Basal ganglia pathology associates with physical and cognitive disability in multiple sclerosis

A study by means of Phase Sensitive Inversion Recovery

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Background

Basal ganglia (BG) atrophy was suggested to play a role in determining cognitive impairment and fatigue in multiple sclerosis (MS). Nevertheless, no data are available in literature about the impact of focal lesions (FL) and Virchow Robin Spaces (VRS) in determining BG atrophy and their role in clinical and cognitive decline. Phase Sensitive Inversion Recovery (PSIR), a MRI sequence with a high signal-to-noise ratio, may help to inspect FL and VRS in the BG of MS patients.

Objectives

We compared T1, FLAIR and PSIR for the detection of VRS and FL in the BG of MS patients, in order to analyse possible correlations between BG volume, FL/VRS in this site and clinical, cognitive and fatigue parameters.

Methods

43 MS patients [21 clinically isolated syndrome (CIS)/early relapsing-remitting (eRRMS), 15 RRMS, 7 progressive (PMS)], and 9 normal controls (NC) were studied. 3DT1, 3DFLAIR and 2DPSIR images were obtained with a 3T MRI and analysed in parallel. BG volume was calculated by means of Freesurfer, while VRS and lesion number/volume/site with manual segmentation (ITKSNAP). All patients underwent clinical (EDSS), cognitive (Rao's BRB, DKEFS) and fatigue (FSS) assessment. The two groups were selected in order to avoid possible age-related bias (no significant differences in mean age)(Table 1).
All patients underwent neurological examination with Expanded Disability Status Scale (EDSS) and neuropsychological assessment with Rao's Brief Repeatable Battery of Neuropsychological Tests (BRB-NT). Patients were considered cognitively impaired if their neuropsychological assessment showed at least 1 test with z-score < -2 or 2 tests with z-score < -1.5.

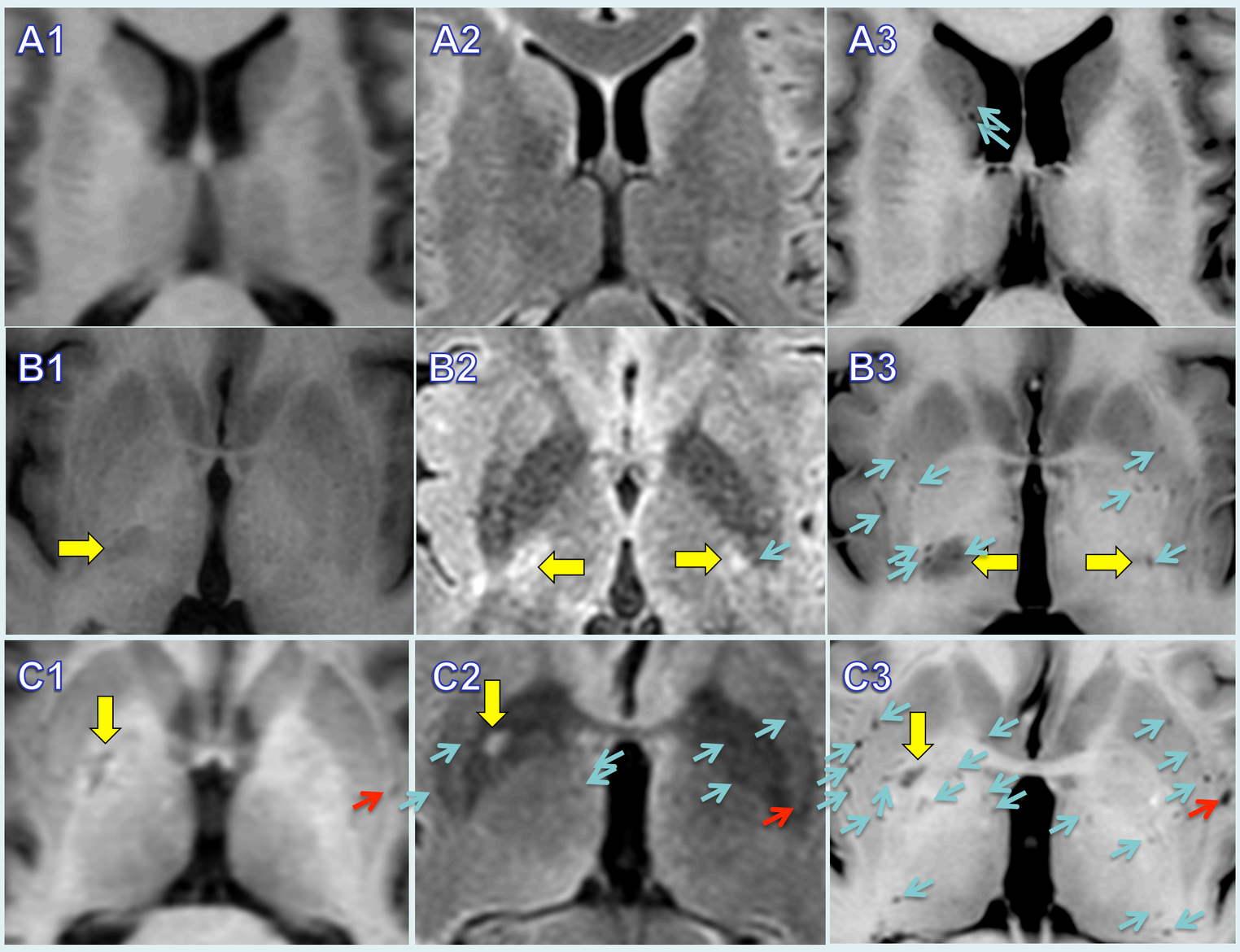

Figure 1: T1 (1), FLAIR (2) and PSIR (3) sequences of a CIS (A), a RRMS (B) and a PMS (C) patient. The yellow arrows indicate lesions in BG, the red and blue arrow indicate the VRS laying in the BG. PSIR sequence allowed the identification of more VRS than FLAIR and T1.

Results

PSIR versus FLAIR versus T1 images.
PSIR disclosed higher VRS number and volume in thalamus, caudatus, pallidus and putamen compared to both FLAIR and T1 ($p<0.001$ for all comparisons).
The volume but not the number of focal inflammatory lesions in the BG was higher when analysed by PSIR compared to FLAIR and T1 ($p<0.02$ for both comparisons).
Both PSIR and T1 did not disclose significant differences in BG volume either before or after subtraction of VRS or focal lesions or both.

BG pathology in CIS, RRMS and PMS.
VRS number and volume were higher in CIS compared to HC ($p<0.05$). CIS differed from RRMS in the volume and number of VRS ($p<0.05$), but not in the number and volume of focal inflammatory lesions ($p=0.8$). CIS differed from PMS in the volume of VRS ($p=0.0008$) and in the number of focal inflammatory lesions ($p<0.01$) in all the BG. Moreover, the volume of left thalamus, right caudatus, right pallidus and left and right putamen, was significantly lower in PMS compared to CIS. Caudatus, putamen and pallidus volume but not thalamus volume was reduces in PMS compared to RRMS ($p<0.05$). Increased number and volume of both VRS and focal inflammatory lesions were found in the thalamus of RRMS compared to CIS ($p<0.05$).

Correlation analysis.
An inverse correlation was found between patient age and the volume of the nucleus caudatus either before or after of VRS (r= -0.54).
The pyramidal functional system (FS) score of the EDSS correlated with bot number (FLAIR: r= 0.58; PSIR: r=0.52) and volume (FLAIR: r= 0.58; PSIR: r=0.46) of the inflammatory lesions in the BG considered as a whole. BG lesions also correlated with the cerebellar FS (r= 0.53) and with the brain stem FS (r= 0.57), but not with sensory and visual FS.
The SDMT inversely correlated with bot number (FLAIR: r= -0.56; PSIR: r= -0.57) and volume (FLAIR: r= -0.51; PSIR: r= -0.57) of the inflammatory lesions in the right thalamus. A weaker inverse correlation was also noted between the number and volume of VRS in the thalamus and SDMT (r ranging from 0.37 to 0.50). Interestingly, the right thalamus volume also correlated with SPART D (r= 0.51), while the number and volume of the inflammatory lesions in the BG inversely correlated with WLG (r=- 0.58 and r=-0.54, respectively).
The number and volume of inflammatory lesions in the right thalamus and in the BG considered as a whole inversely correlated with DKEFS-SR (r= -0.6). Finally, the right and left thalamus volume correlated with the FSS score (r= - 0.57).

Discussion

In this study, PSIR proved to be superior to both FLAIR and T1 in evaluating both VRS and lesions, but was almost comparable to T1 in measuring thalamus and BG volume. PSIR allowed a more correct and comprehensive view of deep GM pathology. As expected, we also found that the evolution of the disease course from CIS to PSM was associated with the progressive accumulation of enlarged VRS and inflammatory lesions in thalamus and BG, and by a progressive reduction of their volume. These findings further indicate that the deep grey matter is a site of relevant inflammatory and neurodegenerative damage in MS.
The possibility of a better analysis of BG pathological changes by PSIR allowed to find some interesting correlations with clinical parameters of physical disability, such as the pyramidal and the cerebellar FS of the EDSS. Worth of particular interest, however, are the correlations observed between the inflammatory lesion load in the thalamus and SDMT (that evaluates the information processing speed), SPART D (spatial learning) and DKEFS-SR (executive functions) scores, that further point out a role for thalamic pathology in the cognitive decline in MS.