

## **Rethinking Alzheimer's disease and its treatment targets**

September 22 2009, By Mark Wheeler

(PhysOrg.com) -- Psychiatry professor George Bartzokis introduces a new theory about the fundamental cause of Alzheimer's and other neurodegenerative diseases.

The standard explanation for what causes Alzheimer's is known as the amyloid hypothesis, which posits that the disease results from of an accumulation of the peptide amyloid beta, the <u>toxic protein</u> fragments that deposit in the brain and become the sticky plaques that have defined Alzheimer's for more than 100 years.

Billions of dollars are spent yearly targeting this toxic peptide — but what if this is the wrong target? What if the disease begins much earlier, fueled by a natural process? Reporting in the current edition of the journal *Neurobiology of Aging*, UCLA professor of psychiatry George Bartzokis argues just that and says that a better working hypothesis is the "myelin model."

"The greatest promise of the myelin model of the human brain is its application to the development of new therapeutic approaches," Bartzokis said.

Like insulation around wires, myelin is a fatty sheath that coats our <u>nerve</u> <u>axons</u>, allowing for efficient conduction of nerve impulses. It is key to the fast processing speeds that underlie our higher cognitive functions and encoding of memories.



But the lifelong, extensive myelination of the human brain also makes it uniquely vulnerable to damage. The myelin model's central premise is that it is the normal, routine maintenance and repair of myelin throughout life that ultimately initiates the mechanisms that produce degenerative diseases like Alzheimer's. That is, the amyloid-beta peptide and the tau peptide, which is also implicated in Alzheimer's, as well as the signature clinical signs of the disease, such as memory loss and, ultimately, dementia, are all byproducts of the myelin breakdown and repair processes.

"The pervasive myelination of our brain is the single most unique aspect in which the human brain differs from other species," said Bartzokis, who is a member of the Laboratory of Neuro Imaging in the UCLA Department of Neurology and a member of UCLA's Brain Research Institute. Myelin is produced by oligodendrocytes, specialized glial cells that themselves become more vulnerable with age.

Bartzokis notes that myelination of the brain follows an inverted Ushaped trajectory, growing strongly until our 50s, when it very slowly begins to unravel as we age. The myelin that is deposited in adulthood ensheaths increasing numbers of axons with smaller axon diameters and so spreads itself thinner and thinner, Bartzokis said. As a result, it becomes more susceptible to the ravages of age in the form of environmental and genetic insults and slowly begins to break down faster than it can be repaired.

The exclusive targeting of the amyloid-beta peptide for many years is understandable because the same genes and enzymes involved in controlling myelination and myelin repair are, ironically, also involved in the production of amyloid-beta proteins. Bartzokis' point is that the amyloid beta may actually develop as a result of the natural process of the repair and maintenance of myelin.



"So the breakdown that leads to Alzheimer's and other age-related brain diseases, such as Parkinson's, may begin much earlier, before the formation of the protein deposits that are used to define these diseases," Bartzokis said.

Most drugs being developed for Alzheimer's are targeting amyloid beta, but little if any clinical improvement is being seen. This is, according to Bartzokis, "similar to cleaning up a house that's been flooded by water but never repairing the actual pipe that created the flood.

"For drug development then, the targets should be much further upstream, earlier in the process before the AB plaques even develop," he said.

Instead of focusing on reducing amyloid beta, Bartzokis argues, the myelin model suggests entirely different approaches to treatment and prevention of <u>Alzheimer's disease</u> that precede plaque formation. With modern brain imaging technology, clinicians could track the dynamic changes taking place in the <u>brain</u> and intercede well before any signs of Alzheimer's are seen.

"With earlier intervention," Bartzokis said, "we could reduce and potentially eliminate the increasingly catastrophic burden of dementia on the individual and their family, the health care system, and our society."

Provided by University of California Los Angeles (<u>news</u> : <u>web</u>)

Citation: Rethinking Alzheimer's disease and its treatment targets (2009, September 22) retrieved 5 May 2024 from https://medicalxpress.com/news/2009-09-rethinking-alzheimer-disease-treatment.html



This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.