Global Brain Iron Deficiency in Restless Legs Syndrome Examined by an Increase of T2-Values

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Introduction

Restless Legs Syndrome (RLS) is with a prevalence of 5-15 % a very common sensormotor disorder. In idiopathic RLS patients CSF examinations demonstrate decreased ferritin and increased transferrin levels despite normal serum levels, which suggest brain iron deficiency as one major pathophysiologic factor (1). Hypoechogenicity of the substantia nigra (SN) is a sonographic marker for RLS, which is supposed to indicate decreased SN iron storage (2). First MRI and histological studies could demonstrate decreased iron content by an increase of T2 in the SN and the putamen only (3, 4). In this study we examined alterations of the T2 relaxation outside the nigrostriatal system in RLS patients.

Material and Methods

6 idiopathic RLS patients with sonographic SN hypoechogenicity and 19 age matched healthy controls with normal SN echogenicity were examined. The MRI was performed on a 1.5 Tesla scanner (Avanto, Siemens, Germany) with a four-array head coil. A three-echo twodimensional Turbo spin-echo sequence was used (TE 14 ms, 85 ms and 156 ms, TR 9,9 s, slice thickness 3.5 mm, FOV 100, 256*256 matrix). 30 slices with the SN in the central slice were examined. Images were interpolated to a spatial resolution of 0.8 mm. T2-maps were calculated from signal intensities of the first two echoes. Circular ROIs were bilaterally placed in the first echo images for the following ten regions: 1 pallidum, 2 red nucleus, 3 dentate nucleus, 4 putamen, 6 temporal white matter, thalamus (5 dorsolateral, 7 medial, 8 ventral), 9 head of the caudate and 10 hippocampus. The T2 values of all pixels within single ROIs were visualized in cumulative histogram plots. These histograms were averaged for each group and region separately. Mean and standard deviation (SD) of the averaged T2 values were compared between both groups for each region.

Results

In every examined brain region the average T2 value histogram plots were remarkably shifted to higher T2 intensities in the RLS patient group (Fig. 1). Differences of the mean T2 values between the RLS patient and the control group were highly significant for red nucleus, head of the caudate and thalamus and less significant for temporal white matter and putamen (Fig. 2).

Discussion

Increased T2 values in RLS patients compared to controls suggest decreased iron content in all examined brain regions. Those group differences were not significant for all regions, what may be explained by the distribution of T2 values in single ROIs which results in SDs that may mask group differences. One reason for the differing results between this spin-echo sequence study and previous MRI studies using gradient-echo sequences (3, 5) may be a higher signal-to-noise ratio in this approach which possibly enables a more sensitive visualization of changes in signal intensity. Moreover, we demonstrated that the evaluation of only two echoes can be sufficient to assess group differences with high levels of significance. This MRI approach underlines the relevance of brain iron metabolism for the development of idiopathic RLS and is the first proof of a pathophysiologic condition that involves the whole brain of RLS patients.

References

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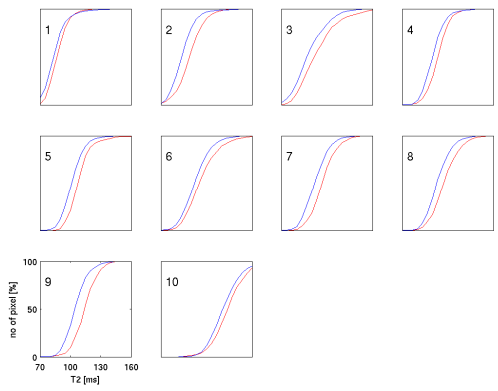

Fig. 1: Average cumulative T2 value histogram plots for RLS patients (red) and controls (blue) for the ten assessed brain regions (numbers explained in the text). The scale is unique for all images

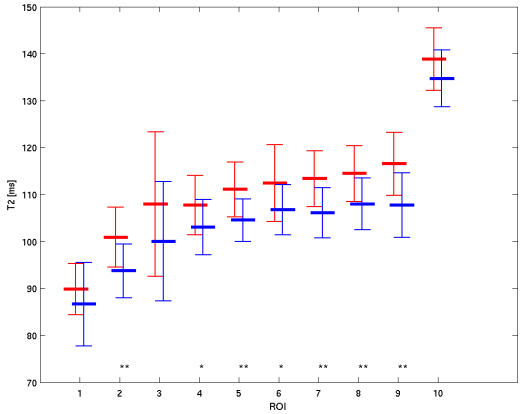

Fig. 2: Mean and SD for T2 values of RLS patients (red) and controls (blue) by region (numbers explained in the text). * p<0.05, ** p<0.005.