Research article

The role of width of pars compacta of substantia nigra and the midbrain area in patients with Parkinson’s disease and progressive supranuclear palsy with healthy aged individuals

Mamatha Hosapatna¹, Aparna Verma¹, Antony Sylvan D’Souza², Lokadolalu Chandracharya Prasanna¹

¹Department of Anatomy, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India
²Department of Anatomy, Father Muller Medical College, Mangalore, Karnataka, India

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Corresponding author: Prasanna LC. Email: prasanna.lc@manipal.edu

ABSTRACT

Introduction and Aim: Though numerous image processing software exists to analyse the images, measurement of substantia nigra width and midbrain area are simple yet definite tools to distinguish and diagnose the Parkinson’s disease (PD) and progressive supranuclear palsy (PSP) when complimented with clinical findings. Comparing the brainstem parameters in healthy, (neurodegenerative) diseased, and during the treatment helps us to assess the disease monitoring i.e., severity and progress of the disease, and formulate the best treatment strategies. This study aimed at comparison of the thickness of substantia nigra (SN) in Parkinson's disease (PD) and progressive supranuclear palsy (PSP) with aged healthy individuals by magnetic resonance (MR) imaging.

Material and Methods: This observational study includes the evaluation of MR images of 50 aged healthy individuals with no obvious neurological diseases, 35 classical PD, and 15 PSP patients from the Department of Radiology. Quantitative planimetric evaluation of midbrain area was calculated and the width of substantia nigra (SN) was evaluated as per standard reference criteria with computer assisted image analysis and interpretation program.

Results: The parameters like means of midbrain area and the pars compacta thickness on both right and left sides were compared both in PD and PSP patients with healthy individuals. MR image analysis showed significant decrease in the thickness of pars compacta of SN in PD patients than in PSP patients when compared with age matched healthy aged individuals.

Conclusion: Parkinsonian diseases are always associated with the neuronal loss leading to volume alterations by causing midbrain atrophy. Magnetic resonance imaging of the thickness of SN is simple and reliable imaging markers to differentiate PD and PSP when combined with clinical symptomatology.

Keywords: Neurodegenerative diseases; Parkinson’s; pars compacta; midbrain; imaging.

INTRODUCTION

Midbrain resides neurologically vital nuclei and white matter tract with diverse functions and associated with distinct clinical syndromes. It can be anatomically segmented into dorsal area with superior and inferior colliculi and ventral area with cerebral peduncles, crus cerebri, corticobulbar fibers, and SN, and (1). On cross sections, SN appears as a curved sheet with a dorsal concavity between the anterolateral crus cerebri and posteromedial ascending lemniscal fibres. It is divided into darker, dorsal pars compacta and lighter, ventral pars reticulate (2, 3).

Numerous studies were established the cardinal pathologic feature of PD as the depleted dopaminergic neurons in the SN and intracytoplasmic inclusions in the intact SN neurons (4-7). Spectrum of abnormal movement diseases which do not match with classical PD are grouped as Parkinson plus diseases. This includes PSP, corticobasal degeneration, multisystem atrophy, Lewy body disease, and olivopontocerebellar atrophy (8,9). The diagnosis of these diseases may be difficult by their motor symptoms alone because of overlapping such symptoms are seen in wide range of Parkinson plus diseases that lead to misclassification and affect the specific treatment strategy. Most studies have reported the reduced width of hyperintense SN on axial T2w images of midbrain as an index of SN neurodegeneration. This in turn causes smudging of the hypointense SN with hypointense red nucleus. The concentration of ferritin in the brain produces local heterogeneity and hence the signal loss areas observed in T2w images (10,11).

PSP typically affect the posterior cranial fossa structures. Further, brain appears normal to mild atrophy, shrunken globus, atrophy and hyperintense of midbrain, atrophy of red nucleus, and hypopigmented SN (8,9,12-14). With significant focal parenchymal loss in the superior part and global atrophy of the midbrain, the normal superior profile of midbrain which normally appears convex, gradually becomes flat and concave in more severe cases (1, 9, 13, 15). The present study aims to compare the pars compacta thickness of SN and the midbrain area in PD and PSP.
patients with healthy aged individuals by MR imaging. Such simple yet reliable morphometric data help us to diagnose the PD and PSP patients accurately as well as to monitor the disease progress throughout its course which in turn improves patient care.

MATERIALS AND METHODS

Data collection

Upon approval from the institutional ethical clearance (approval letter IEC 512/2014) from our institute, this retrospective observational study was conducted on the MR images of neurologically aged healthy aged individuals as control group and neuroimages of PD and PSP patients admitted, diagnosed, and treated in our hospital from September 2014 to August 2016 were included. Brain MR images of 100 patients (50 neurologically normal aged healthy individuals, 35 patients of PD and 15 patients of PSP disease) were considered for the evaluation of the midbrain area and width of SN. The inclusion criteria were as follows: (a) age greater than 45 years, (b) no history of any neurological disease, (c) availability of brain MRI images, (d) confirmed cases of PD and PSP patients by clinical and laboratory data and MR image analysis. The exclusion criteria were (a) MR images of patients with head injuries, and neurological diseases like cerebrovascular accidents and any space-occupying within the brain, (b) alternative diagnosis concluded during MRI examination.

MR imaging analysis

All the MR images (5-mm thick midsagittal images; TR = 1000/echo time; TE = 30) were studied with 1.5-T units (GE Medical Systems, Milwaukee). For analysis, we used an image analyzer and a computerized interpretation program. After anonymization, images were sent to a senior radiologist who is blinded to all patient data for critical analysis. The midsagittal image was taken at the level of the midbrain and the image was sectioned through the centers of the cerebral aqueduct and the interpeduncular cistern. The axial images of the midbrain centered with the red nucleus and mammillary bodies were obtained for the SN measurement in both cases and control patients (Fig. 1). Axial plane images showed SN as a crescent area. The width of the minor axis of the SN was considered as SN “thickness” as shown in Fig. 2. A senior radiologist who was unaware of patient details in our study was given MR images to evaluate the midbrain area and pars compacta SN thickness. The area of the midbrain (Fig. 3) was plotted above the inferior pontine notch to the superior pontine notch.

Fig. 1: Axial section of midbrain at superior colliculi level - Pars compacta appears as hyperintense band between red nucleus and hypointense (darker) pars reticularis

Statistical analysis

The measurements obtained were analyzed with SPSS statistical software (version 6.0). The parameters like means of midbrain area and the thickness of pars compacta on both right and left sides were compared with control, PD and PSP patients. Pairwise comparisons of midbrain area, Pars compacta on right and left sides between PD and PSP groups with control individuals were made. The mean difference is significant at the 0.05 level.

Fig. 2: Axial sections of midbrain at superior colliculi level. Fig.2a: Appears dark or hypointense due to increased iron accumulation. Thickness of pars compacta of SN (arrow) is very less. Red nucleus and pars reticularis are distinctly visible. Fig. 2b: Demarcation of SN and red nucleus is difficult as the iron deposition is not so pronounced (arrow).
RESULTS

The average age of MR imaging was higher among the controls (in males, 54±12.1 and in females, 45±6.7 years). The average age of PD and PSP patients included for the study were belonged to 61 to 70 years. Men and women were not considered separately to determine the changes that might related to gender in our study. Available literature indicates that gender does not affect differences in the midbrain among the PD, PSP and normal control groups.

Table 1: Imaging data of midbrain parameters

<table>
<thead>
<tr>
<th>Groups</th>
<th>MBA</th>
<th>PCR</th>
<th>PCL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (C)</td>
<td>Mean</td>
<td>.328196</td>
<td>.345958</td>
</tr>
<tr>
<td>Total individuals</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>.303341</td>
<td>.064954</td>
<td>.0742015</td>
</tr>
<tr>
<td>Parkinson’s Disease (PD)</td>
<td>Mean</td>
<td>.413429</td>
<td>.401400</td>
</tr>
<tr>
<td>No of cases</td>
<td>35</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>.305094</td>
<td>.104879</td>
<td>.0834817</td>
</tr>
<tr>
<td>Progressive supranuclear palsy (PSP)</td>
<td>Mean</td>
<td>.370000</td>
<td>.338000</td>
</tr>
<tr>
<td>No of cases</td>
<td>15</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>.359465</td>
<td>.0589188</td>
<td>.0758005</td>
</tr>
<tr>
<td>P value</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Mean pars compacta thickness was maximum in healthy aged group on both sides (Right side: 0.49±0.33 cm; left side 0.52±0.35 cm). Pars compacta thickness on right side in PD and PSP patients were 0.427±0.07 cm, 0.364±0.05 cm respectively and on the left side it was 0.4±0.08 cm, 0.343±0.08 cm respectively. Thus, reduction of SN thickness was seen more in PD and PSP groups. The thickness of the right and left pars compacta in patients with PD versus control patients was found to be statistically significant.

DISCUSSION

The variations in the brainstem morphometric about age and sex are controversial till today. Oguro et al. (16) noted that the changes in the brainstem morphometric data depends on the various factors like regions, genetics, and the slice thickness. They found no significant changes between age and sex. Pathologies within the midbrain parenchyma may result in distinct diseases because of their proximity to various vital nuclei and fiber tracts. Thereby result in in overlapping symptomatology as well as the diagnostic difficulties (1).

Literature survey revealed that the midbrain profiles in PD and parkinsonian plus diseases is not easy to distinguish by routine MR imaging (1,4,6,9,10,15). Differentiating PD from PSP by imaging is important in predicting response to the accurate early diagnosis, choosing a specific treatment strategy, and predicting the rate of prognosis.

Table 2: Pairwise comparisons of midbrain parameters

<table>
<thead>
<tr>
<th>Midbrain parameters</th>
<th>Group A (cases)</th>
<th>Group B (control)</th>
<th>Mean Difference (A-B)</th>
<th>Std. Error</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBA</td>
<td>PD C</td>
<td>PSP C</td>
<td>-.2240816</td>
<td>.0687572</td>
<td>.003</td>
</tr>
<tr>
<td>PCR</td>
<td>PD C</td>
<td>PSP C</td>
<td>.0852327</td>
<td>.0177518</td>
<td>.000</td>
</tr>
<tr>
<td>PCL</td>
<td>PD C</td>
<td>PSP C</td>
<td>.0418042</td>
<td>.0327125</td>
<td>.151</td>
</tr>
</tbody>
</table>

(MBA=Midbrain area, PCR=Pars compacta right side, PCL=Pars compacta left side) between different groups of patients with control individuals. (PD = Parkinson disease, PSP = Progressive supranuclear palsy and C= Control (healthy) individuals. Dunnett t (2-sided) applied. * The mean difference significant at 0.05 level.
The SN extending along the entire length of the midbrain is primarily involved in neurodegenerative diseases by dopaminergic neuronal loss. Pars compacta of SN has darkly pigmented neurons containing neuromelanin granules, called as nigrosomes. T2-weighted images of MRI allow visualization of these nigrosomes as hypertensive signal area in the pars compacta of SN and its absence in PD patients is thought to be due to the loss of melanized neurons and the increase of iron deposition. Pars reticulata of SN consists of clusters of neurones intermingled with descending fibres of crus cerebri. Most pars reticulata neurones are containing high deposits of iron pigment. Added to this, Hirsh and Hunot (6), Atasoy et al., (17) demonstrated that the neuronal loss in SN is caused by excessive oxygen free radicals generated by increased iron content. The fact is as the age advances, the iron concentration increases. This results heterogeneity and appears as areas of signal loss in T2 weighted images (10,11).

In PD, increased iron deposition and depleted dopaminergic neurons results in reduction in the width of the pars compacta of SN. Decrease in the width of hyperintense pars compacta causes smudging of the hypointense pars reticulata with the hypointense red nucleus. Present study revealed that the thickness of the SN found to be reduced in PD and more so in patients with PSP. However, Galazka et al., (18) reported that the total amount of iron in pars compacta of SN remain same both in patients of PD and in control group. Adachi opined that the thickness of pars compacta of the substantia nigra in PD patients is reduced when compared with control individuals (19). However, we found significant difference in the pars compacta thickness between the control group and in the case (PD and PSP patients) groups.

The percentage of pigmented neurons in the SN was found to be increased in patients with PD. However, the number of nonpigmented neurons was not reduced (12). In PSP, gliosis is shown in the entire SN. It is therefore possible that the volume of the SN does not markedly decrease even if pigmented neurons disappear from the pars compacta of the SN.

The midbrain area was found to be reduced in patients with PSP than with PD (9) and the midsagittal images showed atrophied midbrain. Atrophied midbrain in imaging appeared as decrease in the anteroposterior diameter and in midbrain. It could be due to loss of neurons in the periaqueductal grey mater, Edinger Westphal nucleus, pretectal area, and rostral nucleus of medial fasciculus and cuneiform. Literature revealed, the midbrain tegmentum area showed highest diagnostic accuracy among volumetric variables and is significantly reduced in PSP than in PD (8,9,12,14). Present study showed reduced midbrain area more in patients with PSP than PD.

The superior outline of the midbrain normally appears convex. Atrophy of the midbrain causes the superior profile to become flat, and it becomes concave in severe cases. It is caused by significant focal parenchymal loss in this area which coexists with global atrophy of the midbrain (1,15,20). Staining studies showed severe loss of neurons present in the cranial and dorsal part of the midbrain especially the periaqueductal grey mater, Edinger Westphal nucleus, nucleus interstitialis of Cajal, pretectal area, rostral nucleus of medial fasciculus and cuneiform nucleus (18). In our study, the superior profile was found to be convex in 57.14%, 60%, and 78% in PD, PSP, and in control subjects respectively. The abnormal superior concavity was least in all participants (14.28% in PD, 13.33% in PSP, and 2% in normal control).

Limitations of the present study

The main limitation of the study is the lack of neuropathological confirmation of the diagnosis. Other limitations are its retrospective character, and the numbers of men and women in the different groups were not balanced. Our study had several positive aspects. First, all patients included in our study were evaluated in a standardized fashion by a radiologist and a neurologist who had more experience in movement disorders to avoid diagnostic errors. Two independent radiologists in the Department of Radiodiagnosis, who were blinded to the patient’s diagnosis, evaluated all MR images.

CONCLUSION

Morphometric data of brainstem by MR images help us to compare the anatomical details in healthy aged individuals with PD and PSP patients. Among the brainstem parameters, estimation of the width of substantia nigra and midbrain volumes found to be most reliable in diagnosis of PD and PSP when combine with clinical symptomology, monitoring of disease progression, and treatment of patients.

CONFLICT OF INTEREST

None of the authors have a conflict of interest.

REFERENCES


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