Exploring families' interest in understanding genetic FTD

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1. The Association for Frontotemporal Degeneration;
2. 2. The FTD Disorders Registry

State of the Art

Frontotemporal degeneration (FTD) encompasses a genetically heterogeneous group of complex neurodegenerative conditions broadly characterized by changes in cognition, behavior, language, and movement. The diverse range of clinical presentations contributes to the challenge of an accurate diagnosis, resulting in delayed diagnosis and underdiagnosis of FTD. Barriers to receiving a timely and accurate diagnosis is one of the key challenges in identifying potential candidates to participate in clinical trials, many of which focus on genetic forms of FTD.

FTD and amyotrophic lateral sclerosis (ALS) share common neuropathology and share several causative genes, indicating the two conditions comprise a spectrum of neurodegenerative disorder.

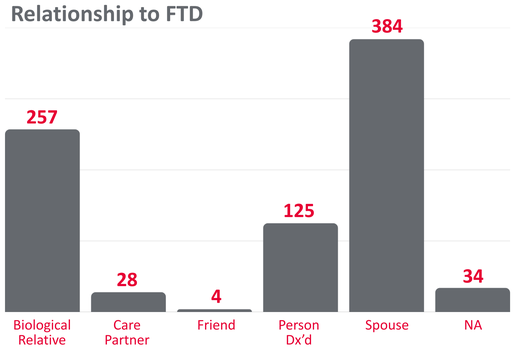
Approximately 20-30% of FTD has an underlying genetic etiology, whereas 10-15% of ALS has an identifiable genetic cause (De Marchi et al. Genes.2023;14 1658). Diagnostic guidelines recommend genetic counseling with an option to pursue genetic testing for ALS, yet similar guidelines have not yet been developed for the diagnosis of FTD (Roggenbuck et al. Ann Clin Transl Neurol.2023;10 2074-2091). Several potential therapies are under investigation for GRN-FTD and C9orf72-FTD-ALS, highlighting the importance of detecting individuals with genetic FTD to broaden the pool of eligible participants for clinical trials and to identify people who may benefit from a successful treatment.

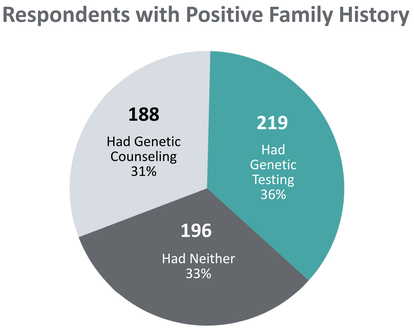
Methodology

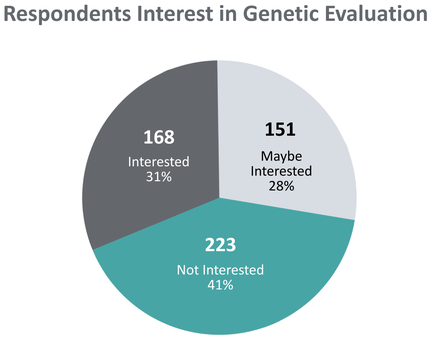
The FTD Disorders Registry deployed an anonymous 10 question survey to explore if, how, and when the subjects of genetic counseling (GC) and genetic testing (GT) arose between healthcare providers and persons diagnosed with FTD and their care partners.

Survey questions included when in the FTD diagnostic process genetics was discussed, who first raised the issue of genetics, the time from symptom onset to discussion of genetics, and whether they were offered pre- and/or post-test genetic counseling. The survey also queried about whether there was a known family history, defined as two or more biological relatives, diagnosed with FTD or a related disorder, such as ALS, Parkinson disease, Lewy Body dementia, Alzheimer's disease, other dementia, aphasia, or psychiatric disorder.

Results







- Total of 832 respondents, of whom 452 (54%) reported a positive family history.
- After a clinical diagnosis of FTD, the subject of genetics was first raised an average of 2.37 years for those with a positive family history and 2.44 years for people with presumed simplex FTD.
- The request for a genetic evaluation originated from the person diagnosed or their care partner in approximately 12% of cases, whereas 30% reported the healthcare provider raised the issue of genetics. The remaining 58% of respondents did not recall when or by whom genetics had been raised.
- A neurologist was often the first healthcare provider to discuss genetic counseling or testing (42% families asked the neurologist; 61% neurologists asked the family).
- 67% of respondents who had genetic counseling, reported simplex FTD (no known family history).

Conclusion

We hypothesized that people with a positive family history would be offered genetic counseling and the option to pursue genetic testing earlier and more often than those with an apparently simplex form of FTD.

- Approximately 5-10% of individuals with no known family history, have an identifiable genetic cause for their FTD.
- Data suggest a positive family history had minimal influence on if genetic counseling and testing were offered even when the family history includes more than one person with an FTD spectrum diagnosis.
- Data suggest a positive family history had minimal impact on when in the diagnostic process the subject of genetics was raised.

Genetic counseling and testing can facilitate well-informed decisions about testing, shorten the diagnostic odyssey, ensure an accurate diagnosis, reduce the anxiety of uncertainty, inform future life planning, and may offer the opportunity to participate in disease-modifying clinical trials. Moreover, many families are interested in or at least open to discussing genetics.

Clinical trials for a rare disease, such as FTD, struggle to identify eligible participants needed to produce sufficiently robust data to support the efficacy of an intervention. Recent diagnostic guidelines for ALS call for universal genetic counseling with the option to test should as standard of care. Given ALS is within the spectrum of FTD disorders, it stands to reason the same standard of care should apply to the diagnosis of FTD, allowing families to make an informed decision about whether testing is right for them and open opportunities to participate in clinical trials targeting specific FTD-causing genetic variants as well as future approved therapies.

Additional Resources

AFTD and the FTD Disorders Registry have information and resources for people interested in participating in research as well as researchers who want to better understand the lived experience of FTD.

www.theaftd.org

www.ftdregistry.org