Characteristic Magnetic Resonance Imaging Findings in Machado-Joseph Disease

Yoshio Murata, MD; Shinya Yamaguchi, MD; Hideshi Kawakami, MD; Yukari Imom, MD; Hirofumi Maruyama, MD; Tetsuo Sakai, MD; Toshinari Kazuta, MD; Toshiyuki Ohtake, MD; Masataka Nishimura, MD; Takahiko Saidai, MD; Susumu Chiba, MD; Takekazu Oh-i, MD; Shigenobu Nakamura, MD

**Objective:** To clarify the characteristic magnetic resonance imaging (MRI) findings in patients with Machado-Joseph disease (MJD) diagnosed by genetic analysis.

**Patients and Methods:** Using MRI, we examined 31 patients genetically diagnosed as having MJD, 20 patients with sporadic olivopontocerebellar atrophy, and 26 control subjects.

**Results:** The MRIs of patients with MJD disclosed remarkably reduced width of the superior cerebellar peduncles, atrophy in the frontotemporal lobes, diminished transverse diameter of the globus pallidus, and decreased anteroposterior and transverse diameters of the pons, which correlated with the width of the middle cerebellar peduncle. The width of the superior cerebellar peduncles also correlated with the diameter of the dentate or red nucleus in patients with MJD, but not in controls or in patients with sporadic olivopontocerebellar atrophy. On T2- and/or proton-weighted axial MR imaging, a high signal intensity in the transverse pontine fibers was observed in 14 (45.2%) of 31 patients with MJD and in all patients with sporadic olivopontocerebellar atrophy, but not in any controls.

**Conclusion:** Affected afferent and efferent cerebellar tracts and atrophy of the frontotemporal lobes and globus pallidus are characteristics of MRI of patients with MJD.


---

**RESULTS**

The Table summarizes the MRI findings of 31 patients with MJD, 20 patients with sOPCA, and 26 control subjects. The MJD group had severe atrophy of the pons, middle, and superior cerebellar peduncles, and the globus pallidus compared with controls. The anteroposterior and transverse diameters of the midbrain and the anteroposterior diameter of the medulla oblongata were significantly different between the MJD and control groups (*P*<.05). We observed a significant enlargement of the fourth ventricle in patients with MJD (*P*<.05). The area of the cerebellum was significantly smaller in patients in the MJD group than in controls (*P*<.01). Significant atrophy was observed in the frontotemporal lobes in patients in the MJD group (*P*<.05), but not in the parietal or occipital lobes.

There was a significant correlation between the width of the superior cerebellar peduncle and the diameter of the dentate nucleus (*r*=0.54; *P*<.05) or of the red nucleus (*r*=0.52; *P*<.05) in patients with MJD (Figure 2, top), but not in patients with sOPCA (Figure 2, center) or in controls (Figure 2, bottom). A significant correlation also was found between the width of the middle cerebellar peduncle and the anteroposterior (*r*=0.40; *P*<.05) or transverse diameter of the pons (*r*=0.56; *P*<.005) in patients with MJD.

Transverse pontine fibers were observed in 14 (45.2%) of 31 patients with MJD and in all patients with sOPCA, but in none of the controls. The proton-
**PATIENTS AND METHODS**

We studied 31 patients with MJD (16 men and 15 women; mean±SD age, 50.3±13.7 years; mean±SD duration of illness, 12.9±6.6 years), 20 patients with sporadic olivopontocerebellar atrophy (sOPCA) (6 men and 14 women; mean±SD age, 55.1±11.6 years; mean±SD duration of illness, 3.2±3.1 years), and 26 age-matched control subjects without intracranial lesions (11 men and 15 women; mean±SD age, 49.6±17.2 years). The condition of patients with MJD was diagnosed by genetic analysis and by symptoms and signs, including cerebellar ataxia, pyramidal tract signs, extrapyramidal symptoms, and amyotrophy. The condition of patients with sOPCA was diagnosed by the clinical criteria proposed by Quinn, excluding familial spinocerebellar degeneration by genetic analysis. Informed consent for the genetic analysis was obtained from all patients.

Patients with sOPCA and normal volunteers were examined using 1.5-T MRI. T1-weighted axial images (repetition time [TR], 450 milliseconds; echo time [TE], 30 milliseconds), T2-weighted axial images (TR, 2000 milliseconds; TE, 80 milliseconds), and proton-weighted axial images (TR, 2000 milliseconds; TE, 30 milliseconds) were obtained in the transaxial plane (5-mm thickness and 2.5-mm gap). Patients with MJD were examined using 0.5- to 1.5-T MRI. T1-weighted axial images (TR, 300-600 milliseconds; TE, 15-30 milliseconds), T2-weighted axial images (TR, 2000-4000 milliseconds; TE, 80-102 milliseconds), and proton-weighted axial images (TR, 2000-4000 milliseconds; TE, 15-30 milliseconds) were obtained in the transaxial plane (5- to 8-mm thickness and 0- to 2.5-mm gap). Measurements were performed separately by 3 neuroradiologists (Y.M., S.Y., and Y.I.) who did not know the clinical or genetic status of the subjects.

Anteroposterior and transverse diameters of the pons, midbrain, medulla oblongata, and fourth ventricle were measured on T1-weighted axial images. The width of the middle cerebellar peduncle was also measured on T2-weighted axial images. It was difficult to measure the width of the superior cerebellar peduncle directly on the transaxial T1 MRI, so we evaluated the diameter of the midbrain at the level of the superior cerebellar peduncle, which would indirectly reflect the width of the superior cerebellar peduncles. The diameter of the dentate nucleus, red nucleus, and globus pallidus was determined on T2-weighted axial images. The area of the cerebellum was evaluated on T1-weighted axial images. We tried to exclude the sulcal indentations in the outline of the cerebellum at the edge shown in Figure 1 using a computer software package (MacSCOPE, Mitani Co, Fukui, Japan) on a Macintosh computer. The threshold was determined to represent the edge of the cerebellum accurately and the binary image was made. Thereafter, pixels in the cerebellar area were counted and the area of the cerebellum was measured. The degree of atrophy in the frontal, temporal, parietal, and occipital lobes was visually divided into 4 grades (0, none; 1, mild; 2, moderate; and 3, severe) by observers (Y.M., S.Y., and Y.I.) unaware of the subject status. The appearance of the abnormal signal intensity of transverse pontine fibers was assessed on T2- and/or proton-weighted axial images.

All data were analyzed using the computer software package JMP 3.0 (SAS Institute Inc, Cary, NC) on a Macintosh computer. Differences between the groups were examined by analysis of variance. Frontal, temporal, parietal, or occipital lobe atrophy was analyzed by the Wilcoxon rank sum test. Probability values less than 5% were accepted as significant.

*Figure 1. Measurements on T1- and T2-weighted axial magnetic resonance images. 1 indicates anteroposterior diameter of the globus pallidus; 2, transverse diameter of the globus pallidus; 3, anteroposterior diameter of the midbrain; 4, transverse diameter of the midbrain; 5, width of the superior cerebellar peduncles; 6, width of the middle cerebellar peduncle; 7, diameter of the dentate nucleus; 8, diameter of the red nucleus; 9, anteroposterior diameter of the pons; 10, transverse diameter of the pons; 11, anteroposterior diameter of the fourth ventricle; 12, transverse diameter of the fourth ventricle; 13, anteroposterior diameter of the medulla oblongata; 14, transverse diameter of the medulla oblongata; and 15, area of the cerebellum.*
Moderate cerebellar atrophy and marked brainstem atrophy, especially in the pontine tegmentum, were observed in the MJD group, which is consistent with previous MRI and pathologic studies. Our study also disclosed a moderate to severe atrophy in the frontal and temporal lobes, and remarkable atrophy in the superior and middle cerebellar peduncles and globus pallidus in patients with MJD. Marked dilatation of the fourth ventricle was also observed in patients in the MJD group, which probably could be attributed to the atrophy of the pontine tegmentum and dentate nucleus.

To evaluate the accuracy of measurement in the dentate nucleus, red nucleus, and globus pallidus on 0.5-T MRI, we investigated the size of the dentate nucleus, red nucleus, and globus pallidus in 23 healthy volunteers on 0.5-T MRI and in 26 healthy volunteers on 1.5-T MRI. The dentate nucleus, red nucleus, and globus pallidus were visible and their size was measured on the 0.5-T magnetic field, but we found no significant difference in their size between 0.5- and 1.5-T MRI (dentate nucleus, mean±SD 1.70±0.23 cm and 1.54±0.22 cm; red nucleus, 0.64±0.10 cm and 0.69±0.11 cm; anteroposterior diameter of the globus pallidus, 2.49±0.37 cm and 2.54±0.37 cm; transverse diameter of the globus pallidus, 0.79±0.12 cm and 0.83±0.16 cm, respectively). These data suggest that the size measured on the 0.5-T MRI would not be underestimated compared with that measured on the 1.5-T MRI. Therefore, the size of the dentate nucleus, red nucleus, or globus pallidus would not be influenced by variable magnetic fields, and would therefore be reliable.

The atrophy of the pons or midbrain is age-dependent, because significant reverse correlation was found between age and the anteroposterior diameter of the pons (P<.05) or the anteroposterior diameter of the midbrain (P<.01) in patients in the MJD group. The duration of illness correlated with the decrease in the anteroposterior (r=0.40, P<.05) and transverse diameters (r=0.53, P<.01) of the globus pallidus in patients in the MJD group, and with the degree of temporal or occipital lobe atrophy in MJD (P<.05). These data indicate that changes disclosed by MRI are age-related and develop according to the disease process.

The width of the superior or middle cerebellar peduncle was significantly decreased in patients in the MJD group compared with controls (P<.05). There was a significant correlation between the anteroposterior or transverse diameter of the pons and the width of the middle cerebellar peduncle. The atrophy of the pons and the middle cerebellar peduncle suggests that the afferent cerebellar tract from the pontine nuclei to the cerebellum through the middle cerebellar peduncle is affected in MJD.

To characterize MRI features peculiar to MJD, we compared the MRI findings of 31 patients who had MJD with those of 20 patients who had sOPCA, although sOPCA might include miscellaneous disease entities. There was a significant difference in the duration of illness between the patients with MJD and sOPCA (P<.05), probably due to more rapid progress in patients with sOPCA. In patients with sOPCA, the superior cerebellar peduncle was preserved, but it was atrophied in patients with MJD. Moreover, the correlation was observed between the width of the superior cerebellar peduncles and the diameter of the dentate or red nucleus in patients with MJD, but not in controls or in patients with sOPCA. Although there was no significant difference in the diameter of the dentate or red nucleus among the 3 groups by analysis of variance, the atrophy of the superior cerebellar peduncle seems to proceed in parallel with the atrophy of the dentate and red nucleus in patients with MJD. The dentate or red nucleus and the superior cerebellar peduncle are spared in patients with sOPCA and in controls. Therefore, no close relationship exists between the width of the superior cerebellar peduncles and the diameter of the dentate or red nucleus in patients with sOPCA and in control subjects. In addition, transverse diameter of the globus pallidus was significantly smaller in patients with MJD compared with controls (P<.05 vs the control group) and those with sOPCA (P<.01 vs the control group).


d| Finding | Control | MJD | sOPCA |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pons, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>2.47±0.21</td>
<td>1.81±0.32†</td>
<td>2.15±0.29†</td>
</tr>
<tr>
<td>Trans</td>
<td>3.00±0.25</td>
<td>2.33±0.43‡</td>
<td>2.67±0.34‡</td>
</tr>
<tr>
<td>Midbrain, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>2.62±0.16</td>
<td>2.11±0.35§</td>
<td>2.39±0.25‡</td>
</tr>
<tr>
<td>Trans</td>
<td>3.59±0.40</td>
<td>3.03±0.60‡</td>
<td>3.11±0.38‡</td>
</tr>
<tr>
<td>Medulla oblongata, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>1.66±0.25</td>
<td>1.25±0.23§</td>
<td>1.30±0.17‡</td>
</tr>
<tr>
<td>Trans</td>
<td>1.72±0.16</td>
<td>1.47±0.32</td>
<td>1.42±0.13</td>
</tr>
<tr>
<td>Fourth ventricle, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>1.11±0.26</td>
<td>1.47±0.45¶</td>
<td>1.06±0.32</td>
</tr>
<tr>
<td>Trans</td>
<td>1.44±0.37</td>
<td>1.88±0.57‡</td>
<td>1.41±0.54</td>
</tr>
<tr>
<td>Middle cerebellar peduncle, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>1.75±0.24</td>
<td>1.16±0.46‡</td>
<td>1.45±0.25‡</td>
</tr>
<tr>
<td>Trans</td>
<td>2.00±0.12</td>
<td>1.47±0.27‡</td>
<td>1.86±0.14</td>
</tr>
<tr>
<td>Dentate nucleus, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>1.54±0.22</td>
<td>1.81±1.26</td>
<td>1.76±0.25</td>
</tr>
<tr>
<td>Red nucleus, cm</td>
<td>0.69±0.11</td>
<td>0.83±0.26</td>
<td>0.83±0.12</td>
</tr>
<tr>
<td>Globus pallidus, cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AP</td>
<td>2.54±0.37</td>
<td>2.31±0.47</td>
<td>2.55±0.31</td>
</tr>
<tr>
<td>Trans</td>
<td>0.83±0.16</td>
<td>0.65±0.33¶</td>
<td>0.81±0.13</td>
</tr>
<tr>
<td>Area of cerebellum, cm²</td>
<td>41.45±6.37</td>
<td>35.16±4.93§</td>
<td>28.50±6.70¶</td>
</tr>
<tr>
<td>Atrophy, grade§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal lobe</td>
<td>0.65±0.75</td>
<td>1.32±0.79§</td>
<td>0.75±0.72</td>
</tr>
<tr>
<td>Temporal lobe</td>
<td>0.77±0.71</td>
<td>1.29±0.82¶</td>
<td>1.10±0.91</td>
</tr>
<tr>
<td>Parietal lobe</td>
<td>0.96±0.77</td>
<td>0.87±0.81</td>
<td>1.20±0.41</td>
</tr>
<tr>
<td>Occipital lobe</td>
<td>0.46±0.65</td>
<td>0.35±0.49</td>
<td>0.15±0.37</td>
</tr>
</tbody>
</table>

* Values are given as mean±SD. MJD indicates Machado-Joseph disease; sOPCA, sporadic olivopontocerebellar atrophy; AP, anteroposterior diameter; and trans, transverse diameter.
†P<.05 vs the control group.
‡P<.01 vs the control group.
§Graded as 0, none; 1, mild; 2, moderate; and 3, severe.

©1998 American Medical Association. All rights reserved.
dition, sOPCA progresses more rapidly than MJD, so disproportionate atrophy may be present in sOPCA. Furthermore, the atrophy of the dentate nucleus seems to be related to the pontocerebellar tract, but not to the dentatorubrothalamic tract. These findings indicate intact efferent fiber systems in sOPCA, which has been indicated by previous reports in contrast to MJD. The involvement of the efferent dentatorubral system, which runs through the superior cerebellar peduncle in MJD shown by autopsy studies, seems to characterize the MRI of patients with MJD.

A high signal intensity in the transverse pontine fibers on T2-weighted axial image was previously reported to be characteristic in sOPCA. In the present study, almost half (14 of 31) of patients with MJD had the pontine high signal intensity, which presum-

Figure 2. Correlation between the width of the superior cerebellar peduncle and the diameter of the dentate and red nuclei in patients with Machado-Joseph disease (top), in patients with sporadic olivopontocerebellar atrophy (center), and in controls (bottom). There was a significant correlation between the width of the superior cerebellar peduncles and the diameter of the dentate nucleus (r = 0.54, P < .05) and of the red nucleus (r = 0.52; P < .05) in patients with Machado-Joseph disease, but not in patients with sporadic olivopontocerebellar atrophy or in controls.
ably reflects the gliosis and myelin sheath loss along the degenerated pontocerebellar fibers elucidated by morphological studies on MJD.14,17 Age-related pathological changes in pontocerebellar fibers may contribute to the appearance of a high signal intensity in the transverse pontine fibers on T2 and/or proton-weighted MRIs, which can be detected in various cerebellar diseases.18 Moreover, the pons or midbrain decreases its size and is packed according to aging. Consequently, an abnormal high signal intensity in the pons could be observed in older patients with MJD and is not specific to sOPCA.

Frontal or temporal lobe atrophy or decrease in the transverse diameter of the globus pallidus and the aforementioned findings may fortify the neuroradiological diagnosis of MJD. These MRI findings and the clinical features characteristic of MJD may prompt us to identify the gene responsible for MJD. These results also seem to help the differentiation of MJD from sOPCA.

**REFERENCES**


Figure 3. The proton-weighted axial magnetic resonance images of a 64-year-old woman with Machado-Joseph disease. A high signal intensity in the transverse pontine fibers is observed (arrow). The duration of illness was 3 years.

Accepted for publication June 3, 1997.

This work was supported by a grant-in-aid from the Research Committee of Central Nervous System Degenera-tive Diseases, the Ministry of Health and Welfare of Japan.

We thank Kiyoshi Harada, MD (Department of Neurology, Shizuoka General Hospital, Shizuoka, Japan), and Yuichiro Inatomi, MD (Department of Neurology, Iizuka Hospital, Fukuoka, Japan), for referral of patients, and to Kaori Katayama for photography.

Reprints: Yoshio Murata, MD, Third Department of Internal Medicine, Hiroshima University School of Medicine, 1-2-3 Kasumi, Minami-ku, Hiroshima 734, Japan.

©1998 American Medical Association. All rights reserved.