Frontotemporal Degeneration (FTD): A Cruel and Often Misdiagnosed, Mistreated Form of Dementia

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Meet the Speaker

Dr. Ulen is a senior clinical pharmacy specialist and serves as the founding PGY-2 Geriatric residency program director at Upstate University Hospital's Community Campus in Syracuse, NY. The residency program was recently accredited for the maximum duration of 8 years. She is a board-certified geriatric pharmacist. She has several publications in geriatrics pertaining to safe medication use in the older patient and deprescribing and is currently involved in a New York State funded study on deprescribing. She serves as preceptor for PGY1 and PGY2 residents, and APPE students.

Disclosure

- Dr. Ulen will discuss off-label use of the following medications: trazodone, citalopram, sertraline, quetiapine, risperidone, rivastigmine, galantamine, donepezil, olanzapine, memantine, aripiprazole, carbidopa/levodopa, and topiramate.

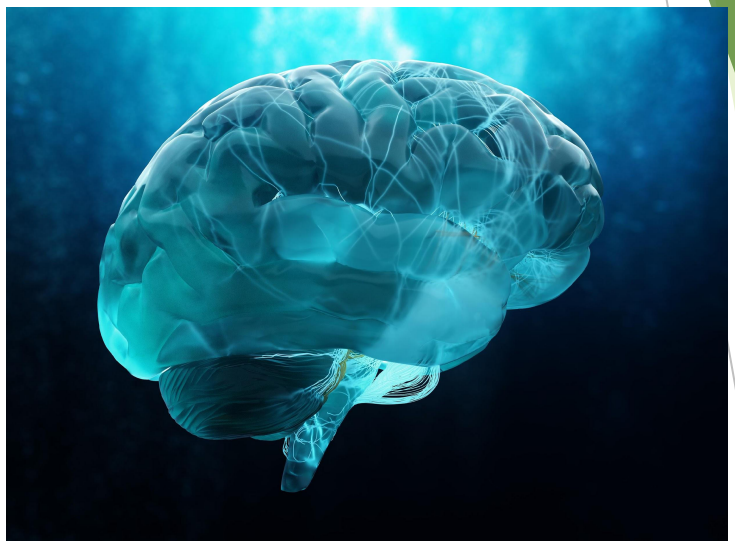
Learning Objectives

1. Describe the clinical presentations and complications of Frontotemporal Dementia (FTD)
2. Identify the subtypes of FTD
3. Identify a hallmark sign of behavioral variant FTD (bvFTD)
4. Create an appropriate medication regimen for a patient with bvFTD
5. Provide appropriate counseling points to patients with FTD, their family and caregivers

Photo by Sarah Heppell

Frontotemporal Degeneration (FTD)

- Frequently referred to as frontotemporal degeneration, frontotemporal dementia or Pick's disease
- FTD represents a group of brain disorders caused by degeneration of the frontal and/or temporal lobes of the brain
- The hallmark of FTD is a gradual, progressive *decline in behavior and/or language*; it can also cause a decline in *motor function*



Miller B, Llibre Guerra JJ. Frontotemporal dementia. *Psychopharmacology of Neurologic Disease*. 2019:33-45. doi:10.1016/b978-0-444-64012-3.00003-4
Godefroy V, Tanguy D, Bouzigues A, et al. Frontotemporal dementia subtypes based on behavioral INHIBITION DEFICITS. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*. 2021;13(1). doi:10.1002/dad2.12178

Prevalence of Frontotemporal Degeneration

- The estimated point prevalence is 15-22/100,000, and incidence 2.7-4.1/100,000 globally
  - **Approx. 60,000 cases in the USA**
- Equal distribution of gender
- Frequently familial and hereditary, Non- genetic risk factors have not yet been identified
- Survival similar to Alzheimer's Disease

Hogan DB, Jetté N, Fiest KM, et al. The Prevalence and Incidence of Frontotemporal Dementia: a Systematic Review. *Can J Neurol Sci*. 2016;43 Suppl 1:S96-S109. doi:10.1017/cjn.2016.25

FTD

- Most common cause of early-onset dementia

Mean age of onset is 60 years young

- Life expectancy is 7.5 years

Average survival time from first symptoms

- On average, takes almost 4 years to diagnose!

Mimics many psych disorders

Miller B, Llibre Guerra JJ. Frontotemporal dementia. *Psychopharmacology of Neurologic Disease*. 2019:33-45. doi:10.1016/b978-0-444-64012-3.00003-4
Godefroy V, Tanguy D, Bouzigues A, et al. Frontotemporal dementia subtypes based on behavioral INHIBITION DEFICITS. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*. 2021;13(1). doi:10.1002/dad2.12178
Fast Facts about Frontotemporal Degeneration. Association for Frontotemporal Degeneration. http://www.theaftd.org/wp-content/uploads/2009/02/Fast-Facts-Final-6-11.pdf. accessed August 2, 2021.

Alzheimer's Vs FTD

Alzheimer's Dementia	FTD
Most common dementia in **older** people	Most common dementia in **younger** people
Usually begins with **memory loss**	Usually begins with **behavior** or **language disorder**
Odds of having AD **increase** as you get older	Odds of having FTD **decrease** as you get older

Ftd misdiagnosis. Memory and Aging Center. https://memory.ucsf.edu/dementia/ftd/ftd-misdiagnosis. Accessed August 17, 2021.

FTD Impact on the Brain

Frontal Lobe Functions	Temporal Lobe Functions
Motor function	Visual memory
Social and Sexual behavior	Language comprehension
Problem solving	Emotion association
Impulse control	Formation of language

Atrophy in the frontal and temporal lobes

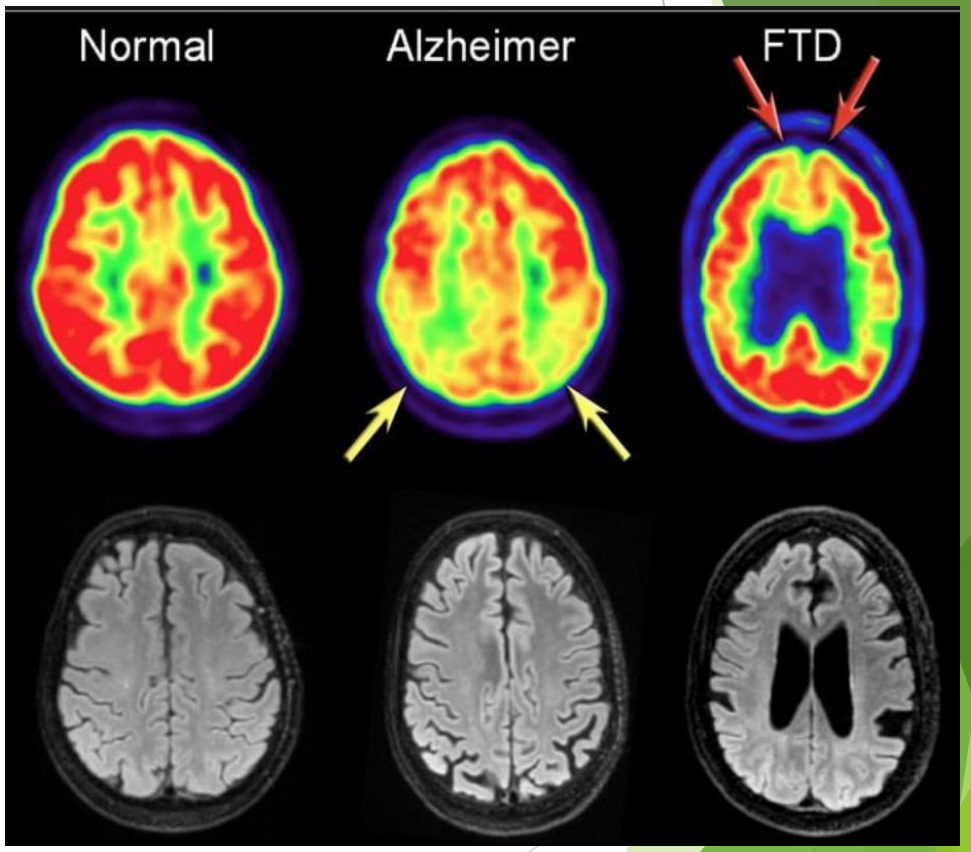


Image from What is FTD. OPEN HAND FOUNDATION. https://theopenhand.org/about-ftd. Accessed August 2, 2021.

Huang J. Overview of cerebral function - neurologic disorders. Merck Manuals Professional Edition. https://www.merckmanuals.com/professional/neurologic-disorders/function-and-dysfunction-of-the-cerebral-lobes/overview-of-cerebral-function#v1033945. Published June 2020. Accessed August 2, 2021.

Rabins PV, et al. American Psychiatric Association practice guidelines: treatment of patients with Alzheimer's disease and other dementias. psychiatryonline 2007.

What Happens Where?

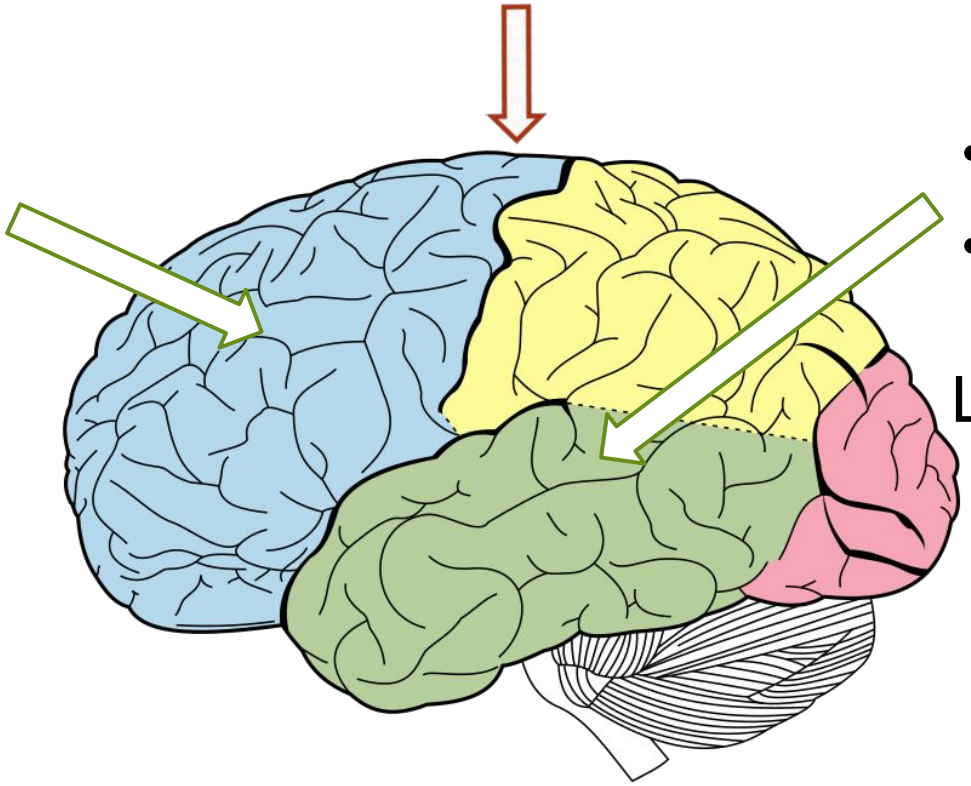
Frontal Lobes

Prefrontal cortex

- Reasoning, decision making
- Control of behavior
- Executive functions (Planning, organizing)
- Problem solving
- Attention, concentration
- Emotional control

Motor & Pre-Motor

- Initiating action
- Physical movement



Temporal Lobes

Processing sensory information

Right Lobe

- Visual memory, pictures, shapes and faces, art
- Sounds, music
- Inhibition of speech

Left Lobe

- Verbal memory
- Understanding words and names
- Differentiating smells and sounds

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Clinical Presentation

- Depression is a commonly seen symptom in all neurodegenerative dementias and should be treated
- Cardinal features for the primary progressive aphasia (PPA)
  - Difficulty with understanding words
  - Problems with reading
  - Problems with writing
- Cardinal features for the behavioral variant of FTD (bvFTD)
  - Disinhibition
  - Apathy
  - Lack of empathy
  - Compulsive behavior
  - Altered eating habits

Huang J. Overview of cerebral function - neurologic disorders. Merck Manuals Professional Edition. https://www.merckmanuals.com/professional/neurologic-disorders/function-and-dysfunction-of-the-cerebral-lobes/overview-of-cerebral-function#v1033945. Published June 2020. Accessed August 2, 2021.
Rabins PV, et al. American Psychiatric Association practice guidelines: treatment of patients with Alzheimer's disease and other dementias. psychiatryonline 2007.

FTD: A Cluster of Complex Disorders

Progressive Behavior/ Personality Change

Behavioral Variant FTD (bvFTD)

Also called:

Frontotemporal Dementia

Pick's Disease

Progressive Language Change

Primary Progressive Aphasia (PPA)

Subtypes:

Nonfluent/Agrammatic Variant

Semantic Variant

Logopenic Variant

Progressive Motor Function/ Movement Change

Corticobasal Syndrome (CBS/CBD)

Progressive Supranuclear Palsy (PSP)

FTD + Motor Neuron Disease (ALS-FTD)

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FTD has subtypes, called variants

- **Primary progressive aphasia** (PPA) is characterized predominantly by the gradual loss of the ability to speak, read, write and understand what others are saying

PPA Diagnosis Criteria
1. There is gradual impairment of language (not just speech)
2. The language problem is initially the only impairment
3. The underlying cause is a neurodegenerative disease

Huang J. Overview of cerebral function - neurologic disorders. Merck Manuals Professional Edition. https://www.merckmanuals.com/professional/neurologic-disorders/function-and-dysfunction-of-the-cerebral-lobes/overview-of-cerebral-function#v1033945. Published June 2020. Accessed August 2, 2021.
Rabins PV, et al. American Psychiatric Association practice guidelines: treatment of patients with Alzheimer's disease and other dementias. psychiatryonline 2007.

Primary progressive aphasia (PPA)

Clinical Description	Possible Symptoms	Type of Pathology Seen in Brain
Deterioration in ability to produce speech, understand words, recognize objects	Hesitant, effortful speech Comprehension of speech may be preserved in the early stages Typically lack features of bvFTD	Tau protein pathology found

Huang J. Overview of cerebral function - neurologic disorders. Merck Manuals Professional Edition. https://www.merckmanuals.com/professional/neurologic-disorders/function-and-dysfunction-of-the-cerebral-lobes/overview-of-cerebral-function#v1033945. Published June 2020. Accessed August 2, 2021.
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Behavioral Variant FTD (bvFTD)

Clinical Description	Possible Symptoms	Type of Pathology Seen in Brain
Changes in personality, emotions, and/or behaviors	Hyperoral (ex. only eating ***sweets*** or a certain type of food) Disinhibited actions (ex. making inappropriate comments) Apathy, lack of motivation to do things Lack of insight (unaware of impact of symptoms on others) Impaired decision making	Associated with tau or AD pathology

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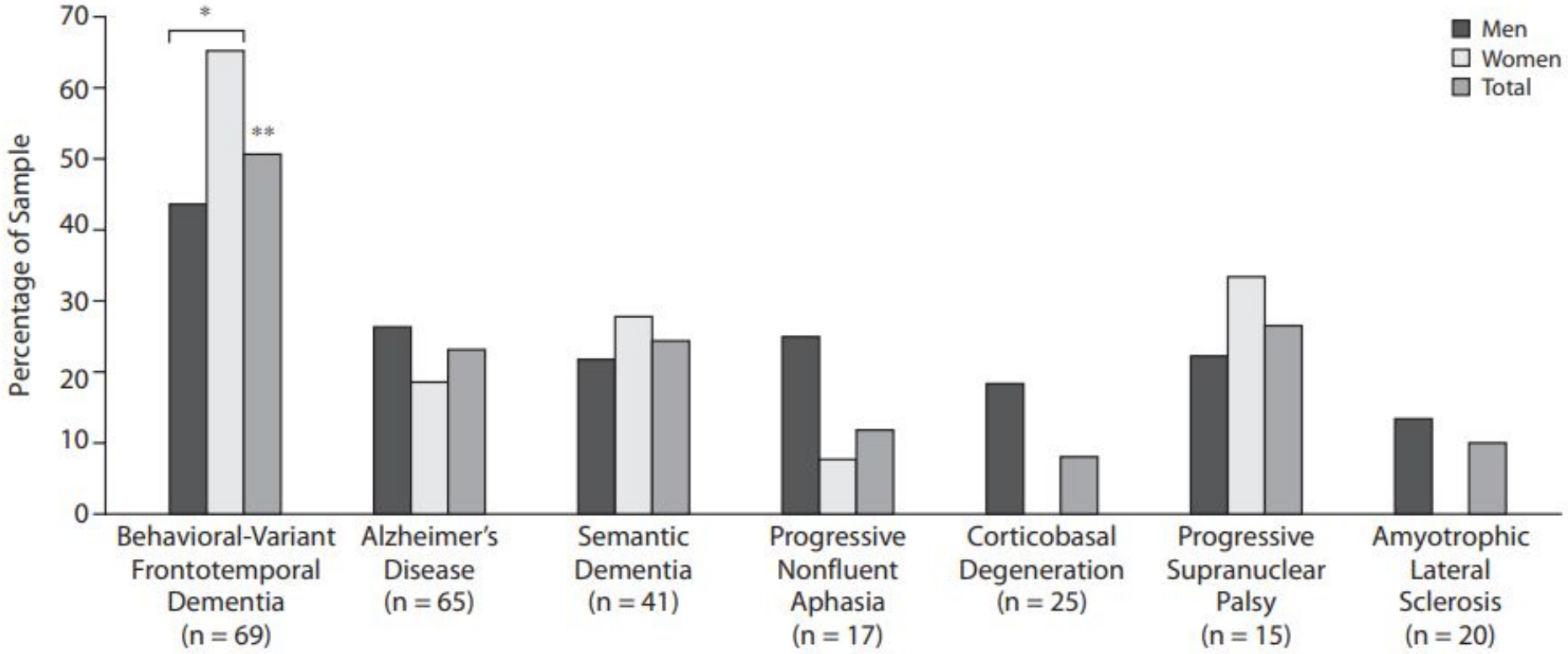
Misdiagnosis

Figure 1. Rates of Psychiatric Diagnosis Within Each Neurodegenerative Disease[a]



[a]Percentage of patients given a psychiatric diagnosis for symptoms that eventually led to a neurodegenerative disease diagnosis, separated by gender.
*$P < .05$ for comparison of rates of psychiatric diagnosis in men versus women with behavioral-variant frontotemporal dementia.
**$P < .01$ for rates of psychiatric diagnosis in patients with behavioral-variant frontotemporal dementia compared to patients with other forms of neurodegenerative disease.

Woolley JD, Khan BK, Murthy NK, Miller BL, Rankin KP. The diagnostic challenge of psychiatric symptoms in neurodegenerative disease. *The Journal of Clinical Psychiatry*. 2011;72(02):126-133. doi:10.4088/jcp.10m06382oli

Misdiagnosis

- FTD sometimes misdiagnosed as AD mainly because of executive function
  - Disorganization
  - Distraction
  - Poor Planning
  - Poor performance on cog testing (executive fxn)

Woolley JD, Khan BK, Murthy NK, Miller BL, Rankin KP. The diagnostic challenge of psychiatric symptoms in neurodegenerative disease. *The Journal of Clinical Psychiatry*. 2011;72(02):126-133. doi:10.4088/jcp.10m06382oli

Self Assessment Question

When does FTD disease onset usually occur?

A. In the 2nd decade of life
B. In the 6th decade of life
C. In the 9th decade of life
D. In the 10th decade of life

Self Assessment Question

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Genetics of FTD

- A family history of dementia or psychiatric conditions is present in **40% of patients**, but without a clear inheritance pattern

- Researchers have identified three genes that account for the majority of mutation-associated hereditary FTD cases
  - C9orf72
  - Progranulin (GRN)
  - Microtubule associated protein tau (MAPT)

- Clinical trials for anti-tau drugs, progranulin-elevating therapies, and compounds to block the dipeptide repeat proteins in *C9ORF72* are underway
  - AFTD - The Association for Frontotemporal Degeneration (theaftd.org) is a great resource for ongoing clinical trials that are actively recruiting

Huang J. Overview of cerebral function - neurologic disorders. Merck Manuals Professional Edition. https://www.merckmanuals.com/professional/neurologic-disorders/function-and-dysfunction-of-the-cerebral-lobes/overview-of-cerebral-function#v1033945. Published June 2020. Accessed August 2, 2021.
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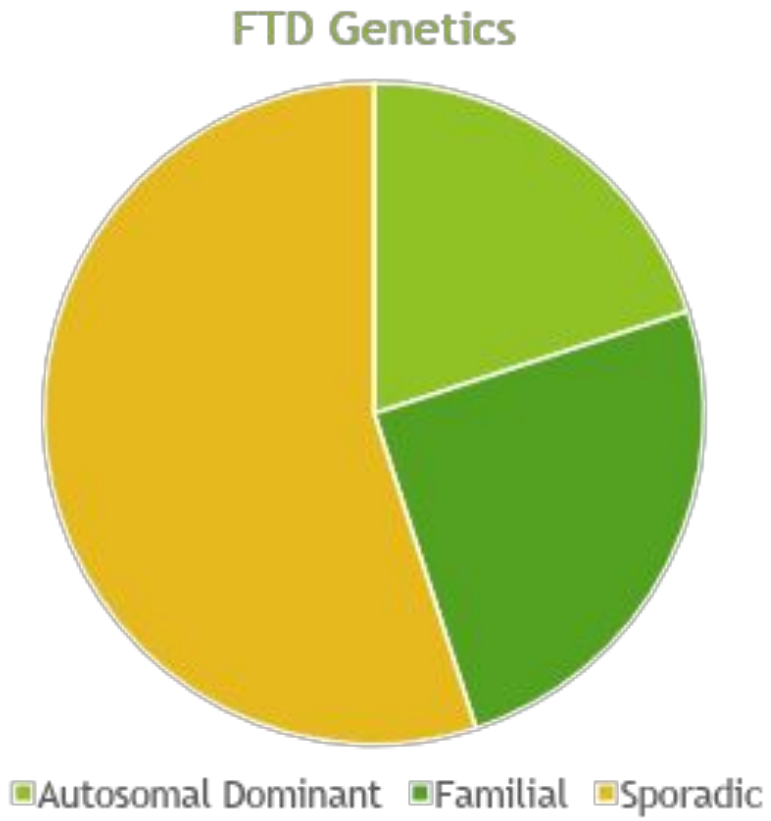
Is FTD Inherited?



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Management

- There are currently no effective disease-modifying treatments for FTD
- Both pharmacologic and nonpharmacologic interventions are aimed at ameliorating symptoms, particularly the behavioral symptoms of FTD.

Tsai RM, Boxer AL. Therapy and clinical trials in frontotemporal dementia: past, present, and future. *J Neurochem*.

Treatment for Behavioral Symptoms

Drug Class	Examples of Preferred Medications	Effect	Highest Level of Evidence
Antidepressants	Sertraline, Citalopram, Trazodone	May improve behavioral symptoms	RDBPC* trial
Antipsychotics	Quetiapine, Aripiprazole, risperidone, olanzapine	May improve behavioral symptoms	Case-Series

*randomized double blinded PCB controlled

Tsai RM, Boxer AL. Therapy and clinical trials in frontotemporal dementia: Past, present, and future. *Journal of Neurochemistry*. 2016;138:211-221. doi:10.1111/jnc.13640

Treatment for Behavioral Symptoms- Antipsychotics

- Clinicians must weigh the pros and cons of using antipsychotics in general
- There are no evidence-based analyses to assist the clinician in making these decisions
- The usual dictum is critical: “Start low and go slow” when any medication in the antipsychotic class is commenced, and titrate upward as necessary and tolerated
- Always start with nonpharmacological interventions
- Assess need for an antidepressant before starting antipsychotics

Tsai RM, Boxer AL. Therapy and clinical trials in frontotemporal dementia: past, present, and future. *J Neurochem*.
2016;138 Suppl 1(Suppl 1):211-221. doi:10.1111/jnc.13640

Treatment for Behavioral Symptoms- Nonpharmacological

- Nonpharmacologic interventions include
  - An exercise program
  - Modification of the home environment
  - Increased supervision
  - Physical therapy
  - Occupational therapy
  - Speech therapy
  - Behavioral modification techniques
  - Redirection replaces correction and explanation
  - **Primary caregiver support and respite**

Shinagawa S, Nakajima S, Plitman E, et al. Non-pharmacological management for patients with frontotemporal dementia:
a systematic review. *J Alzheimers Dis*. 2015;45(1):283-293. doi:10.3233/JAD-142109

Treatment for Cognitive Symptoms

Drug Class	Examples of Preferred Medications	Effect	Highest Level of Evidence
Acetylcholinesterase inhibitors	Donepezil, galantamine, rivastigmine	No improvements, may worsen behavioral symptoms	RDBPC trial
NMDA-antagonist	Memantine	No improvements, may worsen behavioral symptoms	RDBPC trial

*randomized double blinded PCB controlled

Tsai RM, Boxer AL. Therapy and clinical trials in frontotemporal dementia: Past, present, and future. *Journal of Neurochemistry*. 2016;138:211-221. doi:10.1111/jnc.13640

Treatment for Cognitive Symptoms- Donepezil

- Donepezil was studied in a 6 month, open label study of 24 FTD patients
- The groups did not differ on most variables at baseline or at six months; however, the donepezil group had greater worsening on the FTD Inventory
- Discontinuation of donepezil resulted in abatement of behavioral symptoms, which was replicated in other recent studies
- There were no changes in global cognitive performance or dementia severity; however, a subgroup of patients with FTD can experience worsening of symptoms with donepezil

Mendez MF, Shapira JS, McMurtray A, Licht E. Preliminary findings: behavioral worsening on donepezil in patients with frontotemporal dementia. *Am J Geriatric Psychiatry*.

Memantine in FTD

Purpose	To determine if memantine is effective in treating patients with FTD
Intervention	Patients diagnosed with FTD received 10mg of memantine twice daily for 26 weeks or placebo (initially titrated from 5mg daily) 42 patients in the placebo group 39 patients in the memantine group
Results	Change in Neuropsychiatric Inventory (NPI) score & Clinical Global Impression of Change (CGIC) NPI: mean difference from baseline to the end of the 26 weeks: 2.2 [95% CI (-3.9-8.3); P=0.47] → **not significant** CGIC: mean difference from baseline to the end of the 26 weeks: 0 [95% CI (-0.4-0.4); P=0.90] → **not significant**
Limitations	Recall bias with the NPI scoring tool Possible poor internal validity due different healthcare providers using the CGIC

Boxer A, et al. The Lancet . 2013Feb1;12(2):149-56.

Treatment for Movement Symptoms

Drug Class	Examples	Effect	Highest Level of Evidence
Dopamine Replacement	Carbidopa/Levadopa	Modest to no benefit	Case Series

Tsai RM, Boxer AL. Therapy and clinical trials in frontotemporal dementia: Past, present, and future. *Journal of Neurochemistry*. 2016;138:211-221. doi:10.1111/jnc.13640

Self Assessment Question

FTD can cause a decline in:

A. Touch sensation
B. Vision
C. Hearing
D. Ability to manage finances

Self Assessment Question

FTD can cause a decline in:

A. Touch sensation
B. Vision
C. Hearing
D. Ability to manage finances

Frank

- 65 years old M with PMH of CVA (L cerebellum), hyperlipidemia and insomnia comes for evaluation of new onset behavioral issues
- Partner reports that for the last 2 years he has not been himself
  - He lashes out easily
  - Has developed some new obsessions with cleanliness, organization and eating sweets
  - Has been touching or kissing strangers, urinating in public without concern
  - Makes offensive remarks in inappropriate contexts
  - He is otherwise independent functionally

Frank's Medication List

Drug	Indication
Donepezil 5 mg daily	Dementia
Memantine 10 mg daily	Dementia
Pantoprazole 20 mg daily	GERD
Acetaminophen 650 mg daily as needed for pain	Back Pain

Optimize Frank's Med List

- Keep patient on a daily routine
- Engage patient in sensory stimulation, music therapy, animal therapy, daily physical activity and cognitive exercises
- Care Partner/Caregiver should develop care team and respite plans
- Discontinue donepezil and memantine
- Start trazodone 25 mg qhs
  - I would also consider starting sertraline or citalopram, but start one new medication at a time

Multidisciplinary Team For FTD

- Primary Care doctor
- Neurologist
- Pharmacist
- Psychiatrist
- Geriatrician
- Movement disorder specialist
- Speech and language pathologist
- Physical therapist
- Occupation therapist
- Psychologist
- Social worker or case manager

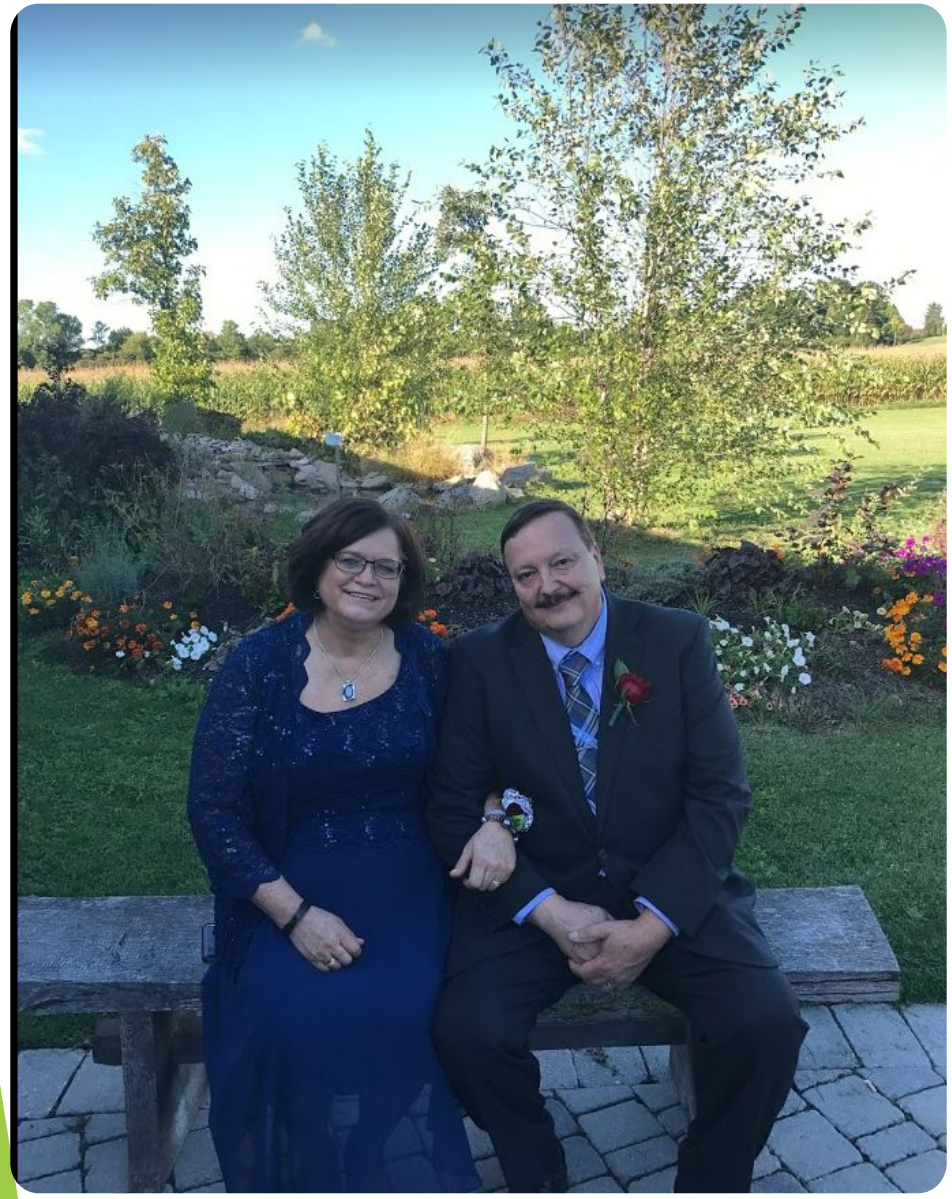
Counseling points for care partner/caregiver

- Adult Day services
- Pharmacist to review medications
- Health care proxy, Power of attorney, advance medical directives
- In home services
  - Make sure they are trained in FTD
    - Teepa Snow is an excellent source
- FTD support groups
- Keep a diary
  - Track changes between office visits

My Mom’s Journey

My Mom's Journey

- November 2019 increased anxiety and depression interfering with ability to work
  - Had her PCP take her out on FMLA
  - We suspected issue with depression
- January 2020 went to Aruba
  - That trip changed my perspective from depression to something more
  - Impulsive- taking more medications than she should
  - Overwhelmed- couldn't sit with my 9-month-old son
  - Combative- lashed out at me



My Mom's Story

- 6/11/20 confirmed on PET scan, checking all the boxes for bvFTD
- 64 years young
- Impulsive- wants to get in the hot tub- gets in fully clothed, swears a lot, & acts like a child
- Struggles to use a cell phone
- Can no longer handle finances
- Combative (mostly towards my Dad)

My Mom's Journey

- Rapid progression of symptoms
  - 1.5 years ago, helping with newborn grandson overnights
- Asked to leave day program after 2 visits
- Kicked out of assisted living after one week
- Had FTD trained aides coming into the home >40 hours per week
  - Too much to handle for my Dad

My Mom's Journey

- Now in SNF, doing well there, no longer walking
- Memory preserved, for now
- Hallucinations
  - Conversations
  - People

Lessons Learned

- Toll on the primary caregiver/care partner
  - Denial is prevalent. Watch for lack of engagement with information on FTD
  - Grief is recurring. Can exacerbate depression
- Encourage therapy, support groups
- Encourage taking time for own hobbies
- Encourage letting hired help provide solo care

- Educate caregiver/care partner on scams
  - Identify theft protection services
  - Credit Freeze
  - Lower credit card limits
- Help develop hobbies if they don't already have one
  - Have hobbies!

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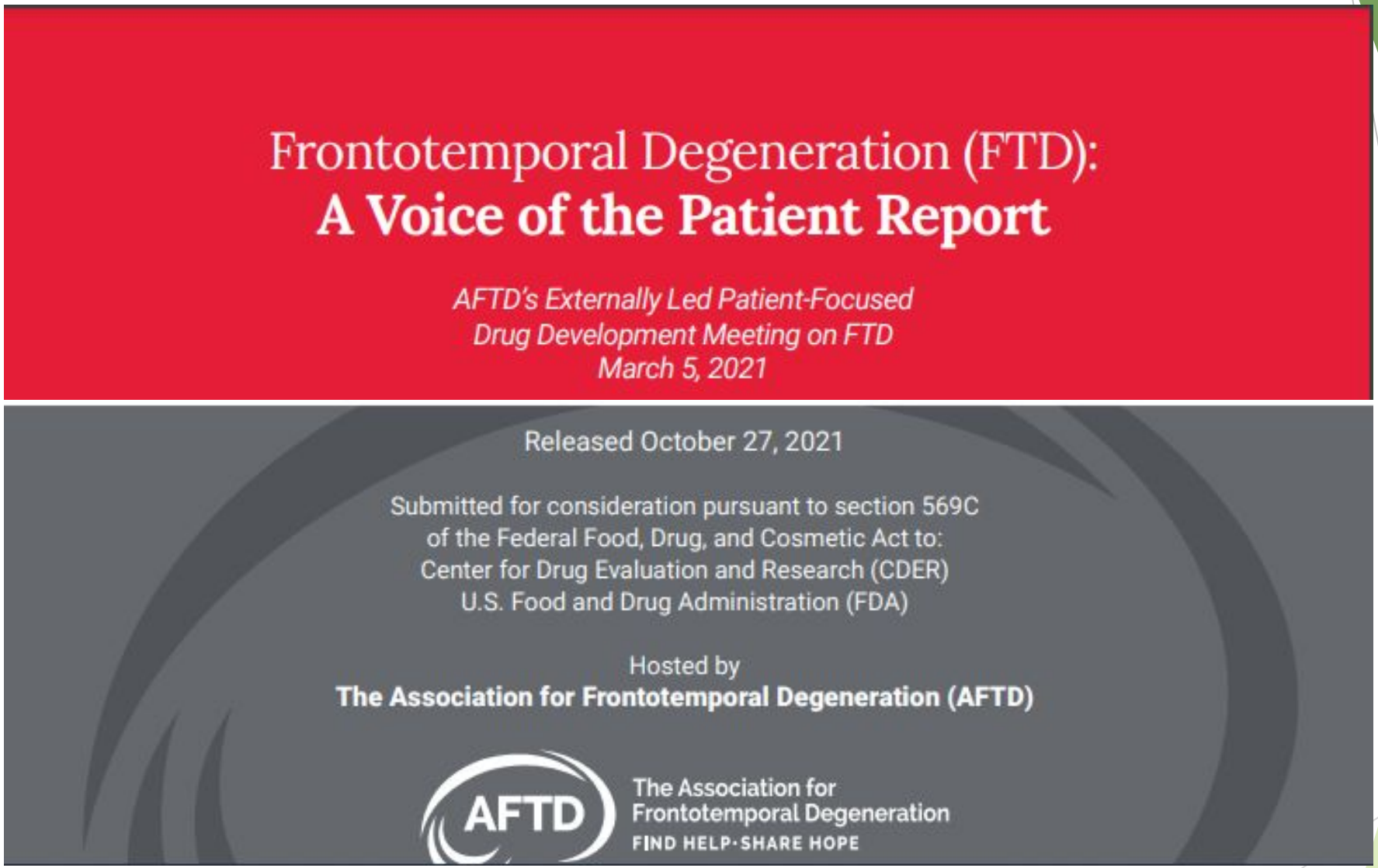

Dodge S, Dacks P, Niehoff D, et al. Frontotemporal Degeneration (FTD): A Voice of the Patient Report. AFTD. https://www.theaftd.org/. Published October 27, 2021. Accessed January 12, 2022.

Executive Summary: Key Themes

- Devastating impact of FTD symptoms
- Difficulty obtaining reliable FTD diagnoses
- Impact of familial FTD
- Lack of effective treatment for FTD
- Research participation

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Are FTD patients aware of their symptoms?

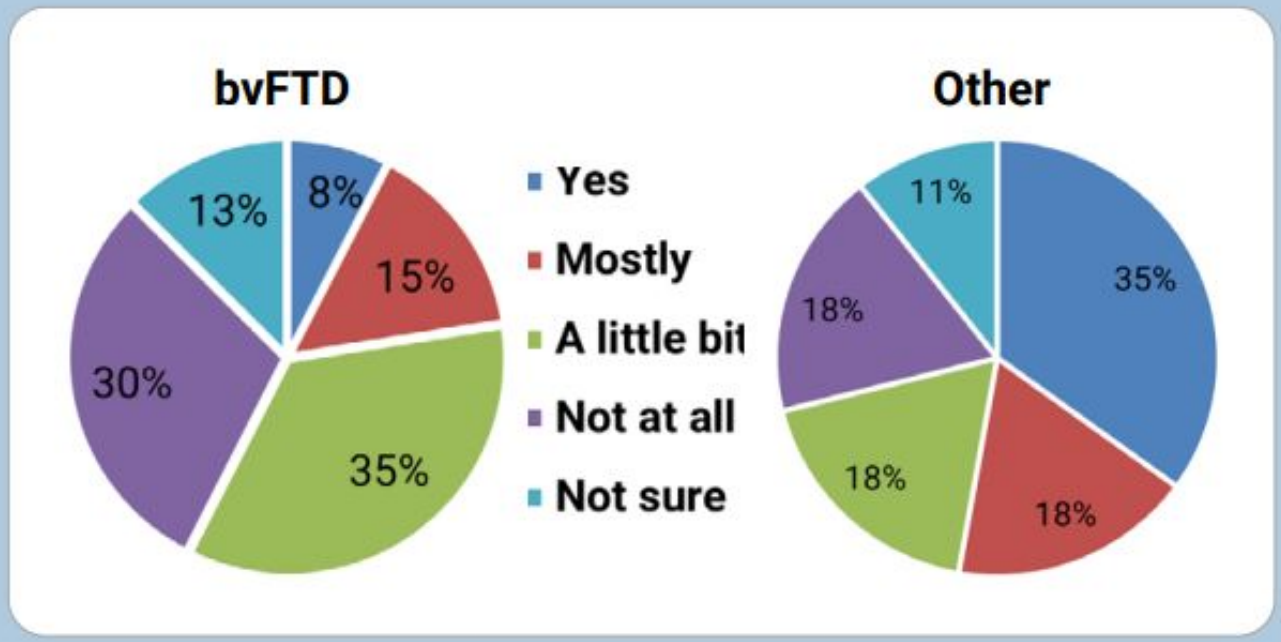

Figure 1. Are people diagnosed with FTD aware of their symptoms? *n= 549 Data from current care partners only. bvFTD group (n=369) includes diagnoses of behavioral variant frontotemporal degeneration and Pick's disease. Other group (n=180) includes PPA (svPPA, nfvPPA, lvPPA), PSP, CBS/ CBD, FTD with ALS or neuron disease, and unknown diagnoses. Data are available broken down by specific diagnoses, but the patterns represented in the graphs held within the smaller diagnostic groups.*

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Health Effects & Daily Impacts

Gail, a caller from Florida and former caregiver to her husband, who had bvFTD, noted:

"He was diagnosed at 50, though his symptoms started in his forties. It took us seven years to get a diagnosis."

Aisha from Georgia, who cares for her mother with bvFTD, described the impact of initial misdiagnoses:

"Diagnosis took a couple of years and ranged from generic stress to menopause-related anxiety and depression, during which time her symptoms remained untreated and continued to become more extreme."

Dawn from Illinois cares for her daughter, who started exhibiting changes in personality and behavior in her 20s, but spent two years seeking a diagnosis:

"She was diagnosed at the age of 29, but the actual [symptoms began at] 27. We didn't actually realize, because she was diagnosed with postpartum depression and then psychosis...due to her young age, it was not on their radar that she could have dementia."

Dan, who was diagnosed with bvFTD in 2019, described what was he was told by clinicians about the disorder:

"PET scans, MRIs, labs, and spinal tap confirmed sporadic behavior variant, frontotemporal dementia diagnosis. Treatment: none. Prognosis: fatal. Symptoms: progressive."

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First indication of something wrong

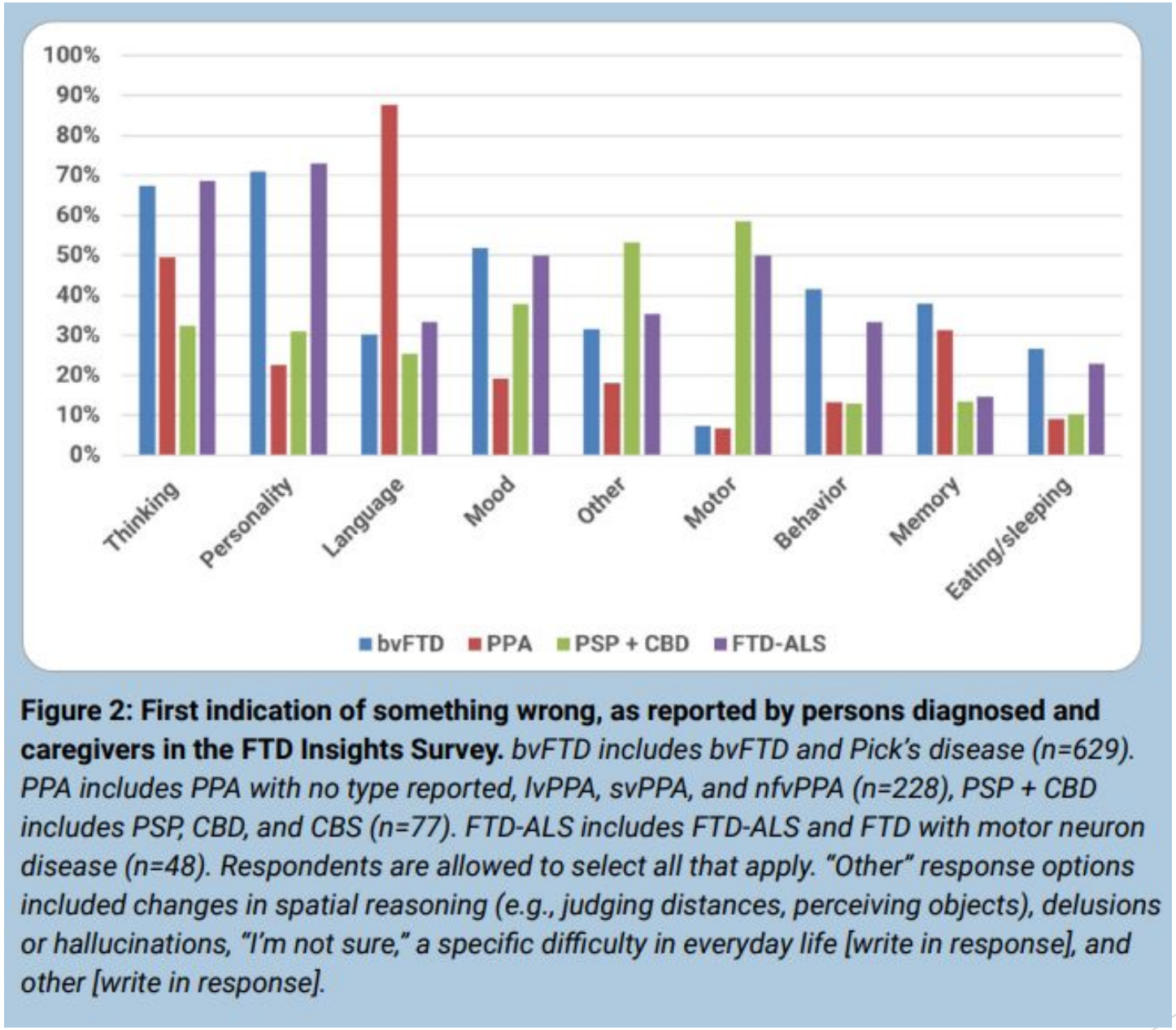

Figure 2: First indication of something wrong, as reported by persons diagnosed and caregivers in the FTD Insights Survey. *bvFTD includes bvFTD and Pick's disease (n=629). PPA includes PPA with no type reported, lvPPA, svPPA, and nfvPPA (n=228), PSP + CBD includes PSP, CBD, and CBS (n=77). FTD-ALS includes FTD-ALS and FTD with motor neuron disease (n=48). Respondents are allowed to select all that apply. "Other" response options included changes in spatial reasoning (e.g., judging distances, perceiving objects), delusions or hallucinations, "I'm not sure," a specific difficulty in everyday life [write in response], and other [write in response].*

Jennifer from Alabama noted how her PPA language symptoms have worsened:

"Sometimes when I try to speak, nothing comes out. Sometimes, it's guttural sounds that come out, or nothing at all. Even when the words are in my mind, I can't get them to come out of my mouth. Sometimes, it feels as if my mind is buffering."

Dodge S, Dacks P, Niehoff D, et al. Frontotemporal Degeneration (FTD): A Voice of the Patient Report. AFTD. https://www.theaftd.org/. Published October 27, 2021.

Current & Future Approaches to Treatment

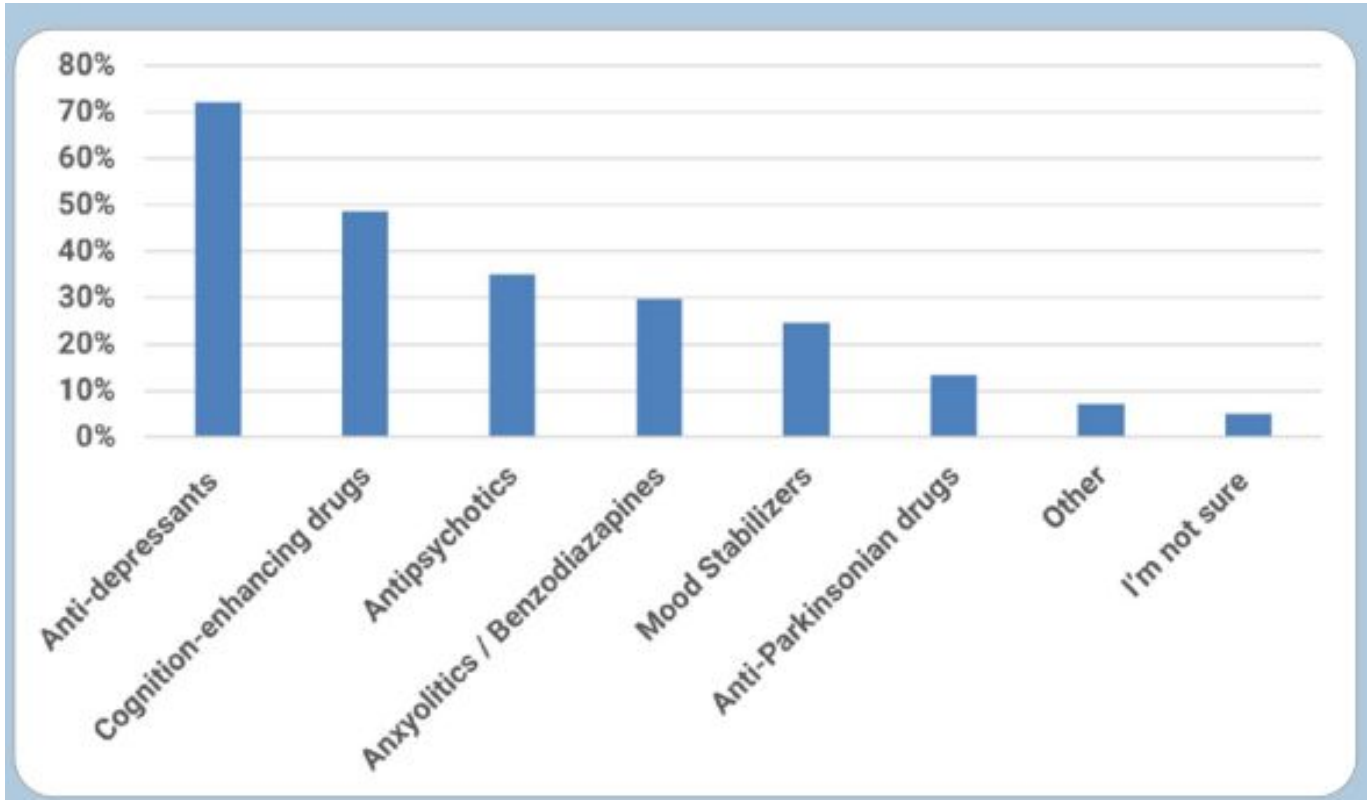

Figure 5. Past use of prescription medications as reported in the FTD Insights Survey. *n=841. Results include reports from individuals with an FTD diagnosis (n=89), current care partners (n=422), and past care partners (n=330) who indicated that they had taken prescription medications. Survey also included response option "I prefer not to say" (only endorsed in n=1). Free text from the "Other" category is available as well as data broken down by diagnosis, and reports from current care partners can be broken down by disease severity level. Respondents are allowed to select all that apply.*

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Cognition Enhancing Drugs

"Nearly half of FTD Insights Survey respondents indicated that they or their loved one had been prescribed cognition enhancing drugs, despite evidence to contraindicate their use, including lack of benefit and evidence that they exacerbate behavioral symptoms of the FTD disorders."

Dodge S, Dacks P, Niehoff D, et al. Frontotemporal Degeneration (FTD): A Voice of the Patient Report. AFTD. https://www.theaftd.org/. Published October 27, 2021. Accessed January 12, 2022.

Current & Future Approaches to Treatment

Dorian described a desperate and painful journey of changing from one ineffective medication to another:

"Meds offered short-lived and fluctuating relief and we were constantly adjusting the dosages every three months or less. All were imperfect tools, but the only tools we had. None impacting the underlying pathology. None of the medications Matthew was prescribed ever managed his impulse control."

Brandon from California became a primary caregiver for his mother when he was 19. A VCP genetic variant runs in his family:

"Her symptoms have constantly been progressing and changing so we've constantly been evaluating the medications that she's been taking, making adjustments to her dosages…It's a constant struggle to gauge the benefit of an antipsychotic or a mood stabilizer or a sleep medication with the negative effects that it has at the same time."

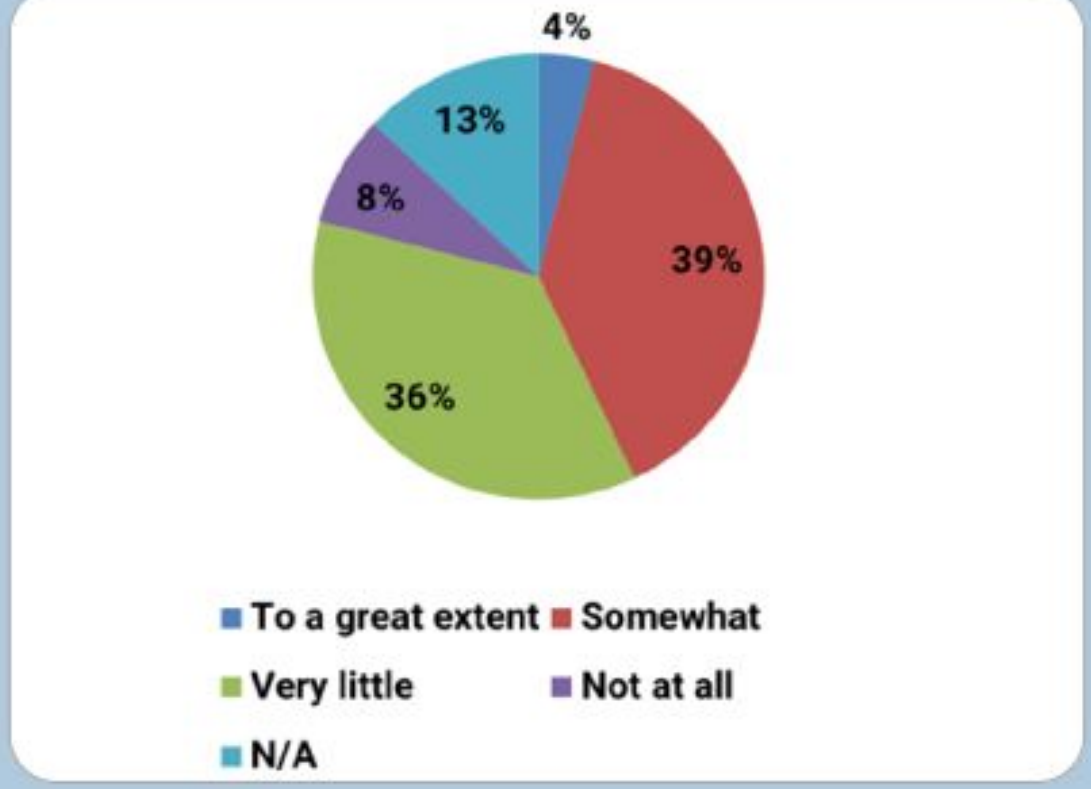
Halima, a geriatrician from Maryland spoke about her father, who has been diagnosed with PPA:

"When thinking about drawbacks of our current treatment approaches: side effects I think is the biggest, also number of pills, as well as questions of effectiveness."

Dodge S, Dacks P, Niehoff D, et al. Frontotemporal Degeneration (FTD): A Voice of the Patient Report. AFTD. https://www.theaftd.org/. Published October 27, 2021. Accessed January 12, 2022.

How well does current regimen control symptoms?

Figure 6. How well does the current regimen control important symptoms of the condition?
Asked of meeting participants during live polling, n=113



Dodge S, Dacks P, Niehoff D, et al. Frontotemporal Degeneration (FTD): A Voice of the Patient Report. AFTD. https://www.theaftd.org/. Published October 27, 2021. Accessed January 12, 2022.

Current & Future Approaches to Treatment

Cindy, who was diagnosed with bvFTD in 2011 at the age of 58, described how FTD has taken the lives of her grandmother, her mother, her aunt, and her uncle. It was not until several of her relatives had died from the disease that her neuropsychiatrist diagnosed Cindy with FTD and realized that autosomal dominantly inherited FTD was running through her family. Cindy fears for the children in her family:

"I would willingly participate in any research studies or drug trials, even if there is a risk to my life. I am that desperate to have this disease end with me… FTD has now taken a family member in every decade. I pray that this disease can end with me."

Hannah, a police officer in the U.K., illustrated the amplified trauma of genetic FTD:

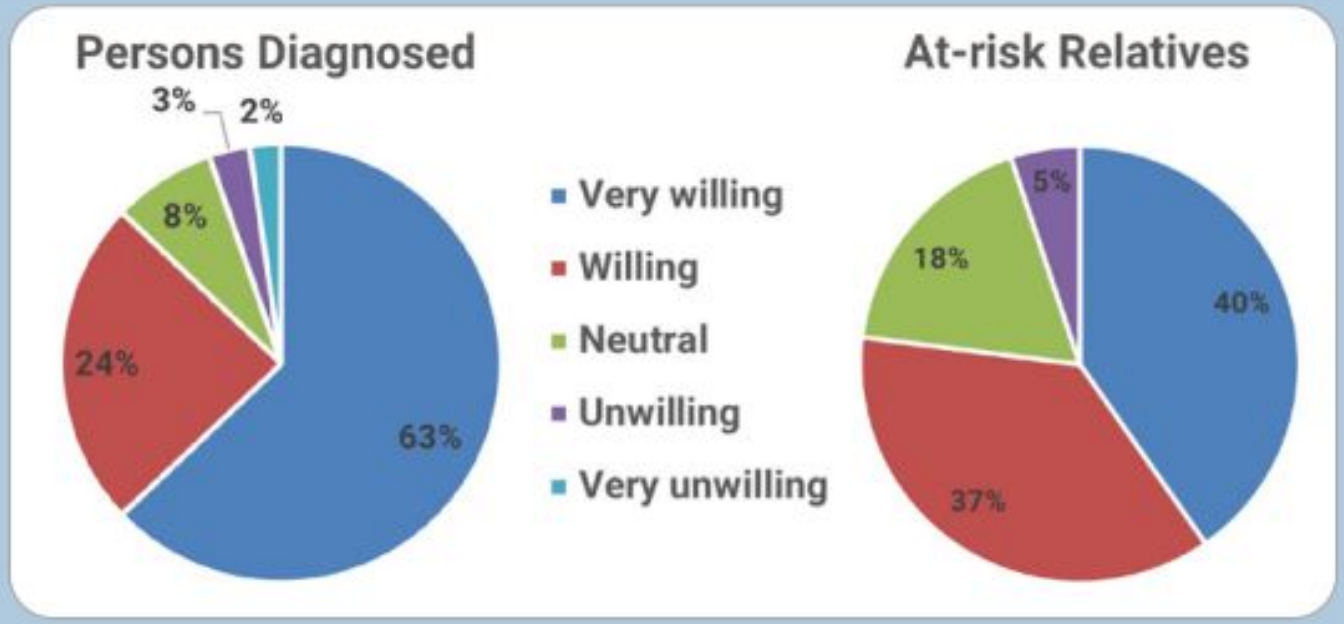
"With my dad's diagnosis came another blow, it was genetic. I debated over having the test, but I realized that I could live better with the result, whatever it was. Then, I was given the bad news. I am to suffer the same fate as my dad, giving my children a 50% chance too. I look at my children every day, as they run and play with their friends, knowing that I am responsible for this brutal condition potentially affecting them, and that kills me."

Dodge S, Dacks P, Niehoff D, et al. Frontotemporal Degeneration (FTD): A Voice of the Patient Report. AFTD. https://www.theaftd.org/. Published October 27, 2021. Accessed January 12, 2022.

Willingness to participate in research

Figure 7.

Figure 7. Rate your willingness to participate in a clinical trial to develop an FTD treatment. *n=328. Results broken down by those with a current FTD diagnosis (n=132) and at-risk relatives (n=196). Data are also available for current care partners. Results suggest that the majority (>75%) of individuals diagnosed with FTD and at-risk relatives would be willing to participate in clinical trials to develop an FTD treatment*



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Plea to clinical researchers

Aisha *summarized the urgent plea to clinical researchers and regulatory agencies:*

"Frontotemporal dementia is the cruelest, most unrelenting disease that completely strips its victims of their identity and robs families of a piece of their soul. We need relief, and it cannot come soon enough."

Dodge S, Dacks P, Niehoff D, et al. Frontotemporal Degeneration (FTD): A Voice of the Patient Report. AFTD. https://www.theaftd.org/. Published October 27, 2021. Accessed January 12, 2022.

In Conclusion

- FTD symptomatically complex
  - Symptoms come from anatomy
- FTD is pathologically, genetically complex
  - Multiple pathologies
  - Overlap with other syndromes
- Diagnosis is multimodal
  - Proper clinical characterization
  - Imaging
- Current treatments limited
- Future treatments will be aimed at specific proteinopathy for patients with genetic mutations

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AFTD Resources for Healthcare Providers

- Partners in FTD Care: quarterly publication focuses on a specific care issue or topic
  - www.theaftd.org/for-health-professionals/partners-in-ftd-care
  - Only Part of the Answer: Medications and FTD
    - www.theaftd.org/wp-content/uploads/2019/10/PinFTDcare_Newsletter_Fall_2019.pdf
- Clinical presentations of symptoms:
  - www.theaftd.org/for-health-professionals/clinical-features/
- Webinars and Annual Conference
- AFTD Helpline: 1-866-507-7222 or info@theaftd.org

For additional info, go to www.theaftd.org/for-health-professionals/partners-in-ftd-care/ or contact the AFTD Helpline.

AFTD Resources for Families

HelpLine: info@theaftd.org
866-507-7222

Websites: www.theaftd.org
www.aftdkidsandteens.org

Publications: *Help & Hope*
Partners in FTD Care
The Doctor Thinks It's FTD. Now What?
What About the Kids?
Understanding the Genetics of FTD

Grants: Respite, Travel to conferences, Quality of Life

Support www.theaftd.org/living-with-ftd/aftd-support-groups

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Questions?

References

Miller B, Llibre Guerra JJ. Frontotemporal dementia. *Psychopharmacology of Neurologic Disease*. 2019:33-45. doi:10.1016/b978-0-444-64012-3.00003-4

Godefroy V, Tanguy D, Bouzigues A, et al. Frontotemporal dementia subtypes based on behavioral INHIBITION DEFICITS. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*. 2021;13(1). doi:10.1002/dad2.12178

Hogan DB, Jetté N, Fiest KM, et al. The Prevalence and Incidence of Frontotemporal Dementia: a Systematic Review. *Can J Neurol Sci*. 2016;43 Suppl 1:S96-S109. doi:10.1017/cjn.2016.25

Fast Facts about Frontotemporal Degeneration. Association for Frontotemporal Degeneration. http://www.theaftd.org/wp-content/uploads/2009/02/Fast-Facts-Final-6-11.pdf. accessed August 2, 2021.

Ftd misdiagnosis. Memory and Aging Center. https://memory.ucsf.edu/dementia/ftd/ftd-misdiagnosis. Accessed August 17, 2021.

Huang J. Overview of cerebral function - neurologic disorders. Merck Manuals Professional Edition. https://www.merckmanuals.com/professional/neurologic-disorders/function-and-dysfunction-of-the-cerebral-lobes/overview-of-cerebral-function#v1033945. Published June 2020. Accessed August 2, 2021.

Rabins PV, et al. American Psychiatric Association practice guidelines: treatment of patients with Alzheimer's disease and other dementias. psychiatryonline 2007.

Woolley JD, Khan BK, Murthy NK, Miller BL, Rankin KP. The diagnostic challenge of psychiatric symptoms in neurodegenerative disease. *The Journal of Clinical Psychiatry*. 2011;72(02):126-133. doi:10.4088/jcp.10m06382oli

Tsai RM, Boxer AL. Therapy and clinical trials in frontotemporal dementia: past, present, and future. *J Neurochem*. 2016;138 Suppl 1(Suppl 1):211-221. doi:10.1111/jnc.13640

Shinagawa S, Nakajima S, Plitman E, et al. Non-pharmacological management for patients with frontotemporal dementia: a systematic review. *J Alzheimers Dis*. 2015;45(1):283-293. doi:10.3233/JAD-142109

Mendez MF, Shapira JS, McMurtray A, Licht E. Preliminary findings: behavioral worsening on donepezil in patients with frontotemporal dementia. *Am J Geriatr Psychiatry*. 2007;15(1):84-87. doi:10.1097/01.JGP.0000231744.69631.33

Boxer A, et al. The Lancet . 2013Feb1;12(2):149–56.