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Original article

SPECTRUM OF MAGNETIC RESONANCE IMAGING IN MOVEMENT DISORDER: A CROSS-SECTIONAL STUDY IN A TERTIARY CARE TEACHING HOSPITAL.

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Abstract

Background

Movement disorders share an overlapping manifestation in many cases making a clinical diagnosis alone challenging. There are no standard objective tests available for the diagnosis currently. This study attempts to illustrate the comprehensive magnetic resonance imaging (MRI) spectrum of brain abnormalities in patients with different movement disorders and to observe the agreement of clinical and radiological diagnosis.

Methodology

A descriptive cross-sectional study was conducted in a tertiary care teaching hospital over two years from 2020 to 2022. The study will include 50 patients with all patients with movement abnormalities who were prescribed to get an MRI.

Results

The most commonly affected site was substantia nigra seen in 19 cases (38%), followed by midbrain in 10 cases (20%), putamen in 9 patients (18%), and caudate in 5 patients (10%). Most patients had absent swallow tail signs (38%), forming a diagnosis of Parkinson's disease. The Hummingbird sign of PSP was observed in 6 patients (12%). Only one patient had a box-like configuration which is seen in Huntington's disease. Clinico- radiological correlation was 72%.The diagnostic validity of the MRI in identifying movement disorders was 100% specific, with varying sensitivity for all.

Conclusion

MRI is currently the preferred modality for diagnosing movement disorders, owing to its ability to provide details on the structural pathologies of the brain with high resolution and sensitivity. The present study's findings corroborated with the results of previously worldwide conducted studies. A significant agreement was observed between the clinical and radiological diagnoses.

Recommendation

MRI can be used as a diagnostic tool in clinically challenging cases and to confirm the clinical diagnosis. We recommend more studies on the same with a larger sample size and dedicated disease study to analyze other ancillary MRI findings as well.

Keywords: Magnetic resonance imaging, movement disorders, Parkinson's disease Submitted: 2023-06-01 Accepted: 2023-06-06

1. Introduction

Based on the clinical presentation, movement disorders are broadly studied as akinetic and hyperkinetic disorders. Parkinsonism is one of the most prevalent neurodegenerative movement disorders affecting several brain neuronal circuits, commonly presenting with rigidity, bradykinesia, and resting tremors. The movement disorders overlap in many cases, making a clinical diagnosis challenging. There are no standard objective tests available for the diagnosis currently. Hence, imaging modalities are relied upon extensively for their diagnosis. Parkinson's disease (PD) is a commonly occurring movement disorder with many overlapping symptoms with atypical Parkinsonism, and the characteristic features of atypical Parkinsonism are not well understood. Thus brain MRI is the investigation of choice and can suggest specific forms of atypical Parkinsonism. [1] Clinical guidelines for movement disorders, MRI can be performed once during the disease. [2]Parkinsonism includes Idiopathic Parkinson's Disease and Parkinson's Plus Syndromes. "Parkinson Plus" (P+) means Parkinson's disease with other clinical symptoms, including multiple system atrophy (MSA), degeneration of basal cortical regions, and Progressive Supranuclear Palsy (PSP). The P+ with MSP is the most commonly prevalent type. One of the primary causes of Idiopathic Parkinson's Disease is age-associated changes in the neurons of dopaminergic nature located in the SubstantiaNigra (SN).MSA contains features of Idiopathic PD and additional Dyskinetic features and is of two types, MSA-P (Parkinsonism predominant type) and MSA-C(cerebellar ataxia dominant type). In PSP, the patient's movement is slowed, limb movements become rigid, they undergo repeated falls due to movement changes, and also present with limitations in downward gaze(supranuclear vertical gaze palsy)and dementia. PSP is associated with atrophy of the midbrain with sparing of the pons. Corticobasal degeneration, a part of Parkinson's plus, is a progressive condition with extrapyramidal, cognitive, and neuropsychiatric problems. In this condition, the neurons of the posterior frontal and parietal lobes are affected asymmetrically. The corticospinal tract and basal ganglia are affected more commonly. [1] Asymmetrical cortical atrophy may be seen on MRI. Huntington's disease is a polyglutamine disorder that is autosomal dominant and is brought on by the amplification of a CAG triplet codon responsible for the formation of the huntingtin protein. The most prevalent inherited type of mental retardation, fragile X tremor ataxia syndrome (FXTAS), is due to the CGG triplet in the FMR1 gene, which expands by more than 200 base pairs. Most mothers of individuals with Fragile X syndrome do not have mental retardation, although they do have FMR1 CGG repeats. Adult males having permutation gradually present with tremors, cerebellar ataxia, and cognition impairment. These symptoms are similar to MSA or ataxia. Wilson's disease (WD) is associated with copper metabolism dysfunction, which has an autosomal recessive inheritance. The copper (Cu) transport protein ATP7B has recorded over 200 mutations. Because of the genetic flaws, there are decreased plasma values of ceruloplasmin protein and higher amounts of free Cu that build up and harm various organs, including the liver and brain. MRI, a noninvasive technique without the involvement of harmful radiation, is the currently preferred modality over the other imaging techniques due to its ability to provide details on the structural pathologies of the brain with high resolution and sensitivity. [3, 4] More advances in molecular, structural, and functional neuroimaging techniques are coming up in the current days. The functional MRI PET and SPECT have allowed a better understanding of the disease pathologies. With these advances, neurological biomarkers specific to each brain disorder are researched to be mapped. Brain MRI improves the accuracy of diagnosis in movement disorders primarily based on the region of the brain affected. MRI can identify the underlying etiologies of movement disorders, such as cerebrovascular damage and abnormal pressure hydrocephalus. The study aims to evaluate the role

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of MRI in diagnosing various movement disorders.

2. Methodology

This descriptive cross-sectional hospital-based study was conducted over two years, from 2020 to 2022. Patients who attended neurology OPD of our hospital with suspected movement disorder over the mentioned two-year period were referred to the radiology department for an MRI study. After meeting the inclusion and exclusion criteria a total of 50 patients were enrolled in the study, which was calculated by a statistician on the basis of the frequency of such patients over past years. Patients with contraindications to MRI (Claustrophobia, metallic Implant, etc.) and unwilling to participate in the study were excluded from our research. The study was approved by Institutional Ethics Committee and Informed consent was obtained using a self-designed questionnaire approved by the Institutional Scientific Review Committee (ISRC).

2.1. Statistical Analysis

Analysis was conducted in IBM SPSS 26. Categorical variables were expressed in frequencies and proportions. Mean (SD) and Median (IQR) were calculated for continuous variables. Cohen's kappa was calculated to test the signed agreement between each movement disorder's clinical and radiological diagnoses. The sensitivity, specificity, positive predictive value, and negative predictive value of the MRI findings for each movement disorder were calculated. A p-value of <0.05 is considered statistically significant.

3. Results

Patients of any age range who attended Neurology OPD with a suspected movement disorder and who were referred to our department for an MRI study and had informed consent for participation in the study were included. Those who did not give informed consent or were having MRI incompatible implants in the body were excluded from the study. Based on patient data collected by the statistician over past years, the sample size was calculated and limited to 50. The patients in our study were of age ranging from 22- 80 years with a mean age of 60.72 years, with a male: female ratio of 2.1:1. Out of 50 patients, 26 (52%) patients had a provisional diagnosis of Parkinson's disease, followed by nine patients of PSP (18%), 7 of MSA-P (14%), 4 of Wilson's disease (8%), 3 of MSA- C (6%) and 1 of Huntington's disease (2%). On neuroimaging, multiple brain areas were observed to be affected in the same individual [Table 1].

The most commonly affected site was substantia nigra seen in 19 cases (38%), followed by midbrain in 10 cases (20%), putamen in 9 patients(18%), and caudate in 5 patients (10%). An equal involvement of pons, MCP, cerebellum, and white matter tract was observed with a 2 (4%) frequency. Radiological diagnosis was made based on site affected and signs characteristic to specific diseases. Most patients had absent swallow tail signs (38%), forming a diagnosis of Parkinson's disease [Figure 1].

The Hummingbird sign in PSP was observed in 6 patients (12%) [Figure 2]. Only one patient had a box-like configuration seen in Huntington's disease. Out of 50 patients, 10 (20%) were observed to have no significant MRI findings. The face of the giant Pandasign was present in 4patients with Wilson's Disease [Figure 3, Table 2]. A hot cross bun sign was observed in 2 patients (4%) [Figure 4]

A clinical-radiological correlation was found to be 72%, i.e., 36 patients out of 50 were found to have a radiological diagnosis corresponding to a clinical diagnosis. Upon calculation of Cohen's kappa, a significant agreement was found between clinical and radiological diagnosis of all movement disorders observed in the study(p-value 0.01)[Table 3]. The diagnostic validity of the MRI in identifying movement disorders was 100% specific, with a sensitivity of 73.1% for Parkinson's disease, 66.7% for PSP and MSA-C, and 57.1% for MSA-P. The sensitivity of MRI was observed to be 100% in identifying Huntington's and Wilson's diseases.

Table 1: Clinical diagnosis and site involved in neuroimaging

Clinical diagnosis	Area Involved n (%) **Substantia Nigra**	**Mid-brain**	**Pons**	**MCP***	**Caudate**	**Putamen**	**Cere-bellum**	**WMT****
Parkinson's Disease	19 (73.1)							
PSP		6 (66.7)						
Wilson's Disease		4 (100)			4 (100)	4 (100)		
MSA-C			2 (66.7)	2 (66.7)			2 (66.7)	2(66.7)
MSA-P						4 (100)		
Huntington's Disease					1 (100)	1 (100)		

***Middle cerebellar peduncle**
**** White matter tract**

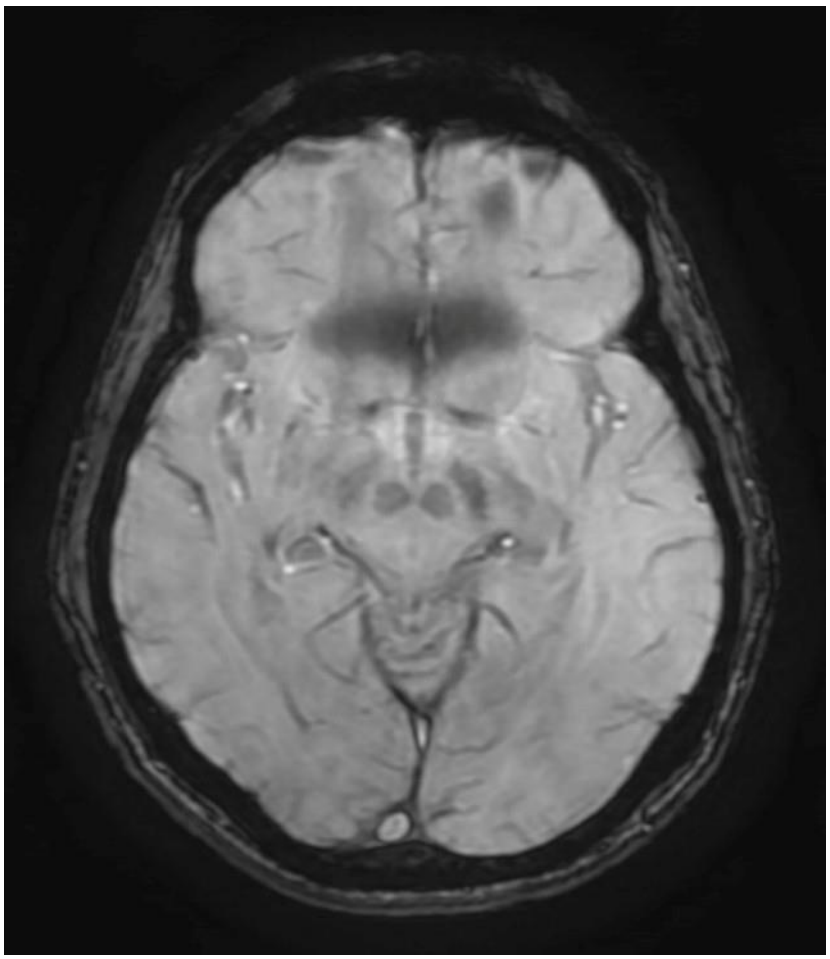

Figure 1: Loss of normal hyperintense signal in substanitanigra. (Absent swallow tailsign-Parkinson's disease)

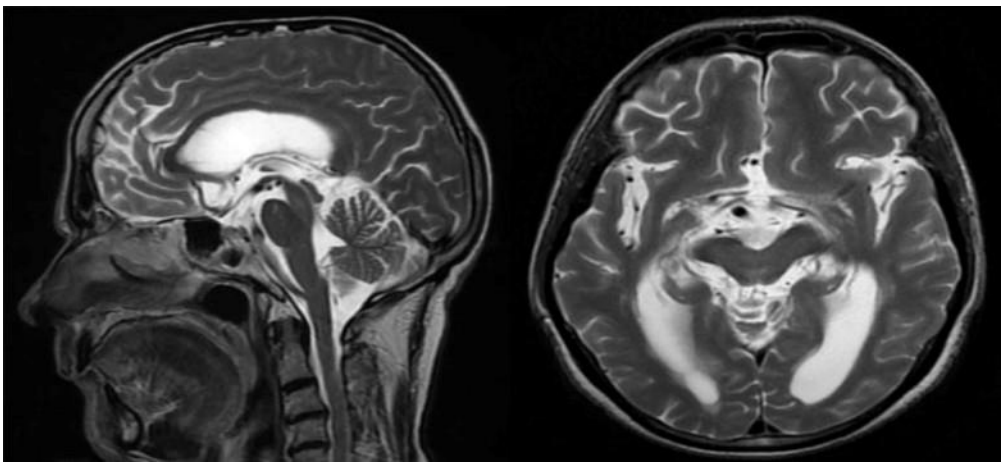

Figure 2: T2W midbrain atrophy with subtle hyperintensesignal in parenchyma and mild flattening of superior surface of pons. (PSP)

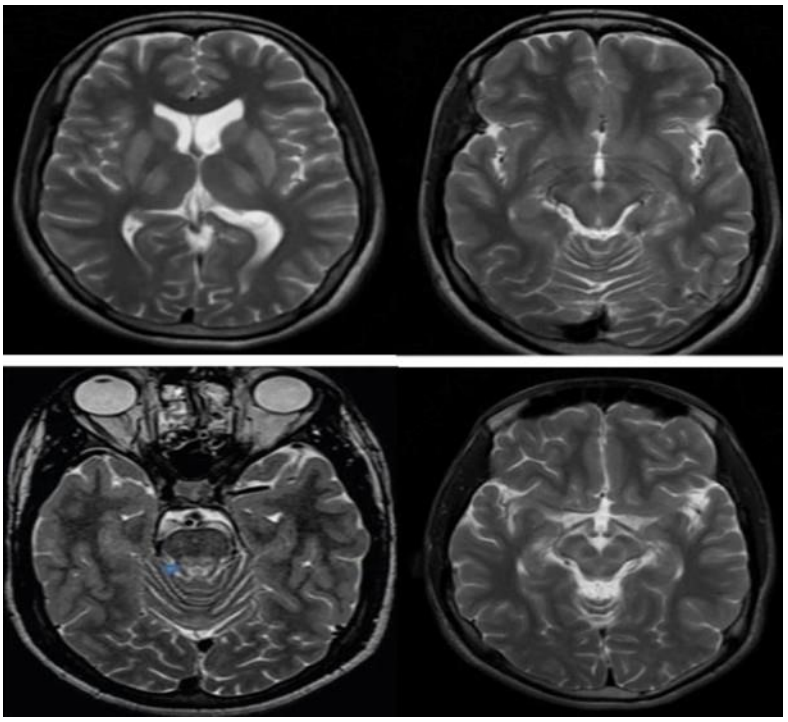

Figure 3: T2/FLAIR hyperintensities in bilateral basal ganglia, thalami, tegmentum and midbrain involvement forming a classical sign "FACE OF GIANT PANDA".(Wilson's disease)

4. Discussion

The current study evaluated the role of MRI and its validity in movement disorders at a tertiary care center in Odisha, India, among 50 patients. While the present study included multiple movement disorders in the spectrum, previous studies have focused on specific movement disorders. In the present study, the mean value of the patient's age was 60.72 years. This aligns with the patients included in the Meijer et al. (mean= 61.9-65.5 years) and Ponticorvoet al. (mean=59.5-64.3 years). [5, 6]In contrast, Hu et al. and Tinaz et al.included patients of younger age (22.36 years & 43.2 years) than our study. [7, 8] While males were the majority in our study, Meijer et al.reported a mixed proportion of gender distribution in the atypical Parkinsonism and Parkinson's disease. [5] Ponticorvo et al. and

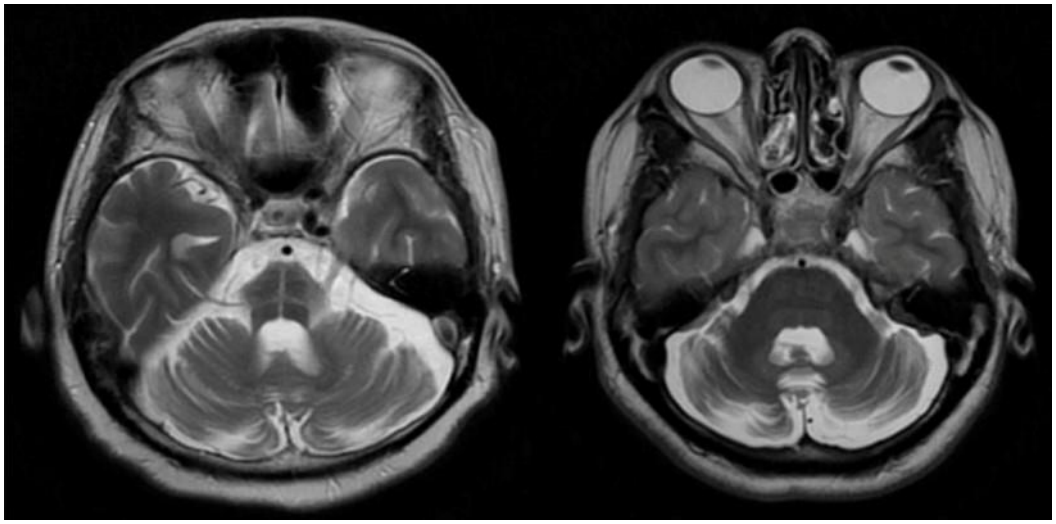

Figure 4: Cruciform T2 hyperintense signal seen in pons (HOT CROSS BUNSIGN)with diffuse cerebellar atrophy in young patient(MSA-C)

Table 2: **Observed signs of neuroimaging and radiological diagnosis**

Signs on MRI	Radiological diagnosis	Frequency	Percentage
Absent swallow tail	Parkinson's Disease	19	38.0
Hummingbird sign	PSP	6	12.0
Face of Giant Panda sign	Wilson's Disease	4	8.0
Putamen Rim Sign	MSA-P	4	8.0
Hot Cross Bun Sign	MSA-C	2	4.0
"Box" Like Configuration	Huntington's Disease	1	2.0
Normal		10	20.0
Others		4	8.0
Total		50	100.0

Table 3: Agreement between Clinical & Radiological Diagnosis

	kappa	**P-value**
Parkinson's Disease (PD)	0.723	<0.001
PSP	0.766	<0.001
Wilson's Disease (WD)	1.000	<0.001
MSA-C	0.790	<0.001
MSA-P	0.696	<0.001
Huntington's Disease (HD)	1.000	<0.001

Hu et al. reported males as the majority, which aligned with our study. Tinaz et al.included females as the majority in their study. [6–8]

Based on the clinical evidence, making an initial differential diagnosis of degenerative Parkinsonian illnesses might be problematic. In this background, MRI may be used as a supplemental tool to improve the diagnostic accuracy of the disease. The proportion of PD among those with movement disorders was 52% on clinical examination and 38% on radiological findings, similar to the study by Meijer et al., where 50% of cases had Parkinson's disease on neuroimaging. [9] Among those with movement disorders, 14.0% and 8% had MSA-P as clinical and radiological diagnoses, respectively. In contrast, Meijer et al. recorded a higher percentage of about 20% MSA-P. [9] Among those with movement disorders, 18%, and 12% had PSP on clinical and radiological diagnosis, respectively, contrary to a lower proportion of about 5% had PSP observed by Meijer et al. [9]

In their comparative study between PSP, MSA-P, and PD, Oba et al. reported that mid-brain MRI findings could differentiate PSP from Parkinson's disease and multiple-system atrophy-P. In the present study, among the clinically diagnosed PSPs, 66.7% showed a positive sign in the mid-brain in the MRI. [10] Yagishita et al.also noted that most patients with clinical PSP had shown diffuse signals in the mid-brain. [11] Among the clinically diagnosed MSA-C, 66.7% showed a positive sign in the Middle cerebellar peduncle, pons, white matter tract, and cerebellum in the MRI. In previous studies, putamen showed almost half the volume reduction from baseline in patients with severity ranging from mild-moderate Huntington's disease, while caudate showed a 28-29% reduction in its volume. [12] Among the clinically diagnosed MSA-P in the present study, 100% showed putamen involvement in MRI [Figure 3]. This is in line with Ponticorvo et al.findings, which also reported the involvement of putamen bilaterally. [6] In the most recent iteration of the clinical diagnostic criteria for MSA, the presence of atrophy seen in the regions of the putamen, MCP, pons, and cerebellum in MRI is considered an add-on indication that may point to the fact of MSA. MRI studies have also demonstrated the involvement of the brainstem and cerebellum in MSA-P and the striatum in MSA-C. When a diagnosis of MSA cannot be determined solely based on clinical features, the presence of these characteristics is diagnostic. [13]

MRI can be considered a helpful tool in detecting disorders of movement owing to its high specificity reported in our study. The diagnostic validity of MRI in identifying Parkinson's Disease and PSP was found to be 73.1% and 66.7% sensitive, respectively. Clinico-radiological diagnosis correlation was 72%. Bacchi et al. evaluated the role of MRI in diagnosing PSP and reported a high sensitivity of about 95%. Still, the specificity (95%) was lower than our findings. [14] The difference might be due to the smaller sample size in the present study and the differential study settings. A swallowtail sign was absent in 38% of the participants in the current study. Among the clinically diagnosed Parkinson's disease, 73.1% showed involvement of substantia nigra in the MRI. Ponticorvo et al. also showed that Substantianigra was affected in those with MSA significantly and reduced in patients with Parkinson's disease. [6] Putamen changes were present in 18% of patients. Both in MSA and Parkinson's disease bilaterally, reduced putamen volume was recorded by Ponticorvo et al.as well as, seen significantly more in MSA-P. [6]

The 'hummingbird sign,' also described as the 'penguin sign,' indicating mid-brain atrophy, is a classical sign of PSP on sagittal view. In this study, the Hummingbird sign was present in 12% of patients. Meijer et al.also reported that the Hummingbird sign had a high diagnostic value with 100% sensitivity and 97.8% specificity for diagnosing PSP. [9] While 4% of the cases were found to show a hot cross bun sign, none of the patients in Meijer et al.showed the sign. [9] Hot cross bun sign had been known to occur in the pons regions in the MSC-C type, where it is classical. [15] Putamen Rim Sign is a sign which is relatively more associated with MSA-P. This sign was reported by 8% of the patients in this study, leading to a diagnosis of MSA-P; Meijer et al. observed Parkinson's disease (30%), atypical (37%), and

Parkinsonism (33%) in MSA-P as well as PSP. Mestre et al. found that 30% of their patients who had MSA-P had typical MRI signs before making a clinical diagnosis. [16]

Classical signs in MRI brain which are specific for certain disorders include the swallow tail sign in Parkinson's disease, the face of a giant panda in Wilson's disease, the Hummingbird sign in PSP, Putamen rim sign in MSA-P, Box like configuration of frontal horns in Huntington' disease, Hot cross bun sign in MSA-C. These findings are particular for specific diseases, however, their absence does not rule out the diagnosis when clinical findings are classical. MRI is used as an adjunct to make or confirm a clinical diagnosis.

5. Conclusion

Overall, the clinical-radiological correlation for detecting movement disorders using MRI was 72%. Significant agreement existed between the clinical and MRI diagnosis of all the movement disorders. The most common brain area which showed changes in the MRI was the substantia nigra followed by the mid-brain. Wilson's disease, Huntington's, and MSA-P had 100% positive MRI findings with characteristic signs. The diagnostic validity of MRI in identifying movement disorders was found to be 100% specific for all with variable sensitivity. To better understand the implications of these results, further multicentric studies must be conducted with an adequate sample size for each movement disorder.

6. Limitation

Although our findings corroborated with the results of previously worldwide conducted studies, like all research, our study also has its limitations. It is a single-centric study; hence, the findings cannot be applied to other settings and regions. The duration of the diseases and the disease control status were not assessed, which could have revealed the predictive value. Since multiple movement disorders were included, the sample size was small for individual diagnosis, leading to the limited internal validity of the findings.

Recommendation: MRI can be used as a diagnostic tool in clinically challenging cases and to confirm the clinical diagnosis. We recommend more studies on the same with a larger sample size and dedicated disease study to analyze other ancillary MRI findings as well.

7. List of Abbreviation

MRI: Magnetic Resonance Imaging
PD: Parkinson's disease
P+: Parkinson Plus
MSA: Multiple System Atrophy
PSP: Progressive Supranuclear Palsy
SN: Substantia Nigra
FXTAS: Fragile X Tremor Ataxia Syndrome
CAG: Cytosine –adenine- guanine
CGG: Cytosine -guanine - guanine
WD: Wilson's disease
Cu: Copper
PET:Positron emission tomography
SPECT:Single photon emission computed tomography
SD: Standard Deviation
IQR: Interquartile range
MCP:Middle cerebellar peduncle

8. Conflict of Interest:

There is no conflict of interest.

9. Source of funding:

None

10. Author Biography:

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