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Original Research Paper

Radiology

ROLE OF MRI AND PET-MRI FUSION IN CHARACTERISATION OF ATYPICAL PARKINSON'S DISEASE

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ABSTRACT With the revolution in medical diagnostics & science; 18F-FDG PET MRI fusion is the latest novel method for the diagnosis and differentiation of atypical Parkinson's disorder. We found an abnormal midbrain profile on MRI was useful in distinguishing PSP from different type of atypical Parkinson's disorder which consist AP diameter of midbrain, midbrain to pons ratio and magnetic resonance Parkinsonism index. We explained the pattern of regional hypometabolism in different type of atypical Parkinson's disorder. PET-MRI fusion is better sensitive modality in diagnosis of different types of disease in which MRI has limited role like in DLB and CBGD. The literature as well as this study concluded that alterations in the PSP measurement profile, structural changes in brain and metabolic pattern in different parts of brain are very much helpful in the diagnosis of APD. It can be concluded that FDG-PET-MR fusion is highly valuable imaging technique for documentation of atypical Parkinson's disorder in the new era of diagnosis.

KEYWORDS : PET MRI fusion Atypical Parkinson's disease Progressive supranuclear palsy (PSP) Multiple system atrophy (MSA) Cortico-basal ganglionic degeneration (CBGD) Dementia with Lewy bodies (DLB)

INTRODUCTION

Positron emission tomography (PET) is a noninvasive diagnostic imaging procedure that enables medical professionals to view the human body's biological functions and to study disease processes(1).It is the most sensitive and specific imaging modality in the detection of metabolic changes but presents limited spatial resolution. On the other hand, MRI presents a significant spatial resolution, besides evaluating soft tissue signal intensity with excellent contrast resolution (2). Fusion technology melds functional and anatomic information and holds great promise for diagnostic imaging and improved patient care.

Clinically differentiating among parkinsonian syndromes may be very difficult. Morphological studies such as CT and MRI are usually used to rule out other causes that may be leading to secondary Parkinsonism. FDG-PET may be utilized in dubious cases (2).Parkinson's symptoms consist of tremor, rigidity and hypokinesia. Tremors are typically pin rolling on rest. The other non-motor symptoms include autonomic, neuropsychiatric symptoms, sleep and sensory symptoms. These features are also present in atypical Parkinson's disease.Apart from the usual Parkinson's symptoms, atypical Parkinson's has overlapping symptoms that make it difficult to diagnose only on the basis of clinical symptoms.

Early in the course, APS can be easily misdiagnosed as idiopathic PD because of the symptom overlap, lack of objective diagnostic biomarkers and, for some patients, a symptomatic improvement with Levodopa. Waning medication benefit, development of additional characteristic signs and symptoms, and more rapid progression of disease may eventually differentiate these conditions from PD, although this can take years.

Neuro-imaging may support clinical impression and/or exclude conditions that may require (or respond better) to other treatments. Structural imaging (CT or MRI), for example, may reveal vascular disease or normal pressure hydrocephalus (both of which may present with clinical features similar to those seen in neurodegenerative parkinsonism).

MRI may be normal or show mild diffuse atrophy in PD or DLB but demonstrate distinct patterns of atrophy in the other APS, particularly with advancing disease (e.g., midbrain atrophy in PSP). DaTscans, which approximate the pre-synaptic binding activity of dopamine transporters, may be helpful to distinguish neurodegenerative (PD or APD) from drug-induced or vascular forms of parkinsonism or essential tremor, but cannot differentiate among APS, or between them and PD(3).

Atypical Parkinson's disease encompasses group of neurodegenerative disease naming:-

1. Progressive supranuclear palsy (PSP)
2. Multiple system atrophy (MSA)
3. Cortico-basal ganglionic degeneration (CBGD)
4. Dementia with Lewy bodies (DLB)

Definitive diagnosis of APD can be made only through neuropathological confirmation, the hallmark of which is intracellular protein deposition. Abnormal accumulation of alpha- synuclein is characteristic of PD, DLB, and MSA (the synucleinopathies); tau protein aggregates in PSP and CBD (the tauopathies).

We performed the study to assess role of mri and pet-mri fusion in characterisation of atypical parkinson's disease The objectives of the study were:

1) To evaluate 3T MR imaging features of atypical Parkinson's disease.
2) To evaluate the role of PET-MRI fusion for imaging of atypical Parkinson's disease.
3) To outline the advantages of PET- MR Fusion over MRI alone and its clinical impact.

METHODS

In this study a total of 32 patients were analyzed by PET images, Cortex-ID, MRI images and software co registered PET-MR images. PET images were obtained in a dedicated PET-CT machine and then Magnetic Resonance Imaging of brain was separately performed on a 3T MRI machine. Both the data were fused by matching the corresponding sections of brain on CT and MR images, using fusion software such that a co-registered PET-MR brain image is obtained. Cortex - ID was generated from PET data using special software.

1) Mr Imaging (3- TESLA Whole body scan, PHILIPS ACHIEVA

with 16 array channel coil).

Magnetic Resonance Imaging was performed on 3.0 Tesla MR scanner (Philips – Achieva X series) using dedicated head sense 16 channel coil. In addition to padding, chin and forehead straps were used to reduce patient motion.

MR imaging with high resolution specific serial sections was obtained including:

A) T2 AXIAL(90 degrees FLIP ANGLE,3000ms TR,90msTE,400X252 MATRIX ,230 mm2 FOV, 20 SLICE, 5.5 mm SLICE THICKNESS,1 mm GAP,1 NSA)
B) T2 FLAIR(90 degrees FLIP ANGLE,10000ms TR, 119msTE,284X138 MATRIX ,240 mm2 FOV, 20 SLICE, 5.5 mm SLICE THICKNESS,0.7 mm GAP,1 NSA)
C) 3D T1 (8 degrees FLIP ANGLE,7.6ms TR, 3.6msTE, 228X227 MATRIX ,250 mm2 FOV, 290 mm SLICE THICKNESS)
D) VENO BOLD- AXIAL(15 degrees FLIP ANGLE,14ms TR, 19msTE, 192 X150 MATRIX ,230 mm2 FOV, 130mm SLICE THICKNESS)
E) Diffusion Weighted Imaging (DWI) sequence (AXIAL)

DW-MRI were obtained with motion-probing diffusion gradient (b = 0 and 1000 s/mm2) being applied on each of three orthogonal directions (90 degrees FLIP ANGLE,1363ms TR,45msTE,112X89 MATRIX ,230 mm2 FOV, 15 SLICE, 6 mm SLICE THICKNESS,2mm GAP,1 NSA)

2)pet Ct

Scanner BGO plus, Full Ring PET-CT (GE Discovery STE) Radio-isotope: 18F-FDG-370 MBq & 45 minute uptake periods. Study Mode: PET-3D Mode and CT- 120 kV auto mA (Image slices for PET-CT- 125, Slice thickness- 1.25 mm, Interstice distance- 1.25 mm, Total axial field of view- 20 cm,Matrix size- 512 × 512,Extent Of study: Vertex to base of skull)

3)pet Mri Fusion Data Acquisition Technique

PET-MR fusion is done by using advantage fusion software provided in the AW workstation on GE PET-CT machine. The advantage fusion is software developed for easy comparison of 3D image sets from different modalities.

After loading the two sets of images to be compared (CT images of brain and 3D T1W MRI images), a minimum of 3 pairs of matching points are defined using anatomical landmarks that can be clearly identified in both sets of images.

The application then uses a 6 DoF(linear scaling, translation and rotation) transform calculation algorithm to register(align) the co-ordinates of the reference examination. This allows 3D registering of images from two different examinations, where the modality used in each examination may be the same or different (for instance CT& MR).

The registering process was semiautomatic with manual definition of common points on the two exams, and an optional computer assisted enhanced selection mode as well as an automatic set up procedure, which can at times provide a faster & more accurate registering.

Generation of Cortex-ID maps:

Cortex ID maps were generated by the Cortex –ID software provided in the AW workstation on GE PET-CT machine. Cortical ID maps aids in identifying the patient's metabolic changes in comparison to a database of age-matched normal subject and to check for any abnormalities indicative of brain function alterations by neurodegenerative processes.

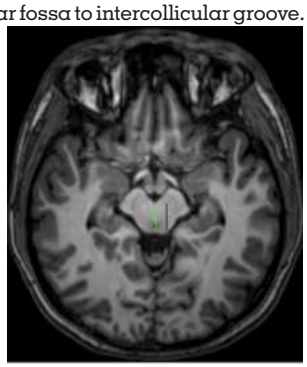
It combines fully automated 3D-stereotactic surface projection (SSP) and an age-stratified normal PET database with rich image review capabilities and enables easy clinical reporting.

Data collection and data analysis:

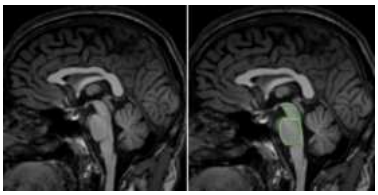
Data was collected and analyzed for different parameters:-

1) AP diameter of midbrain:

AP diameter of midline midbrain was obtained on axial 3D T1W image at the level of superior colliculus from interpeduncular fossa to intercollicular groove.

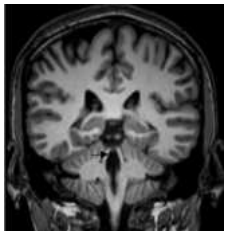


2) Mid brain to pons area ratio: MP ratio was measured in midsagittal line on 3D T1W images

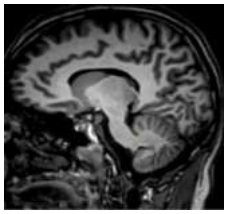


3) Magnetic resonance parkinson's index (MPRI): It was obtained by the formula- Area of pons in mid sagittal plane (P) x Width of middle cerebellar peduncle (MCP) Area of midbrain in mid sagittal plane (M) x Width of superior cerebellar peduncle(SCP)

A. Both superior peduncles width was measured on coronal view on 3D T1W images and mean SCP value is half of summation of each SCP.



B.Middle cerebellar peduncle width was measured in parasagittal view, the linear distance between the superior and inferior borders of the MCP located between the pons and the cerebellum. Mean MCP value is the half of summation of Each MCP (left and right).



4) Atrophy in different lobes and parts of the brain.

5) Hypometabolism in different part of the brain- assessed by visual assessment and with the help of the cortex ID and Z-score. A Z score of ≤ -2 was considered to be significant.

RESULTS

Out of our study on 32 clinically diagnosed atypical parkinson's patients in our institution GUJARAT MRI centre Pvt. Ltd., Samved hospital with 3Tesla MRI and PET scan machine

under the topic "ROLE OF MRI AND PET-MRI FUSION IN CHARACTERISATION OF ATYPICAL PARKINSONS DISEASE" for period of two years, there were 16 patients of PSP, 8 of MSA, 6 of CBGD and 2 of DLB. We studied on the atypical Parkinson's disease patients aged from 40 to 79 years (overall mean age was 63.09 ± 8.57 years). The mean age was 66.25 ± 9.05 years, 58 ± 9.24 years, 61.16 ± 9.60 years and 64 ± 2.82 years for PSA, MSA, CBGD and DLB groups respectively. In our study, there was no significant difference in the age group of different subtypes. Overall atypical Parkinson's disease incidence was more in male as compared to female with female to male ratio 1: 2.2

The mean value of AP diameter of midbrain was 11.44 mm ± 1.42 mm, 14.21 mm ± 1.45 mm, 13.46 mm ± 1.49 mm and 13.9 mm ± 0.56 mm in PSP, MSA, CBGD and DLB groups respectively .Total 13 patients out of 16 patients (81.2 %) of PSP have AP diameter of midbrain less than 12 mm.(Figure I)

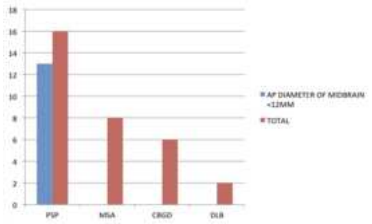


Figure I

The mean value of Midbrain to pons ratio was 0.167 ± 0.028, 0.348 ± 0.064, 0.355 ± 0.070 and 0.37 ± 0.113 in PSP, MSA, CBGD and DLB groups respectively. Midbrain to pons ratio < 0.24 was presented in 100 percent of 16 PSP patients, while the rest of the groups had ratio > 0.24.

The mean value of MRPI was 13.76 ± 4.842, 8.823 ± 1.318, 9.228 ± 0.921 and 11.26 ± 0.24 in PSP, MSA, CBGD and DLB groups respectively. MRPI > 13.55 was presented in 50 percent of PSP patients of total 16 patients. But rest of the subtypes had MRPI < 13.55.(Figure II)

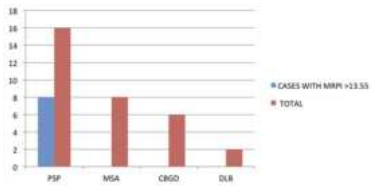


Figure II

In our study we found hot cross bun sign, atrophy of brachium pontis,cerebellar atrophy and hyperintensity along MCP in pons only in MSA patients, whereas hummingbird sign was only seen with PSP patients.(Figure III)

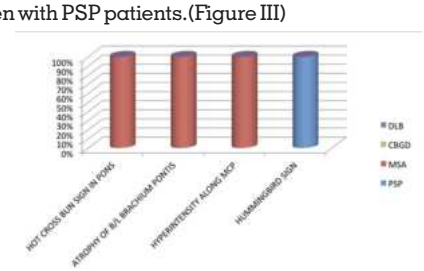


Figure III

In our study, MSA patients had pontine and cerebellar hypometabolism while DLB patients had occipital region hypometabolism on FDG-PET.

DISCUSSION

Advances in clinically available functional and metabolic imaging techniques, such as U.S. Food and Drug Administration (FDA) approval of fluorine 18 (18F) florbetapir positron emission tomography (PET) in 2012, combined with the increasing use of semiquantitative 2- [fluorine-18]fluoro-2-deoxy-d-glucose (FDG) PET, highlight the need for radiologists to become familiar with the most common imaging patterns of parkinsonism .

When these techniques are used in combination with conventional magnetic resonance imaging (MRI) and a thorough clinical examination, an accurate diagnosis can frequently be made. Differentiation between subtypes of atypical Parkinson's disease is necessary for the treatment of each subtype, although there is no specific treatment. For example, with the promise of neuroprotective treatments, early diagnosis is increasingly important. For example, a more extensive cholinergic deficit has been observed in DLB compared with AD. This observation explains the beneficial effects of cholinergic therapy in DLB (cholinesterase inhibitor), which has been shown to improve impaired cognitive functions.

We studied on 32 clinically diagnosed atypical parkinson's patients in our institution GUJARAT MRI centre Pvt. Ltd., Samved hospital with 3 Tesla MRI and PET scan machine under the topic "ROLE OF MRI AND PET-MRI FUSION IN CHARACTERISATION OF ATYPICAL PARKINSON'S DISEASE" for period of two years from November 2015 to November 2017.

There were 16 patients(50%) of PSP, 8 patients (25%) of MSA, 6 patients of CBGD and 2 patients of DLB in our study. We studied the atypical Parkinson's disease patients aged from 40 to 79 years. The mean age was 66.25 ± 9.05 years, 58 ± 9.24 years, 61.16 ± 9.60 years and 64 ± 2.82 years for PSA, MSA, CBGD and DLB groups respectively. In our study, there was no significant difference in the age group of different subtypes.

Overall atypical Parkinson's disease incidence was more in male as compared to female (female : male ;1: 2.2).

In our study, the mean value of AP diameter of midbrain was 11.44 mm ± 1.42 mm, 14.21 mm ± 1.45 mm, 13.46 mm ± 1.49 mm and 13.9 mm ± 0.56 mm in PSP, MSA, CBGD and DLB groups respectively. 81.2 % of PSP had an AP diameter of midbrain less than 12 mm.Monika Warmuth-Metz et al in their study ,showed significantly lower midbrain diameters (mean 13.4) than patients with PD and MSA-P and control subjects (P<.001).(4)

Although previously many authors found a clear cutoff value separating PSP from PD, we found an important overlap, and the observed threshold value of 12 mm included too few PSP subjects to be of practical use. This discrepancy can be explained by differences in the measurement methods: we traced our measurement on axial, 3-mm-thick, T2-weighted sections perpendicular to the main axis of the midbrain, and all images were acquired with the same protocol. In contrast, Warmuth-Metz et al (4) and Schrag et al (5) traced the AP diameter on axial 5–7-mm-thick sections obtained with different MR units. Therefore, our measurement might be accurate given the better spatial resolution and the smaller technical variability between imaging sessions.

The mean value of Midbrain to pons ratio was 0.167 ± 0.028, 0.348 ± 0.064, 0.355 ± 0.070 and 0.37 ± 0.113 in PSP, MSA, CBGD and DLB groups respectively. Midbrain to pons ratio < 0.24 was presented in 100 percent of 16 PSP patients, while the rest of the groups had ratio > 0.24.(Figure 1)

Our results support previous findings indicating a significantly decreased midbrain pons ratio in PSP. Quattrone A et al also demonstrated in their patients that Pons / Midbrain

values patients with PSP (median, 6.67; range, 4.35–9.09) was significantly larger than that observed in patients with MSA-P (median, 3.22; range, 2.17–5.26; P < .001) and with PD (median, 4.0; range, 2.94–6.25; P < .001) and in control participants (median, 3.85; range, 2.78–5.56; P < .001).(6)

Figure 1a

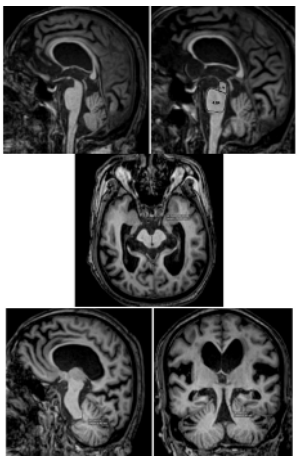


Figure 1b

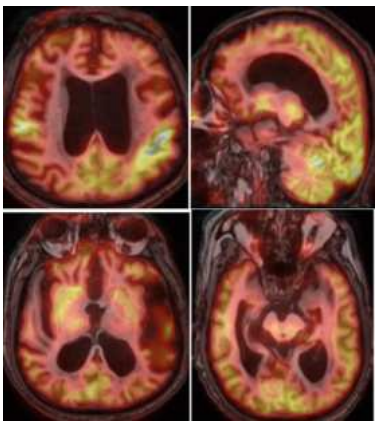


Figure 1c

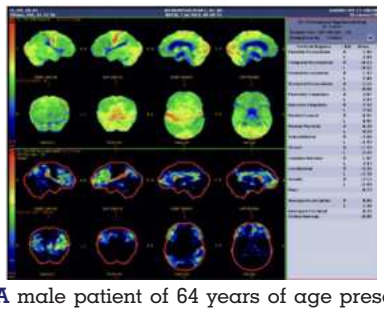


Figure 1 -A male patient of 64 years of age presented with complaints of tremors and imbalance with history of frequent fall since 4 years and diagnosed as PSP type of APD.MRI shows flattening of superior surface of midbrain giving "hummingbird sign". Midbrain to pons ratio as 0.16, AP diameter of midbrain as 10mm and MRPI as 19.5.(1a)

PET-MRI fusion images show hypometabolism involving the frontal cortex, anterior cingulate gyrus and basal ganglia (LT>RT).(1b)CORTEX ID confirms the findings with Z score > 2.(1c)

Magnetic resonance parkinson's index was measured with the help of midbrain pons ratio, superior peduncle width and middle cerebellar width. The mean value of MRPI was 13.76 ± 4.842, 8.823 ± 1.318, 9.228 ± 0.921 and 11.26 ± 0.24 in PSP, MSA, CBGD and DLB groups respectively. MRPI > 13.55 was presented in 50 percent of PSP patients of total 16 patients. But rest of the subtypes had MRPI < 13.55.

Our results support previous findings indicating a significantly increased MRPI in PSP patients. Quattrone A et al also showed in their study that patients with PSP had highest MRPI with respect to all other groups (patients with PSP vs patients with MSA-P, P < .001; patients with PSP versus patients with PD, P < .001; patients with PSP vs control participants, P < .001). There was no overlap of individual values for the MR parkinsonism index between the patients with PSP (median, 19.42; range, 14.39–40.11) and those with MSA-P (median, 6.53; range, 3.87–11.3), those with PD (median, 9.40; range, 6.33–12.71), and control participants (median, 9.21; range, 6.29–12.77). (6)

But in our study there was significant overlap of the MRPI value in PSP patients as compared to MSA and CBGD patients. Midbrain to pons ratio is the most sensitive measurement for diagnosis of PSP seen in 100 percent PSP patients. AP diameter of midbrain is less sensitive than midbrain pons ratio with 82.5 percent to diagnose PSP on MRI. And MRPI is least sensitive among all three measurements with only 50 percent in PSP patients.

AP diameter of midbrain <12mm, midbrain to pons ratio < 0.24 and MRPI >13.55 are more specific for PSP to diagnose it on MRI.

Criss cross hyperintensity was seen in pons giving appearance of "Hot cross bun". It was seen in 100 percent of MSA patient. (Figure 2) It was not found in the rest of the subtype of atypical parkinson's disease. Along with this atrophy of bilateral brachium pontis is also seen only in MSA subtype with 75 percent of the total patients.

Hyperintensity along bilateral middle cerebellar peduncle is also seen only in MSA group of patients with 37 percent. So this finding is specific for MSA disease but not sensitive.(Figure 2)

Figure 2a

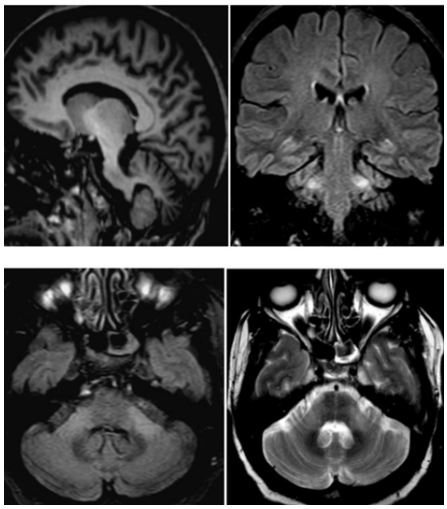


Figure 2b

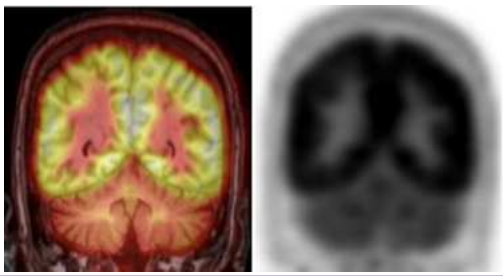


Figure 2c

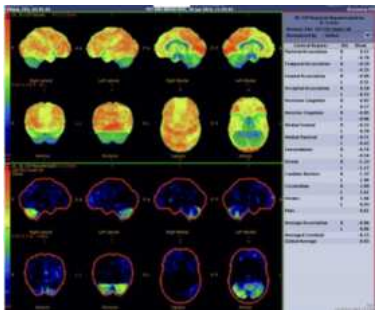


Figure 2-A female of 52 yrs presented with complaints of imbalance in walking, abnormal speech & incontinence in urine. It was diagnosed as MSA type of APD.

T1W 3D sagittal image shows mild atrophy of middle cerebellar peduncle. FLAIR coronal and axial images shows hyperintense signals in middle cerebellar peduncle. T2W axial image shows hot cross bun sign in pons.(2a)

PET coronal and PET-MRI fusion images show marked symmetrical hypo-metabolism in both cerebellum hemisphere with Z-score >2.5.(2b and c)

Giuseppe Nicoletti et al studied on 16 MSA patients they found that eight had cruciform hyperintensity, five had brainstem atrophy, and two had hyperintensity of the MCP.

They also found that there was mild reduction in the width of middle cerebellar peduncle. 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 < .001) or control subjects (9.80 mm ± 0.66, P < .001) (7).

So according to our study hot cross bun sign, atrophy of bilateral brachium pontis and hyperintensity along bilateral middle cerebellar peduncle are more specific finding for MSA disease to diagnose it on MRI, but only hot cross bun sign is most sensitive as compared to other findings.(Figure 3)

Our findings were supported by recent previous studies. Broski et al demonstrated that increased T2 signal in the pons, middle cerebellar peduncles, and cerebellar white matter, with sparing of the corticospinal tracts and superior cerebellar peduncles produce a cruciform T2 hyperintensity within the basis pontis, popularly referred to as the hot cross bun sign This sign has relatively high sensitivity for MSA-C, being reported in up to 80% of patients however, it is not specific for MSA, since it is also seen in many spino-cerebellar ataxia subtypes.(8)

Figure 3a

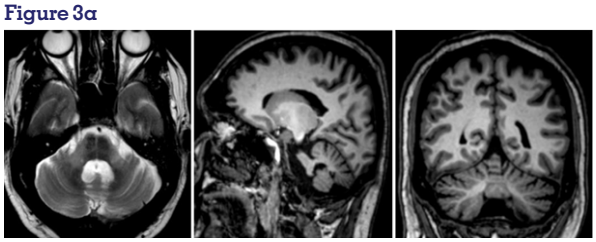


Figure 3b

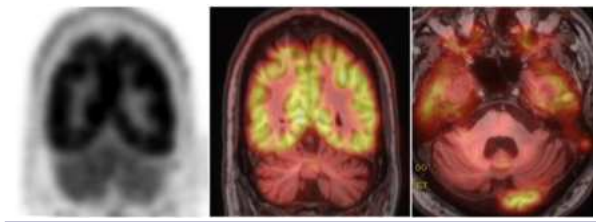


Figure 3c

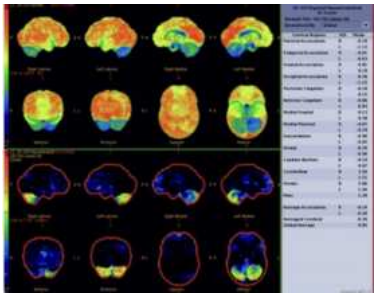


Figure 3- A male of 56 yrs presented with complaints of tremor, rigidity, slurred speech and loss of muscle coordination since 5 yrs. It was diagnosed with MSA type of APD.

T2W axial image demonstrate cerebellar atrophy with "hot-cross bun" sign in pons & hyperintensity along bilateral middle cerebellar peduncle. Sagittal 3D T1W image shows atrophy of middle cerebellar peduncle. FLAIR coronal image reveals marked atrophy of cerebellum(3a).

PET-MRI fusion images shows marked hypometabolism involving bilateral Cerebellar hemispheres.(3b) Cortex ID confirms this finding with Z score >3.5 (3c)

Flattening of superior aspect of midbrain gives the "Hummingbird sign". It was only seen in patients with PSP. 56 percent of PSP patients had hummingbird sign.(Figure 4) So according to our study, it is specific for PSP but not much sensitive for PSP subtype of disease.

Figure 4a

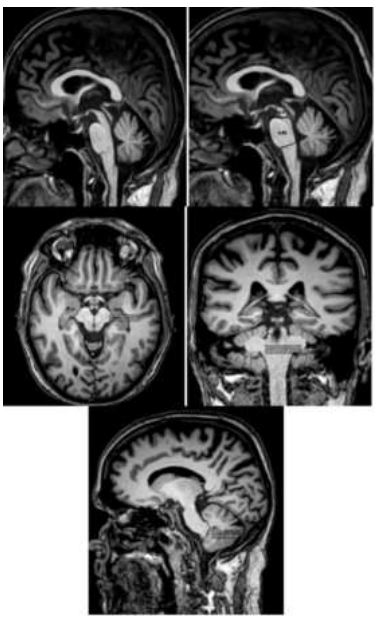


Figure 4b

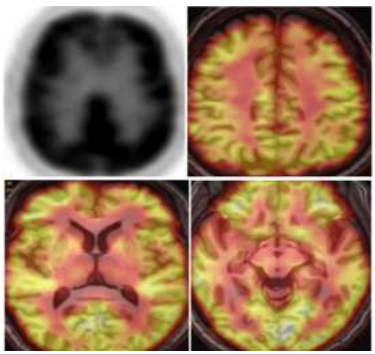


Figure 4c

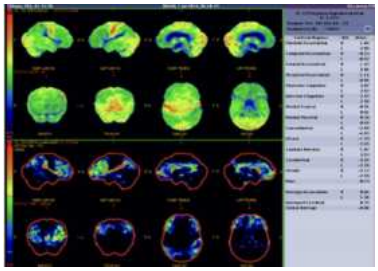


Figure 4- A 62 yrs male patient presented with complaints of rigidity and imbalance in walking with a history of fall since one and half years. He was diagnosed as PSP type of APD.MRI findings show flattening of the superior surface of midbrain giving "hummingbird sign". Midbrain to pons ratio was 0.10, AP diameter of midbrain was 10.3 mm and MRPI was 22.6.(4a) PET and PET-MRI fusion images reveal hypometabolism involving bilateral median frontal cortex and anterior cingulated gyrus. (4b) CORTEX ID confirms the findings with high Z score. (4c)

Atrophy of cerebrum on MRI was assessed by global cortical atrophy scale. It divides cortical atrophy in mild, moderate and severe forms. Regional atrophy was assessed in different parts of brain.

Frontal and parietal cortical atrophy was found in 25 percent of PSP patients. 12.5 percent of PSP patients also had anterior cingulate gyrus atrophy.(Figure 4)

Figure 4a

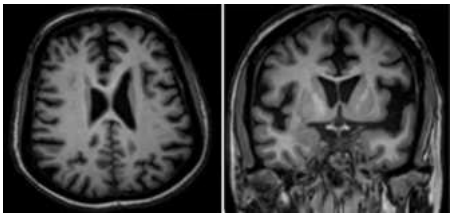


Figure 4b

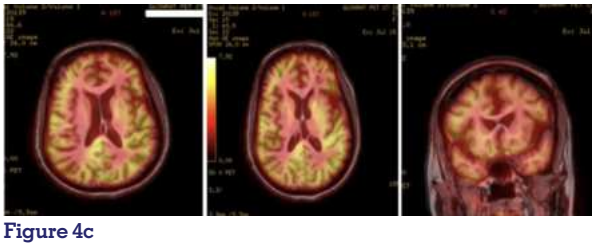


Figure 4c

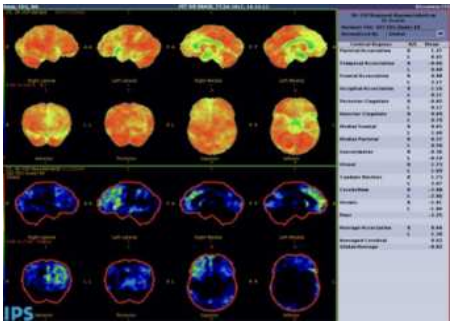


Figure 4 -
56 yrs of female patient presented with complaints of gait disturbance and whole body rigidity with frequent fall since 2 yrs. It was diagnosed with PSP type of APD.

3D T1W axial and sagittal images show atrophy involving bilateral frontal cortex, perisylvian regions and along anterior cingulate gyrus(4a). PET MRI fusion images reveals hypometabolism in bilateral frontal cortices and caudate nucleus (Left > Right) with Z score of >2.17 and 2.67 respectively(4b). CORTEX ID confirms metabolic findings(4c).

Cerebellar hemisphere atrophy was seen in MSA patients with 100 percent cases. But cerebellar atrophy is also seen in 12.5 percent of PSP patients. Few patients with MSA subtype also had midbrain & pons atrophy.

100 percent of CBGD patients had typically peri-rolandic region atrophy. (Figure 7) Perirolandic atrophy was specific for CBGD subtype, however frontal cortex atrophy was also seen in 67 percent of CBGD patients.

Figure 5a

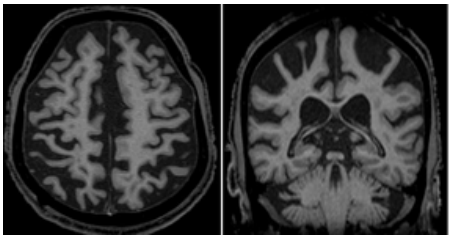


Figure 5b

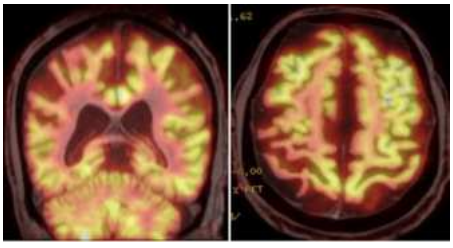


Figure 5c

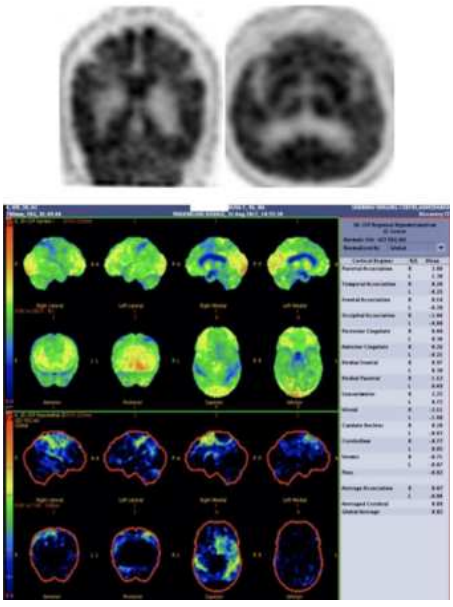


Figure 5 - 66 yrs old left handed male presented with complaints of difficulty in speech and writing with left hand. He was diagnosed as CBGD type of APD.

3DT1W axial and coronal images show bilateral fronto-parietal cortical atrophy with marked asymmetric atrophy in right perirolandic parietal cortex.(5a)

PET and PET-MR fusion images show asymmetric marked hypometabolism in right perirolandic parietal lobe and right basal ganglia.CORTEX ID confirms findings with Z-score 2.25.(5b and c)

With the revolution in medical diagnostics & science; 18F-FDG PET MRI fusion is the latest novel method for the diagnosis and differentiation of atypical Parkinson's disorder. We found an abnormal midbrain profile on MRI was useful in distinguishing PSP from different type of atypical Parkinson's disorder which consist AP diameter of midbrain, midbrain to pons ratio and magnetic resonance Parkinsonism index. We explained the pattern of regional hypometabolism in different type of atypical Parkinson's disorder. PET-MRI fusion is better sensitive modality in diagnosis of different types of disease in which MRI has limited role like in DLB and CBGD.

The literature as well as this study concluded that alterations in the PSP measurement profile, structural changes in brain and metabolic pattern in different parts of brain are very much helpful in the diagnosis of APD. It can be concluded that FDG-PET-MR fusion is highly valuable imaging technique for documentation of atypical Parkinson's disorder in the new era of diagnosis.

Our findings were supported by previous studies. Broski et al revealed that asymmetric atrophy centered in the posterior frontal and parietal lobes develops in a significant proportion of patients with CBGD subtype. (8)

Patients with DLB subtypes had occipital atrophy in 59 percent cases. No other regional atrophy was seen in these patients.

In our study 68.7 % PSP patients had frontal association cortex hypometabolism, and 43.7% patients had basal ganglia hypometabolism. PSP patients also had anterior cingulate gyrus hypometabolism in 31.2 percent patients, parietal cortex hypometabolism in 18.7 patients, temporal association cortex hypometabolism in 12.5 percent patients.

Tripathi et al studied on 165 parkinsonism patients. They found hypometabolism in the midbrain and anterior cingulate cortices in PSP patients. Decreased metabolism was also seen in the basal ganglia and insular cortices. (9) Broski et al studied demonstrated that PSP patients had decreased glucose metabolism in the basal ganglia, midbrain, and midline frontal lobes—in particular, the anterior cingulate cortices. (8)

In this study, patients with MSA subtype had cerebellar hypometabolism in 100 percent of patients and pontine hypometabolism in 50 percent of patients. No other cortical hypometabolism was seen in patients with MSA disease.

Valentine Berti et al studies with FDG PET in MSA showed significant metabolic decrease in the striatum, particularly in the putamen, as well as in the brainstem and cerebellum, when compared to both normal subjects and patients with PD. Patients with MSA-P subtype showed more pronounced striatal hypometabolism, whereas MSA-C-subtype patients exhibited cerebellar hypometabolism, which may helped to distinguish between these forms of MSA.(10) Daniela Perani et al studied on MSA disease patients with FDG PET. They demonstrated that patients with olivo-pontine atrophy had a prevalent hypometabolism in the cerebellum, while the patients with striatonigral degeneration type (N=9) had a prevalent impairment in the pallidum-putamen complex.(11) Broski et al demonstrated that patients with MSA-C showed reduced FDG activity in the cerebellar hemispheres and middle cerebellar peduncles. Interestingly, cerebellar hypometabolism may be seen in patients without clinical signs of cerebellar dysfunction, and also in patients with MSA-P. These patterns are useful in distinguishing MSA from Parkinson disease, which demonstrates normal putaminal and cerebellar metabolism. (8) Tripathi et al demonstrated in their study that metabolic pattern of MSA was characterized by hypometabolism in both basal ganglia predominantly posteriorly with or without hypometabolism in the cerebellar hemispheres in the olivopontocerebellar atrophy variant. Reduced metabolism was also observed in the pons in their patients. (9)

100 percent patients (6 out of 6) with CBGD subtype had asymmetric parietal association hypometabolism. Hypometabolism was predominantly in sensorimotor cortex on contralateral side of affected limb. 50 percent of CBGD patients also had basal ganglia hypometabolism predominantly on contralateral side of affected limb. Frontal cortex, anterior cingulate gyrus and pons were also affected in CBGD patients with 33 percent, 17 percent and 17 percent respectively.

Martin Niethammer et al studied on CBGD patients by FDG-PET. It characterized by asymmetrical metabolic reductions (worse in the left hemisphere, i.e. contralateral to the more affected body side) in the cerebrum, lateral parietal and frontal regions and thalamus, with relative bilateral increases in occipital regions.(12)

Our results support previous researched findings indicating a significantly reduced metabolism in contralateral parietal lobe and basal ganglia. Broski et al demonstrated that FDG PET showed asymmetric basal ganglia and cortical glucose hypometabolism contralateral to the affected side. Tripathi et al found in their study that patients with CBGD had asymmetrical tracer distribution with hypometabolism in basal ganglia and parietal cortices contralateral to the clinically more affected side. (9)

But some studies have shown that patients with CBD can have increased FDG activity in the basal ganglia and cortex ipsilateral to the clinically affected side. (13) It can happen because metabolic assessment was done on the visual assessment which can consider hypermetabolism in affected side as compared to unaffected side or hypometabolism in unaffected side as compared to affected side.

100 percent of patients with DLB subtype typically had occipital association hypometabolism with involvement of visual cortex. No other cortical atrophy was found in DLB patients.(Figure 6)

Figure 6a

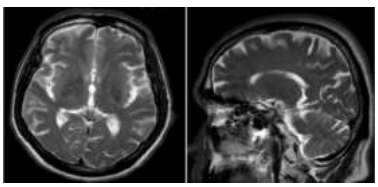


Figure 6b

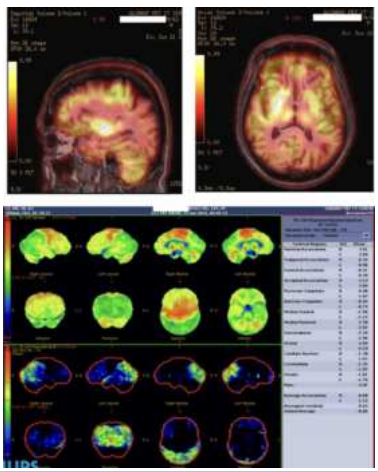


Figure 6- A male of 62 yrs presented with complaints of dementia, imbalance, weight loss and loss of appetite. He was diagnosed with Dementia with Lewy Body (DLB) type of APD.

MRI didn't reveal any major abnormality except age related cerebral and cerebellar atrophic changes.(6a)

PET MR FUSION images show marked symmetric hypometabolism in bilateral occipital lobes involving bilateral visual cortex with Z score>3.5(6b)

Siroos Mirzaei et al studied 5 patients of DLB with FDG-PET. They found diffuse reduced glucose uptake in the entire cortical region with relative sparing of the central region but including the occipital cortex was determined in all the patients, which was less remarkable in patient number 2.(14) Broski et al demonstrated that FDG PET shows generalized decreased FDG activity, with more profound decreased metabolism in both occipital and parieto-occipital regions. This pattern appears to have good sensitivity in distinguishing DLB from Alzheimer disease, which shows decreased metabolism centered more anteriorly in the temporoparietal lobes, with relative sparing of the visual cortex. (8)

Our findings were supported by previous studies. However our study did not showed generalized cortical hypometabolism in DLB patients. It can be explained by visual assessment as our eyes are more prone to pick significant changes as compared to generalized hypometabolism.

PET-MRI fusion was more helpful in diagnosing the different subtype of disease which MRI can't diagnose it alone. CBGD patients can be better diagnosed on PET-MRI fusion compared to MRI alone because this subtype don't has significant findings on MRI to diagnose, while PET-MRI fusion gives the metabolic status in parietal lobe and basal ganglia region. PET-MRI fusion is superior as compared to MRI alone to give functional information in form of glucose metabolic activity as well as structural information

SUMMARY & CONCLUSION

With the revolution in medical diagnostics & science; 18F-FDG PET MRI fusion is the latest novel method for the diagnosis and differentiation of atypical Parkinson's disorder. We found an abnormal midbrain profile on MRI was useful in distinguishing PSP from different type of atypical Parkinson's disorder which consist AP diameter of midbrain, midbrain to pons ratio and magnetic resonance Parkinsonism index. We explained the pattern of regional hypometabolism in different type of atypical Parkinson's disorder. PET-MRI fusion is better sensitive modality in diagnosis of different types of disease in which MRI has limited role like in DLB and CBGD.

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