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ASSOCIATION OF METHYLATION STATUS AND SNP VARIATION OF BDNF AND SUICIDE

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Introduction: Suicide is complex, multifactorial phenomenon, and is an outcome of interplay of environmental, genetic, and epigenetic factors. Brain-derived neurotrophic factor (BDNF), which mediates neural plasticity, different behaviours, and stress response has been associated with stressful life events or childhood adversity in depression and suicidal behaviour in various psychopathologies, and it may as well modulate antidepressant response.
Methods: We genotyped 600 subjects, suicide victims and controls, for polymorphism Val66Met (rs6265), and performed methylation analysis on 44 subjects. Different subgroups were formed to test impact of specific variables (violent and non-violent methods, psychiatric disorders, suicide in victims with/without stressful childhood experience) on suicide and genetic component.
Results: The frequency of the combined Met/Met and Met/Val genotypes and the homozygous Val/Val genotype was significantly different between female suicide victims and controls, between female suicide victims who used violent suicide methods and controls, and between all included suicide victims with or without stressful life events. Postmortem brain samples from suicide subjects showed a statistically significant increase of DNA methylation at specific CpG sites in promoter/exon IV compared with controls. Higher methylation degree corresponded to lower mRNA levels. BDNF promoter/exon IV was frequently hypermethylated in postmortem brain of suicide subjects irrespective of genome-wide methylation levels, indicating that a gene-specific increase in DNA methylation could cause or contribute to the downregulation of BDNF expression in suicide subjects.
Conclusions: DNA variation and methylation stauts of the BDNF could be very importnant prognistic factors for increased vulnerability to suicidal behaviour, and therefore significant target of future studies.

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