

## Chronic Cerebrospinal Venous Insufficiency and Iron Deposition on Susceptibility-Weighted Imaging in Patients with Multiple Sclerosis

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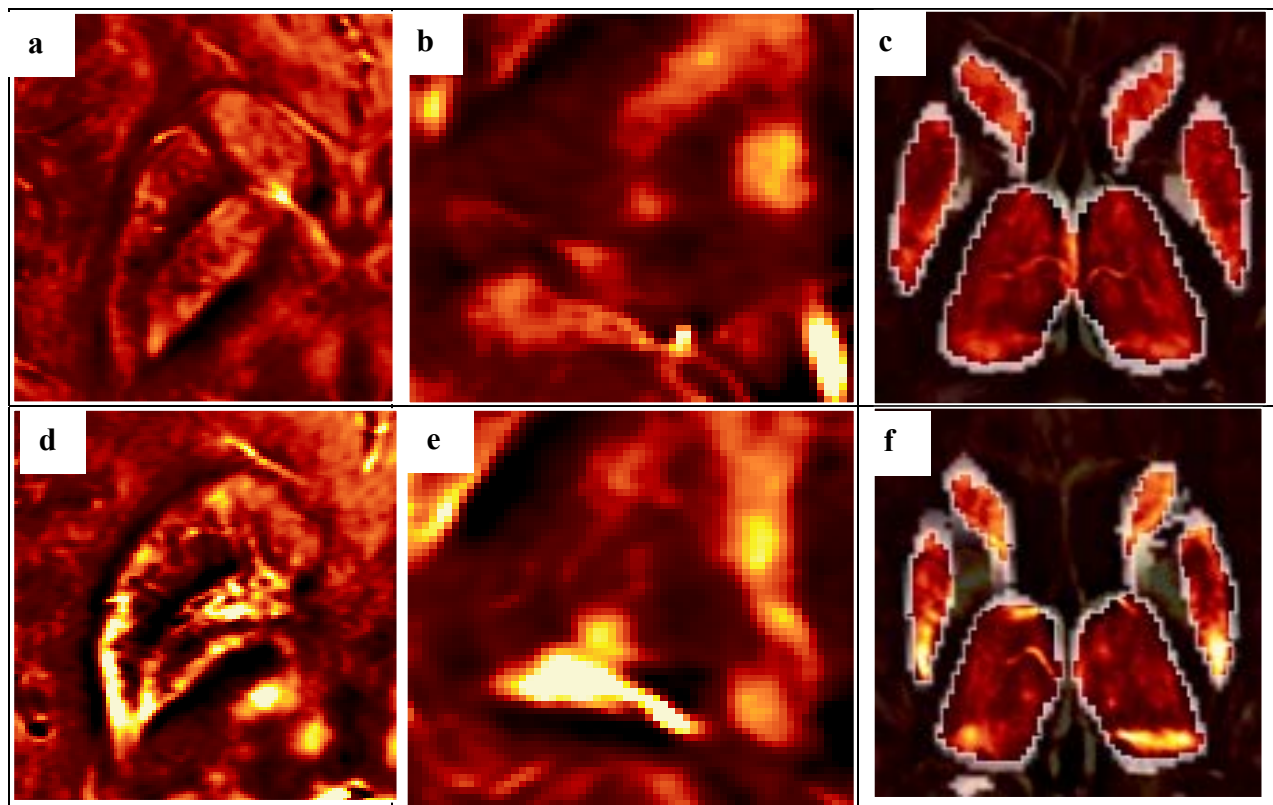
**Objective:** To investigate the relationship between chronic cerebrospinal venous insufficiency (CCSVI) and iron deposition in the brain of multiple sclerosis (MS) patients by correlating venous hemodynamic (VH) parameters and iron concentration in deep-gray matter (DGM) structures and lesions, as measured by susceptibility-weighted imaging (SWI). To preliminarily explore the relationship between iron measures and disability outcomes.

**Background:** CCSVI is a vascular picture recently described in MS patients that is characterized by stenoses affecting the main extracranial venous outflow pathways and by a high rate of cerebral venous reflux that may lead to increased iron deposition in the brain.

**Methods:** Sixteen (16) consecutive relapsing-remitting MS patients (mean age  $36.1 \pm 7.3$  yrs, mean disease duration  $7.5 \pm 1.9$  yrs and median EDSS 2.5) and 8 age- and sex-matched normal controls (NC) were scanned on a GE 3T scanner, by using SWI. Iron concentration was measured in the following DGM structures: thalamus, caudate, putamen, globus pallidus, hippocampus, amygdala, nucleus accumbens, red nucleus and substantia nigra. Iron concentration was also measured in T2, T1, SWI phase and SWI magnitude lesions. Diagnosis of the CCSVI was established based on the previously published VH Doppler criteria (Zamboni, JNNP, 2009).

**Results:** All 16 MS patients fulfilled the diagnosis of CCSVI (median VH=4) and none of the NC. There was a significant association between higher number of VH criteria and higher iron concentration in T2 ( $r=0.64$ ,  $p=0.007$ ) and T1 ( $r=0.56$ ,  $p=0.023$ ) lesion volumes. The only DGM structure that correlated significantly with VH criteria was globus pallidus ( $r=0.58$ ,  $p=0.019$ ). No relationship was observed for NC. Higher iron concentration in DGM structures was strongly associated with higher disability status (EDSS) in almost all examined regions. The highest correlations were detected for thalamus ( $r=0.79$ ,  $p<0.0001$ ) and red nucleus ( $r=0.7$ ,  $p=0.005$ ), but strong correlations were found in caudate, putamen, hippocampus, amygdala, nucleus accumbens and substantia nigra.

**Conclusion:** The findings from this pilot study suggest that CCSVI may be an important mechanism leading to iron deposition in brain parenchyma of MS patients. In turn, iron deposition, as measured by SWI, is a strong predictor of disability progression in patients with MS.



**Figure 1.** Deep gray matter iron maps in normal controls (NC) (a, b, c) and in patients with multiple sclerosis (MS) (d, e, f). Yellow-black color scale indicates higher concentration of iron. Higher concentration of iron has been detected in caudate, putamen and globus pallidus (a, d), pulvinar thalamus (b, e) and in other DGM structures including thalamus and hippocampus (c, f) in MS patients vs NC. High concentration of iron was strongly related to higher disability.

