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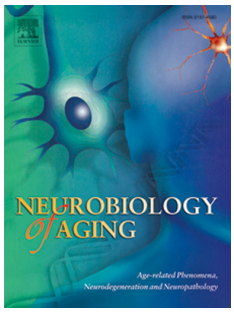

Variations in the APOE allele or BDNF Val66Met polymorphism are not associated with changes in cognitive function following a tertiary education intervention in older adults: The Tasmanian Healthy Brain Project

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NEGATIVE RESULT

Variations in the APOE allele or BDNF Val66Met polymorphism are not associated with changes in cognitive function following a tertiary education intervention in older adults: The Tasmanian Healthy Brain Project

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5 Supplement files for online access

Abstract

The APOE ε4 allele and the Met variant of the BDNF Val66Met polymorphism are associated with reduced cognitive function in older adults. The aim of this study was to examine the independent and interactional effect of the APOE ε4 allele and BDNF Val66Met polymorphism on cognitive function in a cohort of healthy older adults who had undertaken further university level education. Multiple group Latent Growth Curve Modelling revealed no change in cognitive function over time in APOE ε4-carriers or in BDNF Met-carriers, nor in carriers of both APOE-ε4 and BDNF-Met alleles. Further, the results indicate that allelic variation in either APOE or BDNF does not modify the beneficial effects of a university based education intervention on cognitive function over a four-year period following the intervention.

Introduction (see Supplement 1 for extended Introduction)

Carriers of the apolipoprotein (APOE) ε4 allele demonstrate poorer performance compared to non-carriers across a range of cognitive functions, including episodic memory, executive function and general cognition (Wisdom, et al., 2011); with the cognitive decline in ε4-carriers becoming more pronounced with age (Wisdom, et al., 2011). Similarly, brain derived neurotrophic factor (BDNF) is thought to contribute to variance in adult cognitive function, with several studies reporting that healthy older BDNF-Met carriers display reduced cognitive function relative to Val-homozygotes (Egan, et al., 2003).We examined the influence of the APOE ε4 allele and BDNF Met polymorphism on the longitudinally assessed cognitive performance of healthy older adults who have undertaken an education intervention. This intervention has been shown to result in improved cognitive reserve in this sample (Lenehan, et al., 2016).

Methods (see Supplement 2 for extended Method)

A total of 444 healthy adults aged between 50 and 79 years were recruited from the Tasmanian Healthy Brain Project (THBP) participant pool (Summers, et al., 2013). The intervention group (n = 344) had completed a minimum of 12 months part-time or full-time university study comprising a minimum of two units at undergraduate or post graduate levels. The remaining 100 participants were a control reference group who had not undertaken any intervention. The project was approved by the Human Research Ethics Committee (Tasmania) Network and further details of the study protocol have been previously published (Summers, et al., 2013). All participants in the THBP completed a comprehensive testing battery (see Supplement 2; Summers, et al., 2013). DNA was extracted from saliva samples with APOE and BDNF genotype being determined using a one-step ARMS-PCR.

Core Data (see Supplement 2 for extended description of Analyses)

Multiple Group Latent Growth Curve Modelling (LGCM) using maximum likelihood estimation was used to compare group differences in APOE genotype (control non-ε4 carrier; control ε4-carrier; intervention non-ε4 carrier; and, intervention ε4-carrier), BDNF genotype (control Val-homozygote; control Met-carrier; intervention Val-homozygote; and intervention Met-carrier), and APOE/BDNF genotype (ε4/ Met, non- ε4/ Met, ε4/ Val, non-ε4/ Val) in longitudinal performance on composite measures of episodic memory, working memory, executive function and language processing. For APOE (see Supplement 3), the intervention ε4 group displayed higher working memory performance at baseline compared to the control group non- ε4 carriers. In addition, there was a significant difference between the rate of change in language processing over time between the control non-ε4 group (decrease over time) and the intervention non-ε4 group (increase over time). There were no significant APOE group differences in episodic memory or executive function over time. For BDNF (see Supplement 4) the control Met-carrier group displayed lower baseline episodic memory than the intervention Val-carrier group and both intervention groups (Val-

homozygote and Met-carrier) displayed significantly higher linear slopes in language processing compared to the control Val-carrier groups. For the interactive effect of APOE/BDNF (see Supplement 5) no differences between groups on any of the cognitive domains were detected at baseline, nor over time.

Discussion of data (see Supplement 1 for extended Conclusions)

No significant differences in baseline score or linear rate of change over time to working memory, episodic memory, executive function or language processing capacity were found between: intervention group ε4-carriers and non-ε4 carriers or between control group ε4-carriers and non-ε4 carriers (Supplement 1); between Val-homozygotes and Met-carriers or between control group Val-homozygotes and Met-carriers (Supplement 2); or between any combination of APOE/BDNF genotype (Supplement 3). Further, there was no evidence of a genotype specific enhanced benefit of education-based intervention on cognitive function, with no differences in the linear slope of the intervention subgroups (APOE or BDNF) across any of the four cognitive domains. These results suggest that in a group of healthy older adults the APOE and BDNF genotypes are unrelated to cognitive performance or to the four-year trajectory of cognitive change.

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