Metabolite Difference between Multiple System Atrophy of Parkinsonian Type and Parkinson's Disease Assessed with Quantitative Proton MR Spectroscopy

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Introduction: Multiple system atrophy (MSA) is a sporadic progressive neurodegenerative disease of unknown etiology. Based on clinical presentations, MSA can be classified into two main types, Parkinsonian (MSA-P) and cerebella variants. The differential diagnosis between MSA-P and Parkinson's disease (PD) is often difficult, but of great clinical importance, as their prognosis and treatment options differ considerably. The aim of this study is to assess differential metabolic changes of the brain in patients with PD and MSA-P.

Subjects and Methods: The subjects of the study consisted of 45 healthy controls (20 men and 15 women; age, 51.8±5.0 years), 27 patients with PD (14 men and 13 women; age, 56.2±8.8 years; median disease duration, 3 years; range of disease duration, 6 months to 9 years) and 40 with clinically probable MSA-P (22 men and 18 women; age, 54.3±5.2 years; median disease duration, 2 years; range of disease duration, 6 months to 6 years). The three groups did not differ significantly in age ($P>0.05$) and gender ($P=0.917$). Diagnoses were made according to the diagnostic criteria for PD and MSA[1,2]. All the subjects underwent proton MR spectroscopy (MRS) on a 3.0T MR scanner (GE Signa VH*i* Excite II) with an 8-channel head coil. MRS was performed using the point resolved spectroscopy sequence (TR 1500ms, TE 35ms, NAV 128) in pons (6 ml), left basal ganglia (6 ml) and left precentral gyrus (8 ml) (Fig 1). Spectra were evaluated with LC Model which provided user-independent quantification.

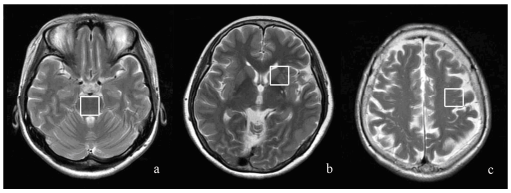

Fig 1 Localization of voxels in pons (a), left basal ganglia (b) and left precentral gyrus (c).

Results: There was significant difference in absolute concentration of creatine (Cr) and myoinositol (mI) in the pons, left basal ganglia and left precentral gyrus between MSA-P and one or both of the other two groups (Table 1-3). Specifically, in MSA-P patients Cr and mI increased and N-acetyl aspartate (NAA) decreased significantly in pons compared with PD and controls. Concentration ratio of NAA/(mI+Cr) in pons of MSA-P (0.684±0.178) was significantly lower than those of PD (1.007±0.118) and controls (0.997±0.103) (both $P=0.000$, one-way ANOVA analysis) (Fig 2).

Table 1 Metabolite absolute concentration (mmol/l) and concentration ratios in the pons of controls, PD and MSA patients

	Cr	mI	NAA	tNAA	Cho	tNAA/Cr	Cho/Cr	mI/Cr
value	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Control	5.538 (1.100)	6.054 (1.470)	8.486 (1.744)	11.423 (2.136)	2.960 (0.586)	2.086 (0.238)	0.541 (0.073)	1.089 (0.220)
PD	5.532 (1.067)	6.194 (1.652)	8.600 (1.757)	11.624 (2.140)	3.151 (0.744)	2.128 (0.281)	0.575 (0.097)	1.115 (0.178)
MSA-P	6.064 (1.030)$^{*\#}$	8.270 (1.846)$^{*\#}$	7.006 (1.741)$^{*\#}$	9.539 (2.163)$^{*\#}$	2.862 (0.716)	1.589 (0.325)$^{*\#}$	0.472 (0.088)$^{*\#}$	1.363 (0.203)$^{*\#}$

tNAA, NAA+N-acetyl aspartyl glutamate; Cho, choline. Significant difference is indicated by * $P<0.05$ compared with controls, and $^{\#}$ $P<0.05$ compared with PD patients (one-way ANOVA analysis).

Table 2 Metabolite absolute concentration (mmol/l) and concentration ratios in the left basal ganglia of controls, PD and MSA patients

	Cr	mI	NAA	tNAA	Cho	tNAA/Cr	Cho/Cr	mI/Cr
value	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Control	7.345 (1.149)	5.130 (1.305)	8.441 (0.967)	8.647 (0.830)	2.138 (0.413)	1.195 (0.140)	0.291 (0.037)	0.703 (0.163)
PD	6.827 (1.299)	4.450 (1.320)	7.895 (1.410)	8.194 (1.292)	2.122 (0.338)	1.220 (0.182)	0.316 (0.054)*	0.665 (0.170)
MSA-P	6.559 (1.340)*	5.477 (1.697)$^{\#}$	7.248 (1.339)*	7.621 (1.201)*	2.139 (0.477)	1.192 (0.222)	0.328 (0.037)*	0.827 (0.255)$^{*\#}$

tNAA, NAA+N-acetyl aspartyl glutamate; Cho, choline. Significant difference is indicated by * $P<0.05$ compared with controls, and $^{\#}$ $P<0.05$ compared with PD patients (one-way ANOVA analysis).

Table 3 Metabolite absolute concentration (mmol/l) and concentration ratios in the left precentral gyrus of controls, PD and MSA patients

	Cr	mI	NAA	tNAA	Cho	tNAA/Cr	Cho/Cr	mI/Cr
value	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Control	6.130 (0.579)	4.668 (0.585)	8.915 (1.120)	9.991 (1.191)	1.634 (0.316)	1.636 (0.194)	0.268 (0.052)	0.761 (0.089)
PD	6.403 (0.552)	4.659 (0.735)	9.116 (0.669)	10.253 (1.013)	1.798 (0.192)*	1.605 (0.128)	0.282 (0.031)	0.728 (0.095)
MSA-P	6.585 (0.741)*	5.102 (0.636)$^{*\#}$	8.733 (1.226)	9.745 (1.201)	1.746 (0.276)	1.485 (0.145)$^{*\#}$	0.266 (0.035)	0.785 (0.100)$^{\#}$

tNAA, NAA+N-acetyl aspartyl glutamate; Cho, choline. Significant difference is indicated by * $P<0.05$ compared with controls, and $^{\#}$ $P<0.05$ compared with PD patients (one-way ANOVA analysis).

Conclusions: Our results exhibit that absolute concentration of Cr differs significantly in MSA-P from those of PD and/or controls in all the three locations, which indicates Cr is not stable as presumed previously and not appropriate as an internal reference in MSA-P. Absolute concentration of brain metabolites demonstrates changes of metabolites more intuitively than concentration ratios, and may aid in understanding the changes of concentration ratios in the previous reports[3]. Furthermore, according to the changes of individual metabolite, more sensitive concentration ratios may be defined, such as NAA/(mI+Cr) ratio in pons, to differentiate MSA-P from PD and healthy controls. Our results suggest absolute quantitative proton MRS is sensitive to detect the metabolic changes caused by neurodegenerative process in MSA, which is compatible with the histopathological findings. Most important of all, absolute metabolite concentration and concentration ratios of MSA-P patients differ from those of PD patients in all the three locations, especially in the pons. The metabolite changes assessed with absolute quantitative MRS may be valuable for differential diagnosis between MSA-P and PD.

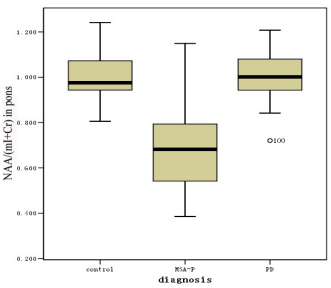

Fig 2 Box plot of NAA/(mI+Cr) ratio of the controls, MSA-P and PD patients in pons.

References

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