Unraveling Frontotemporal Dementia and Primary Progressive Aphasia: Clinical Subtypes, Genes, and Neuroimaging

Antonios Chatzipanagiotou
Deree – The American College of Greece | PS4965A1 – Topics in Neuropsychology
Supervisor: Dr. Ionas Beratis

A. Abstract

This review summarizes clinical, genetic, and imaging findings in frontotemporal dementia (FTD) and its primary progressive aphasia (PPA) subtypes. It examines variant-specific presentations of svPPA and nfPPA, key genes involved (MAPT, C9orf72, GRN), and neuroimaging patterns. Treatment remains symptomatic, and diagnostic overlap with Alzheimer's disease complicates clinical management. This poster highlights emerging biomarker and genetic research and emphasizes the need for clearer classification to improve care pathways.

B. Introduction to FTD & PPA

FTD is the third most common form of dementia, especially among younger adults. It was first described by Arnold Pick in 1892 and later classified by Alois Alzheimer. FTD is often confused with Alzheimer's due to shared genetic components like C9orf72 and TDP-43. Key clinical features include behavioral changes and executive dysfunction.
Subtypes:

- Behavioral variant FTD (bvFTD)
- Primary Progressive Aphasia (PPA), with three variants:
  - Semantic (svPPA)
  - Non-fluent/agrammatic (nfPPA)
  - Logopenic (lvPPA, often linked to Alzheimer's)

D. Genetic Pathways

Gene Mutations in FTD:

- MAPT: Motor symptoms, tau interaction, medial temporal atrophy
- C9orf72: Executive dysfunction, ALS overlap, thalamic atrophy
- GRN: Verbal fluency loss, frontoparietal atrophy
- 60% of FTD cases involve these genes

Neuroinflammation & Stress Response:

- C9orf72 interacts with glial cells and stress granule formation
- TREM2 may link to tauopathies but evidence is inconclusive

E. Clinical Symptoms & Diagnosis

- Behavioral Variant (bvFTD):

Disinhibition, apathy, loss of empathy, compulsive behaviors

- svPPA:

Loss of word meaning, naming difficulty, preserved grammar

- nfPPA:

Effortful, agrammatic speech, speech motor errors

- lvPPA:

Word-finding pauses, impaired repetition, often Alzheimer-related

- Diagnostic Frameworks:

Neary et al. (1998), revised by Rascovsky et al. (2011)
Gorno-Tempini criteria (2011) for PPA classification

F. Treatment & Challenges

No approved treatments for bvFTD or PPA.
Management includes speech and behavioral therapy.
Experimental Approaches:

- Clinical trials for genetic forms
- Transcranial direct current stimulation in nfPPA

Challenges:

- Mixed variants complicate classification
- Biomarkers not yet clinically viable

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