Symposium

2025年9月26日(金) 16:30 ~ 18:00 Session Room 7 (Conference Room C)

[Symposium 53] How does the gut microbiota contribute to elucidating the mental health in children and adolescents?

Moderator: Katsunaka Mikami (Department of Psychiatry, Tokai University School of Medicine), Chaiyavat Chaiyasut (Innovation Center for Holistic Health, Nutraceuticals, and Cosmeceuticals, Faculty of Pharmacy, Chiang Mai University)

[SY-53]

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Katsunaka Mikami[1], Chaiyavat Chaiyasut[2], Eiji Miyauchi[3], Tomokazu Hata[4], Natsure Watanabe[1] (1.Department of Psychiatry, Tokai University School of Medicine(Japan), 2.Innovation Center for Holistic Health, Nutraceuticals, and Cosmeceuticals, Faculty of Pharmacy, Chiang Mai University(Thailand), 3.Institute for Molecular and Cellular Regulation, Gunma University(Japan), 4.Department of Psychosomatic Medicine Graduate School of Medical Sciences, Kyushu Universit(Japan))

[SY-53-01]

Influences of probiotic supplementation on the mental health of humans

*chaiyavat chaiyasut[1], Sivamaruthi Bhagavathi Sundaram[2], Kesika Periyanaina[2], Suchanat Khongtan[1], Pranom Fukngoen[2] (1.Faculty of Pharmacy, Chiangmai University, Chiangmai, Thailand(Thailand), 2.Office of Research Administration, Chiang Mai University, Chiang Mai 50200, Thailand(Thailand))

[SY-53-02]

Dog ownership, microbiota, and adolescent mental health: insights from human and mouse studies

*Eiji Miyauchi (Institute for Molecular and Cellular Regulation, Gunma University(Japan))

[SY-53-03]

Association Between Gut Microbiota and Eating Disorders

*Tomokazu Hata (Department of Psychosomatic Medicine, Kyushu University Hospital (Japan))

[SY-53-04]

The Oral-Gut-Brain Axis: Impact of Maternal Oral Dysbiosis on Offspring Gut Colonization and Early-Life Behavior.

*Natsuru Watanabe, Katsunaka Mikami (Department of Psychiatry, Tokai University School of Medicine(Japan))

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キーワード：microbe-gut-brain axis、mental health、early in life、children、adolescents

It is becoming clear that gut microbiota plays a crucial role in brain development and function. The gut and brain communicate bidirectionally via mechanisms such as hormones, cytokines, the vagus nerve and the central nervous system via spinal afferent fibers. Recently, the gut microbiota has been attracting particular attention in this mechanism. This new system is the recently proposed bidirectional “gut microbiota-gut-brain axis (MGBA)”.

It has also become clear that biologically active substances derived from intestinal bacteria affect stress responses, behavior, and mental states. Plasma ACTH and corticosterone levels in response to restraint stress (i.e., activation of the hypothalamic-pituitary-adrenal (HPA) axis) were higher in germ-free (GF) mice than in specific pathogen-free (SPF) mice. The resident microbiota may affect the postnatal development of the HPA stress response in mice. Furthermore, GF mice were shown to be more active, anxious, and aggressive than Ex-GF mice. These results suggest that the intestinal microbiota may strongly affect not only the stress response but also the host's behavior and mental state. This symposium will focus on the effect of MBGA on the behavior and mental status of children and adolescents and discuss them from the perspectives of basic researchers and clinicians. The speakers will introduce the latest topics in this interesting field of microbial research. From a clinical perspective, the presentation will focus on the pathology of anorexia and stress intervention methods in relation to MBGA. From a basic science, the presentation will focus on mouse aggression and early developmental intervention, as well as the effects of dog ownership and adolescent microbiota on mental health.

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[SY-53-01] Influences of probiotic supplementation on the mental health of humans

*chaiyavat chaiyasut[1], Sivamaruthi Bhagavathi Sundaram[2], Kesika Periyanaina[2], Suchanat Khongtan[1], Pranom Fukngoen[2] (1.Faculty of Pharmacy, Chiangmai University, Chiangmai, Thailand(Thailand), 2.Office of Research Administration, Chiang Mai University, Chiang Mai 50200, Thailand(Thailand))

キーワード：Probiotics、Prebiotics、Mental health、Stress、Synbiotics

Probiotic consumption is increasing globally due to their well-documented health benefits. Research has shown that probiotics are effective as adjuvant therapeutic agents for various conditions. Mental health issues affect around 20% of people worldwide, underscoring the urgent need for effective treatments and preventative strategies. Good mental health means feeling well emotionally and mentally. It allows one to handle everyday stress, work effectively, and participate in the community. The connection between gut health and mental well-being is gaining increasing attention, as emerging research suggests that the gut microbiome plays a crucial role in regulating mental health. Probiotics may help modulate these processes by supporting healthy gut microbiota and offer promising adjuncts to traditional mental health treatments. We have investigated the effect of synbiotic supplementation (*Lactobacillus paracasei* HII01 and *Bifidobacterium animalis* subsp. *lactis*, 5 g galactooligosaccharides, and 5 g oligofructose) on stress-related parameters in Thai subjects. In the stressed group, administering synbiotics led to a significant reduction in negative scores on the Thai Stress Test and a decrease in tryptophan levels. In the non-stressed group, administration of synbiotics resulted in a notable reduction in tryptophan. At the same time, levels of dehydroepiandrosterone sulfate, tumor necrosis factor-alpha, 5-hydroxyindoleacetic acid, and short-chain fatty acids (SCFAs) increased significantly. In both groups, synbiotic supplementation lowered cortisol and lipopolysaccharide (LPS) levels, while increasing the anti-inflammatory mediator interleukin-10 (IL-10) and immunoglobulin A (IgA). In conclusion, administering synbiotics helped alleviate negative feelings by modulating the hypothalamic-pituitary-adrenal (HPA) axis, enhancing IL-10 and IgA levels, and reducing LPS. In contrast, while synbiotics did not significantly impact stress levels in the non-stressed group, they did promote favorable changes in SCFA profiles, the HPA axis, and tryptophan metabolism. These findings suggest that synbiotics may offer therapeutic potential for stress-related disorders and gut microbiome remodeling, depending on the individual's baseline stress status.

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[SY-53-02] Dog ownership, microbiota, and adolescent mental health: insights from human and mouse studies

*Eiji Miyauchi (Institute for Molecular and Cellular Regulation, Gunma University(Japan))
キーワード：Dog ownership、Adolescent mental health、Microbiota–brain axis

Adolescence is a critical period for neurodevelopment and social maturation, during which mental health can be shaped by environmental influences. Among these, the presence of companion animals—especially dogs—has been linked to improved emotional well-being. However, the biological basis of this association remains unclear. In our recent study, we examined whether dog ownership during adolescence could influence mental health via changes in the microbiota. Using data from a longitudinal adolescent cohort in Tokyo, we observed that adolescents living with dogs had lower scores for social and behavioral problems compared to their peers. To further explore this connection, we transplanted microbiota from dog-owning and non-dog-owning adolescents into germ-free mice. Interestingly, mice colonized with microbiota from dog-owning adolescents showed enhanced social behavior, suggesting a functional link between microbiota composition and sociality.
These findings suggest that the positive psychological effects of living with dogs may be mediated, at least in part, by the microbiota. Our work points to a novel “dog–microbiota–brain” axis that may underlie the emotional benefits of dog companionship during adolescence. This axis could have important implications for understanding how everyday environmental exposures influence mental health trajectories, and may offer insights into microbiota-based strategies for supporting adolescent development.

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[SY-53-03] Association Between Gut Microbiota and Eating Disorders

*Tomokazu Hata (Department of Psychosomatic Medicine, Kyushu University Hospital (Japan))

キーワード：gut microbiota、eating disorder、anorexia nervosa、uremic toxin

Anorexia nervosa (AN) is a psychiatric disorder with one of the highest mortality rates, and effective treatment strategies remain under investigation. Various psychotherapeutic approaches, including cognitive behavioral therapy for eating disorders, have been developed to date. In addition, research utilizing genome-wide association studies (GWAS) and neuroimaging has advanced our understanding of the disorder. Our laboratory is currently exploring the therapeutic potential of gut microbiota modulation.

We hypothesize that patients with AN, who often suffer from nutritional imbalances, exhibit dysbiosis of the gut microbiota, and that the gut microbiota–gut–brain axis may play a role in the pathophysiology of the disorder. In fact, the gut microbiota composition in patients with AN differs significantly from that of healthy controls. To investigate this further, we conducted fecal microbiota transplantation (FMT) experiments using germ-free mice, transplanting fecal samples from either AN patients or healthy individuals. Mice that received microbiota from AN patients showed impaired weight gain and increased anxiety-like behaviors.

To identify potential mediators of host alterations caused by dysbiosis, we conducted serum metabolomic analysis. In AN patients, several uremic toxins—metabolites known to be produced by gut bacteria—were detected at higher concentrations compared to healthy controls. Recent studies from other countries have also reported similar findings, with elevated levels of uremic toxins in AN patients. These toxins may serve as key factors in the gut microbiota–gut–brain axis underlying AN. Although a unified consensus has yet to be established, it is hypothesized that therapeutic strategies aimed at reducing uremic toxins and enhancing short-chain fatty acid production could be beneficial in alleviating the symptoms of AN.

In this presentation, we will review recent developments in gut microbiota research, share data from our laboratory, and discuss the therapeutic potential of microbiota-targeted interventions for eating disorders.

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[SY-53-04] The Oral-Gut-Brain Axis: Impact of Maternal Oral Dysbiosis on Offspring Gut Colonization and Early-Life Behavior.

*Natsuru Watanabe, Katsunaka Mikami (Department of Psychiatry, Tokai University School of Medicine(Japan))

キーワード：gut microbiome、oral dysbiosis、microbiota-gut-brain axis、maternal transmission、neurodevelopment

Background/aims:
Recent advances in microbiome research have revealed the critical role of early-life gut microbiota in neurodevelopmental health. While the gut microbiome has been extensively studied in this context, emerging evidence suggests that maternal oral microbiota may also significantly shape the initial gut colonization of offspring. Given the known associations between oral dysbiosis and systemic inflammatory diseases, we hypothesized that maternal oral dysbiosis could negatively affect offspring gut microbiota composition and, consequently, early-life behavioral development. This study aimed to explore the effects of maternal oral dysbiosis on offspring gut colonization and anxiety-like behavior during the early postnatal period.

Methods:
Oral dysbiosis was induced in female mice by ligature placement to model experimental periodontitis prior to mating. Offspring born to these dams and control dams were evaluated at 4 weeks of age. Anxiety-like behavior was assessed using the marble burying test. As a positive control for microbiota disruption, offspring of dams treated with cefoperazone, a broad-spectrum antibiotic, were also analyzed. Gut microbiota analysis was conducted to correlate microbial shifts with behavioral outcomes.

Results:
Anxiety-like behavior in offspring was assessed at 4 weeks of age using the marble burying test. Pups born to dams treated with the antibiotic cefoperazone prior to delivery or to dams with ligature-induced periodontitis exhibited a significant decrease in the number of marbles buried compared to offspring of control dams. Importantly, there were no observable deficits in general activity or short-term memory, indicating that the behavioral changes were not due to motor impairment. These findings suggest that early-life disturbances in gut microbiota, driven by maternal microbiota dysbiosis, can influence neurobehavioral development in offspring, particularly with respect to anxiety-related behavior.

Conclusions:
This study reveals two significant findings. Maternal oral dysbiosis can greatly impact the gut microbiota composition of offspring during the early stages of life. Such changes are linked to observable behavioural modifications in offspring, particularly anxiety-like responses during the initial stages of development. These results support the existence of an oral-gut-brain axis, which was previously underappreciated, and emphasise the importance of maternal oral microbiota in determining neurodevelopmental outcomes in offspring. This research provides foundational evidence for the development of science-based public health strategies, including perinatal oral hygiene education.