Geropathology Research Notes
www.geropathology.org
Volume 1, 2022

Confirmation of Alzheimer's Disease Neuropathology in Old Pet Cats

Jackson Wezeman[1], Zhou Jiang[1], Warren Ladiges[1*]

1. Department of Comparative Medicine, School of Medicine, University of Washington, Seattle

Abstract

Alzheimer's disease (AD) is complex and a common neurodegenerative disease in humans. Disease-modifying treatments have proven difficult as there are not yet ways to evaluate early signs and risk factors associated with early AD as well as not having a predictable animal model. AD is diagnosed by the presence of amyloid plaques and tau tangles during brain autopsy, decades after the pathology in the brain has appeared. Preliminary data shows amyloid plaques and tau tangles have been discovered to develop spontaneously in aging domestic cats in similar fashion to humans. One additional benefit is house cats share the same environment as their owners which validates the results further. Pet cats have the potential to provide a competitive and unique animal model for studies of AD. The purpose of this study is to validate the naturally occurring aging lesion pathology of AD in old pet cats is comparable to human AD patients. Immunohistochemistry (IHC) will then be done on formalin-fixed paraffin embedded slides from old pet cat brains with Amyloid Beta-42 and phosphorylated tau antibodies to examine location and severity of lesions. Additional IHC staining with microglia and astrocyte targeted antibodies will be performed to validate the expression of glial cells around AD associated histology lesions. Finally, a landmark correspondence software package will be used to merge slide images with different staining for comparing the heat map intensity level of each antibody expression around certain lesions of interest. The observations made during this experiment are important and far-reaching as having a reliable animal model for AD would significantly help researchers to develop interventions as well as develop clinical tests for early signs of AD.

**Corresponding Author Warren Ladiges, wladiges@uw.edu*

Introduction

Alzheimer's disease (AD) is a complex and a common neurogenerative disease in humans. Treatments have proven difficult as there are no ways yet to identify risk factors and early signs, as well as the lack of a predictable animal model. AD is diagnosed currently through autopsy, with the presence of amyloid beta plaques and tau tangles. Microglia cells and astrocytes are indicators of a reactive response to AD lesions. Preliminary data suggest these lesions develop spontaneously in cats, comparable to human patients. Because cats share the same environment as humans and exhibit similar comorbidities, they represent a potentially interesting and highly translational model for AD pathogenesis and therapeutic investigations.

Objective

Our objective was to confirm the presence of Alzheimer's disease neuropathology in the brains of old pet cats.

Materials and Methods

Formalin fixed brain samples from a human and cat tissue bank were stained using Immunohistochemistry. The slides contained hippocampus and cerebral cortex sections. Abeta 42 was detected using 6E10 antibody. pTAU was detected using AT8 antibody. Astrocytes were detected using GFAP antibody. Microglia were detected using Iba1 antibody. Imaging software (QuPath) was used to analyze the images and create detection maps for better visualization of the staining.

Results and Discussion

Stains for Abeta42 and pTAU show diffuse amyloid plaques and tau fibrillary tangles in brains of old cats but not young cats. Similar pathology is seen in aging human brains (Figure 1). The red intensity indicates presence of astrocytes and glial cells in the cortex and hippocampus in the brain of a 14-year-old cat with amyloid plaques and tau tangles (Figure 2). The brain from a 75-year-old man with Alzheimer's disease shows similar lesions to the old cats. Amyloid plaques and tau tangles can be seen in brains of old cats but not young cats similar to the evolution of human AD neuropathology. Reactive astrocytes and glial cells are seen in association with AD lesions. These observations help confirm AD neuropathology in old pet cats similar to humans. More studies are needed to determine the role of these lesions in cognitive impairment in cats.

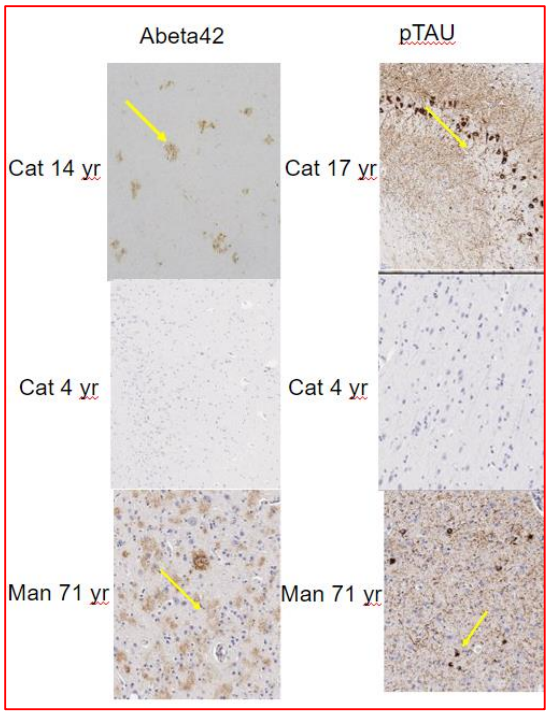

Figure 1. Abeta42 and pTAU staining of young and old cat brains and AD human brain.

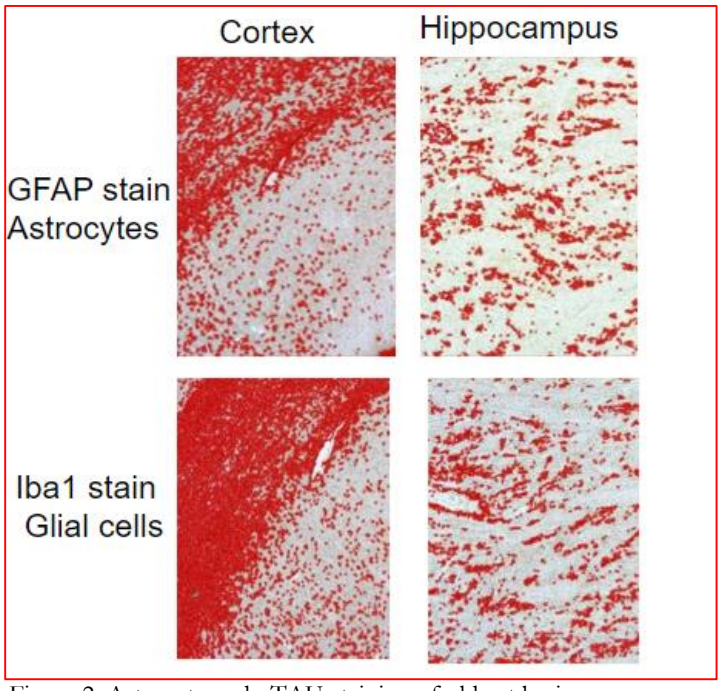

Figure 2. Astrocyte and pTAU staining of old cat brain.

Acknowledgements

Funding was provided by the NIH. (Ladiges, PI)