistical analyses were performed in Stata.

TABLE 1. Characteristics of Study Participants (n=20)

Characteristic	
Age, yrs	71 ± 6 (59-82)
Women, No. (%)	8 (40)
Education, y	17 ± 3
Mini Mental State Exam	28 ± 2
WM volume, % total intracranial	43 ± 2
Fazekas visual rating score:	
Deep, No. subjects with score > 1	1 (0-2), 3
Periventricular , No. subjects with score > 1	1 (0 -2), 3
WMH volume, mL:	
Deep	0.55 ± 0.49
Periventricular	3.0 ± 2.9

Mean (SD) or median (range), unless otherwise noted

Results

As shown in Figure 1, T1 times were significantly increased in both periventricular (+27%) and deep (+10%) WMHs compared to normal appearing white matter (NAWM). No group or gender differences in T1 times were observed (Fig. 2).

No significant difference in vb was observed in pWMHs compared to NAWM. However, dWMHs showed a 24% reduction in vb compared to NAWM and pWMHs (P= 0.0002 and 0.02, respectively) (Fig. 3). Univariate correlates of vb are shown in Table II.

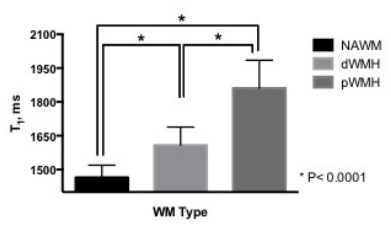

Figure 1. T1 (pre-CR) is significantly increased in both dWMH and pWMH cf. NAWM

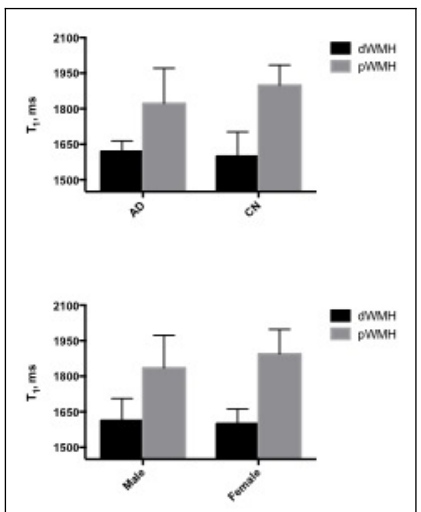

Figure 2. No significant differences in T1 times of dMWHs and pWMHs

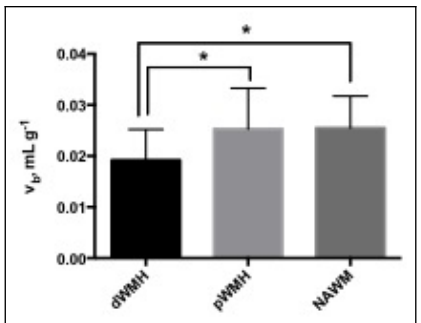

Figure 3. Differences in mean blood volume (vb)

Table II. Univariate correlates of vb in WMHs and NAWM

	v_b (mL g^{-1})	r	P Value[a]
NAWM	0.025 ± 0.006		
Age, yrs		-0.48	0.032
Volume, Total brain[b]		0.24	0.30
dWMH	0.019 ± 0.006		
Age, yrs		-0.25	0.31
Volume[b]			
Total brain		029	0.24
Ventricles		0.093	0.71
pWMH	0.025 ± 0.008		
Age, yrs		-0.17	0.54
Volume[b]			
Total brain		0.33	0.22
Ventricles		-0.48	0.060
Ventricular CR permeability (ΔR_1 min^{-1})		0.51	0.044

(a) Uncorrected; (b) % total intracranial volume

Conclusions

Although further studies will be necessary to confirm these results, we conclude that in elderly patients with minimal vascular risk factors:

Small, focal hyperintensities in the deep WM have T1 times that are significantly increased compared to NAWM, consistent with an increased water:macromolecule ratio. In combination with the observed reduction in intravascular water fraction, these results suggest that dWMHs- at least in the early stages- may represent ischemic damage resulting in edematous tissue with reduced vessel density and/or vasoconstriction.

T1 times are also increased in early pWMHs. However, no discernible difference in vb compared to NAWM is observed. In contrast to dWMHs, mild pWMHs appear more likely to represent areas of periventricular edema with negligible damage to the vessels. The apparent association of vb with CR permeability and ventricular volume (Table II) supports the idea that pWMHs may be related to the integrity of the tissue-fluid interface at the ventricular surface.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the role of vascular changes in the etiology of WMHs; 2) Appreciate the role of advanced MRI techniques in the study of cerebrovascular function.