Symposium | Schizophrenia：[Symposium 75] Current Topic of Biological Psychiatry: Synapse, Glia and Inflammation

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[Symposium 75] Current Topic of Biological Psychiatry: Synapse, Glia and Inflammation

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[SY-75-03] Study the Immunoinflammatory mechanisms of Depression: The role of protein tyrosine phosphatase receptor type Z1 and astrocyte-microglia interactions

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キーワード：Neuroinflammation、Chronic stress、Cytokines、Astroglia-microglia interaction

Major depressive disorder (MDD) is a highly disabling mental disorder characterized by persistent low mood, anhedonia, and cognitive impairment. Its etiology is complex, and the neuroinflammatory responses are considered a critical pathogenic mechanism of MDD, with the homeostatic balance of inflammatory cytokines and the immunoregulatory functions of glial cells being essential for maintaining normal neuroimmune function. Protein tyrosine phosphatase receptor type Z1 (PTPRZ1) has recently been identified as a key molecule involved in the regulation of neuroinflammation, and its genetic variations have been associated with the pathogenesis of MDD. We used the post-witness social defeat stress model, which has been validated for studying the immune mechanisms of MDD. We found the notably increased the expression of PTPRZ1 protein, the significant enhancement of PTPRZ1 phosphatase activity in the hypothalamus and the higher levels of proinflammatory cytokines in stressed mice. The behaviors and immune response could be reversed by both the typical antidepressants (fluoxetine) treatment and administration of the PTPRZ1 phosphatase inhibitor MY10. And additionally, MY10 treatment significantly inhibited the overactivation of microglia in the hypothalamus of stressed mice, reduced the number of M1 pro-inflammatory microglia, and increased the number of M2 anti-inflammatory microglia. This study first unveiled the critical role of PTPRZ1 in the neuroimmune regulation of the hypothalamus in chronically stressed mice. The Immune-inflammatory and astrocyte-microglia interactions play the important role in the pathology of MDD. this immune response. Additionally, this study found that the PTPRZ1 phosphatase inhibitor MY10 modulates microglial polarization and effectively alleviates depressive-like behaviors in stressed mice. These findings provide new theoretical insights into the pathogenesis of MDD and offer potential therapeutic targets for developing novel PTPRZ1-based treatment strategies.