FTD-ALS Fact Sheet

Updated 11/27/2024

In 2011, researchers identified a variant in the *C9orf72* gene as the most common cause of both genetic FTD and genetic amyotrophic lateral sclerosis (ALS). Previously, ALS was thought to be purely a movement disorder, while FTD was considered purely a cognitive or behavioral form of dementia. Today, we know that FTD and ALS exist along a spectrum of neurodegenerative diseases.

FTD is a group of disorders characterized by the degeneration, or loss of nerve cells, of the brain's frontal and temporal lobes. As nerve cells in the brain die, one's behavior, personality, and capacity for producing and understanding language may change significantly, fundamentally altering how they interact with others and handle daily tasks. ALS, meanwhile, is marked by the deterioration and loss of motor neurons in the brain and spinal cord. The brain loses its ability to initiate and control muscle movement, leading to muscle weakness, atrophy (loss of muscle mass), and eventually paralysis.

FTD and ALS can occur in the same person, a clinical subtype known as FTD-ALS. Describing this unique clinical syndrome has been an area of active research, and our knowledge of its underlying genetics, pathology, and clinical features is increasing.

FTD-ALS Symptoms

In persons with FTD-ALS, symptoms of one of the FTD disorders (usually behavioral variant FTD) are often first to appear, and can include changes in behavior, personality, and language. Motor symptoms that are more typically associated with ALS – including difficulty walking, swallowing, and/or using one's hands – develop later. The former symptoms are caused by the degeneration of the brain's frontal and temporal lobes, while the latter are a result of the deterioration of the nerves in the spinal cord that communicate with muscles in the rest of the body.

Motor symptoms may include muscle weakness: a progressive inability to move the arms, legs, face, tongue, and/or neck. Muscle weakness often begins on just one side of the body, and ultimately leads to paralysis.

Other **motor symptoms** associated with FTD-ALS are:

- Weakness in legs leading to frequent trips, stumbles, and falls
- Difficulty lifting arms above the head
- Clumsiness with hands or fingers that cause difficulties with fine motor skills (tying shoes, grasping a cup or pen, etc.)
- Changes in walking speed or stride
- Drooling, difficulty swallowing, or slurred speech
- Difficulty breathing, including choking, gagging, and coughing
- Impaired swallowing

Language difficulties may also be present, such as:

- Trouble recalling the names of objects or finding the right word
- Difficulty recalling the meanings of words
- Omitting words or making consistent word usage errors
- Struggling to understand long sentences

FTD-ALS can cause **behavioral changes**, such as:

- Making uncharacteristically rude or offensive comments
- Being inappropriate with strangers (e.g. touching them without permission)
- Acting impulsively or recklessly (e.g. shoplifting, excessive spending, etc.)
- Uncharacteristic aggression or frustration
- Having a lack of insight into their own diagnosis
- Loss of interest in work or hobbies
- Indifference toward long-established relationships with family or friends
- Neglect of personal hygiene
- Loss of initiative
- Difficulty planning daily activities
- Uncharacteristic mistakes at work
- Challenges with managing finances
- Trouble with problem-solving

FTD-ALS

Treatment, Management, and What to Expect

Interventions should be tailored to the individual, and should consider both cognitive and functional needs. FTD-ALS requires comprehensive and coordinated care to adequately address its complexity. Managing FTD-ALS involves a combination of medical treatment, supportive therapies, and emotional support for both the person living with the diagnosis and their family.

There is no cure for FTD or FTD-ALS. Notably, in 2023 the U.S. Food and Drug Administration approved tofersen as a treatment for ALS caused by a variant in the SOD1 gene. Although tofersen does not treat FTD or FTD-ALS, its success offers promise that a treatment for those conditions is possible.

Riluzole, the first drug approved for use in the treatment of ALS, has been shown to slow the progression of ALS and increase survival in some persons diagnosed.

Rasagiline, developed for Parkinson's disease, is a drug designed to block the breakdown of neurotransmitters but also found to demonstrate neuroprotective action. It has been used to treat ALS, and, in a recent randomized controlled study, appears to increase survival. Other medications may help relieve the symptoms of muscle cramping and spasticity.

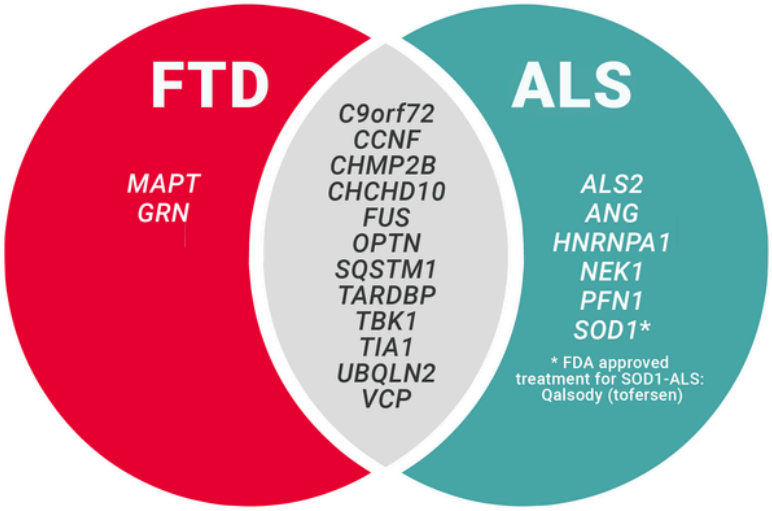
Today, there are no approved medicines specifically for FTD, although medications developed for other disorders may be prescribed to treat certain symptoms.

Genetics

If you have a family member with FTD and other relatives with ALS, or one family member with FTD-ALS, an inherited genetic cause is likely to be present. Genetic counseling is strongly recommended for anyone interested in learning whether there is a genetic cause for their symptoms.

A variant in the *C9orf72* gene is the most common cause of FTD-ALS. The variant produces an expansion of an area of the gene consisting of six nucleotides, called a hexanucleotide repeat. Typically, people have fewer than 25 repeats. When this region expands into several dozen or even hundreds to thousands of repeats, the person is at risk of developing FTD, ALS, or FTD-ALS. We cannot currently predict which symptoms will develop and when.

The image shows which genes can cause symptoms of FTD (red), ALS (teal), or both FTD and ALS (gray).



Other genes have preliminary evidence suggesting an association with FTD and/or ALS, and there are likely additional genes that have yet to be discovered.

The above information is current as of October 2024. To learn more about genetic FTD, visit theaftd.org/what-is-ftd/genetics-overview.

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theaftd.org/what-is-ftd/ftd-and-als-ftd-als