FTD and PPA:
Research Update 2009

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Why combine PPA and FTD in the same conference?
Dementia: a condition caused by a disease

- Affects all thinking abilities, behavior, personality

- Gradual change from a prior level

- Progressive decline

- Customary activities of daily living, work and social relations are impaired

- Shortens one’s life expectancy
DEMENTIA IS A SYMPTOM OF DISEASE IN THE BRAIN
LIKE FEVER IS A SYMPTOM OF DISEASE IN THE BODY
DEMENTIA SYMPTOMS COME IN DIFFERENT FORMS

LOSS OF SHORT TERM MEMORY - PrAD

LOSS OF LANGUAGE: NAMING, UNDERSTANDING - PPA

LOSS OF JUDGMENT, SOCIAL SKILLS - bvFTD

LOSS OF VISUAL PERCEPTION - progressive visuospatial dysfunction
WHAT **CAUSES** DEMENTIA?

DAMAGE TO BRAIN CELLS AND CONNECTIONS

- MULTIPLE STROKES
- NEURODEGENERATIVE DISEASES OF THE BRAIN

ALZHEIMER’S DISEASE
Amyloid, tau

PROTEIN=TAU

Pick’s Disease
CBD
PSP

FRONTOTEMPORAL LOBAR DEGENERATION

PROTEIN=TDP-43

FTDU-MND

NEW PROTEIN?
FTLD PATHOLOGY PRODUCES

TWO CLASSES OF DEMENTIA SYMPTOMS

LANGUAGE TYPE

PRIMARY PROGRESSIVE
APHASIA (PPA)

Progranulin mutations
Young onset (<65)

BEHAVIORAL TYPE

Behavioral Variant
Frontotemporal Dementia (BvFTD)

Tau and Progranulin mutations
Young onset (<65)
Behavioral Variant FTD

Initial: decline in social/interpersonal conduct; poor judgment and/or loss of initiative; no memory or language loss INITIALLY

Loss of typical emotional responses

Progresses: to affect other cognitive functions

Early neuroimaging: prefrontal cortex

Unaware of personality and cognitive changes
Primary Progressive Aphasia = PPA

Initial: finding words while speaking; no memory loss; no behavioral change INITIALLY

Progresses: other language deficits (understanding conversation, reading, writing)

Progresses: to affect other cognitive and behavioral functions

Early neuroimaging: language brain regions

Affected individuals are aware of illness
DEMENTIA OF ALZHEIMER’S DISEASE

Short term memory loss; spatial (space) and temporal (time) disorientation

DEMENTIA OF FRONTOTEMPORAL LOBAR DEGENERATION

Type 1 Behavioral variant FTD: Deficits in executive functions, social skills, personality

Type 2 Primary Progressive Aphasia: Impairments in speaking, understanding, Reading and writing
We have no biomarkers* either for AD or for FTLD. We base our diagnosis on the TYPES OF SYMPTOMS in the clinical examination.

* biomarkers=blood tests, spinal fluid chemicals, MRI markers. Brain biopsy is the only test and without viable treatment it is not appropriate.
CLINICAL
What the doctor diagnoses during life: Symptoms

PATHOLOGY
What the neuropathologist diagnoses after brain autopsy: Cell Abnormalities

PPA
Aphasia
Language Disorder

bvFTD
Personality
 Judgment

“Probable
AD”
Short Term Memory

80%

70%

80%

90+%

FTLD-T
FTLD-U

AD

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## Different Types Of Research

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<th>Observing and measuring behavior</th>
<th>Memory loss vs aphasia vs behavior change</th>
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<td>Inspecting brain regions on MRI</td>
<td>Which regions? How do they differ from normal?</td>
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<td>Inspecting brain tissue</td>
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<td>Developing and testing drugs</td>
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<td>Testing other intervention</td>
<td>What works for management and coping?</td>
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Pace is SLOW

“Breakthroughs” come after many years of work and many different laboratories bringing together their findings: 5+ YEARS FOR DRUGS

Participation in clinical studies: how the disease affects the person and their loved ones; risk factors for illness

Participation in brain imaging studies: find new ways to diagnose the disease

Participation in brain donation programs: discover new proteins for drug development
Northwestern New Funding

GRANT FOR INTERNATIONAL REGISTRY FOR PPA to Dr. Nancy Johnson

IMPPACT: International PPA Consortium

SOCIAL SECURITY ADMINISTRATION HEARING ON YOUNG ONSET DEMENTIA- RAISE AWARENESS OF PPA and bvFTD (AFTD, AA)
CLINICAL DIAGNOSIS

Subtyping: different forms of aphasia can improve prediction of pathology in the brain

BRAIN IMAGING STUDIES

Cortical Thickness Mapping shows different regions of cell loss depending on the type of language deficit

PROTEINS AND GENES

Progranulin mutations responsible for PPA in two families

What role does TDP-43 play in brain pathology?
Emotional signals are processed abnormally in people with bvFTD. They cannot interpret negative emotion but have an easier time understanding positive emotion.
PPA Project

Funded by the National Institute on Deafness and Communication Disorders (NIDCD)

36 Individuals with PPA recruited in first year (16 above target!)

Continuing to recruit and now following up initial participants

WHAT WILL THIS TELL US?

Different symptoms predict different forms of pathology

How does the disease progress in different individuals behaviorally? In the brain?
Future Research at Northwestern

TREATMENT TRIALS: Memantine for bvFTD

What are the best ways we know now to intervene and live with PPA and bvFTD? ADEAR Booklet

Midwest-Southwest Consortium for FTD

Improve diagnostic accuracy and standardize the way in which we make the pathologic diagnosis of diseases that cause bvFTD (Bigio)

PPA Program years 3-5

How does illness progress and what are early signs that predict different routes of progression?
FROM CELLS.....

Neuropathologic features of FTLDs

Longitudinal Study Of Language In PPA

Electrophysiological Brain

Neuropsychiatric Symptoms In bvFTD and PPA

Neuroimaging of PPA and bvFTD

Treatment of PPA and bvFTD

Education and Support for bvFTD and PPA

TO SOCIAL WORK
Thank you to all the individuals with PPA and bvFTD and to their families and friends for your unwavering support and commitment to our research efforts.