Original Article

The Cerebral to Middle Cerebellar Peduncle Width Ratio: An Imaging Biomarker for Differentiating Multiple System Atrophy from Degenerative Parkinsonism

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Abstract

Introduction: The differentiation between Parkinson's disease (PD) and atypical parkinsonian syndromes (APS) is clinically challenging. Magnetic resonance imaging (MRI) measurement of the cerebral peduncle (CP) and middle cerebellar peduncle (MCP) axial widths have not been investigated. The objective was to evaluate the utility of the CP and MCP axial widths in the differentiation of degenerative parkinsonian syndromes and their clinical correlations.

Methods: The CP and MCP were retrospectively measured based on the axial T1-weighted MRI in 100 patients with probable PD, multiple system atrophy (MSA), progressive supranuclear palsy, Lewy body dementia, or Alzheimer's disease from the movement disorders clinic at Thammasat University Hospital between January 2018 and December 2021 and in ten controls. Diagnostic accuracy was determined based on the final diagnosis. The Schwab & England activity of daily living (ADL), the Hoehn & Yahr (H&Y), and the levodopa equivalence dose (LED) were evaluated.

Results: Patients with parkinsonian syndromes had smaller mean CP and MCP axial widths than controls. Patients with probable MSA had the largest axial CP widths and the smallest MCP axial widths. A CP to MCP width ratio ≥ 0.88 suggested the diagnosis of probable MSA (sensitivity 90.0%, specificity 91.2%, AUC 0.93). There was no difference in the CP width between probable PD and APS. The small CP width correlated with advanced age and poor ADL, while the small MCP width was associated with poor ADL, advanced H&Y, and low LED.

Conclusion: This study shows the benefit of using CP and MCP axial widths as an imaging biomarker for patients with degenerative parkinsonian syndromes and could help differentiate MSA patients from others with parkinsonism.

Keywords: Parkinson's disease, Multiple system atrophy, Atypical parkinsonism, Magnetic resonance imaging, Biomarker

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Introduction

Atypical parkinsonian syndromes (APS) describe a group of neurological disorders that comprise parkinsonism and additional clinical features that are not typically seen in Parkinson's disease (PD). In current clinical practice, a diagnosis of APS mainly relies on clinical findings. Differentiating between PD and APS, as well as among the various APS subtypes is clinically challenging, especially in the early stages of the disease. Evidence indicates that the diagnostic accuracy of PD is low initially but improves to 88% after five years of follow-up.[1] Continuous clinical evaluation and the use of additional diagnostic tools will provide valuable clues and improve the accuracy of distinguishing PD and APS over time. Several studies have demonstrated the benefits of neuroimaging techniques in improving diagnostic accuracy and differentiating APS from PD. While most research has focused on characteristic signs, volumes, and diameters based on sagittal plane imaging, the measurement of the cerebral peduncle (CP) and middle cerebellar peduncle (MCP) axial widths has not been extensively investigated. CP and MCP are crucial for the integration and coordination of motor control, particularly in transmitting signals from the cerebral cortex to the brainstem and from the brainstem to the cerebellum. Our research aimed to evaluate the utility of CP and MCP axial widths as imaging biomarkers for differentiating degenerative parkinsonian syndromes and their clinical correlations.

Methods

The first available brain MR images of 75 patients with parkinsonian syndromes who attended a movement disorders clinic at Thammasat University Hospital between January 2018 and December 2021, 22 patients with Alzheimer's disease (AD), and 10 healthy control subjects were retrospectively reviewed. Clinical diagnoses of probable PD,[2] multiple system atrophy (MSA),[3] progressive supranuclear palsy (PSP),[4] Lewy body dementia (LBD) including PD with dementia (PDD),[5] dementia with Lewy bodies (DLB),[6] and AD[7] were determined based on established criteria. The subtypes within each Parkinsonian syndrome were classified according to clinical manifestations: PD with tremor-dominant (TD), postural instability and gait difficulty (PIGD), and indeterminate subtype (ID); MSA cerebellar subtype (MSA-C) and MSA with parkinsonism subtype (MSA-P); PSP Richardson syndrome (PSP-RS), and PSP with progressive gait freezing (PSP-PGF). Subjects with uncertain clinical diagnosis or MRI abnormalities such as basal ganglia, brainstem infarctions, and brain tumors were excluded from the study. All patients with parkinsonian syndromes had at least 1 year of follow-up. The following demographic and clinical data were collected for each patient: current age, age at onset, age and disease duration at the first MRI scan, clinical parkinsonian subtype, the Schwab and England Activities of Daily Living Scale (SE-ADL), the modified Hoehn and Yahr (H&Y) scale, the current levodopa equivalent dose (LED), Thai mental state examination (TMSE), and co-morbidities. The study received approval from the Human Research Ethics Committee of Thammasat University.

MRI and measurement protocol. Brain MRIs were performed according to the routine brain MRI protocol using a 1.5 or 3.0 T MRI system (Siemens Magnetom Aera 1.5, Siemens Magnetom Skyra 3.0). All MR examinations included axial and sagittal T1-weighted spin echo images (section thickness, 5 mm), axial and sagittal T2-weighted turbo spin echo (section thickness, 5 mm), axial T2 fluid-attenuated inversion recovery with fat suppression (section thickness, 5 mm), axial and coronal T2-weighted gradient-echo (section thickness, 5 mm), axial resolve diffusion-weighted imaging and apparent diffusion coefficient mapping (section thickness, 5 mm). Patients with an additional PD protocol will receive axial proton density-weighted turbo spin echo (section thickness, 3 mm), axial T2-weighted turbo spin echo (section thickness, 3 mm), and axial 3D susceptibility-weighted imaging (SWI, section thickness, 0.7 mm). Two independent raters experienced in neurology and who were blinded to the patient's diagnosis evaluated all MR images. All measurements were made using Synapse 5 (version 5.7.100, Fujifilm medical system, USA). To assess the interrater reliability, a second evaluation was made 2 weeks later by another rater. The interrater reliability of the axial CP and MCP widths was 0.96 (interrater ICC range 0.92-0.98). The mean value of these two measurements was used for statistical analyses. The brain structures that were measured are shown in

Figure 1. The CP and MCP widths were measured on an axial T1-weighted image. The left and right CP were identified on the axial view at the plane of the red nucleus and the mamillary body. The CP axial width was measured as the maximum perpendicular width from the anterior surface at the interpeduncular fossa to the posterior surface bilaterally. The MCP was measured as the maximum width from the anterior to the posterior surface of each side of the MCP that was best exposed at the level of the mid pons. The width of each side of the CP and MCP was measured, and the mean value of each side was calculated. In addition, the sagittal view of the midbrain to pons ratio and the mean MCP sagittal height were measured. The conventional brain MR images were visually inspected for the presence of loss of swallow tail sign, hummingbird/penguin sign, the hot cross bun sign, the putaminal rim sign, and the degree of cerebellar atrophy. The medial temporal atrophy (MTA) scale score, the Fazekas scale score for white matter lesions, and the Evans index were defined.

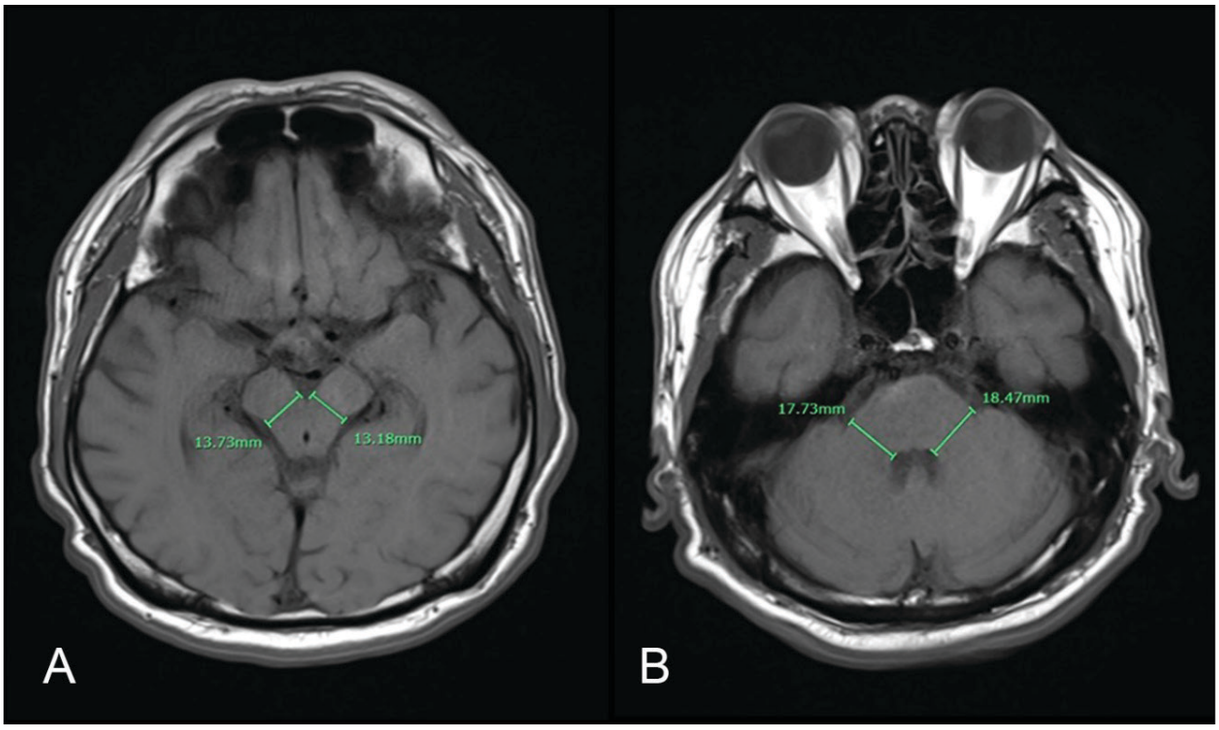

Figure 1 Measuring the axial width of the cerebral peduncle (A) and the middle cerebella peduncle (B) using axial T1-weighted magnetic resonance images.

Statistical analysis. Statistical analysis was performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Data are presented as the mean ± standard deviation (SD), the median with interquartile range (IQR), or percentages. One-way analysis of variance (ANOVA) or the Kruskal-Wallis test was used to determine differences between groups. The independent samples t-test or the Mann-Whitney test was used to compare different means between the groups. All tests were two-sided and $p < 0.05$ was statistically significant. The interrater reliability was assessed by the intraclass correlation coefficient (ICC). Diagnostic accuracy and the optimal cut-off point was determined by receiver operating characteristic (ROC) curve analysis, including sensitivity, specificity, and area under the curve (AUC).

Results

Demographic data. Data and brain MR images from a total of 107 subjects were evaluated. Of these, 7 subjects were excluded due to uncertain clinical diagnosis (3) and the presence of a large cerebral or brainstem infarction (4). The demographic and clinical characteristics of the clinically diagnosed groups are summarised in Table 1. Sex was not different between the groups. The mean duration of clinical parkinsonism before the first MRI brain scan was 3.79 ± 3.51 years. Fifty-four subjects (79.41%) had an MRI brain scan performed within the first five years of their clinical parkinsonian onset. The mean duration of clinical follow-up was 4.85 ± 2.63 years. In subjects without dementia, there was no difference in age at MRI scan between patients with parkinsonian syndromes and controls. However, MSA patients were significantly younger at the first MRI scan compared to PSP patients (59.70 ± 3.65 vs 67.50 ± 5.47 years, $p < 0.001$). Patients with non-demented PD had significantly better SE-ADL functions, higher LED, and a lower H&Y stage than other atypical parkinsonian groups. In patients with dementia, there was no difference in age at scan between patients with probable Lewy body dementia (LBD), which included PDD and DLB, and patients with probable AD. There was a significant difference in the duration of clinical parkinsonian symptoms before the first MRI brain scan between the groups (chi-square = 13.15, $p = 0.004$).

Imaging features. Table 2 shows a comparison of the MRI measurements between the groups. Patients presenting with parkinsonian symptoms exhibited significantly smaller mean CP axial width (12.75 ± 1.26 vs 13.99 ± 0.75 mm, $p < 0.01$) and MCP axial width (16.10 ± 2.02 vs 17.94 ± 1.21 mm, $p = 0.07$) than controls. The mean CP axial width in controls was significantly larger than in patients with PD ($p = 0.010$), PSP ($p = 0.001$), LBD ($p = 0.001$), or AD ($p = 0.002$). Moreover, patients diagnosed with MSA had significantly larger mean CP axial width than patients with PSP ($p = 0.044$) or LBD ($p = 0.041$). Subgroup analysis within each parkinsonian subtype revealed a significantly smaller mean CP axial width in PSP-RS compared to PSP-PIGF (12.02 ± 0.94 vs 13.56 ± 1.00 mm, $p = 0.010$) and in PDD compared to DLB (11.77 ± 0.99 vs 14.01 ± 1.44 mm, $p = 0.012$). There were no significant differences in the mean CP axial width among the various subtypes of PD and MSA.

The mean MCP axial width in controls was also significantly larger than in patients with PSP ($p < 0.001$), MSA ($p < 0.001$), LBD ($p = 0.020$), or AD ($p < 0.001$). There was no difference in the mean MCP axial width between PD patients and controls. Compared to patients with PD, the mean MCP axial width was significantly smaller in patients with PSP ($p < 0.001$), MSA ($p < 0.001$), or AD ($p = 0.002$). Patients with MSA demonstrated the smallest mean MCP axial width. Among patients with parkinsonian syndromes, a mean MCP axial width of less than 14.50 mm suggests a diagnosis of MSA (sensitivity 80.0%, specificity 89.7%, AUC 0.82, $p < 0.001$). The mean CP to MCP width ratio was significantly higher in patients with MSA compared to the other groups (Figure 2). Subgroup analysis revealed a significantly smaller mean MCP axial width in MSA-C compared to MSA-P (12.56 ± 1.80 vs 18.11 ± 1.83 mm, $p < 0.001$), although the mean CP to MCP width ratio did not show statistically significant differences between MSA-C and MSA-P (1.05 ± 0.16 vs 0.81 ± 0.10 mm, $p = 0.079$). A CP to MCP width ratio of 0.88 or higher suggests the diagnosis of probable MSA (sensitivity 90.0%, specificity 91.2%, AUC 0.93, $p < 0.001$) (Figure 3).

There were significant correlations between the CP axial width and the age at scan ($r = -0.33$, $p = 0.001$) and the SE-ADL scale ($r = 0.23$, $p = 0.046$). Furthermore, the MCP axial width was correlated with the CP axial width ($r = 0.32$, $p = 0.001$), the SE-ADL scale ($r = 0.55$, $p < 0.001$), the H&Y stage ($r = -0.50$, $p < 0.001$), LED ($r = 0.43$, $p < 0.001$), the MCP sagittal height ($r = 0.66$, $p < 0.001$), the mean MTA scale score ($r = -0.26$, $p = 0.008$), and the Evans index ($r = -0.29$, $p = 0.003$). There was no correlation between the CP or MCP axial width and the duration of parkinsonian symptoms or TMSE score.

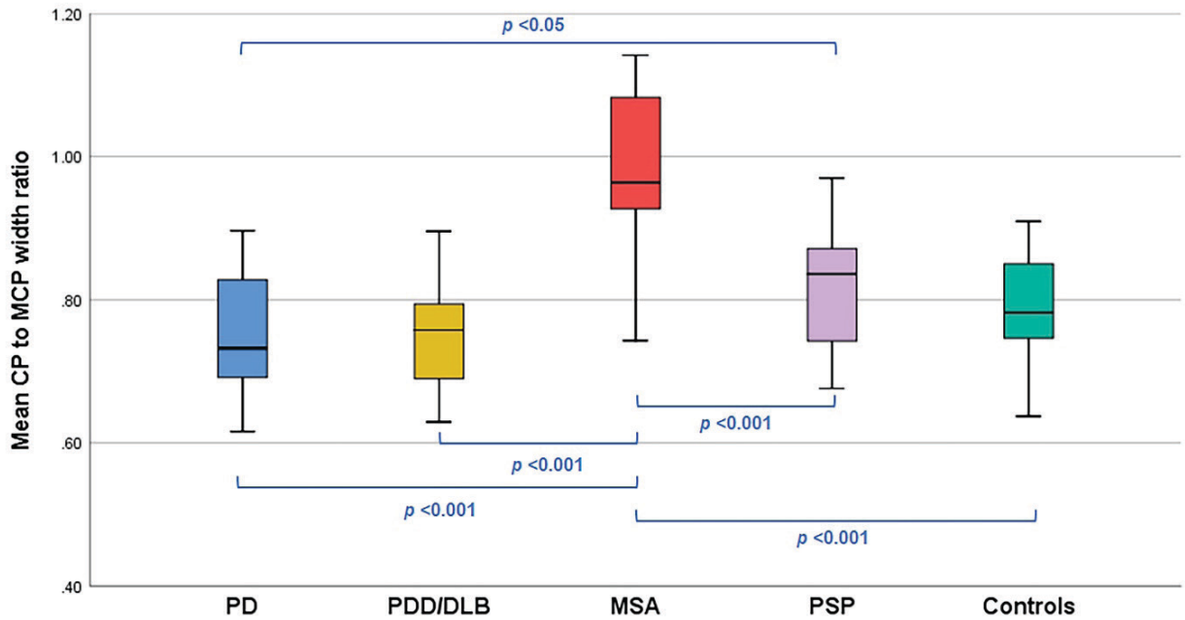

Figure 2 The cerebral peduncle (CP) to middle cerebella peduncle (MCP) axial width ratio in patients with parkinsonism and controls. Abbreviations: PD = Parkinson's disease, PDD = Parkinson's disease with dementia, DLB = dementia with Lewy bodies, MSA = multiple system atrophy, PSP = pro gressive supranuclear palsy.

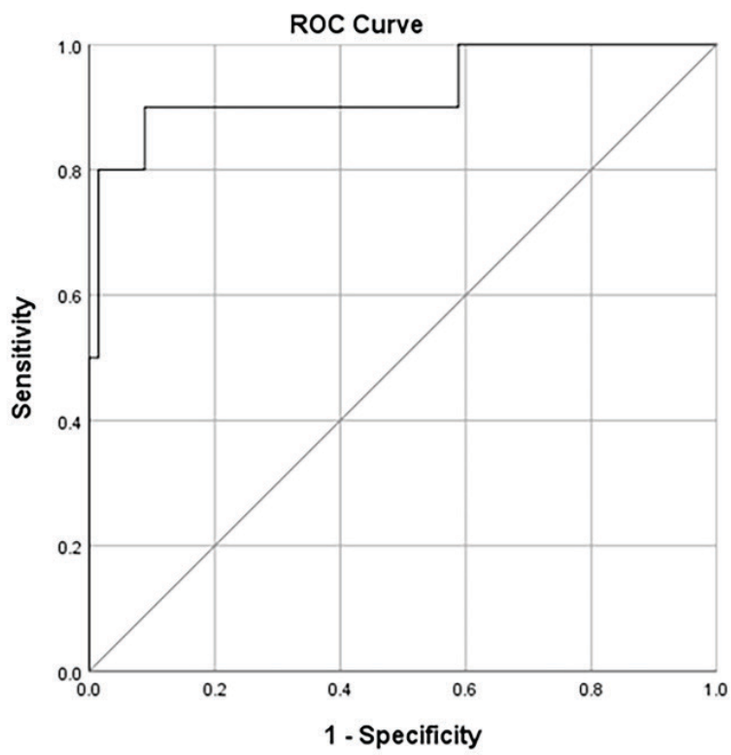

Figure 3 The receiver operating characteristic (ROC) curve of the CP to MCP axial width ratio to differentiate patients with multiple system atrophy (MSA) from other parkinsonism.

Discussion

MRI plays an important role in the diagnosis of various neurological diseases and provides *in vivo* biomarkers that inform the underlying neurodegenerative processes. Numerous quantitative assessments of regional brain size and volume facilitate early diagnosis and could also be useful to follow disease progression. Generally, conventional brain MRI does not show specific abnormalities in the early stage of parkinsonism. However, subtle changes in terms of size and volume may help differentiate and support the clinical diagnosis in some patients.

This study has shown the utility of quantitative assessment using the CP and MCP axial widths as an imaging biomarker for patients with degenerative parkinsonian syndromes and might be helpful in differentiating MSA patients from others with parkinsonism. The mean CP axial width was smaller in patients with PD, PSP, LBD, or AD compared to those with MSA and controls. This finding aligns with previous MRI studies that demonstrated a significant reduction in the midbrain volume in patients with PSP or AD.[8-10] Additionally, the preserved CP axial width in MSA may indicate that the pathology predominantly affects the lower brainstem and cerebellar connections, rather than the upper brainstem and cerebral connections, as seen in other parkinsonian syndromes.[11] Furthermore, the reduction in CP axial width in our patients was associated with advancing age and severe motor disability, but not with the duration of parkinsonism. These findings may indicate that patients and/or their caregivers recognized parkinsonian symptoms later than their actual onset. Although the CP axial width was not correlated with the TMSE score, it was significantly smaller in the demented group and in PSP patients, who often develop dementia. This reduction reflects the degenerative process of the cortico-striatal pathway, which is relevant to their cognitive and behavioural symptoms.

The average width of the MCP, measured in both the axial and sagittal planes, was reduced in MSA patients, particularly in those with MSA-C. This finding is consistent with previous MRI studies showing a reduction in MCP width in the sagittal plane[12] along with pathological findings of pontocerebellar atrophy in MSA-C.[8,12-14] Measurement of the MCP axial width helped discriminate MSA from those with other parkinsonian syndromes. In addition, a reduced MCP axial width suggests poorer motor function and a more advanced stage of parkinsonism. Patients with MSA had a significantly greater mean CP to MCP width ratio than the other groups. This finding probably results from an inappropriate atrophy of the MCP compared to the CP in MSA patients. Measurement of the CP to MCP width ratio in the axial view helped differentiate MSA patients from patients with other parkinsonism syndromes. Although, subgroup analysis in patients with MSA-P did not show a reduction in MCP axial width or an increased in CP to MCP width ratio, as observed in MSA-C. This finding might suggest that neuronal loss in MSA-P is more prominent in the striatum and substantia nigra rather than in the pontine nuclei or cerebellum and olivary nucleus. However, caution should be exercised in interpreting these results due to the small sample size for MSA-P. It is important to note that 80% of MSA cases in this study were the MSA-C subtype, which is prevalent in East Asia.[15] Cerebellar and pontine involvement is likely a major factor contributing to the decreased MCP size and poorer motor function in these patients. In addition, there was a significant reduction in the midbrain to pons ratio in the PSP group and an increase in the ratio in the MSA group, a finding similar to a previous study.[16]

In terms of qualitative visual inspection of the MRI, there was an absence of dorsolateral nigral hyperintensity in SWI or 'loss of swallow tail sign' in approximately 63.3% of patients with PD and 83.3% of patients with LBD. This finding has also been frequently reported in patients with other APS and idiopathic rapid eye movement (REM) sleep behaviour disorder (RBD).[17,18] The presence of this sign is probably due to abnormal iron deposition in subjects with parkinsonian syndromes,[19] and could be a useful sign to discriminate patients with parkinsonian syndromes from healthy controls. With standard sagittal T1-weighted imaging, the flat or concave aspect of the midbrain tegmentum known as the hummingbird or penguin sign was demonstrated in 81.3% of patients with PSP, but in all patients with PSP- Richardson syndrome (PSP-RS). This feature also occurred in some patients with AD. This finding might reflect the involvement of upper brainstem pathology and the dopaminergic system

in the pathophysiology of AD.[20] Although this sign is highly specific for PSP-RS, it has low sensitivity, especially in patients with early stages of the disease and in PSP variants.[21] In the present study, the hot cross bun sign which describes a cross-shaped increase in signal intensity that affects the transverse pontine fibres on an axial T2-weighted image was found in 60% of patients with MSA and 75% of patients with MSA-C. Although this feature was not found in other groups in the present study, the specificity is limited because it could be found in patients with hereditary cerebellar ataxia.[22] The hyperintense rim at the lateral edge of the dorsolateral putamen on T2-weighted images, known as the putaminal rim sign, was observed in 40% of patients with MSA in the present study and was occasionally observed in patients with PD and in controls. This finding supports that the putaminal rim sign is a nonspecific finding, as mentioned in previous studies.[23,24]

The strength of this study lies in the extended follow-up period, providing valuable insights into the precise subtype of each disease. With an average follow-up duration of approximately 5 years, the clinical diagnostic accuracy is significantly improved. However, the present study has some limitations. First, the findings could not be validated with neuropathological data. All groups were defined according to a probable diagnosis based on their clinical symptoms and progression. Consequently, the clinical diagnosis may not be consistent with the pathological diagnosis, particularly in aging patients who might have multiple coexisting pathologies. Second, this study was based on retrospective reviews of the MRI image and patients's records from a single center with a Thai population, and the number of subjects was limited. Therefore, the results may vary in different populations. To minimize discrepancies in future studies, standardand consistent imaging protocols should be implemented, along with a multi-center registry and a larger sample size. Third, the timing of the clinical examinations and imaging study varied among patients. Although most imaging studies were performed within the first five years after the clinical onset, quantitative MRI measurement might not be sensitive enough to detect the difference in the early stage of the diseases. Fourth, the measurement of a single axial plane MRI could be complicated in patients with multiple brain pathologies and previous brain lesions. The clinical signs and progression of symptoms together with qualitative and quantitative MRI inspection would be the best way to obtain the most accurate diagnosis. Lastly, there was no follow-up data in the control group. It is possible that some of them may develop neurodegenerative disorders later.

Conclusion

This study provides a simple and validated MRI measurement procedure for the differentiation of MSA from other degenerative parkinsonian syndromes. Measurement of CP and MCP widths on the axial MRI plane could be an MRI biomarker for patients with degenerative parkinsonian syndromes and might help differentiate patients with MSA from others with degenerative parkinsonism.

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None reported

Ethical compliance statement

The study protocol was approved by the local ethics committee. Informed consent was given a formal waive because of the retrospective design by the institutional ethics committee. All the methods were carried out in accordance with the relevant guidelines and regulations.

Conflicts of Interest

There are no conflicts of interest.

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Table 1 Demographic and clinical features of the clinically diagnosed groups.

	Subjects without dementia (n = 66)				Subjects with dementia (n = 34)	
	PD (n = 30)	**MSA (n = 10)**	**PSP (n = 16)**	**Control (n = 10)**	**LBD (n = 12)**	**AD (n = 22)**
Subgroup	TD: 2 (6.7%) PIGD: 9 (30%) ID: 19 (63.3%)	MSA-C: 8 (80%) MSA-P: 2 (20%)	PSP-RS: 12 (75%) PSP-PGF: 4 (25%)	-	PDD: 9 (75%) DLB: 3 (25%)	-
Male sex (%)	20 (66.7%)	6 (60.0%)	8 (50.0%)	5 (50%)	7 (58.3%)	10 (45.5%)
Age (years)	67.74 ± 8.05	64.60 ± 5.23	70.38 ± 5.77	64.10 ± 5.57	76.75 ± 4.49	75.68 ± 7.27
Age at onset (years)	60.37 ± 8.41	58.70 ± 3.37	64.44 ± 4.95	-	65.67 ± 7.10	-
Age at scan (years)	64.37 ± 8.10	59.70 ± 3.65	67.50 ± 5.47	62.40 ± 5.50	72.25 ± 5.08	72.73 ± 6.90
Duration of parkinsonism before scan (years)*	3.00 (3.75)	1.00 (1.13)	2 (3.75)	-	3.5 (8.75)	-
Duration of follow-up (years)*	4.50 (4.00)	3.50 (6.50)	3.50 (3.75)	-	6.00 (2.50)	-
TMSE	28.61 ± 1.78	27.00 ± 1.00	28.00 ± 2.00	30.00 ± 0.00	20.80 ± 1.79	19.69 ± 5.25
SE-ADL scale	73.00 ± 10.88	40.00 ± 12.47	45.00 ± 10.33	-	45.83 ± 15.05	-
H&Y scale	2.53 ± 0.60	4.10 ± 0.57	4.06 ± 0.68	-	3.54 ± 0.72	-
LED (mg/day)	698.10 ± 326.38	294.00 ± 269.49	400.00 ± 237.07	-	642.58 ± 368.97	-

* Median with interquartile range.

Abbreviations: PD = Parkinson's disease, MSA = multiple system atrophy, PSP = progressive supranuclear palsy, LBD = Lewy body dementia, AD = Alzheimer's disease, TD = tremor-dominant subtype, PIGD = postural instability and gait difficulty subtype, ID = indetermined subtype, MSA-C = MSA cerebellar subtype, MSA-P = MSA parkinsonism subtype, PSP-RS = PSP Richardson syndrome, PSP-PGF = PSP with progressive gait freezing, PDD = Parkinson's disease dementia, DLB = dementia with Lewy bodies, TMSE = Thai mental stage examination, SE-ADL = Schwab and England Activities of Daily Living Scale, H&Y = Modified Hoehn and Yahr Scale, LED = levodopa equivalent dose

Table 2 Imaging parameters in clinical diagnosed groups.

	Subjects without dementia (n = 66)				**Subjects with dementia** (n = 34)		
	PD (n = 30)	**MSA** (n = 10)	**PSP** (n = 16)	**Controls** (n = 10)	**LBD** (n = 12)	**AD** (n = 22)	**Group comparison**
Mean CP width (mm)	12.92 ± 1.23	13.33 ± 1.10	12.40 ± 1.15	14.00 ± 0.75	12.33 ± 1.45	12.59 ± 0.88	Control > PD†, PSP*, LBD*, AD* MSA > PSP†, LBD†
Mean MCP width (mm)	17.18 ± 1.05	13.67 ± 2.90	15.35 ± 1.82	17.94 ± 1.21	16.41 ± 1.13	15.82 ± 1.19	Control > PSP*, MSA*, LBD†, AD* PD > PSP*, MSA*, AD* MSA < PD*, PSP*, LBD*, AD*, Control*
CP/MCP width ratio	0.75 ± 0.08	1.01 ± 0.18	0.81 ± 0.09	0.78 ± 0.08	0.75 ± 0.08	0.80 ± 0.07	MSA > PD*, PSP*, LBD*, AD*, Control* PSP > PD†
Midbrain/ pons ratio	0.67 ± 0.08	0.82 ± 0.15	0.52 ± 0.05	0.65 ± 0.03	0.67 ± 0.05	0.65 ± 0.05	PSP < PD*, MSA*, LBD*, AD*, Control*
Mean MCP height (mm)	12.61 ± 1.11	7.91 ± 2.87	12.09 ± 1.60	12.16 ± 0.92	12.19 ± 0.80	11.78 ± 0.99	MSA < PD*, PSP*, LBD*, AD*, Control†
Mean MTA scale	0.37 ± 0.56	0.50 ± 0.53	0.91 ± 0.69	0.25 ± 0.42	0.92 ± 0.76	2.36 ± 0.66	AD > PD*, LBD*, PSP*, Control*
FAZEKAS	0.47 ± 0.57	0.40 ± 0.52	0.75 ± 0.45	0.80 ± 0.63	0.83 ± 0.84	1.36 ± 0.66	AD > PD*, MSA*, PSP†
Evans index	0.25 ± 0.03	0.26 ± 0.01	0.28 ± 0.03	0.23 ± 0.01	0.26 ± 0.04	0.27 ± 0.03	Control < MSA*, PSP*, AD* PD < PSP†, AD†
Swallow tail sign (%) ‡	19/24 (63.3%)	4/7 (70.0%)	9/15 (56.3%)	0/8 (0.0%)	10/12 (83.3%)	1/21 (4.5%)	
Hummingbird sign (%)	2 (6.7%)	0	13 (81.3%)	0	1 (8.3%)	4 (18.2%)	
Hot cross bun sign (%)	0	6 (60.0%)	0	0	0	0	
Putamina rim sign (%)	3 (10.0%)	4 (40.0%)	2 (12.5%)	1 (10.0%)	4 (33.3%)	1 (4.5%)	

*$p < 0.01$, †$p < 0.05$

‡ Assessment based on available susceptibility-weighted imaging (SWI).

Abbreviations: PD = Parkinson's disease, MSA = multiple system atrophy, PSP = progressive supranuclear palsy, LBD = Lewy body dementia, AD = Alzheimer's disease, CP = cerebral peduncle, MCP = middle cerebellar peduncle, MTA = medial temporal atrophy