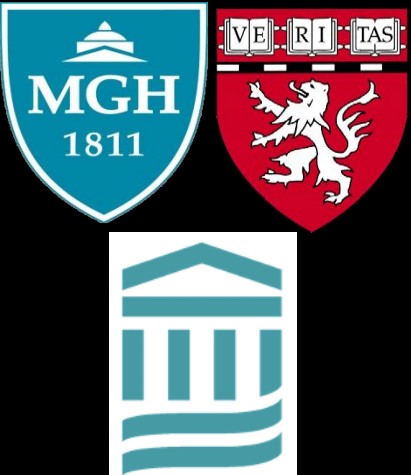




Painting by Kemon Sermos
(lived with frontal variant AD)



The Neuropsychiatry of Frontotemporal Dementias

MGB Neuropsychiatry CME Course 2026

Brad Dickerson, MD

Director, MGH FTD Unit & Imaging Core Leader, Mass Alz Dis Research Center

Disclosures

Data Safety Monitoring Board:

Lilly, Merck

Consulting:

Arkuda, Biogen, Cervomed, Eisai, Lantheus, Lilly,
Merck, Novo Nordisk, Quanterix,
Med Learning Group

Best Doctors.com, GrandRounds.com

Royalties/paid editorial duties:

Oxford University Press (*Dementia: Comprehensive Principles and Practice*, 2014)

Cambridge University Press (*Hodges' Frontotemporal Dementia*, 2016)

HIS WIFE SAID MIDLIFE CRISIS.

HIS THERAPIST SAID DEPRESSION.

HIS DOCTOR SAID ALZHEIMER'S.

NOBODY SAID FTD.

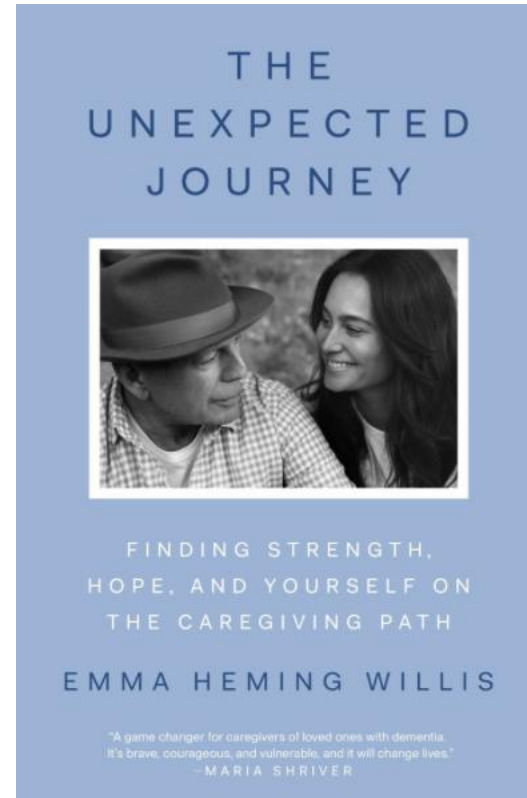
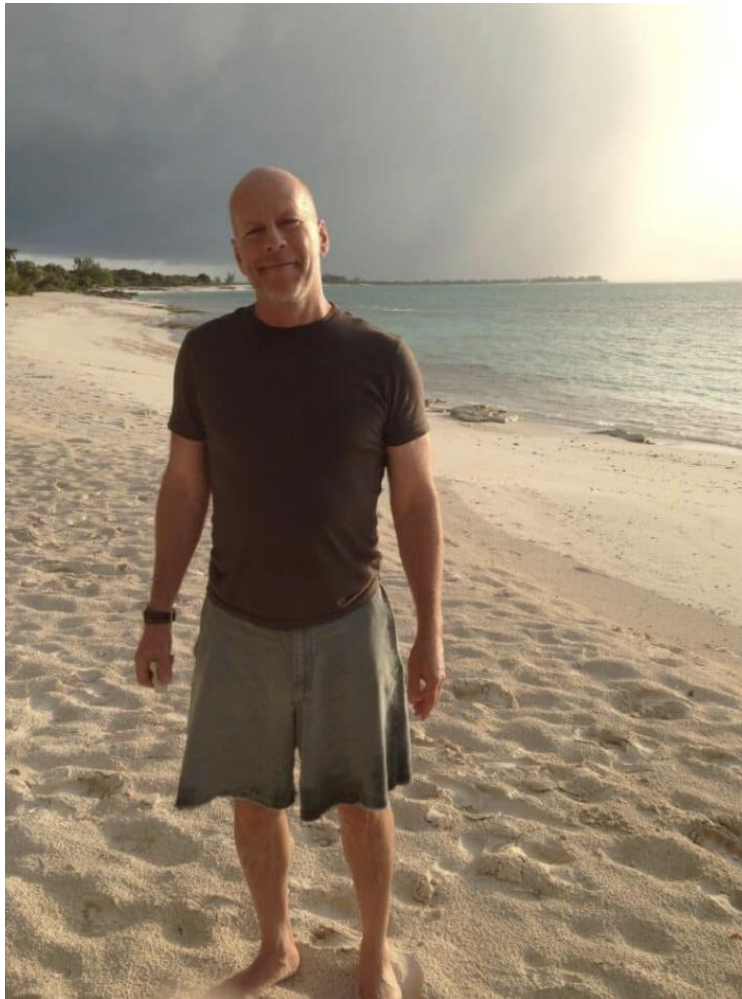


A Statement from the Willis Family

February 16, 2023



Since we announced Bruce's diagnosis of aphasia in spring 2022, Bruce's condition has progressed and we now have a more specific diagnosis: frontotemporal dementia (known as FTD). Unfortunately, challenges with communication are just one symptom of the disease Bruce faces. While this is painful, it is a relief to finally have a clear diagnosis.

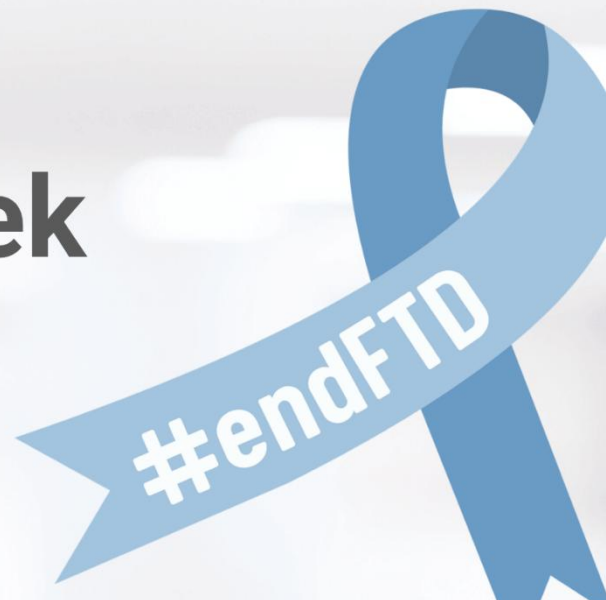


World FTD Awareness Week

Put a Spotlight on FTD

September 28 - October 4, 2026

[Learn More](#)



ISFTD ²⁰₂₆
PHILADELPHIA

15th International Conference on Frontotemporal Dementias

**October 8–11, 2026
Philadelphia, PA**

FTD: Demographics

- ~3rd most common neurodegenerative dementia
 - After AD and DLB
 - 5 - 15% of dementias
- Estimated to affect 50-150,000 Americans
- Typically early onset, often 50s – 60s
 - Most common early onset dementia
- Cases have been reported with onset as young as 20s, as old as 80s (MGH FTD Unit: 27 – 86)
- Up to 1/3 cases have positive family history

1. Cognitive Functional Status

Cognitively normal, Subjective Cognitive Concern, Mild Cognitive Impairment, Dementia

2. Cognitive-Behavioral Syndrome

nfvPPA, svPPA, SD, bvFTD, PSP, CBS, FTD-MND

Symptoms

History from patient, informant(s)

Signs

Office based cognitive testing, neurologic exam, psychiatric interview, neuropsychological testing

3. Neurodegenerative (or other) Brain Disease

FTLD tau, FTLD TDP43, AD, CVD, LBD, etc.

Abnormal in Brain Structure?

CT, MRI

Abnormal Brain Function?

FDG PET, SPECT, EEG

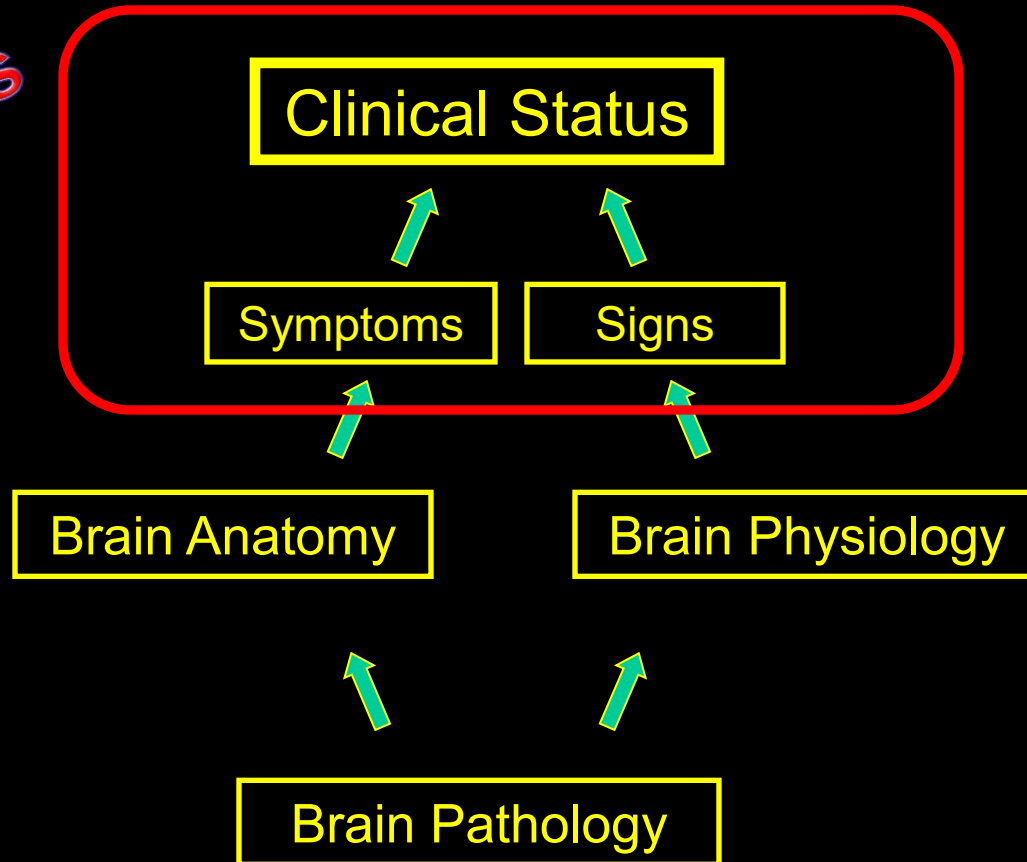
Molecular Brain Pathology

(Amyloid or Tau PET, CSF)

Atri & Dickerson et al.,
Alz & Dementia
2024

Approach to diagnosis

The illness



FTD: Diagnostic Criteria

- slowly progressive decline in behavior / cognition
- not better accounted for by another medical / neurologic / psychiatric disorder
- not a prominent episodic memory or visual/spatial impairment
- behavioral and aphasic variants
 - behavioral variant FTD (bvFTD)
 - Primary Progressive Aphasia (PPA) & its variants
- clinical diagnosis (“possible”)
 - functional / structural imaging as supportive feature (“probable”)

Diagnostic Criteria: bvFTD

- “Possible bvFTD” requires at least 3 of the following early in disease course
 - behavioral disinhibition
 - apathy / inertia
 - loss of sympathy / empathy
 - perseverative / stereotyped / compulsive behavior
 - hyperorality / dietary changes
 - neuropsychological profile: executive deficits with relative sparing of memory and visuospatial abilities
- “Probable bvFTD” additionally requires neuroimaging evidence of frontal or anterior temporal atrophy or hypometabolism

Diagnostic Criteria: PPA

- PPA Dx requires 3 features to be present
 - most prominent clinical feature is difficulty with language
 - language deficits are the principal cause of impaired daily function
 - aphasia is most prominent deficit at symptom onset and for the initial phases of illness
- Dx requires the *absence* of 4 features
 - pattern of deficits better accounted for by another nondegenerative nervous system or medical disorder
 - cognitive disturbance better accounted for by psychiatric dx
 - prominent initial episodic memory, visual memory, or visuoperceptual impairments
 - prominent initial behavioral disturbance

Diagnostic Criteria: PPA subtypes

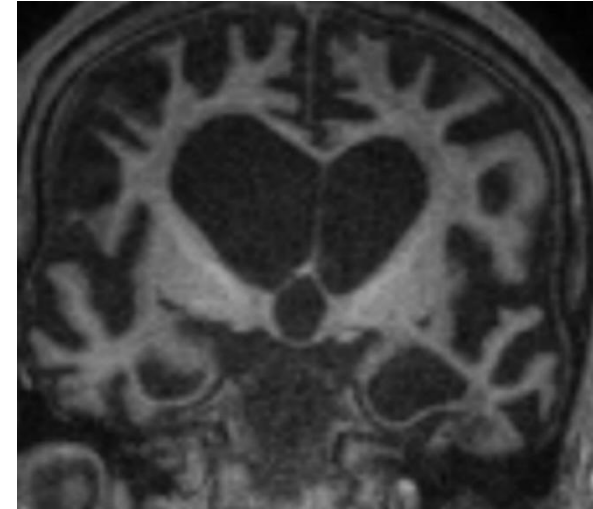
- Non-fluent variant PPA
 - Agrammatism, effortful & halting speech; impaired comprehension of grammatically complex sentences, spared single word comprehension and object knowledge
 - Fronto-insular atrophy/hypometabolism
 - Usually a type of FTLD (usually FTLD tau)
- Semantic variant PPA
 - Impaired naming and single-word comprehension; impaired object knowledge, surface dyslexia; spared repetition, speech production
 - Anterior temporal atrophy/hypometabolism
 - Usually a type of FTLD (TDP43 type C)
- Logopenic variant PPA
 - Impaired word retrieval, repetition; often with phonological errors in speech; spared single-word comprehension, motor speech, absence of frank agrammatism
 - Left posterior perisylvian/parietal atrophy/hypometabolism
 - Usually associated with **Alzheimer's disease** pathology, not FTLD

DSM5: Major/Mild Neurocognitive Disorders of the FTLD type

- Essentially full adoptions of international consensus criteria for bvFTD and PPA, lumped into one diagnostic category (FTLD) with two distinctions based on severity of functional impairment (major vs. minor)

The spectrum of dementias called FTD arise from the neurodegenerative diseases called FTLD

- Behavioral variant FTD
- Non-fluent/agrammatic variant PPA
- Semantic variant PPA
- Semantic dementia
- Progressive Supranuclear Palsy
- Corticobasal syndrome
- FTD with motor neuron disease
- [Dysexecutive/apathetic/amnesic syndromes]
- *Imaging-supported diagnostic criteria*



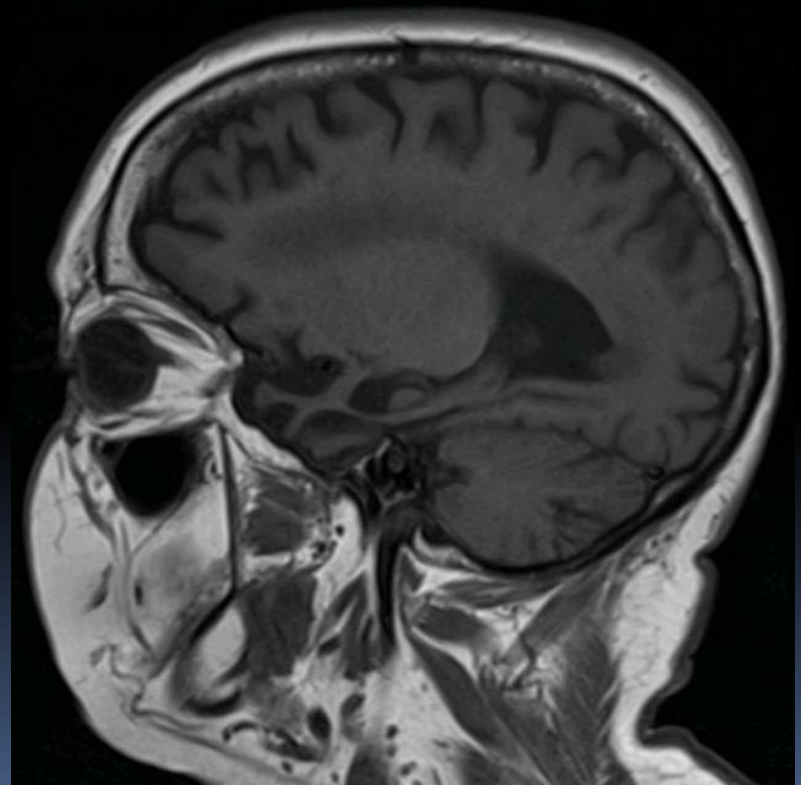
bvFTD: Structural Imaging Findings

MRI: focal atrophy of frontal and temporal lobes

normal

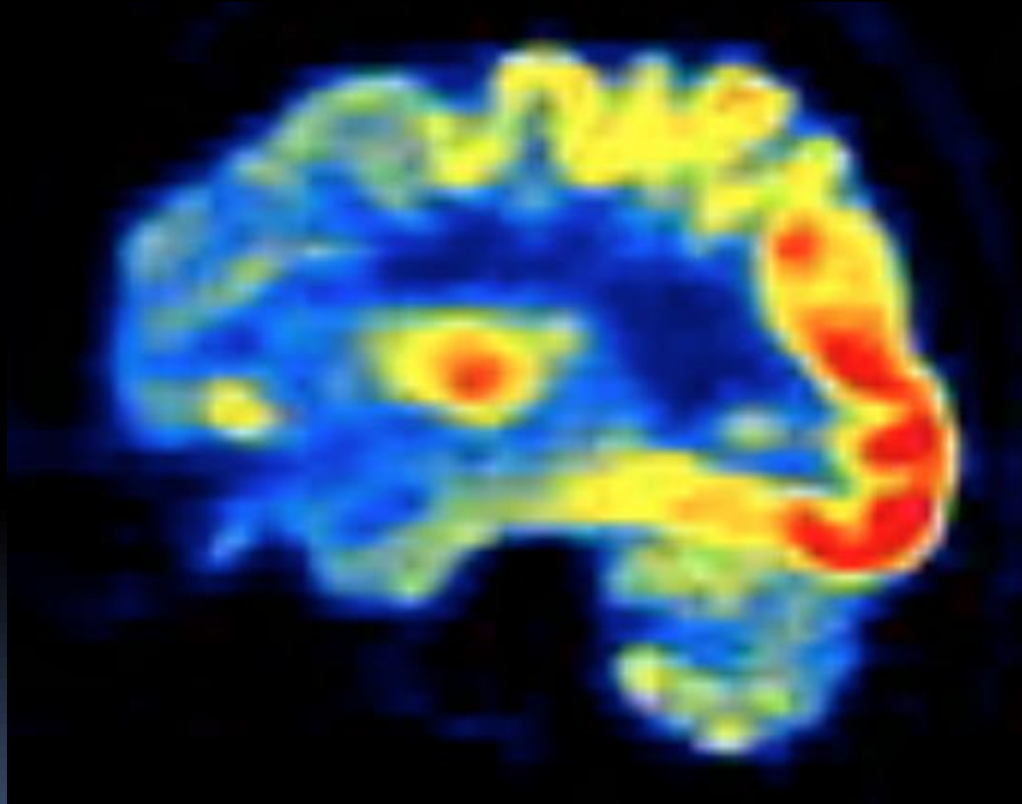


bvFTD



bvFTD: Functional Imaging Findings

PET: hypometabolism of frontal and temporal lobes



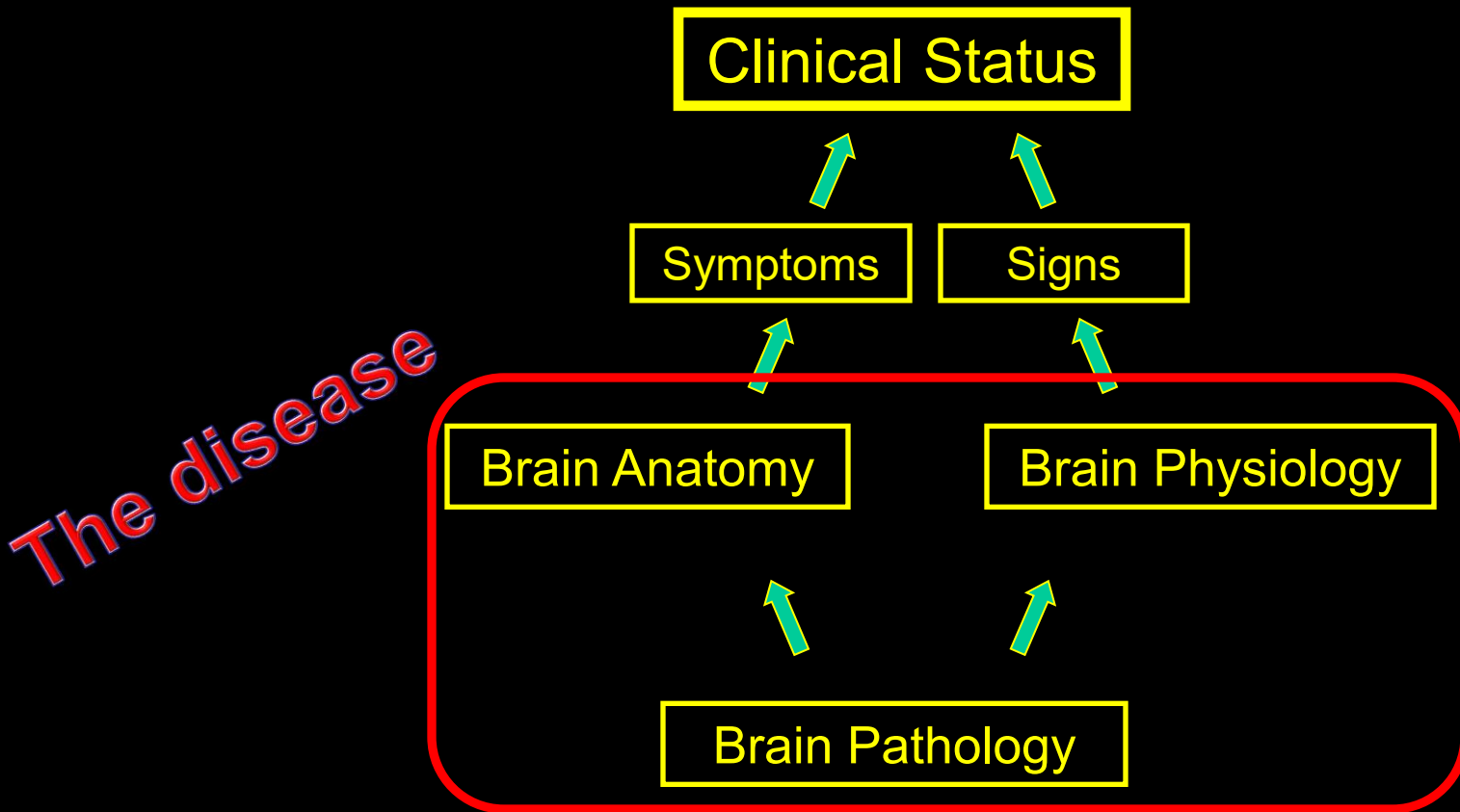
Clinical course of FTD

- Starts out distinctly as one of these variants
- Usually progresses to involve other domains
- Depending on the type and location of changes in the brain, changes in movement may also occur
 - Incoordination
 - Slowing, stiffness
 - Changes in walking/falls
 - Changes in eye movements
 - Impaired swallowing
- Survival is 2 – 20+ years after onset of symptoms
- Average is 7-12 years
 - Depends on how early diagnosis is made

FTD: Current treatment

- Treatment
 - Medicines to slow disease progression: now in clinical trials and further development
 - Medicines to treat symptoms
 - No FDA labeled indication
 - Several studies have shown benefits of antidepressant medications on a variety of symptoms
 - Existing medicines may be helpful for managing various symptoms
 - Antipsychotics, antiseizure medicines, others
 - AD medicines & stimulants are often not helpful and may exacerbate behavioral symptoms
 - Comprehensive interdisciplinary team approach
 - Neurologist, psychiatrist, neuropsychologist, speech pathologist, social worker, nurse, case manager/care coordinator
 - Occupational/physical/cognitive therapist
 - AFTD/Alzheimer's Association/other organizations
 - Community care programs

Approach to diagnosis

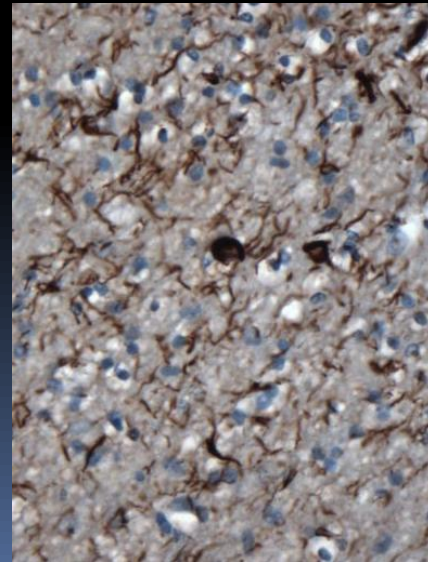
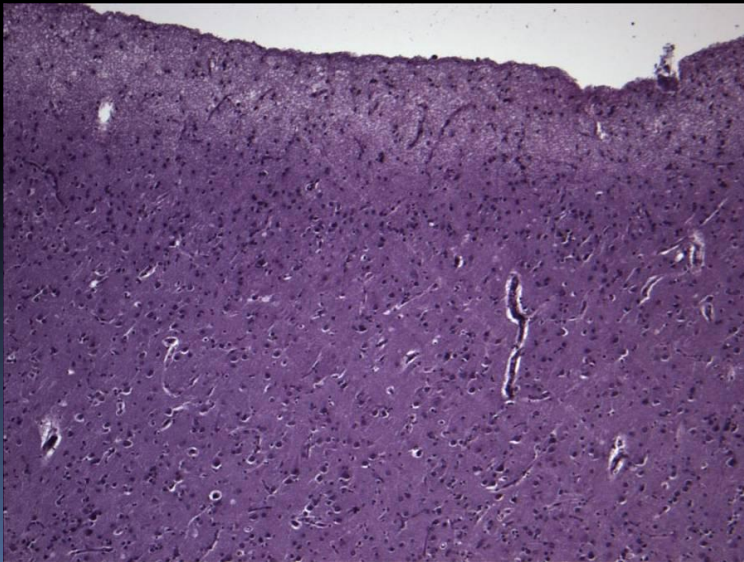


FTD: Neuropathology

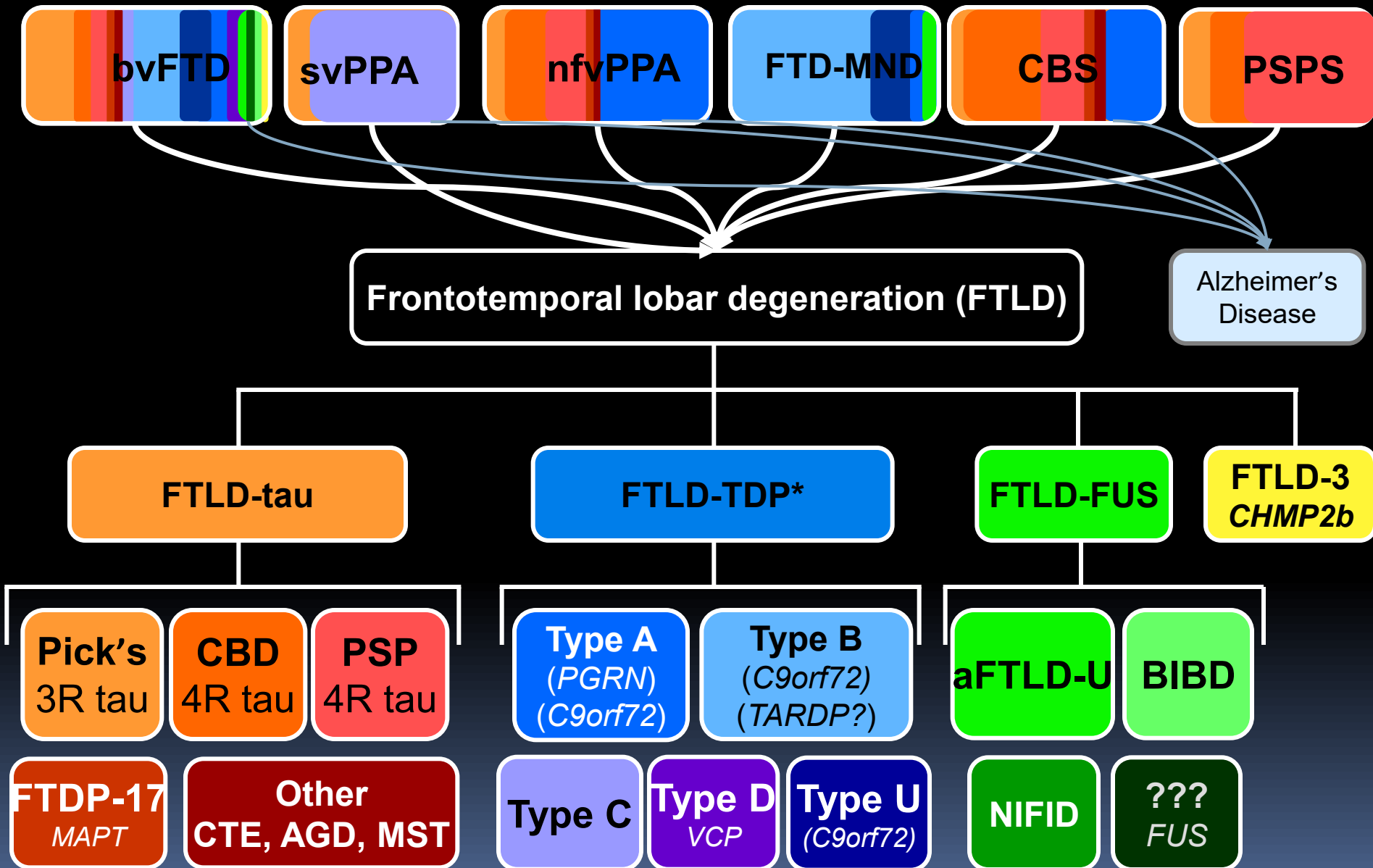


FTLD: Neuropathology

- FTLD cellular morphology: Pick bodies & other types of cellular inclusions, dystrophic neurites, often reactive astrocytes and other glial pathology
- FTLD proteins: tau, TDP-43 >> FUS



FTLD clinicopathologic spectrum

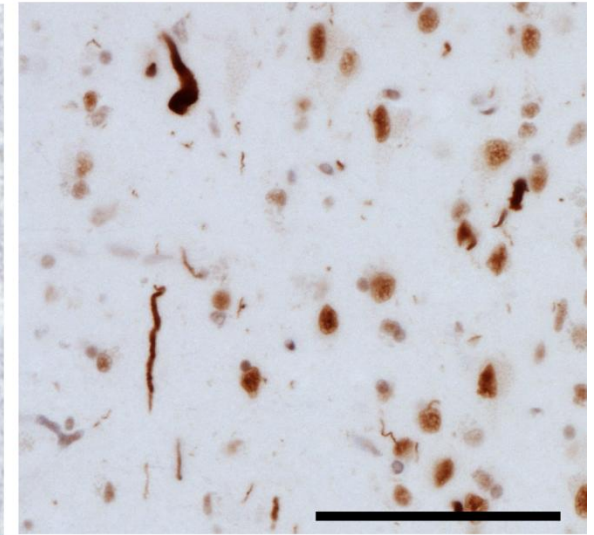
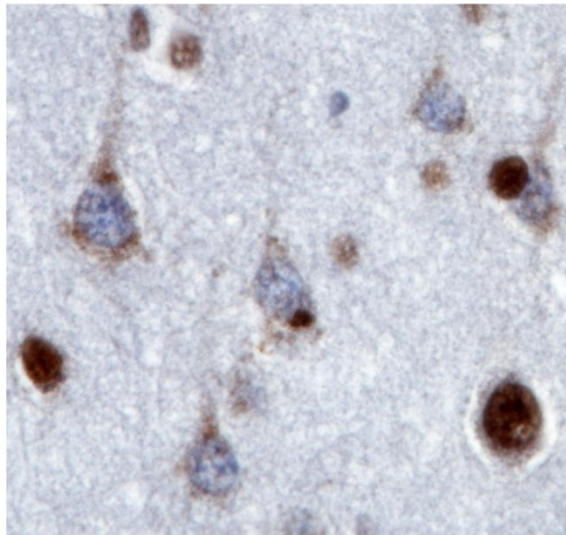
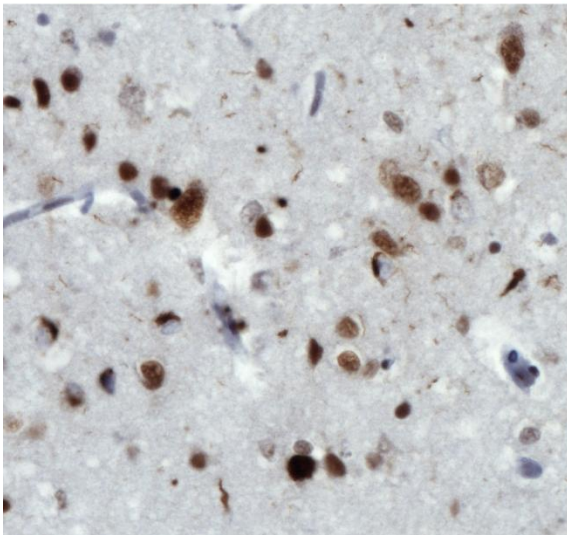
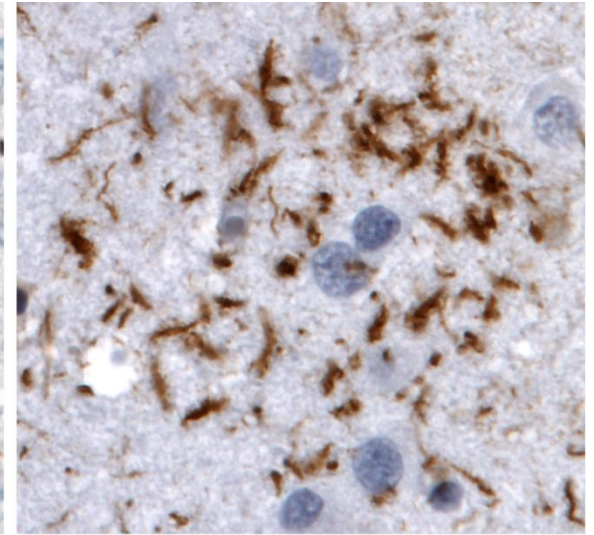
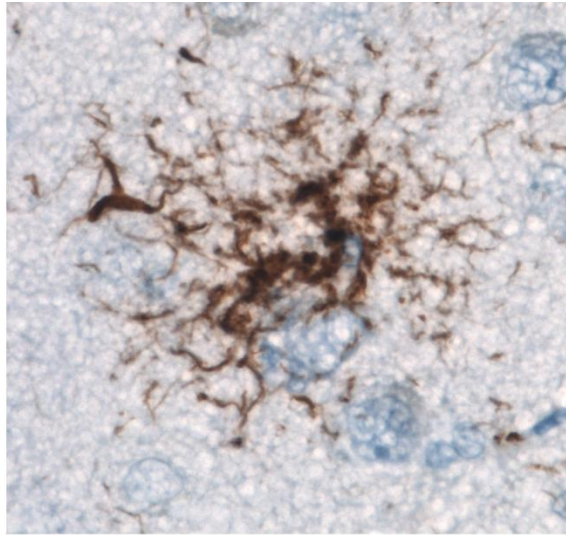
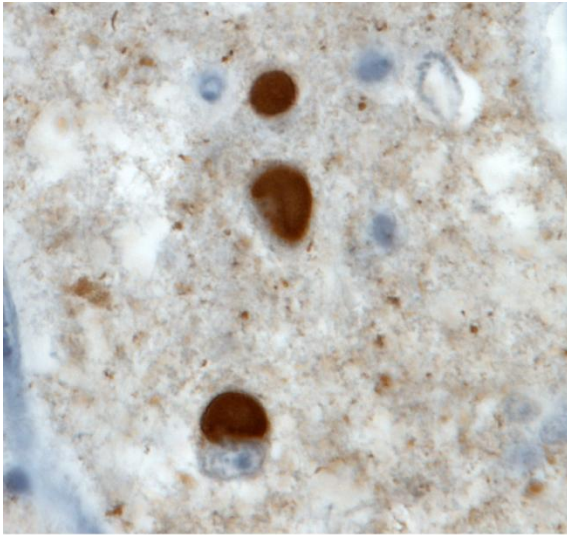


FTLD-tau

PID

PSP

CBD

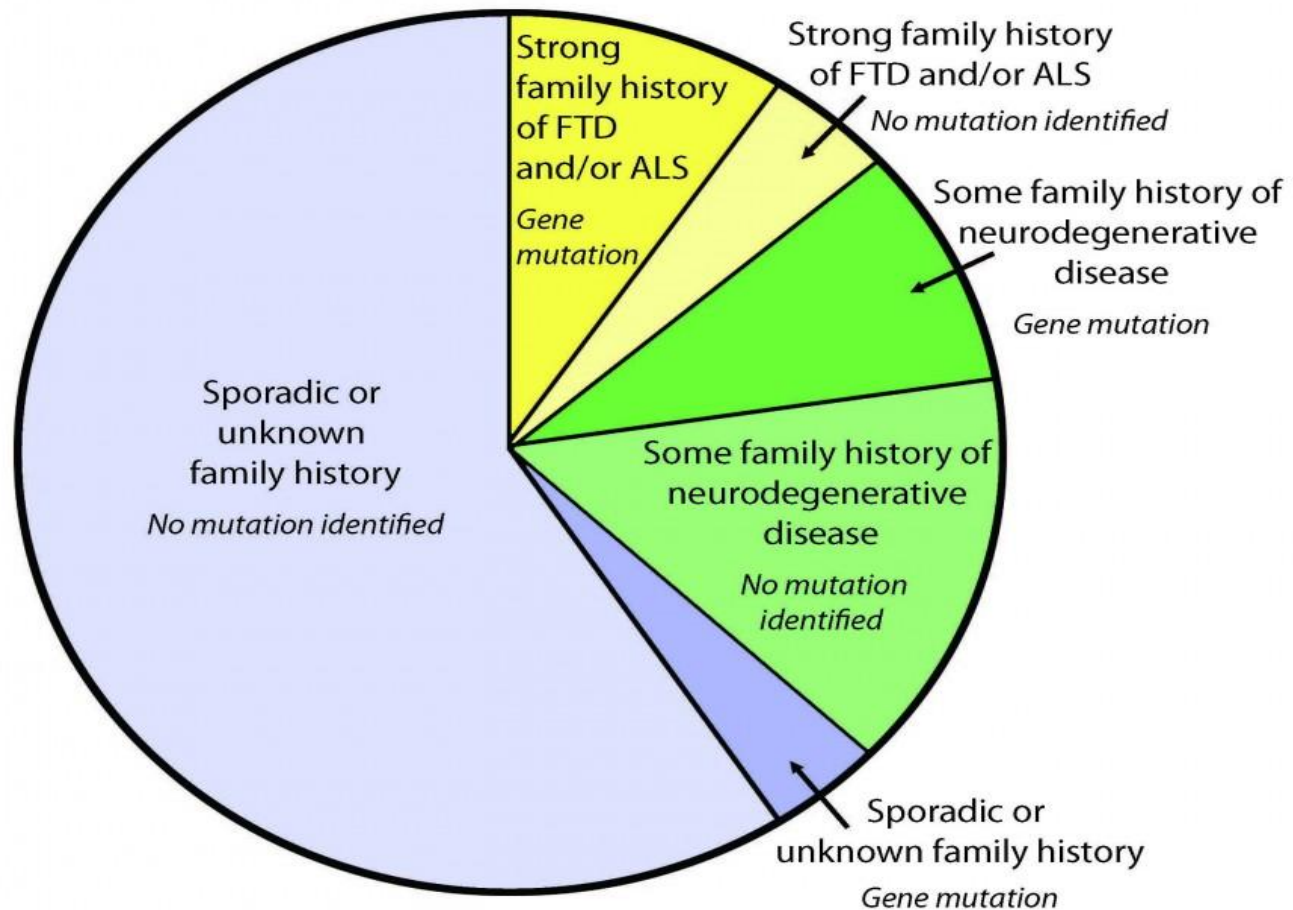


TDP-A

TDP-B

TDP-C

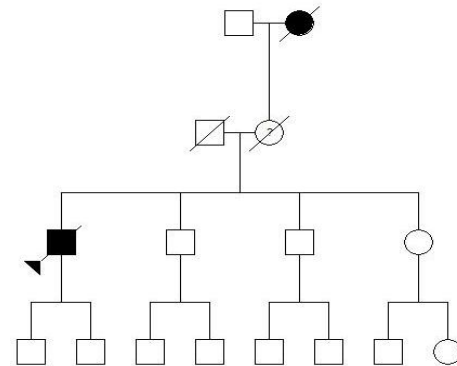
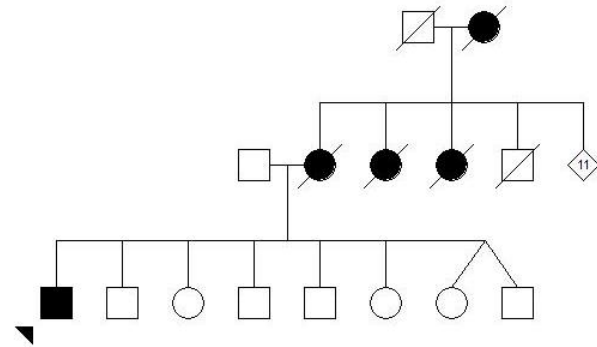
FTLD-TDP



- Strong family history of FTD and/or ALS: Accounts for about 10-15% of FTD. The majority, but not all, can be explained by a mutation in a known FTD gene.
- Some family history of neurodegenerative disease: Accounts for about 20-25% of FTD. Less than half have a mutation in a known FTD gene.
- Sporadic or unknown family history: Accounts for about 60% of FTD. Only a small percentage (less than 10%) have a mutation in a known FTD gene.

FTLD: Genetics

- MAPT (tau)
- Progranulin
- C9ORF72
- FUS and others



Age at symptom onset and death and disease duration in genetic frontotemporal dementia: an international retrospective cohort study

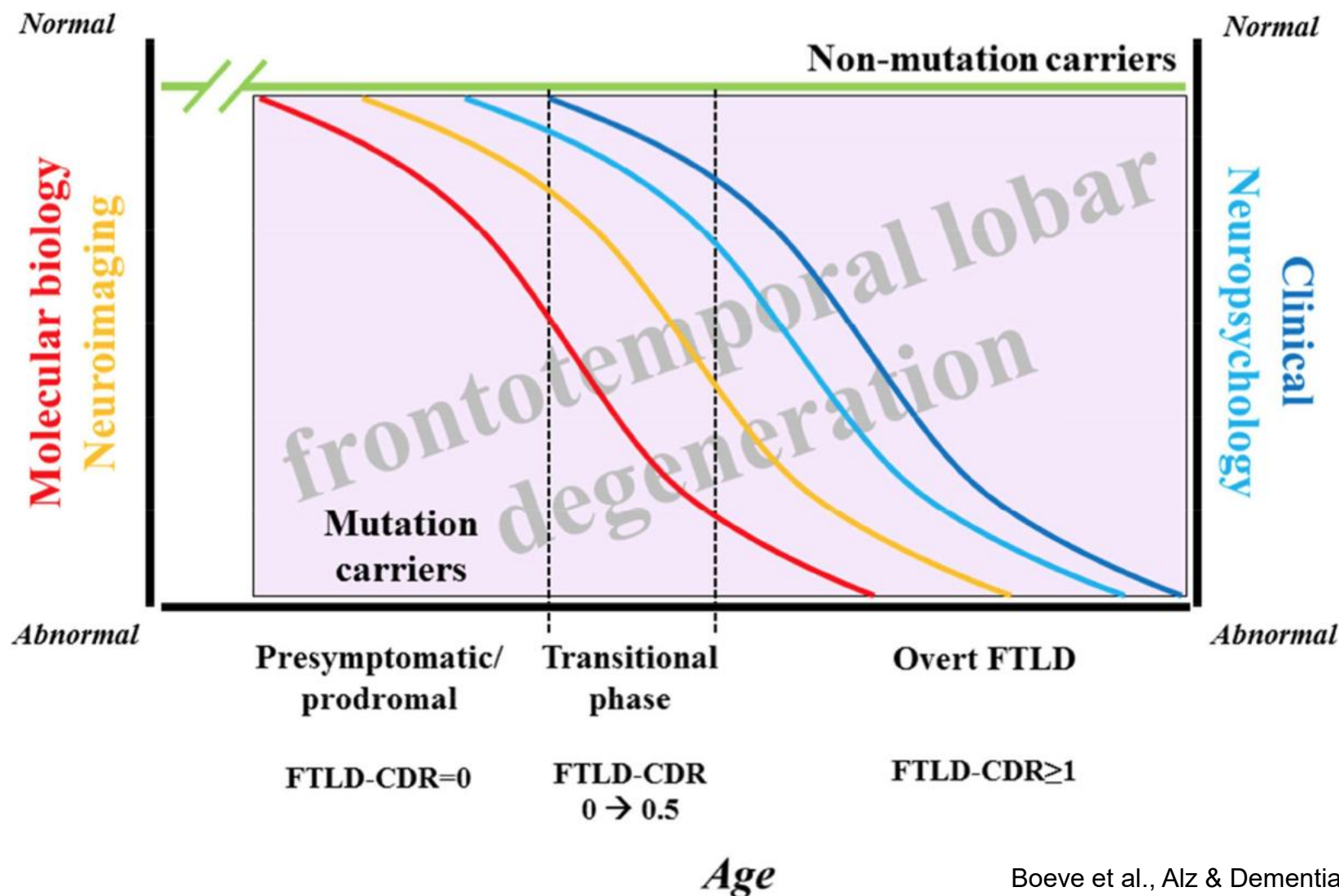
Lancet Neurol 2020; 19: 145–56

Katrina M Moore, Jennifer Nicholas, Murray Grossman, Corey T McMillan, David J Irwin, Lauren Massimo, Vivianna M Van Deerlin, Jason D Warren, Nick C Fox, Martin N Rossor, Simon Mead, Martina Bocchetta, Bradley F Boeve, David S Knopman, Neill R Graff-Radford, Leah K Forsberg, Rosa Rademakers, Zbigniew K Wszolek, John C van Swieten, Lize C Jiskoot, Lieke H Meeter, Elise GP Dopper, Janne M Papma, Julie S Snowden, Jennifer Saxon, Matthew Jones, Stuart Pickering-Brown, Isabelle Le Ber, Agnès Camuzat, Alexis Brice, Paola Caroppo, Roberta Ghidoni, Michela Pievani, Luisa Benussi, Giuliano Binetti, Bradford C Dickerson, Diane Lucente, Samantha Krivensky, Caroline Graff, Linn Öijerstedt, Marie Fallström, Håkan Thonberg, Nupur Ghoshal, John C Morris, Barbara Borroni, Alberto Benussi, Alessandro Padovani, Daniela Galimberti, Elio Scarpini, Giorgio G Fumagalli, Ian R Mackenzie, Ging-Yuek R Hsiung, Pheth Sengdy, Adam L Boxer, Howie Rosen, Joanne B Taylor, Matthis Synofzik, Carlo Wilke, Patricia Sulzer, John R Hodges, Glenda Halliday, John Kwok, Raquel Sanchez-Valle, Albert Lladó, Sergi Borrego-Ecija, Isabel Santana, Maria Rosário Almeida, Miguel Tábuas-Pereira, Fermin Moreno, Myriam Barandiaran, Begoña Indakoetxea, Johannes Levin, Adrian Danek, James B Rowe, Thomas E Cope, Markus Otto, Sarah Anderl-Straub, Alexandre de Mendonça, Carolina Maruta, Mario Masellis, Sandra E Black, Philippe Couratier, Geraldine Lautrette, Edward D Huey, Sandro Sorbi, Benedetta Nacmias, Robert Laforce Jr, Marie-Pier L Tremblay, Rik Vandenberghe, Philip Van Damme, Emily J Rogalski, Sandra Weintraub, Alexander Gerhard, Chiadi U Onyike, Simon Ducharme, Sokratis G Papageorgiou, Adeline Su Lyn Ng, Amy Brodtmann, Elizabeth Finger, Rita Guerreiro, Jose Bras, Jonathan D Rohrer, for the FTD Prevention Initiative*

Gene	Avg age of onset	Avg survival
<i>MAPT</i>	49+/-10	9
<i>Progranulin</i>	59+/-11	7
<i>C9orf72</i>	58+/-9	6

C9orf72 is associated with greater frequency of psychosis at presentation

Autosomal dominant FTLD: Biomarker model of preclinical->clinical trajectory



Active lifestyle is a resilience factor in autosomal dominant FTLD rate of progression

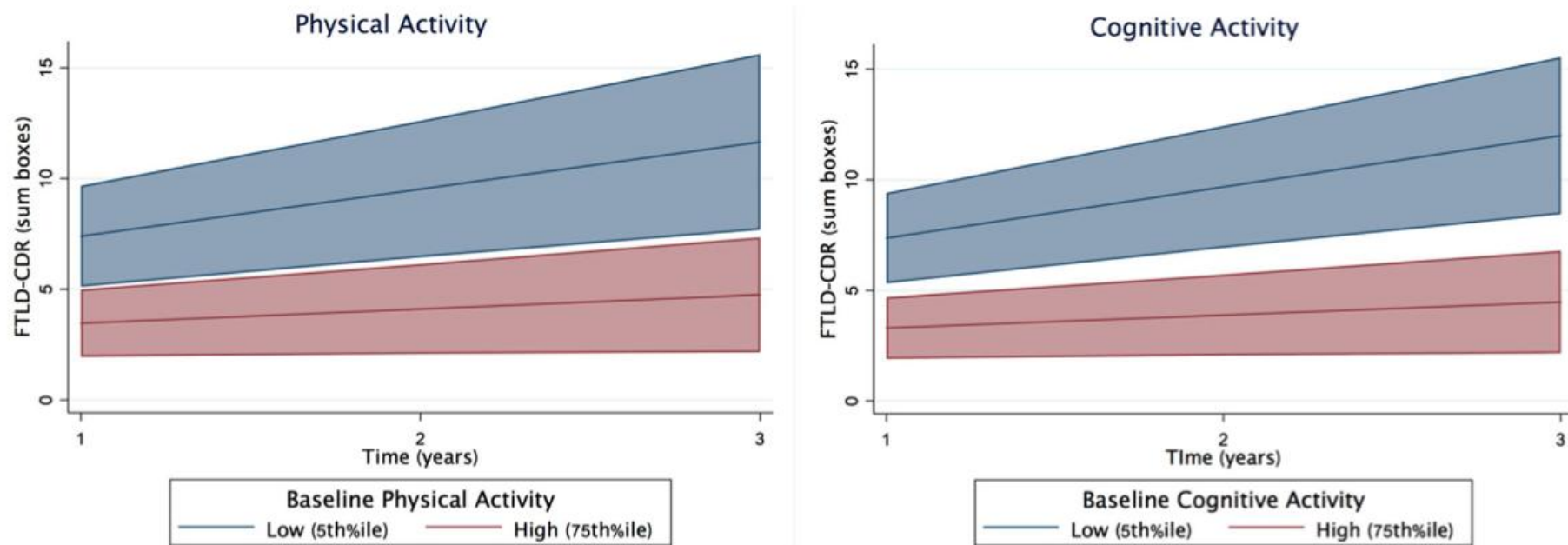
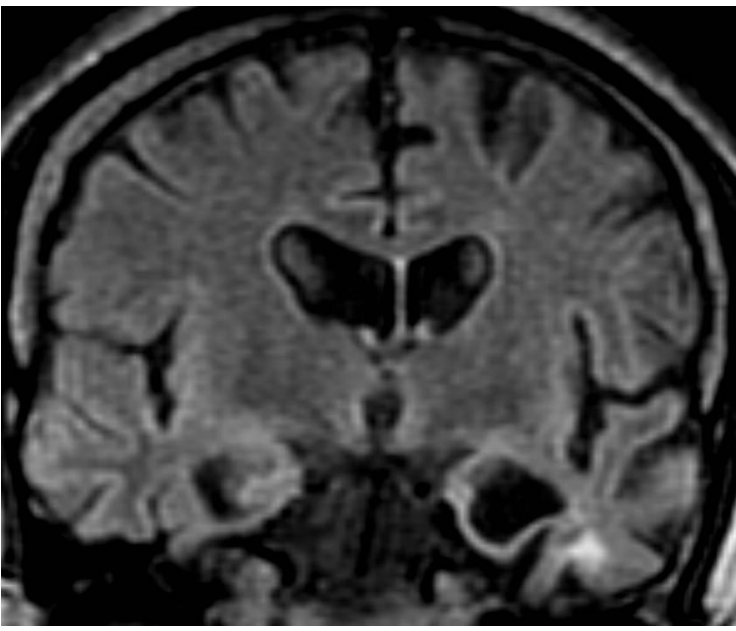
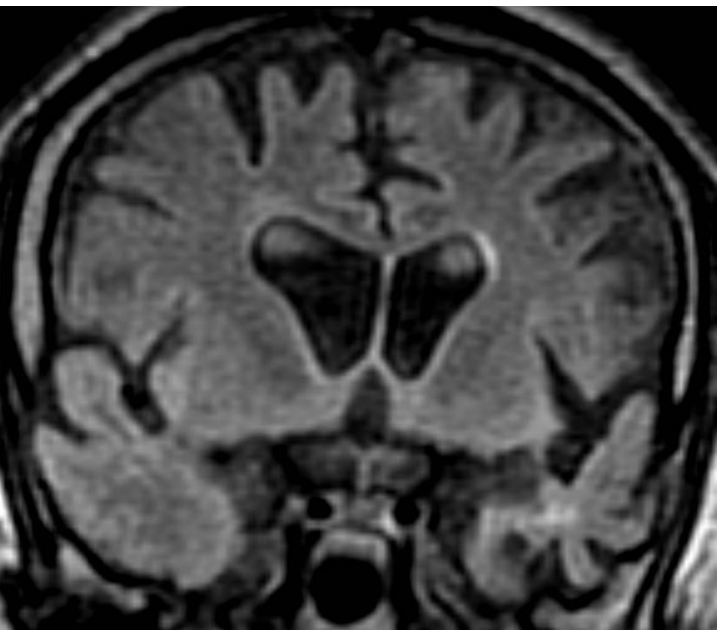
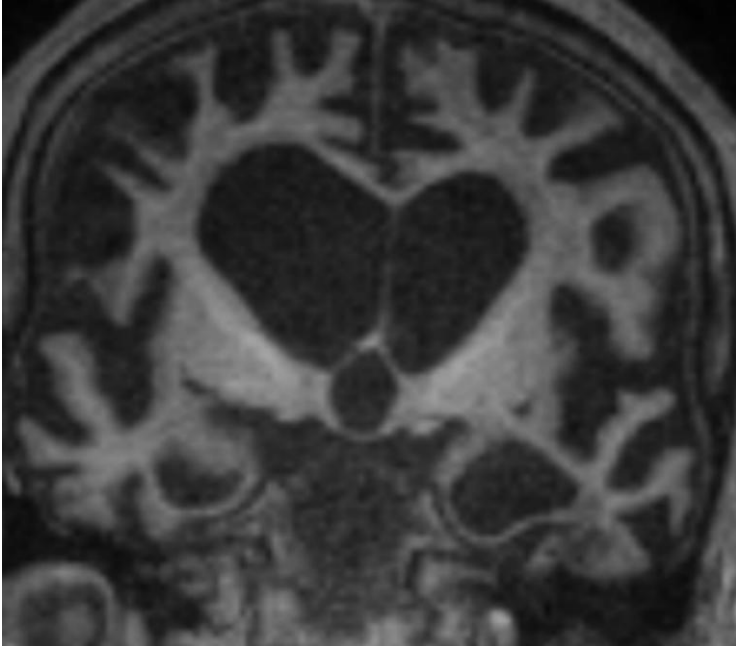
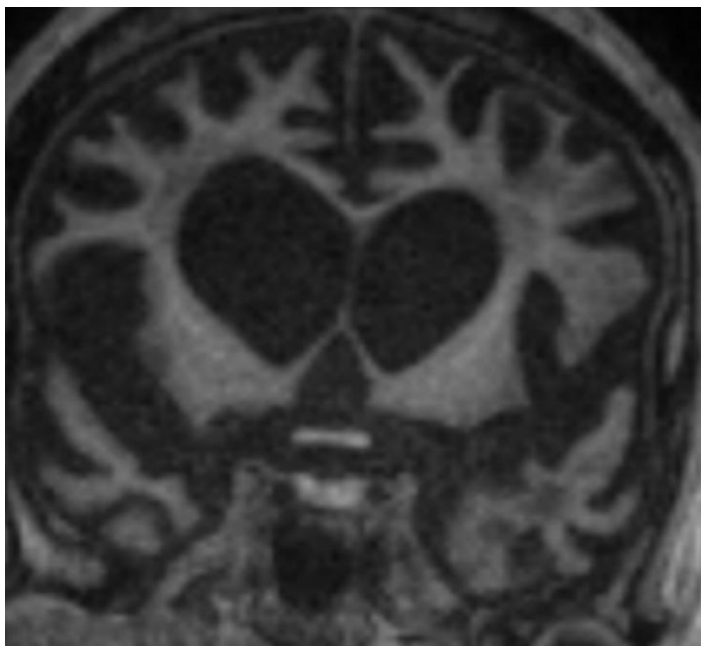


FIGURE 3 Higher levels of baseline physical and cognitive activities are associated with significantly slower clinical decline over time in autosomal dominant FTLD mutation carriers (adjusted for age, sex, education). Bands represent 95% CI



29y man w/
bvFTD

Initial
presentation



2.5 years
later

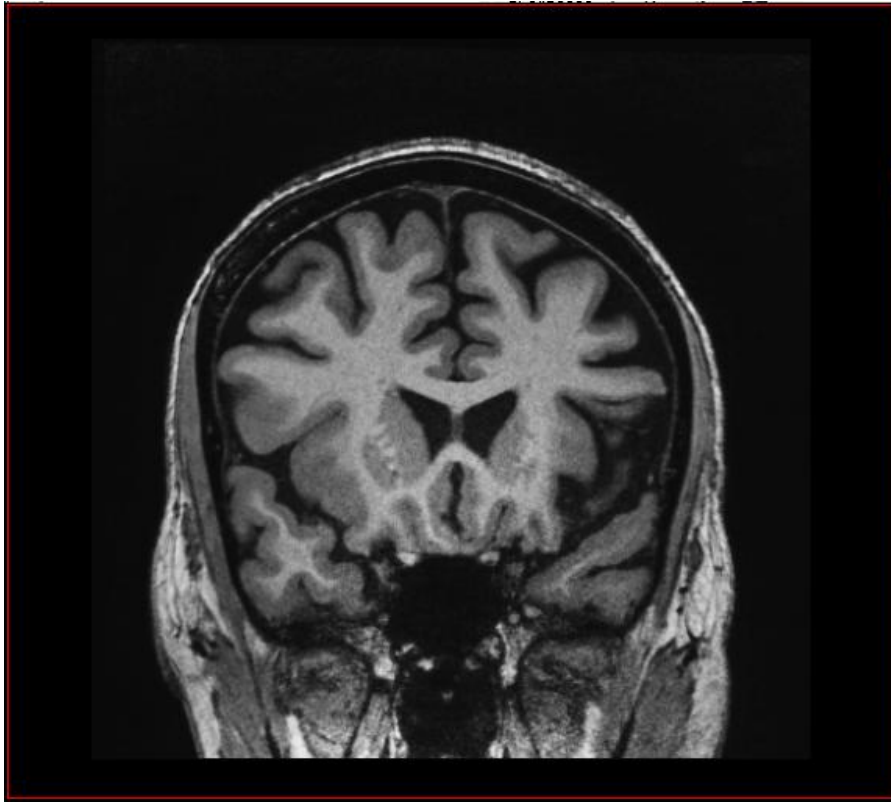
53y F: nfvPPA with normal motor speech

Conversational speech: speaking and writing

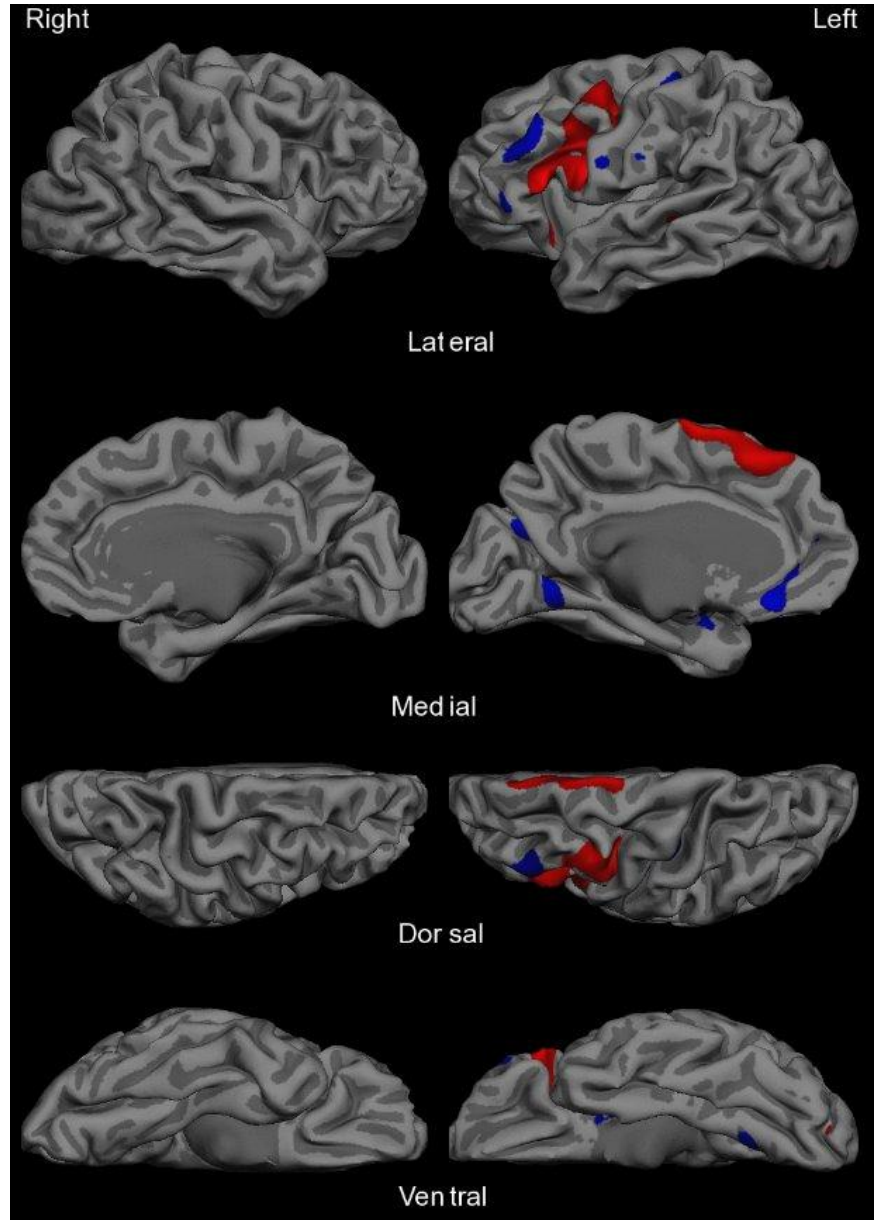
Nonfluent, effortful speech with word retrieval difficulty



53y F: nfvPPA with normal motor speech: MRI



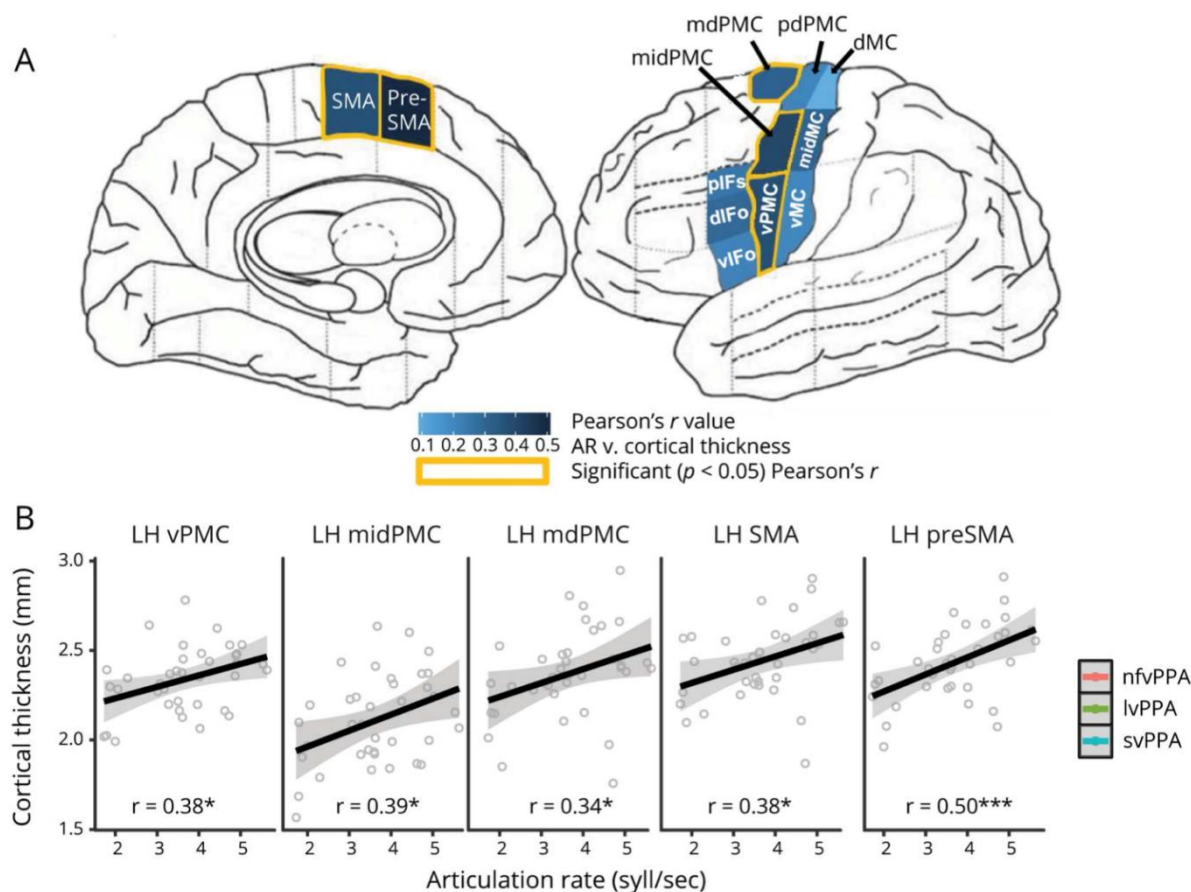
9 year course, Pick's disease
pathology



Slowing of articulation rate correlates with atrophy in motor speech cortical areas from Frank Guenther's DIVA model of speech production

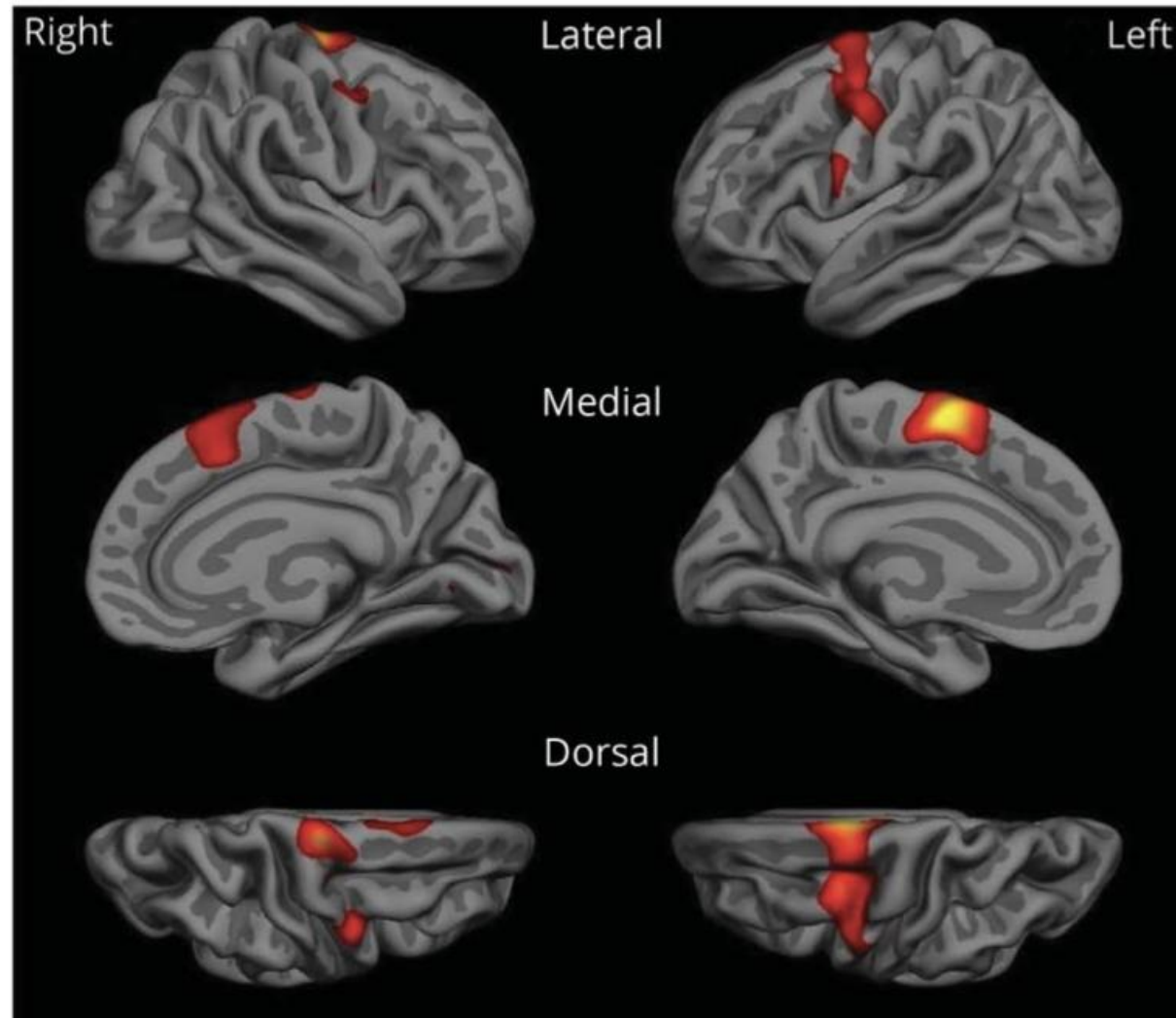
Figure 3 Slower AR is correlated with thinner cortex in select motor speech ROIs

DIVA model
brain regions



N=64 PPA
patients, all
subtypes

Slowest articulation rate occurs in patients with atrophy specific to motor speech cortical areas from the DIVA model of speech production (analysis across the entire cortex)



N=64 PPA
patients, all
subtypes

Most patients with
slowest articulation
rates have apraxia
of speech

57y F w/ 3y slowly progressive difficulty with speech articulation followed by progressive nonfluent aphasia

Spontaneous speech was halting and dysfluent with mild agrammatism with appropriate content

Features of moderate apraxia of speech: inconsistent speech sound distortions, slow articulation rate, sound sequencing errors, vowel distortions, difficulty with multi-syllabic words, equal & excess stress

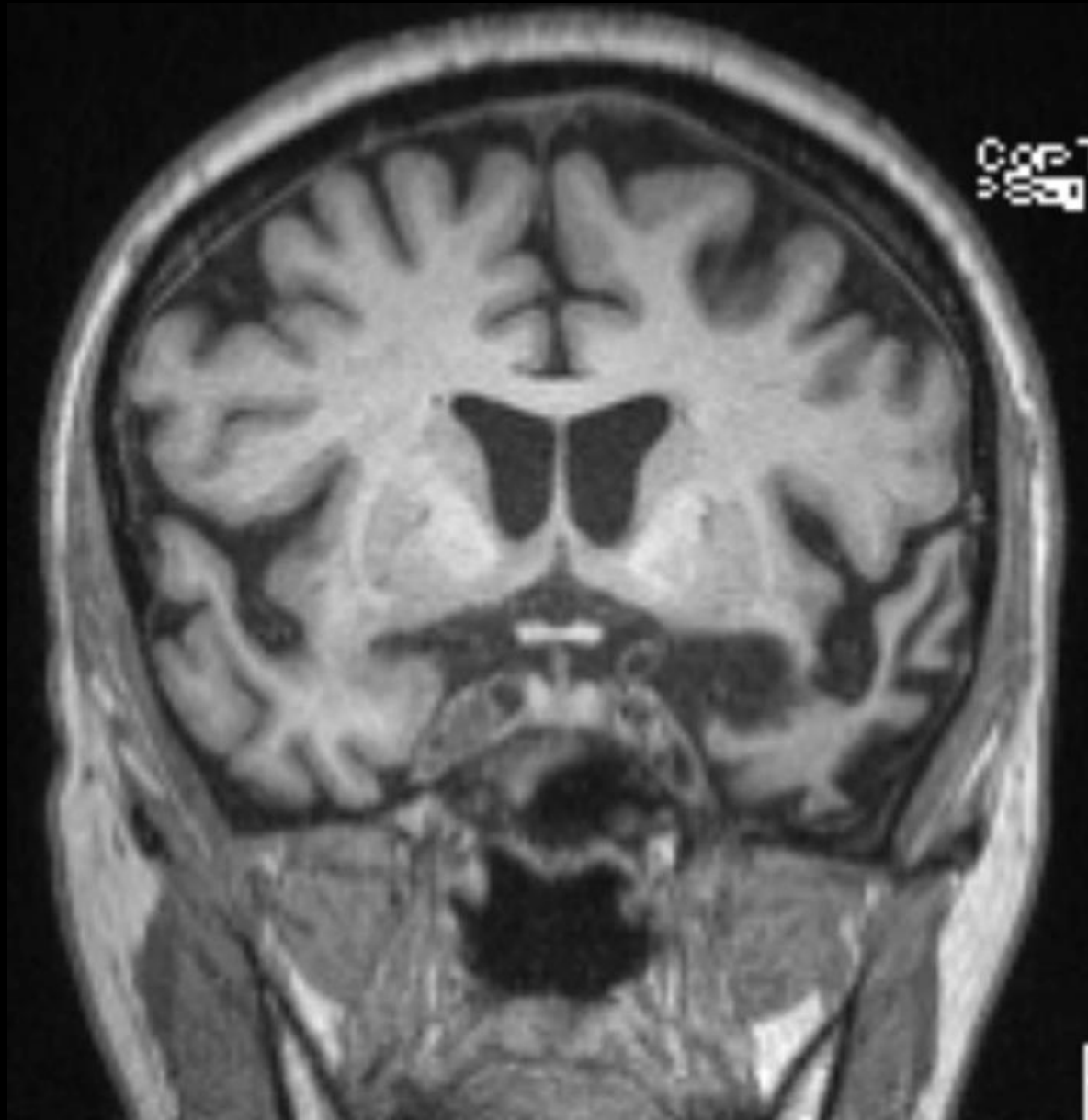


“I know what I want to say and I have the word, but I — over the years I’ve develop... developed a sense of what I can say and can’t say in a specific moment. So, I know what I want to say but I can sense...*when* I can sense that I will not get it out, I s...scan the list of sy-no-nyms and to pause to try are them in my mind and it comes across as a pause.”

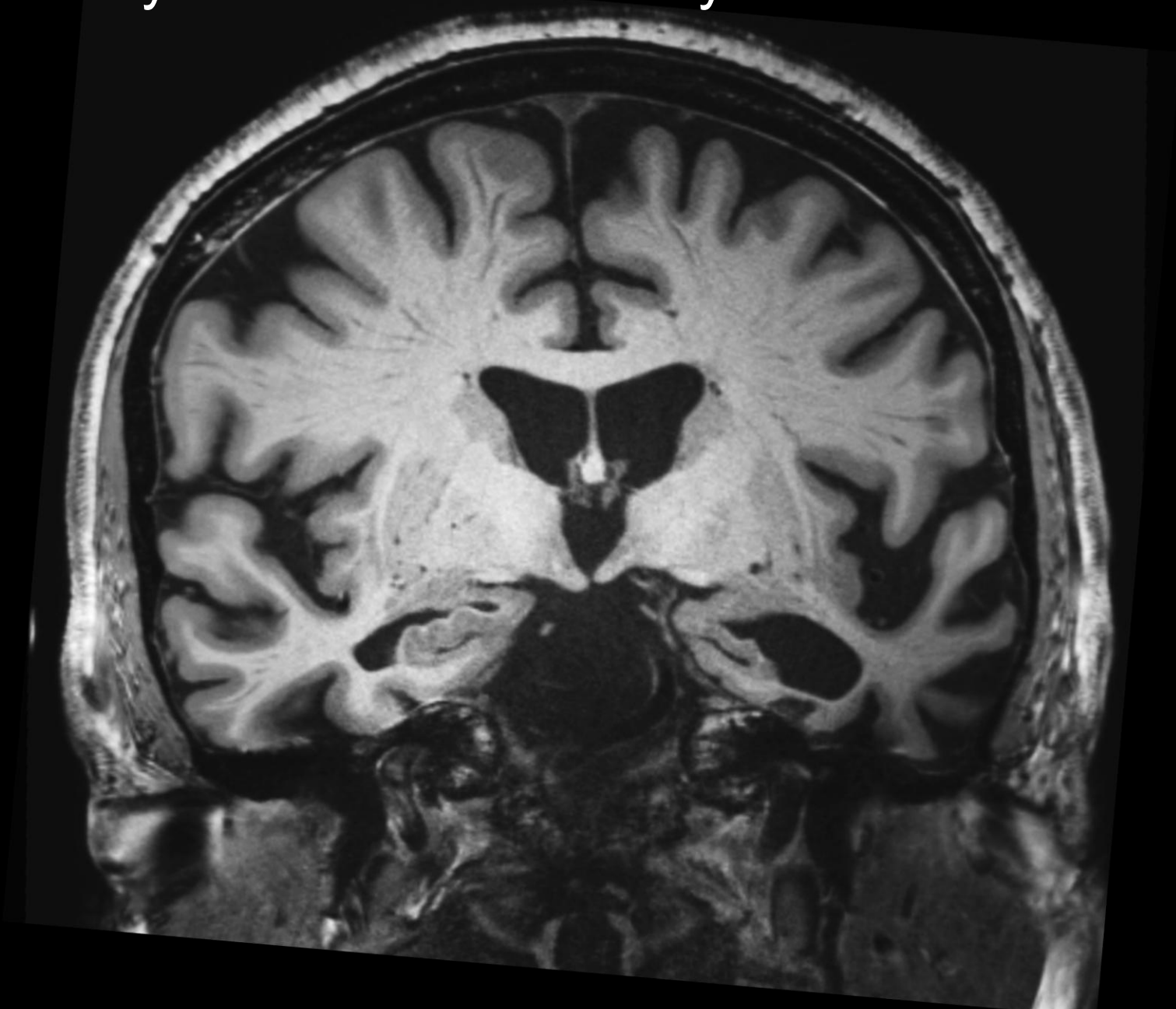
70y F: svPPA



70y woman with clinically classic svPPA

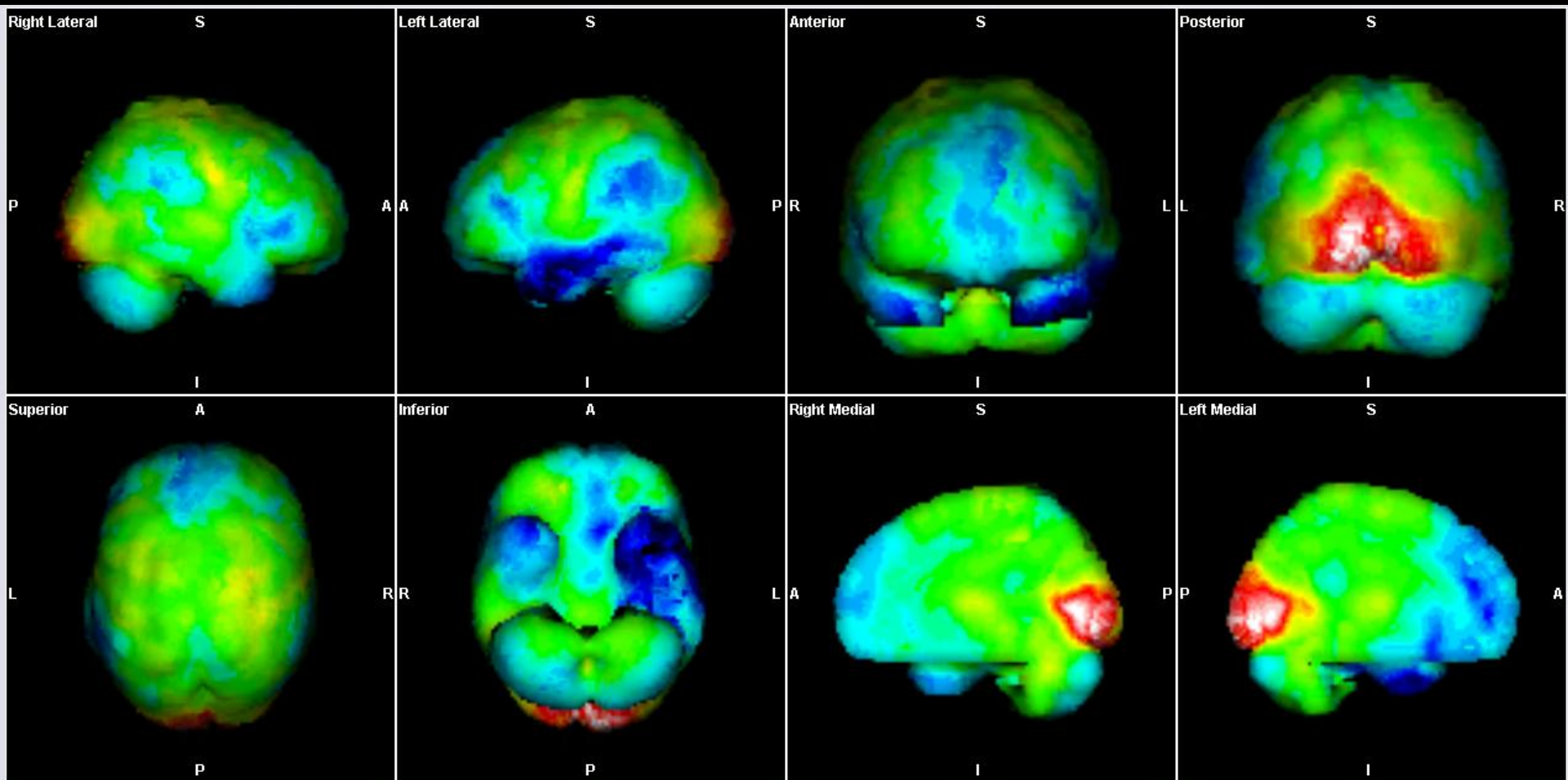


70y woman with clinically classic svPPA

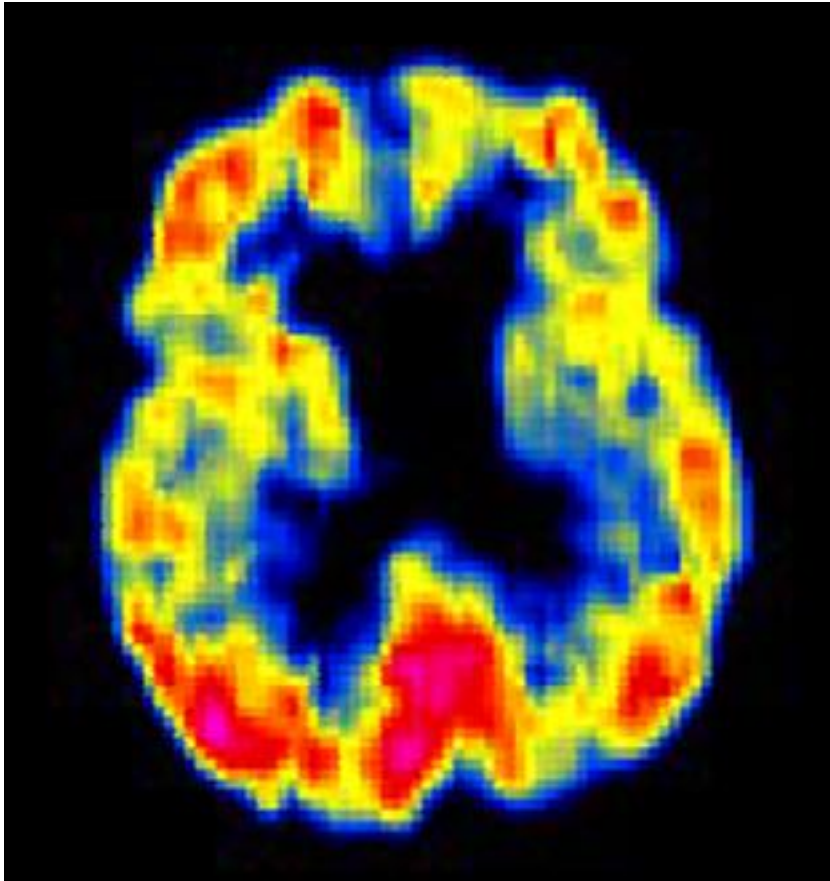


Mesulam, Dickerson, et al., NEJM 2017

FDG PET



Amyloid PET+



- FTLD with TDP-43 inclusions (FLTD-TDP), subtype C
 - With hippocampal sclerosis
- AD neuropathology changes [ADNC]
 - Thal stage 4 of 5 for amyloid;
 - Braak and Braak stage II of VI for tangles;
 - CERAD: sparse for neuritic plaques
 - NIA-AlzAssn score: A3B1C1

MGH FTD Unit: Clinical

- clinical-research unit for FTD and related disorders
- multidisciplinary clinic
 - comprehensive approach to diagnosis and treatment
 - speech / language therapy, neuropsychology, neuropsychiatry, neuroradiology, social work, genetic counseling, autopsy
 - training of neurologists, psychiatrists, speech pathologists, neuropsychologists
 - regular case conference series
 - caregiver and professional education

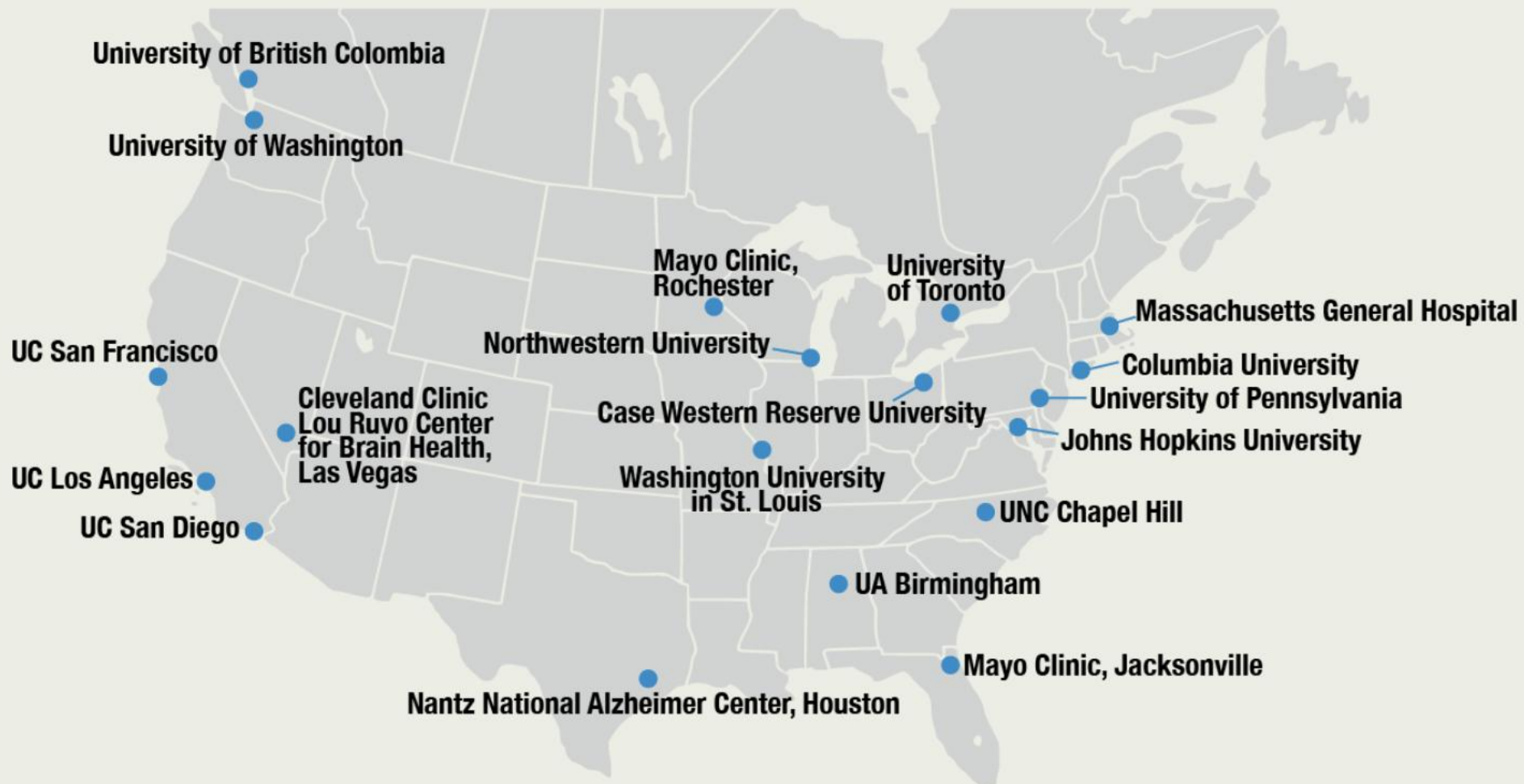
PPA Support group also bvFTD support groups



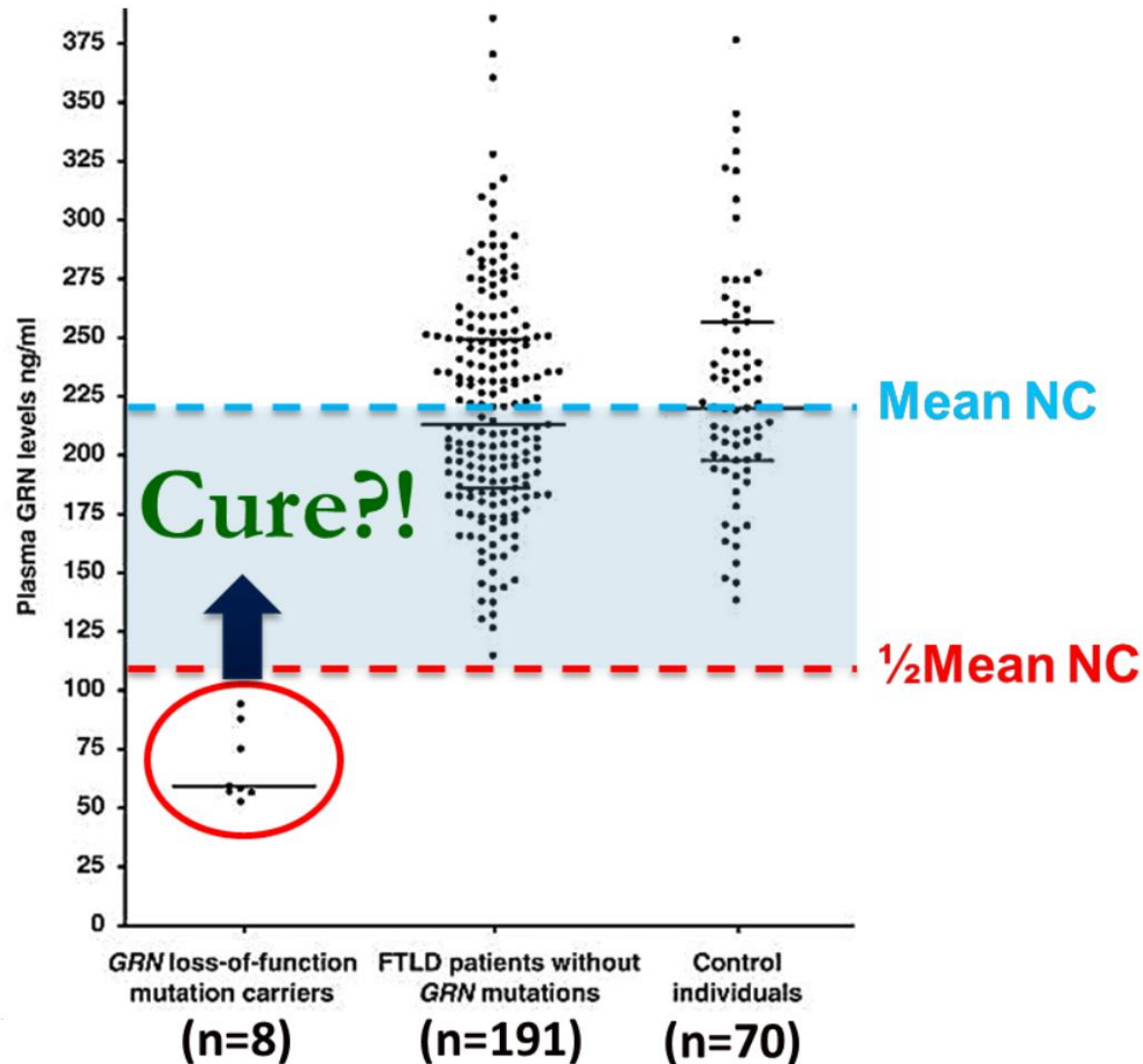
MGH FTD Unit: Research

- quantification of cognitive and behavioral symptoms (including Prodromal stage)
 - Progressive Aphasia Severity Scale (PASS)
 - Social Impairment Rating Scale (SIRS)
- quantitative structural, functional, molecular neuroimaging
- biofluid / genetic / tissue studies
 - blood, urine, CSF, skin biopsy (iPS cell lines), autopsy
- multicenter longitudinal observational & biomarker studies (ALLFTD (ARTFL-LEFFTDS), GENFI, NIFD, 4RTNI, FTD-NACC)
- Presymptomatic and prodromal familial FTD study
- clinical drug trials and new treatment studies (TMS, TACS)

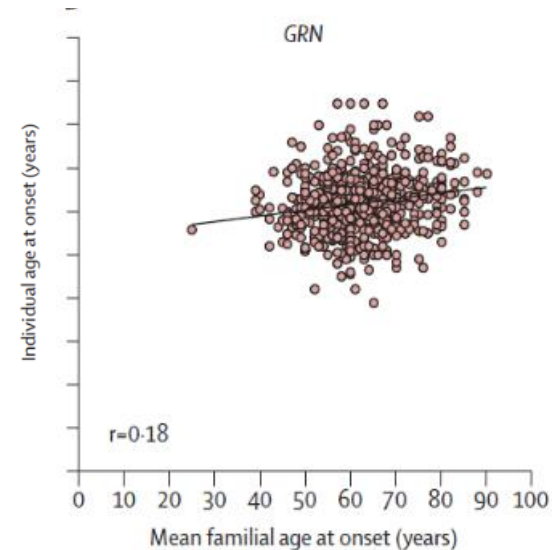
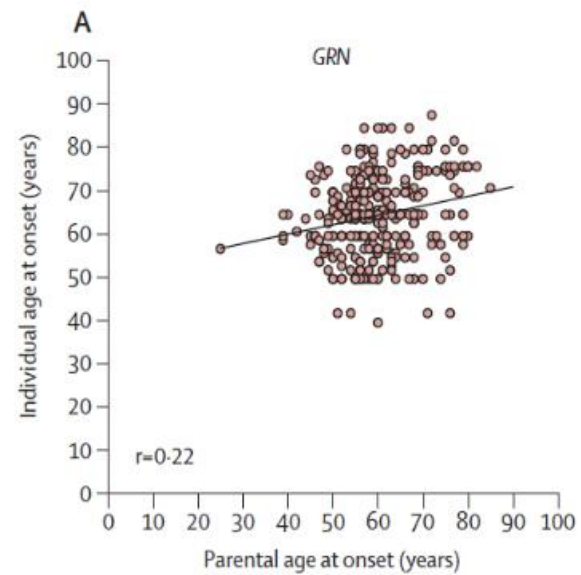
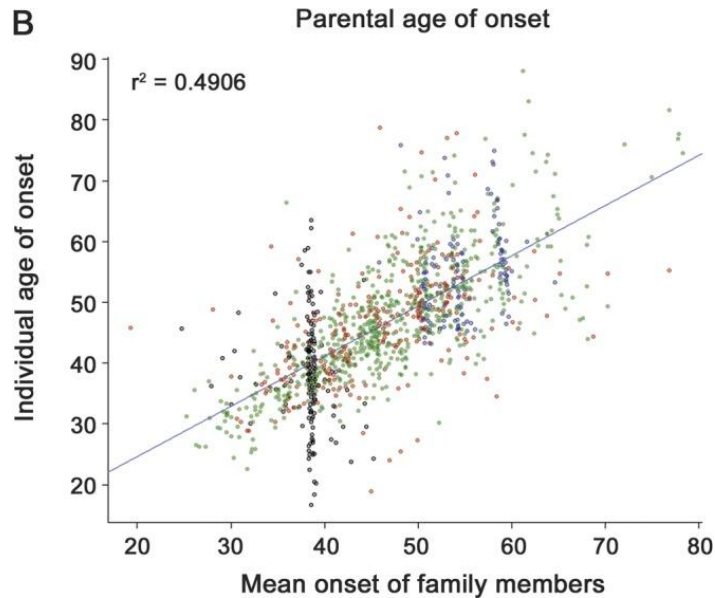
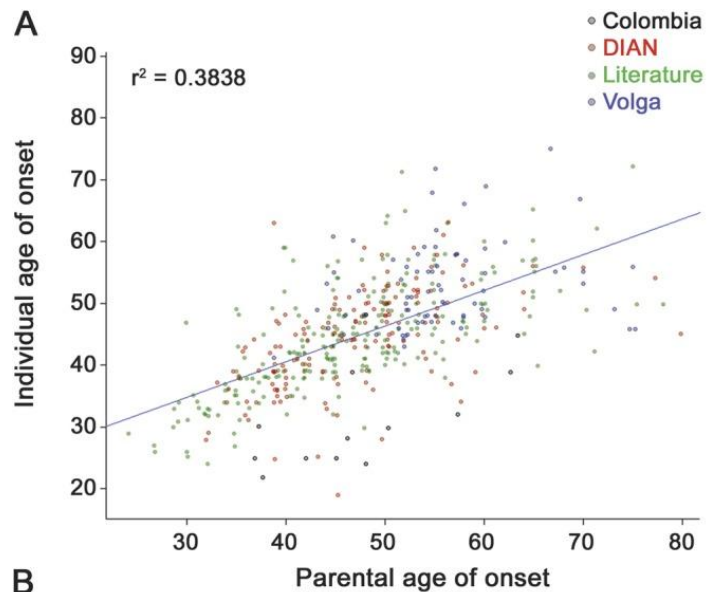
ALLFTD SITES



FTD with GRN mutations: haploinsufficiency



Unlike ADAD, EYO in GRN-FTLD is difficult to predict

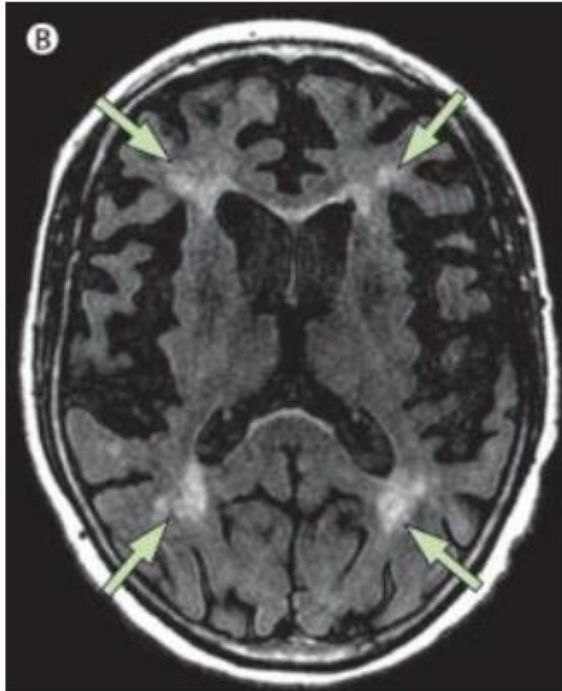


GRN clinical phenotypes

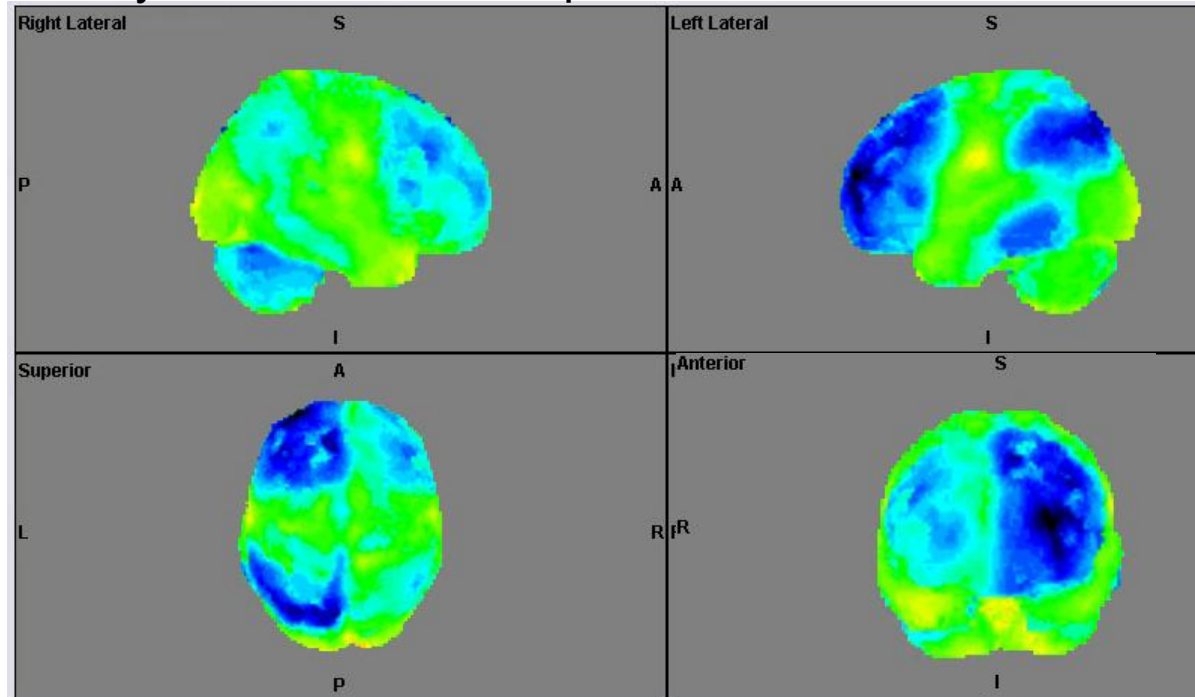
	GRN (n=1179)
Diagnoses within the frontotemporal dementia spectrum	
Behavioural variant frontotemporal dementia	446 (37.8%)
Non-fluent variant primary progressive aphasia	107 (9.1%)
Semantic variant primary progressive aphasia	13 (1.1%)
Logopenic variant primary progressive aphasia	4 (0.3%)
Primary progressive aphasia not otherwise specified*	36 (3.1%)
Frontotemporal dementia with amyotrophic lateral sclerosis	7 (0.6%)
Amyotrophic lateral sclerosis	7 (0.6%)
Corticobasal syndrome	47 (4.0%)
Progressive supranuclear palsy†	0 (0%)
Diagnoses outside the frontotemporal dementia spectrum	
Alzheimer's disease	97 (8.2%)
Huntington's disease	0 (0%)
Parkinson's disease	16 (1.4%)
Dementia with Lewy Bodies	4 (0.3%)
Vascular dementia	9 (0.8%)
Dementia not otherwise specified*	361 (30.6%)
Other	25 (2.1%)

GRN imaging and fluid biomarkers

WMSA are elevated



MRI/FDG neurodegeneration is often very asymmetric with more parietal involvement



Research: CSF and plasma progranulin, neurofilament light, GFAP, lysosomal markers

Clinical: Genetic testing; *coming soon: plasma NfL & GFAP*

Mab

GRN therapeutic strategies

- Ph3: Latozinemab: human mab against sortilin receptor (primary regulator of GRN). INFRONT-3 (Alector Inc, 60mg/Kg) every 4 weeks vs. placebo; readout late 2025

“Brain shuttle”

- Ph 1 / 2: DNL593: progranulin protein fused to an antibody fragment that binds to the transferrin receptor. (Denali Therapeutics Inc); dosing ongoing

Small molecule

- Ph1: VES001 orally available small molecular sortilin receptor antagonist; PGRN uptake inhibitor. SORT-IN-1(Vesper Biotechnologies ApS) VES001 ; readout late 2025

AAV

- Ph 1 / 2: PRO06/LY3884963 (AAV9-GRN) single dose injection into the cisterna magna. PROCLAIM (Prevail Therapeutics); readout 2029; adverse events occurred in all 13 patients (increased white blood cells in CSF, an indication of neuroinflammation, was seen in half. The increase was transient and caused no symptoms in all but one patient, who experienced a hearing impairment that later recovered. Twelve serious adverse events were noted, including multiple instances of blood clots. Deep vein thrombosis in two patients was possibly related to the immunosuppressive therapy in people with multiple risk factors for DVT. There was one death). In all participants, CSF progranulin concentration rose, between 2.1- and 6.9-fold. Most attained normal or supernormal CSF progranulin levels at six or 12 months. [Sevigny et al., 2024](#)
- Ph1b/2a: PBFT02 (AAV1-GRN). Single Dose of PBFT02 Delivered Into the cisterna magna. upliFT-D (Passage Bio, Inc); promising biomarker results; readout 2026
- Ph 1 / 2: AVB-101 Bilateral Intrathalamic Infusion of AAV-GRN. Dosing of 3rd cohort ongoing. ASPIRE-FTD (AviadoBio, Ltd); biomarker data 2026

Thank you!

MGH FTD Unit & Center for Translational Brain Mapping
Affiliated with the Mass ADRC and Martinos Center for Biomedical Imaging



Thanks for funding to:

Support

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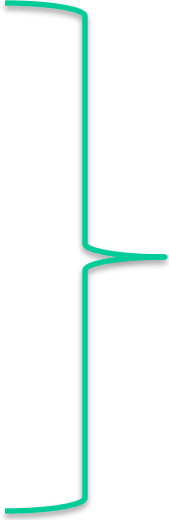
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MGH FTD Unit: Research

- Additional slides with details on research

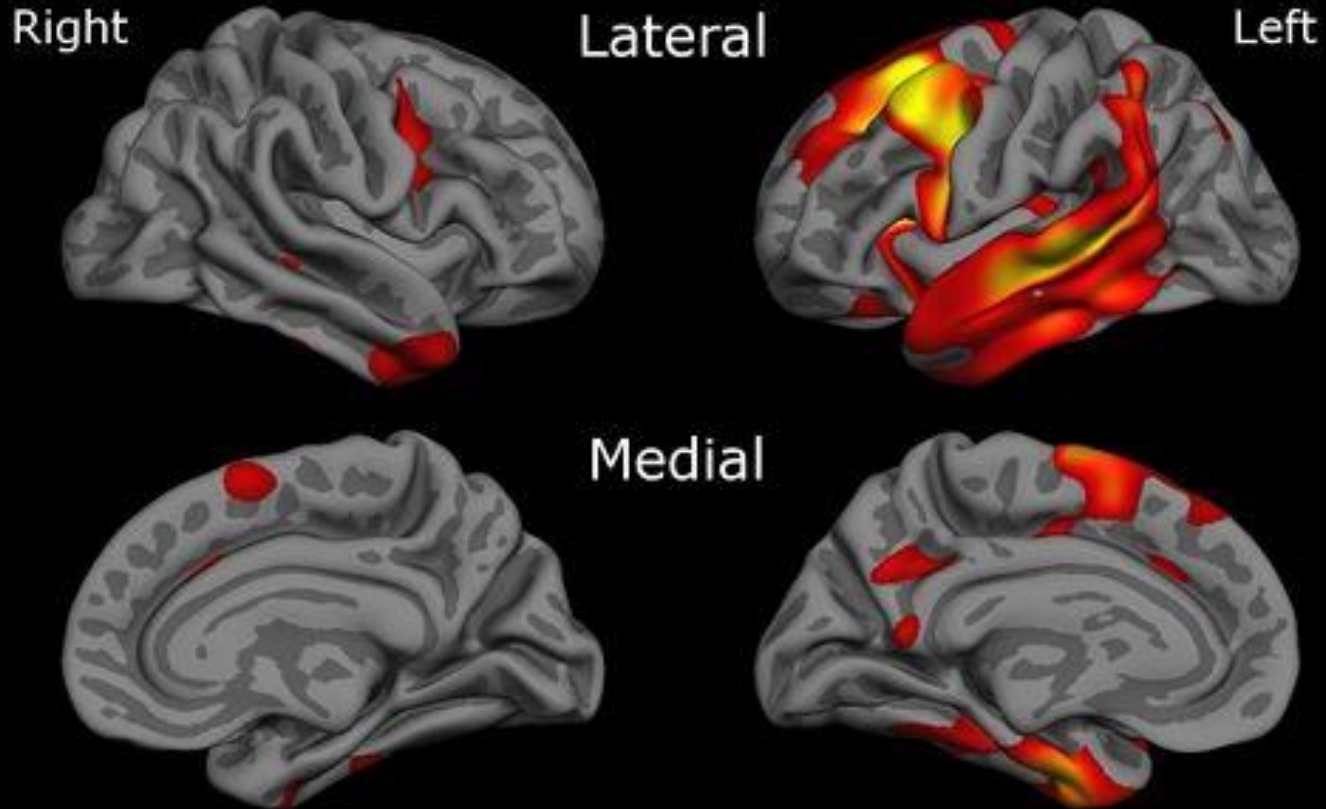
Progressive Aphasia Severity Scale

- Goals
 - Building on CDR-FTLD Language score, to enable clinicians to rate impairment in a variety of specific language domains
 - Identify types as well as grades severity of impairments
- All domains rated as 0, 0.5, 1, 2, or 3, like CDR, using clinical judgment based on history & exam
 - Articulation
 - Syntax/grammar
 - Fluency
 - Word retrieval and expression
 - Repetition
 - Auditory comprehension
 - Single word comprehension
 - Reading
 - Writing
 - Functional communication

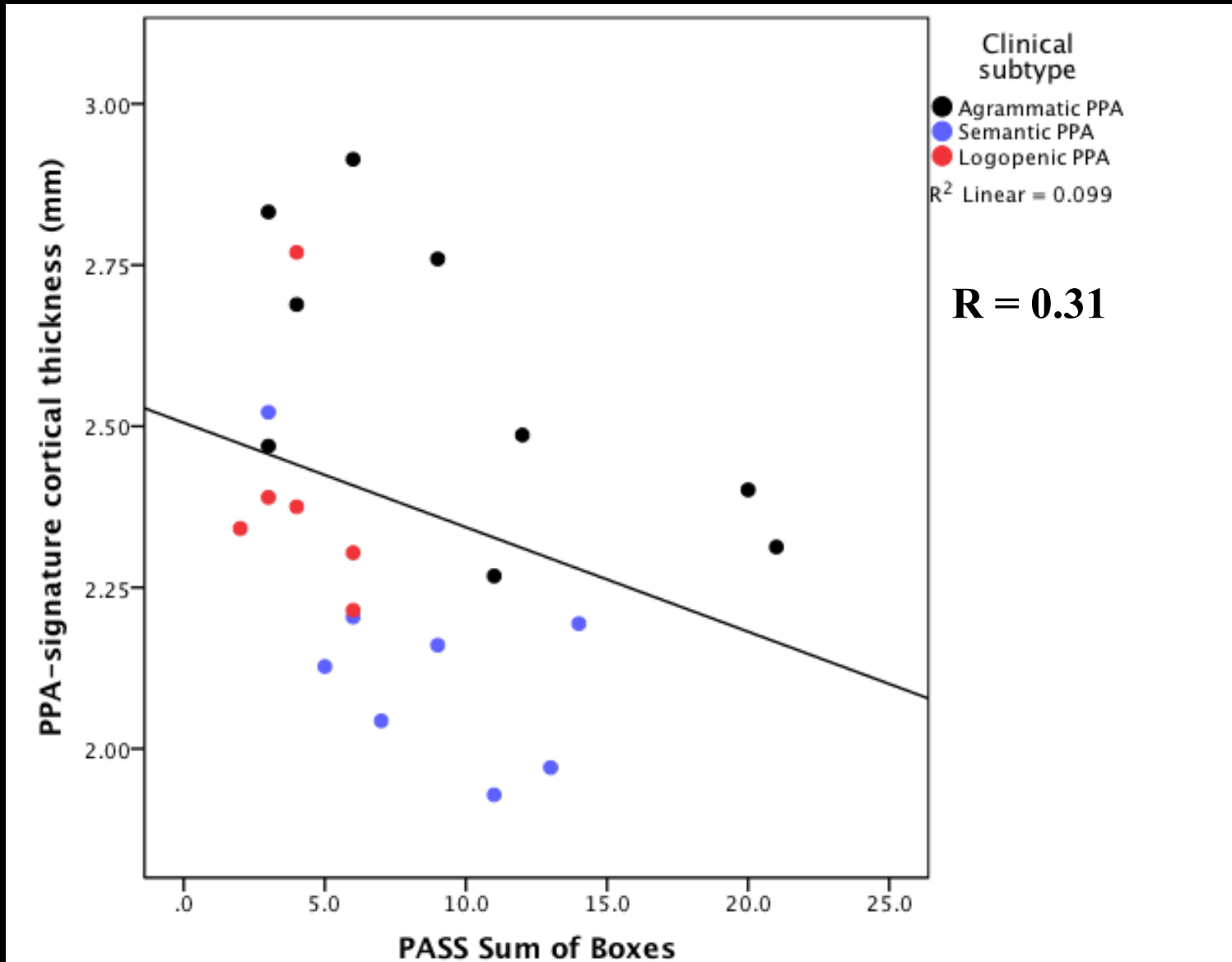


**Generates a
PASS sum of
boxes measure**

Cortical signature of atrophy in PPA



PPA signature MRI marker relates to PASS clinical severity



Social Impairment Rating Scale

Domains of the Social Impairment Rating Scale (SIRS)
Lack of attention/response to social cues
Socioemotional detachment (Lack of empathy or warmth)
Inappropriate trusting or approach behavior
Lack of adherence to social norms
Social withdrawal
Person recognition difficulty

- Modeled after CDR, parses the *Behavior and Personality* supplemental box(Knopman et al., 2009, Brain)
- Each domain is scored on the same scale as the CDR: 0 (none), 0.5 (very mild), 1 (mild), 2 (moderate), 3 (severe)

Table 1 Social Impairment Rating Scale (SIRS) scoring guide

No impairment 0	Questionable or very mild impairment 0.5	Mild impairment 1	Moderate impairment 2	Severe impairment 3
<i>Lack of attention/response to social cues</i>				
No change in attention/response to social cues	Might pay slightly less attention to social cues or respond in a slightly unexpected way; still responds to subtle cues from family member like the raise of an eyebrow or smirk	Pays noticeably less attention to social cues, or sometimes responds awkwardly or unexpectedly to social cues (eg, might make less eye contact, stand closer than normal to others, respond less well to subtle gestures/expressions but understands basic hand pointing and head nods/shakes; might interrupt when another person is speaking).	Pays much less attention to social cues, or often responds awkwardly or unexpectedly to social cues (eg, makes less eye contact, stands closer than normal to others, much less responsive to gestures/expressions; interrupts without noticing expressions of the other person indicating for him/her to stop talking).	Pays almost no attention to social cues, or often responds awkwardly or unexpectedly to social cues (eg, makes less eye contact, stands much closer than normal to others, much less responsive to gestures/expressions; interrupts without noticing expressions of the other person indicating for him/her to stop talking).
<i>Inappropriate trusting or approach behaviour</i>				
No change in judgments of trustworthiness	May be somewhat more gullible or less cautious around others than before but no clear episodes have occurred	Has displayed a few clear but minor acts of poor judgment of other people (eg, may have purchased something from a salesman with less consideration than previously or given out personal information too easily).	Has displayed multiple minor acts or a few major acts of poor judgment of other people resulting in adverse consequences (eg, might have fallen for scams; given personal information away; interacted with strangers without exercising caution such as inviting them into the house).	Has displayed severe, and often recurrent, acts of poor judgment of other people resulting in adverse consequences (eg, might have been sexually abused, lost money, or been involved in a legal case).
<i>Lack of adherence to social norms</i>				
No change in social behaviour	Might be slightly more socially inappropriate such as speaking more loudly than usual	Demonstrates mild but consistent socially inappropriate behaviour at least once per week (eg, mild loss in manners such as leaving the table before others have finished; may make rude or explicit remarks or jokes). Strangers may not perceive that something is 'wrong' with him/her or may question whether something is wrong. These behaviours are mostly observed in the home and around familiar people, whereas in public the patient appears relatively normal.	Demonstrates obvious socially inappropriate behaviour on a daily or near daily basis (eg, spitting, touching private parts or belching; moderate loss in manners such as he/she will eat with hands or 'wolf' down food while others are present; may make crude or sexually explicit remarks or offensive jokes about others; there may have been a minor instance of criminal behaviour such as shoplifting). Strangers perceive that something is 'wrong' with him/her. These behaviours occur in the home and also in public but can be curtailed by family members.	Demonstrates severe socially inappropriate behaviour on a daily or near daily basis (eg, spitting, touching private parts or belching; severe loss in manners such as he/she will eat with hands or 'wolf' down food while others are present; may make crude or sexually explicit remarks or offensive jokes about others; there may have been a major instance of criminal behaviour such as shoplifting). Strangers perceive that something is 'wrong' with him/her. These behaviours occur in the home and also in public and cannot be curtailed by family members.
<i>Person recognition difficulty</i>				
No difference in ability to recognise familiar people	Sometimes has trouble recognising acquaintances or distant coworkers	Often does not recognise acquaintances or distant relatives or friends; usually recognises close friends or family members; may have mistaken an unfamiliar person as familiar	Almost never recognises distant relatives or friends; sometimes does not recognise close friends or family members; or sometimes mistakes an unfamiliar person as familiar	Almost never recognises distant relatives or friends; almost always does not recognise close friends or family members; often mistakes an unfamiliar person as familiar
<i>Social withdrawal</i>				
No change in interest in engaging in social activities	Might be slightly less social or initiate slightly less contact with friends or family, but still enjoys being around them and people in general.	Spends somewhat less time talking to and seeing friends and family; he/she may call or make plans with others less often; is less interested in meeting new people or going to social events. Even if he/she does not initiate plans, the patient will go.	Spends much less time talking to or seeing friends and family; he/she rarely if ever calls or makes plans with friends or family; much less interested in meeting new people or in interacting with close friends and family.	Spends almost no time talking to or seeing friends and family; he/she almost never calls or makes plans with friends or family; almost completely uninterested in meeting new people or in interacting with close friends and family.

Methods & Results

20 FTLD patients and their caregivers

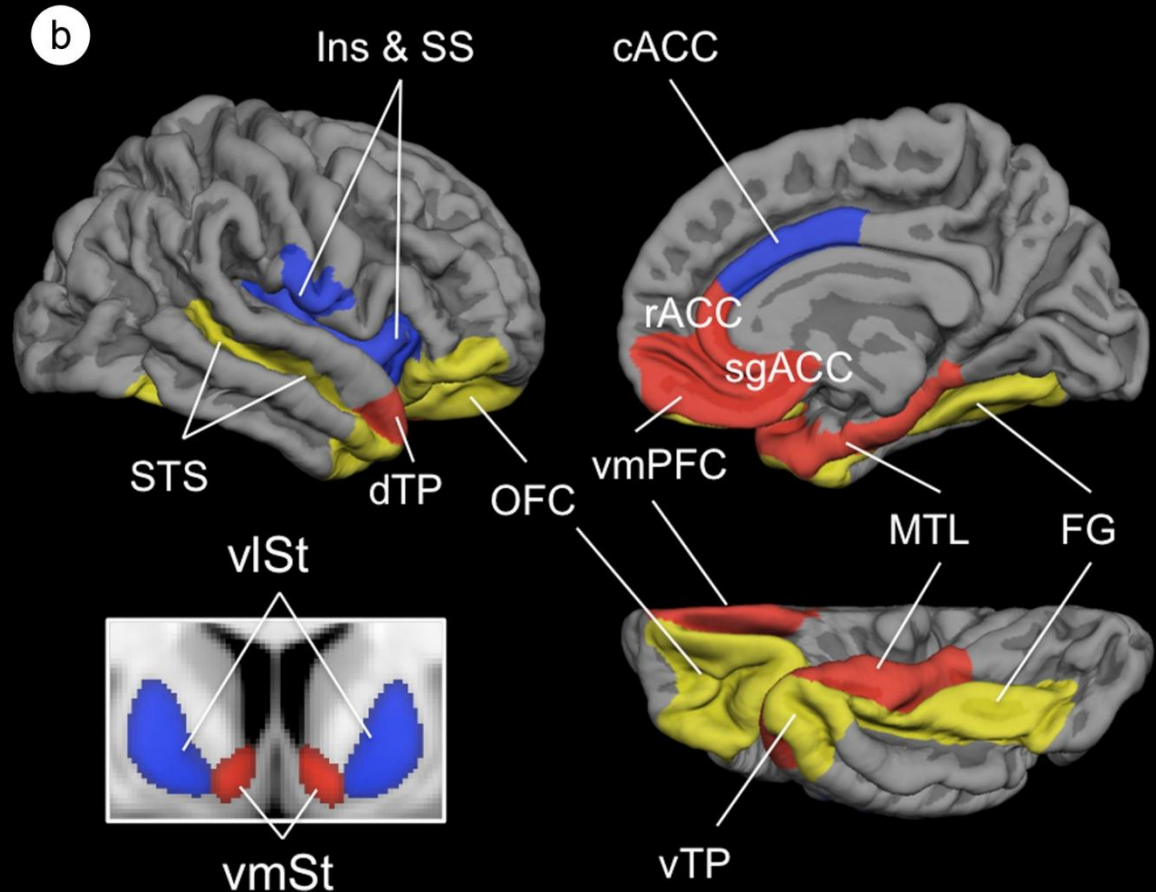
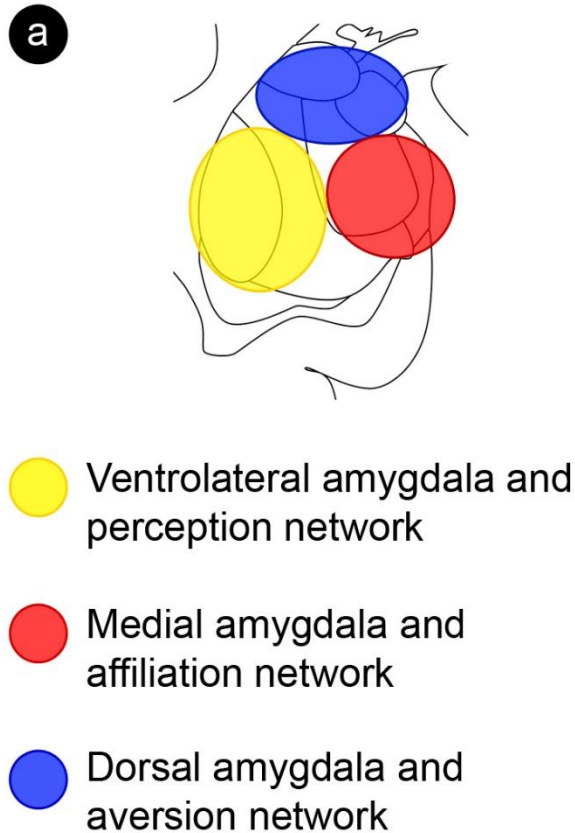
Reliability: SIRS scores were highly reliable across and within two independent raters (most intraclass correlations > 0.90)

Convergent validity: SIRS scores related to an independent rating of global behavior and personality change (CDR-Behav box, $r = 0.59$, $p = 0.008$)

Discriminant validity: SIRS scores did not relate to patient age, gender, education, or global cognitive impairment (MMSE or CDR-SB)

Test hypothesis that atrophy in brain networks identified in prior study (*Bickart et al., J Neurosci 2012*) predict types and severity of impairment in social behavior

Used map of socioaffective brain networks to create ROIs



Some patients showed more prominent social perceptual symptoms: best predicted by perceptual network atrophy

SIRS Domains

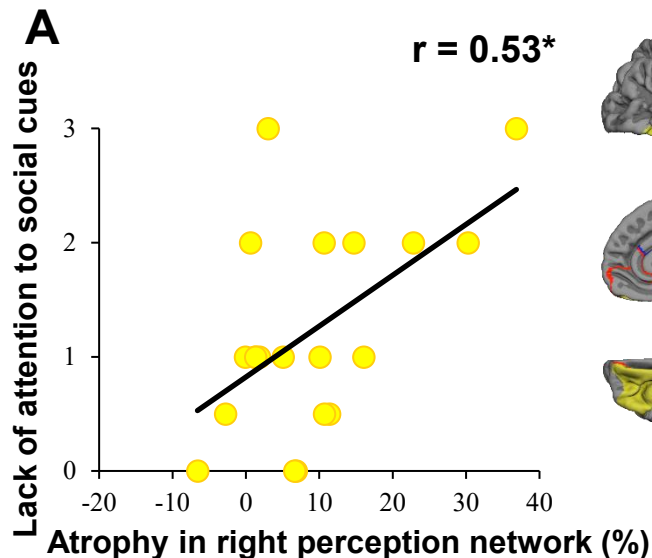
Lack of attention/response to social cues

Socioemotional detachment

Inappropriate trusting or approach behavior

Impaired social perception

- *Less frequent eye-contact*
- *Difficulty following and interpreting body language*
- *Less sensitive to others' facial expressions when behaving inappropriately*



Some patients showed more prominent social affiliative symptoms: best predicted by affiliation network atrophy

SIRS Domains

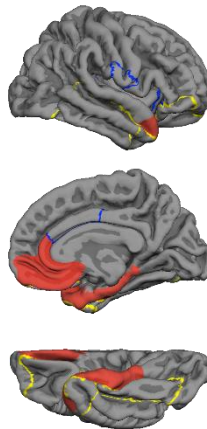
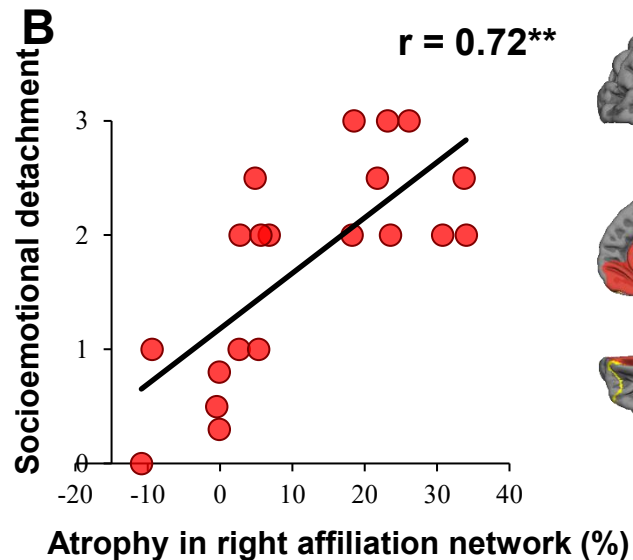
Lack of attention/response to social cues

Socioemotional detachment

Inappropriate trusting or approach behavior

Impaired social affiliation

- *Diminished understanding of others' needs, desires, or feelings*
- *Diminished display of warmth and concern*
- *Cold or cruel*



Some patients showed more prominent social aversive symptoms: best predicted by aversion network atrophy

SIRS Domains

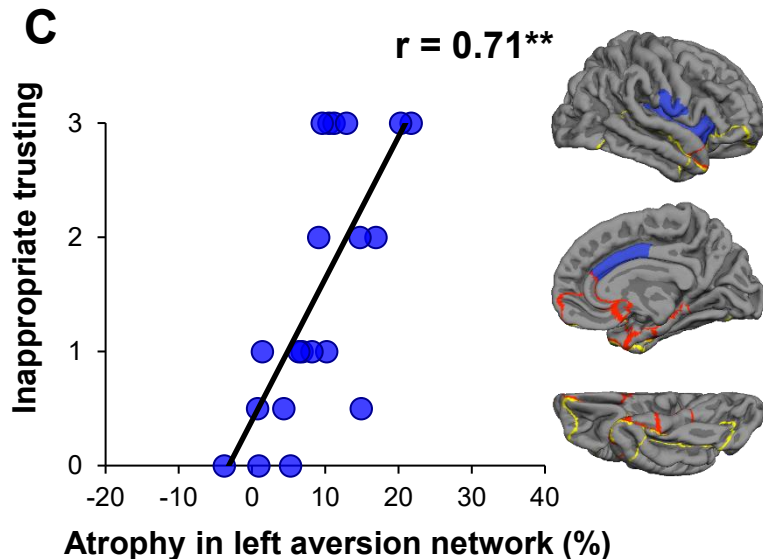
Lack of attention/response to social cues

Socioemotional detachment

Inappropriate trusting or approach behavior

Impaired social aversion

- *Increased willingness to trust, approach, and interact with strangers*
- *Fell for scams from salesmen in person or over the phone*
- *Gave away personal information*



Potential value of PASS and SIRS in clinical research and trials in FTD

CDR and CDR Sum-of-Boxes has been a valuable tool in Alzheimer's research

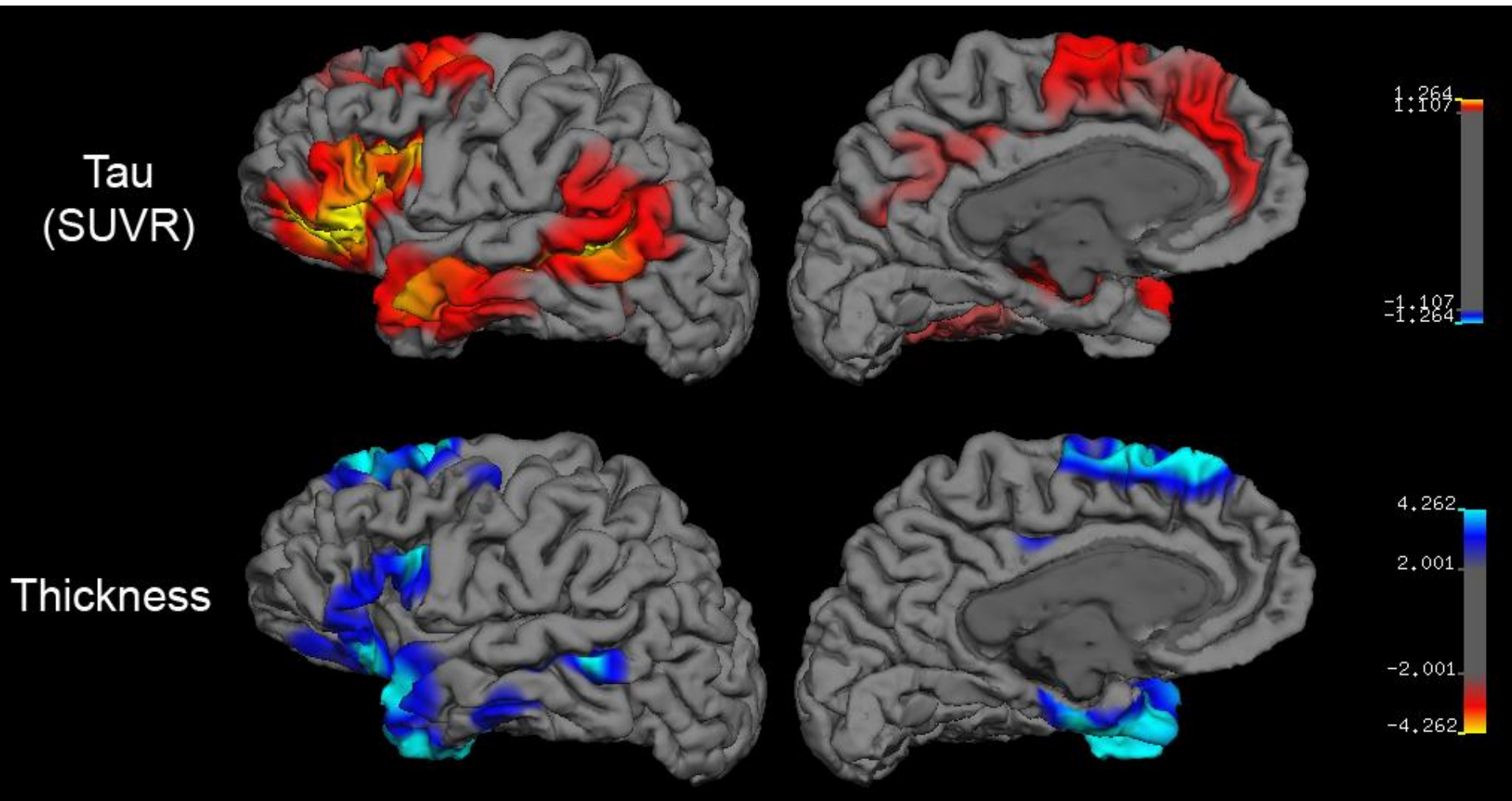
- Provides complementary information to neuropsych testing
- In amnesic MCI, the two types of information together are better than either alone in predicting progression to AD

PASS and SIRS measure core symptoms in FTD

- These and related measures should enable subtle but consistent symptoms, as in prodromal stages, to be measured
- These and other clinician-rating tools (e.g., NPI-c deMedeiros et al., 2010; CBI; etc) may be synergistic with new performance-based tests in dx/prognx/monitoring

Case of nfvPPA

Initial work with Tau PET was encouraging because signal colocalizes with atrophy



But current “Tau PET” is not specific to tau in FTLD; it also binds to something unknown in svPPA—bottom line: not useful at present in FTD

