Phase Sensitive Inversion Recovery improves the detection and the analysis of Virchow Robin spaces in multiple sclerosis brain

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BACKGROUND

Virchow Robin spaces (VRS) are small, interstitial fluid-filled ducts that host small vessels in the subarachnoid space. Even if VRS have been traditionally thought to be a casual MRI finding lacking pathological significance, recent observations have suggested their possible role as MRI marker for various brain pathologies.
Indeed, VRS have been associated with either inflammatory or degenerative MRI parameters. However their involvement in inflammatory brain disorders and the significance of their implication in multiple sclerosis (MS) are still controversial. Discrepancies are probably due to the low number of patients enrolled in the studies, patient age, substantial differences in the MRI methodologies applied, and the strength of the MRI field. Moreover only few and conflicting data are available on enlarged VRS in MS and their association with physical and cognitive impairment in this disease, due to methodological constraints that currently limit their identification and characterization.

OBJECTIVES

We combined 3DT1, PSIR and FLAIR images to study VRS in MS patients and normal controls with the aim to find possible association of VRS with MRI parameters of inflammation or neurodegeneration (brain atrophy) and with physical or cognitive disability.

METHODS

Patients.
Forty-three patients, whose diagnosis was achieved according to the McDonald/Polman's diagnostic criteria, and ten normal controls (NC) were enrolled in the study. Twenty-one patients had a diagnosis if clinically isolated syndrome (CIS) highly suggestive of MS or early relapsing-remitting MS (eRRMS, with disease duration <3 years), 15 had relapsing remitting MS (RRMS), and 7 had progressive MS (PMS). Clinical and demographic features of all the subjects included in the study are summarized in Table 1. All patients underwent clinical (EDSS) and cognitive (Rao's BRB, DKEFS) evaluation, and MRI scan. On the base of literature data, in order to obtain a comprehensive view of VRS number and volume in different disease stages, the patients were selected to comprise a wide range of disease duration (0.33–41.5 years) and disability (Expanded Disability Status Scale (EDSS), range: 1–7.5).

	F/M	Age mean	Disease duration (years)	EDSS
CIS/eRRMS	16/5	36,3 ± 9,3 [17 – 52]	1,0 ± 0,8 [0 – 3]	1,6 ± 0,4 [1 – 2,5]
RRMS	7/8	35,3 ± 9,1 [17 – 55]	8,7 ± 5,9 [0 – 18]	2,2 ± 0,6 [1,5 – 3,5]
PMS	4/3	41,3 ± 11,0 [27 – 56]	13,9 ± 7,4 [8 – 26]	6,0 ± 1,5 [2,5 – 7,5]
Total	27/16	36,9 ± 9,8 [17 – 56]	5,6 ± 7,1 [0 – 26]	2,5 ± 1,8 [1 – 7,5]

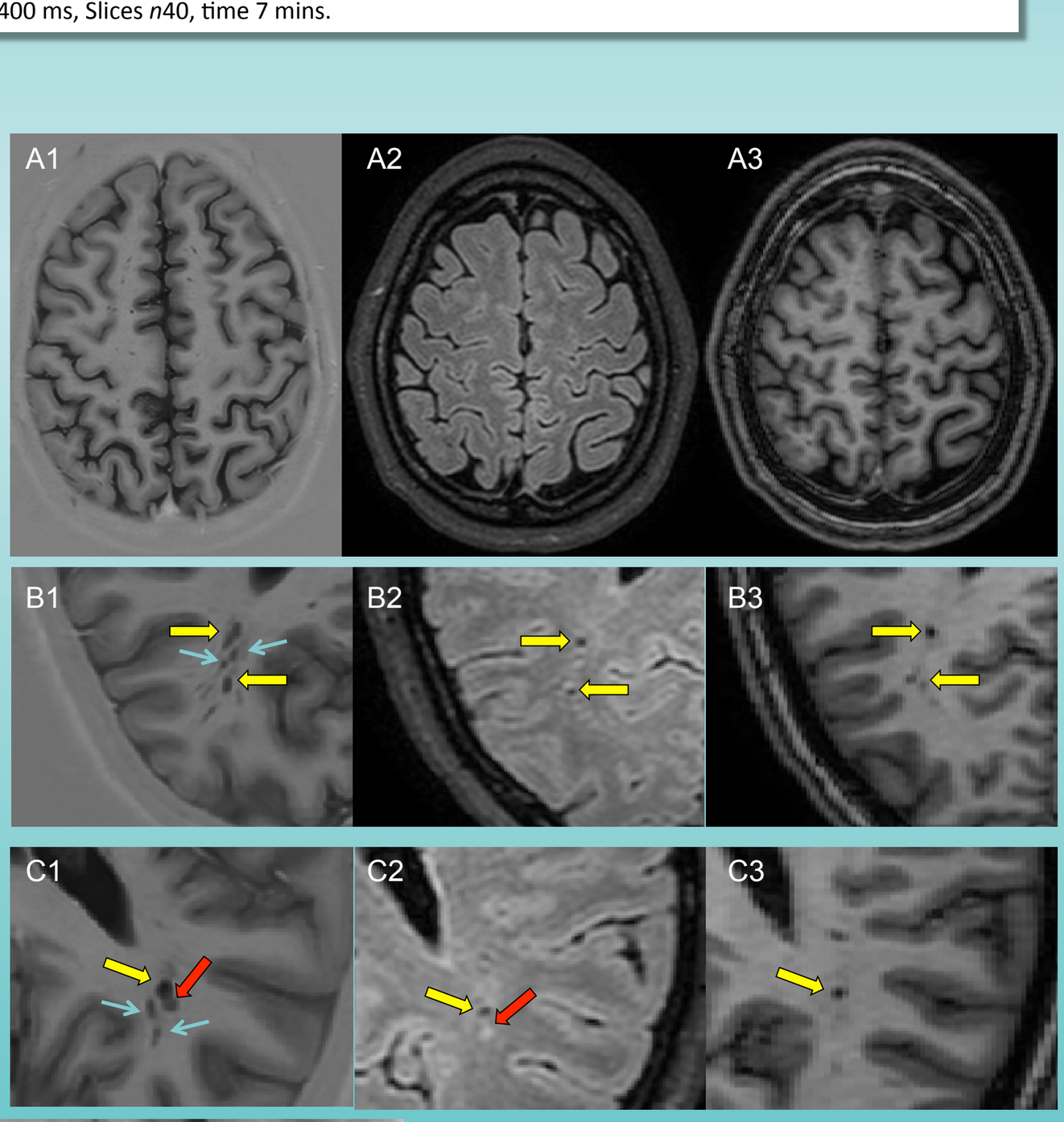
MRI examination.
3DT1, 3DFLAIR and 2DPSIR images were obtained with a 3T Achieva TX system (Philips Healthcare, Best, The Netherlands) with a 64-channel coil, and analysed in parallel by consensus of three examiners. VRS number and volume were calculated by manual segmentation (ITKSNAP). Brain parenchymal fraction (BPF) was assessed by means of Freesurfer.
The acquisition parameters were the following: FLAIR=resolution 0.5x0.5x1; FOV 256x256; TR 4800; TE 300; TI 1656; T1-WEIGHTED: resolution 0.5x0.5x1; FOV 224x224; TR 78; TE 36; ; PSIR: resolution 1×1×3 mm, FOV 230×200 mm, TR 7000 ms, TE 13 ms, TI 400 ms, Slices *n*40, time 7 mins.

RESULTS

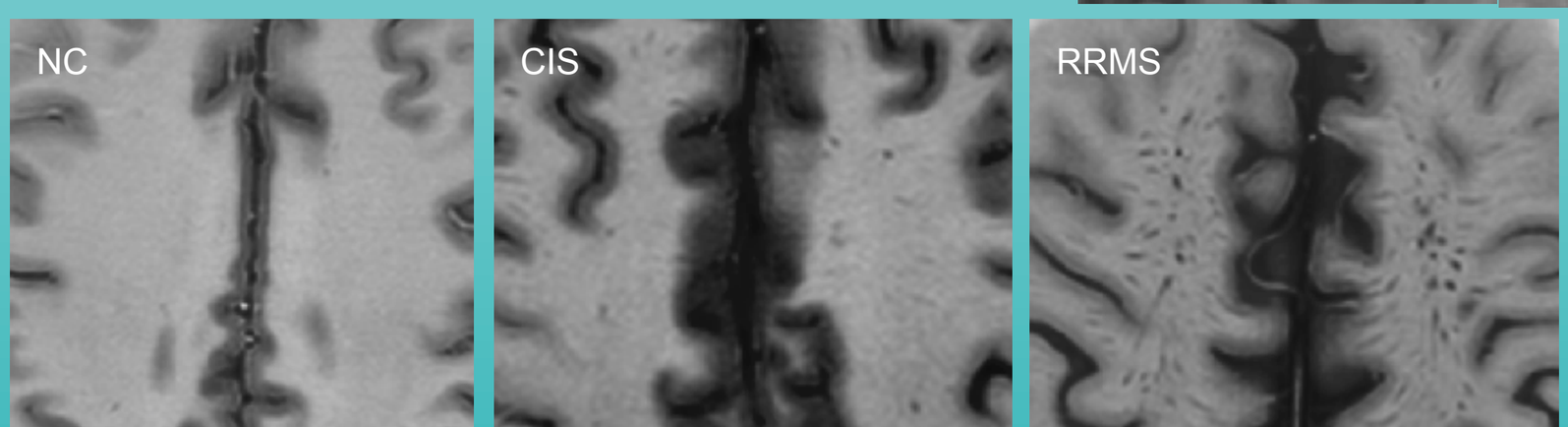
PSIR vs T1 vs FLAIR.
A significantly higher number of VRS was observed on PSIR (mean number 271.26±198.50) images compare to T1 (mean number 120.98±121.62; p<0.001) and FLAIR (mean number 43.34± 38.27; p<0.001). The calculation of VRS volume also gave higher values on PSIR images (mean number 2783.96±2631.70) than in T1 (mean number 490.56±621.38) or FLAIR images (mean number 139.00±2.13) (p<0.001 for both comparisons). T1 was superior to 3D-FLAIR in the analysis of VRS number (p=0.0002) and volume (p=0.00005).

CIS vs RR vs SP vs NC
PSIR disclosed a significant increase in VRS number and volume in CIS/eRRMS compared to NC (p<0.05) and in PMS and RRMS compared to CIS/eRRMS (p<0.05). Interestingly, an higher VRS volume was observed in male compared to female (p<0.05) on PSIR but not on T1 and FLAIR images. (figure 2)

Correlation analysis
On PSIR, but not on T1 and FLAIR images, a correlation between VRS total volume and disease duration was observed (r=0.56). No correlation was found between VRS total number, disease duration and age. VRS volume and number did not correlate with EDSS global and functional system scores.
Mild inverse correlations were found between VRS number and SPART*d* and DKEFS*fs* (r=-0.47 and r=-0.46, respectively).
Finally, no correlation was found between VRS number and volume and the BPF (r=0.2)



▲ **Figure 1**: : T1 (1), FLAIR (2) and PSIR (3) sequences of a CIS (A), a RRMS (B) and a PMS (C) patient.
Yellow arrows: VRS that can be detected from all the three images.
Light blue arrows: VRS observed only in PSIR.
Red arrow: periventricular lesion visible in PSIR and FLAIR sequences



◀ **Figure 2**: PSIR images of the convexity in a normal control (NC), in a CIS and in a RRMS patient.

DISCUSSION

PSIR was superior to T1 and FLAIR in calculating VRS number and volume in the deep grey matter and in the white matter of the convexity. The correlation observed with SPART*d* and DKEFS*fs* suggests that the tissue loss associated with VRS enlargement may contribute to cognitive decline in MS. We observed that male patients had higher VRS volume on PSIR images. This finding is in line with previous literature not only in MS, but also in HC and in people with dementia. Literature and our findings suggest that VRS associate with age, gender, tissue loss and cognitive decline. Thus, increase VRS count and volume could contribute to the progressive reduction in parenchyma brain fraction observed in MS.