

Evaluation of inflammatory process in Parkinson's disease model: Magnetization transfer image histogram parameter and 1H magnetic resonance spectroscopy

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Introduction

Parkinson's disease (PD) is characterized by degeneration of the dopaminergic (DAergic) neurons of the substantia nigra (1). Dopamine denervation induces an increase in corticostriatal glutamate transmission that is central to the pathophysiology of PD (2). The subthalamic nucleus also receives neuromodulatory inputs, notably DAergic axons from the substantia nigra. (3) For PD research, the 1-methyl-1,2,3,6-tetrahydropyridine (MPTP) intoxicated animal model has been widely used because it mimics the neurodegeneration observed in human PD (4). The aim of this study was to investigate whether magnetization transfer ratio (MTR) histogram changes are related to specific PD characteristics and whether any possible relationship between MTR histogram parameters and to analyze in vivo consequences of dopamine depletion on amount of metabolites in a mouse model of Parkinson's disease using proton 1H magnetic resonance spectroscopy (MRS).

Materials and Methods

The study was performed on control mice (n = 6) and MPTP-intoxicated C57BL/6 mice (n = 6) in this MTR and 1H-MRS studies. All MTR and 1H-MRS studies were performed on a 9.4 T/20cm magnet BioSpec 94/20 USR (Bruker Biospin, Germany) using a standard head coil. For obtaining MTR images, proton-density fast spin echo (FSE) images (TR/TE/excitations 6000/11.6 ms/8) and T2-weighted spin echo images (TR/TE/excitations 6000/11.6/46.5 ms/8) were acquired with 1.0 mm slice thickness and no gap. For in vivo MRS acquisitions, outer volume suppression combined with the ultra-short echo-time stimulated echo acquisition mode (STEAM) (TE = 2.2 ms, TM = 20 ms, TR = 5 sec) was used for localized 1H-MRS. The absolute concentrations of metabolites were determined using jMRUI (Lyon, France) from 1H spectra obtained in vivo on striatum.

Results

These images guaranteed precise and reproducible placement of the VOI of MTR images in the striatum and the substantia nigra (SN) (Fig.1). No significant differences between means, modes, volumes and bin widths were observed in the striatum and SN MTR histogram at each MTR histogram measurement (P>0.05). However, the normalized peak height, in the PD model, was significantly lower than in the control group in the striatum and SN (P < 0.05) (Fig.2). 1H-MR spectra were acquired from VOI (2.5x1.5x2.5 mm³) centered in the striatum (Fig. 3). The Glx/Cr ratio (6.2353±1.21570) in PD model, was significantly increased compared to the normal control (4.8974±2.19358, P=0.024) and the NAA/Cr ratio in the PD models was a little significantly decreased compared to the normal control. However, there was a little difference in the Cho/Cr ratio between the PD and control groups.

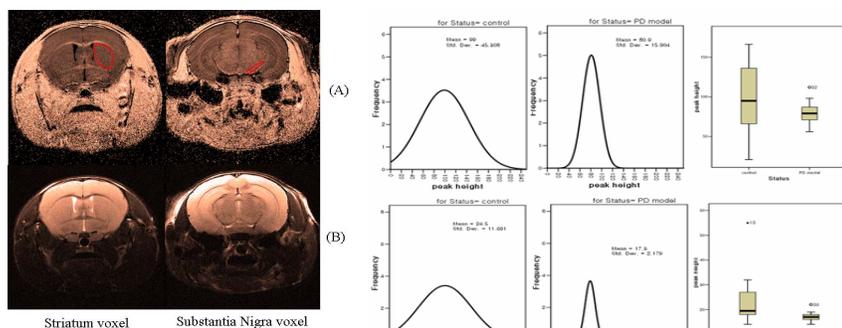


Fig.1 In midbrain and basal ganglia the ROIs, localized on MTR images (striatum, 1pars reticulata of the substantia nigra and 1 pars compacta of the substantia nigra) (A), were copied and pasted on T2-weighted images, performed with identical graphic prescription (B).

Fig.2 MTR histograms in control and PD model group in striatum (Top; A,B,C) and SN(Bottom; A,B,C). The normalized peak height in PD model was significantly lower than that in control group in the striatum and SN. (C) Solid line indicates a median of P<0.05. The lower peak height of the MTR histogram in PD model compared with healthy controls is consistent with mode.

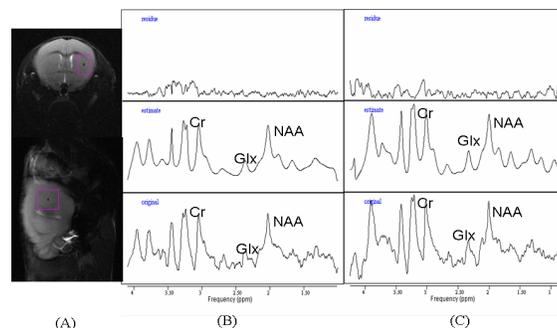


Fig.3 (A) Coronal and sagittal RARE image of the mouse brain with the volume of interest VOI (squares) of the striatum. (B) Data analyses of proton MR spectra using jMRUI in the control group. (C) Data analyses of proton MR spectra in the PD model group. Bottom row: original spectrum. Middle row: fitted individual components using the HLTLS algorithm. Top row: residuals signal after subtraction of the individual components from the original data set. Cr: creatine; Glx: glutamate, glutamine and GABA.

Discussion

The present study demonstrated that the highest peak height value of the MTR histogram, as well as the increase in the Glx/Cr ratio was observed in the striatum of the PD group. In the conclusion, we demonstrated that MTR histogram changes were associated with metabolic changes by 1H-MRS, and that the pathological studies in PD model clearly demonstrate the presence of disseminated activated microglial-like inflammatory cells in the central nervous system.

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