Northwestern Cognitive Neurology And Alzheimer's Disease Center
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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

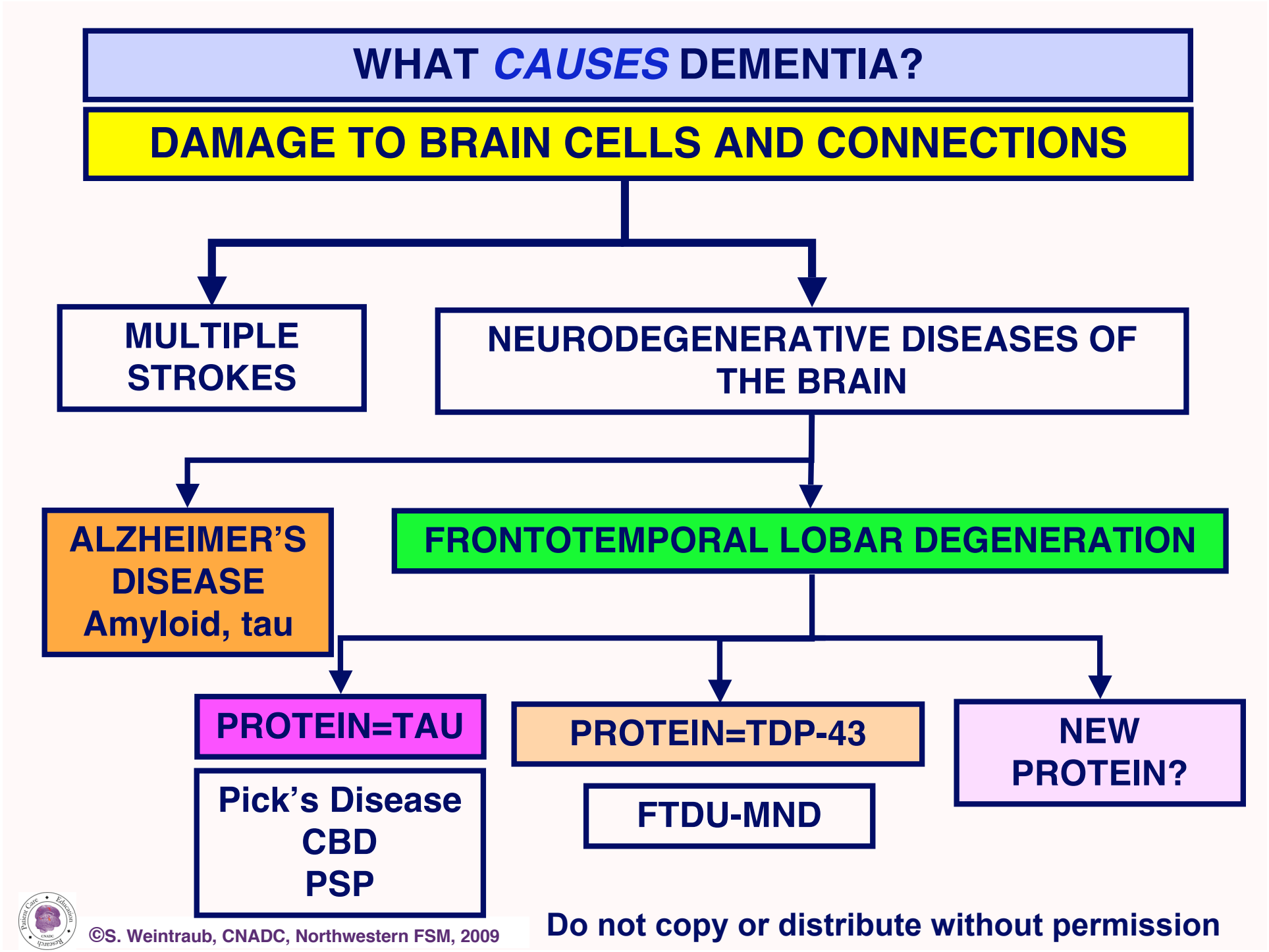
DEMENTIA SYMPTOMS COME IN DIFFERENT FORMS

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



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)

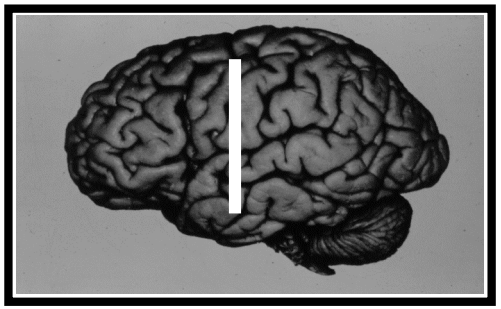
Progresses: to affect other cognitive and behavioral functions

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



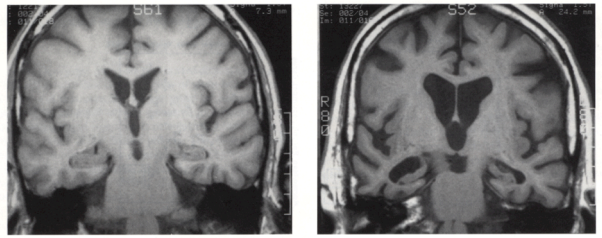
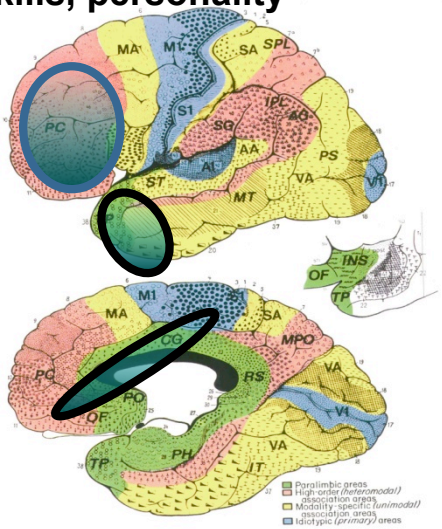


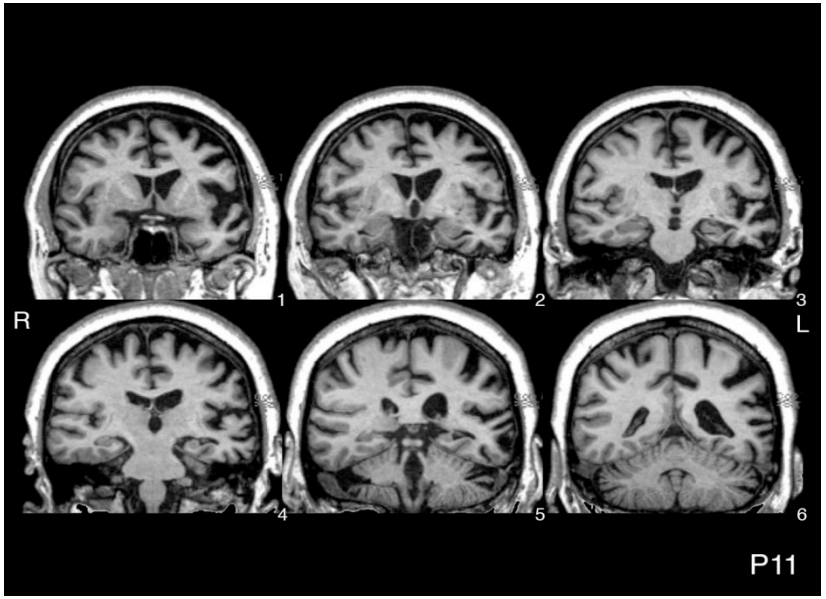
FIG. 2. Coronal images from a 78-year-old normal control subject (left hand side) and a 74-year-old patient with a clinical diagnosis of Alzheimer's disease (right hand side). The patient belonged to the third group of AD cases and had a MMSE score of 15.

DEMENTIAS 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.

S. Weintraub, CNADC, NUFSM, 2009

CLINICAL
What the doctor diagnoses during life: Symptoms

PPA
Aphasia
Language Disorder

bvFTD
Personality
Judgment

"Probable AD"
Short Term Memory

70%

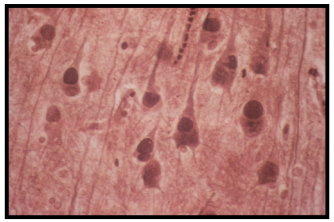
80%

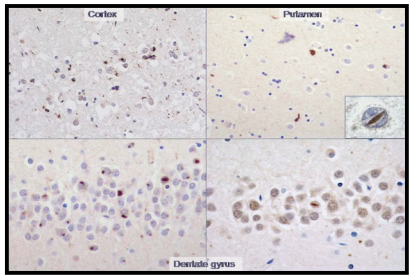
90+%

PATHOLOGY
What the neuro-pathologist diagnoses after brain autopsy: Cell Abnormalities

FTLD-T
FTLD-U

AD





Wieneke & Weintraub

Different Types Of Research

Observing and measuring behavior	Memory loss vs aphasia vs behavior change
Inspecting brain regions on MRI	Which regions? How do they differ from normal?
Inspecting brain tissue	Measuring proteins, genes
Developing and testing drugs	Based on which proteins and genes are involved
Testing other intervention	What works for management and coping?

RESEARCH PROGRESS

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?

UNDERSTANDING SYMPTOMS IN BVFTD (Osher)

Emotional signals are processed abnormally in people with bvFTD. They cannot interpret negative emotion but have an easier time understanding positive emotion.

BANKRUPTCY

PROMOTION

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

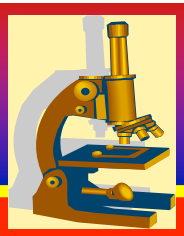
What are the best ways we know now to intervene and live with PPA and bvFTD? ADEAR Booklet

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

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