Prefrontal Ultrasound Stimulation Prevents Schizophrenia-Like Symptoms in Rats

Feng-Yi Yang
Department of Biomedical Imaging and Radiological Sciences, National Yang Ming Chiao Tung University, Hsinchu, Taiwan

Wei-Shen Su
Department of Biomedical Imaging and Radiological Sciences, National Yang Ming Chiao Tung University, Hsinchu, Taiwan

Abstract

Schizophrenia continues to present significant therapeutic challenges, with growing interest in the role of glutamatergic dysfunction, particularly involving NMDA receptor hypofunction. This study assessed the potential of low-intensity pulsed ultrasound (LIPUS) as a non-invasive intervention for schizophrenia-like symptoms induced by dizocilpine (MK-801), an NMDA receptor antagonist. Male rats were divided into four groups and pretreated with or without LIPUS targeting the prefrontal cortex (PFC) for five consecutive days. Following MK-801 (0.3 mg/kg) or saline administration, behavioral assessments—including open field and prepulse inhibition tests—were conducted. Subsequent analysis of brain tissues involved western blotting and immunohistochemistry to evaluate molecular changes. LIPUS pretreatment attenuated MK-801-induced hyperlocomotion, sensorimotor gating deficits, and anxiety-like behavior. Moreover, LIPUS preserved the expression of the NMDA receptor subunit NR1 in the medial PFC, which was otherwise downregulated by MK-801. It also reduced the MK-801-induced increase in c-Fos expression in the medial PFC and ventral tegmental area. These findings suggest that LIPUS modulates NMDA receptor function and neural activation patterns, offering promising neuromodulatory effects that could inform future non-pharmacological strategies for schizophrenia treatment.

Keywords

LIPUS, schizophrenia, positive symptom, NMDA receptor, MK-801.