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PRECISION MEDICINE IN EPILEPSY: A GENDER-BASED OMICS APPROACH

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Abstract

Epilepsy is a complex neurological condition with recurrent seizures and is often accompanied by cognitive impairments and varying drug responses. The recent advances in precision medicine have highlighted the importance of proteomic and metabolomic biomarkers in understanding the heterogeneity of the condition as well as the gender-related differences in drug responses.Proteomic research has shown that there is differential expression of synaptic and receptor-related proteins such as the GABA_A subunits,NMDA receptor-associated proteins and synaptophysin, which are involved in the control of neuronal excitability,synaptic plasticity,memory. Variations in the expression of drug transporter proteins such as P-glycoprotein at the BBB have also been associated with reduced drug penetration and pharmacoresistance in epilepsy patients.Metabolomic profiling has revealed significant alterations in neurotransmitter and energy metabolism pathways, including changes in glutamate,GABA, and lactate levels, which may influence seizure threshold and cognitive function. In addition, inflammatory and neurotrophic biomarkers such as BDNF,interleukin-1β, and tumor necrosis factor-α show differential expression patterns that may vary with sex hormones, contributing to gender-specific differences in disease progression and drug response.Proteomic and metabolomic studies indicate gender differences in epilepsy caused by certain sex hormones such as estrogen, progesterone, testosterone, and a metabolite of progesterone named allopregnanolone. In females, estrogen increases NMDA receptor function and excitatory transmission, and progesterone/allopregnanolone increases GABA_A receptor function, resulting in hormone-dependent modulation of seizure threshold and cognitive function. In males, testosterone and its metabolites may modulate GABA_A and NMDA receptor function, resulting in distinct, though relatively stable, receptor function compared with females. In addition, gender differences in P-glycoprotein, a drug transporter involved in the BBB, might influence the penetration of antiepileptic drugs.. These results demonstrate the relevance of hormone-dependent mechanisms in epilepsy and support the need of gender specific precision therapy

Keywords: Epilepsy, Proteomics, Metabolomics, Biomarkers, GABA, BDNF, P-glycoprotein, Pharmacoresistance, Precision medicine, Personalized therapy.