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Review [J Steroid Biochem Mol Biol](#). 2016 Jun;160:134-47. doi: 10.1016/j.jsbmb.2016.03.012.

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Age, APOE and sex: Triad of risk of Alzheimer's disease

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Abstract

Age, apolipoprotein E ϵ 4 (APOE) and chromosomal sex are well-established risk factors for late-onset Alzheimer's disease (LOAD; AD). Over 60% of persons with AD harbor at least one APOE- ϵ 4 allele. The sex-based prevalence of AD is well documented with over 60% of persons with AD being female. Evidence indicates that the APOE- ϵ 4 risk for AD is greater in women than men, which is particularly evident in heterozygous women carrying one APOE- ϵ 4 allele. Paradoxically, men homozygous for APOE- ϵ 4 are reported to be at greater risk for mild cognitive impairment and AD. Herein, we discuss the complex interplay between the three greatest risk factors for Alzheimer's disease, age, APOE- ϵ 4 genotype and chromosomal sex. We propose that the convergence of these three risk factors, and specifically the bioenergetic aging perimenopause to menopause transition unique to the female, creates a risk profile for AD unique to the female. Further, we discuss the specific risk of the APOE- ϵ 4 positive male which appears to emerge early in the aging process. Evidence for impact of the triad of AD risk factors is most evident in the temporal trajectory of AD progression and burden of pathology in relation to APOE genotype, age and sex. Collectively, the data indicate complex interactions between age, APOE genotype and gender that belies a one size fits all approach and argues for a precision medicine approach that integrates across the three main risk factors for Alzheimer's disease.

Keywords: Age; Alzheimer's disease; ApoE; Bioenergetics; Brain; Mitochondria; Sex difference.

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Figures

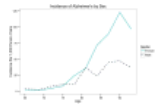


Figure 1 Sex-specific incidence estimates of Alzheimer's...

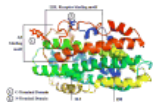


Figure 2 ApoE NMR protein structure. Created...



Figure 3 ApoE serum concentrations by sex...

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