

DIFFERENTIAL METHYLATION PROFILES OF BDNF PROMOTERS I AND IV IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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INTRODUCTION

➤ Epigenetics can be defined as the study of inheritable changes in gene expression that occur with no modifications in the DNA sequence per se. Methylation is the most studied epigenetic change and can lead to promoter gene silencing or loss of its function. The BDNF gene, a member of the neurotrophin family which encodes brain-derived neurotrophic factor (BDNF), is related to differentiation, maturation, survival and cell death in central nervous system. In this study, we evaluate possible epigenetic mechanisms in epilepsy, by analyzed methylation changes in promoters I and IV of the BDNF gene in patients with temporal lobe epilepsy (TLE).

METHODS

➤ Analysis of 172 patients with TLE and 158 healthy controls for metylation status of promoters I and IV of the BDNF gene of peripheral blood and its correlation with the clinical characteristics of TLE. Methylation profile analysis was performed using the High Resolution Melting (HRM) method on a StepOne™ Real-Time PCR System (Applied Biosystems®). As a methylated/unmethylated control, we used the Cells-to-CpG Methylated and Unmethylated gDNA Control Kit (Applied Biosystems®). Methylated was defined as ratios of methylation of 75% or higher.

RESULTS

➤ Patients showed increased methylation in promoter I ($p < 0.047$) and decreased methylation in promoter IV ($p < 0.005$) when compared to controls. Considering only patients with epilepsy, the methylation frequency of BDNF promoter I was 7.6% ($n = 13$), and of promoter IV was 1.7% ($n = 3$), as opposed to the unmethylated status, in which 92.4% ($n = 159$) of patients showed unmethylated status for BDNF promoter I and 98.3% ($n = 169$) for BDNF promoter IV. There were no statistical differences between promoter methylation status regarding main features of TLE, such as sex, age, age of epilepsy onset, mean age at epilepsy, or EEG or neuroimaging findings.

CONCLUSION

➤ It is believed that selective changes in DNA methylation of BDNF promoter regions may highlight the relation of epigenetic factors in epilepsy. Our seminal results may indicate that methylation of selective genes or other epigenetic mechanisms might be important contributing factors for epileptogenesis or its characteristics. Therefore, we believe that these mechanisms and exciting new possibilities need to be further explored.

Funding by:     