

Spectrum of clinical and FDG-PET patterns of patients with frontotemporal dementia (FTD) in a tertiary care hospital

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ABSTRACT

Introduction. Frontotemporal dementia (FTD) is a common cause of cognitive impairment, behavioral changes and language deficits. In this study we assessed the clinical and FDG-PET characteristics of our patients and compared them with available international and Indian data on FTD.

Methods. All patients were evaluated with a neuropsychological battery followed by 18F-FDG-PET scan, in addition to all necessary dementia work-up.

Results. 15 FTD patients (m:f = 11:4) had a mean age of presentation of 67.4 (8.6) years, with a mean interval of 1.7 (0.7) years from the symptom onset to diagnosis. Those with 10 or less years of education had an earlier presentation. A positive family history was present in 20%. The mean MMSE score was 18.8 (4.6). Disinhibition was the most common symptom seen in 60%. Apathy was less frequently noted. FDG-PET scan showed predominantly anterior cingulate and anterior temporal hypometabolism, with asymmetry in 67%. 2 cases diagnosed as fvAD had a revised diagnosis of bvFTD after FDG-PET scan. 1 patient of nfvPPA was mute at presentation with a history of agrammatism with hypometabolism in left inferior frontal and superior temporal regions.

Conclusions. There were significant variations compared to international/Western literature, with later age of presentation, shorter interval from onset to presentation, lower MMSE scores, with disinhibition rather than apathy as the commonest symptom. FDG-PET showed similar areas of involvement but with less extensive hypometabolism compared to other studies with a lesser frequency of asymmetry. FDG-PET scan is a useful adjunct for evaluation of FTD patients.

Keywords: frontotemporal dementia, FDG-PET scan

INTRODUCTION

Frontotemporal dementia (FTD) is a constellation of neurocognitive symptoms that present variably with impairment of executive functioning, alterations in behavior and deficiency in language skills. Its prevalence among people below 65 years is second only to Alzheimer's disease (AD) (1), while its overall prevalence ranks third behind Alzheimer's disease and dementia with Lewy bodies (DLB). The various clinical subtypes of FTD include behavioral variant (bvFTD), semantic variant primary progressive aphasia (svPPA), nonfluent,

agrammatic variant primary progressive aphasia (nfvPPA) and FTD associated with motor neuron disease (FTD-MND). Of the subtypes, bvFTD is the most commonly encountered (2). Other conditions presenting prominent symptoms related to disordered basal ganglia circuits, such as progressive supranuclear palsy (PSP) and the corticobasal syndrome (CBS) have been associated with frontotemporal lobar degeneration. The term frontotemporal lobar degeneration (FTLD) is used for patients who have clinical features consistent with FTD with recognition of a FTD associated

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mutation or a histopathologically proven FTD, by either biopsy or autopsy.

Though FTD is commonest between 45 and 65 years of age, 10% occur before the age of 45 years and 30% after the age of 65 years (1). It has no sex predilection. The hallmark of bvFTD includes disinhibition, apathy, loss of empathy, perseverative/compulsive behavior and hyperorality (3). The classical symptom in svPPA is ‘loss of word meaning’ and there is evidence of naming and single word comprehension deficits. In nfvPPA, there is agrammatism in language production (short, simple phrases with omissions of grammatical morphemes), effortful and labored speech with difficulty in articulation planning (apraxia of speech) (4). While the PPA variants are easy to differentiate, many patients with bvFTD present as an amnesic syndrome, mimicking AD. Thus an accurate differentiation of FTD from other dementing syndromes is important from a diagnostic and therapeutic point of view.

FDG-PET imaging in subjects with underlying neurodegenerative pathology has emerged as a crucial diagnostic tool, extending the neuropsychology-based understanding of the brain/cognition relationship. Patterns of hypometabolism on FDG-PET can distinguish between AD and FTD and its appropriate use can add valuable information to the clinical workup (5). PET imaging typically shows frontal (including medial, orbitofrontal, dorsolateral, anterior cingulate) and temporal hypometabolism in bvFTD. In svPPA, there is asymmetric hypometabolism in the left temporal lobe, predominantly in the anterior temporal pole. In nfvPPA, the hypometabolism is usually over the left inferior frontal and superior temporal lobes.

There are very few studies which have looked at the FDG-PET findings in FTD patients in the Indian population. We attempted to look at the clinical characteristics and FDG-PET findings in our FTD cohort and to compare it with available international and Indian data.

MATERIALS AND METHODS

A cross-sectional observational analysis was done on 35 consecutive patients presenting with cognitive impairment, language dysfunction and behavioral symptoms, attending the Neurology Out-patients department, Cognitive Clinic at Sri

Ramachandra Institute of Higher Education and Research, Chennai, between 1.7.2017 and 31.6.2018. A detailed history was obtained from a reliable caregiver. A detailed history was obtained from a reliable caregiver with special focus on their abilities to retain new information, handle complex tasks, reasoning, language, behavior, spatial ability, orientation, attention and concentration, memory, visuo-spatial perception, praxis, calculation, executive function, mood and thought content followed by neuropsychological evaluation for the diagnosis of cognitive disorders according to the DSM-V criteria.

All other reversible/potentially treatable causes of cognitive impairment were ruled out with a structural neuroimaging study (CT/MRI), serum vitamin B1 and B12, thyroid functions, HIV serology, VDRL, chest roentgenogram, blood and urine toxicology and heavy metal screening, liver and renal function tests. All patients were further evaluated with a 18F-FDG-PET scan. Those patients who satisfied the International Consensus Criteria for behavioral variant frontotemporal dementia (bvFTD) (3) or the Gorno-Tempini classification for primary progressive aphasia (PPA) (4) (of either semantic or nonfluent agrammatic variants) were included.

We looked at 18F-FDG-PET scan images for various patterns of hypometabolism for diagnosis of neurocognitive disorders. 6 age and sex matched normal patients also underwent a FDG-PET scan. The equipment used for 18F-FDG-PET scan was Siemens Biograph Horizon TRUE-V 16 Slice PET CT scanner. The patients were asked to fast overnight. A dose of 5 MBq/kg of 18F-fluorodeoxyglucose (FDG) was administered peripherally via intravenous cannula. The patient was allowed to sit quietly for about 30-60 minutes in a shielded, dimly-lit room, with their eyes open to allow for uniform uptake and distribution of radio-tracer. Low dose CT scan was performed for attenuation correction followed by acquisition of PET data. PET images were reconstructed using a filter. Regional brain metabolism assessment using visual rating method was done. The areas of hypometabolism and asymmetry if any were recorded. FDG-PET imaging findings were rated by an experienced nuclear medicine specialist who was an independent assessor, who was blinded to the clinical diagnosis.

The summary for numerical data was presented with mean (standard deviation) and categorical data with percentages. The data was initially tabulated on MS Excel and the statistical analysis was performed with SPSS version 20 (IBM, USA).

RESULTS

35 patients with cognitive or behavioral symptoms or language deficits presented to us during the study period. After neuropsychological assessment followed by a FDG-PET scan, 15 were classified as FTD, 19 were diagnosed to have AD, 1 was diagnosed as DLB. Of the 15 FTD patients, 13, were diagnosed correctly after neuropsychological assessment. 2 patients thought initially to be frontal variant of AD (fvAD), because of amnesic symptoms preceding the onset of a dysexecutive/behavioral syndrome, were subsequently reclassified as bvFTD after FDG-PET scan. Of the 15 patients, 14 were diagnosed to be bvFTD, 1 was diagnosed as nfvPPA.

The mean age at presentation was 67.4 (8.6) years and mean age at symptom onset for patients with FTD was 65.6 (7.4) years, with a mean interval of 1.7 (0.7) years from the onset of symptoms to diagnosis. 8 of our 15 patients presented after the age of 65 years (53%) whereas 7 presented in the ‘presenile’ age group of 45 to 65 years. We had, 11 (73%) males and 4 (27%) females, with a male to female ratio of 2.75:1. The mean years of education, in our patients was 9.6 (5.6). The mean ages of onset of symptoms for those who had 10 or less years of education was 63.7 (4.2) years and for those with more than 10 years, was 70.6 (10.1) years.

The AD to FTD ratio was 1.3:1. The mean MMSE score was 18.8 (4.6). 3 of our 15 patients (20%) had a positive family history. All of our patients with bvFTD had a ‘frontal lobar’ syndrome with disinhibition being the most commonly observed symptom in 60% of our patients. Ritualistic and compulsive behavior and loss of empathy, each, were noted in 53%. Hyperorality and apathy were seen, less frequently, in 40%. Delusions and hallucinations were noted in 13%. 40% of our patients had amnesic symptoms (Figure 1). In 2 of them, amnesic symptoms occurred early, prompting a diagnosis of frontal variant of AD. One patient was mute at presentation with negligible comprehension, but with a history of a slow, effortful speech with grammatical errors, and was diagnosed both clinically and on FDG-PET to be nfvPPA.

MRI scans in our patients showed fronto-temporal atrophy in 4 (27%) with asymmetric atrophy in 3 (20%). FDG-PET in bvFTD patients showed frontal hypometabolism (including medial frontal, dorsolateral prefrontal regions, anterior cingulate gyrus) and in the anterior temporal lobe (Figure 2).

Hypometabolism was commonest in the anterior cingulate gyrus seen in 13 patients (87%), followed by anterior temporal lobe in 10 (67%) and other areas of the frontal lobe (medial/orbitofrontal/dorsolateral) in 9 (60%) (Figure 3).

All 15 patients had either anterior cingulate gyrus or anterior temporal lobe hypometabolism on FDG-PET scan. Asymmetric hypometabolism was noted in 10 out of 15 cases (67%), right predominant in 5 and left predominant in 5. In our patient of nfvPPA we noticed an asymmetric hypo-

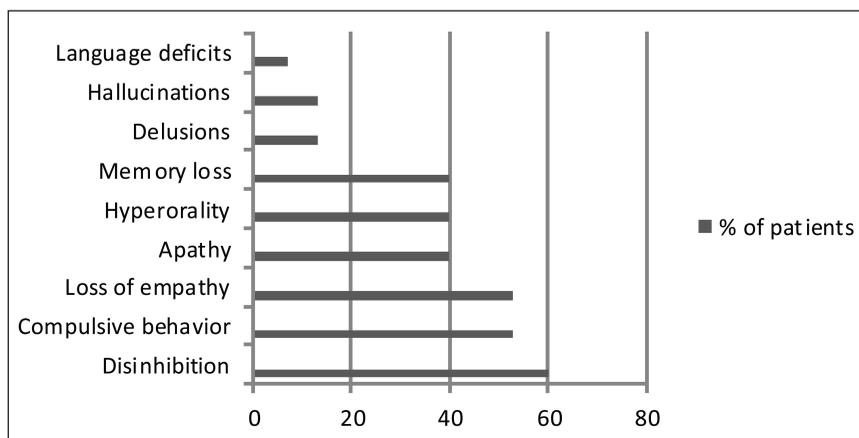


FIGURE 1. Percentage of patients with clinical symptoms consistent with FTD (bvFTD/nfvPPA)

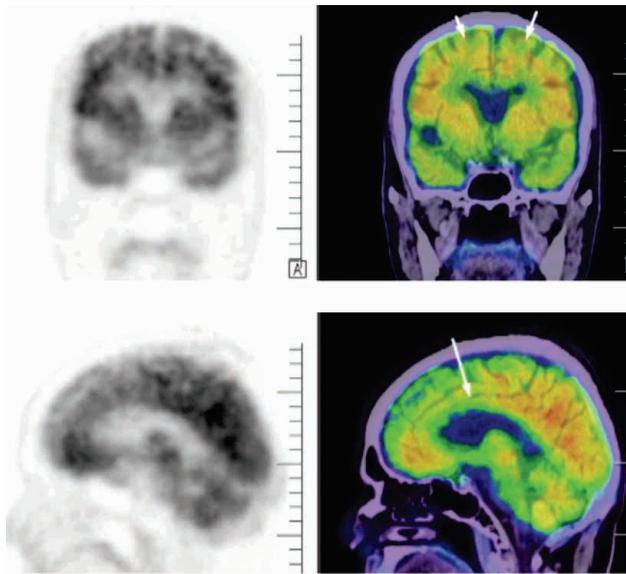


FIGURE 2. FDG-PET scan coronal and sagittal images showing hypometabolism noted in superior frontal gyri and anterior cingulate gyrus, suggestive of behavioral variant of frontotemporal dementia

metabolism of left inferior frontal lobe, anterior part of left superior temporal gyrus and left parietal cortex (Figure 4).

In 13 of the 15 patients (87%), the clinical diagnosis and FDG-PET findings correlated well. In 2 patients with initial clinical diagnosis of fvAD, PET scan showed an alternative diagnosis with a pattern of hypometabolism consistent with bvFTD. The clinical and FDG-PET findings are summarized in Table 1.

DISCUSSION

Our observation on 15 FTD patients revealed various clinical and FDG-PET imaging attributes some of which were at odds with a lot of the available international data on frontotemporal dementias.

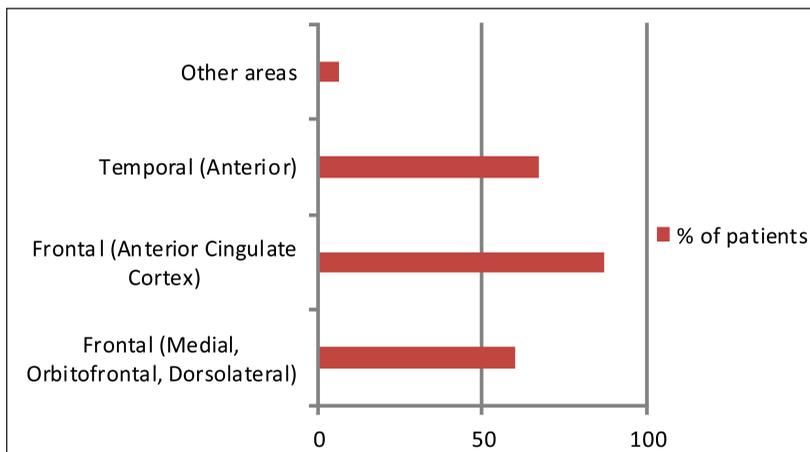


FIGURE 3. Percentage of patients with areas of hypometabolism on FDG-PET scan with FTD (bvFTD/nfvPPA)

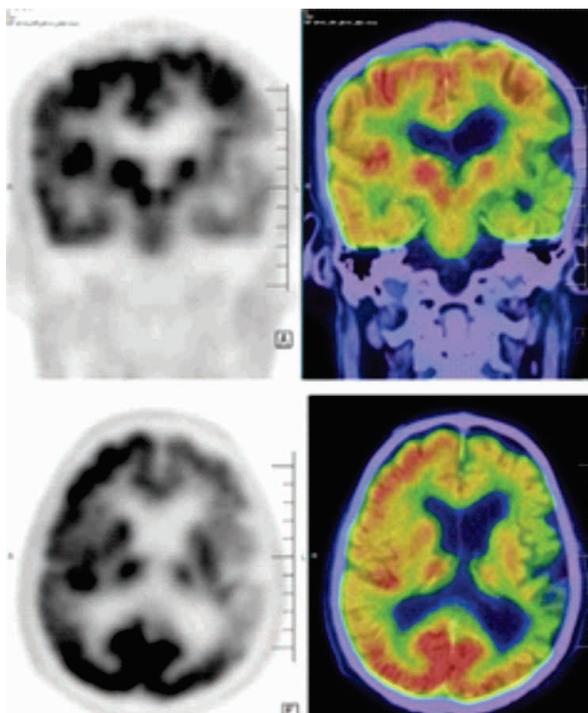


FIGURE 4. FDG-PET scan showing coronal and axial images showing metabolic deficits in left temporal and left frontoparietal lobes suggestive of primary progressive aphasia

TABLE 1. Clinical and FDG-PET profile of FTD patients

| Patient | Age (years) | MMSE | Education (years) | Dis-inhibition | Compulsive behavior | Loss of empathy | Apathy | Hyper-orality | Memory loss | FDG-PET hypometabolism | Asymmetry |
|---------|-------------|------|-------------------|----------------|---------------------|-----------------|--------|---------------|-------------|------------------------|-----------|
| 1 | 73 | 21 | 12 | + | - | - | + | + | + | AC,AT | + |
| 2 | 68 | 23 | 12 | + | - | + | - | + | + | F,AC,AT | + |
| 3 | 54 | 23 | 12 | - | + | + | - | + | + | F,AC,AT | + |
| 4 | 72 | 26 | 14 | - | - | + | + | - | - | AC | - |
| 5 | 72 | 15 | 15 | + | - | + | + | + | + | F,AC,AT | - |
| 6 | 60 | 16 | illiterate | + | + | - | - | - | - | AC | + |
| 7 | 74 | 21 | 15 | - | + | - | + | - | - | F, AC,AT | - |
| 8 | 61 | 26 | 15 | + | + | - | - | + | - | AC | - |
| 9 | 60 | 15 | 8 | - | - | + | + | - | - | F,AT | + |
| 10 | 64 | 18 | 10 | + | + | - | - | - | - | AC,AT | + |
| 11 | 64 | 12 | 5 | + | - | + | - | - | + | AC | + |
| 12 | 91 | 11 | 16 | + | + | - | - | - | + | F,AC | + |
| 13 | 71 | 15 | illiterate | - | + | + | + | - | - | F,AC,AT | + |
| 14 | 68 | 19 | illiterate | - | - | + | - | + | - | F,AT,P | - |
| 15 | 59 | 21 | 10 | + | + | - | - | - | - | F,AC,AT | + |

Legend: MMSE – mini mental status examination, F – frontal lobe areas (including medial, orbitofrontal, dorsolateral prefrontal), AC – anterior cingulate cortex of frontal lobe, AT – anterior temporal lobe, P – parietal

14 of the 15 FTD patients belonged to the behavioral variant of FTD (bvFTD) and 1 was assessed to be nonfluent agrammatic variant PPA (nfvPPA). Nieto et al. (6) in their study of 21 patients has found bvFTD in 76% of them. Other studies have also noted bvFTD to be the commonest among the FTD subtypes (7,8).

In our study, the mean age at presentation was 67.4 years and mean age at symptom onset was 65.6 years. 53% of our patients presented after 65 years of age. The mean ages of onset noted by various studies were in the ‘presenile’ age group ranging between 52 and 60 years (6-13). Unsurprisingly, several studies have echoed our findings as well, Johnson et al. (22) have recognized the existence of late onset FTD (above 65 years) in 25% of their patients. Strikingly however, data from the Swedish Dementia registry (Christer Nilsson et al.) (14) observed that mean age at diagnosis of FTD was 69.6 years and almost 70% of FTD patients (n = 245) were older than 65 years of age. Moreover, the maximum age related incidence was in the 80 to 84 years cohort. A Japanese population based study (Wada-Isoe et al.) (15) found 88% of their FTLD patients (n = 66), were above the age of 65 years while another Japanese study (Ishii et al.) (16) has reported a mean age of 67 years among their patients. These findings and those from our study suggest that increasing age might be just as important a risk factor in FTD as it is in AD and other degenerative dementias.

We noticed a mean interval of 1.7 years from the onset of symptoms to diagnosis. Most of our patients had a later onset of amnesic symptoms, but when the affective and behavioral symptoms, such as disinhibition and apathy became intolerable to family members, they sought a consultation, perhaps explaining why there was no overt delay in diagnosis compared to international studies. Also, a mean interval from onset to diagnosis of less than 2 years is one of lowest reported thus far, raising the possibility that most patients in our study had a more florid clinical presentation to begin with, which necessitated a visit to the hospital. Several Asian studies have also reported that most of their bvFTD patients had more florid manifestations at presentation (17-20). Interestingly, several Asian and European studies have reported a greater mean interval than our study suggesting that mild behavioral symptoms across cultures are often overlooked (6,7,13).

In our study of FTD patients, the mean years of education was 9.6. Those that had 10 or less years of education, tended to have an earlier age of onset (mean 63.7 years) as compared to those who had more than 10 years of education (mean 70.6 years). This was also observed in Diehl et al.’s study (8) (56 vs. 60 years), possibly indicating that the brain’s reserve capacity, improved by greater number of years in education, may have a disease onset modifying effect.

Our study noted an AD to FTD ratio of 1.3:1. The UK based prevalence study (Ratnavalli et al.) (7) reported a AD to FTD ratio of 1.6:1, the difference owing possibly to the fact that in their study FDG-PET was not used as a diagnostic tool. In fact taking FDG-PET scan findings into consideration for diagnosing dementing disorders, 2 patients earlier thought to be frontal variant AD, on neuropsychological examination, because of early amnesic symptoms were subsequently proven to be FTD. Without FDG-PET scan assisting in the diagnosis, the AD to FTD ratio in our study would have been 1.6:1.

Our study observed a male to female ratio of 2.75:1. Although FTD has been considered to have an equal sex incidence (11,12), several studies have in fact reported a male preponderance. Ratnavalli et al. (7) reported a male to female ratio of 4:1, while Diehl et al. (9) also noted a male predilection (62%). Conversely, a Dutch population-based study (Stevens et al.) (10) has reported a female preponderance (60%). Interestingly however, a small study (Heston et al.) (21), on 18 families of Pick's disease, another tauopathy, has reported a significantly higher risk for men.

A positive family history was observed in 20% of our patients, all of them having a first degree relative affected. While most Western studies report a higher incidence of similar symptoms in family members often in excess of 40% (7,10,11,23), most Asian studies report an incidence of less than 30% (13,15,18), and even in less than 5% in one (Wada-Isoe et al.) (15), suggesting that genetic factors may have a lesser role to play in Asian patients with FTD.

Our mean MMSE score was 18.8. Indian FTD studies on patients of Bengali ethnicity (Ghosh et al.) (13) and Southern Indian ethnicity (Chandra et al.) (31) have reported a mean MMSE of 17.1 and 18.1 respectively. Ren R-J et al. (18) (Han Chinese ethnicity), Shimomura et al. (24) and Shinagawa et al. (25) (Japanese ethnicity) have reported a mean MMSE score of 13.9, 18.7 and 16.1 respectively. Contrasting these findings are data from most Western European and North American literature (26-29), with a mean MMSE range of 20 to 25, unequivocally suggestive of a milder phenotype, in comparison to their Asian counterparts, at least at presentation.

Disinhibition was the most common early symptom seen in 60% of our patients, while apathy

which is often an early prominent feature, was less commonly seen in 40%. Even though most Western studies have reported a high frequency of apathy, ranging from 62 to 84% (3,8,28,30), and even certain Asian studies (Hokoishi et al.) (32), there are exceptions. A French Multicenter study (Le-Ber et al.) (29) has observed apathy in a mere 43% of their patients. Several Indian FTD studies (13,31,33) have reported a lower frequency of apathy (26 to 35%), with a higher frequency of disinhibition (in more than 50%) at presentation. Most international studies have reported a reasonably high frequency of disinhibition too, albeit less commonly than apathy (28-30). This observation could be a possible explanation as to why patients in our study have a low mean interval between onset to presentation, as disinhibited behavior such as use of derogatory language, micturating publicly, increased inappropriate bodily contact, noted in varying proportion in our study, have all compelled family members to seek medical advice early.

Compulsive, ritualistic and perseverative behavior was also noted frequently in our study (53%). Various Western studies have reported similar findings ranging from 40 to 64% in their studies (8,30,34). Indian studies contrastingly have noted a lesser frequency, ranging from 18 to 25% (31,33). Loss of empathy towards others was seen in 53%, similar to the findings of the Multicenter French trial (Le Ber et al.) (29), who reported it in 49%. Hyperorality (increased consumption of food, preference for sweet foods and increased smoking and alcohol consumption) was seen in 40% of patients, Ellajosyula et al. (46%) (35), Diehl et al. (30%) (8) have noticed a similar or lesser frequency in their studies, while several others, have all reported a higher frequency of hyperorality ranging from 55 to 79% (3,28,30,31,34). Hallucinations and delusions (13% each) were less frequently noted in our study, similar to certain studies (33,36).

Amnesic symptoms were noted in 40% of our patients. Andrew Graham et al. (37) suggested that some patients with otherwise typical FTD can be amnesic at presentation or present solely with amnesia. In 11% of 71 patients with FTD, memory loss was the predominant complaint, sufficient enough to receive a diagnosis of AD in most. In all patients, behavioral features suggestive of FTD, developed later. 2 of our own patients (13%) had

amnestic symptoms preceding the onset of behavioral symptoms, resulting in an erroneous diagnosis of frontal variant of AD. Other studies have reported memory complaints in varying proportions (28,30,31).

All of our patients underwent an 18F-FDG-PET scan. We assessed for evidence of hypometabolism in areas of the brain consistent with FTD. We noticed hypometabolism in the temporal lobe particularly the anterior temporal lobe (67%), in the frontal lobe including medial, orbitofrontal and dorsolateral prefrontal regions (60%), and most commonly at the anterior cingulate gyrus (87%).

Ishii et al. (16) reported similar patterns of hypometabolism in their FTD patients, predominantly in anterior regions (frontal lobes, including anterior cingulate cortex and anterior temporal cortex). In addition they have noted hypometabolism in hippocampi and subcortical structures. A Korean study by Jeong et al. (38), using voxel-wise analysis, noted widespread hypometabolism in not just the frontal (prefrontal, medial, orbitofrontal and cingulate gyri), and in the anterior temporal lobe, but also in the insula, subcortical basal ganglia structures, left inferior parietal lobule, right cerebellar tonsil, dorsomedial thalamus, hypothalamus and pulvinar. While our study did not show as extensive hypometabolism as these studies, the most common areas showing metabolic deficits remain the same. It is also well known that affliction of the insula would cause among many deficits, apathy, anergia, lethargy and reduced speech output. As our study failed to show a significant proportion of patients to be plagued by apathy, FDG-PET did not show significant involvement of the insula. However, most of our patients underwent neuropsychological assessment and PET scans fairly early in their course of illness, and if on follow-up visits if they had greater degree of apathy, a repeat PET scan may be useful to check for evidence of metabolic deficits in the insula.

Womack et al. (39) have shown that hypometabolism in the anterior cingulate and anterior temporal cortexes have higher specificities and higher likelihood ratios for a diagnosis of FTD than hypometabolism in the temporoparietal cortex has for AD. The three most commonly involved brain regions in their study mirror our findings. Moreover an interestingly similar finding noted between our studies is that while all 15 of our patients have hy-

pometabolism in either the anterior cingulate or anterior temporal cortices, 13 of the 14 patients in their study has either of the aforementioned two specific brain regions involved. Thus it can be safely postulated that more than the presence of frontal hypometabolism alone, hypometabolism in the anterior cingulate and anterior temporal regions is more specific for FTD.

Several studies have reported an extension of hypometabolism into the parietal regions mimicking features consistent with AD. Madhavi Tripathi et al. (40) reported in their study of FDG-PET in dementias, that FTD can have extension of metabolic deficits in the parietal lobe, in which case they may be erroneously construed to be AD. However our study did not note an extension of metabolic deficits in the posterior parts of the brain.

One of our patients, a male, in his seventh decade of life, was diagnosed to have PPA. When the patient presented to us, he was mute with negligible comprehension. His language difficulties, as iterated by his caregivers, began 3-4 years ago, when they noticed a slowing of his speech, it became more effortful over time. He was speaking in a stop-start manner and there were frequent grammatical errors, with poor sentence construction. Also, if they asked him to do something, he would frequently ask them to repeat and would make an attempt to grasp parts of that sentence, separately, and then try to do what was asked of him. Over the next few years, he became completely mute and was unable to comprehend most of what was said to him. He had no history of stroke or head trauma. With the said set of symptoms we diagnosed him to be suffering from nonfluent agrammatic variant of PPA (nfvPPA). Harciarek et al. (41) reported a mean age of presentation of 68.7 years in their cohort of 25 nfvPPA patients, similar to our patient who was 68 years old. Several studies have observed a halting, effortful character of speech in such patients and has suggested among others a significantly higher proportion of grammatical errors to be responsible leading to severely curtailed sentence length (42-44), both of which were observed in our patient. Also, there have been reports of an inability to carry out tasks that assess comprehension (Bak et al.) (45), as was also noted in our patient. Several case reports and studies have observed their nfvPPA patients progressing to mut-

ism (46,47). In our patient we noticed an asymmetric left predominant hypometabolism in the inferior frontal, anterior aspect of the superior temporal gyrus and parietal cortex. Nestor et al. (48) in their landmark study on patients with pure progressive non-fluent aphasia group (PNFA), with a more pervasive dementia, have noted hypometabolism in insular regions and in the posterior regions such as temporo-parietal areas. Our patient too, in an advanced and mute state, showed extension of metabolic deficits in the parietal region. Gorno-Tempini et al. (47) have compared affected brain areas between mute and non-mute nfvPPA patients and have noted that while the left inferior frontal gyrus (pars opercularis), insula and the left superior temporal gyrus was involved in both these cohorts, the damage was more extensive in the those patients who were mute with extension of the damage into the orbitofrontal region, basal ganglia and thalamus.

In our study asymmetric hypometabolic abnormalities were noted in 67% patients, with equal left and right sided asymmetry. Several studies using structural and functional neuroimaging have demonstrated asymmetric deficits in FTD (49-52). Sharma et al. (53) have noted asymmetric hypometabolism in 93% patients, with left and right sided asymmetry being fairly equal. Jeong et al. (38) have observed asymmetric hypometabolism in 90% of their 29 bvFTD patients, with left dominant metabolic deficits in 18 and right dominant metabolic deficits in 8. While in this particular study, those with right sided deficits predominantly had a varied presentation and those with left sided deficits had difficulties with naming, we however found no clinical significance in our bvFTD patients corresponding to which of the hemispheres was affected more. Our nfvPPA patient of course had a definite asymmetry in hypometabolism affecting the left side significantly more than the right.

13 of our 15 FTD patients had their clinical diagnosis corroborated by FDG-PET scan. 2 patients presented with amnesic symptoms first with frontal lobar symptoms thereafter and were diagnosed to have frontal variant AD. FDG-PET scans in these patients failed to reveal significant temporo-parietal metabolic deficits, with predominant involvement of the frontal and anterior temporal cortices and were subsequently reclassified as bvFTD. Jagust et al. (54) in their study on a cohort

of dementia patients (mostly AD) have noted a sensitivity and specificity of 76% and 58% respectively during initial clinical examination, which improved to 84% and 74% respectively on subsequent FDG-PET scan. Mendez et al. (55) have observed that in FTD the sensitivity of a functional neuroimaging study (PET/SPECT) superseded, that of the consensus clinical criteria and a structural neuroimaging study like MRI (90.5% vs. 36.5% vs. 63.5%). Keeping this fact in mind we have allowed our patients which appeared to be frontal variant of AD (fvAD) on clinical evaluation to be reclassified as bvFTD, following a FDG-PET scan evaluation.

CONCLUSIONS

There were significant variations in the neuropsychological and FDG-PET manifestations noted between our study and reported European and North American literature on frontotemporal dementia. We observed an older age of presentation and a shorter mean interval between onset of symptoms and presentation, because of more florid manifestations. Patients with lesser years of formal education had an earlier age of onset. We also reported a lower MMSE score with disinhibition, compulsive ritualistic behavior and loss of empathy to be more common compared to apathy, which was indeed the commonest manifestation noted in most Western literature. FDG-PET assessment showed metabolic deficits, most frequently in the anterior cingulate gyrus and anterior temporal lobe similar to most studies, without the extensive hypometabolism in other areas noted elsewhere. Asymmetric hypometabolism was a less prominent feature noted in our study. The clinical manifestations of agrammatism and poor sentence construction progressing to mutism with asymmetric left inferior frontal, superior temporal and parietal hypometabolism on FDG-PET in our nfvPPA patient was classical of findings reported in literature. In 13 of the 15 patients the neuropsychological and FDG-PET diagnosis concurred. 2 patients diagnosed as fvAD, on neuropsychological testing, because of early amnesic symptoms had their diagnosis revised to bvFTD after PET scan. We advocate the routine use of FDG-PET scan as an adjunct to neuropsychological testing in all patients with suspected degenerative dementias, as there are therapeutic implications in these patients.

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