

BDNF GEN POLYMORPHISM - INFLUENCE ON CLINICAL MANIFESTATIONS AND OUTCOME OF NEUROLOGICAL DISEASES

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BDNF - its role in clinical course of potential brain recovery during multiple sclerosis and stroke

Brain-derived neurotrophic factor (BDNF) belongs to the family of neurotrophins originally described to be crucial for neuronal differentiation and survival. BDNF is known to be involved in myelin formation and promote remyelination in multiple sclerosis (MS) and is also essential for post-stroke recovery in rodents and in brain neurodegeneration.. BDNF-196 G>A (Met/Val) polymorphisms has been shown to have functional consequences, whereas for -270 C>T it has not been fully elucidated. The Met allele has been associated with impairments in intracellular trafficking and activity-dependent secretion of BDNF in neurons and neurosecretory cells. In all brain processes where acute injury or choric degeneration occur accumulation of inflammatory cells may additionally increase production of trophic factors. In our studies we have determined impact of BDNF single nucleotide polymorphisms (SNPs): -196 G>A (Val66Met) and -270 C>T on: 1) MS susceptibility and its the clinical course, 2) human stroke early outcome and 3) post stroke recovery after rehabilitation. According to the study design suitable neurological and outcome measures were used. The tendencies of influence of BDNF polymorphisms on studied parameters have been noticed. For example there was higher occurrence of BDNF -270 CC genotype in pa-

tients with hemorrhagic than ischemic stroke (96% versus 86%,). In hemorrhagic stroke BDNF -196 GG carriers scored better in NIHSS at admission and after 7 days. No effect of determined BDNF polymorphisms on functional motor or language recovery was found. However, in patients who were admitted to the rehabilitation ward within 3 months from ischemic stroke onsets some significant effect of -196 G>A and -270 C>T polymorphisms on stroke outcome differences in men and women were noted. It was found that men with BDNF -196 GG scored in discharge Rankin scale significantly better than women (median 2,0 versus 3,0, $p=0,0142$). Moreover, men with -270 CT scored better than women both in Rankin and Barthel scale at discharge (respectively median 2,0 versus 4,0; $p=0,0139$ and median 18,5 versus 8,5; $p=0,0144$). When BDNF -270 CT and -196 GG were combined, men scored better in both Rankin and Barthel scale at discharge (respectively median 2,0 versus 4,0; $p=0,0079$ and median 18,0 versus 9,0; $p=0,0142$).

Different effect of BDNF SNPs on clinical course and outcome of neurological diseases may be explained by influence of many different genetic and non-genetic factors involved in processes of neurodegeneration and post ischemia brain recovery. Further studies are needed to elucidate influence of endogenous neurotrophic factors in neurological diseases.