



Pick's Disease: Characterization of Pathology with Diverse Stains

Baun, J., Hutchings, S., Ballard, J., Tipton, B., Kieffer, J., Zurhellen, C., Switzer III, R.C.

NeuroScience Associates, 10915 Lake Ridge Drive, Knoxville, TN 37934

Abstract

Pick's Disease (PiD) is a neurodegenerative disease characterized by neuronal cell death in the frontal and temporal lobes of the brain, classifying it as a Frontotemporal dementia (FTD). Symptoms include dementia, changes and difficulty in speech patterns, and many behavioral indicators including anxiety, confusion, attenuated social abilities and disengagement from friends and family. Onset of the disease usually occurs between the ages of 40 and 60, with the average age of onset being 54.

We evaluated the pathology postmortem in the brain of a 68 year old female using various histological and antibody stains. One indicator of PiD is a buildup of amyloid and tau proteins, which was evaluated using Ab 1-42 and AT8 (respectively) as well as other amyloid and tau markers. Several silver stains were also used to detect abnormal pathology. The Campbell-Switzer method revealed amyloid plaques and deposits, which resembled Alzheimer's (AD) pathology but the plaques

were far fewer in number in the PiD brain than an average AD brain. A Silver Protein protocol (Wako, cat # 283-90241), a modified Bodian stain, revealed both amyloid plaques and neurofibrillary tangles. Thionine Nissl and H&E stains showed swollen, "ballooned" neurons, one of the hallmark indicators of PiD. A hypertrophied glial state was observed with both GFAP (astrocytes) and Iba1 (microglia). This battery of stains on near adjacent tissue sections further characterizes the unique pathology of PiD.

Overview

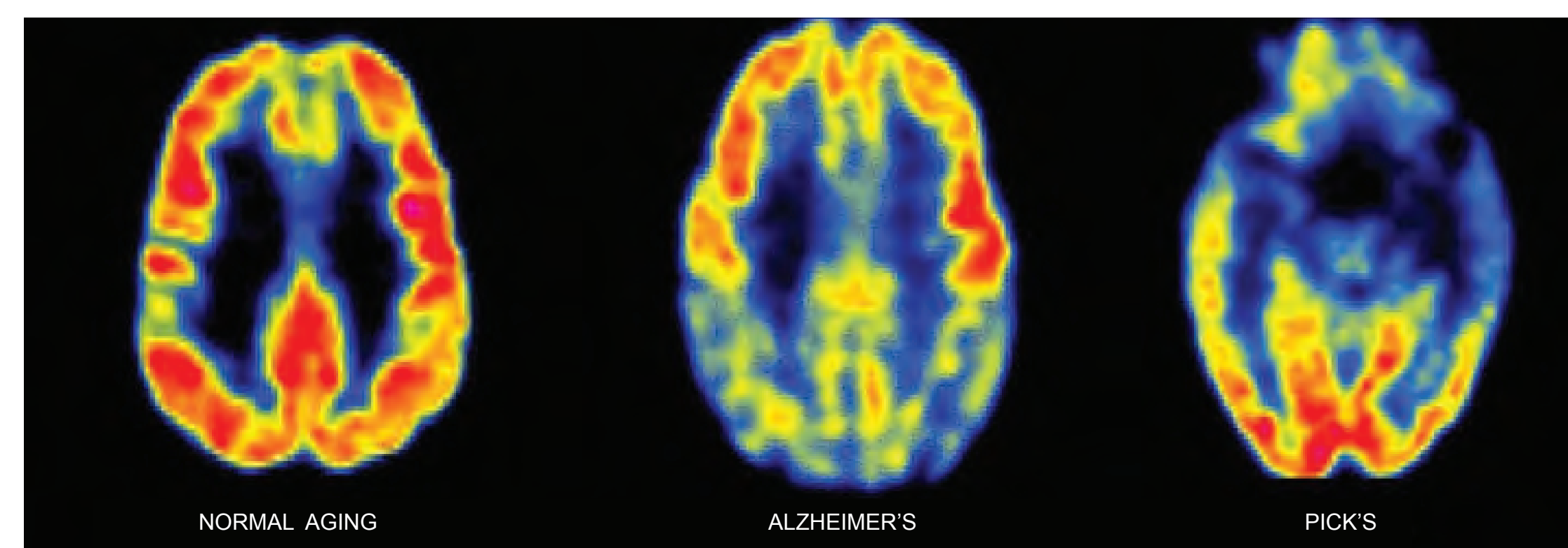
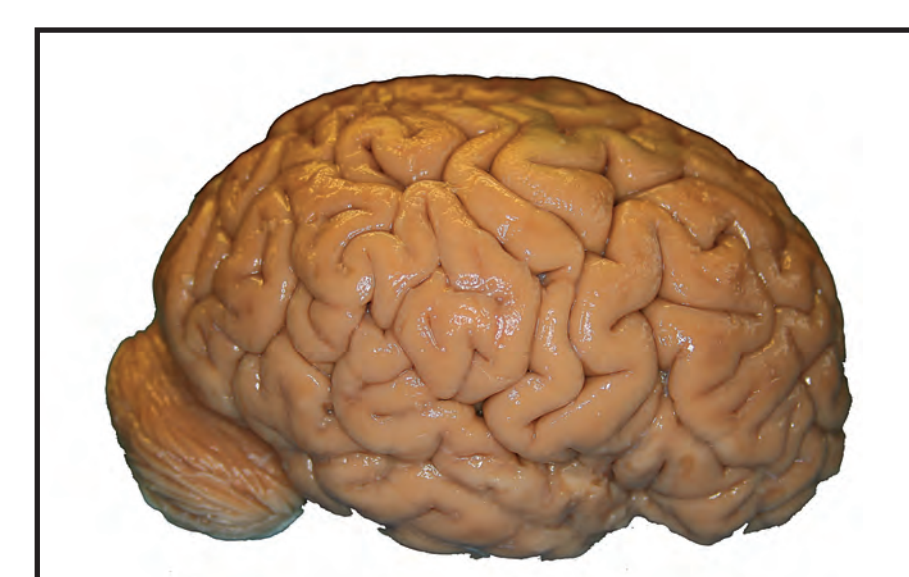


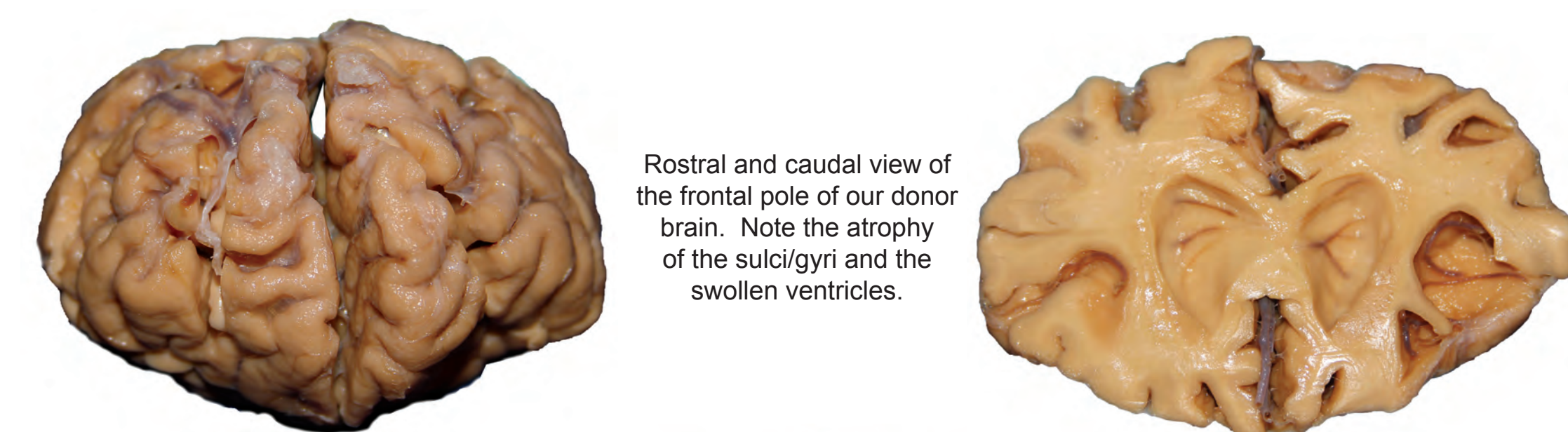
Photo taken from: http://www.massgeneral.org/radiology/news/radrounds/april_2006/ (for demonstration purpose only). MRI images of normal, Alzheimer's, and Pick's brain. Note the difference between AD and PiD brain, with the loss frontal lobe neuronal activity in PiD brain while occipital lobe function is preserved, with the opposite observed in AD brain MRI.



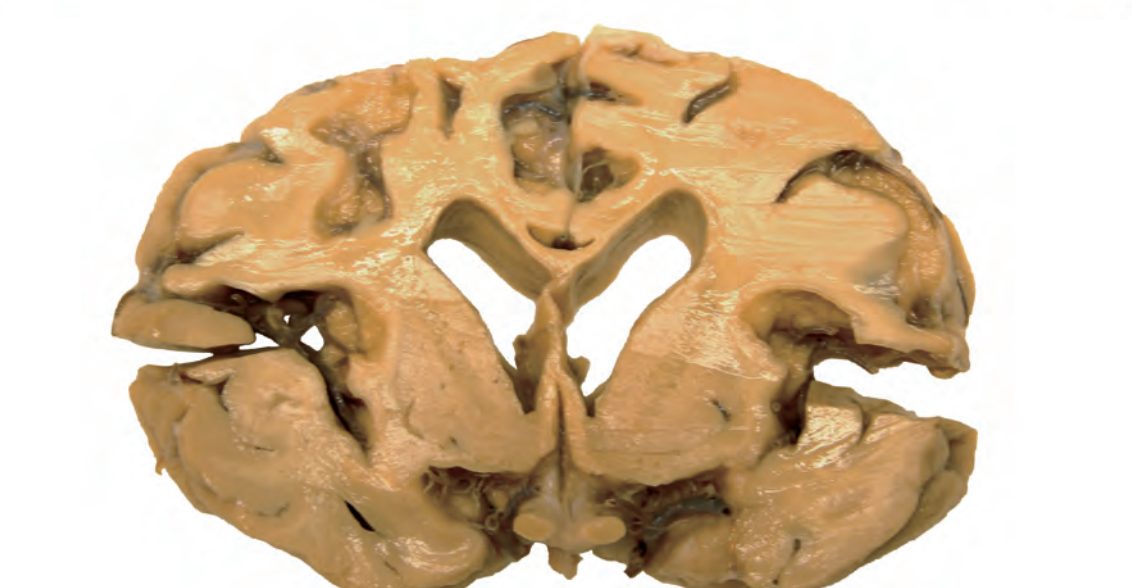
Lateral view of a normal brain. The brain has normal gross pathology.



Lateral view of diagnosed patient who died from complications of PiD. Note the loss of volume in the frontal cortex and temporal lobe, and the atrophy of the sulci and gyri of those areas compared to the Occipital cortex. Photo taken from: http://www.alzheimer-adna.com/Gb/Diseases/Pick_disease.html (for demonstration purpose only).



Rostral and caudal view of the frontal pole of our donor brain. Note the atrophy of the sulci/gyri and the swollen ventricles.



All of the histology presented here was taken from this sample of our donor brain. Areas sampled include striatum, corpus callosum, hippocampus, frontal cortex, and temporal lobe.

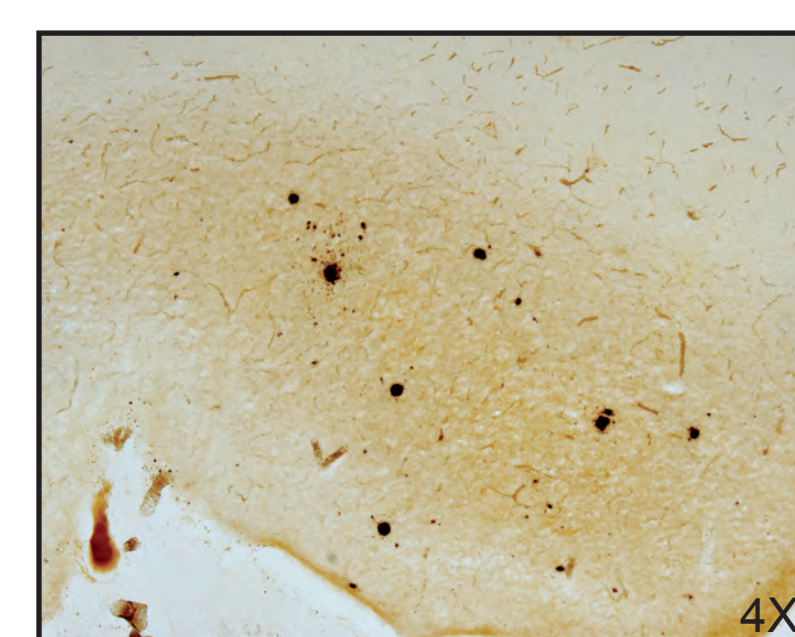
Conclusion

By using a battery of traditional and IHC stains one can gain an understanding of the unique pathological aspects of a chosen disease. Here we have shown the unique anatomical features that contribute to the symptoms of PiD.

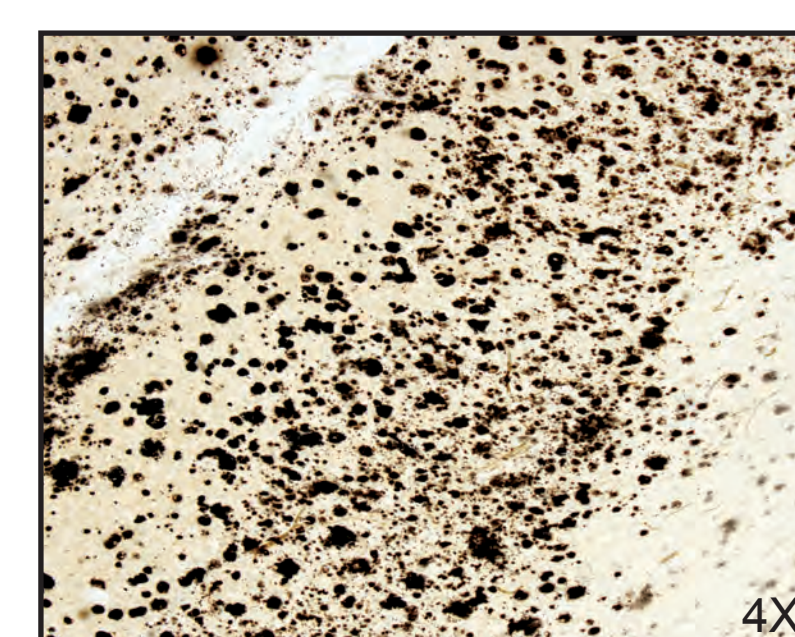
Gaining an understanding of these features and how they present during the course of the disease can lead to better knowledge of the behavioral symptoms and possibly point improved course of treatment and management of symptoms.

Amyloid Proteins

Pick's Disease



Alzheimer's Disease



CSAD
The Pick's brain exhibited far less plaque staining compared to the AD brain.

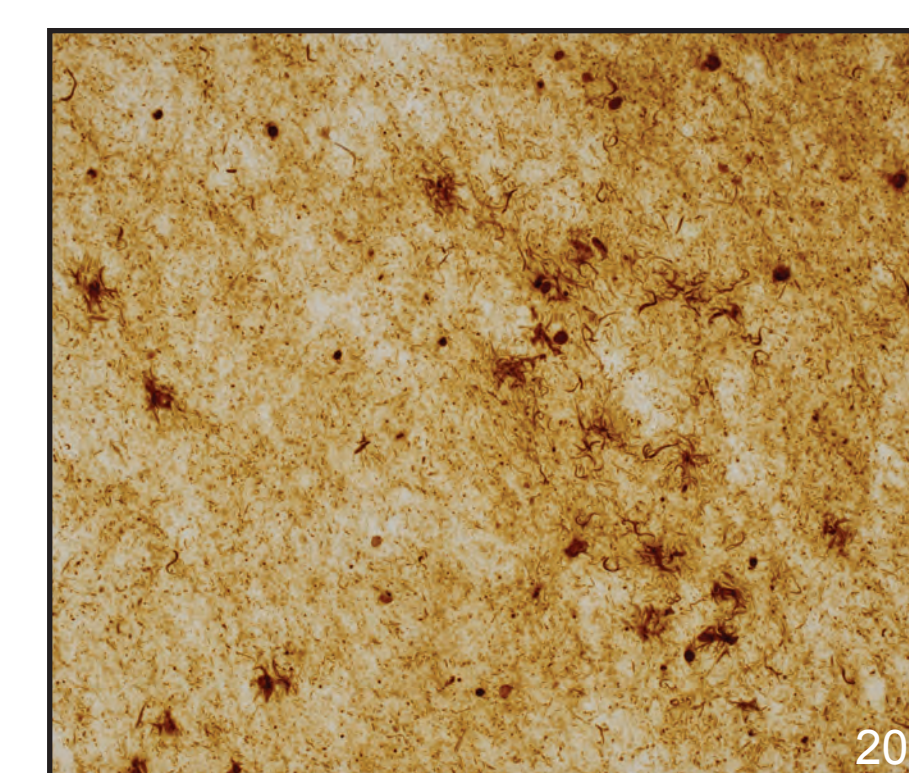
A-beta 1-42
Very little amyloid staining in the Pick's brain while the Alzheimer's brain shows an abundance of amyloid staining.

Silver Protein (modified Bodian's Stain Protocol)
Pick's brain shows few Pick's bodies and neurofibrillary tangles while the Alzheimer's brain pathology reveals an abundance of these features.

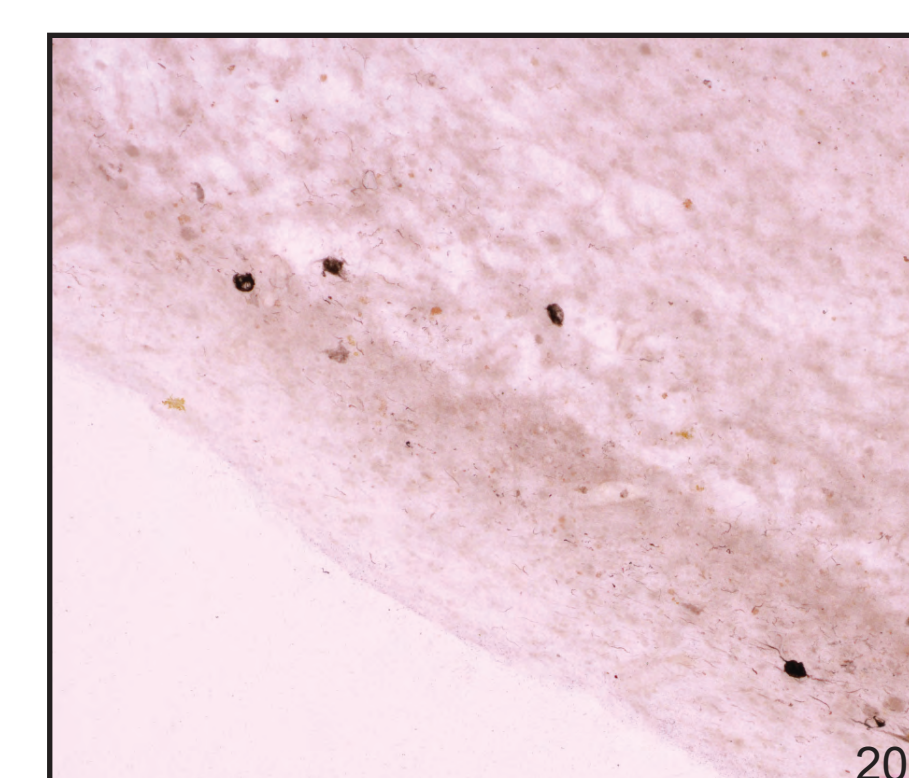
Thioflavin-S
Far less amyloid plaque staining in the Pick's versus Alzheimer's.

Tau Proteins

Pick's Disease

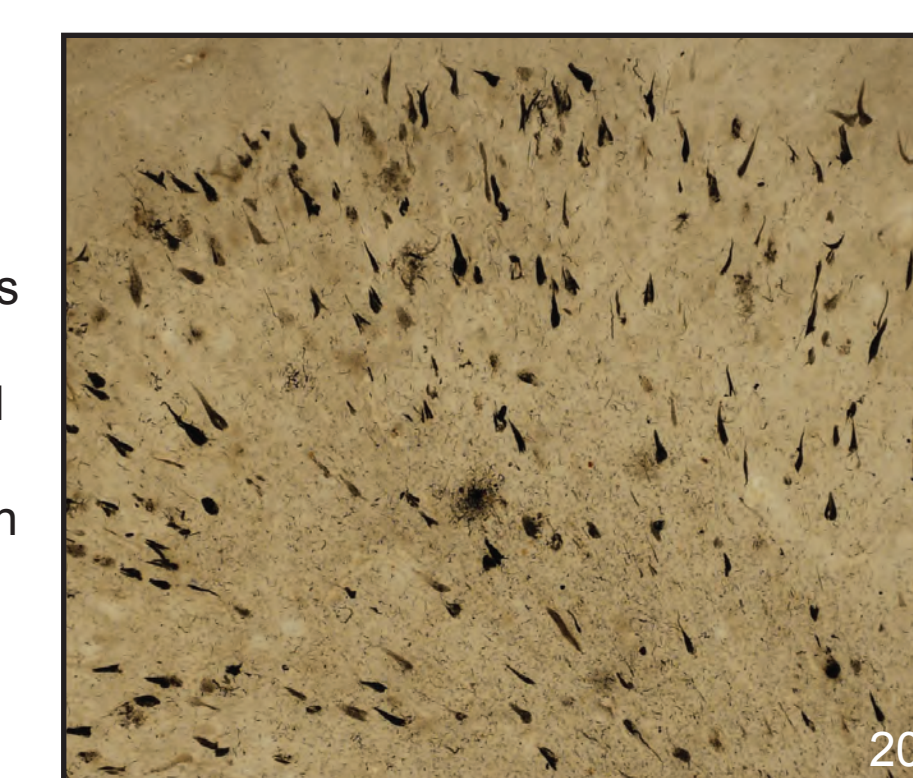
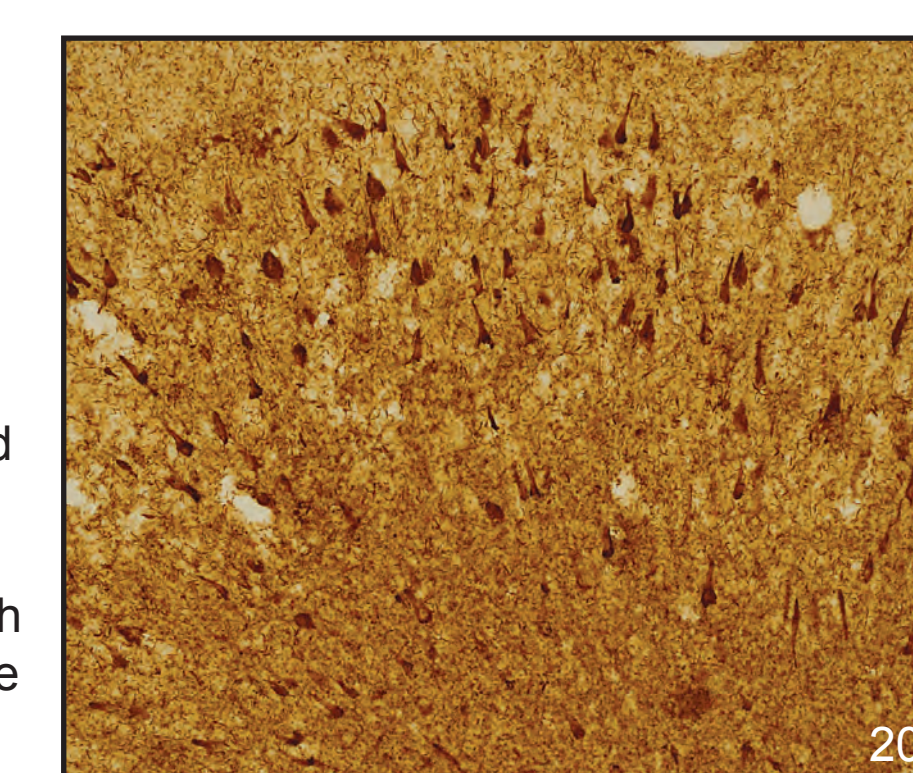


AT8
The Pick's brain shows a significant amount of neurofibrillary tangles as well as hyperphosphorylated tau proteins in the frontal cortex, however, not as much as the AD brain to the right.



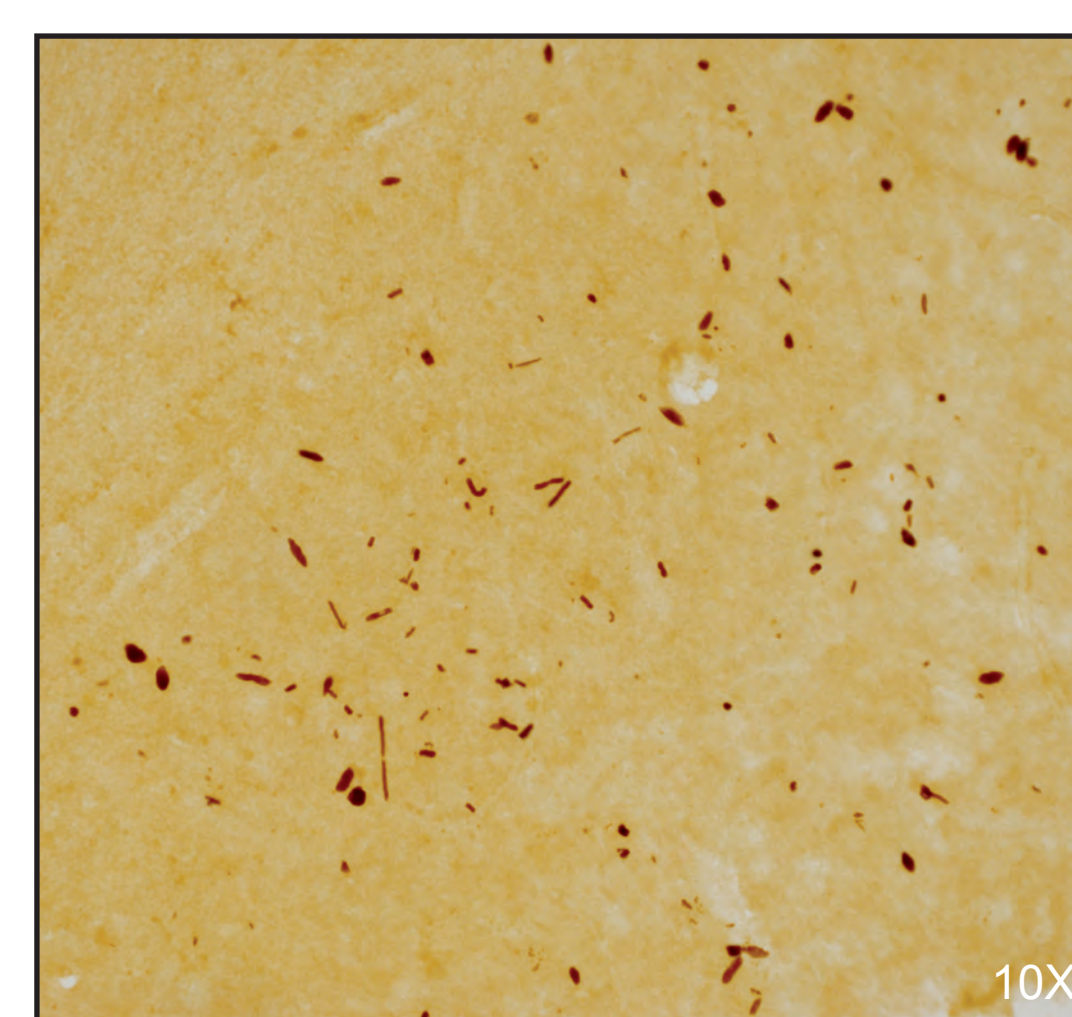
Gallyas
The PiD brain reveals some cells with tangles in the frontal cortex, but not as much as the AD brain to the right.

Alzheimer's Disease



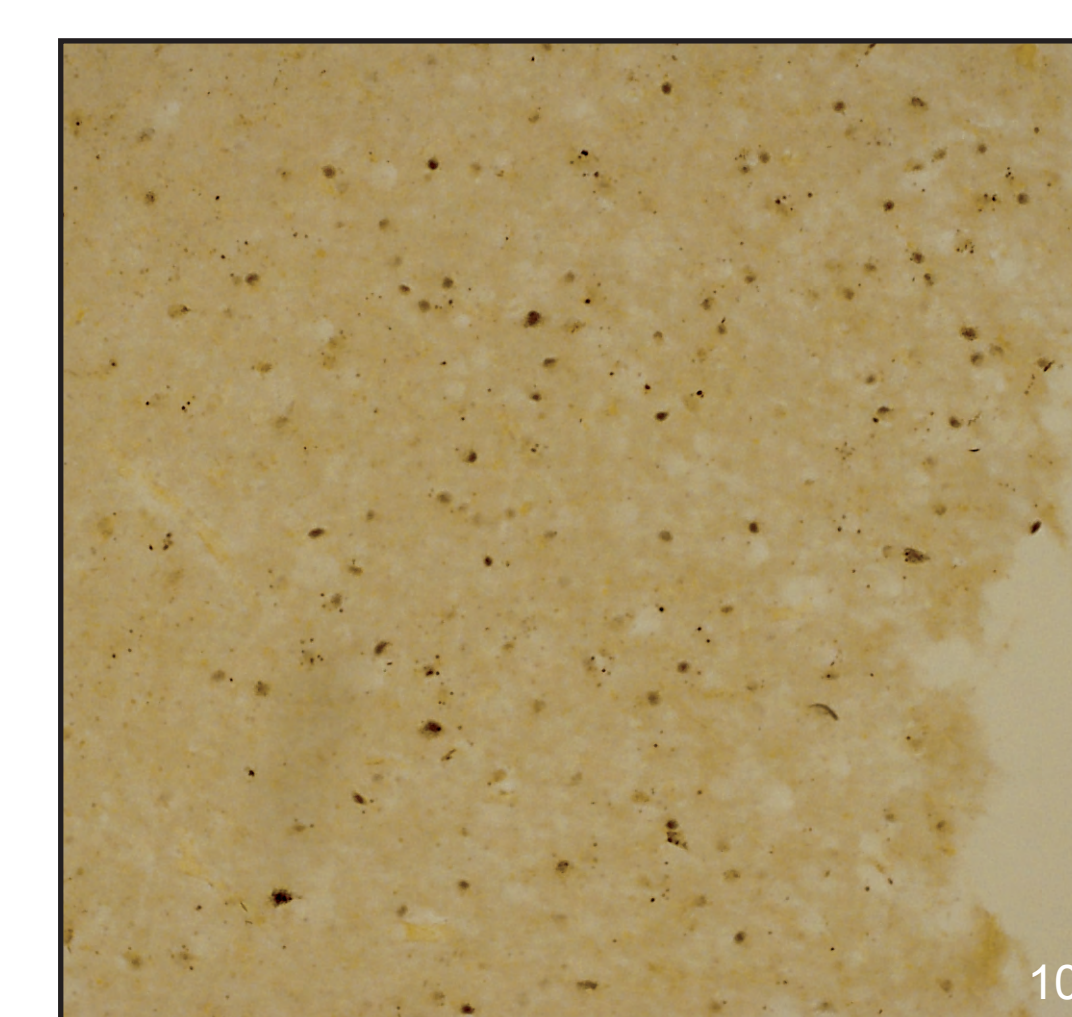
TDP-43 and Ubiquitin Expression

TDP-43



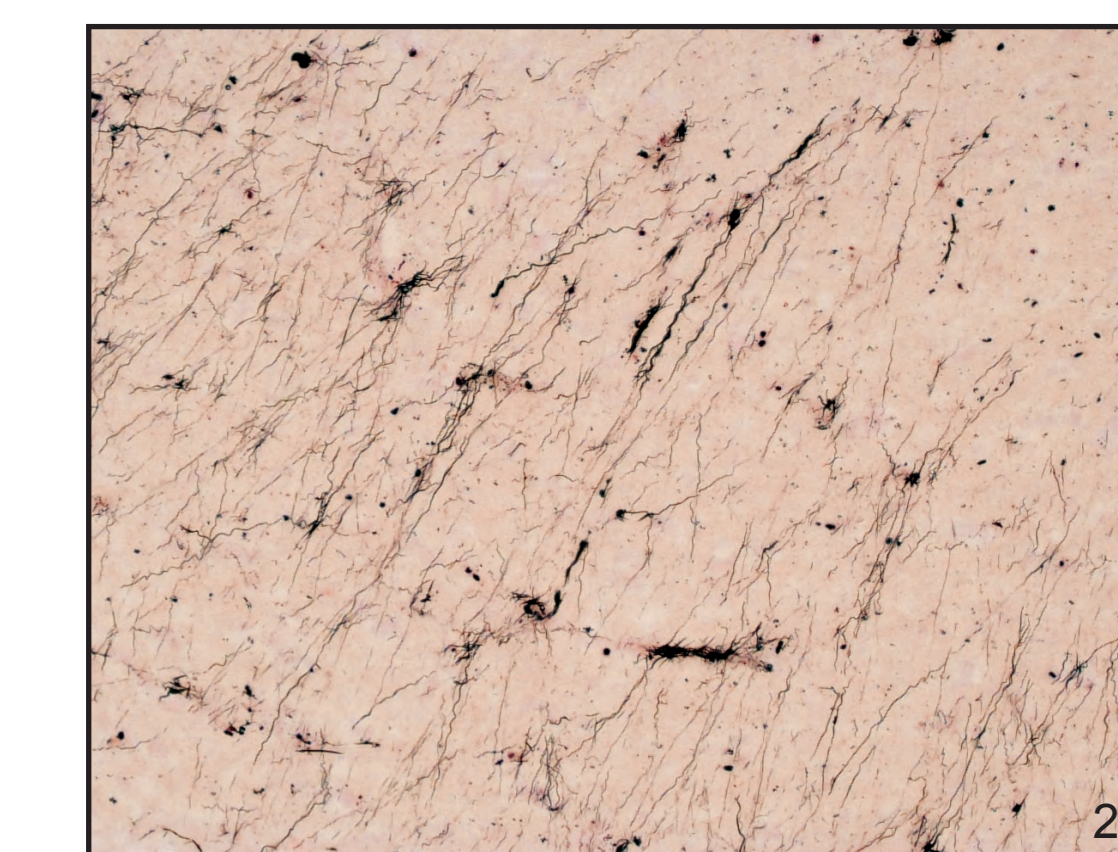
TDP-43 showed positive staining in the hippocampus area.

Ubiquitin

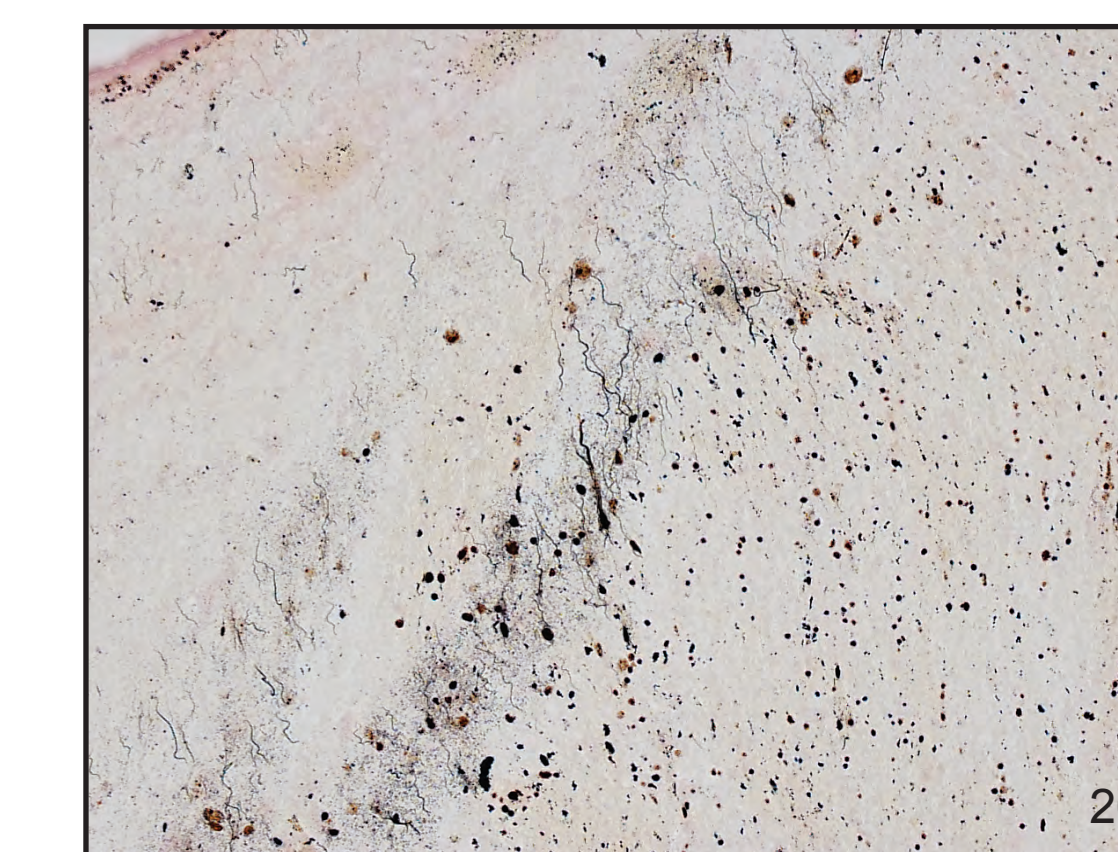


Ubiquitin stains positive in FTLT-DTP brain.

Amino Cupric Silver

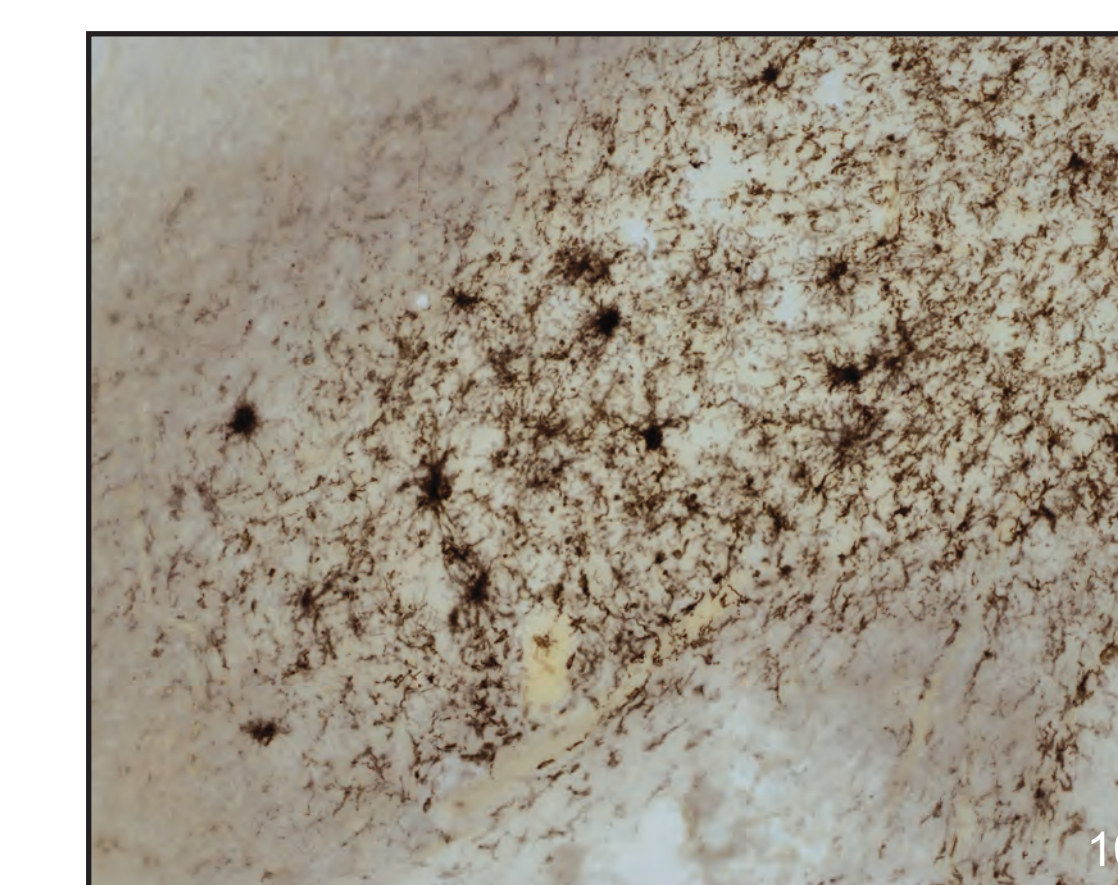


Amino CuAg (deOlmos)
Left image: Reveals argyrophilic cell bodies and axons in cortex.

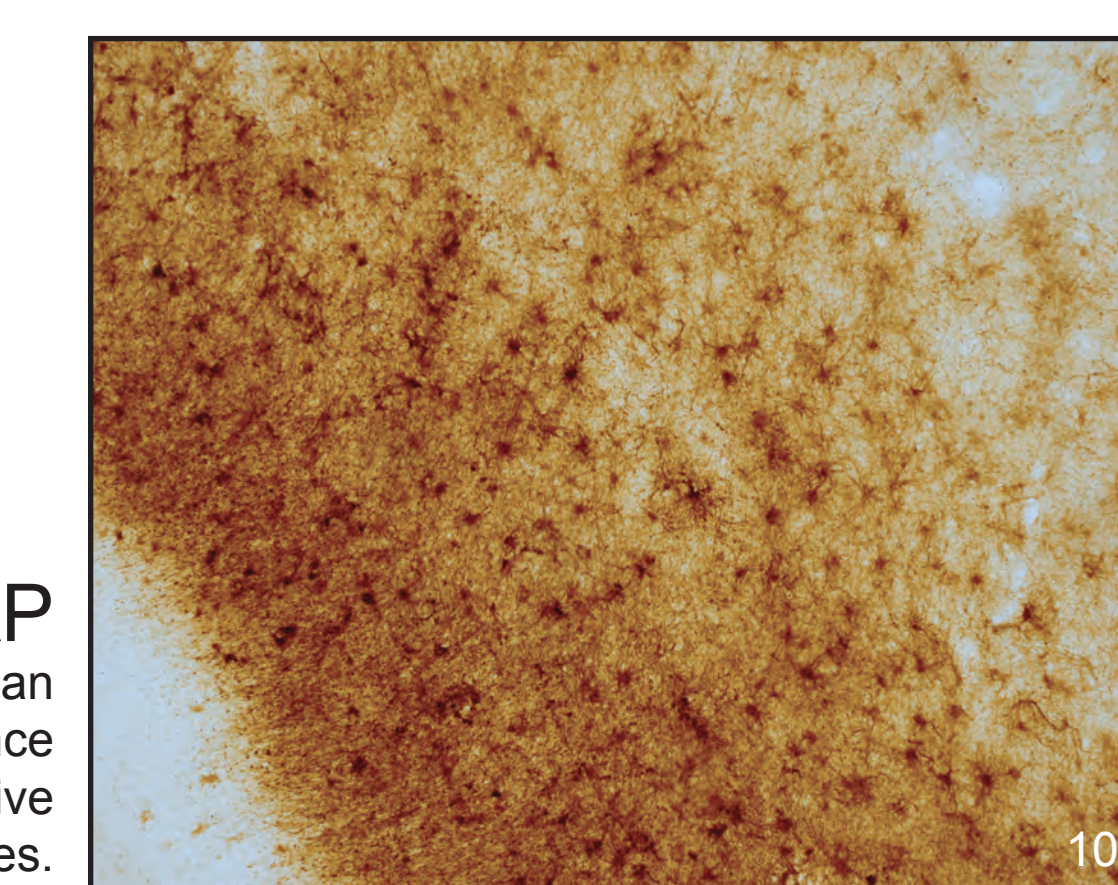


Right image: Argyrophilic cell bodies and processes. (Usually features that are argyrophilic in the amino cupric silver stain are interpreted as being in a disintegrative state).

Hypertrophied Glial State



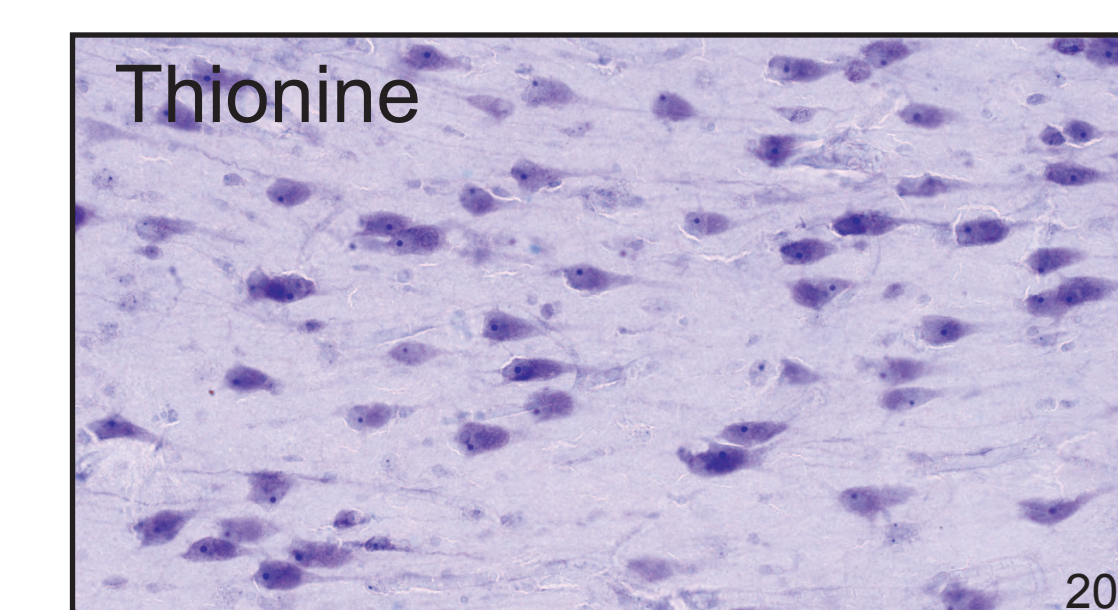
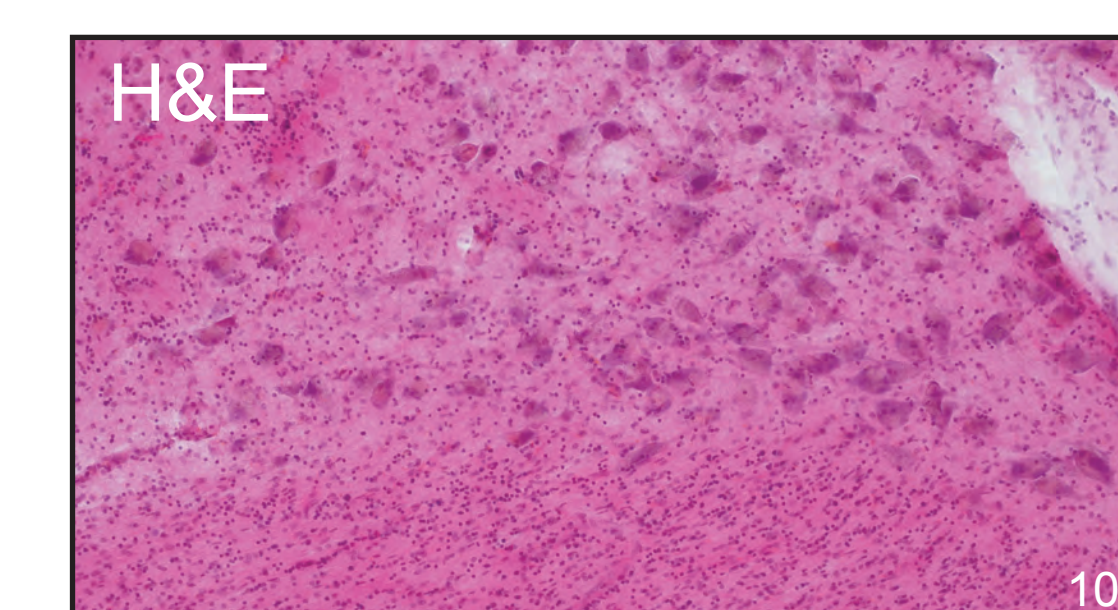
Iba1
There is a significant amount of hypertrophied microglia present in the hippocampus region.



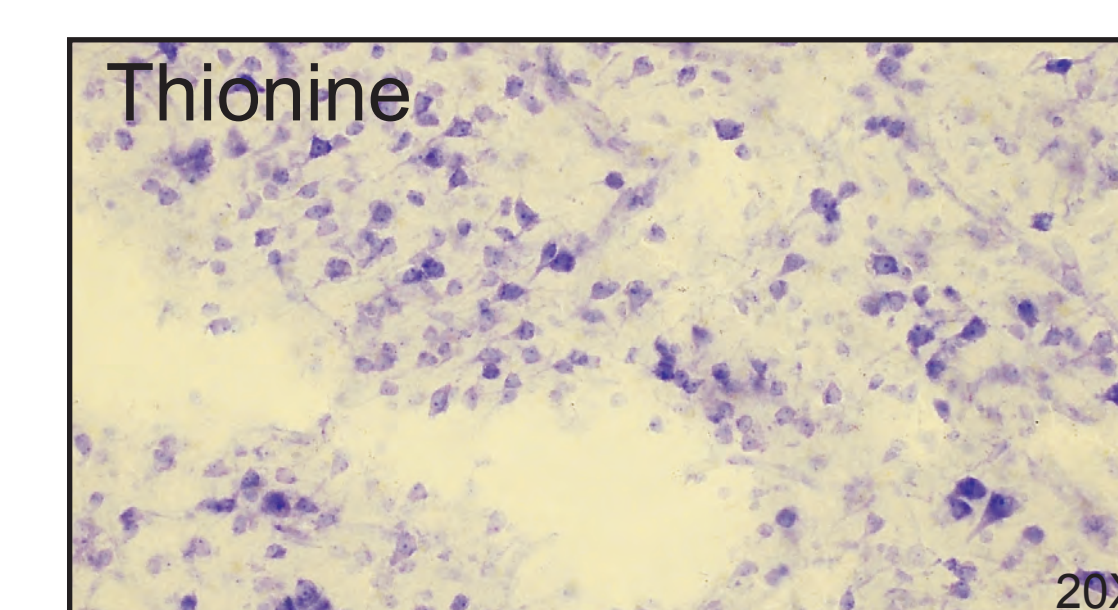
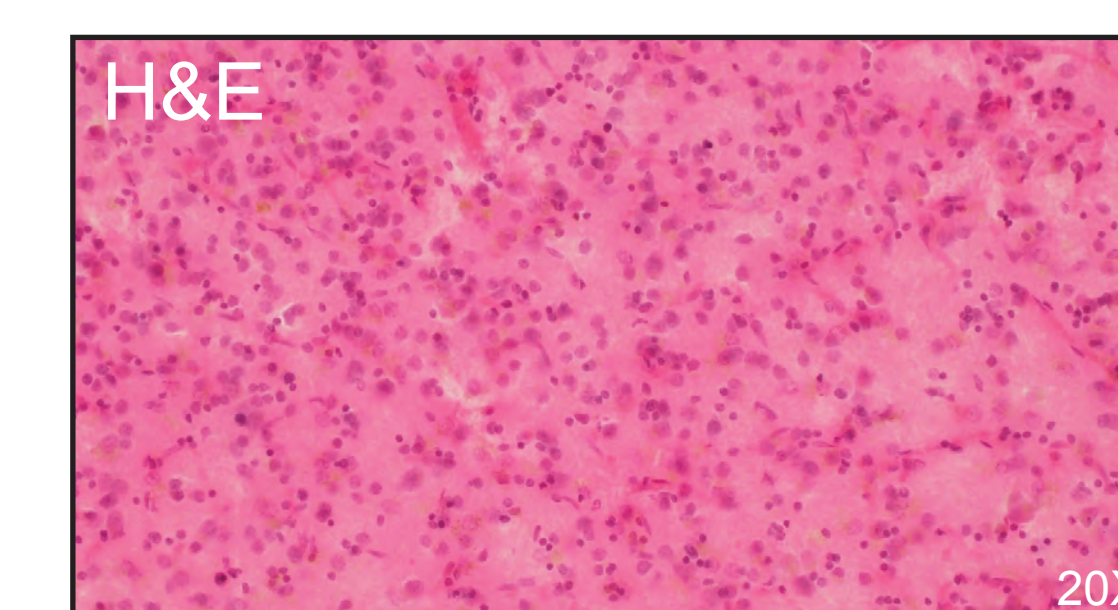
GFAP
Reveals an abundance of reactive astrocytes.

"Ballooned Cells"

Ballooned Cells



Normal Cells



The Hematoxylin and Eosin stain (top left) and Thionine Nissl (bottom left) reveal the nucleus inside the ballooned shaped neurons (Pick bodies).

The top right and bottom right images reveal normal stained cells in the same brain.