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REDUCED FRACTIONAL ANISOTROPY IN THE UNCINATE FASCICULUS IN PATIENTS WITH MAJOR DEPRESSION CARRYING THE MET-ALLELE OF THE VAL66MET BRAIN-DERIVED NEUROTROPHIC FACTOR GENOTYPE

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Objective: Experimental studies support a neurotrophic hypothesis of major depressive disorder (MDD). The aim of this study was to determine the effect of Val66Met brain derived neurotrophic factor (BDNF) polymorphism on the white matter fibre tracts connecting hippocampus and amygdala with the prefrontal lobe in a sample of patients with MDD and healthy controls.
Methods: Thirty seven patients with MDD and 42 healthy volunteers were recruited. Diffusion tensor imaging (DTI) data with 61 diffusion directions were obtained with MRI 3 Tesla scanner. Deterministic tractography was applied with *ExploreDTI* and Val66Met BDNF SNP (rs6265) was genotyped. Fibre tracts connecting the hippocampus and amygdala with the prefrontal lobe, namely uncinate fasciculus, fornix and cingulum were analysed.
Results: A significant interaction was found in the uncinate fasciculus (UF) between BDNF alleles and diagnosis. Patients carrying the BDNF met-allele had smaller fractional anisotropy (FA) in the UF compared to those patients homozygous for val-allele and compared to healthy subjects carrying the met-allele. A significant 3-way interaction was detected between region of the cingulum (dorsal, rostral and parahippocampal regions), brain hemisphere and BDNF genotype. Larger FA was detectable in the left rostral cingulum for met-allele carriers when compared to val/val alelle carriers.
Conclusions: We provide evidence for the importance of the neurotrophic involvement in limbic and prefrontal connections. The met-allele of the BDNF polymorphism seems to render subjects more vulnerable for dysfunctions associated with the UF, a tract known to be related to negative emotional-cognitive processing bias, declarative memory problems, and autonoetic self awareness.

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