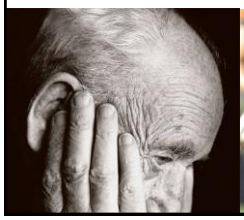
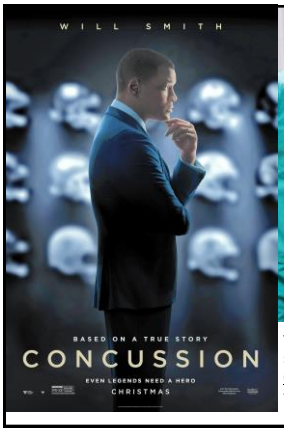
Case Study Example from BIOL362

Case Study #1:
Alzheimer's Disease and Chronic Traumatic Encephalopathy





This image released by Columbia Pictures shows, from left, Will Smith, Dr. Bennet Omalu and director Peter Landesman on the set of the film, "Concussion.

Rules for Case Study #1

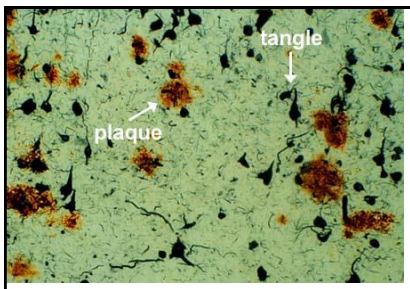
1. Work must be done in your groups. One person should be designated the secretary and take notes on your discussion (you may use your computer for this, as long as you are not using the internet).
2. One person should also be elected as facilitator to help make sure that all voices are being heard and that you stay on task.
3. You may only rely on your class notes, class materials, and your collective knowledge. **NO OUTSIDE SOURCES** (I'm looking at you, Wikipedia!). You can also ask questions of the teaching team.
4. At the end you must fill out the End of Task Group Report.

Unit 2 Case Study

Alzheimer's Disease (AD) is an incurable disease that most commonly affects the elderly. Chronic Traumatic Encephalopathy (CTE) is a brain disorder that has been shown to affect individuals exposed to repeated head impacts (e.g. boxer, football players).

Both are progressive neurodegenerative disorders where the individual loses brain function over time, resulting in confusion, mood swings, memory loss behavioral changes and debilitating dementia. Eventually, body function can also be lost, leading to death.

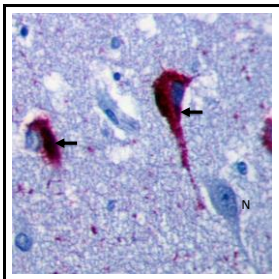
Your task is to examine the evidence presented to try and find a connect between it and the neuronal dysfunction of these diseases.

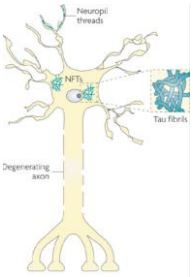


What you know

1. Images of the brain tissue in both diseases show intracellular, proteinaceous 'tangles' in the cytosol, which are composed of the microtubule associated protein, Tau.

Ignore the plaques for today's exercise.





2. Immunohistochemistry for tau protein in the brain of an individual with Alzheimer's shows neurofibrillary tangles (red) visible in some neurons (arrows) but not in others (N).

Cartoon from: Brunden KR, et al. 2009 Nat Rev Drug Discov. Oct;8(10):783-93.

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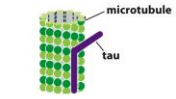
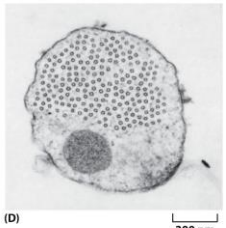


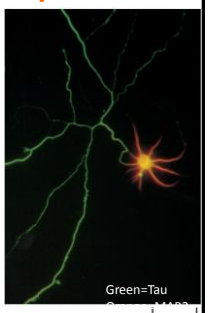
What you know

(B)



(D)

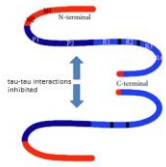
300 nm

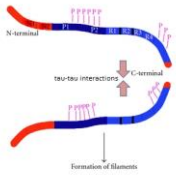


10 µm

3. Figure 16-51 of our textbook tells us that Tau is involved in the formation of the MT network in the axon of neurons

What you know

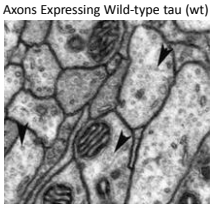




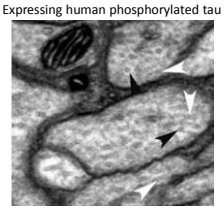
4. Studies have shown that the neuronal tangles of Tau are hyper-phosphorylated and have a different shape, but if they are de-phoshorylated *in vitro*, the protein regains normal shape and function.

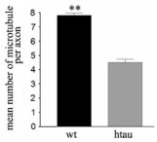
Kolarova M, et al. 2012 International Journal of Alzheimer's Disease doi:10.1155/2012/731526

Axons Expressing Wild-type tau (wt)



Axons Expressing human phosphorylated tau (htau)





The mean number of correctly aligned microtubules is significantly higher (**) for wt tau-expressing neurons

5. In wild type (wt) tau-expressing neurons the axon profiles show numerous regularly-spaced correctly-aligned microtubules (black arrowheads).

In human phosphorylated tau (htau)-expressing axons the microtubules are dramatically disrupted. There are many fewer correctly-aligned microtubules (black arrowheads) than in the wt control and there is additional evidence of disorganised (wrongly oriented) microtubules (white arrowheads)

Cowan CM, et al. 2010 Acta Neuropathol. Nov;120(5):593-604

Case Study 1 - Central Question:

Given this information, can you explain whether there is a relationship between the microtubule associated protein Tau and the neurodegeneration present in AD and CTE? If so, how does Tau contribute to disease pathology?