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Is encephalopathic brain genetically more prone to dementia?

Letter to the Editor

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To the Editor,

Encouraging progress in understanding the genetics of Alzheimer's disease (AD) merely highlights the work that remains. AD and vascular dementia are two commonest dementias. Etiology of AD involves genetic factors in 25–40% [1]. Thus far, three fully penetrate genes' mutations have been identified in patients younger than 60 years.

First, this was assigned to the β amyloid precursor protein gene (*APP*) on chromosome 21and after that to the autosomal dominant gene defects of presenilin-1 (*PS1*) gene on chromosome 14. Presenilin-2 (PS2) gene on chromosome 1 was the last connected to early-onset AD. Each of these mutations causes abnormal proteins to be formed. In 2012 for example, Kamboh identifies nine other genes/loci (CR1, BIN1, CLU, PICALM, MS4A4/MS4A6E, CD2AP, CD33, EPHA1 and ABCA7) for late-onset Alzheimer's disease (LOAD) using genome-wide association studies (GWASs) [2].

With identification of more of the genes involved in development of the disorder, and a greater understanding of their action, AD research holds the hope of reducing or potentially eliminating the burden of this overwhelming disease [1]. The single-gene mutations directly responsible for early-onset Alzheimer's disease do not seem to be involved in late-onset Alzheimer's.

A specific gene causing the late-onset form of the disease has not been identified yet. However, one genetic risk factor does appear to increase a person's risk of developing the disease. This is related to the apolipoprotein E (APOE) gene found on chromosome 19. APOE encodes for a protein that helps carry cholesterol and other types of fat in the bloodstream. APOE comes in several different forms, or alleles. Three forms – APOE ε2, APOE ε3, and APOE ε4 – occur most frequently. APOE ε4 is present in about 25 to 30 % of the population and in about 40 % of all people with late-onset AD. People who develop AD are more likely to have an APOE ε4 allele than people who do not develop the disease.

Testing for the *E-4* allele cannot predict who will get the disease. Two national panels have raised their voice against the use of *apoE-4* as a predictive test for AD. This could be justified even more, if one bears in mind that a great majority of people who carry *E4* will not develop AD, respecting many people who do not.

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Just alike, chronic traumatic encephalopathy (CTE) [3], usually seen in athletes (i.e. TBI-related encephalopathy), affects competitors of different backgrounds, origin and colour of skin and people who inherit one or two APOE ε4 alleles tend to develop the disease at an earlier age than those who do not have any APOE ε4 alleles yet more likely if athletes (see McKee et al.) [4].

Already damaged nervous system is ideal ground for expression of mutations as suggested by Mattson et al. There is always a question, would some dementive disorder come obvious without contact sport history [5]

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