# Original Article

# Neuropsychiatric Symptoms in a Cohort of Patients with Frontotemporal Dementia: Our Experience

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ABSTRACT

**Introduction:** About 20–50% of relatively young onset dementia belongs to frontotemporal type. Most of these patients are diagnosed as psychiatric illness as their memory and instrumental activities of daily living remain unaltered till late and most of these patients do not qualify for dementia by the Diagnostic and Statistical Manual of Mental Disorders-IV criteria. In this study, we analyzed the behavioral symptoms in our patients with radiologically and neuropsychologically proven as probable behavioral variant of frontotemporal dementia (FTD). **Patients and Methods:** Twenty patients qualifying the International Consensus Criteria were included and evaluated using National Institute of Mental Health and Neurosciences neuropsychological battery in addition to all mandatory dementia workup. **Results:** The mean age was 53.9 ± 9.9 years and the mean duration of illness was 2 ± 1.3 years. Sixty percent of them were <60 years. There were 9 males and 11 females. Most common heralding symptom noticed in 85% of the patients was irritability and aggression as against apathy in 100% in western studies. Memory impairment was found in only 11.1% as against 25% in western studies. Disinhibition, eating problems, stereotyped behavior, delusions, and paranoia were comparable between the study population and literature. **Discussion and Conclusion:** There are minor variations in the neuropsychological manifestations in our patients compared to western population. Agitation and aggression are more and memory impairment is very less making the diagnosis of FTD possible only if there is a high degree of suspicion. These symptoms are less amenable for pharmacotherapy and therefore, there is a need to explore the benefits of nonpharmacological treatment options such as yoga and meditation.

**Key words:** *Behavioral symptoms, behavioral variant frontotemporal dementia, neuropsychological features*

## INTRODUCTION

Approximately 20–50% patients with dementia in age group <65 years have frontotemporal dementia (FTD).[1] The early symptoms are almost always misdiagnosed as psychiatric illness.[2,3] There are three typical types described. They are the behavioral variant in which changes in personality and social behavior dominates

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due to the involvement of orbito basal frontal lobes. The semantic variant presents as fluent aphasia of progressive nature due to the involvement of the dominant lateral temporal regions causing breakdown in the conceptual database. The progressive nonfluent type characterized by phonological and syntactic errors due to the involvement of the dominant perisylvian regions.[4] Although the prevalence of this condition is less than AD, the caregiver burden is much more due to the lack of tact and social norms in these patients. The types of behavioral symptoms seen are as follows. Apathy is considered a feature in 95–100% of the patients.[5] They lack interest in activities of daily living as well as in emotional interactions resulting in stopping of all social interactions and neglect of personal hygiene. Disinhibition is seen in about 52% of the patients.[5] They lack socially acceptable patterns of behavior which vary from features such as shoplifting, exhibitionism, inappropriate touching of strangers, and extramarital affairs which are believed to be associated with hypoperfusion in orbitofrontal regions.[6] Agitation and aggression pose a great risk to the patient and the caregiver and are seen in about 45% of the patients.[7] Eating disturbances are seen as increased frequency, larger amount, and food faddism followed slowly by decreasing swallowing ability. Binge eating behavior is found to be linked to ventral insular cortex, striatum, and orbitofrontal cortex.[8] Other behavioral changes seen are repetitive behaviors, stimulus-bound behavior, verbal perseveration, hoarding, and ritualistic tendency. Delusions and paranoia are also seen.[9] Common recommended treatment options are nonpharmacological behavior interventions supported with fluoxetine, sertraline, paroxetine and trazodone, quetiapine, olanzapine, risperidone, etc. Drugs such as donepezil and rivastigmine increased disinhibition, compulsions, and muscle cramps. There are very few effective treatment options which significantly reduce caregiver burden in these patients. Therefore, research is needed to analyze the basis and formulate therapeutic options. Criteria for diagnosis of a behavioral variant of FTD are as follows [Table 1].

**Table 1: International consensus criteria for bvFTD**

| |
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| Neurodegenerative disease |
| Must be present for any FTD clinical syndrome |
| Shows progressive deterioration of behavior and/or cognition by observation or history |
| Possible bvFTD |
| Three of the features (A–F) must be present; symptoms should occur repeatedly, not just as a single instance |
| A. Early (3 years) behavioral disinhibition |
| B. Early (3 years) apathy or inertia |
| C. Early (3 years) loss of sympathy or empathy |
| D. Early (3 years) perseverative, stereotyped, or compulsive/ritualistic behavior |
| E. Hyperorality and dietary changes |
| F. Neuropsychological profile: Executive function deficits with relative sparing of memory and visuospatial functions |
| Probable bvFTD |
| All the following criteria must be present to meet diagnosis |
| A. Meets criteria for possible bvFTD |
| B. Significant functional decline |
| C. Imaging results consistent with bvFTD (frontal and/or anterior temporal atrophy on CT (or) MRI (or) frontal hypoperfusion (or) hypometabolism on SPECT or PET) |
| Definite bvFTD |
| Criteria A, either B or C must be present to meet diagnosis |
| A. Meets criteria for possible or probable bvFTD |
| B. Histopathological evidence of Frontotemporal lobar degeneration on biopsy at postmortem |
| C. Presence of a known pathogenic mutation |
| Exclusion criteria for bvFTD |
| Criteria A and B must both be answered negatively, criteria C can be positive for possible bvFTD but must be negative for probable bvFTD |
| A. Pattern of deficits is better accounted for by other nondegenerative nervous system (or) medical disorders |
| B. Behavioral disturbance is better accounted for by a psychiatric diagnosis |
| C. Biomarkers strongly indicative of Alzheimer's disease or other neurodegenerative process |
| Additional features |
| A. Presence of motor neuron findings suggestive of motor neuron disease |
| B. Motor symptoms and signs similar to corticobasal degeneration and progressive supranuclear palsy |
| C. Impaired word and object knowledge |
| D. Motor speech deficits |
| Substantial grammatical deficits |

FTD – Frontotemporal dementia; bvFTD – Behavioral variant FTD; MRI – Magnetic resonance imaging; SPECT – Single-photon emission computed tomography; PET – Positron emission tomography

## PATIENTS AND METHODS

Patients attending the neurology outpatient department of the authors' team from January 2015 to December 2015 were evaluated. The patients who qualified for the behavioral variant FTD as per International Consensus Criteria were included for the study. Informed consent was taken and was evaluated with National Institute of Mental Health and Neurosciences neuropsychological battery. All of them underwent all the recommended mandatory investigations including magnetic resonance imaging (MRI). Those who had features of mixed dementia,evidence of other neurological diseases and those who were unwilling were excluded. The results are as follows.

## RESULTS

Of the 20 patients having features of FTD as per the International Consensus Criteria for behavioral variant of FTD (bvFTD) were recruited, the mean age was 56.8 ± 10.35 years. The mean age of onset of illness was 53.97 ± 9.9 years and the mean duration from the onset was 2 ± 1.3 years. Twelve (60%) patients were <60 years of age. Eleven (55%) patients were females and 9 (45%) were males. Four patients are from Northeastern states, 4 patients from Kerala state, 8 patients from Karnataka state, 3 patients from Tamil Nadu, and 1 patient from Nepal. Twenty percent of the patients had completed their graduation and were employed. The mean hemoglobin levels, total count, and erythrocyte sedimentation rate values were 13.1 ± 1.59 g%, 8173.89 ± 2663.08 cell/mm$^3$, and 23.65 ± 13.1 mm/1$^{st}$ h, respectively. The mean Hindi Mental Status Examination (HMSE) scores were 18.06 ± 4.84 and the mean Vitamin B12 levels were 512.11 ± 3.84.

The most common heralding symptom noticed in the majority of our patients was behavioral problems in terms of irritability and episodes of anger in 85% of patients. Mental speed assessed by digit symbol substitution test was abnormal in 7 patients (35%). Sustained attention using digit forward and backward tests and category fluency using animal names were abnormal in 9 patients (45%). Attention and verbal working memory assessed using 1-backtest were abnormal in 10 patients (50%) and using 2-back test in 12 patients (60%). Response inhibition using Stroop test and verbal comprehension and learning using auditory verbal test were abnormal in 10 patients (50%). Sixty-seven percent of the patients had scores below the 15$^{th}$ percentile in working memory, response inhibition, and set shifting tested using Wisconsin card sorting test [Figures 1 and 2]. Neuropsychological tests revealed dysfunction in the following areas: 1. Dorsolateral

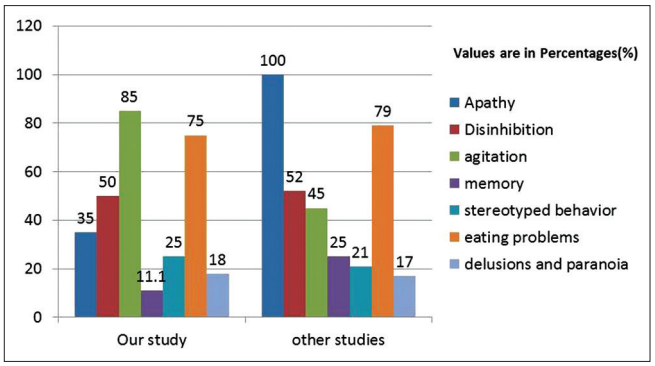


**Figure 1:** Comparison between our study and other study groups

prefrontal cortex(100%), 2. Medial orbitofrontal cortex(100%) and 3. Both temporal cortex( left temporal -75% and right temporal- 70%). Parietal and occipital lobe involvement was seen in only <25% of the patient population. When the patients with lower HMSE scores (<20) were compared with patients with higher HMSE scores (≥20), although not statistically significant, the trend showed that the first group had more of memory problems (11.1%) and the second group had more of behavioral issues (85.7%).

None of the patients had evidence of thyroid deficiency, Vitamin B12 deficiency, elevated homocysteine, or evidence of immunocompromised state or positive venereal disease research laboratory at the end of the screening. MRI showed right, frontal atrophy with mild diffuse atrophy in 14 patients out of the twenty and bifrontal atrophy in 6 patients [Figures 3 and 4]

## DISCUSSION

FTD affects relatively younger males than females. As memory impairment is relatively less (11.1% in our study and 25% in literature) and severe symptoms are seen early, these patients do not qualify for dementia as per Diagnostic and Statistical Manual of Mental Disorders-IV in the early stages.[10] This results in significant diagnostic delay resulting in problems in treatment and prognostication. The incidence of aggression and agitation is seen in 85.7% in our patients as against 45% in literature.[11] Apathy is seen in almost 100% of the patients in literature, but only 35% of our patients. Disinhibition shows similar distribution, 52% in literature and 50% in our patients. Stereotyped behavior is also seen in 25% each in literature and our study group. Eating problems, delusions, and paranoia are also distributed similarly. This study reveals that our patients have more aggression and agitation compared to other study populations [Figure 3].[1] Memory impairment is almost 50% less than found in other studies.[11] Other parameters are similarly affected. This interesting combination of neuropsychological

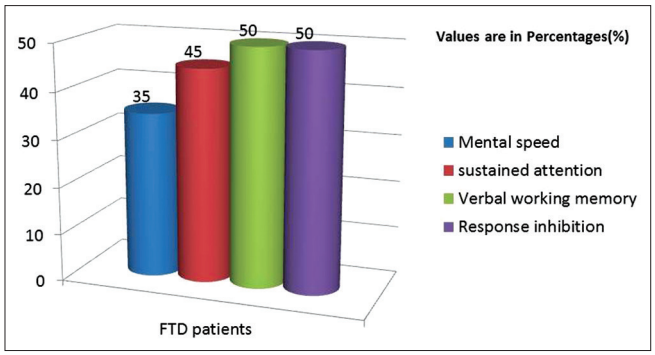


**Figure 2:** Additional Neuropsychological dysfunction in our study group

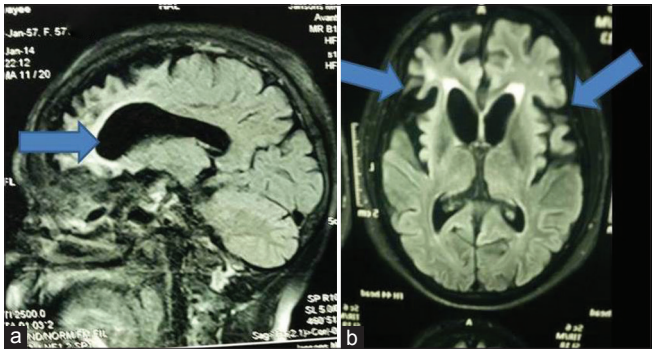


**Figure 3:** (a) Bulbous dilatation of the frontal lobe. (b) Asymmetrical right frontal atrophy

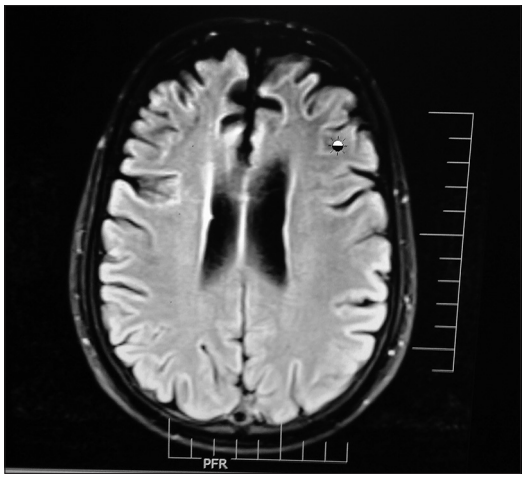


**Figure 4:** Computed tomography scan showing bifrontal atrophy left >right

symptoms in Indian patients makes it more difficult to distinguish organicity from purely late-onset psychosis in these patients. Therefore, it is probably mandatory that all late onset psychosis needs to be evaluated for behavioral variant of FTD in our country. Neither pharmacological nor nonpharmacological tools are effective in controlling most of these symptoms. However, caregiver education in this regard will improve knowledge of the caregivers and thus reduce stress on them. There is an urgent need to explore the role of alternative treatment options such as yoga and meditation in the treatment of these symptoms early in the course of this disease instead of using antipsychotic agents.

## CONCLUSION

There are minor variations in the neuropsychological manifestations in patients with bvFTD in our study population as compared to the western population. Aggression and agitation are more and memory impairment is very less making the diagnosis dilemma more complex in patients with late-onset psychosis. Therefore, it is mandatory to investigate all late onset psychosis for organicity which will help in diagnosis, prognosis, and caregiver education. There is an urgent need to try alternative treatment options such as yoga and meditation as a substitute for psychotropic agents in the early stages of these patients. This study needs to be repeated in a larger population in Indian setting.

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### Conflicts of interest
There are no conflicts of interest.

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