The association of BDNF and cognitive function in patients with Alzheimer's disease and mild cognitive impairment

Matea Nikolac Perkovic[1], Fran Borovecki[2], Natasa Klepac[3], Sanja Hajnsek[3], Dorotea Muck-Seler[1], Nela Pivac [1]

[1]Division of Molecular Medicine, Rudjer Boskovic Institute, Bijenicka cesta 54, 10 000 Zagreb, Croatia

[2]Department for Functional Genomics, Center for Translational and Clinical Research, University of Zagreb School of Medicine, and University Hospital Center Zagreb, Zagreb, Croatia

[3]Department of Neurology, University Clinical Hospital Center Zagreb, Zagreb University School of Medicine, Zagreb, Croatia.

Introduction

Brain derived neurotrophic factor (BDNF) is a neurotrophin found in different brain areas like hippocampus, neocortex, amygdala, cerebellum and hypothalamus. It affects neurogenesis and synaptic plasticity, neurotransmission mediated by different neurotransmitters, cognition, learning and memory. BDNF modulates dopaminergic, cholinergic and serotonergic neurotransmitter system, regulates food intake, pain sensation, mood, behavior and response to stress. The reduction of the BDNF concentration in different brain areas has been associated with dementia and cognitive decline indicating an important role of this neurotrophin in the development of dementia which is characterized by progressive deterioration of intellectual functioning. Alzheimer disease (AD) is a most common type of dementia characterized by progressive loss of cognitive function. Since there is no cure for AD, the studies of the early phases of AD, that are trying to find new biological markers that could serve as early diagnostic indicators, have pointed out the potential importance of early detection of mild cognitive impairment (MCI). MCI is a disorder that has been associated with risk for AD since it represents a transitional state between normal and pathological aging (characterized with cognitive impairments that lead to dementia).

The aim of this study was to define the role of BDNF in the development of cognitive symptoms of dementia by analysing five different BDNF polymorphisms, rs6265 (Val66Met), rs11030104, rs7934165, rs1519480 and rs56164415 (C270T) (Figure 1) and by analysing BDNF plasma concentration.

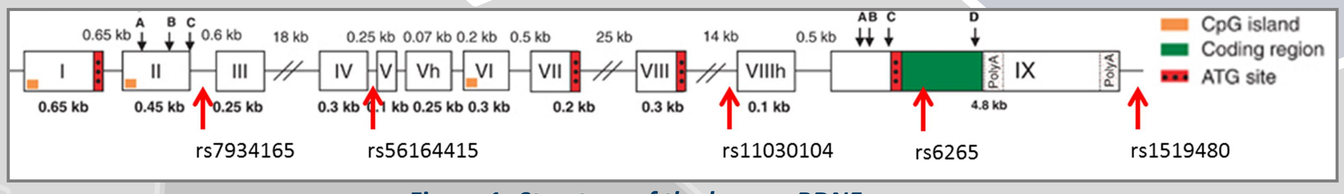


Figure 1. ***Structure of the human BDNF gene***

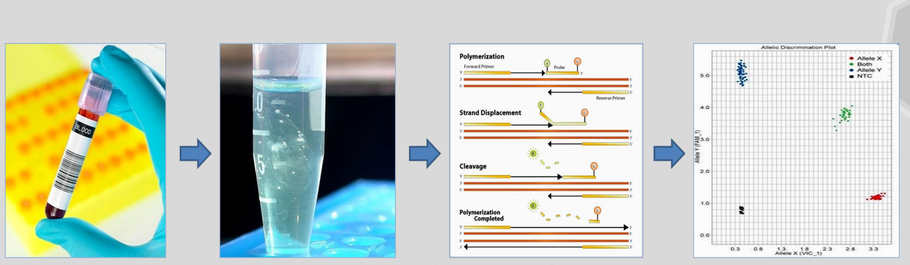


Figure 2. ***Genotyping procedure***

Methods and Materials

The study included 82 patients with AD and 49 patients with MCI. Diagnosis of AD was done according to the NINCDS-ADRDA and DSM-IV criteria. Cognitive impairment was evaluated using Mini-Mental Status Examination (MMSE) and Clock Drawing Test (CDT).

Genomic DNA was extracted from peripheral blood using the salting out method. SNPs were genotyped with the ABI Prism 7000 Sequencing Detection System apparatus (ABI) using the TaqMan® Pre-designed and Custom TaqMan® SNP Genotyping Assay (Figure 2). Plasma BDNF levels were measured using enzyme-linked immunosorbent assay (ELISA) according to the procedures supplied by the manufacturer (R&D Systems GmbH Wiesbaden-Nordenstadt, Germany).

The association of polymorphisms and plasma BDNF levels with cognitive decline in patients with AD or MCI was evaluated using one-way analysis of variance (ANOVA) in Sigma Stat 3.5.

Results

Our results showed an association between rs1519480 and MMSE scores in patients with AD (Table 1).

Our results showed an association between rs1519480 and MMSE and CDT scores in patients with MCI (Table 2).

Alzheimer's disease

Table 1. ***The association of MMSE and CDT scores with BDNF polymorphisms in AD***

	MMSE		CDT	
	ANOVA			
SNP	**F**	**P**	**F**	**P**
rs6265	0.385	0.681	1.502	0.229
rs11030104	0.438	0.647	2.858	0.063
rs7934165	2.070	0.133	0.861	0.427
rs1519480	3.856	**0.025**	1.496	0.231
rs56164415	3.676	0.059	1.583	0.212

Mild cognitive imapirment

Table 2. ***The association of MMSE and CDT scores with BDNF polymorphisms in MCI***

	MMSE		CDT	
	ANOVA			
SNP	**F**	**P**	**F**	**P**
rs6265	0.860	0.358	0.985	0.326
rs11030104	2.252	0.140	1.039	0.313
rs7934165	0.577	0.566	1.615	0.210
rs1519480	3.270	**0.047**	5.453	**0.007**
rs56164415	1.358	0.250	0.242	0.625

Plasma BDNF levels and cognitive symptoms

Our results showed no significant difference in plasma BDNF levels between patients with AD and MCI (Figure 3) and no signifficant association between plasma BDNF levels and MMSE (Figure 4) or CDT scores (Figure 5).

Figure 3.

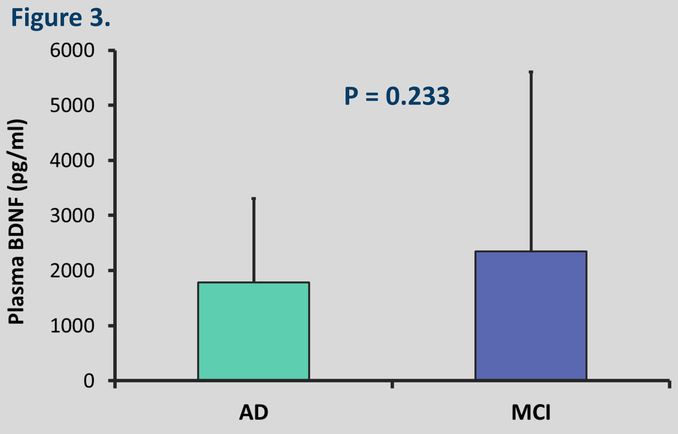


Figure 4.

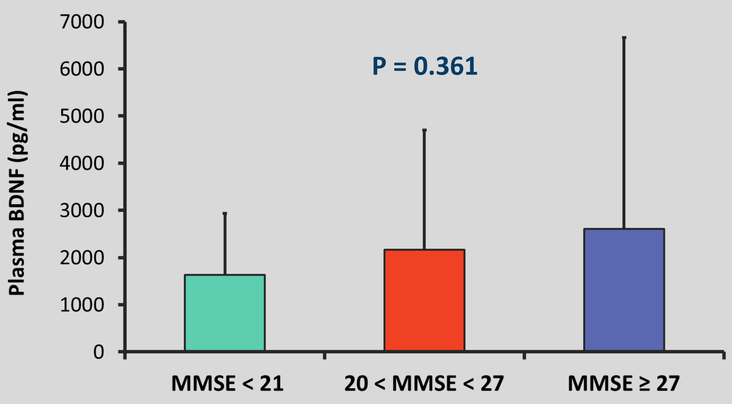
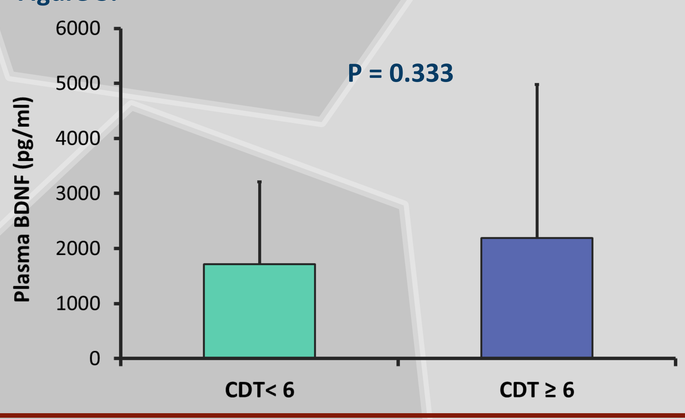


Figure 5.



Conclusion

The present findings suggested a major role of BDNF in AD, and revealed a potential role of BDNF rs1519480 polymorphism in cognitive decline that is characteristic for patients with AD and MCI. The rs1519480 might influences BDNF mRNA expression in the prefrontal cortex and contribute to inter-individual variation in cognitive performance, as well as contributing to the risk for developing psychiatric and neurological conditions.

Analyses utilized to examine the relation between plasma BDNF levels, MMSE and CDT scores did not distinguish between AD and MCI patients and they did not significantly predict global cognitive functioning. However, our results show that there may be a trend toward lower plasma BDNF concentration in patients with lower cognitive abilities.