Symposium

Sat. Sep 27, 2025 3:50 PM - 5:20 PM JST | Sat. Sep 27, 2025 6:50 AM - 8:20 AM UTC Session Room 4 (Large Hall B)

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

Moderator: Takahiro A. Kato (Department of Psychiatry, Hokkaido University Graduate School of Medicine), Shigenobu Kanba (Kyushu University)

[SY-75]

Current Topic of Biological Psychiatry: Synapse, Glia and Inflammation

Takahiro A. Kato[1], Shigenobu Kanba[2], Hsein-Yuan Lane[3], Si Tianmei[4], Masaaki Iwata[5] (1.Hokkaido University(Japan), 2.Kyushu University(Japan), 3.China Medical University/Hospital(Taiwan), 4.Peking University(China), 5.Tottori University(Japan))

[SY-75-01]

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

*Tian-Mei Si[1,2] (1.National Clinical Research Center for Mental Disorders(Peking University Sixth Hospital/Institute of Mental Health)(China), 2.The Key Laboratory of Mental Health, Ministry of Health (Peking University)(China))

[SY-75-02]

Antidepressant Effects of β-Hydroxybutyrate Based on the Neuroinflammation Hypothesis of Depression and Its Potential for Clinical Application

*Masaaki Iwata (Tottori University (Japan))

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Keywords：inflammation、microglia、NMDA

In this symposium, we will discuss the current topic of biological psychiatry expecially focusing on neuro-glia interactions and brain inflammation.

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Keywords：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.

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[SY-75-02] Antidepressant Effects of β-Hydroxybutyrate Based on the Neuroinflammation Hypothesis of Depression and Its Potential for Clinical Application

*Masaaki Iwata (Tottori University (Japan))

Keywords：Depression、Inflammation、beta hydroxybutyrate

The monoamine hypothesis, which attributes depression to reduced function of neurotransmitters such as serotonin and norepinephrine, has long dominated the understanding of depression’s pathophysiology. However, many patients show limited response to monoaminergic treatments, highlighting the need for alternative models. Recently, the neuroinflammation hypothesis has emerged, suggesting that chronic stress and environmental factors activate microglia in the central nervous system, triggering the release of pro-inflammatory cytokines like IL-1β and TNF-α. These disrupt neuroplasticity and may underlie depressive symptoms.We focused on β-hydroxybutyrate (BHB), an endogenous ketone body with anti-inflammatory properties, as a novel therapeutic approach. BHB is produced in the liver during fasting, exercise, or ketogenic diets and crosses the blood–brain barrier to act within the central nervous system. In animal models of stress-induced depression, BHB administration significantly improved depression-like behaviors. Mechanistically, BHB suppressed activation of the NLRP3 inflammasome and reduced brain IL-1β expression. It may also enhance BDNF expression via HDAC inhibition, contributing to both anti-inflammatory and neuroplasticity-promoting effects.Based on these findings, we are currently conducting a specified clinical trial in patients with depression to evaluate BHB’s therapeutic potential. As BHB is already used as a dietary supplement and demonstrates high safety and oral bioavailability, it is a promising candidate for clinical application.This research supports a shift from the monoamine-based model to a molecularly informed neuroinflammatory paradigm of depression, offering a foundation for novel, mechanism-based interventions. Further multi-institutional collaboration is ongoing to clarify BHB’s efficacy and mechanisms, aiming toward its integration into personalized psychiatric care.