*Dissertation on*

# MAGNETIC RESONANCE IMAGING OF ANTEROPOSTERIOR DIAMETER OF MIDBRAIN – DIFFERENTIATION OF PROGRESSIVE SUPRANUCLEAR PALSY FROM PARKINSON DISEASE

Submitted in Partial Fulfillment of Requirements for

**M.D. DEGREE BRANCH VIII**

**RADIO DIAGNOSIS**

*of*

**THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY,**

**CHENNAI**

**MARCH- 2009**

**MADRAS MEDICAL COLLEGE**

**CHENNAI- 600 003.**

## CERTIFICATE

This is to certify that DR. S P. MANICKAM has been a post graduate student during the period May 2006 to March 2009 at Department of Radiodiagnosis, Madras Medical College and Research Institute, Government General Hospital, Chennai.

This Dissertation titled "Magnetic Resonance Imaging Of Anteroposterior Diameter Of Midbrain – Differentiation Of Progressive Supranuclear Palsy From Parkinson Disease"is a bonafide work done by him during the study period and is being submitted to Tamilnadu Dr.M.G.R. Medical University in Partial fulfillment of the M.D. Branch VIII RadioDiagnosis Examination

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## DECLARATION

I solemnly declare that this dissertation titled "**Magnetic Resonance Imaging Of Anteroposterior Diameter Of Midbrain – Differentiation Of Progressive Supranuclear Palsy From Parkinson Disease**"is done by me at Madras Medical College & Govt. General Hospital, Chennai during the academic years 2006-2009 under the guidance and supervision of **Prof.N.Kulasekaran M.D.,D.M.R.D**. This dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Radio Diagnosis (Branch – VIII).

Place: Chennai Dr. S P.MANICKAM

Date:

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## Contents

## Introduction

Progressive supranuclear palsy (PSP), also known as Steele-Richardson-Olszewski syndrome, is a neurodegenerative disease that affects cognition, eye movements, and posture . PSP was first described as a clinico pathologic entity in 1964. Characteristics include supranuclear, primarily vertical, gaze dysfunction accompanied by extra pyramidal symptoms and cognitive dysfunction. The disease usually develops after the sixth decade of life, and the diagnosis is purely clinical.

The mean age at onset is approximately 63 years, with a range of 44-75 years .The median interval between onset and diagnosis is 3 years, with a range of 6 months to 9 years

The onset of PSP is insidious, and usually a prolonged phase of vague fatigue, headaches, arthralgias, dizziness, and depression occurs. Patients also develop subtle personality changes, memory problems, and pseudobulbar symptoms, and family members are often a more accurate source of such information than the patient. The initial symptoms can often involve unexplained imbalance or falls. Over time, dysarthria, dysphagia, and visual symptoms ensue

The most common symptoms at disease onset were postural instability and falls (63%); dysarthria (35%); bradykinesia (13%); and visual disturbances such as diplopia, blurred vision, burning eyes, and light sensitivity (13%) .

The cardinal manifestations of PSP are supranuclear ophthalmoplegia pseudobulbar palsy; prominent neck dystonia; parkinsonism; behavioral, cognitive, and gait disturbances that cause imbalance; and frequent falls.

Although presentations vary and early predominance of a particular symptom is not unusual, a greater spectrum of symptoms inevitably ensues over time. Several other features have been reported, including sleep disturbance with insomnia, clumsiness, impaired handwriting, and oscillopsia. Although the full constellation of symptoms occurring in a progressive fashion over time is characteristic, the vertical gaze palsy is the most distinctive single clinical feature.

Other features that can be prominent include focal or segmental dystonia in the form of limb dystonia or blepharospasm (Barclay, 1997).[ 1]

Patients can also have asymmetric apraxia resembling corticobasal degeneration

**Clinical examination**

Slow vertical saccades and square wave jerks are early signs in most patients. The

classic gaze palsy in PSP is supranuclear ophthalmoplegia. Supranuclear in this context refers to a lesion above the ocular motor nuclei, thus sparing the ocular motor nuclei, nerve fascicles, and neuromuscular junctional and extraocular muscles. Examination features serve to establish that the infranuclear structures are intact and that the lesion lies within the supranuclear domain. A supranuclear vertical gaze limitation is improved following extravolitional pathway activation, such as the vestibular ocular reflex (VOR) or the Bell phenomenon.

The Bell phenomenon consists of upward eye deviation behind closed lids. This can be assessed clinically by partially holding the eyelid open and instructing the patient to try forcefully closing the eye. The vertical VOR can be activated by manually flexing and extending the neck while the patient views a distant target. If the extent of the vertical eye movement limitation is improved with either of these maneuvers, then the lesion is supranuclear in origin.

Measurement of ocular alignment in the cardinal positions of gaze at near and distance viewing often discloses the source of any diplopic symptoms.

Examination of the eyelid position and movements may yield critical information.

The characteristic facies, especially when associated with dysarthria, may provide a nearly pathognomonic clinical picture

The histopathology of PSP involves diffuse brainstem disease. Neuronal loss, NFTs, and gliosis affect the reticular formation and ocular motor nuclei. Early pathology is evident primarily in the mid brain, perhaps explaining the early vertical eye movement characteristics. The pontine nucleus raphe interpositus and pedunculopontine and deep pontine nuclei are also affected.

- The distribution and ultrastructure of NFTs in PSP is distinct from those found in Alzheimer disease. PSP is associated with more subcortical involvement, with 15- to 20-nm wide single tubules, compared to the cortically based paired helicoidal filaments of Alzheimer disease.
- In one series, examination of PSP cases revealed the uniform presence of t-positive cortical lesions. These were found in highest concentration in the precentral and angular gyrus, primarily affecting the deep cortical layers, and involved both small and large neurons. These characteristics are distinct from the NFT pattern observed in Alzheimer disease. NFT concentration analysis appeared to implicate the pedunculopontine nucleus in lesion spread.

Although NFTs are the histologic hallmarks of PSP, neuropil threads have also been found extensively.

Besides the brainstem structures, the striatum, medial pallidum, subthalamic nucleus,

and the substantia nigra are also affected.

The clinical diagnosis of Progressive supranuclear palsy, particularly its differential diagnosis with Parkinson disease (PD), can be difficult, especially in early stages , However, the differential diagnosis between Progressive supranuclear palsy and Parkinson disease is important, because the prognosis of Progressive supranuclear palsy is worse than that of Parkinson disease.

**Clinical criteria**

**Criteria for possible PSP are as follows:**

- Gradually progressive disorder with onset when the individual is aged 40 years or older
- Either vertical supranuclear palsy or both slowing of vertical saccades and prominent postural instability with falls in the first year of onset
- No evidence of other diseases that can explain the clinical features

**Criteria for probable PSP are**

vertical supranuclear palsy with prominent postural instability, falls in the first year of onset, and other features of possible PSP, as follows:

- Symmetric proximal greater than distal akinesia or rigidity
- Abnormal neck posture, especially retrocollis
- Poor or absent response of parkinsonism to levodopa therapy
- Early dysphagia and dysarthria
- Early cognitive impairment with at least 2 of the following: apathy, abstract thought impairment, decreased verbal fluency, imitation behavior, or frontal release sign

In the last 10 years, MR imaging investigations of Progressive supranuclear palsy have shown abnormalities mainly involving the midbrain; such changes include atrophy, abnormal T2 hyperintensity in the tegmentum, and narrowing of the substantia nigra . However, the introduction of MR imaging into the routine workup of patients with suspected Progressive supranuclear palsy or other parkisonian syndromes has been hampered by its low sensitivity and poor specificity and also by high variability, which can be heavily influenced by the neuroradiologist's experience.

Reports have shown that the quantitative evaluation of midbrain atrophy, based on its anteroposterior (AP) diameter calculation, is useful in the differential diagnosis of Progressive supranuclear palsy and Parkinson disease, because it is more reproducible and less affected by reader experience

## Aim of the study

To prospectively asses if AP Diameter of Midbrain , evaluated at MR imaging ,can help to differentiate Progressive supranuclear palsy from Parkinson disease and whether it correlates with age of the patient and duration of disease

## Review of literature

In 2001,MR imaging of midbrain diameter first done by Monica Warmuth-Metz et al [ 2] in T2 W axial image to differentiate Progressive supranuclear palsy from Parkinson disease ,but observed an important overlap in midbrain diameter among Progressive supranuclear palsy and Multiple system atrophy patients

In 2004, Andrea Righini et al ,[ 3 ] performed, MR imaging studies of 25 patients with Progressive supranuclear palsy and 27 with Parkinson disease were reviewed by means of five parameters: midbrain superior profile on midsagittal T1-weighted images, midbrain atrophy, tegmental abnormal T2 hyperintensity, abnormal T2 putaminal hypointensity or hyperintensity on axial proton density–weighted images. We also measured the anteroposterior diameter of the midbrain on axial T2-weighted sections at the level of the superior colliculus. observed The finding of an abnormal superior profile of the midbrain had 68% sensitivity and 88.8% specificity. Midbrain atrophy had 68% sensitivity and 77.7% specificity.

TegmentalT2 hyperintensity had 100% specificity but poor sensitivity (28%). Only 14.8% of patients with PD and 24% of those with progressive supranuclear palsy had abnormal putaminal T2 hypointensity; none had protondensity hyperintensity. With PSP, the average midbrain diameter was smaller than that with PD, but an important overlap was observed. Reader discordance was lower for the midbrain

superior profile sign (eight of 52 cases); this was similar for tegmental hyperintensity (nine of 52 cases) and higher for midbrain atrophy (16 of 52 cases).

In 2005 klaus sepi et al [ 4 ] observed that Magnetic resonance imaging-based volumetry semi-automatic segmentation techniques showed volume loss of different supratentorial and infratentorial brain structures in patients with Multiple System Atrophy (MSA ) and PSP .Patients with MSA showed significant reductions in mean striatal, brainstem and cerebellar volumes , patients with PSP showed significant reductions in whole brain, striatal, brainstem – especially midbrain – and frontal volumes

Magnetization transfer imaging MTI is based on the interactions between highly bound protons within structures such as myelin or cell membranes

and the very mobile protons of free water . By application of irradiation that selectively saturates the energy level of bound protons, exchange of magnetization

between bound and free protons is induced and the signal intensity of bound protons is reduced. The difference between signal intensities with and without

magnetization transfer is measured by calculating the magnetization transfer ratio, which correlates with the degree of myelinization and with axonal density

By using MTI in patients with neurodegenerative parkinsonian disorders, abnormalities of the basal ganglia and substantia nigra were reported in patients with Parkinson’s

disease, MSA and PSP . The most recent of these studies investigated the potential of MTI in the differential diagnosis of neurodegenerative parkinsonism including 37 patients with different parkinsonian syndromes and 20 age-matched controls The main finding in this study was a change in the magnetization transfer ratio in the globus pallidus, putamen, caudate nucleus, substantia nigra and white matter in Parkinson's disease, MSA and PSP patients,matching the pathological features of the underlying disorder. By application of stepwise discriminant analysis, there was a good discrimination of Parkinson's disease patients and controls from the MSA and PSP patients

DWI visualizes the random movement of the water molecules in the tissue by applying diffusion-sensitized gradients between two radio-frequency pulses [5]. The signal of the water molecules decreases with the extent of diffusion between the two radio-frequency pulses. An absolute quantification of the diffusivity is achieved by applying diffusion-sensitized gradients of different degrees in three orthogonal directions and calculating the apparent diffusion coefficient (ADC) for each direction, which forms the trace of diffusion tensor [6]. The central nervous system is highly organized in numerous tracts of myelinated fibre bundles, whereby the movement of the water molecules is restricted perpendicular to these fibre bundles. The resulting anisotropic diffusion is quantified by the fractional anisotropy, which is determined by diffusion-sensitized 372 Movement disorders gradients in at least six directions. Both the diffusivity and the fractional anisotropy form the diffusion tensor [5].

Pathological DWI findings in Parkinson's disease patients are very rare.

In 2006 , Nicoletti et al [ 7 ] reviewed  Sixteen consecutive patients with MSA, 26 consecutive patients with PD, and 14 healthy control subjects examined with MR imaging, Images were interpreted independently by two experienced neuroradiologists blinded to clinical information, who visually inspected the images for the presence or absence of putaminal atrophy, putaminal hypointensity, slitlike hyperintensity in the posterolateral margin of the putamen, brainstem atrophy, hyperintensity of the MCP, and cruciform hyperintensity of the pons. Measurements of MCP width on T1-weighted volumetric spoiled gradient-echo images were performed in all subjects. Differences in MCP width among the groups were evaluated by using the Kruskall-Wallis test, followed by the Mann-Whitney U test for multiple comparisons and Bonferroni correction. All patients (mean age, 63.88 years; range, 55–72 years) with MSA had at least one of the features commonly observed in this disease on MR images, whereas control subjects (mean age, 66.93 years; range, 61–77 years) and all but one patient with PD (mean age, 65.31 years; range, 51–79 years) had normal MR images. The average MCP width was significantly smaller in patients with MSA (6.10 mm ± 1.18 [standard deviation]) than in those with PD (9.32 mm ± 0.77, $P \leq .001$) or control subjects (9.80 mm ± 0.66, $P \leq .001$).

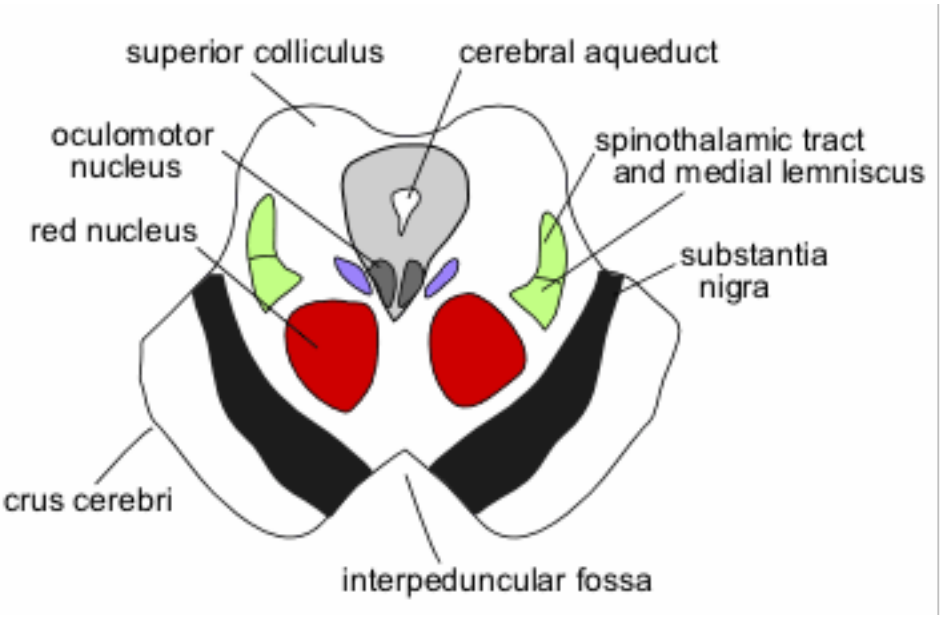
In 2007,quattronne et al [ 8 ] reviewed , MRI of 21 patients with PSP, 23 patients with PD, 25 patients with MSA-P, and 31 age-matched normal control subjects. The areas of the midbrain tegmentum and the pons were measured on mid-sagittal MRI using the display tools of a workstation. The ratio of the area of the midbrain to the area of the pons was also evaluated in all subjects. The average midbrain area of the patients with PSP (56.0 mm2) was significantly smaller than that of the patients with PD (103.0 mm2) and MSA-P (97.2 mm2) and that of the age-matched control group (117.7 mm2). The values of the area of the midbrain showed no overlap between patients with PSP and patients with PD or normal control subjects. However, patients with MSA-P showed some overlap of the values of individual areas with values from patients with PSP. The ratio of the area of the midbrain to the area of pons in the patients with PSP (0.124) was significantly smaller than that in those with PD (0.208) and MSA-P (0.266) and in normal control subjects (0.237). Use of the ratio allowed differentiation between the PSP group

## Anatomy of midbrain

The mid-brain or mesencephalon  is the short, constricted portion which connects the pons and cerebellum with the thalamencephalon and cerebral hemispheres. It is directed upward and forward, and consists of (1) a ventrolateral portion, composed of a pair of cylindrical bodies, named the cerebral peduncles; (2) a dorsal portion, consisting of four rounded eminences, named the corpora quadrigemina; and (3) an intervening passage or tunnel, the cerebral aqueduct, which represents the original cavity of the mid-brain and connects the third with the fourth ventricle

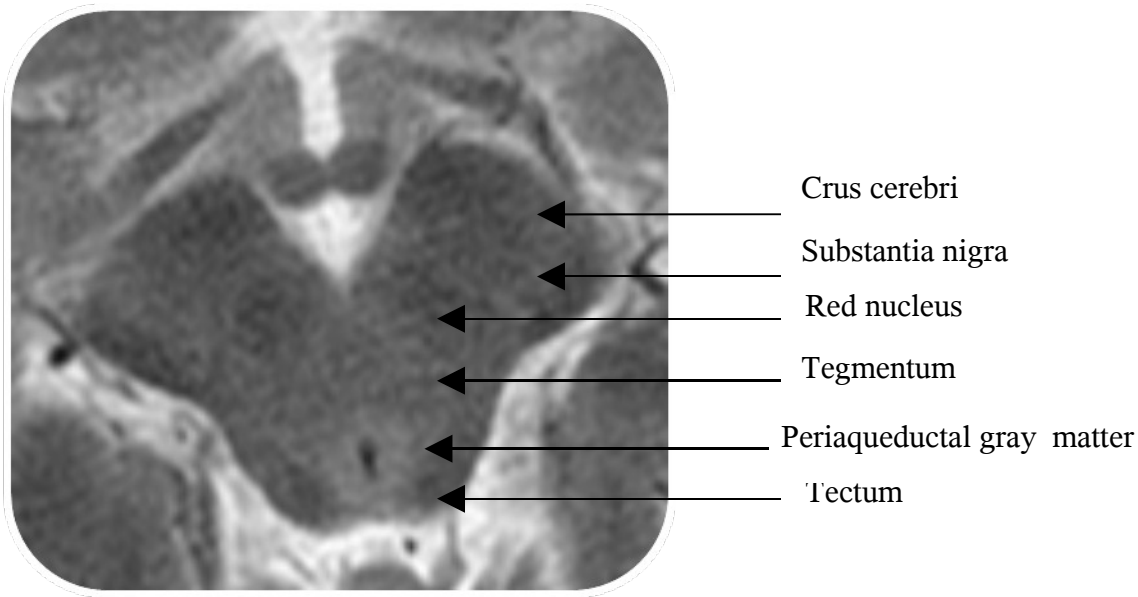
The cerebral peduncles (*pedunculus cerebri; crus cerebri*) are two cylindrical masses situated at the base of the brain, and largely hidden by the temporal lobes of the cerebrum, which must be drawn aside or removed in order to expose them. They emerge from the upper surface of the pons, one on either side of the middle line, and, diverging as they pass upward and forward, disappear into the substance of the cerebral hemispheres. The depressed area between the crura is termed the interpeduncular fossa, and consists of a layer of grayish substance, the posterior perforated substance, which is pierced by small apertures for the transmission of bloodvessels; its lower part lies on the ventral aspect of the medial portions of the tegmenta, and contains a nucleus named the

interpeduncular ganglion , its upper part assists in forming the floor of the third ventricle. The ventral surface of each peduncle is crossed from the medial to the lateral side by the superior cerebellar and posterior cerebral arteries; its lateral surface is in relation to the gyrus hippocampi of the cerebral hemisphere and is crossed from behind forward by the trochlear nerve. Close to the point of disappearance of the peduncle into the cerebral hemisphere, the optic tract winds forward around its ventro-lateral surface. The medial surface of the peduncle forms the lateral boundary of the interpeduncular fossa, and is marked by a longitudinal furrow, the oculomotor sulcus, from which the roots of the oculomotor nerve emerge. On the lateral surface of each peduncle there is a second longitudinal furrow, termed the lateral sulcus; the fibers of the lateral lemniscus come to the surface in this sulcus, and pass backward and upward, to disappear under

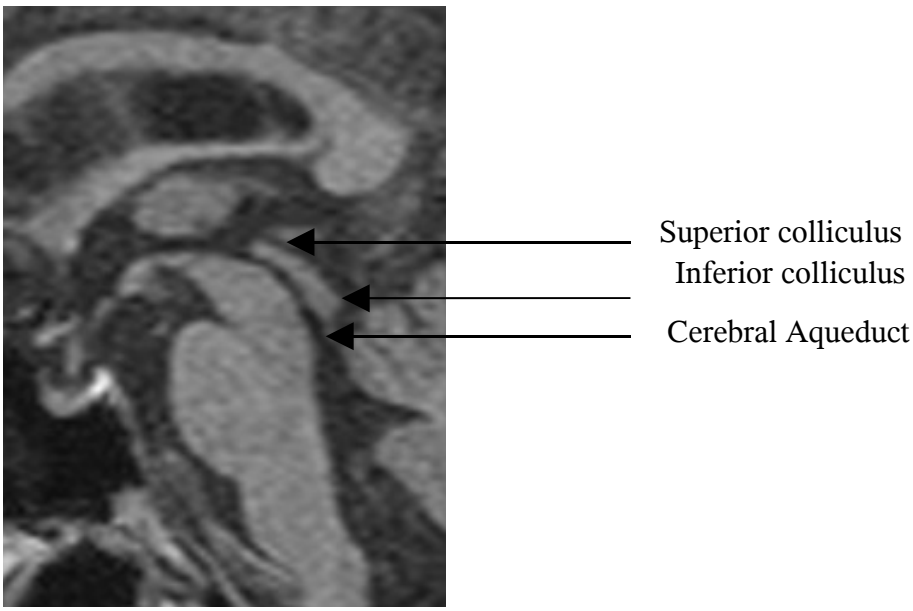



the inferior colliculus.

## T2 W Axial Image of Superior Midbrain




## Mid sagital MRI of Brain stem




Structure of the Cerebral Peduncles, on transverse section, each peduncle is seen to consist of a dorsal and a ventral part, separated by a deeply pigmented lamina of gray substance, termed the substantia nigra. The dorsal part is named the tegmentum; the ventral, the base or crusta; the two bases are separated from each other, but the tegmenta are joined in the median plane by a forward prolongation of the raphé of the pons. Laterally, the tegmenta are free; dorsally, they blend with the corpora quadrigemina.

The base (*basis pedunculi; crusta or pes*) is semilunar on transverse section, and consists almost entirely of longitudinal bundles of efferent fibers, which arise from the cells of the cerebral cortex and are grouped into three principal sets, viz., cerebrospinal, frontopontine, and temporopontine. The cerebrospinal fibers, derived from the cells of the motor area of the cerebral cortex, occupy the middle three-fifths of the base; they are continued partly to the nuclei of the motor cranial nerves, but mainly into the pyramids of the medulla oblongata.

The frontopontine fibers are situated in the medial fifth of the base; they arise from the cells of the frontal lobe and end in the nuclei of the pons. The temporopontine fibers are lateral to the cerebrospinal fibers; they originate in the temporal lobe and end in the nuclei pontis.

The substantia nigra (*intercalatum*) is a layer of gray substance containing numerous deeply pigmented, multipolar nerve cells. It is semilunar on transverse section, its concavity being directed toward the tegmentum; from its convexity, prolongations extend between the fibers of the base of the peduncle. Thicker medially than laterally, it reaches from the oculomotor sulcus to the lateral sulcus, and extends from the upper surface of the pons to the subthalamic region; its medial part is traversed by the fibers of the oculomotor nerve as these stream forward to reach the oculomotor sulcus. The connections of the cells of the substantia nigra have not been definitely established. It receives collaterals from the medial lemniscus and the pyramidal bundles. Bechterew is of the opinion that the fibers from the motor area of the cerebral cortex form synapses with cells whose axons pass to the motor nucleus of the trigeminal nerve and serve for the coördination of the muscles of mastication.

The tegmentum is continuous below with the reticular formation of the pons, and, like it, consists of longitudinal and transverse fibers, together with a considerable amount of gray substance. The principal gray masses of the tegmentum are the red nucleus and the interpeduncular ganglion; of its fibers the chief longitudinal tracts are the superior peduncle, the medial longitudinal

fasciculus, and the lemniscus.

**Gray Substance**.—The red nucleus is situated in the anterior part of the tegmentum, and is continued upward into the posterior part of the subthalamic region. In sections at the level of the superior colliculus it appears as a circular mass which is traversed by the fibers of the oculomotor nerve. It receives many terminals and collaterals from the superior cerebellar peduncle also collaterals from the ventral longitudinal bundle, from Gudden's bundle and the median lemniscus. The axons of its larger cells cross the middle line and are continued downward into the lateral funiculus of the medulla spinalis as the rubrospinal tract ; those of its smaller cells end mainly in the thalamus. The rubrospinal tract forms an important part of the pathway from the cerebellum to the lower motor centers.

The interpeduncular ganglion is a median collection of nerve cells situated in the ventral part of the tegmentum. The fibers of the fasciculus retroflexus of Meynert, which have their origin in the cells of the ganglion habenulæ ,end in it.

From the lateral aspect of each colliculus a white band, termed the brachium, is prolonged upward and forward. The superior brachium extends lateralward from the superior colliculus, and, passing between the pulvinar and medial geniculate body, is partly continued into an eminence called the lateral geniculate body, and partly into the optic tract. The inferior brachium passes forward and upward from the inferior colliculus and disappears under cover of the medial geniculate body.

In close relationship with the corpora quadrigemina are the superior peduncles, which emerge from the upper and medial parts of the cerebellar hemispheres. They run upward and forward, and, passing under the inferior colliculi, enter the tegmentum

Structure of the Corpora Quadrigemina.—The inferior colliculus (*colliculus inferior; inferior quadrigeminal body; postgemina*) consists of a compact nucleus of gray substance containing large and small multipolar nerve cells,

## Imaging in Progressive Supranuclear Palsy

### CT Brain

Most common finding observed in PSP is generalized cerebral atrophy, CT Brain shows reduction in AP diameter of Mid brain ( Midbrain Atrophy) but it is less sensitive and specific than MRI

### MRI

MRI shows atrophy of the mid brain with cisternal and ventricular dilatation, thinning of the quadrigeminal plate, dilation of the third ventricle, and a nonspecific finding of increase in proton density images in the periaqueductal gray matter compatible with gliotic changes Righini [ 3 ]reported the usefulness of midsagittal T1-weighted MRI appearance of the superior profile of the midbrain; the appearance of a flat or concave profile (compared to the normal convex profile) was associated with a 68% sensitivity and an 89% specificity for the diagnosis of PSP compared to patients with Parkinson disease. MR shows Mid brain atrophy i.e. reduced anteroposterior diameter and hyperintensity in tegmentum

MR volumetry shows reduced volume of mid brain in PSP than PD

**PET**

These studies may help reveal physiopathologic aspects of the disease. PET studies have shown a global cerebral hypometabolism with relative selectivity in the frontal cortex , Regional cerebral blood flow and oxygen metabolism are decreased in the caudate and putamen and impaired in the thalamus and the brain stem.,lowered glucose metabolism in the midbrain compared to controls .Fluorodopa (F-dopa) PET has shown a reduction in the F-dopa influx in the caudate and putamen.

**SPECT**

Striatal dopamine receptor binding is reduced in some patients with PSP with I iodobenzamide SPECT

## Materials and Methods

The study was performed on a 1.5 Tesla super conductive whole body MRI scanner SIEMENS MAGNETOM SYMPHONY

During the study the patient is placed on the strong homogenous magnetic field , the hydrogen nuclei ,protons, distributed through the entire body tissue generate signals when stimulated by a radiofrequency pulse . these signals are processed in to images by a computer

**Study place**

Barnard institute of radiology ,Madras Medical College

**Study period**

March 2007 to July 2008

**Patient evaluation and selection**

**Inclusion criteria**

Age > 40 yrs

Clinical diagnosis of idiopathic Parkinson disease and progressive supranuclear palsy

Normal CT brain

**Exclusion criteria**

Age < 40 yrs

Patients having organic cause for Parkinson disease and progressive supranuclear palsy

Patients with contraindication to MR

**Data collection**

All patients provided the informed consent for the study, brief history regarding the nature,duration and age at onset of the disease , history of truma, treatment history significant past and personal history is taken from all patients

Base line CT brain was done

**Methods**

All patients are examined with MRI , the studied parameters include AP diameter and superior profile of midbrain, mean middle cerebellar peduncle width ,tegmental and putaminal intensity, differences In AP diameter of Midbrain among the groups were evaluated by using the Kruskall wallis test ,followed by Mann Whitney U test for bonferroni correction

**Sequence parameters**

T2 WI- axial(3500/85,4mm thickness)

FLAIR axial(8000/120/2000,4mm thickness)

T2*-axial(500/15/4mm thickness)

T1W SPGR sagital(15.2/6.8 thickness .72mm)

**Interpretation**

AP Diameter of midbrain measured in T2 WI axial images at the level of red nucleus between interpeduncular fossa to quadrigeminal cistern in all patients and evaluated using Krus kall wallis test and multiple comparison with Mann – whitney U test and bonferroni correction done

Superior profile of midbrain assessed in T1 WI mid sagital SPGR , convex profile is taken as normal , concave and flat profile is taken as abnormal i.e finding suggestive of supranuclear palsy , then the sensitivity and specificity is assessed using statistical tests

Middle cerebellar peduncle (MCP) width measured in T1 WI para sagital SPGR between superior and inferior cerebellar cistern right and left MCP width is measured in all patients and average of the two is taken and evaluated using Krus kall wallis test and multiple comparison with Mann – whitney U test and bonferroni correction done

Tegmental intensity in assessed T2 WI axial images , hyperintensity in the periaqueductal region is taken as finding suggestive of PSP ,then the sensitivity and specificity is assessed using statistical tests

## Results and Observation

The study was conducted in Twelve consecutive patients with PSP, 18 with PD referred from neurology department , diagnosis were made by the experienced neurologist according to established criteria and in 10 healthy control subjects,

**MEN/WOMEN**

The difference in sex distribution between patients with PSP , patients with PD, and control subjects was evaluated with the chi square test(p= 0.13)

**Table 1- Sex Distribution**

| **Groups** | **Male** | | **Female** | | *p-value*[*] |
|---|---|---|---|---|---|
| | **n** | ***%*** | **n** | ***%*** | |
| PSP | 8 | 66.7 | 4 | 33.3 | 0.13 |
| Parkinsons' | 14 | 77.8 | 4 | 22.2 | |
| Control | 4 | 40.0 | 6 | 60.0 | |

[*] Chi-square test

**Age at the time of study**

There was no difference in age at the time of examination (*P*= .570,ANOVA Test) between patients with PD (mean, 62.2years ± 7 [standard deviation]; and those with PSP(mean, 62years ± 5.; and the control subjects (mean, 65years ± 7)

Table 2- **Age at the time of study**

| **Groups** | **Mean ± SD** | *p-value*[*] |
|---|---|---|
| PSP | 62 ± 5 | 0.57 |
| Parkinsons' | 62 ± 7 | |
| Control | 65 ± 7 | |

[*] ANOVA test

**Mean Duration of disease**

There was no difference in disease duration (P = .626) between patients with PD (mean, 3.75 years) and those with PSP (mean, 3.25 years )

**Table 3- Mean duration of disease**

| **Groups** | **Mean duration** | **P value** |
|---|---|---|
| PSP | 3.25 years | 0.62 |
| PD | 3.75 years | |

## Age at onset

There was no difference in age at onset of disease( P =0 .848) between patients with PSP (mean, 58.75 years) and those with PD (mean, 58.5 years )

**Table 4- Age at onset**

| Groups | Age at onset | P value |
|---|---|---|
| PSP | 58.75 years | 0.84 |
| PD | 58.5 years | |

## Mid Brain AP Diameter

**Table 5- Mid Brain AP Diameter**

| Groups | Maximum AP(cm) | Minimum AP(cm) | Mean AP (cm) | P value* |
|---|---|---|---|---|
| PSP | 1.34 | 1.14 | 1.29 | 0.00 |
| PD | 1.58 | 1.82 | 1.70 | |
| CONTROL | 1.65 | 1.81 | 1. 74 | |

## Mean MCP width

MCP width does not differ significantly among the groups (P= 0.54),PSP ( mean -0.99cm),PD(mean -0.97 cm) and control (mean-0.97 cm)

**Table 6-Mean MCP width**

| Groups | Maximum MCP(cm) | Minimum MCP(cm) | Mean MCP (cm) | P value* |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| PSP | 1.1 | 0.87 | 0.99 | 0.54 |
| PD | 1.05 | 0.89 | 0.97 | |
| CONTROL | 1.06 | 0.88 | 0.97 | |

*Anova test

## AP Diameter of Mid brain

AP diameter of midbrain measured in T 2 W axial images ( AP diameter < 15mm)

Has 100% sensitivity and specificity in differentiating PSP from PD and control

**Table 7 - Mid Brain AP Diameter**

| **Groups** | **Total no of patients** | **No of patients having AP diameter < 15 mm** |
|---|---|---|
| PSP | 12 | 12 |
| PD | 18 | 0 |
| CONTROL | 10 | 0 |

## Superior profile of midbrain

Abnormal Superior profile of midbrain ( flat or concave profile) has 75 % sensitivity and 86% specificity in differentiating PSP from PD and control.

**Table 8 - Superior profile of midbrain**

| **Groups** | **Total no of patients** | **No of patients having Abnormal superior profile** |
|---|---|---|
| PSP | 12 | 9 |
| PD | 18 | 3 |
| CONTROL | 10 | 1 |

## Tegmental hyper intensity

Tegmental hyper intensity assessed in T2 W axial images has 25 % sensitivity and 100% specificity in differentiating PSP from PD and control.

**Table 9 - Tegmental hyper intensity**

| Groups | Total no of patients | No of patients having Tegmental hyper intensity |
|---|---|---|
| PSP | 12 | 3 |
| PD | 18 | 0 |
| CONTROL | 10 | 0 |

**Age and AP diameter**

Age and AP diameter of both PSP and PD groups were evaluated using spearmans co efficient (P> 0.05), there fore there is no correlation between Age and AP diameter of midbrain in both groups

**Table 10 - Age and AP Diameter**

| Disease | Spearmans coefficient | P value |
|---|---|---|
| **PSP** | 0.08 | 0.82 |
| **PD** | 0.36 | 0.15 |

**Duration and AP diameter**

Duration and AP diameter of both PSP and PD groups were evaluated using spearmans co efficient (P> 0.05), there fore there is no correlation between duration and AP diameter of midbrain in both groups

**Table 11 - Duration and AP Diameter**

| Disease | Spearmans coefficient | P value |
|---|---|---|
| PSP | 0.43 | 0.16 |
| PD | 0.16 | 0.52 |

**AP Diameter of Mid brain**

The mean anteroposterior midbrain diameter significantly smaller in PSP( 1.29 cm ±0.06 cm ; ) than PD (1.70 cm ±0.08 cm) and control 1.74 cm ±0.05 cm)

P value = 0.001

**Table 12- Mid Brain AP Diameter**

| Group | Mean (SD) | P value * |
|---|---|---|
| PSP | 1.29cm (0.06 cm) | 0.001 |
| PD | 1.70 cm (0.08 cm) | |
| CONTROL | 1.74 cm (0.05 cm) | |

*-kruskall wallis test

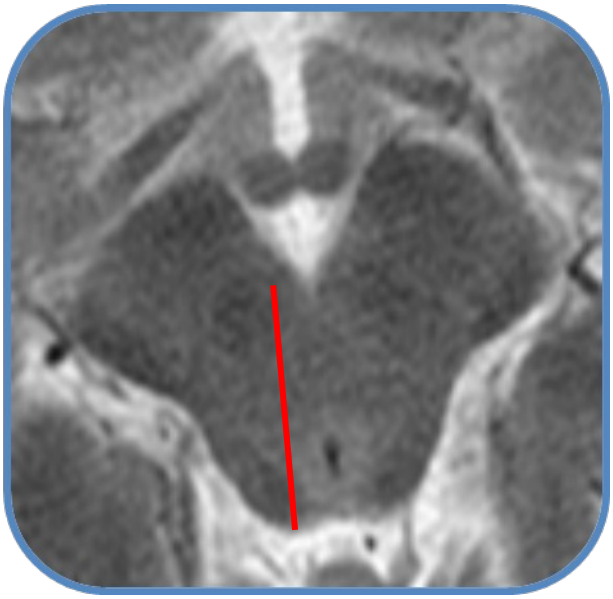
Multiple comparisons of mean PSP"s diameter with Mann-Whitney U test with bonferroni correction was done.

**Table 13- sensitivity and specificity of parameters in differentiating PSP from PD and control groups**

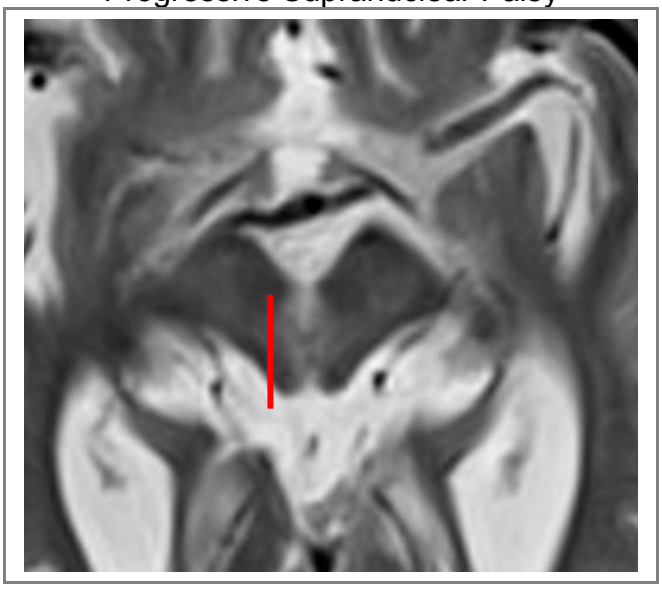
| Parameter | Sensitivity | Specificity | Positive predicitivity | Negative predictivity |
|---|---|---|---|---|
| **Abnormal superior profile** | 75% | 86% | 69% | 89% |
| **AP diameter of midbrain <15mm** | 100% | 100% | 100% | 100% |
| **Tegmental hyperintensity** | 25% | 100% | 100% | 76% |

## AP DIA METER OF MID BRAIN

Parkinson Disease

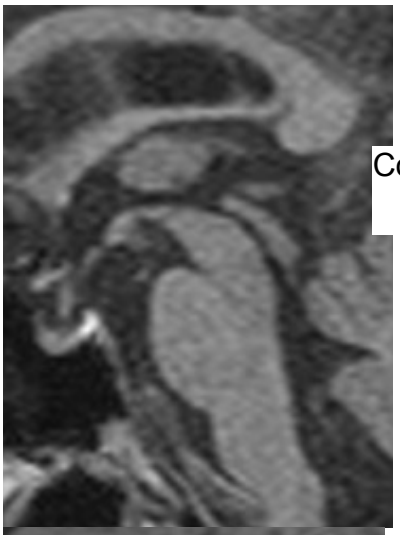


Progressive Supranuclear Palsy

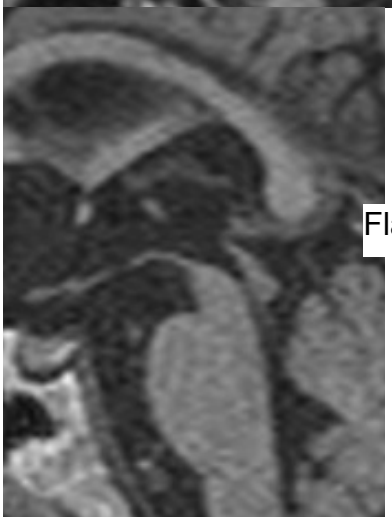


**Superior Profile of Midbrain**

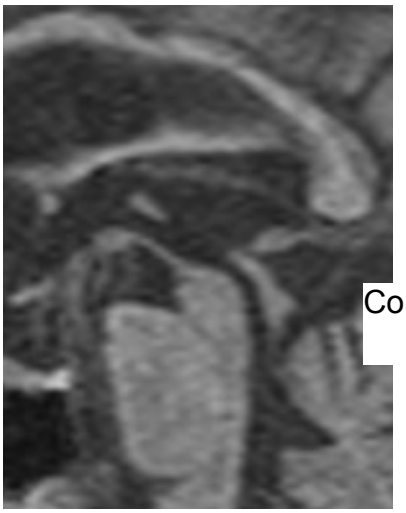
Superior Profile of Midbrain



Convex profile

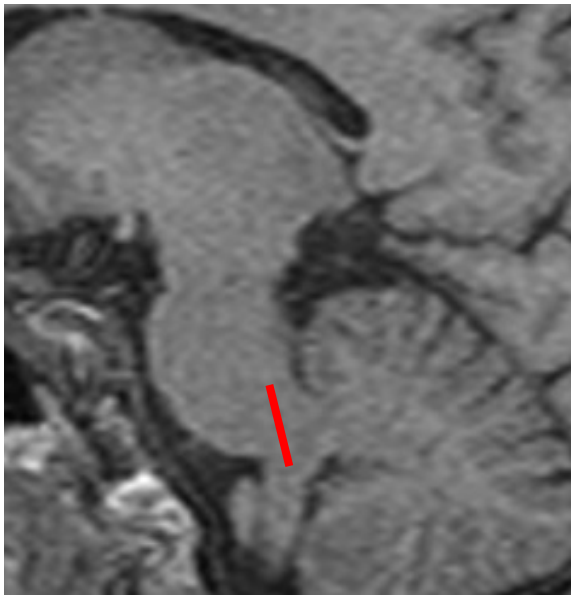


Flat Profile

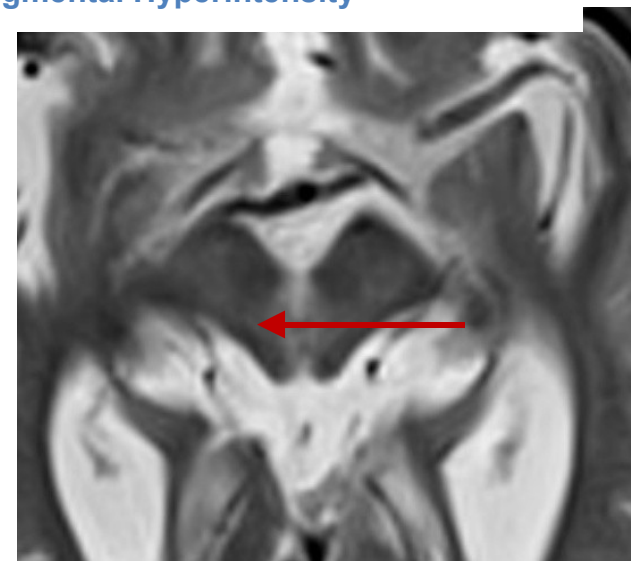


Concave Profile

## MCP width



## Tegmental Hyperintensity



## Discussion

MRI can be used to differentiate Progressive supranuclear Palsy from Parkinson disease

Total of 40 patients including 10 controls , twelve PSP and Eighteen PD Patients formed the study group , most of the patients belong to $5^{th}$ to $7^{th}$ decade.

There is no statistically significant difference in men and women as (P= 0.13) among the groups Chi-square test

Age at onset ,mean duration of disease does not differ significantly among the groups

***For diagnosis of PSP***

The AP diameter of Midbrain at the level of Red nucleus between interpeduncular fossa to quadrigeminal cistern is measured in T2 W axial images ,AP diameter less than 15 mm is taken as positive finding i.e suggestive of progressive supranuclear palsy

Superior Profile of Midbrain assessed in Mid sagital T1 SPGR images convex profile is taken as Normal, Flat and Concave Profile is Taken as abnormal i.e

A finding suggestive of PSP

Tegmental hyperintensity in T2 W axial images is also taken as finding suggestive of PSP

AP diameter of Midbrain in all PSP patients is less than 15 mm, but none of the PD and Control subjects .

The right and left Middle cerebellar Peduncle width measured in Parasagittal T1 w spoiled gradient echo images in all patients is greater than 8mm and does not differ significantly among the groups

Tegmental hyperintensity assessed in T2 w image is observed only 3 out of 12 patients with PSP and none of the PD and control group have tegmental hyperintensity , it is 100% specific but has low sensitivity of 25% only.

Superior profile of midbrain assessed in Mid sagital T1 w is abnormal ( flat or concave profile ) in 9 out of 12 patients, 3 out of 18 patients and one in control group has 75 % sensitive and 86 % specific in identifying PSP from PD and control group

AP diameter of Midbrain measured in T 2 W axial images shows significant reduction in all PSP patients( < 15 mm), but none of the Parkinson disease and control patients have AP diameter less than 15 mm evaluating with statistical tests

It has 100 % sensitivity and Specificity in differentiating PSP from PD and control patients

AP diameter of Midbrain also has 100 % positive and negative Predictive value

In differentiating PSP from PD and Control group as there is no over lap in AP diameter among the PSP and PD groups

Superior Profile of Midbrain is less sensitive and specific than AP diameter of midbrain

**Limitations**

Limitation in our study , diagnosis is not validated with neuro pathology as none is proved by brain biopsy or autopsy after death

Clinical diagnosis may be in error, but the possibility of diagnostic error is unlikely as diagnosis were made according to established criteria by an experienced neurologist, and all patients had one of the finding commonly observed in PSP

And none of the PD and Control group had AP diameter of midbrain less than 15 mm in T2 W images

## Conclusion

MR imaging plays a major role in differentiation of Parkinson and Parkinson Plus syndromes as it shows excellent anatomic detail

There is no significant difference in Age at onset and Mean duration of disease, in PSP and PD groups

There is no sex predilection in all three groups

Measurement of AP diameter of midbrain in T2 WI axial images at the level of Red nucleus between interpeduncular fossa to quadrigeminal cistern is simple, reliable and accurate method to differentiate PSP from PD

AP Diameter of Midbrain less than 15 mm in T2 W images is 100% sensitive and specific in differentiating PSP from PD

None of the PSP patients have Mean MCP width less than 8mm ,A finding more in favour of MSA

There is no correlation between AP diameter and duration of disease and age of the patient so MR imaging help us to reach the diagnosis much early than clinical examination

Measurement of AP Diameter of Midbrain in T2 W images can help to clinch the diagnosis of PSP in patients with movement disorder

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## Proforma

Name-
Age /Sex-
Address
Chief complaints
Clinical finding

1. Autonomic dysfunction
2. Cerebellar ataxia
3. Pyramidal signs
4. Gaze palsy
5. Pseudobulbar palsy

Duration of disease
Age at onset
Levodopa response
MR Findings

| Parameter | PSP | PD | CONTROL |
|---|---|---|---|
| R MCP width | | | |
| L MCP width | | | |
| MEAN MCP Width | | | |
| AP Diameter of Midbrain | | | |
| Superior Profile of Midbrain | | | |
| Tegmantal hyperintensity | | | |

## Master Chart

PSP patients

| Sno | Age | Sex | Duration (years ) | Age at Onset | AP (cm) | Sup profile | Tegmenta l hyper | Mean MCP width(cm) |
|---|---|---|---|---|---|---|---|---|
| 1 | 70 | male | 4 | 66 | 1.34 | abnormal | + | 0.97 |
| 2 | 69 | female | 3.5 | 65.5 | 1.31 | abnormal | - | 1.03 |
| 3 | 54 | male | 2 | 52 | 1.14 | abnormal | - | 0.87 |
| 4 | 61 | male | 6 | 55 | 1.32 | abnormal | - | 0.99 |
| 5 | 64 | female | 5 | 59 | 1.29 | abnormal | - | 1 |
| 6 | 59 | female | 2 | 57 | 1.3 | normal | - | 0.96 |
| 7 | 58 | male | 4 | 54 | 1.22 | abnormal | + | 1.04 |
| 8 | 64 | male | 3 | 61 | 1.26 | abnormal | - | 0.89 |
| 9 | 60 | male | 2.5 | 57.5 | 1.27 | abnormal | - | 0.98 |
| 10 | 56 | female | 1 | 55 | 1.36 | normal | - | 1.02 |
| 11 | 62 | male | 2 | 60 | 1.32 | normal | - | 1.1 |
| 12 | 67 | male | 4 | 63 | 1.38 | abnormal | + | 1.07 |

**PD patients**

| Sno | Age | Sex | Duration (years) | Age at Onset | AP(cm) | Sup profile | Tegmental hyperintensity | Mean MCPwidth (cm) |
|---|---|---|---|---|---|---|---|---|
| 1 | 65 | male | 3 | 62 | 1.76 | normal | - | 1.025 |
| 2 | 82 | female | 15 | 67 | 1.69 | normal | - | 1.015 |
| 3 | 61 | male | 2 | 59 | 1.68 | normal | - | 0.925 |
| 4 | 57 | male | 2 | 55 | 1.62 | normal | - | 0.965 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 5 | 58 | male | 1 | 57 | 1.67 | normal | - | 0.98 |
| 6 | 60 | male | 1.5 | 58.5 | 1.68 | normal | - | 1.015 |
| 7 | 68 | male | 7 | 61 | 1.62 | normal | - | 0.94 |
| 8 | 63 | male | 3 | 60 | 1.72 | abnormal | - | 0.94 |
| 9 | 64 | male | 2 | 62 | 1.63 | normal | - | 0.99 |
| 10 | 62 | male | 4 | 58 | 1.76 | normal | - | 0.96 |
| 11 | 70 | male | 5 | 65 | 1.81 | normal | - | 0.91 |
| 12 | 63 | male | 3 | 60 | 1.68 | normal | - | 0.89 |
| 13 | 66 | male | 2 | 64 | 1.82 | normal | - | 0.92 |
| 14 | 55 | male | 4 | 51 | 1.76 | normal | - | 0.98 |
| 15 | 60 | female | 3 | 57 | 1.58 | abnormal | - | 0.99 |
| 16 | 54 | male | 5 | 49 | 1.82 | abnormal | - | 1.045 |
| 17 | 54 | female | 2 | 52 | 1.59 | normal | - | 1 |
| 18 | 58 | female | 3 | 55 | 1.77 | normal | - | 0.99 |

Control patients

| S.no | Age | Sex | AP(cm) | Sup profile | Tegmental hyperintensity | Mean MCP width (cm) |
|---|---|---|---|---|---|---|
| 1 | 58 | male | 1.74 | normal | - | 1.06 |
| 2 | 67 | female | 1.79 | normal | - | 0.98 |
| 3 | 59 | female | 1.74 | normal | - | 0.94 |
| 4 | 76 | female | 1.71 | normal | - | 1.01 |
| 5 | 55 | male | 1.76 | normal | - | 1.03 |
| 6 | 72 | female | 1.69 | normal | - | 0.96 |
| 7 | 59 | male | 1.77 | normal | - | 0.99 |
| 8 | 64 | female | 1.81 | abnormal | - | 1 |
| 9 | 71 | female | 1.65 | normal | - | 0.89 |
| 10 | 64 | male | 1.7 | normal | - | 0.92 |

**Glossary**

MR------ Magnetic Resonance

AP------- Anteroposterior

PSP----- Progressive Supranuclear Palsy

PD ------ Parkinson Disease

MSA---- Multiple System Atrophy

MCP--- Middle Cerebellar Peduncle