Current Event Reflection
Tau-dependent microtubule disassembly initiated by prefibrillar β-amyloid

A&P II
Alex Chun
2/10/09

Alzheimer's disease is a common form of progressive dementia that effects millions and currently lacks a cure due to its complex pathology and the poorly understood interactions between its suspected mechanisms of action. My family was personally affected by Alzheimer's when my grandmother was diagnosed with dementia in the later years of her life. We struggled to cope with the daily challenges posed by her loss of short term memory as well as the emotional pain of her progressive forgetting of loved ones' names and eventual inability to coherently interact with others.

While there is no definitive theory unifying the body of research on the causes of Alzheimer's disease, beta amyloid plaques, the tau protein, and neurofibrillary tangles are widely accepted pathologic indicators and lie at the heart of a recent research article by King et. al appearing in the *Journal of Cellular Biology.* What makes this article so interesting and relevant to Anatomy and Physiology II is its focus on the role of axonal microtubule degradation as a primary cause of Alzheimer's-related neurodegeneration and the link proposed between beta amyloid and tau. Their findings suggest that pathogenic beta amyloid causes devastating microtubule disassembly in neurons, with the endogenous tau in neurons (which normally stabilize microtubules) hyper-sensitizing the cells to the effects of beta amyloid.

This article really reinforces the principle of "structure begets function" in my mind and points out that the least glamorous, often overlooked components of any system are often the most vital to its proper function. Though microtubules are probably among the least exciting structures one comes across when studying the neuron, the simple

phosphorylation of one supporting protein class can eventually impair virtually all higher brain function in an Alzheimer's sufferer. I think the very basic image of structural collapse within the neuron is useful for reminding ourselves that Alzheimer's is not just a disease of the short term memory. Although this is the first and most memorable stage we experience when loved ones begin to forget things, Alzheimer's disease also causes behavioral changes, exhaustion, language deficits, and even muscle atrophy and motor impairment in its most advanced stages.

I hope that continuing research will someday elucidate the mechanisms behind Alzheimer's to the point where we can call the disease curable rather than simply slow the inevitable. There is a clear genetic component to Alzheimer's disease and I sometimes wonder if I've inherited any pathogenic polymorphisms. That, along with the many environmental and nutritional risk factors such as lead exposure and aspartame, make me especially hope for a cure before I reach the 65+ cohort!

Article Citation:

King ME, Kan HM, Baas PW, Erisir A, Glabe CG, Bloom GS. 2006. Tau-dependent microtubule disassembly initiated by prefibrillar β-amyloid. *The Journal of Cell Biology* 175(4): 541-546.