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

Support from NIH (AG066597, AG017586, AG054519, AG052943),
generosity of the Newhouse Foundation, Wyncote Foundation,
Robinson Family foundation, and patients and families
No conflict of interest to declare
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
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
• 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
• 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

![Graph showing f0 Quantiles per Clinical Phenotype](image)

![Graph showing # errors/100 words](image)

Ash et al, 2009

Cho et al, in press
NON-FLUENT/AGRAMMATIC PPA

- 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

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

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

Parjane et al, under review

Sun et al, in prep
SEMANTIC VARIANT PPA

- 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

Cho et al, 2020

Cho et al, in press
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

- CSF neurofilament light elevated in TDP
- Elevated NfL related to cognition

- Concreteness and ambiguity related to left temporal atrophy

Zhang et al. 2020

Bonner et al. 2013

Cho et al. 2020
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
• 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
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

quantitative analysis

BEHAVIORAL VARIANT FTD
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?