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Neurodegeneration with brain iron accumulation: T2 Relaxometry as a diagnostic tool.

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Abstract

The deposition of iron in the basal ganglia is an age-dependent physiological event, however, increased deposits has been shown in the central nervous system in many neurodegenerative diseases (including Friedreich's Ataxia - FA, Machado-Joseph Disease - MJD, Amyotrophic Lateral Sclerosis - ALS and Parkinson's Disease - PD) and, in this context, the use of Magnetic Resonance Imaging (MRI) trhough the analyses of transversal relaxation time (RT2) can be a powerfull diagnostic tool by the detection of brain iron deposits. We selected 191 patients (32 AF, 48 MJD, 58 ALS, 53 PD) and compared four structures of basal ganglia (thalamus, dentate nucleus, pallidum and substantia nigra) RT2 values with control group (n = 207, using normal values from previous study of the same group of researchers), trying to determine paterns of brain iron depositions that can be used as diagnostic tool. We found statistically significance in the avaliation of left dentate nucleus in FA patients (p = 0,03), rght substantia nigra in MJD (p = 0,01) and left thalamus in ALS (0,01), with probable physiopathological and clinical correlations. The RT2 MRI is a relevant technique in the evaluation of neurodegenerative diseases and can be used as an important diagnostic tool in the clinical practice.

Key words:

Relaxometry, Brain Iron Deposits, Neurodegeneration.

Introduction

The deposition of iron in the basal ganglia is an age-dependent physiological event. Increased iron has been shown in the central nervous system in many neurodegenerative diseases (such as Parkinson disease - PD, amyotrophic lateral sclerosis - ALS, Machado-Joseph disease - MJD and Friedreich's ataxia - FA). In this context, the use of Magnetic Resonances Imaging (MRI) through the analyses of transverse relaxation time (RT2) can be a powerful diagnostic tool for estimating in vivo iron deposits in central nervous system. This project aims to: a) compare the value or RT2 from healthy subjects obtained from previous study (from the same group of researchers) with the RT2 obtained from MRI images of patients with PD, ALS, MJD and FA; b) determine the estimated concentration of iron on the basal ganglia; c) determine sensibility and specificity of the RT2 evaluation on the determination of healthy subjects and patients.

Results and Discussion

Methodology: T2 Multiecho images from 191 patients will be used for this study (32 AF, 48 MJD, 58 ALS, 53 PD). For each subject, four structures were chosen on both sides from MRI 3T images (with T2 multiecho sequence): thalamus (T), globus pallidus (GP), substantia nigra (SN) and dentate nucleus (DN). For each structure, values of RT2 were determined with the software Aftervoxel, by selecting 3 Regions of Interest (ROI) on 3 consecutive slices. The final RT2 value was defined as the average of the 3 ROIs. For each disease, the values of RT2 was compared with the control data (from the previous study) and a ROC curve was created to determine the sensibility and specificity of the method. **Results and discussion:** comparing with the previous data from the control group (n = 207, age 9-82 years, obtained from the previous study with the same group of researchers), there was evidence of higher brain iron deposits in the dentate nucleus in FA (p = 0,03, probably related with the physiopathology of the disease, which includes alterations of the iron metabolism by the mutation of frataxin gene, which contributes on the pattern of iron deposition), in right substantia nigra in MJD (p = 0,01, probably related to the parkinsonism symptoms in the role of the disease, which includes degeneration of neurons in this area) and left thalamus in ALS (p = 0,01, probably associated with the superior motor neuron pathway, which is also damaged in this disease), while there was no difference in the analysis of substantia nigra in patients with PD (probably related to the heterogenous population in the present study). The correlation of brain iron deposits as a cause or consequence of neurodegenerative diseases is not well understood, but the presence of the deposits and the determination of its pattern of deposition has important diagnostic and prognostic values [1,2].

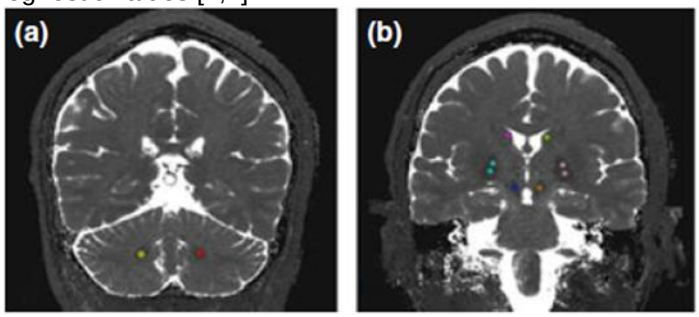

Figure 01: Representation of the coronal slices of Magnetic Resonance Images of brain, showing the detection of ROIs: dentate nucleus (red and yellow, *a*), substantia nigra (dark blue and orange, *b*) and caudate nucleus (light green and pink, *b*).

Conclusions

The MRI RT2 is a relevant technique in the evaluation of patients with neurodegenerative diseases, with can be used as an important diagnostic and prognostic tool in the clinical practice.

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[1] Schenck JF. Magnetic Resonance Imaging of Brain Iron. *Journal of Neurological Sciences* 2003; **207**: 99-102.

[2] Guan X, Xuan M, Gu Q, *et al*. Regionally progressive accumulation of iron in Parkinson's disease as measured by quantitative susceptibility maping. *Wiley Online Library*, 2015; DOI: 10.1002/nbm.3489.