Measurement of the Midbrain Diameter on Routine Magnetic Resonance Imaging

A Simple and Accurate Method of Differentiating Between Parkinson Disease and Progressive Supranuclear Palsy

Monika Warmuth-Metz, MD; Markus Naumann, MD; Ilona Csoti, MD; Laszlo Solymosi, MD

Anteroposterior diameters of the suprapontine midbrain, the pons, and the collicular plate were measured in 50 patients with various parkinsonian syndromes (Parkinson disease [PD] \(n=20\), progressive supranuclear palsy [PSP] \(n=16\), and multiple-system atrophy of striatonigral type \(n=14\)) and 12 age-matched healthy control subjects by means of axial T2-weighted magnetic resonance images. While no differences in midbrain diameter were found between patients with PD (mean, 18.5 mm) and control subjects (mean, 18.2 mm), patients with PSP had significantly lower midbrain diameters (mean, 13.4 mm) than patients with PD and control subjects \((P<.001)\), without any overlap between these 2 groups. However, midbrain diameters of patients with multiple-system atrophy were also significantly lower than those of control subjects and patients with PD, with individual values showing overlap with the PSP, PD, and control groups. Pons and collicular plate diameters did not contribute additional information. We therefore conclude that measurement of anteroposterior diameter of the midbrain on axial T2-weighted magnetic resonance images is a reliable means to differentiate patients with PSP from those with PD and should be incorporated into the diagnostic criteria for PSP.

Arch Neurol. 2001;58:1076-1079

Differentiation of Parkinson disease (PD) from atypical parkinsonian syndromes such as progressive supranuclear palsy (PSP) and multiple-system atrophy of striatonigral type (MSA-P) on clinical grounds can be inaccurate at the beginning or even in later stages of the disease.\(^1,2\)

Novel imaging techniques, including positron emission tomography,\(^3\) single-photon emission computed tomography,\(^4,5\) magnetic resonance (MR) spectroscopy,\(^6,7\) and MR morphometry,\(^4,5,8\) have improved the accuracy of diagnosis of parkinsonian syndromes on the basis of abnormalities of basal ganglia or brainstem morphologic characteristics or receptor density. Magnetic resonance imaging studies in MSA-P have shown alterations of striatal signal intensity and volume,\(^9,10\) whereas patients with PSP frequently show an atrophy of midbrain structures that is most pronounced in the superior colliculi of the tegmental plate\(^11-16\) but also of the pons.\(^16-16\) However, the reduction of midbrain diameter as a morphologic hallmark of PSP has not been analyzed and quantified systematically by contemporary imaging examinations such as MR imaging. The definition of a distinct cutoff point between PD and PSP has not yet been provided.

Therefore, the aim of our retrospective study was to evaluate and quantify the anteroposterior diameters of the pons, the midbrain, and the collicular plate on routine MR images in various parkinsonian syndromes and healthy age-matched control subjects to obtain additional neuroimaging criteria for the differentiation of parkinsonian syndromes.

RESULTS

MIDBRAIN ATROPHY

There was no difference in midbrain diameters between patients with PD and control subjects. Patients with PSP showed significantly lower midbrain diameters than patients with PD and MSA-P and control subjects.

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PATIENTS AND METHODS

Fifty patients with various parkinsonian syndromes and 12 age-matched healthy volunteers were studied between October 20, 1996, and June 22, 1999. Twenty patients had typical PD according to the UK Brain Bank Criteria,17 16 patients had PSP (5 possible and 11 probable cases, 2 of which were later confirmed by autopsy) on the basis of National Institute of Neurological Disorders and Stroke criteria for PSP,18 and 14 patients had MSA-P (4 possible and 10 probable cases) according to the consensus criteria.19 Mean age, sex, disease severity according to the Unified Parkinson’s Disease Rating Scale (UPDRS; motor section and global score),20 and disease duration are given in Table 1.

Magnetic resonance imaging was performed according to our routine imaging protocol on 2 scanners at 1.5-T field strength (Magnetom Vision; Siemens, Erlangen, Germany; and Gyroscan SI3; Philips, Eindhoven, the Netherlands). Axial conventional T2-weighted spin-echo double-echo sequences with a slice thickness of 6 or 7 mm were available for every patient. In all except the patients with PD, additional sagittal T1-weighted MR images with a maximum slice thickness of 5 mm were available. The maximum midsagittal anteroposterior diameters of the pons, midbrain, and collicular plate were measured with the scanners’ internal distance measurement device (Figure 1). The evaluation was performed blinded to the individual diagnosis.

For statistical analysis, the Mann-Whitney rank sum test was used to compare the individual groups. For the evaluation of correlation, the Spearman rank order test was used. For the evaluation of statistical differences between multiple groups, the Kruskal-Wallis analysis was used.

ATROPHY OF THE COLLICULAR PLATE

The diameter of the collicular plate was analyzed only in patients with PSP and MSA-P and control subjects, because in patients with PD, sagittal MR images were not available. The diameter was lowest in patients with PSP. There was a small but significant difference between patients with MSA-P and those with PSP (P = .04) and between patients with PSP and control subjects (P = .02).

CORRELATION WITH CLINICAL OR DEMOGRAPHIC DATA

In patients with PSP, no statistically significant correlation was found between reduced midbrain diameters and patients’ age (r = -0.19), duration (r = 0.16), or severity of disease as evaluated by the motor (r = 0.11) and total (r = 0.21) score of the UPDRS. Patients with PSP with a

<table>
<thead>
<tr>
<th>Sex, No.</th>
<th>PSP (n = 16)</th>
<th>MSA-P (n = 14)</th>
<th>PD (n = 20)</th>
<th>Control (n = 12)</th>
<th>P†</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/F</td>
<td>12:4</td>
<td>6:8</td>
<td>10:10</td>
<td>8:4</td>
<td>NA</td>
</tr>
<tr>
<td>UPDRS</td>
<td>30.2 ± 10.8</td>
<td>34.8 ± 17.6</td>
<td>16.7 ± 5.2</td>
<td>NA</td>
<td>.001</td>
</tr>
<tr>
<td>Motor score</td>
<td>41.9 ± 15.6</td>
<td>47.9 ± 21.7</td>
<td>19.0 ± 69.8</td>
<td>NA</td>
<td>.04</td>
</tr>
<tr>
<td>Age, y</td>
<td>64.5 ± 8.1</td>
<td>57.7 ± 8.3</td>
<td>67.0 ± 10.4</td>
<td>62.2 ± 9.4</td>
<td>.06</td>
</tr>
</tbody>
</table>

*Values are mean ± SD. PSP indicates progressive supranuclear palsy; MSA-P, multiple-system atrophy of striatonigral type; PD, Parkinson disease; NA, not applicable; and UPDRS, Unified Parkinson’s Disease Rating Scale.
†By Kruskal-Wallis tests of statistical differences.

Figure 1. Measurement of the midsagittal anteroposterior diameters of the pons (line 1, A and B), midbrain (line 1, C and D), and quadrigeminal plate (line 2, A) on sagittal T1- and axial T2-weighted magnetic resonance images with the imagers’ internal distance measurement device.

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Table 2. Diameters of Midbrain, Pons, and Collicular Plate in 50 Patients With Parkinsonian Syndromes and 12 Control Subjects*

<table>
<thead>
<tr>
<th></th>
<th>PSP (n = 16)</th>
<th>MSA-P (n = 14)</th>
<th>PD (n = 20)</th>
<th>Control (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midbrain diameter, mm</td>
<td>13.4 (11-15)</td>
<td>16.7 (14-19)</td>
<td>18.5 (17-19)</td>
<td>18.2 (17-20)</td>
</tr>
<tr>
<td>Pontine diameter, mm</td>
<td>20.1 (18-21)</td>
<td>20.1 (16-22)</td>
<td>21.0 (20-23)</td>
<td>21.9 (20-26)</td>
</tr>
<tr>
<td>Collicular plate, mm</td>
<td>3.5 (2.5-4)</td>
<td>4.0 (2.5-5)</td>
<td>NA</td>
<td>4.2 (3-5)</td>
</tr>
</tbody>
</table>

*Values are mean (range). PSP indicates progressive supranuclear palsy; MSA-P, multiple-system atrophy of striatonigral type; PD, Parkinson disease; and NA, not available.

mean disease duration of longer than 39.4 months showed nearly the same mean midbrain diameter (13.5 mm) as did patients with a mean disease duration of less than 39.4 months (13.2 mm). No significant difference in midbrain diameters could be demonstrated between more or less severely affected patients (mean UPDRS motor [30.9] or total [52.7] score).

In 3 patients with PSP, we were able to evaluate a follow-up MR image after 1 year. Only 1 showed a mild decrease in the midbrain diameter of 1 mm, while the increase in UPDRS rating scale values were nearly identical in all 3 patients (10 points of average worsening of the total score).

**COMMENT**

This MR imaging study on brainstem diameters in various parkinsonian syndromes showed that the simple measurement of the midbrain anteroposterior diameter may differentiate patients with PSP from those with PD or control subjects on an individual basis. However, although midbrain diameters were also significantly reduced in patients with MSA-P, there was overlap with patients with PSP and PD and control subjects.

Novel imaging techniques such as positron emission tomography, single-photon emission computed tomography with ligands binding to the nigrostriatal system, and MR spectroscopy are of additional value to further substantiate the diagnosis but are not widely accessible. Routine imaging techniques are therefore of particular practical value.

Atrophy of the midbrain is one of the typical neuropathologic features in PSP and has already been described in pneumencephalography and in a few computed tomographic series. However, these studies included only small numbers of patients whose clinical diagnoses were based on early criteria that might have been less accurate than those currently proposed for PSP.

In patients with MSA, degeneration of neurons in the basal ganglia with resultant signal changes are prominent on MR imaging and imaging.

Most MR imaging studies confirm the diagnostic value of midbrain atrophy in PSP, but evaluation methods vary widely and include subjective estimation or measurement of the transverse or craniocaudal diameter of the midbrain peduncles. Therefore, it is not surprising that, in addition to reduced midbrain diameters, normal-appearing midbrains have been reported in PSP. A recent report on MSA, PSP, corticobasal degeneration, and healthy controls confirmed the value of anteroposterior measurement of the midbrain diameter in PSP. However, clinicians endeavor to identify and differentiate patients with atypical parkinsonian syndromes from those with typical PD rather than from healthy subjects. Our study, therefore, provides individual values of midbrain diameters in PD, atypical parkinsonian syndromes including MSA-P and PSP, and healthy controls from routine MR imaging and clearly shows that the simple measurement of the midsagittal mesencephalic anteroposterior diameter on routine MR imaging may differentiate PSP from typical PD on an individual basis. Anteroposterior midbrain diameters less than 16 mm strongly argue against the diagnosis of PD, with values less than 14 mm found only in patients with PSP. The observation that midbrain diameters measured by a neuroradiologist blinded to clinical diagnosis clearly allowed patients with PSP to be classified as a distinct group without overlap with PD underlines the value of the National Institute of Neurological Disorders and Stroke criteria for the clinical diagnosis of PSP. Interestingly, there was no correlation between duration or severity of PSP and midbrain diameters, indicating that this measure might also be useful for an early diagnosis of PSP.

Our study confirmed previous MR imaging findings of occasional brainstem atrophy in patients with MSA-P. In view of the broad overlap between PD and MSA-P values, however, they do not contribute to the differential diagnosis. The same is true for the pontine or teg-
mental plate diameters, which—although significantly smaller in patients with MSA-P and PSP than PD—showed a considerable overlap between the groups.

In conclusion, the midsagittal mesencephalic diameter measured on standard routine T2-weighted MR images can be used as a reliable measure to differentiate between patients with typical PD and those with PSP in vivo. This simple additional measure should be incorporated in the diagnostic criteria of PSP.

Accepted for publication January 3, 2001.

This research was performed by the National Parkinson Foundation, Center of Excellence, Clinical Office, at the Department of Neurology, University of Würzburg, Würzburg, Germany.

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REFERENCES