

## Does It Run in the Family?: The Genetics of FTD

### Introduction

**M**ost cases of FTD are sporadic, meaning that there is no clear-cut, singular genetic cause. Many cases, however, are said to be familial: Neurodegenerative diseases such as ALS, Parkinson's, and FTD recur throughout the family tree. A variety of factors can contribute to a family's propensity for developing FTD, but the most direct cause is a genetic variant that can be inherited from a parent and passed onto one's children.

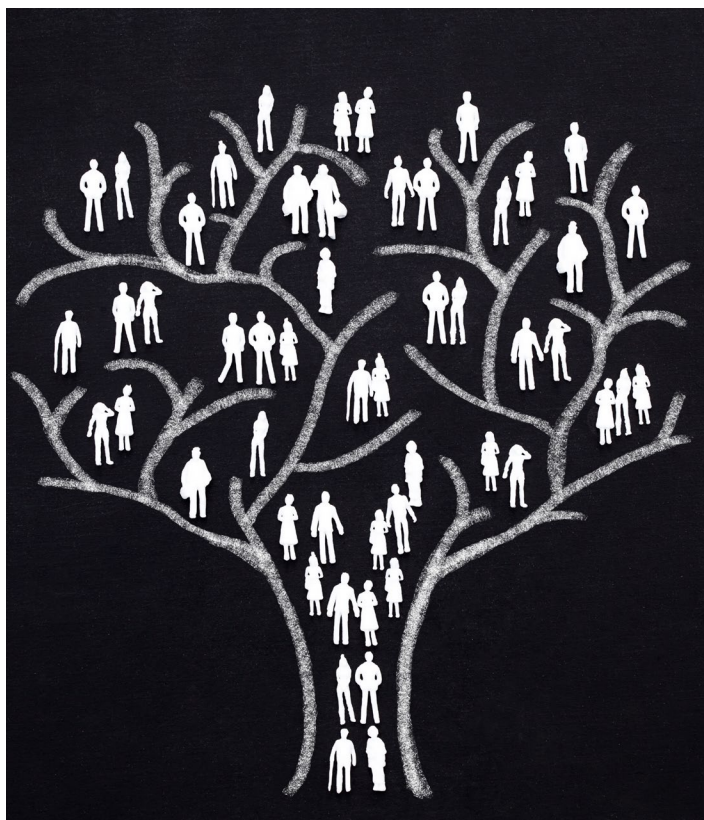
In the following case study, Brian S. begins showing FTD symptoms in his 50s. After reviewing his family's health history – which includes relatives with vaguely defined and undiagnosed neurological conditions – a genetic counselor expresses concern that Brian's FTD may be familial, and perhaps even have a specific genetic cause. With the genetic counselor's help, Brian's daughter Sarah must prepare to learn the results of her father's genetic testing – and then, if a gene variant is present, decide whether to get tested herself.

### The Case of Brian S.

Brian S. was a loving father and lawyer from a close-knit family. When he was 52, his only daughter, Sarah, noticed he seemed less interested in her, and that he no longer called her back when she left voicemails. His wife, Rose, sensed that he was feeling overwhelmed at work, which was unusual for him. At his wife's urging, Brian saw his family doctor, who suspected he might be experiencing job-related stress and anxiety and encouraged him to meditate and take more frequent vacations. Nine months later, after Brian started dressing in unwashed clothes, his wife convinced him to return to the doctor for additional investigations. A brain CT scan yielded normal results, as did routine bloodwork. But with his symptoms worsening, Brian was referred to a specialty neurology clinic for further evaluation.

During Brian's initial assessment at the specialty clinic, a behavioral neurologist provided a complete neuromedical assessment and reviewed his CT images. Although the CT scan was reported as "normal," the neurologist noticed subtle signs of atrophy in Brian's frontal lobes. The neurologist said he suspected that Brian's symptoms represented the early stages of frontotemporal degeneration (FTD) and arranged for an MRI and detailed neuropsychological testing. He scheduled a follow-up appointment in a few months to review the results.

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By the time of the follow-up appointment, Brian was on leave from his job. Throughout the appointment, Brian said he did not understand why he was there, and repeatedly asked if he could go home. The neurologist explained that his MRI revealed atrophy of the frontal and temporal regions of the brain, and that the results of his neuropsychological testing were also in keeping with frontotemporal degeneration. He said that he was quite certain that Brian had behavioral variant FTD.

Sarah and Rose had spent the past year reading about FTD symptoms, so this news did not surprise them. In some ways, it was a relief for them to have a concrete explanation for Brian's symptoms and a better understanding of what to expect. The neurologist said he would arrange for the family to speak with the clinic social worker for information about additional resources and supports.

Genetic FTD is suspected when someone reports several close relatives with FTD or related conditions.

#### Is It Genetic?

Increasingly anxious that her father's FTD may have a genetic cause, Sarah scheduled a session with a genetic counselor. The genetic counselor recorded Brian's family history: his parents were alive and well in their late 70s, his two older siblings were likewise healthy and in their 50s, and there was no known family history of dementia or other neurological disorders.

The genetic counselor provided some reassuring information about FTD's genetic nature. In the majority of FTD cases, she noted, the condition is **sporadic**, meaning it does not run in the family. Meanwhile, some people with FTD have a family history of dementia, psychiatric illness, or movement disorders such as ALS or Parkinson's disease; these cases are considered **familial** and reflect an elevated, but unclear, risk of inheritance. In a portion of these cases, the disease is genetic or inherited, caused by variants in single genes. These cases of **genetic** FTD are suspected when someone reports several close relatives over several generations with FTD or other neurodegenerative conditions.

After the session, Sarah spent time contacting her father's relatives to learn more about his family's health history. She reached out to the genetic counselor to share her findings. While no one else in the family was known to have FTD, Sarah learned that one of her father's paternal uncles had died in his 80s with "some type of neurological condition" that started just a couple of years before he died and required him to use a wheelchair. Sarah also learned that her father's paternal grandmother showed "odd behavior" and lived in isolation before dying in her 70s.

Sarah was newly concerned about the possible genetic implications of her father's diagnosis. The genetic counselor said that Brian's FTD could still very well be sporadic; she noted his father's good health, his uncle's and grandmother's longevity, and the lack of detail about their conditions. However, the updates to the family history were significant: the genetics of FTD are highly complex, and several FTD-causing genes have been discovered over the past two decades. Variants in these FTD-causing genes can give rise to a wide variety of symptoms and trigger different ages of onset, even in the same family. This "variable expression" of FTD-causing genetic variants means that FTD, parkinsonism, ALS, and/or psychiatric conditions can all appear within a single family in which genetic FTD is present. Furthermore, some people who carry an FTD genetic variant live into their 80s or 90s without ever developing a neurological condition. This "reduced penetrance" of some FTD gene variants means that in some families, FTD may appear to come out of nowhere or skip a generation.

With this added information, Sarah expressed a strong interest in genetic testing. The counselor explained that several clinical genetics laboratories offer testing for known FTD gene variants. The testing process would begin by analyzing a DNA sample from Brian. A positive genetic test result would confirm he has genetic FTD – and would also confirm that Sarah and each of Brian's siblings have a 50% of chance developing FTD in the future. Predictive genetic testing could determine whether those relatives carried the same gene variant as the one identified in Brian.

Sarah, who was ready to start a family, wanted to know if she was going to develop FTD or another neurological disease so that she could plan accordingly. She worried, however, about putting her father through the stress of any more testing and said that she would rather take the genetic test herself.

The counselor explained that Sarah's testing would be more informative if they were first able to confirm that Brian's FTD was caused by a detectable FTD gene variant. If Sarah were tested first and received a negative result (no variant found), this could mean that her father had an FTD-causing gene variant and did not pass it on to Sarah. But it could also mean that her father's FTD is sporadic, or caused by a variant in a gene that has yet to be discovered. Sarah's own likelihood of developing FTD would remain difficult to assess.

The family understood and decided to proceed with Brian's genetic testing. Brian was no longer able to make decisions about his medical care; as his medical representative, Rose authorized her husband's genetic testing and signed the requisite consent forms on his behalf. Using a saliva collection kit, she helped administer the test. The family agreed to pay privately for testing, given that its costs were much lower than they had anticipated.

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## THE ROLE OF GENETICS IN FTD: AN OVERVIEW

Frontotemporal degeneration (FTD) is a group of disorders caused by the degeneration of the frontal and/or temporal lobes of the brain, bringing progressive changes to behavior, personality, language, and/or movement. The FTD disorders occur when specific proteins accumulate and clump together in a person's neurons. Three such proteins have been identified: tau, TDP-43, and FUS. The accumulation of any of these proteins in the neurons interferes with brain cell function and longevity, eventually leading to the symptoms of FTD.

### What Causes FTD?

For most people with FTD, the accumulation of tau, TDP-43, or FUS protein in their neurons happens for unknown reasons. These individuals have no family history of FTD; their condition occurs as a random-chance, or **sporadic**, event.

Sporadic cases of FTD have a multifactorial etiology (meaning they are caused by a combination of multiple different factors). These factors have yet to be clearly established, but likely include aging, lifestyle/environment, and susceptibility genes that make us more (or less) vulnerable to developing sporadic FTD in our lifetime. None of these factors will cause FTD on their own, but their complex interactions somehow result in the abnormal accumulation of tau, TDP-43, or FUS protein in the brain cells. Exactly how or why this happens continues to be studied.

Up to 40% of people with FTD will report a family history of FTD or other neurological conditions such as amyotrophic lateral sclerosis (ALS) or Parkinson's disease. These cases of FTD are described as **familial**.

In some families, these clusters of FTD or other neurological disorders are suspected to have a multifactorial etiology, and they are seen in multiple relatives because of significant sharing of underlying genetic susceptibility and/or lifestyle factors. In these families, FTD isn't directly passed on from one generation to the next, but the close relatives of affected individuals may have an increased chance of developing FTD, as compared to the general population.

In other families, having multiple cases of FTD or other neurological disorders represents a purely **genetic, or inherited**, form of familial FTD. In these families, persons with FTD have abnormal TDP-43, tau, or FUS protein accumulation in their brain cells because of a variant in a single causative gene that can be directly passed on from one generation to the next. All known purely genetic forms of familial FTD are autosomal dominant, meaning that if an individual has an FTD-causing gene variant, each of their children will have a 50% chance of inheriting it.

Although most individuals with purely genetic forms of FTD will have a family history of FTD and/or other neurological disorder, family history doesn't always tell the whole story. The gene variants that cause purely genetic forms of FTD have **variable expression**; the same variant can cause a wide range of symptoms and ages of onset, even in the same family. Furthermore, some of these FTD gene variants have **reduced penetrance**, meaning that an individual can carry the variant but live their entire life without developing FTD or a related condition. Researchers have found a small percentage of familial FTD gene variants in people with apparently sporadic FTD (i.e. no family history of FTD or other neurological disease).

More than a dozen causative familial FTD genes have been identified. Variants in three of these genes (*C9orf72*, *GRN*, and *MAPT*) explain the majority of purely genetic FTD cases. Variants in the other genes (including *VCP*, *CHMP2B*, *TARDBP*, *FUS*, *SQSTM1*, *CHCHD10*, *TBK1*, *OPTN*, *CCNF*, and *TIA1*) are rarer, with some being identified in only a handful of families around the world. Researchers anticipate that additional causative familial FTD genes will be identified in the future.

### Common familial FTD genes include:

- **C9orf72** – FTD-causing *C9orf72* variants consist of a section of the genetic code that gets repeated over and over, creating an expanded version of the *C9orf72* gene. This expansion disrupts the gene's normal function, leading to a cascade of events that result in abnormal accumulation of TDP-43 protein in the brain cells, along with another protein called GA dipeptide. Current research suggests that the combination of TDP-43 and GA dipeptide protein is only found in individuals with *C9orf72* expansions. *C9orf72* expansions are known to cause both FTD and ALS. Some *C9orf72* expansion carriers can also present with psychiatric illness such as schizophrenia or bipolar disorder.

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- **GRN (Progranulin)** – The *GRN* gene provides instructions for making progranulin, a protein that is involved in cell survival and the regulation of inflammation. FTD-causing variants in *GRN* lead to reduced progranulin levels. For reasons that remain unclear, decreased levels of progranulin result in the abnormal accumulation of TDP-43 protein in brain cells. Individuals with *GRN* variants most often develop FTD symptoms, but some individuals present with parkinsonism.
- **MAPT (Microtubule-associated protein tau)** – The *MAPT* gene provides instructions for making the tau protein, which plays a role in the assembly and stabilization of neurons. Variants in *MAPT* result in an abnormal form of tau, which can accumulate in the brain cells. Individuals with *MAPT* variants most often develop FTD symptoms, but some individuals present with parkinsonism.

### Genetic Testing for FTD

Genetic testing for familial FTD is available at several clinical genetics laboratories in the U.S. and Europe. The testing must be ordered by a physician and involves analysis of the known causative familial FTD genes using a DNA sample from blood, saliva, or cheek cells.

Genetic testing ideally begins with a family member who has an FTD diagnosis. A positive result – meaning that a gene variant is identified – would confirm that they have a purely genetic form of FTD, and that each of their children and siblings have a 50% chance of carrying the same variant. Those first-degree relatives would then be able to undergo predictive genetic testing.

A negative result can provide some reassurance that an individual's FTD is multifactorial. However, it would not rule out the possibility that they have a purely genetic form of familial FTD caused by a variant in a gene that has yet to be discovered. In this scenario, predictive genetic testing is not available to family members.

Deciding to have genetic testing can be difficult. Each family making this decision will have unique motivations, perspectives, and values. Testing should only be completed upon careful consideration of all test limitations and implications, including medical, social, psychological, and insurance consequences. Pre-test genetic counseling is recommended to ensure that individuals and families considering genetic testing are informed and supported during the decision-making process and beyond. ■

About eight weeks later, the genetic counselor invited Rose and Sarah to review Brian's results. (Brian had just moved into a care facility and was no longer able to travel.) Brian's genetic testing confirmed that he carried a disease-causing, or "pathogenic," variant in the *C9orf72* gene. Variants in this gene are known to cause symptoms of FTD, ALS, and psychiatric illness, and are also known to have reduced penetrance. The counselor gently told Rose and Sarah that this finding confirmed the inherited nature of Brian's condition, and that each of Brian's first-degree relatives had a 50% chance of carrying the same variant. All of these relatives would now have the option of predictive *C9orf72* genetic testing for themselves.

### Next Steps

Rose and Sarah were understandably saddened to learn that Brian's condition was genetic, and that Sarah and other relatives could develop FTD and/or ALS in the future. The genetic counselor explained that Brian's FTD was most likely inherited from his father, and that the neurological symptoms displayed by his older paternal relatives most likely resulted from a *C9orf72* gene mutation.

A positive genetic test result for Sarah would indicate that she is likely to develop FTD and/or ALS.

Rose acknowledged that it was difficult to process this information. She had just learned that Brian's older brother was about to undergo testing for symptoms which could be caused by ALS. She hadn't realized that there was a connection between FTD and ALS until Brian started the genetic testing process. She also hadn't understood that FTD can develop so late in life; most of what she had read about FTD suggested onset before age 60. This meant that Brian's father, though nearing 80, could still develop FTD before he died.

Sarah said that she wanted to proceed with predictive genetic testing to find out her own *C9orf72* status. The genetic counselor explained that such testing would only be done after an additional session to review the implications of a positive and negative test result, motivations for testing, psychological readiness, and support systems.

Sarah returned to the clinic with her husband for pre-test genetic counseling. The counselor explained that a positive test result would indicate that Sarah will most likely develop FTD and/or ALS in her lifetime, but that her specific age of onset, disease progression, and symptoms would remain unknown. The genetic counselor also noted that there is still no way to prevent the onset of FTD or ALS in a *C9orf72* gene variant carrier, but that human clinical trials of *C9orf72*-specific therapies are now underway.

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## PROVIDING SUPPORT TO THOSE CONSIDERING GENETIC TESTING: GUIDANCE FOR HEALTHCARE PROFESSIONALS

For many people facing potential FTD caused by a genetic variant, either for themselves or a family member, deciding to undergo genetic testing can be complicated and challenging. The decision to know (or not know) one's genetic FTD status can feel overwhelming, and invariably comes at an already vulnerable time in one's life. Families should be encouraged and empowered to take advantage of genetic counseling and mental health services available during this time, to help process the complex emotions involved before, during, and after they make their decision. Regardless of how they proceed, families should not have to privately struggle with their decision – they should be given easy access to genetic counseling, psychological counseling, and other coping tools as needed.

It is strongly recommended that individuals and families who are considering testing first meet with a genetic counselor. However, if they indicate that they want to forgo this step, consider referring them to a mental health specialist who works with families living with dementia. Talking to a specialist about why they are hesitant to see a genetic counselor can reduce one's anxiety around this first meeting. Also, make sure that families understand that having a first meeting with a genetic counselor to discuss their concerns and questions does not commit them to moving forward with a genetic test.

For some, knowing the results of a genetic test (even if positive for a genetic variant) is less distressing than living in uncertainty. Research indicates that the majority of those tested demonstrate effective coping skills and absence of negative psychological reactions after several months and found the testing beneficial (Steinbart et al., 2001). More study on this subject and the long-term effects of testing for young-onset dementia is needed.

In addition to helping inform the decision around genetic testing, genetic counselors can also help families learn about coping and adaptation skills. This might include the concept of “post-traumatic growth,” defined as a positive change or changes resulting from one's struggle to deal with a trauma and its consequences. One type of therapy that supports these counseling goals is cognitive behavioral therapy (CBT), which is based upon the relationships between our thoughts, behaviors, and emotions. It focuses not only on what a person knows about their genetic condition or risk, but also on the things they think and believe, elements that inform their emotional response.

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CBT techniques can assist in coping with genetic-test results, as well as identifying the “distorted thoughts” and “irrational beliefs” that are often the source of emotional distress (Biesecker et al., 2017). Consider referring an individual or family to a CBT specialist or another therapist with experience in dementia to treat psychological distress.

Ongoing support is vital. The genetic testing process can cause anxiety, depression, fear, and guilt; a positive test can have significant impact on one's lifestyle, insurance rates, and choices about family planning. It is therefore vital for families to know they are not alone in coping with the possible outcomes – there are skilled professionals who are available to provide help. Through information, knowledge, and psychological support, genetic counselors and mental health service providers can equip families to face the decisions ahead – and, regardless of a family's decision, serve as an important resource to help them cope. ■

### Sources:

- Biesecker B, Austin J, Caleshu C. Theories for Psychotherapeutic Genetic Counseling: Fuzzy Trace Theory and Cognitive Behavior Theory. *J Genet Couns.* 2017; 26(2):322-330. doi:10.1007/s10897-016-0023-1.
- Lerman C, Croyle RT, Tercyak KP, et al. Genetic Testing: Psychological Aspects and Implications. *J Consult Clin Psychol* 2002; 70:784–97.
- Sexton, A, West K, Gill G, Wiseman A, Taylor J, Purvis R, Fahey M, Storey E, Walsh M, James P. Suicide in Frontotemporal Dementia and Huntington Disease: Analysis of Family-Reported Pedigree Data and Implications for Genetic Healthcare for Asymptomatic Relatives. *Psychol Health.* 2020 Nov.; 24:1-7. doi: 10.1080/08870446.2020.1849700. Epub ahead of print. PMID: 33232178.
- Steinbart EJ, Smith CO, Poorkaj P, Bird TD. Impact of DNA Testing for Early-Onset Familial Alzheimer Disease and Frontotemporal Dementia. *Arch Neurol.* 2001 Nov; 58(11):1828-31.
- Tibben A, Stevens M, de Wert GM, Niermeijer MF, van Duijn CM, van Swieten JC. Preparing for Presymptomatic DNA Testing for Early Onset Alzheimer's Disease/Cerebral Haemorrhage and Hereditary Pick Disease. *J Med Genet.* 1997 Jan; 34(1):63-72.

### To Test or Not to Test?

Although a part of Sarah wanted to know if she carried a *C9orf72* gene variant, she was simultaneously nervous about the possibility of a positive test result. Knowing her genetic status before she started a family was important – she would not want to pass the disease to her future children. But at the same time, the experience of caring for her father weighed heavily upon her; she wasn't entirely sure she could cope with a positive test result given her life's current stressors. A positive test result would likely be detrimental to her current mental health and well-being.

Given her wish to avoid potential transmission of a *C9orf72* gene variant to her children, Sarah asked the genetic counselor about

assisted reproductive technologies, such as in vitro fertilization (IVF) with donor eggs or IVF with pre-implantation genetic diagnosis. These could be done without Sarah learning her own *C9orf72* status, the counselor noted.

Ultimately, Sarah decided not to proceed with predictive genetic testing for the time being. She and her husband would seek out additional information about assisted reproductive technologies from the local fertility clinic. The genetic counselor invited them to reach out should Sarah wish to proceed with predictive testing in the future, for periodic updates regarding *C9orf72*-specific therapies, or if they had any additional questions or concerns. ■

### FROM A CAREGIVER'S PERSPECTIVE: DECIDING TO LEARN ONE'S GENETIC STATUS by A. Parker

FTD runs in my father's side of the family. My paternal grandmother almost certainly had it, although she was never officially diagnosed. But three of my father's four siblings had FTD, and so did my father, who displayed symptoms starting in his 40s before dying in 2009 at age 60.

Before my father died, I got a phone call from some kind of government health worker, possibly a genetic counselor. (I was a busy undergrad and don't remember exactly.) She told me that my father's FTD was caused by a genetic variant – one that I may have inherited. She recommended that I look into genetic testing to determine for sure if I shared the variant, explaining that there was a 50/50 chance that my brain was genetically hardwired to deteriorate prematurely.

This news completely overwhelmed me, and I coped by trying not to think about it. Instead, I spent that time doing what many people that age do – starting my career, socializing with friends, dating. I was still a little naïve as to what FTD entailed, and how bad it would eventually get for my dad.

Eventually, however, the anxiety of not knowing got to be too much. My coin-flip chances of getting FTD literally affected every part of my life, from my career to my relationships to the idea of someday having children. So when I was 24, my brother and I went to the University of California, San Francisco, to undergo testing. The staff there was extremely supportive. Their interest in me and my family was genuine and sincere, which made me feel special and important. They set me up with a genetic counselor, who graciously answered all my questions. Over the course of several days, I took numerous tests (memory quizzes, word problems, reflex testing) and submitted to blood tests and MRIs. The counselor asked my brother and me a long series of questions about our family's medical history. The UCSF staff said that my results would not be immediately available, and that they would not share them with me until I asked for them and underwent counseling.

Shortly after I got home, my dad's FTD went from bad to worse. Seeing him at the end of his life brought on intense anxiety and depression, as I saw first-hand how severely debilitating late-stage FTD is. I found it impossible to grieve properly when my dad died, knowing that his fate could one day be mine.

At this point I started becoming paranoid, thinking that any slight abnormality in my behavior confirmed my nascent FTD. Was my handwriting getting worse? Could that be a sign of FTD creeping in? (My dad's handwriting changed drastically in his final years.) I stopped laughing at jokes that everyone else found funny – was the part of my brain responsible for my sense of humor already dying?

I had kept in contact with the genetic counselor and reached out to her when I finally felt ready to learn my test results. My best friend accompanied me to the counselor's office. The genetic counselor asked me one final time if I was sure I wanted to learn the results. I told her yes, and she opened an envelope and read from a piece of paper: My results were negative.

FTD remains very much a part of my family's life. Some of my cousins on my dad's side have asked me about my experience of getting tested, and whether they should get tested themselves. I tell them that only they can make that decision. For me, knowing my genetic status felt necessary. But I will never forget what my genetic counselor once told me: For some people, not knowing their status is a way to hold on to hope. Even a little hope can be very powerful; taking it away can have devastating mental-health consequences.

Then again, someone who has a confirmed genetic mutation told me that he is glad to know his positive status. Knowledge is power, after all. Either way, the decision to learn one's genetic status is not one that can be made lightly. ■

## WHAT TO KNOW BEFORE ORDERING GENETIC TESTING

Frontotemporal degeneration is a progressive, terminal neurological disease with no FDA-approved treatments. Because of the seriousness of the condition and the potential implications for extended family members, particular care and consideration need to be given to the emotional, privacy, and legal/financial needs of the person receiving genetic testing. Asymptomatic family members of persons diagnosed with FTD often feel distressed when discussing both their risk of developing FTD and the idea of undergoing predictive genetic testing (Wong et al., 2021). Genetic counselors can help people to better understand the goals of genetic testing, review their family history, and provide a risk assessment. AFTD recommends those considering genetic testing first be referred to a genetic counselor.

Our understanding of FTD's causes has grown greatly over the last 20 years. Thirty to fifty percent of cases have a family history of dementia, a major psychiatric condition, or progressive challenges in movement. A subset of these familial cases is genetic, or hereditary, in nature (Goldman & van Deerlin, 2018). FTD is genetically heterogeneous, with at least 13 genes being associated with autosomal dominant cases. Most of the heritability is found in three genes: *MAPT*, *GRN*, and *C9orf72*. Because of the chance that FTD can be inherited, many people who have a family member diagnosed with FTD want to learn more about the genetic risk of getting FTD themselves.

Clinicians may recommend genetic testing in the presence of a strong family history or clinical presentations, as in the case of FTD-ALS. Because family history may not be complete or conclusive, all persons diagnosed with FTD should be offered

genetic counseling to help get answers and assuage any concerns they or their family might have (Goldman & van Deerlin, 2018). For many people, learning their genetic risk can relieve anxiety resulting from the unknown.

The lack of disease-modifying treatments in FTD can lead to increased stress around testing (Roggenbuck, Quick & Kolb, 2017). However, as potentially disease-modifying treatments in FTD enter clinical trials, people with known genetic variants can participate and advance the science of FTD.

Those considering genetic testing face many complex considerations; their empowerment and emotional well-being should be of the utmost priority. Individuals decide to undergo genetic testing for different reasons; a person's genetic status can inform their financial future, the decision to raise a family, and long-term care planning. Regardless, the decision to undergo genetic testing is a personal one, and necessary support should be offered. ■

### Sources:

Goldman, JS, & Van Deerlin, VM (2018). Alzheimer's Disease and Frontotemporal Dementia: The Current State of Genetics and Genetic Testing Since the Advent of Next-Generation Sequencing. *Molecular Diagnosis & Therapy*, 2018; 22(5), 505–513. <https://doi.org/10.1007/s40291-018-0347-7>.

Roggenbuck, J, Quick, A, & Kolb, SJ. Genetic Testing and Genetic Counseling for Amyotrophic Lateral Sclerosis: An Update for Clinicians. *Genetics in Medicine*, 2017; 19(3), 267-274.

Wong, B, et al. Knowledge Assessment and Psychological Impact of Genetic Counseling in People at Risk for Familial FTD. *Alzheimer's & Dementia*, 2021; 13(1): e12225.

## Partners in FTD Care Advisors

The Partners in FTD Care initiative is the result of collaboration among AFTD, content experts, and family caregivers. Advisors include:

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## What to Do About... The Decision to Learn One's Genetic FTD Status

Deciding whether to learn if one has a genetic variant that will someday lead to FTD can be overwhelming. Fortunately, there are knowledgeable genetic counselors who can provide information, guidance, and resources to make that decision a little easier. Following are tips and strategies that can help healthcare professionals point families to effective genetic counseling, as well as a checklist of things that families facing FTD should be aware of before meeting with a counselor.

### Guidance for Healthcare Professionals

- Learn the importance of genetics and genetic status for individuals and families living with FTD.
- Share the link to the FTD Genetics section of AFTD's website ([theaftd.org/ftd-genetics/what-causes-ftd](http://theaftd.org/ftd-genetics/what-causes-ftd)) with persons diagnosed with FTD and family members who want to know more about whether FTD can be inherited.
- Recommend that families consider genetic counseling as a first step to answer questions about genetic status.
- Consider that a genetic counselor can evaluate the likelihood that FTD may have a genetic cause, help families think through the benefits and risks of testing, and provide ways that families can talk with other family members.
- Learn about the availability of genetic counselors in your area and be able to provide guidance to help families find one. The National Society of Genetic Counselors' website ([findageneticcounselor.nsgc.org](http://findageneticcounselor.nsgc.org)) enables families and clinicians to search for genetic counseling (in-person or via telemedicine), including those with a neurogenetic specialization.
- Learn about current FTD research opportunities via the FTD Disorders Registry ([ftdregistry.org](http://ftdregistry.org)).
- Share with families that there is currently a reason for hope for potential FTD treatments. Among other research, trials to find a disease-altering treatment based on FTD genetic status are ongoing.
- Be aware that not all sponsored genetic testing is the same and does not necessarily include pre- and post-test genetic counseling, both of which are important to ensure that those considering or taking a genetic test have all the information and support they need.
- Connect those with FTD and their families to resources to help them understand the differences in the no-cost sponsored genetic testing currently available. AFTD ([theaftd.org/ftd-genetics/no-cost-genetic-testing](http://theaftd.org/ftd-genetics/no-cost-genetic-testing)) and the FTD Disorders Registry ([ftdregistry.org/genetics-ftd](http://ftdregistry.org/genetics-ftd)) provide unbiased information specific to the benefits and limitations of current cost-free genetic testing.
- Consider making a referral to a mental health specialist, especially one who has experience with progressive neurodegenerative illness, for individuals and families who may need support to discuss their concerns and fears about deciding whether to pursue genetic counseling.



## Guidance for Individuals with FTD and Family Members

- Consider genetic counseling as a first step to answering your questions about FTD genetic status, whether you have a personal or family history of FTD, or if a past misdiagnosis could potentially be masking one.
- Know that a person can see a genetic counselor individually, or with a family member or friend.
- Consider that genetic testing is never a required part of genetic counseling.
- Assemble, as best you can, a thorough family health history before meeting with a genetic counselor. Know that FTD can present with a wide variety of symptoms and remains frequently misdiagnosed, even today.
- Reach out to other family members to confirm or learn more about your family health history.
- Recognize that a complete understanding of family history should include a history of dementia, major psychiatric conditions, or progressive challenges in movement that may have been misdiagnosed in the past within your family.
- Ask the genetic counselor about your personal genetic risk and your family risk; about future family planning, insurance, and confidentiality concerns; and for guidance on talking with other family members.
- Recognize that a person with FTD who can provide informed consent for a medical procedure is the one who decides for themselves whether to get a genetic test.
- Understand that for any person with FTD who can no longer provide informed consent, the person they have identified as their healthcare proxy or power of attorney for healthcare can provide consent for a genetic test.
- Learn about how both a genetic test and a brain autopsy can provide valuable information in relation to an FTD diagnosis. While genetic testing cannot by itself diagnose FTD, it can be used—along with an evaluation of clinical symptoms, imaging, and other assessments—to help determine if someone has FTD. A positive genetic test for an FTD gene will not necessarily determine the specific FTD disorder.
- Plan ahead if there is an interest in genetic testing when arranging for a brain autopsy, as it is not done routinely.
- Join the FTD Disorders Registry ([ftdregistry.org](https://ftdregistry.org)) to learn about current FTD research studies and how to get involved. Joining the Registry does not require research participation.

For more information on FTD genetics, please go to: [www.theaftd.org/ftd-genetics/what-causes-ftd](https://www.theaftd.org/ftd-genetics/what-causes-ftd).