Neural Network Properties as a Function of Age and ApoE Genotype

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Introduction

The apolipoprotein E (apoE) gene has been implicated in various functions involved in brain health including neural development, regeneration, neuroprotection, and plasticity. Human apoE exists in 3 isoforms - E2, E3, E4 - that differ according to the presence of either a cysteine or arginine at two positions (residues 112 and 158). These substitutions affect not only the structure and function but also risk or resilience for various insults and diseases (e.g,. Alzheimer's disease, TBI). The E2 and E3 alleles are thought to confer relative superiority over E4.

Objective

To investigate brain function in cognitively healthy participants according to apoE genotype.

Methods

A total of 165 cognitively healthy (MoCA 26+) participants (153 women, 12 men) ranging from 28-99 y old were genotyped for apoE and resting state brain function was recorded using magnetoencephalography (MEG).

We analyzed properties of the neural network, including the flexibility and variability of interactions between MEG sensor pairs.

- flexibility = the absolute value of the covariance = ACOV
- variability = the product of the standard deviations = PSD

ApoE genotype was transformed into a new variable to reflect the corresponding number of cysteine residues per mole (CysR/mole).

Genotype	CysR/mole	N (%)
E2/E2	4	2 (1.2)
E2/E3	3	17 (10.3)
E2/E4	2	5 (3)
E3/E3	2	102 (61.8)
E3/E4	1	34 (20.6)
E4/E4	0	5 (3)

Results

(1) Network flexibility increased from E4 to E2 genotype (Fig. 1).

(2) Network variability decreased from E4 to E2 genotype (Fig. 2).

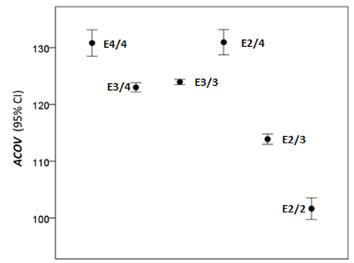

Fig. 1. Network flexibility for each apoE genotype. Lower ACOV indicates more flexible network.

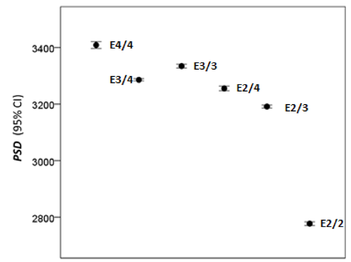

Fig. 2. Network variability.

(3) Plotting network properties by decade and genotype revealed that both network properties were relatively stable up to the 7th decade of life. After that, the network properties differed substantially according to CysR/mole. Genotypes with more CysR/mole evidenced healthier network properties (i.e., increased flexibility, decreased variability). (Fig. 3 and Fig. 4).

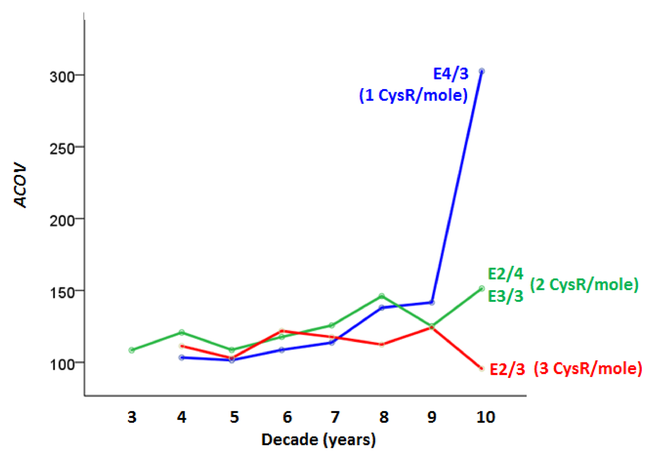

Fig. 3. Network flexibility as a function of age and CysR/mole
Lower ACOV indicates more flexible network.

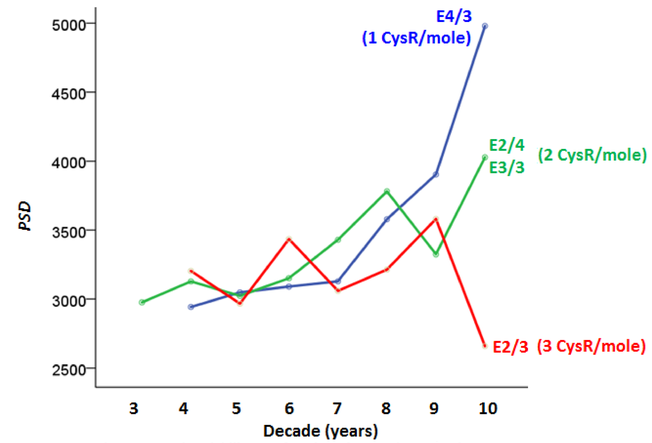

Fig. 4. Network variability as a function of age and CysR/mole

Conclusions

ApoE genotype is associated with systematic neural network changes with age, even in the absence of cognitive decline.

The effects of apoE on neural network functions are manifested more clearly with increasing age.

These findings are in accordance with the prevailing literaure highlighting the relative benefit of the E2 allele over E4.

Neuroprotective effects of the E2 allele extend beyond Alzheimer's disease risk and may promote overall brain health.

These effects may be conferred by the presence of additional cysteines (and enhanced plasticity) relative to other isoforms.

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