FRONTOTEMPORAL DISORDERS

Information for Patients, Families, and Caregivers

LEARN ABOUT:

- Frontotemporal dementia
- Primary progressive aphasia
- Movement disorders

National Institute on Aging
National Institutes of Health

The National Institute on Aging (NIA), part of the National Institutes of Health, leads the Federal Government effort conducting and supporting research on Alzheimer's disease and other forms of dementia. NIA's Alzheimer's Disease Education and Referral (ADEAR) Center offers information and publications on dementia and caregiving for families, caregivers, and professionals. For more information, visit *www.nia.nih.gov/alzheimers* or call **1-800-438-4380**.

CONTENTS

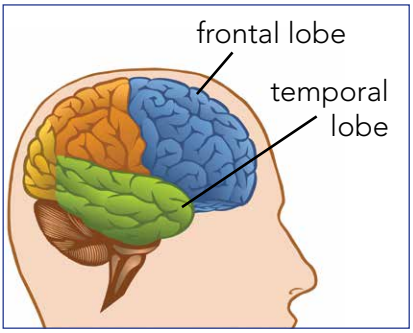
Introduction

Few people have heard of frontotemporal dementia and other brain disorders that affect personality, behavior, language, and movement. These disorders are little known outside the circles of researchers, doctors, patients, and caregivers who study and live with them. Although frontotemporal disorders remain puzzling in many ways, researchers are finding new clues that will help them solve this medical mystery and better understand other common dementias.

The symptoms of frontotemporal disorders are devastating. They gradually rob people of basic abilities—thinking, talking, walking, and socializing—that most of us take for granted. They often strike people in the prime of life, when they are working and raising families. Families suffer, too, as they struggle to cope with the person's daily needs as well as changes in relationships and finances.

This booklet is meant to help people with frontotemporal disorders, their families, and caregivers learn more about these conditions and resources for coping. It explains what is known about the different types of disorders and how they are diagnosed. Most importantly, it describes how to treat and manage these difficult conditions, with practical advice for caregivers. A list of resources begins on page 27.

The Basics of Frontotemporal Disorders



Frontotemporal disorders are the result of damage to neurons (nerve cells) in parts of the brain called the frontal and temporal lobes. As neurons die in the frontal and temporal regions, these lobes atrophy, or shrink. Gradually, this damage causes difficulties in thinking and behaviors controlled by these parts of the brain. Many possible symptoms can result, including strange behaviors, emotional problems, trouble communicating, or difficulty with walking and other basic movements.

A Form of Dementia

Frontotemporal disorders are a form of dementia caused by a family of brain diseases known as frontotemporal lobar degeneration (FTLD). Dementia is a severe loss of thinking abilities that interferes with a person's ability to perform daily activities such as working, driving, and preparing meals. Other brain diseases that can cause dementia include Alzheimer's disease and strokes. Scientists estimate that FTLD may cause up to 10 percent of all cases of dementia and may be about as common as Alzheimer's among people younger than age 65.

People can live with frontotemporal disorders for 2 to 10 years, sometimes longer, but it is difficult to predict the time course for an individual patient. The disorders are progressive, meaning symptoms get worse over time. In the early stages, people have one type of symptom. As the disease progresses, other types of symptoms appear as more parts of the brain are affected.

No cure or treatments for frontotemporal disorders are available today. However, research is improving awareness and understanding of these challenging conditions. This progress is opening doors to better diagnosis, improved care, and, eventually, possible new treatments.

FTD? FTLD? Understanding Terms

One of the challenges shared by patients, families, clinicians, and researchers is confusion about how to classify and label frontotemporal disorders. A diagnosis by one doctor may be called something else by a second, and the same condition or syndrome referred to by another name by a pathologist who examines the brain after death.

For many years, scientists and physicians used the term *frontotemporal dementia* (FTD) to describe this group of illnesses. After further research, FTD is now understood to be just one of several possible variations and is more precisely called *behavioral variant frontotemporal dementia*, or bvFTD.

This booklet uses the term *frontotemporal disorders* to refer to changes in behavior and thinking that are caused by underlying brain diseases collectively called *frontotemporal lobar degeneration* (FTLD). FTLD is not a single brain disease but rather a family of neurodegenerative diseases, any one of which can cause a frontotemporal disorder (see "Causes," page 11). Frontotemporal disorders are diagnosed by physicians and psychologists based on a person's symptoms. FTLD can be identified definitively only by brain autopsy after death.

Changes in the Brain

Frontotemporal disorders affect the frontal and temporal lobes of the brain. They can begin in the frontal lobe, the temporal lobe, or both. Initially, frontotemporal disorders leave other brain regions untouched, including those that control short-term memory.

The frontal lobes, situated above the eyes and behind the forehead both on the right and left sides of the brain, direct executive functioning. This includes planning and sequencing (thinking through which steps come first, second, third, and so on), prioritizing (doing more important activities first and less important activities last), multitasking (shifting from one activity to another as needed), and monitoring and correcting errors.

What's going on?

Brian, an attorney, began having trouble organizing his cases. In time, his law firm assigned him to do paperwork only. Brian's wife thought he was depressed because his father had died 2 years earlier. Brian, 56, was treated for depression, but his symptoms got worse. He became more disorganized and began making sexual comments to his wife's female friends. Even more unsettling, he neither understood nor cared that his behavior disturbed his family and friends. As time went on, Brian had trouble paying bills and was less affectionate toward his wife and young son. Three years after Brian's symptoms began, his counselor recommended a neurological evaluation. Brian was diagnosed with bvFTD.

When functioning well, the frontal lobes also help manage emotional responses. They enable people to control inappropriate social behaviors, such as shouting loudly in a library or at a funeral. They help people make decisions that make sense for a given situation. When the frontal lobes are damaged, people may focus on insignificant details and ignore important aspects of a situation or engage in purposeless activities. The frontal lobes are also involved in language, particularly linking words to form sentences, and in motor functions, such as moving the arms, legs, and mouth.

The temporal lobes, located below and to the side of each frontal lobe on the right and left sides of the brain, play a major role in language and emotions. They help people understand words, speak, read, write, and connect words with their meanings. They allow people to recognize objects, including faces, and to relate appropriate emotions to objects and events. When temporal lobes are dysfunctional, people may have difficulty recognizing emotions and responding appropriately to them.

Which lobe—and part of the lobe—is affected first determines which symptoms appear first. For example, if the disease starts in the part of the frontal lobe responsible for decision-making, then the first symptom might be trouble managing finances. If it begins in the part of the temporal lobe that connects emotions to objects, then the first symptom might be an inability to recognize potentially dangerous objects—a person might reach for a snake or plunge a hand into boiling water, for example.

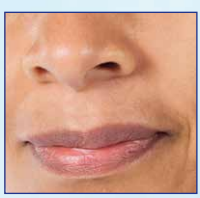
Types of Frontotemporal Disorders

Frontotemporal disorders can be grouped into three types, defined by the earliest symptoms physicians identify when they examine patients.

- **Progressive behavior/personality decline**—characterized by changes in personality, behavior, emotions, and judgment (e.g., behavioral variant frontotemporal dementia).
- **Progressive language decline**—marked by early changes in language ability, including speaking, understanding, reading, and writing (e.g., primary progressive aphasia).
- **Progressive motor decline**—characterized by various difficulties with physical movement, including shaking, difficulty walking, frequent falls, and poor coordination.

It can be hard to know which of these disorders a person has because symptoms and the order in which they appear can vary widely from one person to the next. Also, the same symptoms can appear in different disorders. For example, language problems are most typical of primary progressive aphasia but can also appear in the course of behavioral variant frontotemporal dementia. The table on page 6 summarizes the three types of frontotemporal disorders and lists the various terms that could be used when clinicians diagnose these disorders.

Trouble with words



Alicia's first symptom was trouble talking. She spoke more slowly and thought she sounded stilted. She could understand people well enough, but finding the right words when she was talking became harder and harder. Also, Alicia, 49, could not write words like "and" and "it" but could write words like "alligator." Her doctor recommended a neurological exam, which helped diagnose agrammatic PPA.

Types of Frontotemporal Disorders	
Diagnostic Terms	Main Early Symptoms
Progressive Behavior/Personality Decline	
• Behavioral variant frontotemporal dementia (bvFTD) • Temporal/frontal variant FTD (tvFTD, fvFTD) • Pick's disease	• Apathy, reduced initiative • Inappropriate and impulsive behaviors • Emotional flatness or excessive emotions • Memory generally intact
Progressive Language Decline	
• Primary progressive aphasia (PPA) • Progressive nonfluent aphasia • Semantic dementia	• Semantic PPA (also called semantic dementia): can't understand words or recognize familiar people and objects • Agrammatic PPA (also called progressive nonfluent aphasia): omits words that link nouns and verbs (such as to, from, the); difficulty swallowing • Logopenic PPA: trouble finding the right words while speaking, hesitation, and/or pauses in speech
Progressive Motor Decline	
• Corticobasal syndrome (CBS)	• Muscle rigidity • Difficulty closing buttons, operating simple appliances • Language or spatial orientation problems
• Progressive supranuclear palsy (PSP)	• Progressive problems with balance and walking • Slow movement, falling, body stiffness • Restricted eye movements
• FTD with parkinsonism	• Movement problems similar to Parkinson's disease, such as slowed movement and stiffness • Changes in behavior or language
• FTD with amyotrophic lateral sclerosis (FTD-ALS)	• Combination of FTD and ALS (Lou Gehrig's disease) • Changes in behavior and/or language • Muscle weakness, shrinkage, jerking

Behavioral Variant Frontotemporal Dementia

The most common frontotemporal disorder, *behavioral variant frontotemporal dementia* (bvFTD), involves changes in personality, behavior, and judgment. People with this dementia can act strangely around other people, resulting in embarrassing social situations. Often, they don't know or care that their behavior is unusual and don't show any consideration for the feelings of others. Over time, language and/or movement problems may occur, and the person needs more care and supervision.

In the past, bvFTD was called Pick's disease, named after Arnold Pick, the German scientist who first described it in 1892. The term Pick's disease is now used to describe abnormal collections in the brain of the protein tau, called "Pick bodies," which can only be seen under the microscope after death. Some patients with bvFTD have Pick's disease, and some do not.

Primary Progressive Aphasia

Primary progressive aphasia (PPA) involves changes in the ability to communicate—to use language to speak, read, write, and understand what others are saying. Problems with memory, reasoning, and judgment are not apparent at first but can develop over time. In addition, some people with

"What do you mean by salt?"

Jane, 62, a university professor, began having trouble remembering the names of common objects while she lectured. She also had a hard time following conversations, especially when more than one person was involved. Her family and co-workers were unaware of Jane's difficulties—until she had a hard time recognizing longtime colleagues. One night at the dinner table, when Jane's husband asked her to pass the salt, she said, "Salt? What do you mean by salt?" He took her to a neurologist, who diagnosed semantic PPA. As her illness progressed, Jane developed behavioral symptoms and had to retire early.

PPA may experience significant behavioral changes, similar to those seen in bvFTD, as the disease progresses. As symptoms get worse, people with PPA cannot live alone safely.

Currently, there are three types of PPA, categorized by the kind of language problems seen at first. Researchers do not fully understand the different types of PPA. But they hope one day to link specific language problems with the abnormalities in the brain that cause them.

In *semantic PPA*, also called semantic dementia, a person slowly loses the ability to understand single words and sometimes to recognize the faces of familiar people and common objects.

In *agrammatic PPA*, also called progressive nonfluent aphasia, a person has trouble saying words that link nouns and verbs together—for example, "of," "from," and "for." Eventually, the person may no longer be able to speak at all. He or she may also have difficulty swallowing and develop movement symptoms similar to those seen in corticobasal syndrome.

In *logopenic PPA*, a person has trouble finding the right words during conversation but can understand words and sentences. The person does not have problems with grammar.

Movement Disorders

Two rare neurological disorders associated with FTLD, *corticobasal syndrome* (CBS) and *progressive supranuclear palsy* (PSP), occur when the nerves attached to muscles malfunction and cause problems with movement. The disorders may affect thinking and language abilities, too.

CBS is caused by corticobasal degeneration—gradual atrophy and loss of nerve cells in specific parts of the brain. This degeneration causes progressive loss of movement and muscle rigidity, typically beginning around age 60. Symptoms may appear first on one side of the body, but eventually both sides are affected. Occasionally, a person with CBS first has language problems or trouble orienting objects in space and later develops movement symptoms.

PSP causes serious problems with balance and walking. People with the disorder typically move slowly, fall, and have body stiffness, especially in the neck and upper body—symptoms similar to those of Parkinson's disease. A hallmark sign of PSP is trouble with eye movements, such as involuntary closing of the eyelids, difficulty opening and closing the eyes, trouble looking way up and way down, and limited blinking. These symptoms may give the face a fixed stare. Behavior problems can also develop.

Other movement-related frontotemporal disorders include *frontotemporal dementia with parkinsonism* and *frontotemporal dementia with amyotrophic lateral sclerosis* (FTD-ALS).

Confusing symptoms

Carol had a tingling sensation and numbness in her upper right arm. Then her arm became stiff. She had to change from cursive handwriting to printing. Carol, 61, told her doctor that she had trouble getting her thoughts out and described her speech as "stumbling." She had increasing trouble talking but could still understand others. Eventually, she was diagnosed with CBS.

Trouble with walking

For a year and a half, John had trouble walking and fell several times. He also had trouble concentrating. He couldn't read because the words merged together on the page. John, 73, also seemed less interested in social activities and projects around the house. His wife noticed that he was more irritable than usual and sometimes said uncharacteristically inappropriate things. John's primary care doctor did several tests, then referred him to a neurologist, who diagnosed PSP.

Frontotemporal dementia with parkinsonism is an inherited disease caused by a genetic mutation. Symptoms include movement problems similar to those of Parkinson's disease, such as slowed movement, stiffness, and balance problems, and changes in behavior or language.

FTD-ALS is a combination of bvFTD and ALS, commonly called Lou Gehrig's disease. Symptoms include the behavioral and/or language changes seen in bvFTD as well as the muscle weakness, shrinking, and jerking seen in ALS. Symptoms of either disease may appear first, with other symptoms developing over time. Mutations in certain genes have been found in some patients with FTD-ALS.

Causes

Frontotemporal lobar degeneration (FTLD) is not a single brain disease but rather a family of brain diseases that share some common molecular features. Scientists are just beginning to understand the biological and genetic basis for the changes observed in brain cells that lead to FTLD.

Scientists describe FTLD in terms of physical changes in the brain seen in an autopsy after death. These changes include loss of neurons and abnormal amounts or forms of proteins called tau and TDP-43. These proteins occur naturally in the body and help cells function properly. When the proteins don't work properly, for reasons not yet fully understood, neurons in the frontal and/or temporal lobes are damaged and disease results.

About 20 to 40 percent of people with frontotemporal disorders have a family history of them. About 10 percent of people inherit them directly from a parent. In most cases, the cause is unknown.

Familial and inherited forms of frontotemporal disorders are often related to mutations (permanent changes) in certain genes. Genes are basic units of heredity that tell cells how to make the proteins the body needs to function. Even small changes in a gene may produce an abnormal protein, which can lead to changes in the brain and, eventually, disease.

Scientists have discovered several different genes that, when mutated, can lead to frontotemporal disorders:

- **Tau gene (also called the MAPT gene)**—A mutation in this gene causes abnormal tau to form, which leads to the destruction of brain cells. Inheriting a mutation in this gene means a person will almost surely develop a frontotemporal disorder, usually bvFTD, but the exact age of onset and symptoms cannot be predicted.

- **PGRN gene**—A mutation in this gene can lead to lower production of the protein progranulin, which in turn causes TDP-43, a cellular protein, to go awry. The result is familial bvFTD and possibly a higher chance of developing PPA.
- **VCP gene and CHMP2B gene**—Mutations in these genes lead to very rare familial types of frontotemporal disorders.
- **C9ORF72 gene**—An unusual mutation in this gene appears to be the most common genetic abnormality in familial frontotemporal disorders. It is also the most common genetic abnormality in familial ALS and occurs in some cases of sporadic ALS.

Scientists are continuing to search for other genes and proteins that may play a role in frontotemporal disorders. For example, some researchers are exploring the FUS gene, which causes a type of familial ALS. Scientists are also trying to understand how mutations in a single gene lead to different frontotemporal disorders in different family members.

Diagnosis

No single test, such as a blood test, can be used to diagnose a frontotemporal disorder. A definitive diagnosis can be confirmed only by a brain autopsy after a person dies. To diagnose a probable frontotemporal disorder in a living person, a doctor—usually a neurologist, psychiatrist, or psychologist—will:

- record a person's symptoms, often with the help of family members or friends
- compile a personal and family medical history
- perform a physical exam and order blood tests to help rule out other similar conditions
- conduct a neuropsychological evaluation to assess behavior, language, memory, and other cognitive functions
- use brain imaging to look for changes in the frontal and temporal lobes.

Different types of brain imaging may be used. A magnetic resonance imaging (MRI) scan shows changes in the size and shape of the brain, including the frontal and temporal lobes. It may reveal other causes of the person's symptoms, such as a stroke or tumor. In the early stage of disease, the MRI result may appear normal. In this case, other types of imaging, such as positron emission tomography (PET) or single photon emission computed tomography (SPECT), may be

Is it depression?

Ana's husband was the first to notice a change in his 55-year-old wife's personality. Normally active in her community, she became less interested in her volunteer activities. She wanted to stay home, did not initiate conversations, and went on her daily walks only if her husband suggested it. Ana's family thought she might be depressed. A psychologist referred her to a neurologist, who diagnosed bvFTD.