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

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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.