

Alzheimer's disease is an age-related disease

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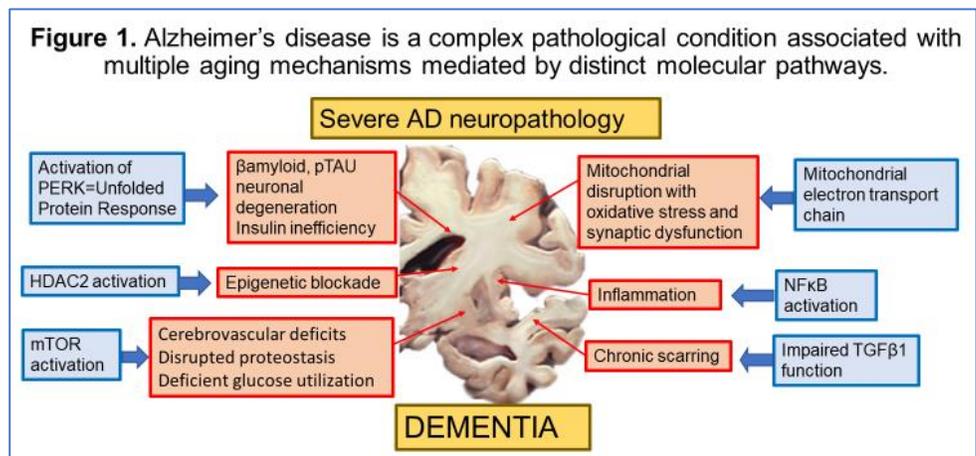
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Late onset Alzheimer's disease is a disease of the elderly, and accounts for greater than 95 percent of all Alzheimer's disease (AD) cases. Therefore, it could be said that AD is an age-related disease. But what does this really mean? It means that mechanisms involved in aging are also implicated in AD and include such processes as

inflammation, epigenetic changes, vascular deficits, oxidative stress, mitochondrial and autophagic impairment (Figure 1).

Many neuroscience purists do not agree with this labeling of AD, and in fact, consider neurological dysfunction unrelated to systemic organ disease relative to the development and progression of AD neuropathology. No wonder attempts to treat and prevent AD have consistently resulted in abysmal failure. Neuroscience grant review groups in the United States routinely reject grant applications that focus on aging as a driving factor in AD, and as such, are denying opportunities to extend AD research into aging research.

Aging research has made exponential progress over the last twenty years, with first genetic approaches



to aging intervention, and then pharmacological approaches using molecular targets identified from genetic studies. Aging grant review groups in the United States are now funding grants to target multiple mechanistic pathways, because aging is a complex multifactorial process. So why not consider AD as an aging condition and use a similar multidrug approach? This is obviously a platform that does not resonate well with established AD research groups engrained in neuroscience approaches designed to unravel a singular neurological target for the one magic bullet that would cure AD. Rather, if AD is viewed as a systemic aging problem in the elderly, then pharmacological testing can begin using drug cocktails. Such an approach will require preclinical testing of drug combinations in various cellular and

animal models that attack distinct mechanisms known to be involved in aging as well as AD.

Figure 2 is an example of such a globalistic approach. Most mechanisms are conserved pathways so drug cocktail studies could start in invertebrates progressing to rodents then to clinical trials. Many questions would need to be addressed, such as type of drug, dosage, timing, prevention or treatment.

