NAPA Advisory Council Meeting

Research on ADRD: Frontotemporal Lobar Degeneration

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Disclosures

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Frontotemporal Lobar Degeneration
Outline

- Terminology
- Epidemiology
- Impact
- Diagnosis
- Syndromes, Pathologies and Genetics
- ADRD Research Recommendations for FTLD
- Progress and Gaps on Recommendations
- Resources and Programs
- Considerations for Governmental Agencies

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Frontotemporal Lobar Degeneration
Terminology

Frontotemporal dementias (FTD)

- Behavioral variant frontotemporal dementia (bvFTD)
- Primary progressive aphasia (PPA)
  - Semantic variant PPA (svPPA)
  - Nonfluent/agrammatic variant PPA (nfvPPA)

Frontotemporal lobar degeneration (FTLD)

- Spectrum of pathologies that are manifested clinically by syndromes associated with prominent frontal and/or temporal dysfunction
- Primary pathologic entities
  - Tauopathies – reflect pathology associated with tau protein dysfunction
  - TDPopathies – reflect pathology associated with TDP-43 protein dysfunction

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Frontotemporal Lobar Degeneration
Epidemiology and Demographics

Epidemiology

- Incidence: 1-8/100,000 person-years
- Prevalence: 2-20/100,000
- Incidence/prevalence increases with age, plateaus around age 70
- Incidence/prevalence is similar to AD in those with symptoms preceding age 60

Demographics

- Male = female
- Seemingly uncommon in non-White populations - sampling biases, biologic differences, or other factors?

Turcano et al, 2020; Onyike and Diehl-Schmid, 2013; Hendriks et al, 2021; Nilsson et al, 2014; Heuer et al, 2020

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Frontotemporal Lobar Degeneration
Personal/Family/Societal Impact

Consequences of altered behavior and cognition

- fractured relationships with family members and friends
- divorce
- poor job performance and loss of one's job and the associated loss of income, medical insurance, and pension
- sexual indiscretion
- gambling or excessive spending
- financial devastation because of poor business decisions
- tragic accidents

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Frontotemporal Lobar Degeneration
Personal/Family/Societal Impact

Costs and quality of life

- costs > 2x reported costs for AD dementia
- caregivers rated the quality of life of their loved ones with bvFTD as “worse than dead”

Galvin et al, Neurology 2017

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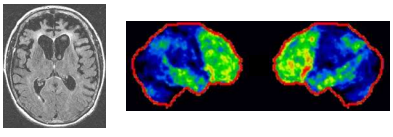
Frontotemporal Lobar Degeneration
Diagnosis

- **Clinical features**
- **Neuropsychological profile**
- **MRI +/- FDG-PET features**
- **Absense of alternate etiology**

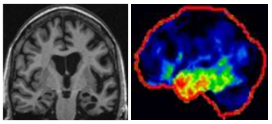
bvFTD
- disinhibition
- apathy
- loss of sympathy and empathy
- perseverative, stereotyped or compulsive / ritualistic behavior
- hyperorality and dietary changes
- attention/executive deficits on neuropsych
- imaging – frontal and/or temporal changes



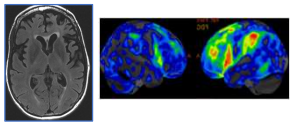
Rascovsky et al., Brain 2011

PPA
- prominent and early loss of language functioning with relative sparing in other domains
- language deficits on neuropsych
- imaging – frontal and/or temporal changes in the dominant (usually left) hemisphere

svPPA



nfvPPA



Gorno-Tempini et al., Neurology 2011

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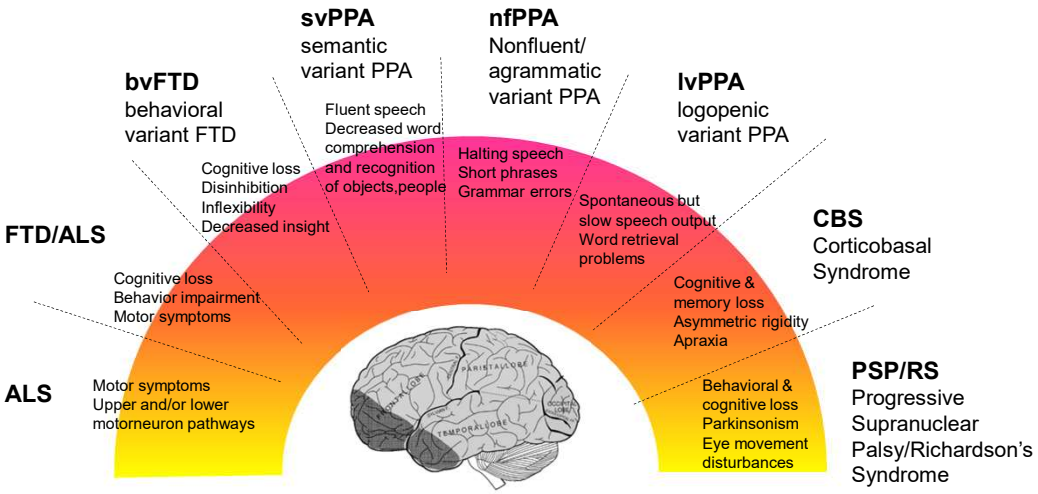
Frontotemporal Lobar Degeneration
Clinical Syndromes



Courtesy: Association for Frontotemporal Degeneration

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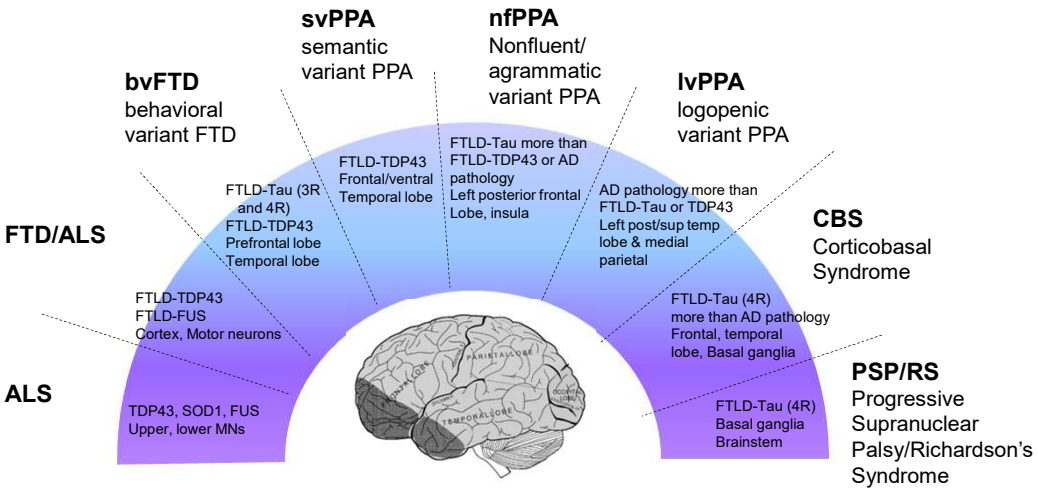
Frontotemporal Lobar Degeneration
Syndrome – Pathology Associations



Courtesy: Association for Frontotemporal Degeneration

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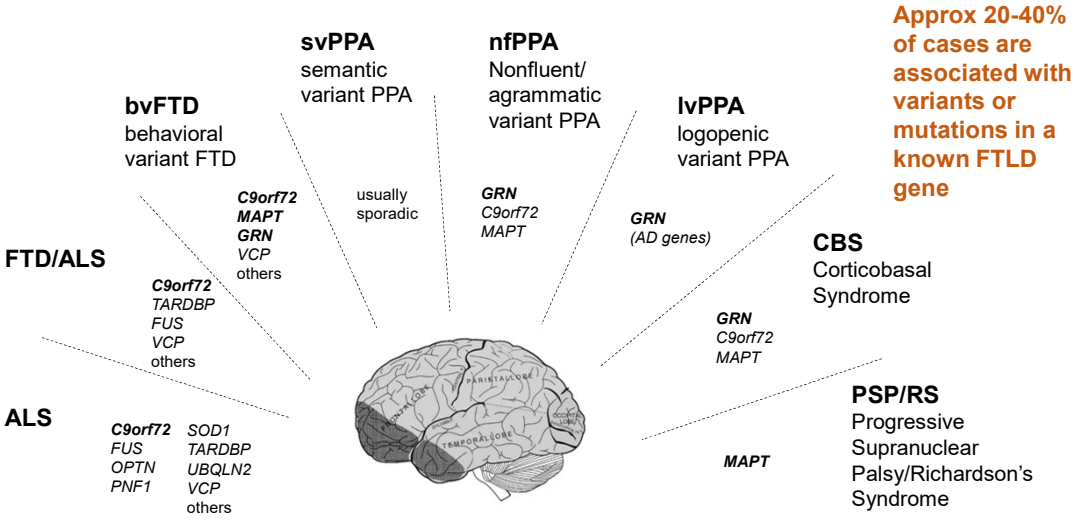
Frontotemporal Lobar Degeneration
Syndrome – Genetic Associations



Courtesy: Association for Frontotemporal Degeneration

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2022 NAPA ADRD Summit – Research Recommendations for FTLD

- Recommendation 1 – Priority 1. Understand FTD epidemiology and genetics in diverse populations, including how socioeconomic and ethnocultural status affects disease risk and manifestations. (1 - 5 years)
- Recommendation 2 – Priority 2. Develop an array of FTD biomarkers for diagnosis, prediction, disease monitoring, target engagement, and patient stratification for clinical trials. (2 - 7 years)
- Recommendation 3 – Priority 3. Accelerate the evaluation of novel FTD treatments by developing new clinical trial resources and FTD-specific designs, and by conducting new prevention and treatment trials. (1 - 5 years)
- Recommendation 4 - Priority 4. Identify overlapping pathogenic mechanisms between FTD and other neurodegenerative disorders and syndromes. (2 - 7 years)
- Recommendation 5 – Priority 1. Advance understanding of FTD and identify therapeutic targets through the creation, validation, and use of pre-clinical and translational tools and resources. (7 - 10 years)
- Recommendation 6 – Priority 2. Accelerate pre-clinical disease-modifying and symptomatic therapeutic development in FTD. (2 - 7 years)
- Recommendation 7 – Priority 3. Elucidate the mechanisms of cell type vulnerability and cell-intrinsic and – extrinsic effects on FTD pathogenesis, with the goal of accelerating development of therapeutic targets. (3 - 10 years)
- Recommendation 8 – Priority 4. Define genetic and molecular modifiers of FTD (including in diverse populations). (3 - 10 years)

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Progress and Gaps Regarding the ADRD Recommendations for FTLD

Recommendation 1 – Priority 1. Understand FTD <u>epidemiology and genetics in diverse populations</u>, including how socioeconomic and ethnocultural status affects disease risk and manifestations.

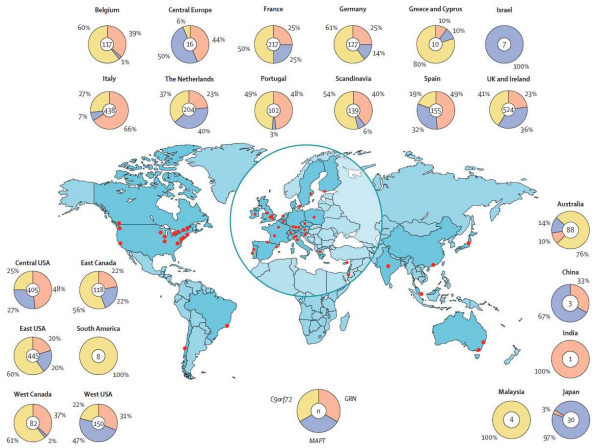
<u>Sporadic + familial FTLD in the US</u>

Primary clinical diagnosis, most recent visit	Race								Non-White
	WHITE	Black or AfricanAmerican	American Indianor Alaska Native	Native Hawaiianor Pacific Islander	Asian	Multiracial	Unknown or ambiguous	All	
Progressive supranuclear palsy (PSP)	250	7	0	2	16	0	8	283	9%
Corticobasal degeneration (CBD)	309	5	1	0	6	8	3	332	6%
FTLD with motor neuron disease (e.g., ALS)	58	0	0	0	1	1	1	61	3%
FTLD, other (including bvFTD and PPA)	2155	53	1	2	51	38	37	2337	6%

Primary clinical diagnosis, most recent visit	Hispanic ethnicity			Hispanic
	NO	Yes	Unknown	All	
Progressive supranuclear palsy (PSP)	269	13	1	283	5%
Corticobasal degeneration (CBD)	321	11	0	332	3%
FTLD with motor neuron disease (e.g., ALS)	57	4	0	61	7%
FTLD, other (including bvFTD and PPA)	2220	93	24	2337	4%

NACC database accessed 1/15/24

<u>Genetic FTLD - international</u>



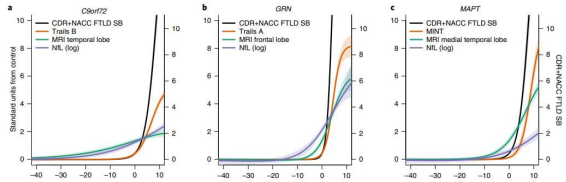
Moore et al, Lancet Neurol 2019

Progress and Gaps Regarding the ADRD Recommendations for FTLD

Recommendation 2 – Priority 2. Develop an array of FTD <u>biomarkers</u> for diagnosis, prediction, disease monitoring, target engagement, and patient stratification for clinical trials.

Current 'reasonably-established' measures and biomarkers for diagnosis and/or tracking

- CDR® plus NACC FTLD module scale
- Neuropsychological measures
- Volumetric MRI
- Plasma neurofilament light chain (Nfl)



Presymptomatic prevention trial (CDR+NACC-FTLD Global = 0)

Genetic group	Estimated number of eligible participants	Inclusion criteria	Primary endpoint: sample size estimates (50% treatment effect)							
			CDR+NACC-FTLD-SB		Neuropsychological tests		NfL (log)		MRI volume	
			2 yr	4 yr	2 yr	4 yr	2 yr	4 yr	2 yr	4 yr
C9orf72 MRI = temporal NP = Trails B	171	All CDR 0	>10,000	4,994	>10,000	6,784	3,397	699	1,639	394
	13	CDR 0 and NfL (log) > 3	582	334	1,113	386	>10,000	638	537	173
	38	CDR 0 and DA > −5	508	224	657	184	527	153	424	119
	20	CDR 0 and DA > −2.5	266	111	364	96	439	123	402	102
GRN MRI = frontal NP = Trails A	168	All CDR 0	3,144	1,526	3,844	1,576	684	271	826	459
	7	CDR 0 and NfL (log) > 3	250	179	250	140	158	51	71	46
	26	CDR 0 and DA −5	297	182	267	130	99	**30**	52	**27**
	10	CDR 0 and DA −2.5	182	104	159	79	84	26	37	**24**
MAPT MRI = MTL NP = MINT	94	All CDR 0	7,073	2,733	>10,000	3,741	3,059	802	1,492	526
	4	CDR 0 and NfL (log) > 3	283	188	373	220	>10,000	501	147	72
	19	CDR 0 and DA −5	362	190	641	265	595	149	108	39
	14	CDR 0 and DA −2.5	191	97	311	134	438	117	72	**24**

Early symptomatic treatment trial (all CDR+NACC-FTLD Global = 1 enriched with 0 and 0.5 participants)

Genetic Group	Estimated number of eligible participants	Inclusion criteria	Primary endpoint: sample size estimates (50% treatment effect)							
			CDR+NACC-FTLD-SB		Neuropsychological tests		NfL (log)		MRI volume	
			1.5 yr	2 yr	1.5 yr	2 yr	1.5 yr	2 yr	1.5 yr	2 yr
C9orf72 MRI =temporal NP = Trails B	94	ALL CDR 0.5 and 1	188	129	340	203	811	483	639	367
	37	All CDR 1 and (CDR 0 and 0.5 if NfL > 3)	161	115	370	222	1,806	782	645	358
	83	All CDR 1 and (CDR 0 and 0.5 if DA > −2.5)	176	124	400	207	740	423	678	360
	67	All CDR 1 and (CDR 0 and 0.5 if DA > 0)	117	**79**	275	161	628	384	669	359
GRN MRI = frontal NP =Trails A	67	ALL CDR 0.5 and 1	**76**	**66**	115	**79**	133	**76**	**44**	**30**
	33	All CDR 1 and (CDR 0 and 0.5 if NfL > 3)	97	84	124	92	182	110	49	**36**
	48	All CDR 1 and (CDR 0 and 0.5 if DA > −2.5)	79	68	105	74	127	75	**36**	**26**
	38	All CDR 1 and (CDR 0 and 0.5 if DA > 0)	**39**	**32**	62	**41**	124	72	**32**	**22**
MAPT MRI = MTL NP = MINT	43	ALL CDR 0.5 and 1	175	136	300	196	845	437	124	74
	11	All CDR 1 and (CDR 0 and 0.5 if NfL > 3)	89	66	138	91	1,719	769	95	59
	43	All CDR 1 and (CDR 0 and 0.5 if DA > −2.5)	164	120	244	163	779	419	109	63
	31	All CDR 1 and (CDR 0 and 0.5 if DA > 0)	96	66	150	104	627	359	83	48

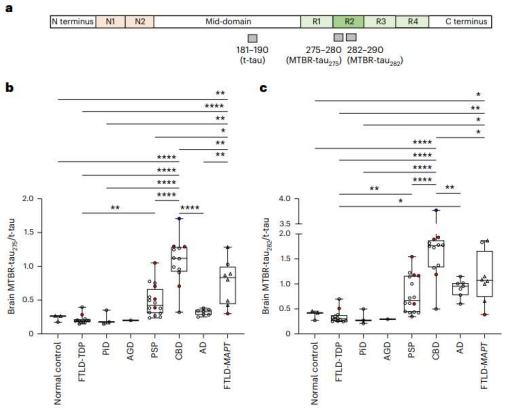
Staffaroni et al, Nature Med 2022

Progress and Gaps Regarding the ADRD Recommendations for FTLD

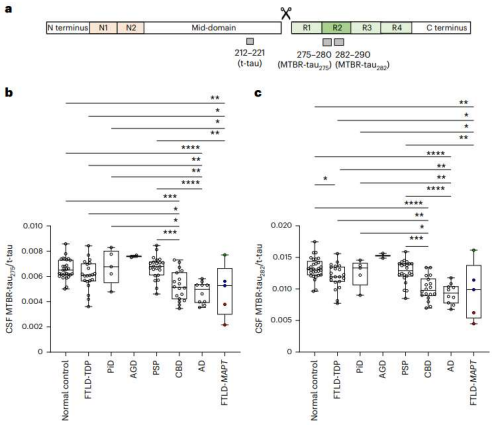
Recommendation 2 – Priority 2. Develop an array of FTD biomarkers for diagnosis, prediction, disease monitoring, target engagement, and patient stratification for clinical trials.

Encouraging findings for a 4 repeat tau-specific biomarker

4R-specific insoluble brain MTBR-tau is enriched in CBD, FTLD-*MAPT*, AD and PSP



4R-specific CSF MTBR-tau decreases in CBD, FTLD-*MAPT* and AD



Horie et al, Nature Med 2022

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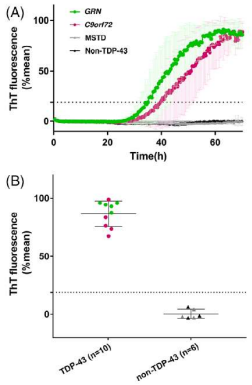
Progress and Gaps Regarding the ADRD Recommendations for FTLD

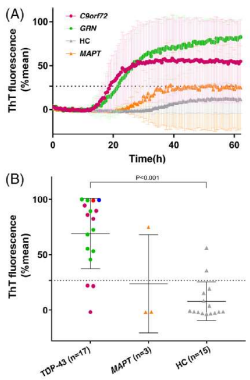
Recommendation 2 – Priority 2. Develop an array of FTD biomarkers for diagnosis, prediction, disease monitoring, target engagement, and patient stratification for clinical trials.

Encouraging findings for a TDP-43-specific biomarker

TDP-43 seeding activity in frontal cortex of FTLD-TDP and non–FTLD-TDP



TDP-43 seeding activity in olfactory mucosa of FTLD-TDP and non–FTLD-TDP



Fontana et al, Alz & Dem 2023

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Progress and Gaps Regarding the ADRD Recommendations for FTLD

Recommendation 2 – Priority 2. Develop an array of FTD biomarkers for diagnosis, prediction, disease monitoring, target engagement, and patient stratification for clinical trials.

Major gaps/concerns

- No established blood or CSF marker that clearly distinguishes a primary tauopathy vs TDPopathy vs other for stratification, or for tracking progression
- Other than Nfl (which is a nonspecific marker of neurodegeneration), no clear blood or CSF marker that tracks with disease progression
- While volumetric MRI and FDG-PET measure disease progression reasonably well, they are markers of neurodegeneration and thus not direct markers of proteinopathy
- No established PET ligand for 4R- and 3R-predominant tau
- No established PET ligand for TDP pathology

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Progress and Gaps Regarding the ADRD Recommendations for FTLD

Recommendation 3 – Priority 3. Accelerate the evaluation of novel FTD treatments by developing new clinical trial resources and FTD-specific designs, and by conducting new prevention and treatment trials.

	Mechanism	Indication	Phase	ClinicalTrials.gov identifier	Status
Potential therapies for *GRN* haploinsufficiency					
Nimodipine	Calcium channel blocker	Frontotemporal lobar degeneration due to *GRN* haploinsufficiency	1	NCT01835665	Negative
FRM-0334	Histone deacetylase inhibitor	Frontotemporal lobar degeneration due to *GRN* haploinsufficiency	2	NCT02149160	Negative
AL001	Anti-sortilin antibody	Frontotemporal lobar degeneration due to *GRN* haploinsufficiency	2/3	NCT03987295, NCT04374136	Active
PBFT02	AAV1-based gene therapy	Frontotemporal lobar degeneration due to *GRN* haploinsufficiency	1	NCT04747431	Active
PR006	AAV9-based gene therapy	Frontotemporal lobar degeneration due to *GRN* haploinsufficiency	1	NCT04408625	Active
Potential therapies for *C9orf72* expansion					
BIIB078	Antisense oligonucleotide	Amyotrophic lateral sclerosis due to *C9orf72* expansion	1	NCT03626012	Active
AL001	Anti-sortilin antibody	Frontotemporal lobar degeneration due to *C9orf72* expansion	2/3	NCT03987295, NCT04374136	Active
LAM-002A	PIKfyve kinase inhibitor	Amyotrophic lateral sclerosis due to *C9orf72* expansion	2	NCT05163886	Active
TPN-101	LINE1 reverse transcriptase inhibitor	Amyotrophic lateral sclerosis due to *C9orf72* expansion, frontotemporal lobar degeneration due to *C9orf72* expansion	2	NCT04993755	Active
WVE-004	Antisense oligonucleotide	Amyotrophic lateral sclerosis due to *C9orf72* expansion, frontotemporal lobar degeneration due to *C9orf72* expansion	1/2	NCT04931862	Active
Metformin	Non-canonical translation inhibition	Amyotrophic lateral sclerosis due to *C9orf72* expansion, frontotemporal lobar degeneration due to *C9orf72* expansion	2	NCT04220021	Active
Symptomatic frontotemporal lobar degeneration treatments					
Oxytocin	Augmenting social apathy	Frontotemporal dementia	2	NCT01386333	Active
Transcranial direct current stimulation	Electrical current stimulation	Frontotemporal lobar degeneration due to *GRN* haploinsufficiency	NA	NCT02999282	Active
Transcranial magnetic stimulation	Magnetic field stimulation	Primary progressive aphasia, behavioural variant frontotemporal dementia	NA	NCT03406429	Active

	Mechanism	Indication	Phase	ClinicalTrials.gov identifier	Status
Tau directed therapies for tauopathies (frontotemporal lobar degeneration or Alzheimer's disease)					
Tilavonemab (ABBV-8E12)	Anti-tau antibody (N-terminus)	Progressive supranuclear palsy	2	NCT03413319	Negative
Gosuranemab (BIIB092)	Anti-tau antibody (N-terminus)	Alzheimer's disease; progressive supranuclear palsy; corticobasal degeneration, nonfluent variant primary progressive aphasia, traumatic encephalopathy syndrome, *MAPT* mutation	2; 2; 1	NCT03352557, NCT02658468, NCT03658135	Negative; Negative; Terminated
Zagotenemab (LY3303560)	Anti-tau antibody (N-terminus)	Alzheimer's disease	2	NCT03518073	Negative
Semorinemab (RO7105705)	Anti-tau antibody (N-terminus)	Alzheimer's disease	2	NCT03289143	Negative
UCB0107	Anti-tau antibody (mid domain)	Progressive supranuclear palsy	1	NCT04658199	Active
JNJ-63733657	Anti-p-tau217 antibody (mid domain)	Alzheimer's disease	1	NCT03375697	Active
Lu AF87908	Anti-tau antibody (C-terminus)	Alzheimer's disease	1	NCT04149860	Active
BIIB076	Anti-tau antibody (monomer and filament)	Alzheimer's disease	1	NCT03056729	Active
AADvac1	Tau vaccine	Non-fluent variant primary progressive aphasia	1	NCT03174886	Active
TPI-287	Microtubule stabilisation	Alzheimer's disease, progressive supranuclear palsy, corticobasal degeneration	1	NCT01966666, NCT02133846	Negative
BIIB080	*MAPT* antisense oligonucleotide	Alzheimer's disease	2	NCT03186989	Active
NIO752	Antisense oligonucleotide	Progressive supranuclear palsy	1	NCT04539041	Active
TRx0237 (LMTM)	Tau aggregation inhibition	Behavioural variant frontotemporal dementia	3	NCT03446001	Negative
E2814	Tau aggregation inhibition	Alzheimer's disease	1/2	NCT04971733	Active
Salsalate	Tau acetylation inhibition	Progressive supranuclear palsy	1	NCT02422485	Negative
Lithium carbonate	Glycogen synthase kinase inhibitor	Behavioural variant frontotemporal dementia	2	NCT02862210	Active
RT001	Lipid oxidation inhibitor	Progressive supranuclear palsy	2	NCT04937530	Active
Young plasma transfusions	Alter peripheral cell signalling	Progressive supranuclear palsy	1	NCT02460731	Negative

Boeve et al, Lancet Neurol 2022

- There are 0 FDA-approved treatments for FTD/FTLD as of January 2024
- Many clinical trials are in progress (in addition to those listed in the tables above) or planned

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Progress and Gaps Regarding the ADRD Recommendations for FTLD

Recommendation 4 - Priority 4. Identify <u>overlapping pathogenic mechanisms</u> between FTD and other neurodegenerative disorders and syndromes.

Observations and gaps

- TDP-43 pathology is frequently present in those with AD, DLB and vascular dementia
- AD pathology may co-occur in those with typical FTLD pathology
- LBD pathology occurs with relative frequency in those with *GRN* mutations

The pathophysiologic and clinical significance of these and related associations are not clear

James et al, Brain 2016; Josephs et al, Acta Neuropathol 2019; Buciuc et al, NeuroImage Clin 2022; among many others

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Progress and Gaps Regarding the ADRD Recommendations for FTLD

Recommendation 5 – Priority 1. Advance understanding of FTD and identify therapeutic targets through the creation, validation, and use of <u>pre-clinical and translational tools and resources</u>.

A Comprehensive Resource for Induced Pluripotent Stem Cells from Patients with Primary Tauopathies

Celeste M. Karch,[1,*] Aimee W. Kao,[2] Anna Karydas,[2] Khadijah Onanuga,[1] Rita Martinez,[1] Andrea Argouarch,[2] Chao Wang,[1] Cindy Huang,[1] Peter Dongmin Sohn,[1] Kathryn R. Bowles,[1] Salvatore Spina,[3] M. Catarina Silva,[4] Jacob A. Marsh,[1] Simon Hsu,[1] Derian A. Pugh,[1] Nupur Ghoshal,[1] Joanne Norton,[1] Yadong Huang,[4] Suzee E. Lee,[2] William W. Seeley,[2] Panagiotis Theofilas,[3] Lea T. Grinberg,[3] Fermin Moreno,[5] Kathryn McIlroy,[5] Bradley F. Boeve,[6] Nigel J. Cairns,[7] John F. Crary,[9,10] Stephen J. Haggarty,[8] Justin K. Ichida,[11] Kenneth S. Kosik,[12] Bruce L. Miller,[2] Li Gan,[4] Alison M. Goate,[1,13] Sally Temple[1,13,*] Tau Consortium Stem Cell Group

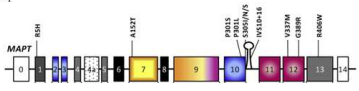

Table 2. Dermal Fibroblast Bank to Model Primary Tauopathies

MAPT	Classification	Clinical Presentation	Tau Isoform	Mean AAO*	Mean Disease Duration*	Fibroblasts	Families
A152T	PSP, CBD, FTLD-Tau	bvFTD	4R	57.5	N/A	8	N/A
P301L	FTLD-Tau	bvFTD	4R	52.6	6.7	13	3
S305I	FTLD-Tau/AGD	bvFTD	4R	39	2	2	1
IVS10+16	FTLD-Tau	bvFTD/AD	4R	49.1	10.3	4	1
V337M	FTLD-Tau	bvFTD	3R & 4R	51.5	15.4	4	2
G389R	FTLD-Tau	bvFTD	3R & 4R	39.8	2.5	3	1
R406W	FTLD-Tau	AD	3R & 4R	56.3	11.5	9	2
R406W/R406W	FTLD-Tau	bvFTD	3R & 4R	34	7	1	1
WT	PSP	PSP-S	4R	N/A	N/A	12	N/A
WT	CBD	CBS	4R	N/A	N/A	5	N/A
WT	PSP/CBD mixed	PSP-S/CBS/mixed	4R	N/A	N/A	10	N/A
WT	normal	N/A	N/A	N/A	N/A	69	N/A

Karch et al, Stem Cell Reports 2019

- This report is an example of many evolving tools and resources that are being used to advance understanding of FTD/FTLD

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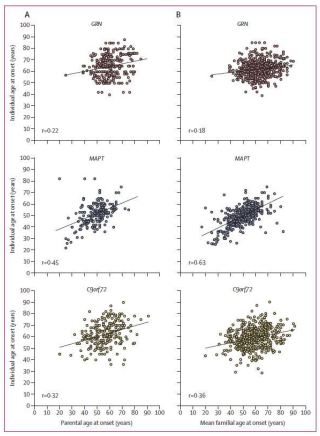
Progress and Gaps Regarding the ADRD Recommendations for FTLD

Recommendation 8 – Priority 4. Define genetic and molecular modifiers of FTD (including in diverse populations).



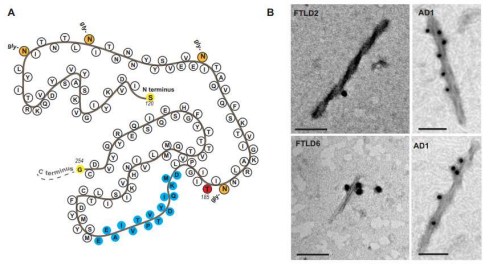
Moore et al, Lancet Neurol 2019

- Only modest correlation between individual and familial age of onset in genetic FTLD

The protective haplotype in *TMEM106B* is associated with:

- modifies penetrance/age of onset in those with *GRN* mutations and the *C9orf72* expansion
- reduced TDP-43 burden in the frontal cortex in those with FTLD-TDP pathology
- slowed progression of TDP-43 pathology in individuals without FTLD

Van Blitterswijk et al, Acta Neuropathol 2014; Yu et al, Neurology 2015; Perneel et al, Front Neurol 2023



Findings suggest that prevention of TMEM106B core accumulation is central to the mechanism by which the *TMEM106B* protective haplotype reduces disease risk and slows progression

Marks et al, Sci Transl Med 2024

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Progress and Gaps Regarding the ADRD Recommendations for FTLD

Recommendation 8 – Priority 4. Define genetic and molecular modifiers of FTD (including in diverse populations).

What are the additional genetic/molecular, environmental exposure and social factors that contribute to:

- Development of symptoms in sporadic FTLD?
- Penetrance, age of onset, and eventual phenotype in familial FTLD?
- Rate of progression in sporadic and familial FTLD?

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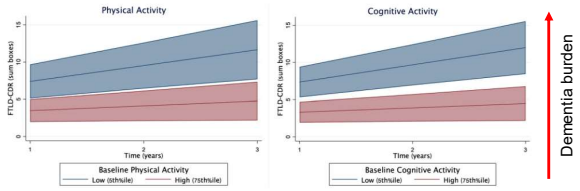
Progress and Gaps Regarding the ADRD Recommendations for FTLD

Related to Recommendation 8 – Define other modifiers of FTD

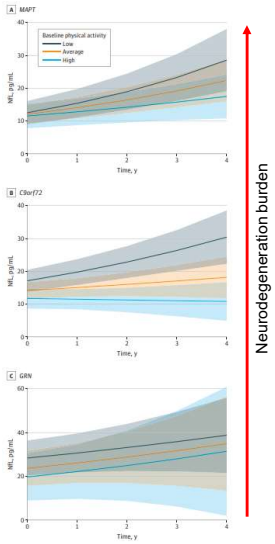


Casaletto et al, Alz & Dem 2020

- Increased physical and cognitive activity is associated with decreased longitudinal clinical burden in familial FTLD

Should a clinical trial involving physical +/- cognitive activities be developed for FTLD?

Should physical and cognitive activity be more strongly recommended in sporadic and familial FTLD?



- Increased physical activity is associated with decreased longitudinal Nfl rate in familial FTLD

Casaletto et al, JAMA Neurol 2023

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Frontotemporal Lobar Degeneration
Key Resources and Programs

NIH National Institute on Aging

NIH National Institute of Neurological Disorders and Stroke

NINDS Information on FTD
https://www.ninds.nih.gov/Disorders/All-Disorders/Frontotemporal-Dementia-Information-Page

National Institute on Aging – Alzheimer's Disease Research Center (ADRC) Program
https://www.nia.nih.gov/research/adc

National Alzheimer's Coordinating Center (NACC)
https://naccdata.org/

National Cell Repository for AD and Related Dementias (NCRAD)
https://ncrad.iu.edu/

Laboratory of NeuroImaging
https://loni.usc.edu/

ClinicalTrials.gov
https://clinicaltrials.gov/search?cond=Frontotemporal%20Dementia

The Association for Frontotemporal Degeneration
www.theaftd.org

Frontotemporal Dementia Disorders Registry
https://ftdregistry.org/

ARTFL LEFFTDS Longitudinal Frontotemporal Lobar Degeneration (ALLFTD) Program
www.allftd.org

Genetic FTD Initiative (GENFI) Program
www.genfi.org

FTD Prevention Initiative (FPI) Program
www.thefpi.org

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Frontotemporal Lobar Degeneration
Considerations for Governmental Agencies

Clinical considerations - encourage efforts to support patients/families

- Support care models (e.g., home health, respite care, skilled care facilities, etc.) that promote quality of life for patients/families while also keeping expenses reasonable/affordable
- Support efforts to cover tests that aid in diagnosis (e.g., novel blood and CSF markers, FDG-PET, future proteinopathy-specific PET ligands/scans, etc.)
- Support and expedite disability processing
- Protect and support individuals with known or suspected mutations (e.g., protection via GINA, coverage for preimplantation genetic testing and in vitro fertilization, etc.)

Research considerations

- Continue to support FTLD research as a high priority in the NAPA AD/ADRD portfolio

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