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Title: 'Evolutionary medicine' perspectives on Alzheimer's

Disease: Review and new directions

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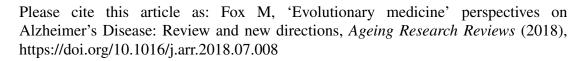
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ACCEPTED MANUSCRIPT

Title: 'Evolutionary medicine' perspectives on Alzheimer's Disease: Review and new directions

Running head: Evolutionary medicine and Alzheimer's

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Highlights

- · 'Evolutionary medicine' explores why we as humans are susceptible to diseases
- · Alzheimer's is an evolutionary enigma in being both harmful and ubiquitous
- · Various theories have been proposed for how natural selection affects Alzheimer's
- An alternative possibility is that Alzheimer's is a 'disease of civilization'
- · Risk factors like chronic inflammation and insulin resistance are novel in human history

Abstract:

Evolution by natural selection eliminates maladaptive traits from a species, and yet Alzheimer's Disease (AD) persists with rapidly increasing prevalence globally. This apparent paradox begs an explanation within the framework of evolutionary sciences. Here, I summarize and critique previously proposed theories to explain human susceptibility to AD, grouped into 8 distinct hypotheses based on the concepts of novel extension of the lifespan; lack of selective pressure during the post-reproductive phase; antagonistic pleiotropy; rapid brain evolution; delayed neuropathy by selection for grandmothering; novel alleles selected to delay neuropathy; by-product of selection against cardiovascular disease; and thrifty genotype. Subsequently, I describe a new hypothesis inspired by the concept of mismatched environments. Many of the factors that enhance AD risk today may have been absent or functioned differently before the modern era, potentially making AD a less common

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