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Proton magnetic resonance spectroscopy (^{1}H-MRS) of motor cortex and basal ganglia in de novo Parkinson's disease patients

C. Lucetti[1] · P. Del Dotto[1] · G. Gambaccini[1]
S. Bernardini[1] · M.C. Bianchi[2] · M. Tosetti[3]
U. Bonuccelli[1] (✉)
[1] Department of Neuroscience, University of Pisa, Pisa, Italy
[2] Neuroradiology Unit of Pisa, Pisa, Italy
[3] Stella Maris Scientific Institute, MR Department, Pisa, Italy

Abstract Proton MR spectroscopy (^{1}H-MRS) has been previously performed in Parkinson's disease (PD) and parkinsonian syndromes to evaluate in vivo concentrations of basal ganglia and cerebral cortex metabolites such as *N*-acetylaspartate (NAA), choline (Cho), and creatine (Cr). However, this technique has never been used to evaluate motor cortex in untreated PD patients. In this study, single-voxel ^{1}H-MRS of basal ganglia and motor cortex was carried out in 10 de novo patients with PD and 10 age-matched healthy controls. A significant reduction in the NAA/Cr ratio was observed in the motor cortex of PD patients compared with controls (p<0.01). Basal ganglia spectra did not allow any evaluation due to the presence of artefacts related to inorganic paramagnetic substances. The motor cortex reduction of the NAA/Cr ratio in de novo PD patients may reflect an altered neuronal functioning due to a loss of thalamocortical excitatory inputs and may represent an in vivo marker for the diagnosis of PD.

Proton magnetic resonance spectroscopy (^{1}H-MRS) is a useful noninvasive method used to study central nervous system pathologies, and allows in vivo investigation of a number of cerebral metabolites such as *N*-acetylaspartate (NAA), choline (Cho), creatine (Cr), myoinositol (My), phosphocreatine (PCr) and lactate. Cho and Cr are present in all brain cells, whereas NAA has been localized mostly in neurons. The NAA/Cr ratio is considered to be a metabolic marker for neuronal function, and a reduction of this ratio indicates damage or degeneration of neuronal and/or axonal structures [1]. The major pathological process in idiopathic Parkinson's disease (PD) involves the degeneration of the dopaminergic neurons of the substantia nigra (SN), even though other areas are involved in the degenerative process and Lewy's bodies, the characteristic pathological findings of PD, are also found in cerebral cortex. ^{1}H-MRS has been widely used to study striatal metabolism in PD patients and conflicting results have been found. Few studies have examined the cortical function and no study has been performed to evaluate metabolic changes in the motor cortex of PD patients using ^{1}H-MRS. The aim of the present study was to investigate whether ^{1}H-MRS is able to detect neurochemical and metabolic changes in the basal ganglia and motor cortex of de novo PD patients. We studied 10 de novo PD patients [(8 men, 2 women; mean age, 58.6 years (SD, 12.4); mean duration of disease, 16.1 years (SD, 10.3); mean Hoehn & Yahr stage, 1.2 (SD, 0.3)]. The patients were diagnosed as idiopathic PD in accordance with the UK Brain Bank criteria. An additional 10 healthy age-matched controls, including 8 men and 2 women of mean age 54.6 years (SD, 15.6) were enrolled. Patients with neuroradiological evidence of brain atrophy and cognitive impairment (Mini-mental state evaluation score ≤ 24) were excluded. All patients and controls underwent single-voxel ^{1}H-MRS of the basal ganglia and the motor cortex, using a PROBE-SV system implemented on a 1.5 tesla scanner (GE Medical System, Milwakee, WI). A short TE stimulated echo acquisition mode (STEAM) technique (TR = 2.0.10 ms, TE = 30 ms, mixing time = 13.7 ms, 256 scans accumulating for signal averaging, volume of interest (VOI) dimension = 3.4 cc) was employed. The VOI was centered on the contralateral putamen and the globus pallidus on the worst affected side and on the medial surface of the motor cortex (both left and right sides were included in the VOI). Cho/Cr and NAA/Cr ratios were obtained. The signal amplitudes of each metabolite were given as relative values with respect to the Cr/PCr peak at 3.05 ppm, taken as the internal reference standard.

No significant metabolic changes in Cho/Cr and NAA/Cr spectra were observed in basal ganglia. However, the short TE we used enhanced the presence of artefacts related to inorganic paramagnetic substances. A significant reduction in the NAA/Cr ratio was observed in the motor cortex of PD patients compared with controls (p<0.05) (Table 1).

Table 1 Metabolite ratios in the motor cortex (mean ± SD)

	Patients (n=10)	Controls (n=10)	
NAA/Cr	1.21 ± 0.12	1.34 ± 0.11	p<0.05
Cho/Cr	0.71 ± 0.11	0.89 ± 0.14	NS
My/Cr	0.66 ± 0.11	0.61 ± 0.15	NS

NS, not significant

Discussion

^{1}H-MRS studies on basal ganglia metabolites are controversial in PD. Some authors reported no change in the striatal metabolism [3-5]; on the contrary, Holshouser et al. [6] found a significant decrease in the striatal NAA/Cho ratio in 27 drug-naive PD patients, and Ellis et al. [7] reported analogous results in 9 de novo PD patients. No significant differences of Cho/Cr and NAA/Cr spectra were observed in basal ganglia of our patients, but data from this study must be viewed in the context of a possible source of error due to the presence of artefacts related to inorganic paramagnetic substances. Few ^{1}H-MRS studies have assessed the cortical function in patients with PD. Tedeschi et al. [5] found no significant cortical changes in NAA/Cho and NAA/Cr ratios in non-demented levodopa-treated PD patients. Recently, a significant temporoparietal cortex reduction in the NAA/Cr ratio in 17 levodopa-treated PD patients without dementia was reported [8]. In agreement with the aforementioned observations, our results indicate that cortical NAA/Cr ratios are significantly depressed in untreated non-demented PD patients. The cortical NAA/Cr reduction in de novo PD may be due to a neuronal functional impairment secondary to the reduction in the thalamocortical glutamatergic imput. This study is still in progress and the number of patients is too small for any definite considerations. However, these data suggest: (1) NAA/Cr ratio could be a measure of functional impairment of cortical neurons in PD; and (2) the motor cortex reduction in the NAA/Cr ratio in de novo PD patients may represent an in vivo marker of PD diagnosis. Thus, ^{1}H-MRS may provide a sensitive tool for studying neuronal dysfunction in the motor cortex of de novo PD patients and may be regarded as a useful technique to monitor disease progression.

References

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