AUTOMATED ANALYSIS OF DIGITIZED SPEECH ABNORMALITIES IN FRONTOTEMPORAL DEGENERATION

Murray Grossman, Naomi Nevler, Sunghye Cho,

Sanjana Shellikeri, Sherry Ash, Mark Liberman

Penn FTD Center, Department of Neurology

and

Linguistic Data Consortium, Department of Linguistics

University of Pennsylvania

FRONTOTEMPORAL DEGENERATION

- Plan of talk
  - What is FTD?
    - Primary progressive aphasia
    - Behavioral variant FTD
  - Digitized speech analysis tools
    - Speech activity detector
    - Part-of-speech analysis
  - Application to FTD
    - Non-fluent/agrammatic primary progressive aphasia
    - Semantic variant primary progressive aphasia
    - Non-aphasic behavioral variant FTD

Arnold Pick

Dementia with Pick Bodies

Penn
Frontotemporal
Degeneration Center
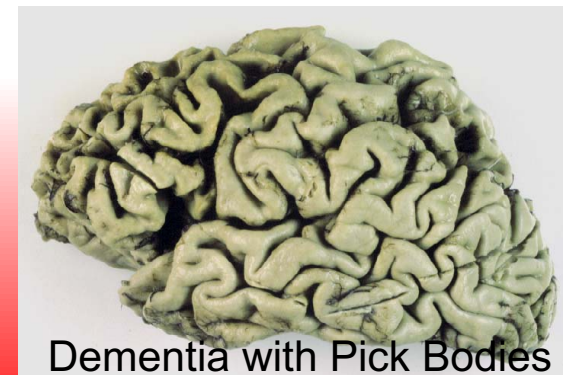
FRONTOTEMPORAL DEGENERATION

- Early-onset neurodegenerative disease
- Two major clinical phenotypes
  - Primary progressive aphasia (45%)
    - Non-fluent/agrammatic variant
    - Semantic variant
  - Disorder of social comportment and executive functioning (55%)
    - Behavioral variant FTD
- Phenotypes are important because they are inexpensive screening markers of pathology

Legend:
- naPPA
- svPPA
- bvFTD

Penn
Frontotemporal
Degeneration Center
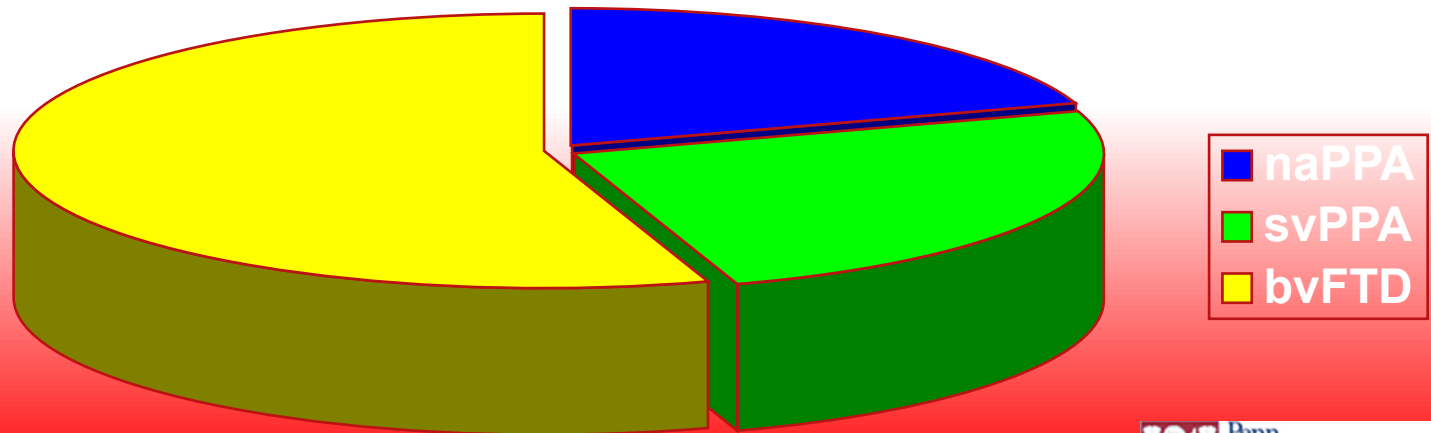
DIGITIZED SPEECH ANALYSIS

- Acoustic analysis
  - Automated speech activity detection
    - Timing of speech activity
      - Total speech time
      - Speech segment duration
      - Pause count
      - Pause duration
      - Pause rate
  - Automated pitch analysis
    - Fundamental frequency (f0)
    - Pitch contour
  - Forced alignment
    - Relate pitch to lexical content
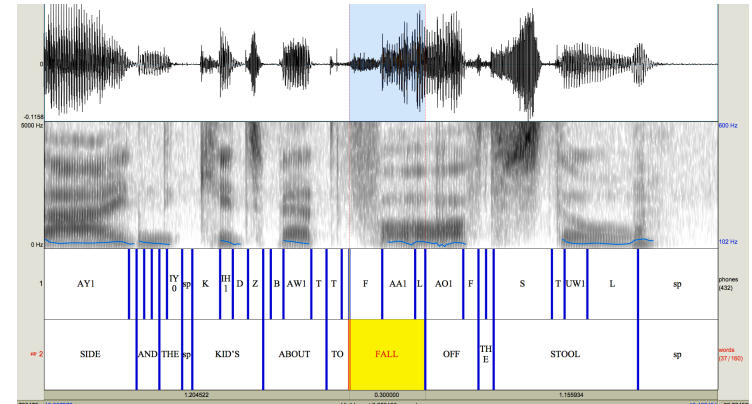
DIGITIZED SPEECH ANALYSIS

- ## Automated lexical analysis
  - Part of speech
    - Major grammatical subcategory
      - e.g. noun, verb, adjective, adverb, conjunction, determiner, pronoun, preposition
    - Speech errors/partial words, interjections
  - Lexical-semantic characteristics
    - Abstractness, frequency, ambiguity, familiarity, age of acquisition

DIGITIZED SPEECH ANALYSIS

- Picture description task
 - Familiar
  - Brief
  - No training for administration
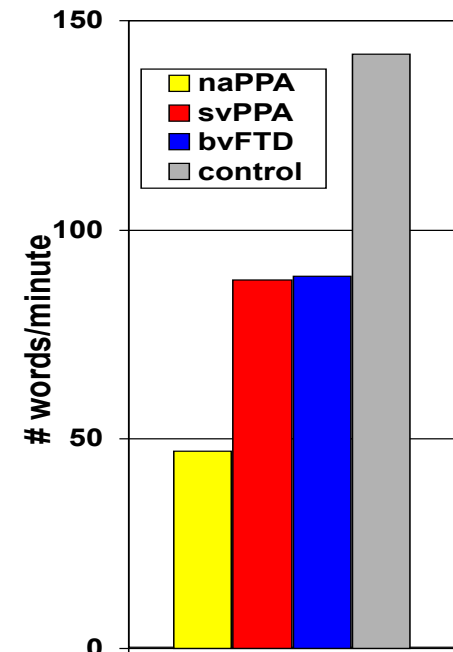

Goodglass and Kaplan, 1972

NON-FLUENT/AGRAMMATIC PPA

- ## Nonfluent/agrammatic PPA
  - Criteria
    - Slow, effortful speech
    - Grammatical impairment
    - Apraxia of speech
  - Significant changes in speech
    - Reduced verbs and inflected verbs
    - Increased speech errors/partial words
    - Limited f0 range
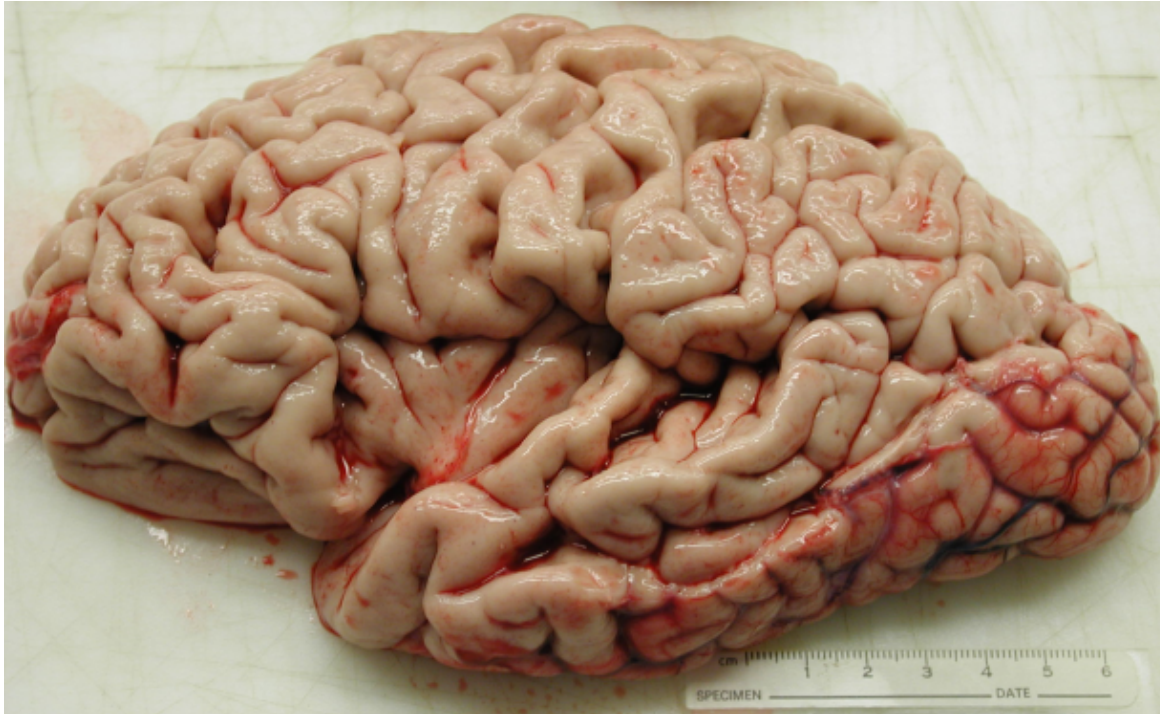
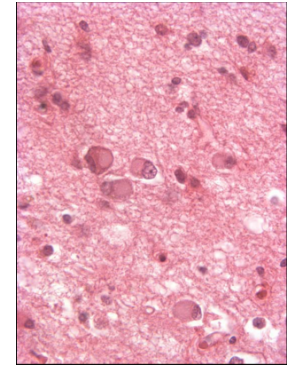Ash et al, 2009

f0 Quantiles per Clinical Phenotype
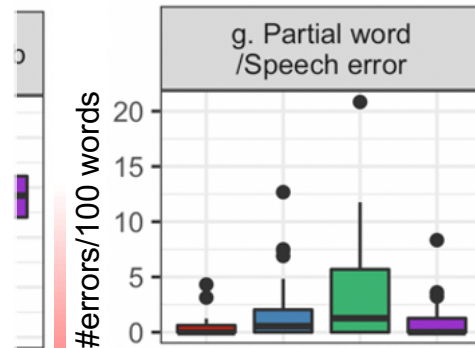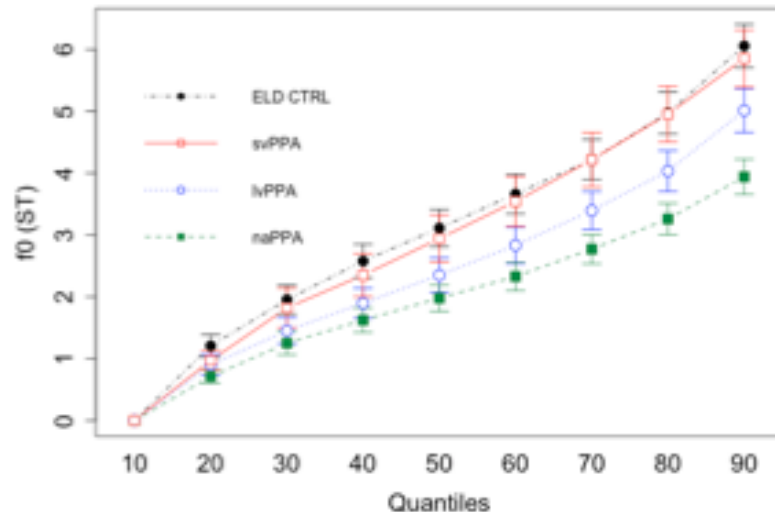
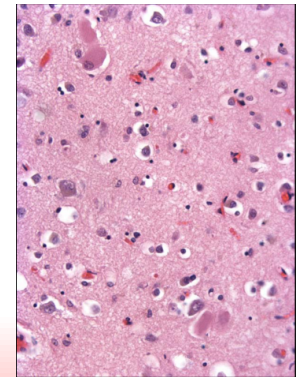Cho et al, in press

NON-FLUENT/AGRAMMATIC PPA

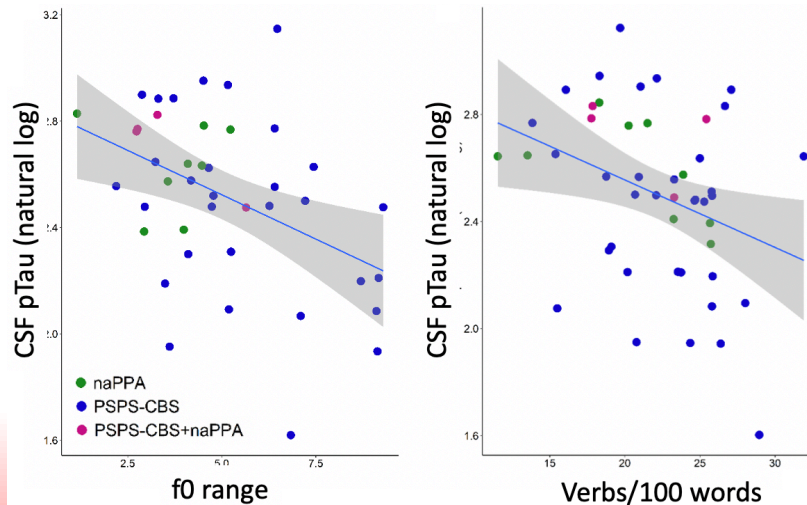Courtesy John Q. Trojanowski MD, PhD

Pick bodies

Balloon cells

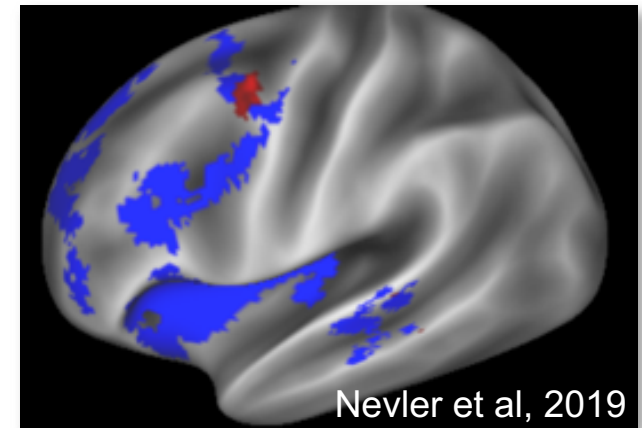- 80% naPPA due to tauopathy such as Pick's disease

NON-FLUENT/AGRAMMATIC PPA

- ## Nonfluent/agrammatic PPA
  - Validation studies directly relating neurobiological measures to speech
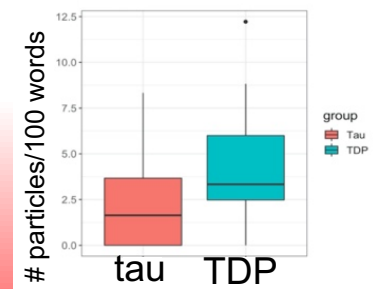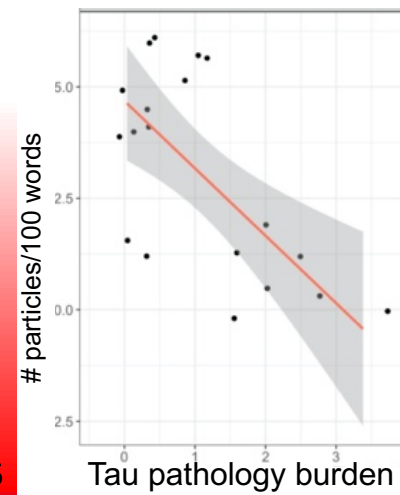   - MRI anatomy
    - Cerebrospinal fluid
    - Pathology

Nevler et al, 2019

- Grammatical and speech deficit related to left frontal atrophy in naPPA

Parjane et al, under review

- Verb use and f0 related to CSF pTau
  - Particle use related to Tau pathology burden in inferior frontal gyrus

Sun et al, in prep

Penn
Frontotemporal
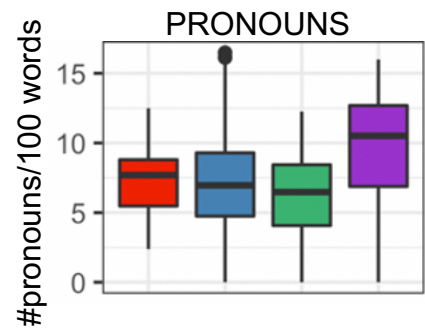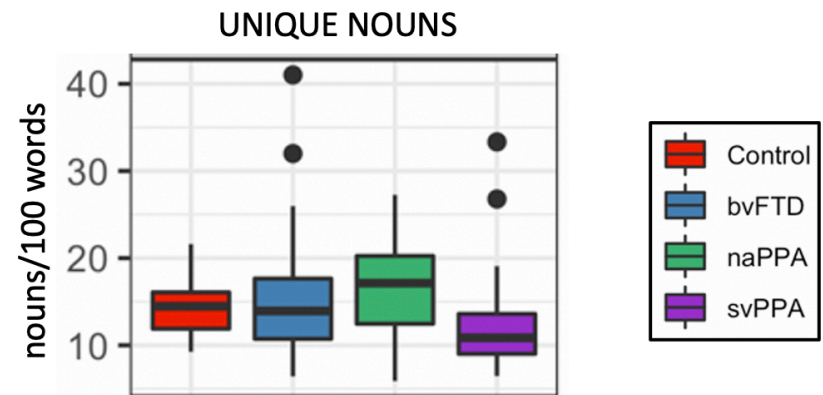Degeneration Center
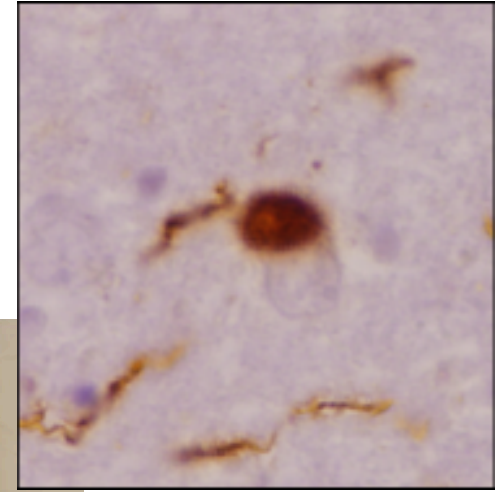
Cho et al, 2020

- **Semantic variant PPA**
  - Criteria
    - Fluent, impaired word-finding
    - Impaired word meaning
    - Impaired object knowledge
  - Significant deficits in speech
    - Fewer nouns
      - Less concrete
      - More ambiguous
    - More pronouns

UNIQUE NOUNS

Legend: Control, bvFTD, naPPA, svPPA

PRONOUNS

ABSTRACTNESS

SEMANTIC AMBIGUITY

Cho et al, in press

Penn Frontotemporal Degeneration Center
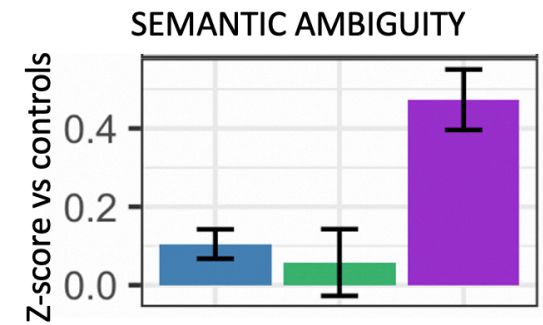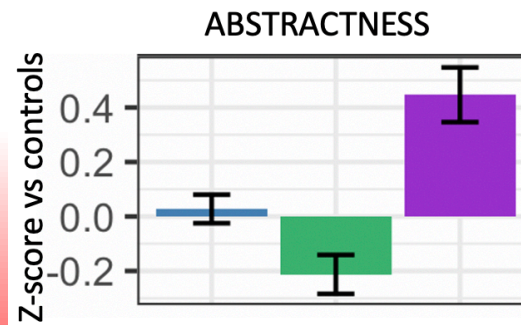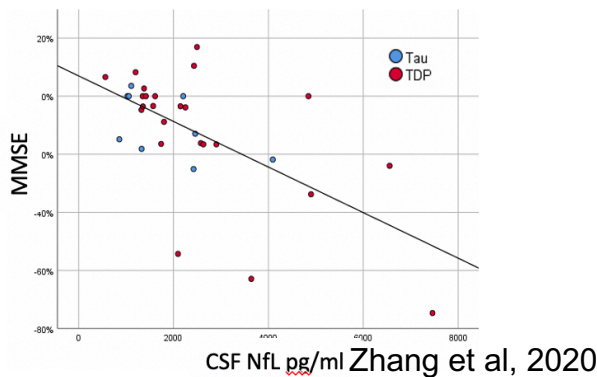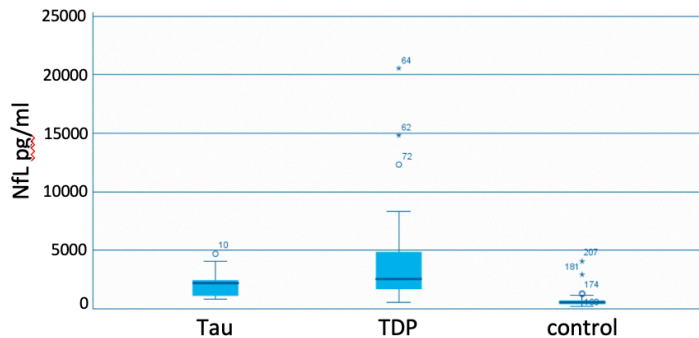
TDP PATHOLOGY IN PPA

- Left temporal atrophy
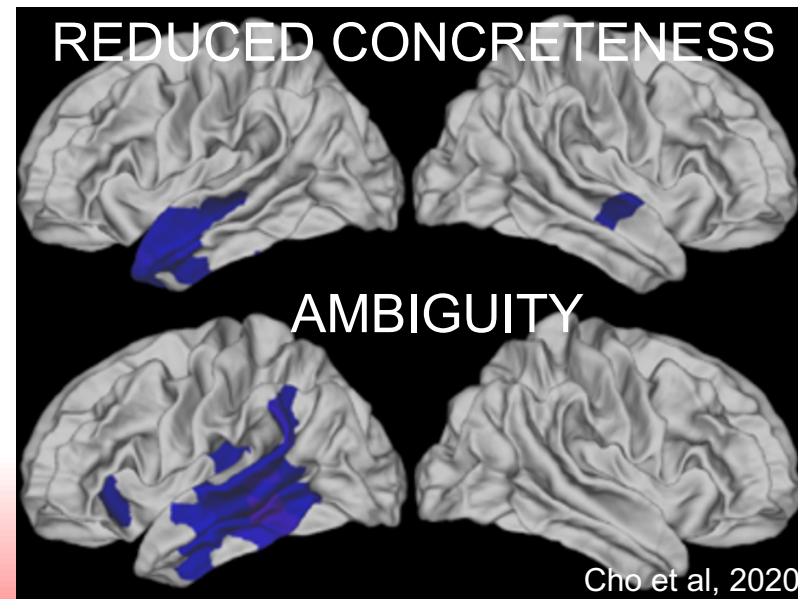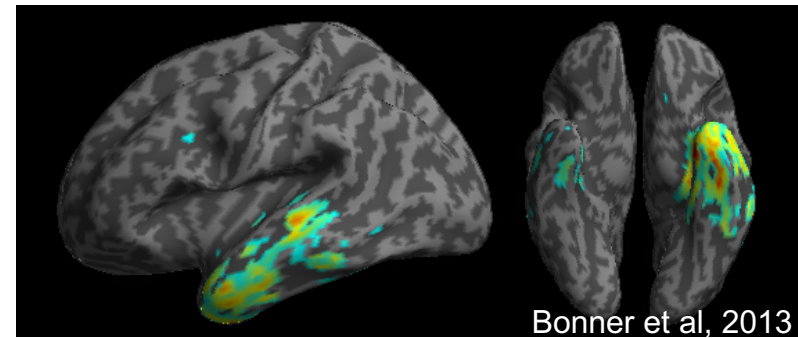- TDP-43 pathology

Courtesy John Q. Trojanowski MD, PhD

SEMANTIC VARIANT PPA

- Semantic variant PPA
  - Validation studies directly relating speech to neurobiological measures
    - MRI
    - Cerebrospinal fluid

Bonner et al, 2013

REDUCED CONCRETENESS

AMBIGUITY

Cho et al, 2020

Zhang et al, 2020

- Concreteness and ambiguity related to left temporal atrophy

– CSF neurofilament light elevated in TDP

– Elevated NfL related to cognition

Penn Frontotemporal Degeneration Center
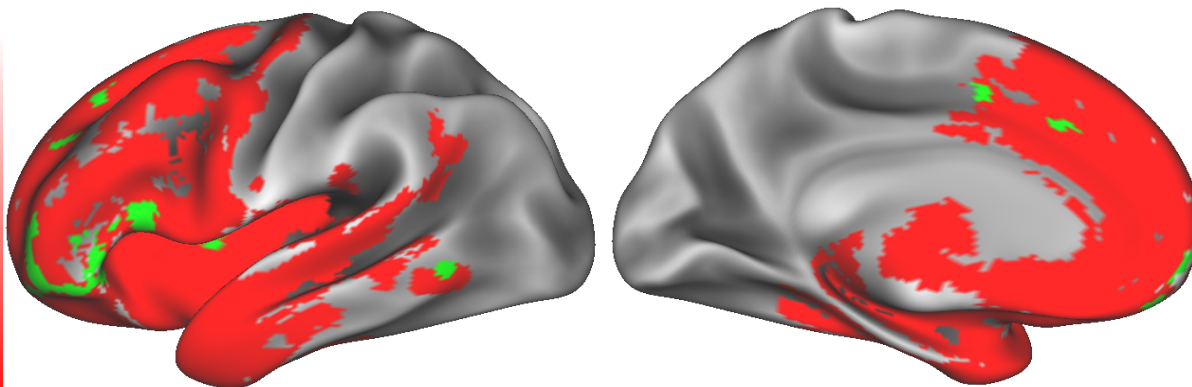
BEHAVIORAL VARIANT FTD

- bvFTD clinical characteristics
  - Poor self-regulation, impulsive, disinhibited, impaired social conduct
  - Rigid, obsessive, rituals
    - Can co-occur with svPPA
  - Apathetic
  - Limited insight
  - Poor empathy
  - Executive deficits
    - Limited judgment
  - bvFTD without clinical aphasia
- Major challenge is establishing objective measures

BEHAVIORAL VARIANT FTD

- Speech and language disorder revealed in bvFTD patients
  - Acoustic features
    - Reduced f0 range
  - MRI atrophy in frontal regions bilaterally
   - Reduced f0 range related to frontal atrophy
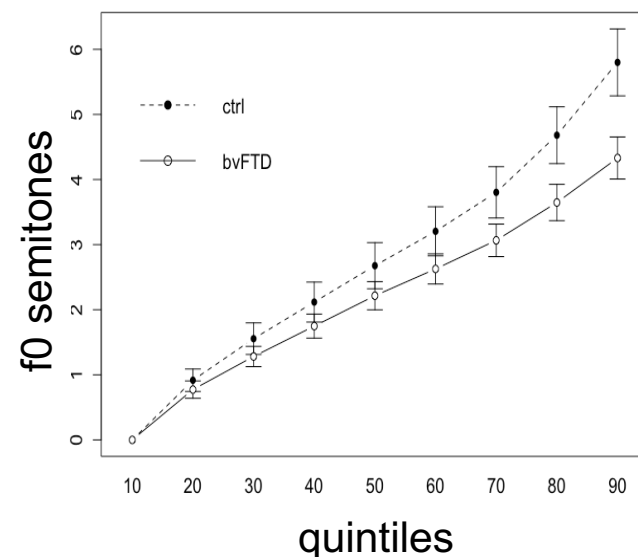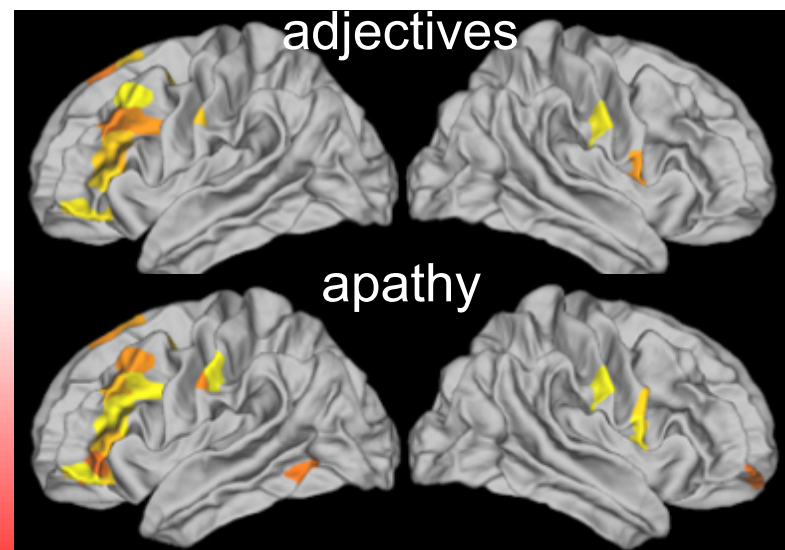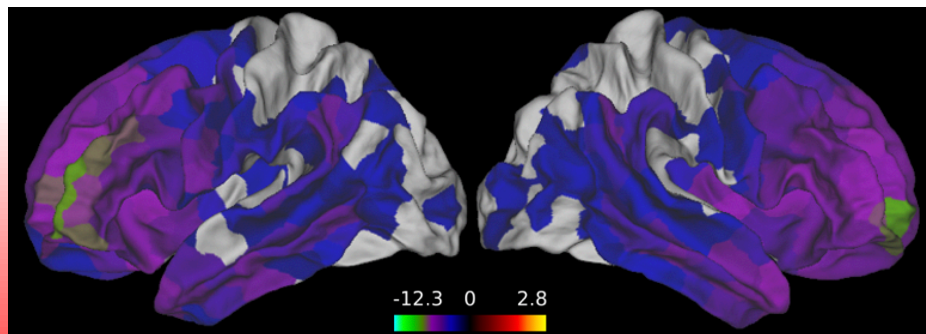

Nevler et al, 2017

BEHAVIORAL VARIANT FTD

- ## Speech and language disorder revealed in bvFTD patients
  - Lexical features
    - Reduced adjective use
    - Related to apathy (r=0.32; p<.01)
  - MRI atrophy in frontal regions bilaterally
    - Reduced adjective use and apathy related to frontal atrophy

Cho et al, in press

adjectives

apathy

Penn
Frontotemporal
Degeneration Center
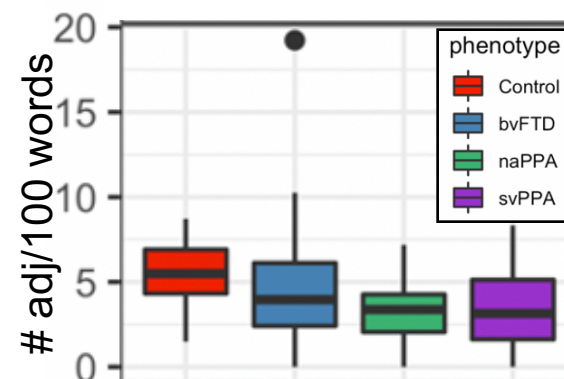
DIGITIZED SPEECH IN FTD

- Digitized speech useful in FTD
  - Objective verification of clinical features
  - Useful for evaluating eligibility for treatment trials
  - Follow patients longitudinally for efficacy and safety during treatment trials
  - Enhance models of the neurobiology of language
  - Clinical marker of spreading pathology in progressive neurodegenerative diseases

THANK YOU!

- Questions?

Penn
Frontotemporal
Degeneration Center