Marsel Mesulam, MD
Northwestern University Cognitive Neurology and Alzheimer's Disease Center (CNADC)

Brain injury can be sudden or slowly progressive over years. Diseases that cause progressive brain injury (atrophy) are known as neurodegenerations. The location of atrophy determines the nature of the deficits: memory, language, and behavioral changes.

Two major neurodegenerative diseases are Alzheimer's disease (AD) and frontotemporal lobar degenerations (FTLD).

The two major types of FTLD are FTLD-Tau and FTLD-TDP.

Primary progressive aphasia (PPA)

- a) impaired usage, retrieval, spelling, or comprehension of words (i.e., aphasia)
- b) the language disorder initially, arises as the principal deficit, (i.e., primary)
- c) The cause is a neurodegenerative disease (i.e., progressive)

Types of PPA and relationship to neurodegeneration

- Agrammatic (PPA-A)
  - consistently low word output
  - disordered grammar
  - good comprehension

- Semantic (PPA-S)
  - good word output & grammar
  - poor comprehension & naming

- Logopenic (PPA-L)
  - word-finding hesitations
  - good grammar & comprehension

Mostly FTLD-Tau, a few AD.

Mostly FTLD-TDP, a few AD.

Mostly AD, a few FTLD.
THERAPEUTIC CONSIDERATIONS - PPA

MEDICAL:
- Is it AD or not determined by Aβ/PET scans and spinal fluid analysis.
- If AD, trazodone, donepezil, rivastigmine, memantine.
- Start treatments appropriate for the diagnosis.
- In other cases, refer to proper clinical trials.

NON-PHARMACOLOGICAL:
- Education: AV13, IMPACT (ppaconnection.org).
- Life enrichment programs & psychosocial interventions.
- Speech therapy: the internet program funded by AFTD.
- TMS?

THE CLINICAL PICTURE INCLUDES THE NEW ONSET OF ONE OR MORE OF THE FOLLOWING FEATURES IN RELATIVE ISOLATION:
1) Diminished motivation (apathy) alternating with loss of restraint (disinhibition, gullibility, indiscretions).
2) Impaired judgment, insight, problem solving, multitasking, flexibility.
3) Emotional blunting with erosion of empathy or concern for the feelings of others.

BEHAVIORAL VARIANT FRONTOTEMPORAL DEMENTIA (bvFTD)

DEFINITE DIAGNOSIS REQUIRES THREE STEPS:
1. Documentation of the clinical picture by history or neuropsychological testing.
2. Documentation of progression.
3. Documentation of abnormality in the frontal lobes by MRI, SPECT or metabolic PET.

IF THE CLINICAL PICTURE LOOKS LIKE bvFTD BUT THERE IS NO DOCUMENTATION OF PROGRESSION OR FRONTAL LOEB ABNORMALITY OR COMBINATION OF THESE TERMS SUCH AS "POSSIBLE" bvFTD OR bvFTD "PHENOCOPY" ARE MORE APPROPRIATE.

NEURODEGENERATIONS IN bvFTD:
(40% FTLD-TAU; 40% FTLD-TDP; 20% AD)

THERAPEUTIC CONSIDERATIONS - bvFTD

THE MEDICAL:
- Is it AD or not?
- If AD, use AD drugs.
- If not, is in FTLD-Tau or FTLD-TDP - a goal for the future.
- In other cases, refer to proper clinical trials.

NON-PHARMACOLOGICAL:
- Education: AV13, IMPACT (ppaconnection.org).
- Life enrichment programs & psychosocial interventions.
- Speech therapy: the internet program funded by AFTD.
- TMS?

QUIZ
1. ARE PPA AND bvFTD MOST COMMONLY CAUSED BY FTLD? YES
2. ARE PPA AND bvFTD ALWAYS CAUSED BY FTLD? NO
3. IS IT POSSIBLE TO HAVE BOTH PPA AND ALZHEIMER'S DISEASE? YES
4. CAN bvFTD BE CAUSED BY ALZHEIMER'S DISEASE? YES