The Usage of Proton Magnetic Resonance Spectroscopy in Parkinson's Disease

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Background: *Parkinson's disease is a degenerative disorder of the central nervous system resulting from neuronal loss in the substantia nigra (a region of the mid brain) and BSG. Proton magnetic resonance spectroscopy (^{1}H-MRS) has been previously performed in Parkinson's disease (PD) to evaluate in vivo concentration of basal ganglia (BSG) and cerebral cortex metabolites. However, this technique has never been used to evaluate the substantia nigra (SN) in PD patients. In this preliminary report, single voxel MRS of BSG and SN was performed in PD and normal control (non-PD) to evaluate the usage of MRS in PD patients*

Material and Method: *Seventeen PD patients including 12 men and five women with a mean age 60.5 years (SD 9.4) and a mean duration of the disease 5.9 years (SD 4.2) based on Hoehn & Yahr stage I to III, and 14 healthy age-matched controls including eight men and six women with a mean age 55.5 years (SD 5.8) were enrolled. Patients with evidence of brain atrophy and cognitive impairment were excluded.*

Results: *A significant reduction in the NAA/Cr ratio was observed in the SN of PD compared with controls ($p < 0.05$). BSG spectra did not allow any evaluation due to the presence of artifacts related to inorganic paramagnetic substances.*

Conclusion: *^{1}H-MRS could be used as a sensitive tool for studying neuronal dysfunction in SN of PD patients and may be a useful technique to monitor the disease. The SN reduction of NAA/Cr ratio in PD patients may be the marker of neuronal loss in SN of patients with PD.*

Keywords: *Parkinson's disease, Spectroscopic imaging, Substantia nigra*

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Parkinson's disease is a degenerative disorder of the central nervous system resulting from neuronal loss in the substantia nigra (a region of the mid brain) and BSG. Proton magnetic resonance spectroscopy (^{1}H-MRS) is a useful noninvasive method used to study pathologies of central nervous system and allow *in vivo* investigation of a number cerebral metabolites such as N-acetyleaspartate (NAA), choline (Cho), creatine (Cr), myoinositol (My), 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 dopamineragic neurons of subtantianigra (SN). ^{1}H-MRS has been widely used to study striatum metabolism in PD patients and conflicting results have been found[2-7]. No study has ever been performed to evaluated metabolic change in the SN of PD patients using ^{1}H-MRS. The aim of the present study was to investigate whether ^{1}H-MRS is able to detect neuro-chemical and metabolic change in the BSG and SN of PD patients.

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Material and Method

Subjects

Seventeen PD patients of Prasat Neurological Institute, including 12 men and five women with a mean age of 60.5 years (SD 9.4) participated in this study. The PD had a mean duration of the disease of 5.9 years (SD 4.2) and were at Hoehn & Yahr stage I to III. Additionally, 14 healthy age-matched controls, including eight men and six women with a mean age 55.5 years (SD 5.8) participated. The study was done between October 1, 2010 and September 30, 2011: Patients with evidence of brain atrophy and cognitive

impairment were excluded. The present study was approved by the PNI Committee on Human Research and all participants provided voluntary informed consent. The small sample was due to limited budget and was designed by a statistician.

MR imaging and MRS

MR imaging and ^{1}H-MRS were performed on a 1.5 tesla MRI scanner (Magnetom vision plus, Siemens, Erlangen, Germany) MRS were obtained by single voxel, PRESS sequences (TR/TE = 1,500/135 ms) with pulse water suppression and avoiding contamination from scalp fat, 256 acquisitions, and automatic shimming. Spectroscopic data is from a cubic volume of 1.5 x 1.5 x 1.5 cms and the acquisition time about 6.3 minutes. The VOI centered on the BSG and SN (both right and left sides). NAA/Cr and Cho/Cr ratios were obtained.

Statistical analysis

All data are reported as means ± SD. Patients and control metabolite ratios were compared using independent sample t-test to compare mean of the PD vs. non-PD. The mean differences were considered to be significant at $p < 0.05$.

Results

Spectra

High quality spectra were obtained from the SN in controls and PD patients (Fig. 1, 2) but spectra with rather low quality from the BSG were observed due to the poor signal to noise ratios from the presence of artifacts related to inorganic paramagnetic substances (Fig. 3, 4).

Metabolite ratio

No significant metabolic changes in the Cho/Cr and NAA/Cr spectra were observed in BSG. A significant reduction in NAA/Cr ratio was found in the SN of PD patients compared with controls ($p < 0.05$) (Table 1).

Discussion

Parkinson's disease is a degenerative disorder of the central nervous system resulting from neuronal loss in the substantia nigra and BSG. ^{1}H-MRS is a useful non-invasive method used to study pathologies of central nervous system and allow *in vivo* investigation of a number cerebral metabolites such as N-acetyleaspartate (NAA), choline (Cho), creatine (Cr). ^{1}H-MRS studies on BSG metabolites are controversial in PD. Some authors reported no change in the striatal metabolism[2-4]. On the contrary, Holshouser et al[6] found a significant decrease in the striatal NAA/Cho ratio in 27 PD patients, and Ellis et al[7] reported similar results in nine PD patients. No significant differences of Cho/Cr and NAA/Cr spectra were observed in BSG of the presented patients. This could be from the possible error due to artifact related to inorganic paramagnetic substances. ^{1}H-MRS study

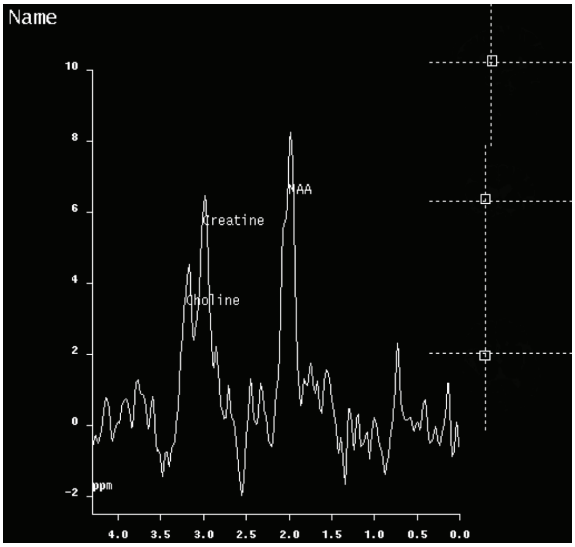

Fig. 1 MRS at SN of patient with Parkinson's disease (PD)

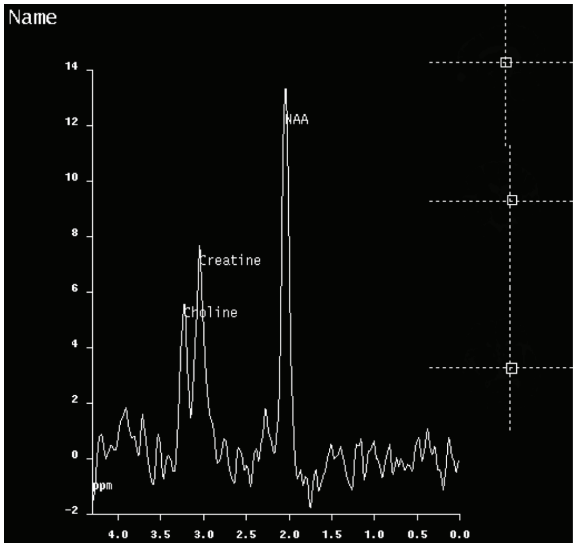

Fig. 2 MRS at SN of healthy control with age match to patient of PD (non PD)

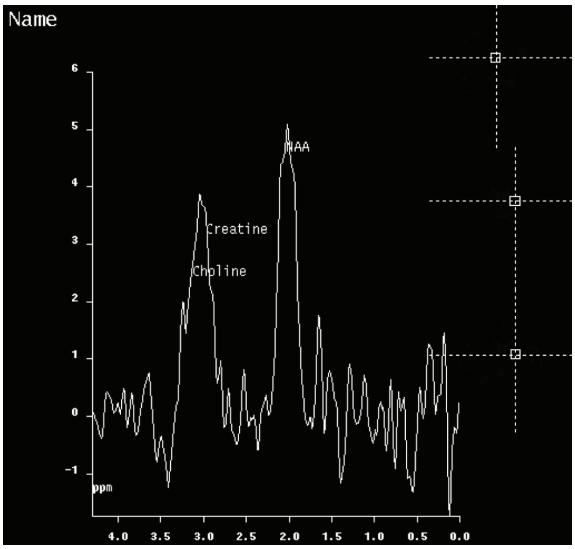

Fig. 3 MRS at BSG region of patient with Parkinson's disease

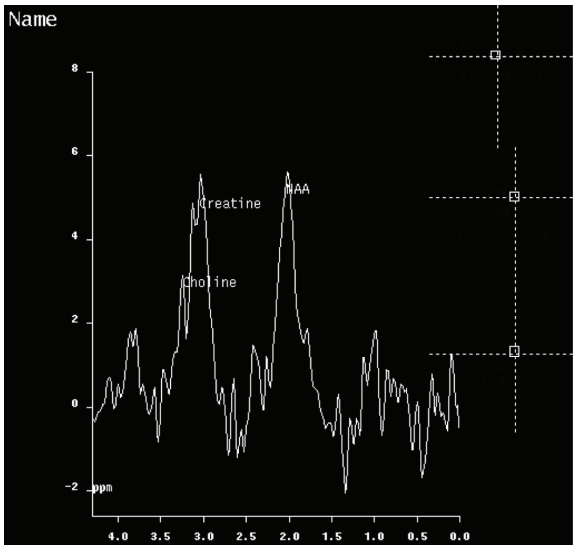

Fig. 4 MRS at BSG region of healthy control

Table 1. Metabolite ratios from MRS spectra in Parkinson's disease patients (PD) and control subjects (non PD)

Metabolites ratio (mean, SD)	PD (n = 17)	Non PD (n = 14)	Mean difference	p-value
NAACRSN1	1.47, 0.19	1.61, 0.18	-0.1455	0.04
NAACRSN2	1.48, 0.23	1.69, 0.23	-0.217	0.02
NAACRBS1	1.19, 0.09	1.25, 0.14	-0.149	0.08
NAACRBS2	1.18, 0.23	1.09, 0.15	-0.153	0.36

NAACRSN1 = NAA/Cr at right substantia nigra; NAACRSN2 = NAA/Cr at left substatia nigra; NAACRBS1 = NAA/Cr at right BSG; NAACRBS2 = NAA/Cr at left BSG

of the SN in patients with PD has never been performed. The present studies indicate that NAA/Cr ratios at the SN are significantly depressed in non-demented PD patients (NAA/Cr = 1.47 as compared to 1.61 in normal control). The reduction may be due to a neuronal functional impairment secondary to the reduction in neuron or neuronal damage. The present study is still in progress and the number of patients is too small for any definite consideration. However, the authors' preliminary report suggests that NAA/Cr ratio was significantly depressed in SN of PD patients and could be an *in vivo* marker of PD diagnosis. Furthermore, ^{1}H-MRS may provide a sensitive tool for studying neuronal dysfunction in SN of PD patients and may be a useful technique to monitor disease progression.

Potential conflicts of interest

None.

References

1. Daniesen ER, Ross B. Ethanol in the brain. In: Daniesen ER, Ross B, editors. Magnetic resonance spectroscopy diagnosis of neurological diseases. New York: Marcel Dekker; 1999: 297-9.
2. Lucetti C, Del Dotto P, Gambaccini G, Bernardini S, Bianchi MC, Tosetti M, et al. Proton magnetic resonance spectroscopy (^{1}H-MRS) of motor cortex and basal ganglia in de novo Parkinson's disease patients. Neurol Sci 2001; 22: 69-70.
3. Zheng XN, Zhu XC, Ruan LX, Zhang LJ, Yuan M, Shang DS, et al. MRS study on lentiform nucleus in idiopathic Parkinson's disease with unilateral symptoms. J Zhejiang Univ Sci 2004; 5: 246-50.
4. Cruz CJ, Aminoff MJ, Meyerhoff DJ, Graham SH, Weiner MW. Proton MR spectroscopic imaging of the striatum in Parkinson's disease. Magn Reson Imaging 1997; 15: 619-24.

5. Bowen BC, Block RE, Sanchez-Ramos J, Pattany PM, Lampman DA, Murdoch JB, et al. Proton MR spectroscopy of the brain in 14 patients with Parkinson disease. AJNR Am J Neuroradiol 1995; 16: 61-8.
6. Holshouser BA, Komu M, Moller HE, Zijlmans J, Kolem H, Hinshaw DB Jr, et al. Localized proton NMR spectroscopy in the striatum of patients with idiopathic Parkinson's disease: a multicenter pilot study. Magn Reson Med 1995; 33: 589-94.
7. Ellis CM, Lemmens G, Williams SC, Simmons A, Dawson J, Leigh PN, et al. Changes in putamen N-acetylaspartate and choline ratios in untreated and levodopa-treated Parkinson's disease: a proton magnetic resonance spectroscopy study. Neurology 1997; 49: 438-44.

ประโยชน์ของ Proton Magnetic Resonance Spectroscopy ในการวินิจฉัยโรคพาร์กินสัน

พิเชษฐ เมธารักษ์ชีพ, สุชาติ หาญไชยพิบูลย์กุล, อัครวุฒิ วิริยเวชกุล, สมศักดิ์ จรรยาวัติวงศ์

วัตถุประสงค์: *โรคพาร์กินสันเป็นโรคที่เกิดจากความผิดปกติของสมองเนื่องจากการเสื่อมสภาพของเซลล์สมองในส่วน substantia nigra ทำให้ขาดสารโดพามิน (Dopamine) ในสมอง พบได้บ่อยในผู้สูงอายุ อาการที่พบบ่อย ได้แก่ อาการสั่นขณะอยู่เฉย ๆ เคลื่อนไหวได้ช้าลง มีอาการตึงของแขนขา และลำตัวเคลื่อนไหวได้ลำบาก จากการสำรวจในปี พ.ศ. 2546 พบว่ามีผู้ป่วยเป็นโรคพาร์กินสัน 1 รายต่อประชากร 1,000 คน มีผู้ที่อายุเกิน 50 ปี ประมาณ 1-5% ป่วยเป็นโรคนี้ ภาพ MRI ธรรมดาไม่สามารถวินิจฉัยโรคพาร์กินสันได้ การวิจัยที่ผ่านมาได้ทำการศึกษาว่า Proton Magnetic Resonance Spectroscopy สามารถวัดการเปลี่ยนแปลงสารเคมี เช่น NAA, Cho, Cr ใน basal ganglia, motor cortex, striatum และ substantia nigra ในโรคพาร์กินสัน แต่ยังมีความแตกต่างในแต่ละงานวิจัย งานวิจัยนี้จึงมีความสำคัญในการสร้างความมั่นใจในประโยชน์ของ Proton Magnetic Resonance Spectroscopy ในการวินิจฉัยโรคพาร์กินสัน*

วัสดุและวิธีการ: *ผู้ป่วยโรคพาร์กินสัน 17 ราย เพศชาย 12 ราย หญิง 5 ราย อายุเฉลี่ย 60.5 ปี และคนปกติ 14 ราย เพศชาย 8 ราย หญิง 6 ราย อายุเฉลี่ย 55.5 ปี ได้รับการตรวจ Proton Magnetic Resonance Spectroscopy*

ผลการศึกษา: *พบว่ามีการลดลงอย่างมีนัยสำคัญของค่า NAA/Cr ที่บริเวณ substantia nigra ในผู้ป่วยโรคพาร์กินสันเมื่อเปรียบเทียบกับคนปกติ*

สรุป: *การตรวจ Proton Magnetic Resonance Spectroscopy ในผู้ป่วยโรคพาร์กินสันน่าจะเป็นเครื่องมือที่ไวต่อการวัดการเปลี่ยนแปลงของการเสื่อมสภาพของเซลล์สมองในส่วน substantia nigra และอาจจะใช้ในการติดตามแต่ละระยะของโรค*