Abstract

Alzheimer's disease (AD) is a slowly progressing neurodegenerative disease characterized by an extracellular accumulation of senile plaques and intracellular neurofibrillary tangles. Apart from these hallmarks, AD is very heterogeneous, especially at the age of onset and the rate of progression. Genetic polymorphisms are key modulators influencing these factors. One of them is a polymorphism for the Brain-derived neurotrophic factor (*BDNF*), a neurotrophin involved in the synaptic plasticity in the hippocampus and medial temporal lobe structures, areas primarily affected in AD. The thesis aimed to investigate the effect of *BDNF* Va66Met polymorphism together with the main genetic risk factor for sporadic AD, Apolipoprotein E (*APOE*) polymorphism, on cognitive functions and structural brain changes. We have shown that the combination of risk alleles *BDNF* Met and *APOE* ε4 is associated with more severe impairment in episodic memory, egocentric orientation and smaller volumes of medial temporal lobe structures in individuals with amnestic mild cognitive impairment (aMCI), and allocentric orientation in cognitively unimpaired individuals compared to non-carriers.

These findings suggest that carriers of the combination of *BDNF* Met and *APOE* ε4 have a higher risk of progression to more severe disease stages, thus supporting the importance of these polymorphisms as clinically relevant genetic markers for identifying asymptomatic individuals at increased risk of developing AD.

Key words:

Alzheimer’s disease, Apolipoprotein E, Brain-derived neurotrophic factor, episodic memory, hippocampus, mild cognitive impairment, spatial navigation