

FTD Research Update

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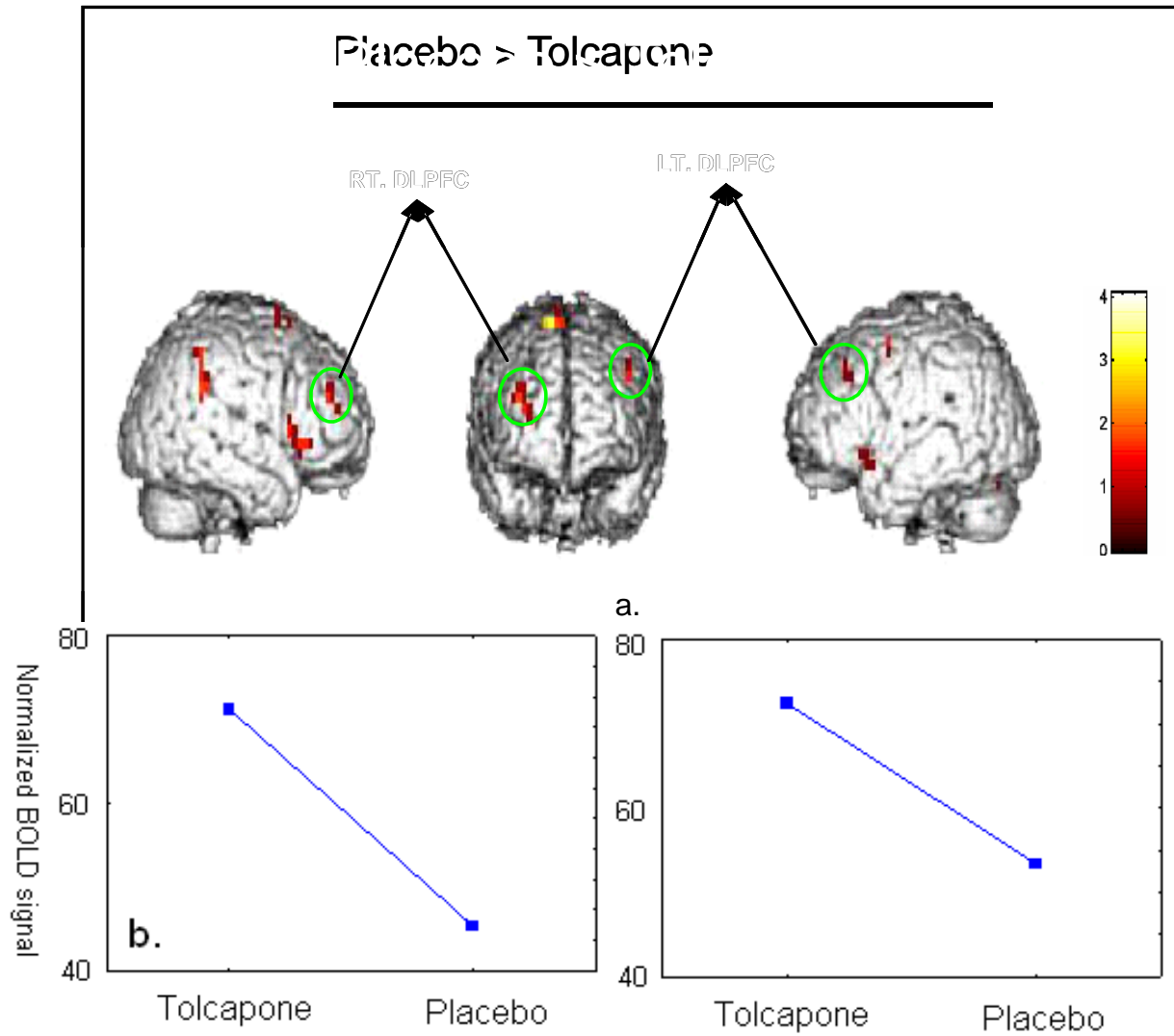
Outline

- Review new findings in
 - Diagnosis
 - Genetics
 - Treatment
- Future directions
- What you can do

Diagnosis / Biomarkers

- Combining imaging, neuropsychology, genetics, and pathology
- Important to develop new measures of diagnosis and treatment response
 - Blood
 - Imaging

Figure 3



Genetics

- Tau
- Progranulin
- TDP-43
- FUS

Potential treatments under investigation for FTD

- Inhibiting tau phosphorylation
 - Valproate
 - Lithium
 - Tau Vaccine
- Memantine
- Symptomatic treatments

Types of treatments

- Symptomatic
- Neuroprotective (disease-modifying)
- Recovery of function

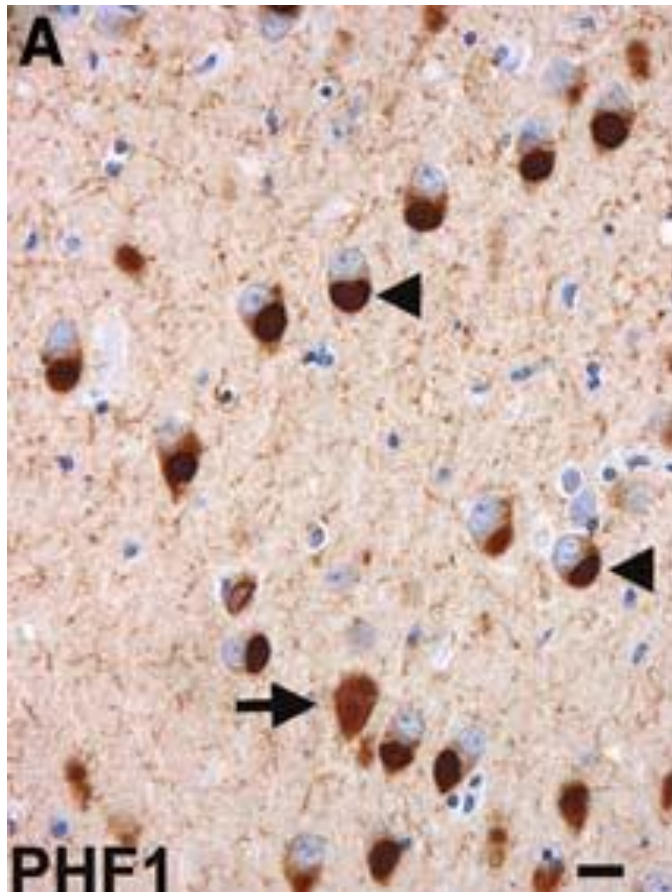
Challenges shared with other neurodegenerative disorders

- Most neurons cannot regenerate
- Lack of biomarkers of treatment efficacy
- Unknowns about mechanism
- Resources

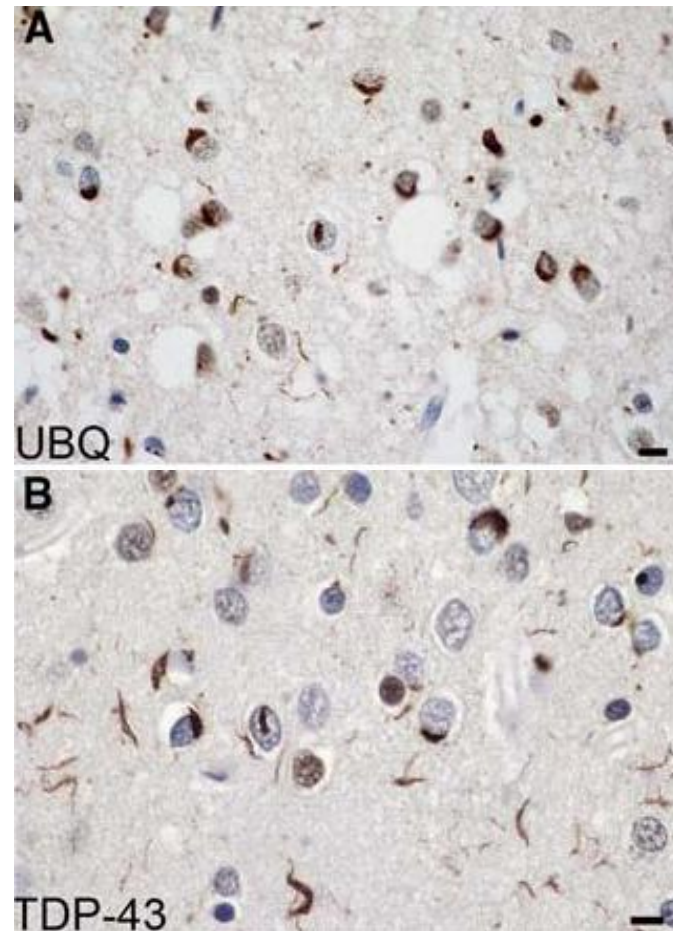
Special challenges of FTD

- Two major neuropathologies
- Lack of good measures of FTD symptoms
- Behavioral symptoms are variable
- Behavioral symptoms can interfere with study participation
- Less prevalent than Alzheimer's disease

Two major FTD neuropathologies



Tau pathology



FTLD-U

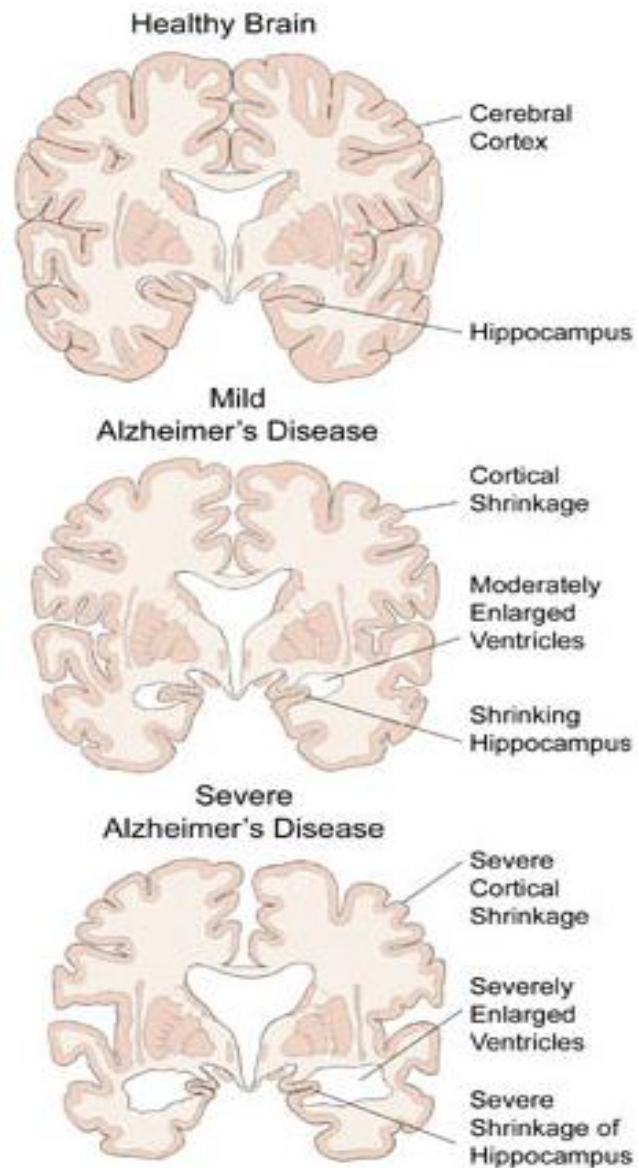
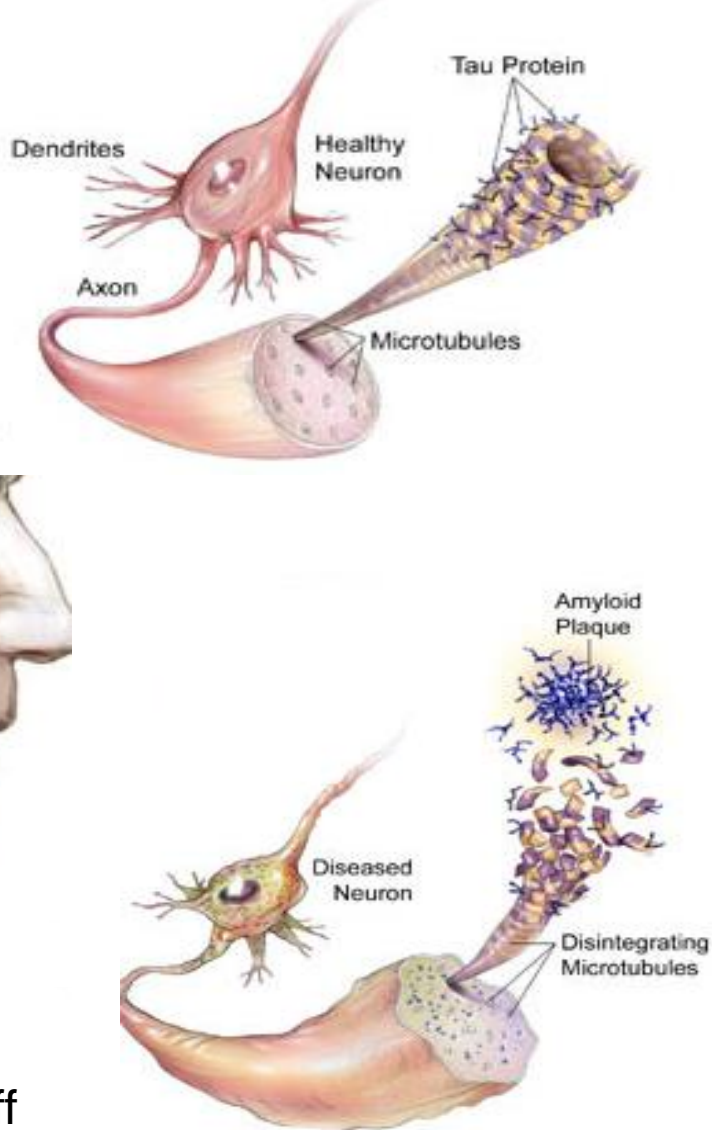
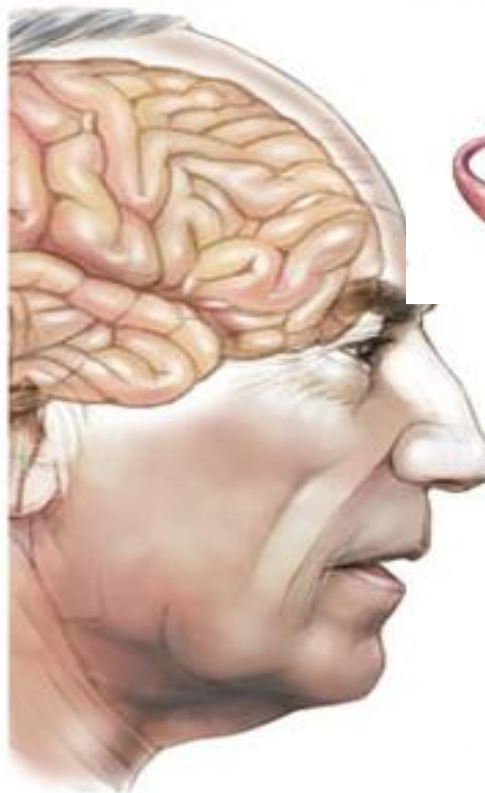
Disadvantages of two pathologies

- Clinically similar
- Disease-modifying treatments likely pathology-specific
 - Problem if treatment has adverse effects
 - Problem for trial design

Advantages of FTD pathology

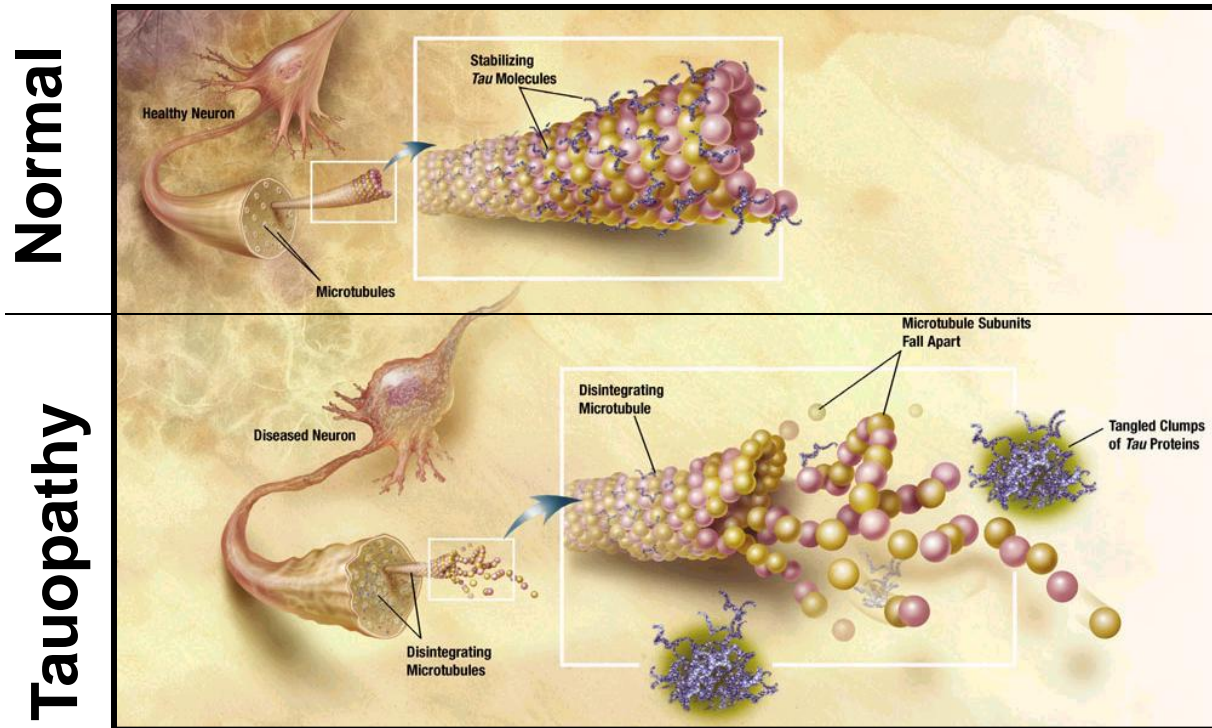
- Alzheimer's disease also involves tau
 - Much is known about tau mechanism
 - Tau-targeted treatments are being investigated for Alzheimer's disease

Alzheimer's disease: Plaques, Tangles, Loss of brain cells



Slide from K. Duff

Neurofibrillary Tangles and Tau protein



Tau (green)/tubulin(red)
overlay (yellow)

- Stabilizes the microtubule network in neurons
- Regulates tubulin polymerization and microtubule dynamics
- Permits axonal transport over long distances
- Located in axons but redistributed to somatodendritic compartment in early stages of disease.

Slide from K. Duff

Targets for drug development in the tauopathies

#1 Suppress mutant tau or isoforms altering the normal 3R:4R = 1

#3 Maintain normal tau conformation

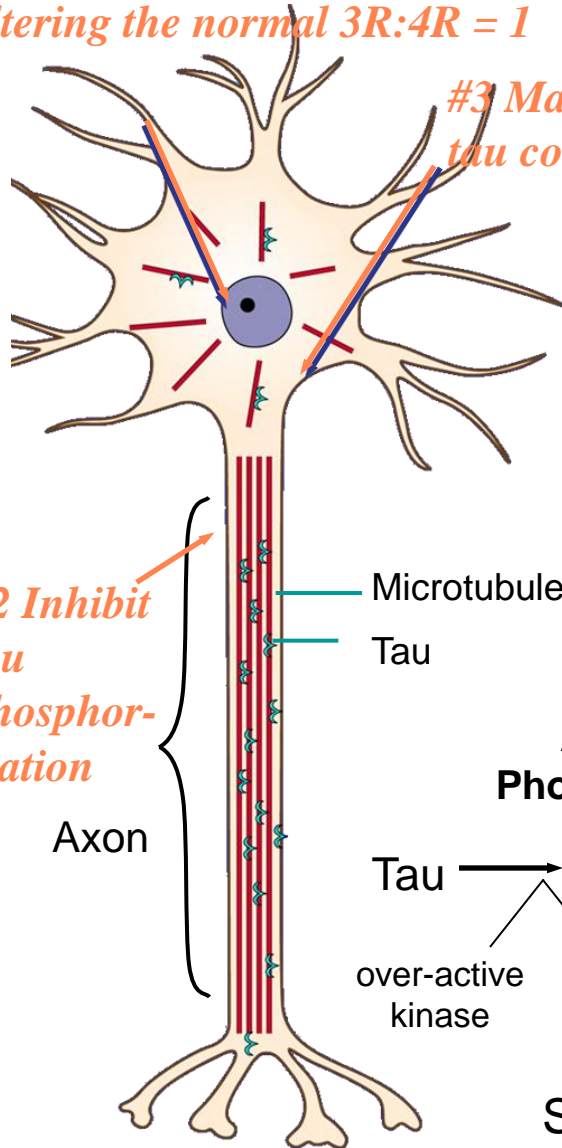
#4 Microtubule stabilization

#5 Increase abnormal tau degradation

#6 Anti-aggregation of abnormal tau

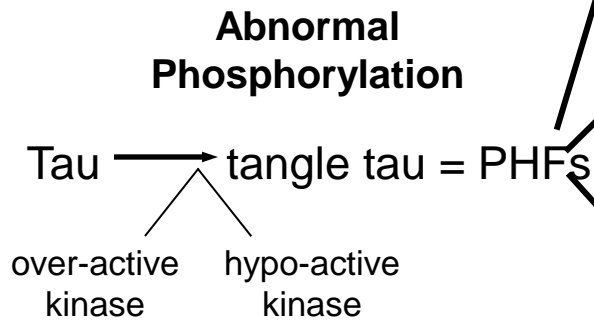
#7 Neuroprotection

#2 Inhibit tau phosphorylation

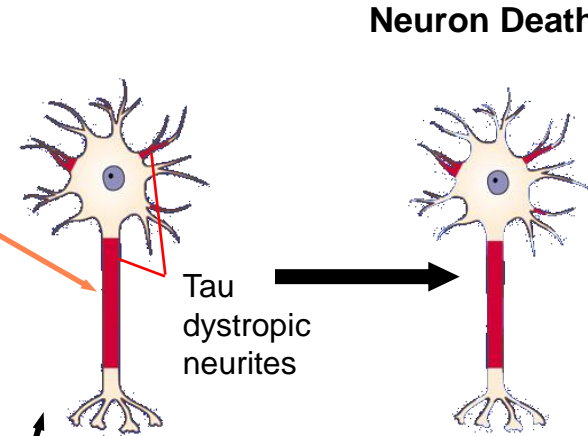


Microtubules
Tau

Axon

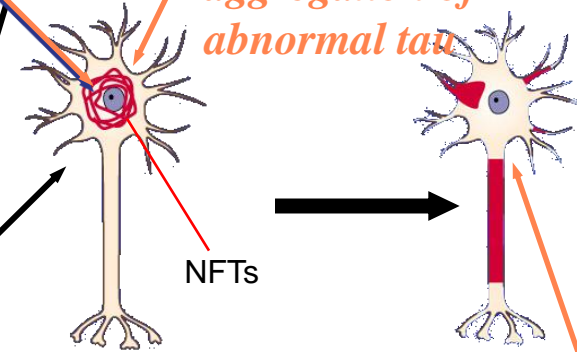


Slide from K. Duff

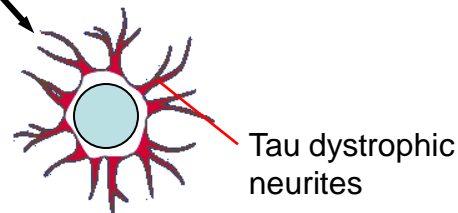


Tau dystrophic neurites

Neuron Death



NFTs



Tau dystrophic neurites

Plaques

Hope for the future

- As we learn more about the basic mechanisms of FTD, treatment opportunities present themselves
- Improving screening of potential medications through better animal models and biomarkers
- “piggybacking” on treatments for other neurodegenerative illnesses

What you can do

- Local trials:
 - Memantine (Lynda Mules at 212-305-2077)
 - Frontal dopamine augmentation and imaging biomarker (Edward Huey at 516-562-0409)
- www.clinicaltrials.gov
- Genetic studies
- Brain donation
- Increasing awareness of FTD www.ftd-picks.org
 - <http://www.ftdsupportforum.com/>
 - http://health.groups.yahoo.com/group/FTD_Spouse_Caregiver_Support/