

FRONTOTEMPORAL DEMENTIA (FTD)

The term "Frontotemporal Dementia" or FTD refers to a group of diseases that are commonly misdiagnosed as Alzheimer's Disease (AD). We use the term FTD as a general term to refer to disorders that are also referred to as:

- Pick's Disease
- Frontotemporal Lobar Degeneration
- Progressive Aphasia
- Semantic Dementia

It is important to identify these patients early in their course and to refer them to physicians in neurology and psychiatry who are experienced with their management. This referral is primarily important because the clinical course of FTD patients is different than patients with AD. Patients with FTD have markedly different behavioral manifestations early in the course of disease and appear to have a longer clinical course overall. In addition, when behavioral symptoms predominate, FTD patients who become ill in mid-life may initially be confused with patients with atypical late life depression, or when the onset is in younger persons, it may be confused with Schizophrenia or Bipolar Disorder.

There have been remarkable advances in the understanding of the underlying pathophysiology and genetic mechanisms of FTD that allow counseling of patients and families in ways that were not possible in the past. In addition, research groups interested in FTD are exploring new therapeutic approaches.

Demographics

FTD occurs primarily between the ages of 35 and 75. The disease affects both sexes equally. About 40% of patients have a clear-cut family history.

Presenting Symptoms

Patients with FTD present with two patterns:

- Gradual and progressive changes in behavior....or
- Gradual and progressive language dysfunction.

Behavioral Presentation of FTD

The most common presentation is an early change in social and personal conduct, characterized by difficulty modulating behavior to the social demands of a situation. This is often associated with a **lack of inhibition**, resulting in impulsive or inappropriate

behavior, such as swearing at inappropriate times, outbursts of frustration, or lack of social tact.

As the disease progresses, this may lead to frank criminal behavior (e.g. shoplifting), poor financial judgment or impulsive buying. At the extreme, the impulsivity can be self-destructive, as when patients try to get out of a moving car. In some individuals, inappropriate sexual behavior occurs.

There may also be **repetitive or compulsive behaviors**. This may include a preoccupation with repeating specific acts (e.g., reading the same book over and over) or repeating specific physical actions (e.g., walking to the same location repeatedly).

Dietary habits and personal hygiene may also change. Overeating is common as well as food fads in which only certain foods are eaten. There is a loss of concern for one's personal appearance and patients may be increasingly unkempt early in the course of disease.

All this occurs in the setting of the patient showing **very little insight** into or personal concern for their actions. Even though there are complaints of memory disturbance, these patients do not have a true amnesic syndrome. They are able to keep track of day to day events and to be oriented.

Language Symptoms in FTD

Early and progressive change in language function is the alternate and less common presentation of FTD. This occurs in the setting of relative preservation of other cognitive domains, such as memory. The majority of such patients present with problems in the expression of language, marked by problems using the correct word, including naming objects or expressing oneself. Difficulties reading and writing then develop. Understanding of word meaning is, however, relatively well preserved in such individuals.

With progression of disease, less and less language is used, until the patient may be virtually mute. Less commonly, patients present with a severe problem with naming and with understanding word meaning. This becomes progressively worse, but patients continue to have otherwise normal speech output as the disease progresses.

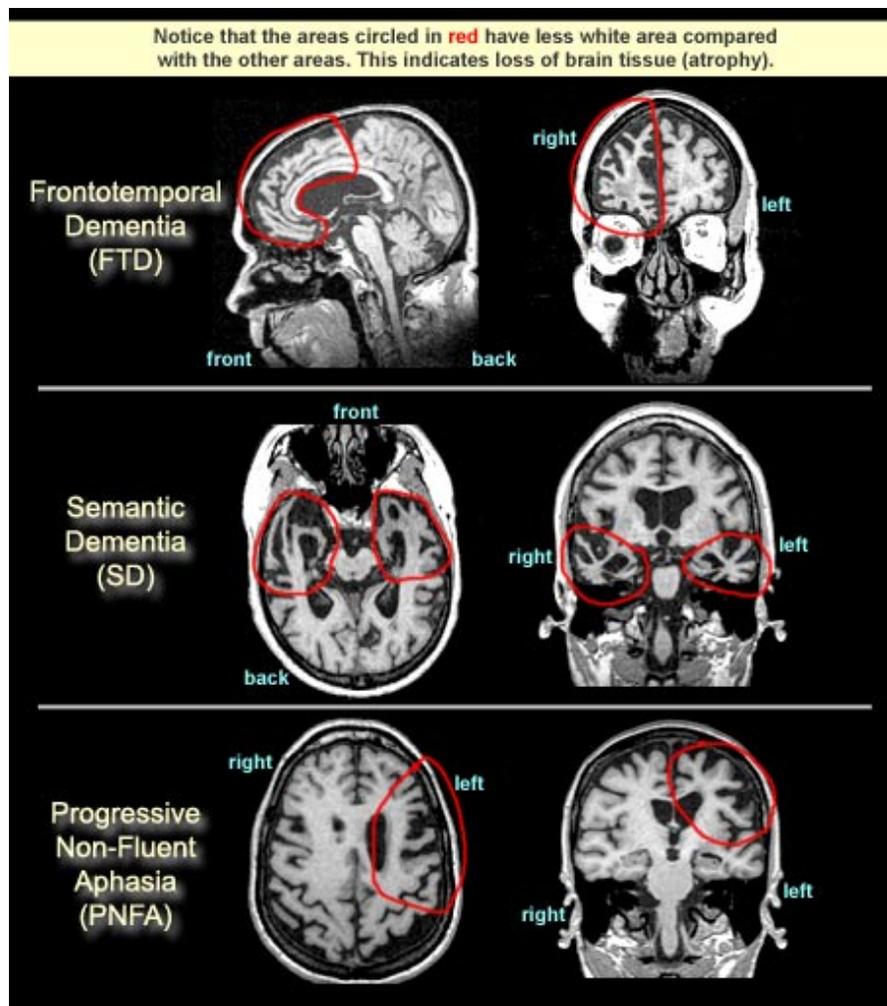
Physiology

One of the most useful tests in the evaluation of FTD is **magnetic resonance imaging (MRI)**. The MRIs below illustrate the areas of the brain affected in patients who have Frontotemporal Dementia, Semantic Dementia, and Progressive Non-Fluent Aphasia.

FTD leads to loss of brain tissue that is visible on MRI scans of patients while patients are still alive. Different areas of the brain are affected (early on) by different types of FTD:

- **FTD (frontal lobes):** responsible for personality, judgement, and planning/organization.
- **SD (anterior temporal lobes):** store general information about the world; very important for language and face recognition.
- **PNFA (left perisylvian cortex):** produces spoken language.

The diagram below shows most commonly affected brain regions (circled in red) in a representative patient with each type of disease.



Genetics of FTD

Approximately 40% of FTD is believed to have a genetic component while 60% occurs sporadically with no apparent hereditary link.

The majority of cases in which genes are involved follow an autosomal dominant inheritance pattern. Thus, 50% of the children of an affected individual are at risk for developing FTD. The presentation of the disease within families can be variable. Some people may have FTD alone while others may develop ALS (Lou Gehrig's disease), parkinsonism, or psychiatric symptoms. Because of this variability, a careful analysis of family medical and social history can help clarify whether an affected person has a sporadic or hereditary form of FTD. Even when a family exhibits autosomal dominant inheritance of FTD, the exact genetic cause may not be known.

One gene, tau on chromosome 17, accounts for up to 15% of hereditary FTD. Recently one FTD family has been linked to chromosome 9 and another to chromosome 3. Ultimately, other FTD genes will be found.

Ancillary Studies

Structural imaging studies, either with Computed Tomography (CT) or Magnetic Resonance Imaging (MRI), may show atrophy of anterior temporal and frontal lobes. Perfusion studies, by Single Photon Emission Computed Tomography (SPECT) or perfusion MRI, typically demonstrate decreased perfusion of frontal and temporal lobes. More widespread atrophy or perfusion deficits, for example involving parietal lobes, is more compatible with AD.

The electroencephalogram (EEG) is usually normal. Thus, a normal EEG does not mean that the behavioral manifestations are primarily the result of a psychiatric illness.

Comparison with Alzheimer's Disease (AD)

Unlike AD, which increases markedly with age, it is rare to have the onset of FTD after 75.

The early appearance of behavioral symptoms, so common in FTD, is distinctly unusual in AD. Unlike patients with FTD, patients with early AD tend to be socially appropriate. Despite their memory deficits, they preserve their social graces and are usually adept at covering up their memory difficulties. As AD progresses, patients may act inappropriately in financial and other situations requiring judgment. This is primarily related to their cognitive problems, rather than impulsiveness or lack of concern for social norms.

Apathy in AD patients is likely to occur in situations that are confusing and overwhelming to the patient, whereas apathy in FTD patients is more pervasive and more often reflects

a lack of concern for others, or is sometimes a generalized lack of initiative and passivity.

Unlike patients with FTD, AD patients have an early and profound difficulty learning and retaining new information. As the disease progresses, memory for new and old information is lost. In contrast, most mildly impaired FTD patients are oriented and able to keep track of recent events, but may be variable in performance on memory testing due to lack of concern or effort in the testing situation.

In FTD, language dysfunction occurs as an isolated cognitive deficit with or without associated behavioral disturbance. In contrast, when language dysfunction occurs in AD, it is almost always associated with some degree of memory abnormality.

In both FTD and AD, early in the course there is difficulty with cognitive flexibility and tasks that require set shifting. Thus, an assessment of these functions will not easily differentiate these patients.

When AD and FTD are in the advanced stages, they often appear very similar. What distinguishes them is the course they took to reach this advanced stage of brain dysfunction.

Caregivers

Being a caregiver of a person with dementia, regardless of whether it's Alzheimer's disease, FTD or another type, can be physically and emotionally exhausting.

However, Frontotemporal dementia can often be even harder on families because:

- The personality changes and behaviors are very distressing
- The diagnosis is often delayed
- There is not as much public awareness about the disease
- Patients affected with FTD are usually younger
- Language problems develop earlier

If you live in the San Francisco Bay Area, we hold a free monthly FTD Support Group for family members or caregivers.