Magnetic Resonance Spectroscopy Findings and Cognitive Function in Patients with Parkinson’s disease

Farzad Ashrafi1, Abdolnasser Rostami2, Mehran Arab Ahmadi1, Behdad Behnam1

1 Functional Neurosurgery Research Center; Shohada Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. 2 Department of Radiology School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

ABSTRACT

Background and Purpose: Cognitive impairment (CI) is one of the most notable disabilities of Parkinson’s disease that is associated with lower quality of life. Early detection of CI is therefore very important for these patients. The purpose of this study was to examine the relationship between cognitive function and the metabolic data from magnetic resonance spectroscopy (MRS) of the patient suffering with Parkinson’s disease.

Methods: Totally, 45 patients with Parkinson’s disease were used in this study. Subjects were divided into three groups based on scales for outcome from Parkinson cognition (SCOPA-COG) test. Patients were classified as non-cognitive impairment (NCI; n=15), mild cognitive impairment (MCI; n=15) and dementia (PDD; n=15). All subjects underwent MRI and 1H-MRS techniques and metabolic changes such as NAA/Cr and NAA/Cho ratios, which were measured in the left hippocampal area of the brain.

Results: The mean and standard deviation of the NAA/Cr ratio in the three cognitive groups (NCI, MCI, PDD) were (2.51±0.037), (2.50±0.033) and (2.47±0.025), respectively. ANOVA test showed a significant difference in the three groups. Furthermore, the Scheffé test showed a significant difference between patients in the MCI and PDD groups (p=0.01). There was no significant difference between the non-cognitive impairment and mild cognitive impairment groups (p=0.54). No significant difference was found in NAA/Cho ratio (p=0.91).

Conclusion: A decreasing NAA/Cr ratio has influence on cognitive function and the development of severe cognitive dysfunction in Parkinson suffering patients. Furthermore, 1H-MRS determinant can be useful to evaluate cognition in Parkinson patients.

Keywords: Magnetic resonance spectroscopy; Cognitive function; Parkinson’s disease

INTRODUCTION

Parkinson’s disease is a degenerative progress disease in the central nervous system. Depression, postural instability, rigidity of the body, slowness of movement, tremor and cognitive impairment are the greatest impacts on quality of life in patients suffering from Parkinson’s disease 1. Parkinson’s disease is considered primarily as a movement disorder. However, studies also show non motor symptoms (NMSs) disorders in these patients. NMS are significant in Parkinson’s patients, more so than in healthy people of same age 2,3. One of the most common non-motor dysfunctions in Parkinson’s disease is cognitive disorders 4. This is indicated in the early stages of the disease and it varies from mild cognitive impairment to dementia 4,5. Mild cognitive impairment can be seen in the early stages of the disease 6. Patients with Parkinson’s disease have a six times higher risk of developing dementia than healthy people 7. Understanding
cognitive changes mechanisms in Parkinson’s disease is very important in relation to the diagnosis, especially in treatment of the disease \(^8\). In the development of dementia, brain imaging shows structural changes in the temporal lobe \(^9,10\), however, several studies were conducted to evaluate cognitive impairment in Parkinson’s disease using brain imaging, and volume changes were not observed in these patients \(^11\). One of the techniques that can be useful in cognitive disorders is magnetic resonance spectroscopy (MRS). This is a non-invasive method that gives researchers information about the tissue metabolic changes \(^12\). Previous studies by \(^1\)H-MRS compared Parkinson’s disease suffers with dementia to healthy control subjects, different areas of the brain, such as the occipital lobes (occipital) and posterior cortex (cingulate), were evaluated in this comparison \(^13,14\). The aim of this study was to investigate the relationship between the cognitive status of Parkinson’s disease and metabolic information by \(^1\)H-MRS in the hippocampus area. The study then went on to predicted metabolites change based on the change in the cognitive status. According to the hypothesis that dementia’s process in Parkinson’s disease patients is associated with the degenerative progress in the limbic and paralimbic system \(^15,16\).

**MATERIALS AND METHODS**

**Patients**

In this study, 45 patients referred to the Movement Disorder Clinic of Shohada Hospital, Tehran, Iran were evaluated. All patients had been diagnosed with Parkinson’s disease by a movement disorder specialist. The patients were matched for age, gender, and educational level.

All patients were examined thoroughly by a neurologist and were excluded if they had other diseases such as Alzheimer’s disease, stroke, vestibular disease, brain surgery, a history of multiple strokes, head trauma, severe atrophy, severe mental illness, and encephalitis. This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences and all patients gave written consent.

**Neuropsychology review**

Patients were categorized as suffering from Parkinson’s disease with healthy cognitive function, Parkinson’s disease with mild cognitive impairment, or Parkinson’s disease with dementia according to the results of a cognition test. The cognitive test used was SCOPA-cog. a short, reliable, valid, and sensitive test to determine cognitive functioning of patients with Parkinson’s disease \(^17,18\). This test has 10 sections and a total of score of 43 with the higher scores showing better cognitive function. Scopa examines memory, attention, executive function, and visual function. Patients who scored lower than 17 were assessed as having dementia, between 17 and 24 as having mild dementia, and those over 24 as having no signs of dementia \(^19\).

**MRI and \(^1\)H-MRS**

The routine images that includes Axial T2W (TR: 3300ms, TE: 111ms, slices thickness: 3.0mm), Coronal T2w (TR:3350ms, TE:110ms, slices thickness:3.0mm), Sagittal T2W, (TR:3300ms, TE:110ms, slices thickness: 3.0mm), imaging matrix 320×256 and 3D Axial T1W MPRAGE (TE=2.81ms, TI=1100ms,flip angle:15) to be taken for all patients.

The MRS protocol was performed with point-resolved spectroscopy (PRESS) volume selection and with volume voxel 2×2×2 cm. automatic shimming was carried out to assure a uniform field in the area. Water saturation was set before receiving data. The areas selected were on T2w images in the coronal-sagittal and axial planes of the left hippocampus. Data was obtained from an area of 2×2×2 cm (Figure 1). Concentrations of NAA, Cr, and Cho metabolites were automatically measured for all patients by the comprehensive software of the MRI system.

**Statistical analysis**

ANOVA and univariate ANCOVA were used to analyze clinical and demographic data between groups. Post hoc Scheffé test was used for assessment of differences between cognitive groups. Pearson’s bivariate correlation was performed for changes in MRS and cognitive function. SPSS software was used in this study.

![Figure 1. The selected area on T2w images in the coronal-sagittal and axial planes of the left hippocampus.](image)
RESULTS

In this study, a total of 45 patients (29 males, 16 females) with a mean age of 59 years were studied. Fifteen cases were arranged as PD-NC (age 58.0±6.4, education 8.7±4.5), fifteen cases as PD-MCI (age 57.4±7.6, education 7.2±3.3) and fifteen cases as PDD (age 61.6±5.1, education 7.1±2.8). One-way ANOVA demonstrate no significant differences in age, sex and education level between groups. However, the duration of disease was significant differences (p= 0.01; Table 1). One-way ANOVA was used to study the changes of NAA / Cr and NAA / Cho in the three groups. This test showed the ratio of NAA / Cr significantly different among the three groups (p <0.001; Figure 2). Because ANOVA test showed significant difference Post hoc Scheffé test was used. This test showed significant difference between PD-MCI and PDD (p=0.013). However, no significant difference between PD-MCI and PD-NC (P=0.54). In the survey groups of the ratio of NAA / Cho no significant difference between groups (p= 0.91; Table 2).

Due to significant difference in the disease duration between cognitive groups, ANCOVA test were execute using disease duration as covariate and this test confirmed significant differences between groups.

Pearson two-tailed bivariate correlations test showed significant correlation between NAA /Cr and total score SCOPA (r=0.568, p<0.01). Also on the Correlation between the NAA / Cr and various items of SCOPA showed significant correlation with memory learning and executive function (r=0.472, p=0.001).

DISCUSSION

Recent epidemiologic studies on patients with Parkinson’s disease have revealed that the prevalence of dementia in these patients is greater than previously thought. The rate of dementia for 10-year prediction was 40% and reached approximately 80% for 8-year prediction 20,21. Cognitive impairment in patients with recently diagnosed Parkinson’s disease is more than 20% 4.

The relationship between cognitive function and reliable biomarkers has significant implications in clinical practice. The present study investigated the relationship between changes in metabolite concentration as measured by 1H-MRS and changes in cognition mode in patients with Parkinson’s disease. Several studies have been conducted on cognitive disorders in patients with Parkinson’s disease. Some have assessed structural changes in MRI images that show changes in the volume of the hippocampus and cortex. Some studies have used 1H-MRS technique to investigate cognitive disorders.

1H-MRS is a non-invasive method. This technique provides researchers with information about metabolic changes in tissue 12. 1H-MRS can be used in clinical cases to quantitatively assess the degree of neuronal damage or damage to different regions of the brain 22,23. N-acetyl-aspartate (NAA) is one metabolite that can be measured by MRS. NAA is an amino acid found in the neurons of the adult brain and is considered a marker of

Table 1. Demographic characteristics of PD cognitive groups.

<table>
<thead>
<tr>
<th></th>
<th>PD-NC</th>
<th>PD-MCI</th>
<th>PDD</th>
<th>P (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ,years</td>
<td>58.0±6.4</td>
<td>57.4±7.6</td>
<td>61.6±5.1</td>
<td>0.15</td>
</tr>
<tr>
<td>Educations, years</td>
<td>8.7±4.5</td>
<td>7.2±3.3</td>
<td>7.1±2.8</td>
<td>0.41</td>
</tr>
<tr>
<td>Mean, %</td>
<td>73</td>
<td>60</td>
<td>60</td>
<td>0.67*</td>
</tr>
<tr>
<td>PD duration, years</td>
<td>5.8±2.6</td>
<td>6.5±3.5</td>
<td>9.3±3.3</td>
<td>0.01</td>
</tr>
<tr>
<td>SCOPA scale</td>
<td>28.13±2.3</td>
<td>21.4±2.2</td>
<td>13.13±2.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are described as means±SD. *:² test

Table 2. NAA/Cr concentration ratio in the left hippocampus in cognitive groups of Parkinson’s patients.

<table>
<thead>
<tr>
<th></th>
<th>NAA/Cr</th>
<th>NAA/Cho</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-CglInt</td>
<td>2.51±0.037</td>
<td>1.49±0.013</td>
</tr>
<tr>
<td>PD-MCI</td>
<td>2.50±0.033</td>
<td>1.50±0.014</td>
</tr>
<tr>
<td>PDD</td>
<td>2.47±0.025</td>
<td>1.49±0.014</td>
</tr>
<tr>
<td>P (ANOVA)</td>
<td>&lt;0.001</td>
<td>0.99</td>
</tr>
</tbody>
</table>

SCOPA (r=0.568, p<0.01). Also on the Correlation between the NAA / Cr and various items of SCOPA showed significant correlation with memory learning and executive function (r=0.472, p=0.001).
neuronal density. It is also associated with the metabolic status of neurons. Choline (Cho) is linked to the cytosolic surface of choline compounds and increases in the cell membrane. Other metabolites include creatine (Cr) which is a measure of metabolism of energy and is the most stable material in MRS 12.

The results show a relationship between cognitive pattern and a decrease in the NAA/Cr ratio. 1H-MRS showed metabolite changes in patients with Parkinson’s disease with mild cognitive impairment or dementia that are similar to the results of previous studies in this area. The use of 1H-MRS to study patients with Parkinson’s disease indicates that a decrease in NAA in the basal ganglia area appears in patients with atypical Parkinsonism and could result from degeneration of the basal ganglia in these patients 24,25.

Previous studies using 1H-MRS that compared patients with Parkinson’s disease without dementia and healthy subjects showed a decreased NAA/Cr ratio in the posterior cingulate cortex area and occipital cortex 13,14. Studies on patients with Alzheimer’s disease and mild cognitive impairment showed a decreased NAA/Cr ratio in the hippocampus when compared to healthy subjects 26,27. Other studies have assessed atrophy of the hippocampus lobe in patients with Parkinson’s disease having cognitive impairment and indicated that hippocampal atrophy is associated with a worsening cognitive state 28.

While studies have compared Parkinson’s patients with healthy subjects, the present study compared patients with Parkinson’s disease based on three levels of cognitive functioning as assessed using the SCOPA-cog test. The findings indicate that the NAA/Cr ratio decreased significantly in patients showing hippocampus cognitive deterioration, especially between groups assessed as having mild cognitive impairment to dementia. This change may be the result of a decrease in NAA, which is accepted as a good marker of health and neuronal density 23,29. These results reinforce those of previous studies which indicate that the development of Parkinson’s disease to dementia is associated with degeneration of the limbic and paralimbic system 15,16. The present study showed a significant correlation between changes shown by 1H-MRS and overall SCOPA-cog score. A review of various SCOPA-cog items for a correlation with changes in NAA/Cr ratio showed a correlation between NAA/Cr ratio and memory, learning, and executive function. These results are similar to those from previous studies showing the relationship between the hippocampus and memory and executive function 30,31.

The limitations of the present study included partial volume effect that could not be completely eliminated, although only the most careful selection of the area was considered. Because the test duration tended to be long, patient tolerance was low and head movement increased over time, preventing assessment of other areas.

CONCLUSION

1H-MRS technique is a noninvasive method to measure metabolites which can identify a patient with Parkinson’s disease who develops dementia at an early stage.

ACKNOWLEDGMENTS

We thank all the staff at the medical imaging center. This project was supported by Functional Neurosurgery Research Center, Tehran, Iran.

REFERENCES

10. Beyer MK, Janvin CC, Larsen JP, Aarsland D. A magnetic resonance imaging study of patients with Parkinson’s disease with mild cognitive impairment and dementia using voxel-
MRS and cognitive function in Parkinson’s disease—Ashrafi et al


