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# Neuropsychiatric Aspects in a Patient Diagnosed with Frontotemporal Dementia: Clinical Case of Low Incidence and Prevalence Disease in Colombia

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## Keywords

Attention · Executive functions · Frontal lobe · Frontal temporal · Frontotemporal dementia · Memory · Neurocognitive functioning · Case report

## Abstract

Frontotemporal dementia (FTD) is a neuropsychiatric pathology characterized by dysfunctions in the frontal lobe of the brain, especially in planning, execution, and inhibition tasks, with an inability to make decisions and handle different sequences, also affecting the temporal lobe. The patient presents alterations to store, consolidate, and recall information. These neurocognitive deficits are accompanied by neurobehavioral disorders such as depression, anxiety, and apathy that contribute to the worsening of the quality of life, with a high impact on the individual, social, and family level. To identify the neurobehavioral disorders and neurocognitive deterioration that present a patient diagnosed with FTD: clinical case of low incidence and prevalence disease in Colombia. A 40-year-old man, with progressive deterioration of his immediate verbal memory, low verbal fluency, aberrant motor behavior, sexual impulsivity, alterations in his executive functions, especially in planning tasks, decision-making, and inhibition was found to have a lesser degree of affectation in his visuospatial functioning and visuoconstructive abilities. It was found

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that the patient presents a severe dysexecutive syndrome associated with a clinical picture of FTD, correlated with an inability to process and recall information, accompanied by disorders such as depression, anxiety, and apathy. It is necessary to generate a functional neurorehabilitation plan that aims to improve the quality of life in these patients. In the same way, it is necessary to create new lines of research and intervention that have the purpose to create a greater field of heuristics or new questions in this type of neurodegenerative pathologies.



## Introduction

Frontotemporal dementia (FTD) is a pathology of low incidence and prevalence worldwide, the recent data that have been obtained point out that epidemiological results are totally changeable; for that reason, it isn't possible to have conceptual clarity in the incidence and prevalence. The FTD is characterized by symptoms that involve the frontal lobe (deficits in executive functions, planning, organization, self-regulation, decision-making, operational memory, and control of immediate behavior) [1], neuropsychiatric disorders (aberrant motor behavior, disinhibition disorder, visual, and auditory hallucinations), and the temporal lobe (inability to process, recall, and consolidate information) [2], this compendium of alterations is related to the dysfunctions that patients present in brain areas such as the dorsolateral cortex, generating a dysexecutive syndrome that is clinically associated with a deficit in the self-control of immediate behavior, affecting the family and social variables that the patient is unable to operate. Other areas that are affected are the superior, middle, and inferior orbitofrontal gyrus, associated with processes of sustained attention, learning, and compliance with the norm, respectively [1]. In relation to the temporal lobe, it has been found that patients with FTD present alterations in the hippocampus, parahippocampal gyrus, middle and superior temporal gyrus, deficits that are related to problems in the memory, auditory alterations, and learning reception [1, 3].

The data obtained from different research have found that patients with FTD present neurobehavioral disorders (Fig. 1) such as depression, anxiety, and apathy [4, 5], which have repercussions on the life quality. Likewise, these alterations are clinically related to the neurocognitive deficit presented by these patients, which is appropriate to design a functional neurorehabilitation treatment plan aimed at improving the neurocognitive deficits presented by patients diagnosed with this pathology.

Depression is one of the most frequent disorders presented by patients with FTD, which is related to frontal atrophy that subjects present, generating deficits in operative memory, immediate verbal memory and states of hopelessness, impulsiveness, and obsessive-compulsive thoughts that inhibit adequate decision-making in patients [4, 5].

Other studies [4, 5] have found that anxiety in patients with FTD has an impact on operative memory and decision-making, while apathy [5–7] has been found to be associated with this emotional disturbance as a predictor for FTD, since it largely affects the frontal lobe brain areas that comprise immediate behavior planning. Currently, scientific literature on FTD is usually scarce, since there are many variants of this pathology, and the consensus at the international level is not clear at present.

## Objective

The objective of this article was to describe the neuropsychiatric disorders presented by a patient diagnosed with FTD, a disease with low incidence and prevalence.

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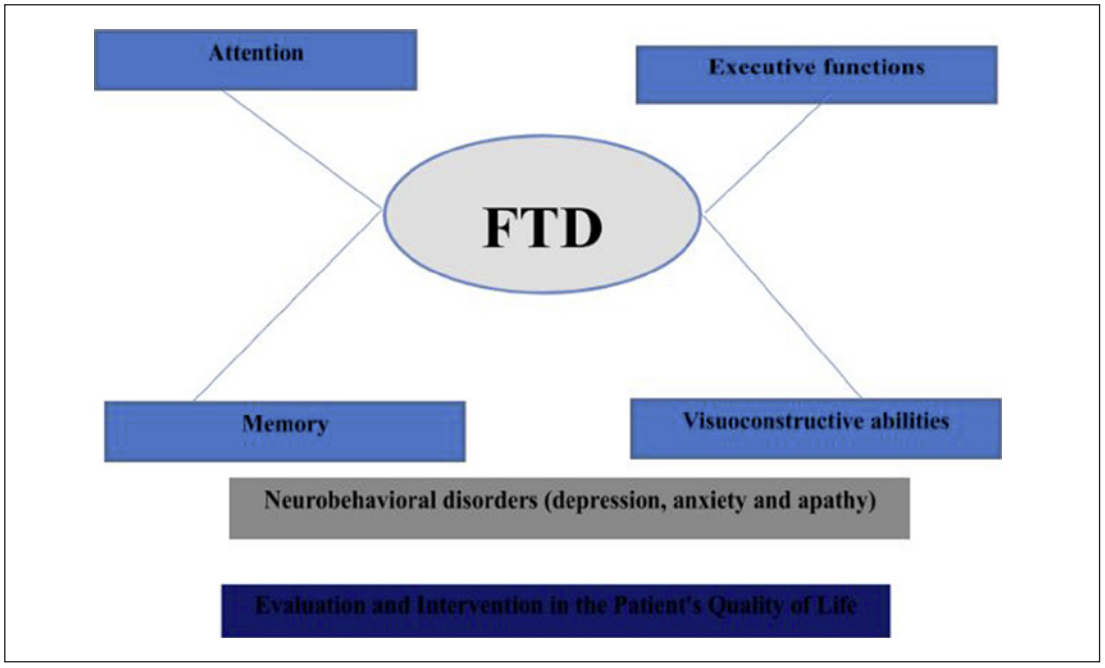


**Fig. 1.** Neurobehavioral disorders such as depression, anxiety, and apathy have an impact on the worsening of the quality of life in patients with FTD. Compromised neurocognitive functioning is also affected by the frontal and temporal lobe injuries that patients present. The DFT is clinically characterized because the patient presents alterations of executive character (frontal lobe) and significant deficiencies in the consolidation, storage, and recall of information (temporal lobe). FTD, frontotemporal dementia.

## Case Presentation

The method was transectional – descriptive. The case report was taken at a clear and specific time to attend the patient and had not been in a long time period.

*Participant*

A 40-year-old patient with progressive deterioration of his immediate verbal memory, low verbal fluency, aberrant motor behavior (delirium, hallucinations, and mood alterations), sexual impulsiveness, alterations in his executive functions, especially in planning, decision-making, and inhibition tasks, was found to have lesser grade impairment on his visuospatial functioning and visuoconstructive abilities. Initially, the patient was diagnosed with bipolar affective disorder. In the evaluation, no clinical correlation was found with this emotional affectation.

The patient presents difficulty in falling asleep, accompanied by low verbal fluency that is characterized by a severe mixed clinical picture of depression and generalized anxiety. It was also found an emotional picture of apathy that is characterized in the patient as a severe difficulty to perform a variety of tasks.

Physical Examination

The patient presents an aberrant motor behavior, excessive motor fluctuations (repetitive movements), and overweight, associated with alterations to his eating behavior possibly due to consumption of medication for his FTD diagnosis. The pharmacological treatment includes the following:

- Valcote® (500 mg per day)
- Sinogan® (100 mg per day)
- Topiramato (100 mg per day)

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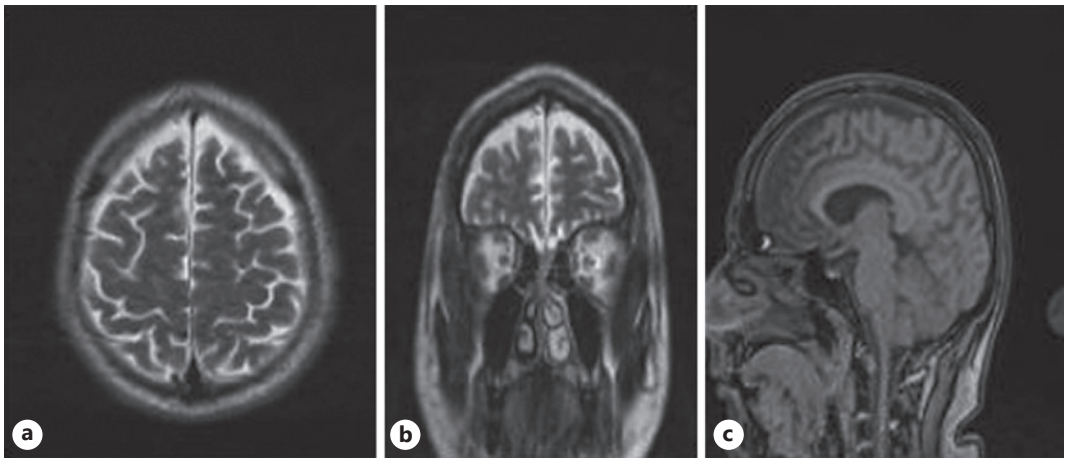


**Fig. 2.** FMRI of a patient diagnosed with FTD. **a** Superior view of the brain. Volumetric reduction and widening of cerebral sulcus due to cortical atrophy is observed. **b** Anterior coronal section. It is an identified widening of cerebral sulcus and affectation of superior frontal gyrus with commitment of operative memory in the patient, medium frontal gyrus with alterations in learning, and consolidation of the information, inferior frontal gyrus, alteration that is related to aberrant motor behavior, hypersexuality, hostility, and/or aggressiveness. **c** Middle sagittal section. It is identified with affectation of the marginal callosum fissure, subparietal sulci, dysfunction in frontal superior gyrus and frontal pole, generating dysexecutive syndrome and/or alteration to plan, take decisions, and control its immediate behavior. FTD, frontotemporal dementia.

- Seroquel® (900 mg per day)
- Sertralina (Zoloft) (100 mg per day)
- haloperidol (1,5 mg per day)
- Akatinol® (20 mg per day)
- Propranolol (80 mg per day)

Diagnosis of Neuroimaging Studies

We use the FMRI to study the evidence about the cortical/subcortical atrophy in the brain as shown in the figure (Fig. 2). We use the following 3 neuroimaging techniques for studying the FTD.

Neuropsychological evaluation:

- Mini-Mental State Examination (MMSE): is a short cognitive screening test, it evaluates cognitive functions, it is made up of 30 sections and grouped into 5 dimensions: orientation (10 points); fixation (3 points); orientation (5 points), calculation, and memory (3 points); language (8 points); and visuoconstructive abilities (1 point) [8].
- Montreal cognitive assessment scale: this is a specific type of neurocognitive test that measures executive functions, attention, immediate and deferred verbal memory, and visuospatial/visuoconstructive domains. It has 90% greater sensitivity and specificity than the MMSE [9].
- Wechsler digit range scale: this is a subtest of the WAIS that aims to measure levels of attention and immediate verbal memory in the subject [10].
- Yesavage geriatric depression scale: is a questionnaire that aims to assess depressive symptoms consisting of 30 items. The scores are 1–9, normal; 10–22 mild, depression, and 23–30, severe depression [11].
- Beck anxiety inventory [12]. This is a Likert-type scale whose objective is to evaluate the symptoms of anxiety consisting of items that are in turn divided into subjective and somatic symptoms. It has a score of 4 points for each question (absolute, mild, moderate, and severe). The sum of its items includes minimal, mild, moderate, and severe anxiety.

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- Trail making test: it is a paper and pencil test that aims to measure levels of attention (part A). The subject must join the numbers 1–25 consecutively, and the executive functions (part B), which consists of joining the numbers 1–25, but alternating with letters (1A-2B-3C-4D-5E successively). The subject should perform the test in the shortest possible time [13].
- Babcock story recall test: it aims to evaluate the verbal and deferred memory. The test is presented by auditory route [14].
- Dementia rating scale: the dementia rating scale is a scale that aims to assess general cognitive aspects, it is an instrument with a high validity for detecting clinical pictures of dementia. It has a total score of 144 points, grouped in 5 subsections: attention (37 points), initiation/perseveration (37 points), construction (6 points), conceptualization (39 points), and memory (25 points) [15].
- Blessed dementia scale: is a specific character scale that aims to evaluate the functionality of the patient with dementia [16].
- GDS geriatric dementia scale: scale that aims to assess neurocognitive functioning in patients [17].
- The apathy evaluation scale: scale that aims to evaluate the unmotivational syndrome. It is composed of 18 items that assess the deterioration of behavioral, affective, and cognitive aspects [18].
- Token test: it is a scale that aims to evaluate the language. In this case, the patients were enrolled with the objective of determining their verbal fluency and semantic knowledge in word recognition [19].
- Clock test: is a neurocognitive test that aims to evaluate the cognitive functioning in patients with neurological or neurodegenerative diseases. It is a highly sensitive test to detect dementia due to Alzheimer's or Parkinson's disease [20].
- Frontal assessment battery: this is a specific test that measures the executive (frontal lobe) functioning or low neurocognitive performance in older people or those diagnosed with a neurodegenerative disease [21].
- Neuropsychiatric inventory: it is a test that aims to evaluate the intensity and frequency of neuropsychiatric disorders. The test is divided into the following subsections: delusions, hallucinations, agitation/aggression, depression, anxiety, euphoria, apathy, disinhibition, irritability, aberrant motor behavior, sleep, and appetite. The frequency scoring system ranges from 0 to 4 and severity from 1 to 3, with a total score of 144 and 123 as the cutoff point for determining a neuropsychiatric profile [22].
- Verbal fluidity: this is a test that aims to evaluate the speed of the subject's information processing. You are asked to name animals and people in 1 min. It is also done in an alternate manner, the subject must name a word, alternating it with a category that the evaluator requires. Your score is obtained by the sum of each of the items.
- General health questionnaire-28: this is a questionnaire that evaluates self-perception of health. The test is grouped into 4 sections of 7 items (somatic symptoms, anxiety/insomnia, social dysfunction, and depression). A score ≥23 points is a possible indicator of a psychiatric condition [23].
- Barthel index: this is a questionnaire that aims to assess the level of functional independence that subjects present when carrying out basic activities of daily living [24].
- Lawton and Brody's scale: a questionnaire to assess the level of functional independence presented by subjects to carry out instrumental activities of daily living [25].

Procedure

The evaluation was carried out taking into account the following steps:

1. Knowledge interview with family members and the patient.

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**Table 1.** Neuropsychological assessment protocol for FTD

| Name of the assessment | Results |
|---|---|
| Dementia rating scale mattis | 6/144 |
| Blessed dementia scale | Positive for dementia |
| GDS geriatric dementia scale | Positive for dementia |
| Yesavage geriatric depression scale | 29/30 |
| Beck anxiety inventory | 62/64 |
| AES | Severe apathy |
| MMSE | 12/30 |
| Digit retention | |
| Direct order | 2/16 |
| Inverse order | 2/14 |
| TMT form A | He can't do it |
| TMT form B | He can't do it |
| Babcock story recall test | 2/21 |
| Babcock story test | 2/21 |
| FAB | 14/18 |
| MOCA | 4/30 |
| Token test | Positive |
| Denomination | 3 severe |
| Clock test order | 1/10 |
| Clock test copy | 0/10 |
| NPI | 4/144 |
| Barthel index | 20/100 |
| Lawton and Brody's scale | 2/8 |
| GHQ-28 | 58/84 |

FTD, frontotemporal dementia; MMSE, Mini-Mental State Examination; MOCA, Montreal cognitive assessment scale; AES, apathy evaluation scale; FAB, frontal assessment battery; NPI, neuropsychiatric inventory; GHQ, general health questionnaire.

2. Review of medical history and records.
3. Neuropsychological evaluation.
4. Neuropsychological report.
5. Functional plan for neurorehabilitation.

The neuropsychological assessment protocol for FTD (Table 1) has 17 different tests that give quantitative and qualitative information about the emotional picture, specific cognitive functioning, and the quality of life of the patient. In the quantitative results, it is important that all tests of the neuropsychological evaluation have a specific score cutoff.

Qualitative Results in the Patient with FTD

Emotional Picture

The values of the scales in depression and anxiety show that the patient presents a mixed clinical picture of depression and generalized anxiety that is directly affecting their quality of life.

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The scores of the scales show a pathological neurobehavioral clinical picture which is affecting his immediate behavior, especially his memory.

Brief Cognitive Tracking

MMSE: the results of the test indicate that the patient is not oriented in time, place, and space at the general level neurocognitive alterations are identified in each one of the subsections of the MMSE. The result in the MMSE demonstrates severe alterations in each one of the components, especially in tasks of inhibition, registry, and control.

## Specific Cognitive Functioning

*Attention*

In the specific tests of neurological and/or neurocognitive functioning, it was found that the patient presents a severe deficit in sustained attention. It was identified by the inability to retain new information, an alteration that is associated with the dysfunction that he presents in his operative memory, which does not allow him to condense and store information immediately. In case of the TMT form A test, the length of time the patient was in the test leads to the clinical inference that his alteration in sustained attention is a predictive factor for the progression to a greater alteration in his attentional processes, specifically related to the fronto-subcortical circuits, which may be generating alterations in motor functions and specific aspects of his behavior.

*Executive Functions*

In the tests that apply this section, it was found that the patient presents moderate alterations to plan, organize, direct, and control his immediate behavior, he is not able to manage several dimensions at the same time, slowly, but he manages to realize them. It was identified that neurobehavioral disorders such as depression and anxiety (especially depression) are clinically correlated with a low neurocognitive performance in tasks that handle different sequences such as TMT form B, and the time it took for the patient in this test leads to infer that there is an alteration of a focused type in his prefrontal cortex and dorsolateral cortex of his brain, brain structures that have as a main component the executive functions and the mastery of immediate behavior. The Montreal cognitive assessment scale test showed the alterations presented by the patient in recording tasks, information coding, and processing deficits in his operating memory.

The above data are confirmed by the frontal assessment battery test (the neurocognitive test of executive functions). The patient had a score below the cutoff point, which may be associated with a clinical picture of advanced dementia, since the results show that he has a clinical picture of dementia, and that the deterioration of their executive functions are a predictive factor to be related to a clinical diagnosis of FTD. For this reason, it is necessary to intervene in a timely manner with a treatment plan for functional neurorehabilitation that aims to slow down their disease and improve their quality of life.

In tasks of verbal fluency, the patient presents capacity in the evocation of information, no alteration is identified that is associated with a language problem. The data obtained by the tests that evaluate executive functioning indicate a deterioration at the cortical and subcortical level that has surely compromised the prefrontal and/or dorsolateral cortex, generating a dysexecutive syndrome that is associated with the loss of neurocognitive flexibility.

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*Memory*

In this section, it was identified that the patient in immediate verbal memory (Babcock's story) has a little capacity to consolidate, store, and recall information, that are clinically associated with a possible dysregulation in the cell wall of the hippocampus and related brain structures such as fimbria and alveus, the data obtained in these scales indicate that the patient may be going through a moderate-severe neurocognitive impairment.

*Visuospatial Functioning/Visuoconstructive Abilities*

In this neurocognitive domain, it was identified that the patient presents serious difficulties in processing information of a mental and/or spatial nature, cannot process or manipulate information in different contexts. The results of the tests in this domain (the clock test) show what we have inferred in the section of executive functions, the deterioration in his visuospatial functioning is related to the deficit he presents in executive functions, specifically in his frontal lobe, where it is necessary to intervene in a timely manner, since the tests used reveal that in the medium term, a worsening of his quality of life.

*Basic, Instrumental, and Advanced Activities of Daily Life*

The patient presents a moderate to severe degree of dependency to perform his daily activities. It is necessary to take into account that as he becomes more dependent, the probability of worsening of his clinical picture of dementia is even greater.

*General Health Questionnaire-28*

The results of this scale indicate that the patient presents a mixed clinical picture of depression and generalized anxiety and a neuropsychiatric profile accompanied by aberrant motor behavior, persecution delusions, and auditory and visual hallucinations.

*Differential Diagnostics*

The following differential diagnoses were made with the aim of preventing errors in the final diagnosis:

- Alzheimer's disease: although the patient presents deterioration at a cortical level, especially in tasks of immediate verbal memory, he does not meet clinical criteria to be diagnosed with Alzheimer's disease, besides, the patient neither present the age (older or equal to 65 years old) nor the history of this pathology at a family level.
- Dementia by Lewy bodies: although it is true that the patient presents a severe neurocognitive deterioration and clinically associated with visual and auditory hallucinations and aberrant motor behavior, the patient does not present age or exacerbated motor fluctuations to be diagnosed with this pathology.
- Frontotemporal dementia: the patient's clinical history is associated with alterations in personality, language, and behavior. The neurocognitive deterioration is centered in its executive functions as predictors for its dementia, later it presents/displays severe alterations in memory, signs, and symptoms that take it to present/display disinhibitory behaviors, accompanied by hostility, aggressiveness, and constant fluctuation in its state of spirit.

## Discussion/Conclusion

The patients who have FTD are characterized because they present an aberrant motor behavior associated with visual and auditory hallucinations, problems in sustained attention, operative memory, and especially, alterations in their executive functions, particularly in tasks of inhibition, conceptualization, and cognitive flexibility [26, 27]. Likewise, it was found

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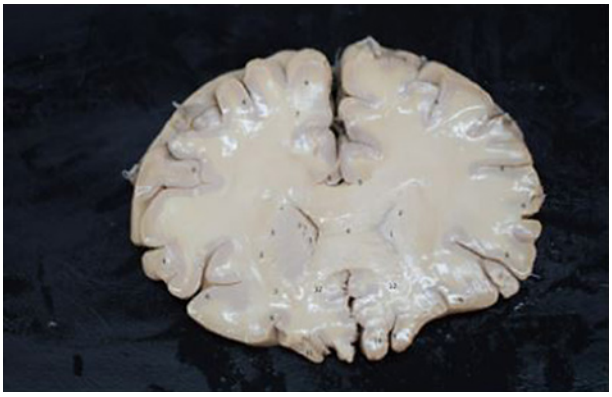

**Fig. 3.** Coronal prefrontal slice at the level of the face of the corpus callosum in a postmortem study of a normal brain. Areas usually involved in FTD are 1. anterior horns for lateral ventricles, 2. Caudate nucleus, 3. Internal capsule, 4. Face of the corpus callosum, 5. Cingulate gyrus or fascicle of the cingulum, 6. Cerebral cortex, 7. Superior frontal gyrus, 8. Olfactory groove, 9. Inferior frontal gyrus, 10. Straight gyrus, 11. Olfactory bulb. FTD, frontotemporal dementia.

that patients present severe alterations to store, consolidate, and recall information. In this case memory, data that are verified by different investigations where they demonstrate that structures surrounding the superior frontal gyrus, middle gyrus, and areas surrounding the hippocampus are altered [28, 29].

In relation to the disinhibitory behavior in the patient, which has relationship of alterations in neuroanatomical structures in the prefrontal cortex in the brain (Fig. 3), our results are compatible with the findings obtained in different investigations, where they argue the lack of social commitment, regulation of the norm, and loss of temporality and spatiality in different contexts where the subject develops [30–32].

Different researches [33–35] point out that neurobehavioral disorders such as depression and anxiety have a repercussion on the deficit of neurocognitive functioning, finding an association between the low performance in executive functions and depressive symptomatology. Likewise, it has been found that anxiety has a repercussion on the decline of operative memory; both entities (depression and anxiety) also have a negative impact on the worsening of the quality of life and self-perception of health. These data corroborate what we found in our clinical case report, the patients present affectation in these neurocognitive domains and in the dimensions that cover the quality of life, especially in areas such as emotional well-being, ADL, memory, and social support.

In relation to apathy, it has been found that this emotional alteration is a predictive factor in the diagnosis of FTD, since the neurological functioning correlate to this pathology (apathy) in the prefrontal cortex and the basal nuclei of the brain (Fig. 4) structures are responsible for defining interest or loss of interest in different activities performed by the patient [36–38].

Regarding the treatment of non-motor symptoms in FTD, we present this proposal, which aims to improve the quality of life of patients, especially in the initial stages of the disease:

1. All patients with an in situ diagnosis of FTD should be operated from the beginning of their neurobehavioral disorders (depression, anxiety, and apathy), with the aim of slowing down the relationship between these emotional disorders and the neurocognitive deficit in patients.
2. It is of great importance to intervene or present a non-pharmacological proposal in front of the decline of neurocognitive domains such as inhibition, planning, and conceptualization, with the purpose of improving decision-making in the patient, likewise, the processes of operative memory must be intervened with tasks that handle different sequences, this will allow the patient to have a greater focus of sustained attention and consolidation and evocation of information.
3. In relation to psychiatric behavior, it is necessary to generate processes of cognitive behavioral character, focused on the handling of irrational ideas, cognitive distortions, and reinforcement of desired behaviors.

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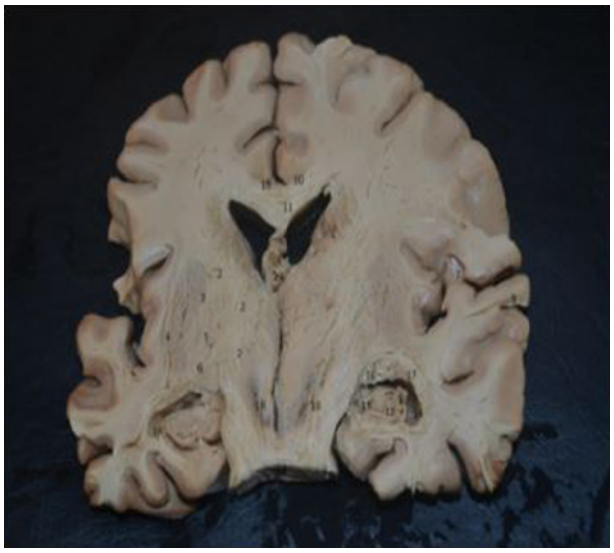

**Fig. 4.** Coronal slice at the level of the temporal lobe in a postmortem study of a normal brain. We saw some areas that are usually involved in FTD are noted, especially those that are related to the behavioral variant of FTD such as the caudate nucleus (1), putamen (3), cingulum bundle (10), hippocampus (12), amygdalin nucleus (16). FTD, frontotemporal dementia.

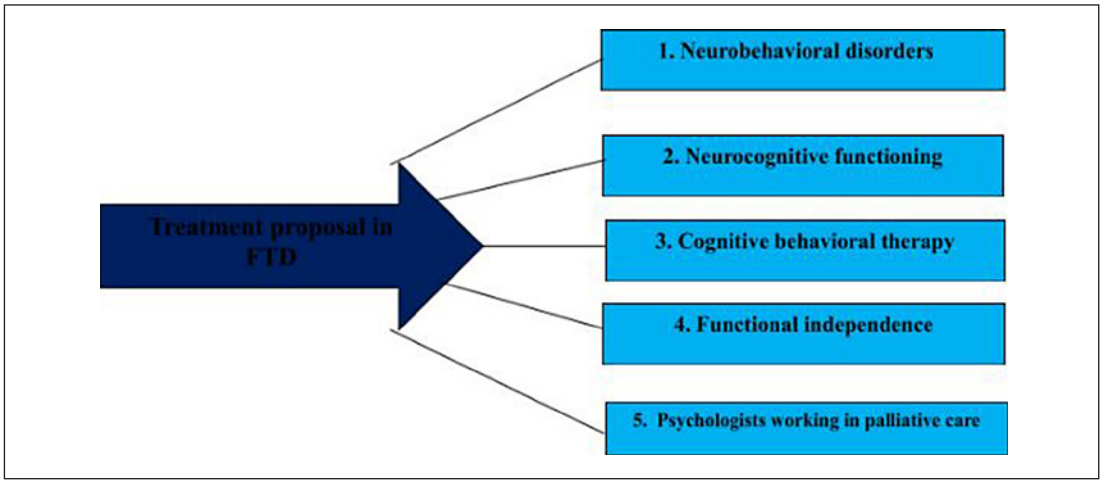


**Fig. 5.** Proposal of functional neurorehabilitation for FTD and the proposal of non-pharmacological treatment in patients with FTD. Initially, neurobehavioral disorders (1) such as depression, anxiety, and apathy should be intervened, seeking to prevent greater wear in the cell wall of the prefrontal cortex, and thus, slow down neurocognitive functioning (2), later a cognitive behavioral treatment focused on the handling of irrational ideas presented by the patients (3); the above will allow a moderate management in the activities of their daily life (4). In advanced stages of the disease, multidisciplinary work is expected to be applied based on the palliative care (5). All of the above has a single objective, to improve the quality of life of patients. FTD, frontotemporal dementia.

4. To generate activities of functionality or independence, it is clear that the ADLs are deteriorating over time, and are also a predictive factor for any type of dementia, which is sought and the patient has it for a time greater functional independence in different contexts.
5. For advanced stages of the disease, we suggest psychological treatment of a palliative nature, that is, generating in the patient a state of emotional rest that does not break into social or behavioral domains.

In this figure, you can see specifics about the proposal of functional neurorehabilitation for FTD (Fig. 5) with the aim to guide the proposal of non-pharmacological treatment in patients with FTD. Unfortunately, the deterioration in FTD is of a progressive nature, and it is hoped that this treatment proposal can be applied in the initial stages of the disease. Likewise, it is hoped to contribute to the creation of new lines of research in intervention with diagnosis of FTD.

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## Statement of Ethics

The patient and his or her companion, in agreement with the researchers, signed an informed consent form indicating the process to be carried out with the patient. They were guaranteed the protection of their personal data. The patient was told that the evaluation was a paper and pencil test and so he/she presented no physical risk. Also, the patient and their immediate caregivers consented to give his/her neuroimaging study for the publication of this case report. The study was carried out taking as the ethical principles for the development of research or experimentation on human beings as a reference, in this case, the Declaration of Helsinki, the Declaration of Bern, and resolution 008430 of 4 October 1993 of the Ministry of Social Protection of the Republic of Colombia for the ethical aspects of research on human beings.

The authors have no ethical conflicts to disclose. The authors state that the patient and their immediate caregiver gave their written approval to write and publish the article, including their clinical history, neuroimaging tests, and the results of the evaluation protocol.

## Conflict of Interest Statement

The authors declare that there are no conflicts of interest.

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## Author Contributions

Juliana Vergel Hernández: summarizing data, first patient contact, and patient examination. María Eugenia Barrera Robledo: summarizing data, first patient contact, and patient examination. Carlos Alberto Hurtado Gonzáles: supervision of the apply assessment, summarizing data, literature search, responsible for the review of the data, and drafted the manuscript for intellectual content. Carlos Steven Marmolejo Escobar: summarizing data, literature search, and patient examination. Sebastián Ospina Otalvaro: summarizing data, literature search, and drafting of the manuscript. Juan David Sánchez Tobón: summarizing data and literature search. Pablo Miguel Arango de la Pava: summarizing data and revising it critically for important intellectual content. Juan José Alvareze: summarizing data and literature search.

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