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■ THE EFFECTS OF GENE POLYMORPHISMS RELATED WITH GABAERGIC SYSTEM ON EVENT RELATED EEG RESPONSES

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Abstract

Neurotransmitter related gene polymorphisms are shown to be important factors in the pathogenesis of neurological and psychiatric disorders, response to the treatment, and cognitive functions. Therefore, investigation of these polymorphisms in the healthy populations might help to understand the neurochemical mechanisms underlying several cognitive processes. GABAergic system is implied to have an outstanding role in generation and/or modulation of event related potentials (ERPs) and event related oscillations (EROs) via its effects on inhibitory and excitatory post-synaptic potentials and local and large scale neuronal synchronizations. The present study was aimed to identify the associations between the single nucleotide polymorphisms (SNP) in GABA_A and GABA_B receptor genes and auditory ERPs and EROs. We investigated an intronic G to A nucleotide exchange in the $\gamma 2$ subunit of GABA_A receptor (GABRG2) gene and three exonic SNPs of the GABA_B R1 gene (Ala20Val, Gly489Ser, and Phe658Phe polymorphisms). The study was carried out on 202 healthy male medical students in order to avoid confounding effects of gender, age,

education, and IQ. Auditory novelty and Go/Nogo paradigms were used to derive ERPs and EROs. The differences in the amplitudes and the latencies of N1, P2, P3 ERP waves, and the mean amplitudes of the evoked and the total ERO activities between the different genotypes for each polymorphisms were tested with repeated measures analysis of variance (ANOVA) designs. In the time domain analysis, the investigated GABA_A receptor polymorphism led to a difference in P3a amplitude, and GABA_B receptor polymorphisms affected N1 and P2 amplitudes and the P2 and P3 latencies. In the time-frequency plane analyses, we found that GABA_A polymorphism mainly affected late responses in the alpha and theta bands, except for an early effect in gamma range, whereas GABA_B polymorphisms were associated with early responses in evoked theta and gamma range. Our results suggest that the genetic variants of GABA_A and GABA_B receptors might produce different effects on cognitive electrophysiological signals.

Keywords: event related potentials, event related oscillations, gamma-aminobutyric acid (GABA), GABA_A receptor, GABA_B receptor, polymorphism