PRIMARY PROGRESSIVE APHASIA
(PPA)

OCTOBER 9, 2003
Memory Disorders Research Society
Chicago

Marsel Mesulam, MD
Cognitive Neurology and Alzheimer's Disease Center
Northwestern University Feinberg School of Medicine

PPA COLLABORATORS

- Sandra Weintraub- Alissa Wicklund
- Nancy Johnson- Chris Fahey
- Darren Gitelman- Siri Sonty
- Cindy Thompson- Ann Oehring
- Deborah Reed
- Dana Small- Ramesh Srinivasan
- Dan Geschwind-Maria Jesus Sobrido (UCLA)
- Roman Alberca-Enrique Montes (Seville, Spain)

Definition of Primary Progressive Aphasia (PPA)

PPA is characterized by a progressive impairment of word usage and comprehension.

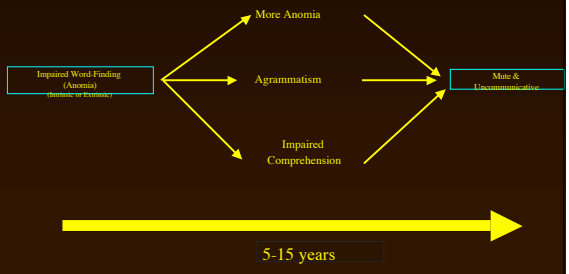
Memory, personality, movement, face and object recognition remain relatively preserved for at least the first 2 years.

Core Features of PPA

- Naming deficits (anomia)
- Impaired fluency: word- finding pauses
- Agrammatism
- Impaired comprehension of word meaning

These features can be dissociated; any one is sufficient for diagnosis. PPA can be fluent or non-fluent.

PROGRESSION OF PPA



The Core and Halo of PPA

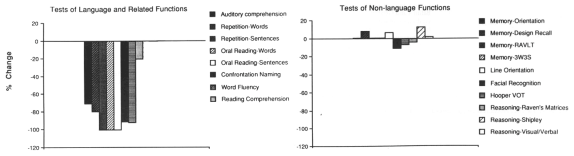
Core Features (Language-Based)

- Impaired fluency: word-finding pauses
- Agrammatism
- Impaired comprehension of word meaning
- Naming deficits (anomia)

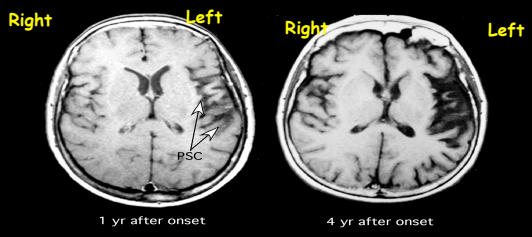
Boundary Features

- Dysarthria
- Idiomotor Apraxia
- Dyscalculia
- Visual recognition deficits
- "Executive" dysfunction
- Poor memory for words- but event memory is preserved.

Longitudinal Investigations
In a PPA Patient Tested 6 and 9 years After Onset (M.K.)

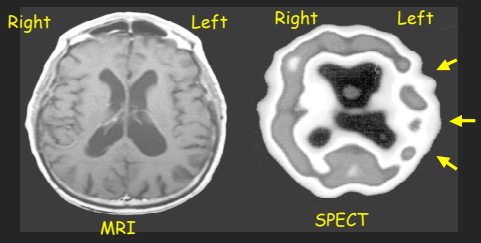


Weintraub, Rubin & Mesulam, Archives of Neurology 1990.



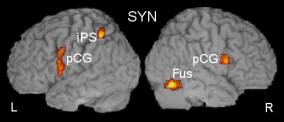
Two MR Scans from the Same Patient
Separated by a 3-yr Interval
Mesulam, Annals of Neurology, 2001

73 yr Old Man With PPA



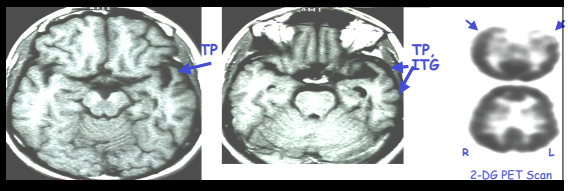
Mesulam, Annals of Neurology 2001

FUNCTIONAL MRI of LEXICAL PROCESSING
11 PPA VERSUS 11 AGE-MATCHED CONTROLS
Sonty, Mesulam, Thompson, Johnson, Weintraub, Parrish, & Gitelman
Annals of Neurology, 2003.



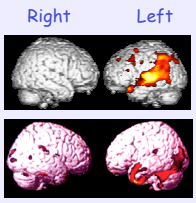
Areas that were more activated in PPA than in controls
during word identification tasks.

FLUENT PPA WITH POOR COMPREHENSION



MRI and 2-DG PET in Patient with PPA
Onset at Age 42 (M. Sc.).

Voxel-Based Morphometry in Fluent vs Non-Fluent PPA



Dementia and Geriatric Cognitive Disorders

Dement Geriatr Cogn Disord 1999;10(suppl 1):33–36

Semantic Dysfunction in Frontotemporal Lobar Degeneration

Julie S. Snowden

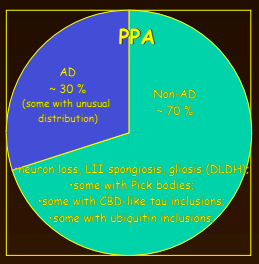
Key Words
Semantic dementia · Word Meaning · Object recognition · Temporal lobes

Abstract
Semantic dementia, characterized by loss of word meaning and impaired face and object recognition, is one of the clinical manifestations of frontotemporal lobar degeneration and is associated with atrophy of the inferior and middle temporal gyri. Patients may present predominantly with problems in naming and understanding words, or in face and object recognition, the verbal or nonverbal predominance reflecting the accent of atrophy on the left or right temporal lobe. Behavioural changes

Introduction

In frontotemporal dementia (FTD) [1- prominent feature is character change an social conduct, instrumental functions c visual perception are relatively intact. Pat progressively less as part of their general namia and eventually become mute, yet t no evidence that they have difficulty un meaning of words or in recognizing objec contrast, some patients with focal cerebr [5–7] in whom the emphasis of the path temporal rather than frontal lobes in wl feature is a profound loss of semantic k may include loss of the ability to underst

NEUROPATHOLOGY OF PPA

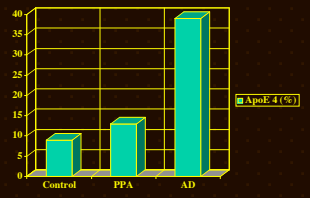


PPA belongs to the FTD-Pick-tauopathy spectrum of diseases, within which the major subtypes are PPA, SD and FLD.

Possible association of the *tau* H1/H1 genotype With primary progressive aphasia

Sobrido, M.-J. MD, PhD; Abu-Khalil, A. BA; Weintraub, S. PhD; Johnson, N. PhD; Quinn, B. MD, PhD; Cummings, J. L. MD; Mesulam, M.-M. MD; Geschwind, D. H. MD, PhD

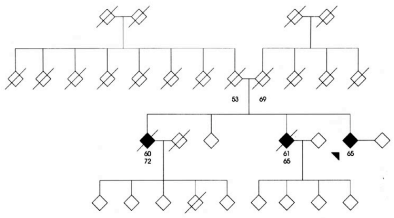
Neurology, 60:862-864, 2003.



ApoE 4 Allele Frequencies

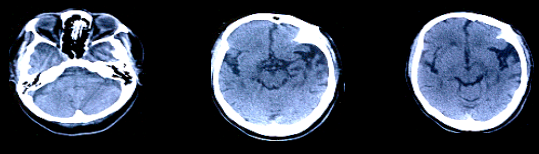
Mesulam, Johnson, Grujic & Weintraub, Neurology, 1997

Familial PPA- Alzheimer Dis Assoc Disord, 17:106, 2003.
Krefft, Graff-Radford, Dickson, Baker, Castellani



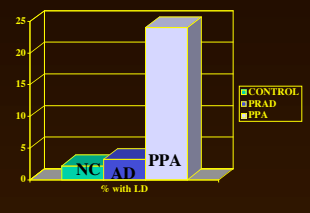
One affected had DLDH,
tau genotyping in another affected is negative.

Left hemicranial craniosynostosis and hypoplasia.
PPA onset at age 63.



Alberca, Montes, Russell, Gil-Néciga, Mesulam- Arch Neurol, in press

PROBANDS AND FIRST DEGREE RELATIVES WITH LEARNING DISABILITY



From Weintraub and Mesulam- La Démence: Pourquoi?, Paris 1995.