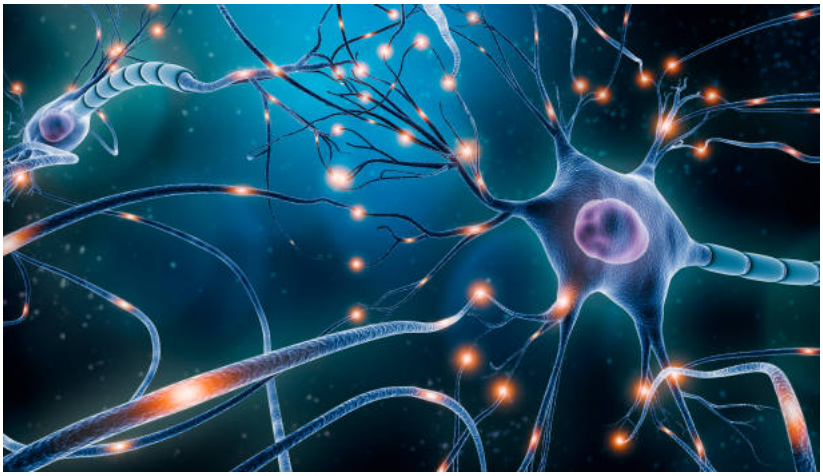
The International Symposium on Oral Neuroscience 2024



Program & Abstract

March 22nd, 2025

Osaka University Graduate School of Dentistry

大阪大学 OSAKA UNIVERSITY

Challenge to Intractable Oral Diseases

Venue: Yumikura Memorial Hall (Building F, 5F)
Osaka University Graduate School of Dentistry, Osaka, Japan

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Dept. of Oral Physiology, Osaka Univ. Grad. Sch. Of Dentistry

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Access map (Osaka University, Suita campus)

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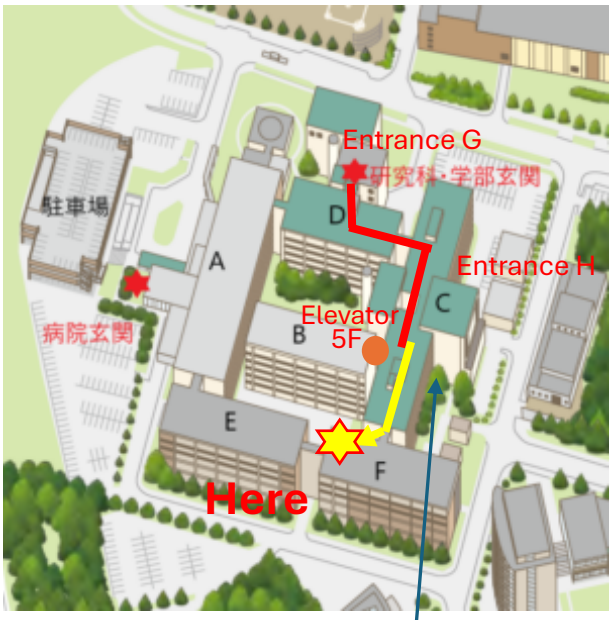
How to get to Yumikura Memorial Hall Building F, 5F



Entrance K is available when you visit the social gathering site, **NSSOL CAFÉ**. (50 m)

NOTE:

Please go up to the 5th floor using the elevators of Building C, and go to Building F from Building C on the 5th floor.

Information

Accommodation

The registration desk will open from 12:00 PM to 4:00 PM that day. Please make sure to receive your name tag.

General (not including speakers): 3,000 yen

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Social gathering: NSSOL CAFÉ

The party will be held from 5:45 PM to 7:45 PM. Please pay the fee at the registration desk.

Buffet style, some foods & drinks (beer, beverage, coffee, etc.)

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- Please bring your presentation on your PC.
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Presentation time for speakers

Please confirm the presentation time you use.

Short talk: The time allowed for the slide presentation is 10 minutes, including 3 minutes for discussion.

Mini-review: The time allowed for the slide presentation is 25 minutes, including 5 minutes for discussion.

Plenary lecture: The time allowed for the slide presentation is 60 minutes, including discussion time.

Oral Neuroscience 2024：Program

12:00-16:00 Registration

13:00-13:05 Opening Remarks Chair Takafumi Kato

13:05-14:05

Plenary Lecture

Chair : Takafumi Kato (Osaka University)

Adaptive Stem Cell Plasticity Enables Circumvallate Papilla Regeneration After Lgr5+ Cell Ablation
Han-Sung Jung
Dept of Oral Biology, Yonsei University College of Dentistry, Soul, Korea

14:05-14:15

Coffee Break

We will prepare drinks and snacks at the beside of the hall.

14:15-

Session 1: Mini-review 1, 2 & Short talk 1, 2

14:15-14:45 (30 min*) * including presentation and question/answer
【Mini-review 1】Chair: Yusuke Yokota (Osaka University)

Projections from the Cerebellar Nuclei Containing Neurons Receiving Jaw Muscle Proprioceptive Signals to Trigeminal Motoneurons and Their Premotoneurons in the Rat Pons and Medulla
Fumihiko Sato
Department of Systematic Anatomy and Neurobiology, Osaka University Graduate School of Dentistry, Suita, Japan

14:45-15:15 (30 min*)
【Mini-review 2】Chair: Yoshihisa Tachibana (Kobe University)

Descending pathway from the insular cortex to the brainstem nuclei facilitates nociception in orofacial area
Yuka Nakaya
Department of Pharmacology, Nihon University School of Dentistry

15:15-15:28 (13 min*)
【Short-talk 1】Chair: Jaerin Sohn (Osaka University)

Involvement of hypoxia inducible factor in intra-oral pain caused by chronic intermittent hypoxia during sleep in ovariectomized rat
Sho Katsura
Department of Oral Physiology, Osaka University Graduate School of Dentistry, Suita, Japan

15:28-15:41 (13 min*)
【Short-talk 2】Chair: Jaerin Sohn (Osaka University)

Elevation of masticatory muscle activity during sleep after inescapable footshock stress
Yiwen Zhu
Department of Oral Physiology, Osaka University Graduate School of Dentistry, Suita, Japan

15:41-15:51

Coffee Break

We will prepare drinks and snacks at the beside of the hall.

15:51-

Session 2: Mini-review 3, 4 & Short talk 3, 4

15:51-16: 21 (30 min*) * including presentation and question/answer
【Mini-review 3】Chair: Tadashi Inui (Hokkaido University)

The neural circuit mechanism underlying the synergistic effect between different tastes
Takaaki Ozawa
Laboratory for Advanced Brain Functions, Institute for Protein Research, Osaka University, Osaka, JAPAN

16:21-16:51 (30 min*)
【Mini-review 4】Chair: Chiho Kudo (Osaka University)

Evaluation of food texture perception in rats
Chihiro Nakatomi
Division of Physiology, Department of Health promotion, Kyushu Dental University

16:51-17: 04 (13 min*)
【Short-talk 3】Chair: Misaki Iwahashi (Osaka University)

A Study on Taste Disturbances in Cancer Chemotherapy: The Effect of S-1 Administration on Taste-Related Genes Expressions
Karen Yamauchi
Department of Oral and Maxillofacial Surgery, Osaka University Graduate School of Dentistry, Suita, Japan

17:04-17:17 (13 min*)
【Short-talk 4】Chair: Misaki Iwahashi (Osaka University)

Maternal hypothyroidism during fetal and neonatal periods causes ADHD-like behavior in mouse offspring
Shiho Mima
Department of Pharmacology, Osaka University Graduate School of Dentistry, Suita, Japan

17:17- Closing Remarks Chair of Oral Neuroscience 2025 Kazuhiro Takuma

Abstract

Plenary Lecture

Adaptive Stem Cell Plasticity Enables Circumvallate Papilla Regeneration After Lgr5+ Cell Ablation

Han-Sung Jung
Dept of Oral Biology, Yonsei University College of Dentistry, Soul, Korea

Taste receptor cells located within the papillae of the oral cavity have a lifespan of 8 to 12 days and are continuously replenished by stem and progenitor cells located outside the taste buds. Previous genetic lineage-tracing studies have identified Lgr5+ stem/progenitor cells in the basal trench of the circumvallate papilla (CVP) as the source of all taste and non-taste epithelial cells during normal functioning and regeneration. However, it is still unclear whether an alternative stem cell population exists within the CVP that can regenerate the epithelium in the absence of Lgr5-expressing cells. In our study, we used Lgr5DTR mice, which allowed for the selective ablation of Lgr5-expressing cells through administration of diphtheria toxin. We observed a complete loss of these cells in the CVP, resulting in rapid degeneration of taste buds, K8-expressing taste receptor cells, basal cells, and the basement membrane within 24 hours post-injection. Remarkably, at 72 hours post-injection, the basal cells and basement membrane had fully regenerated, demonstrating the efficiency of the regeneration process. Although no taste buds were present at this time, they were observed to regenerate 2 weeks post-injection. Lineage tracing with K8CreERT2; R26RtdT revealed that K8-expressing cells from the ducts of Von Ebner's gland contributed to the regeneration of taste buds, indicating that these differentiated cells undergo dedifferentiation to restore taste buds in the absence of the resident Lgr5-expressing stem cell population

Keywords: Epithelial Plasticity, LGR5, Taste Bud

Abbreviated Curriculum Vitae

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ACADEMIC EDUCATION

2022 – 2023 MBA Essentials, The London School of Economics and Political Science, UK

1993 – 1997 Ph.D in Developmental Biology, University College London, UK

1990 – 1993 B.Sc in Anatomy and Development Biology, University College London, UK

RESEARCH & PROFESSIONAL EXPERIENCE

1999 – 2000 Instructor, Harvard Medical School, USA

1997 – 1999 Post-Doctoral Fellow, University of Helsinki, Finland

RECENT PUBLICATIONS

1. Lee DJ, Kim P, Kim HY, Park J, Lee SJ, An H, Heo JS, Lee MJ, Ohshima H, Mizuno S, Takahashi S, Kim SJ, Jung HS, 2024, MAST4 regulates stem cell mai ntenance with DLX3 for epithelial development and amelogenesis, **Experimental & Molecular Medicine** 56(7):1606-1619
2. Kim S, Li S, Jangid AK, Park HW, Lee DJ, Kim K, Jung HS, 2024, Surface En gineering of Natural Killer Cells with CD44-targeting Ligands for Augmented Can cer Immunotherapy, **Small**. 31:e2306738
3. Kim EJ, Kim KH, Kim HY, Lee DJ, Li S, Ngoc Han M, Jung HS, 2024, Harnes sing the dental cells derived from human induced pluripotent stem cells for hard ti ssue engineering, **Journal of Advanced Research**. 61:119-131
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5. Kim J, Kim S, Lee SY, Jo BK, Oh JY, Kwon EJ, Kim KT, Adpaikar AA, Kim EJ, Jung HS, Kim HR, Roe JS, Hong CP, Kim JK, Koo BK, Cha HJ. 2023 Parti al in vivo reprogramming enables injury-free intestinal regeneration via autonomous Ptgs1 induction, **Science Advances**. 24;9(47):eadi8454

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7. Kim S, Li S, Gajendiran M, Jangid AK, Lee DJ, Kim K, Jung HS, 2023, Lipid a nchor-mediated NK cell surface engineering for enhanced cancer immunotherapy, **Chemical Engineering Journal** 473, 145211
8. Kim P, Park J, Lee DJ, Mizuno S, Shinohara M, Hong CP, Jeong Y, Yun R, Par k H, Park S, Yang KM, Lee MJ, Jang SP, Kim HY, Lee SJ, Song SU, Park KS, Tanaka M, Ohshima H, Cho JW, Sugiyama F, Takahashi S, Kim SJ, Jung HS, 2 022, Mast4 determines the cell fate of MSCs for bone and cartilage development, **Nature Communications**, Jul 8;13(1):3960
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11. Mast4 knockout shows the regulation of spermatogonial stem cell self-renewal via the FGF2/ERM pathway., 2021 Lee SJ, Park J, Lee DJ, Otsu K, Kim P, Mizuno S, Lee MJ, Kim HY, Harada H, Takahashi S, Kim SJ, Jung HS, **Cell Death and Differentiation**. May;28(5):1441-1454

Session 1: Mini-review 1

Projections from the Cerebellar Nuclei Containing Neurons Receiving Jaw Muscle Proprioceptive Signals to Trigeminal Motoneurons and Their Premotoneurons in the Rat Pons and Medulla

Fumihiko Sato[1], Yumi Tsutsumi[1,2], Ayaka Oka[3], Takahiro Furuta[1], Jaerin Sohn[1], Yuki Oi[4], Mai Amano[5], Akiko Morita[6], Katsuro Uchino[4], Takafumi Kato[7], Yoshihisa Tachibana[8], Atsushi Yoshida[1,6]

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[7] Department of Oral Physiology, Osaka University Graduate School of Dentistry, Suita, Japan
[8] Division of Physiology and Cell Biology, Kobe University Graduate School of Medicine, Hyogo, Japan

The cerebellum plays a crucial role in sensorimotor control through cerebellofugal projections from the cerebellar nuclei. However, little is known about the cerebellofugal projections involved in jaw sensorimotor control, although the dorsolateral parts of the interposed cerebellar nucleus (IntDL) and medial cerebellar nucleus (MedDL) do receive proprioceptive signals bilaterally from rat jaw-closing muscle spindles (JCMSs). This study aimed to detail the cerebellofugal projection features involved in jaw sensorimotor control. Anterograde tracer was injected into the rat IntDL and MedDL, which contained neurons receiving JCMS proprioceptive inputs (i.e., jcms-IntDL and jcms-MedDL). Axon terminals arising from the jcms-IntDL were labeled bilaterally with an ipsilateral predominance in several pontomedullary regions, although very few terminals were labeled in the dorsolateral and ventromedial divisions (5dl and 5vm) of the trigeminal motor nucleus. In contrast, terminals from the jcms-MedDL were labeled bilaterally with a contralateral predominance in several pontomedullary regions and a few terminals were labeled in the contralateral 5dl and 5vm. Thus, the projections from the jcms-IntDL and jcms-MedDL were well segregated. Subsequent retrograde tracer injections into the pontomedullary regions confirmed these segregated projections, and demonstrated that amongst the entire cerebellar nuclei these projections principally arose from the IntDL and MedDL. Additionally, many premotoneurons for the 5dl or 5vm were widely labeled in the pontomedullary regions where many axons from the jcms-IntDL or jcms-MedDL terminated. The various connections involving the jcms-IntDL and jcms-MedDL may play a crucial role in jaw sensorimotor

control, mainly through indirect cerebellofugal pathways to the 5dl and 5vm via their premotoneurons. (250)

Keywords: muscle spindle, motor control, mastication

Session 1: Mini-review 2

The role of descending projections from the insular cortex to the brainstem nuclei in orofacial pain

Yuka Nakaya[1] and Masayuki Kobayashi[1]
[1] Department of Pharmacology, Nihon University School of Dentistry, Tokyo, Japan

Nociceptive information from the orofacial area is transmitted to the trigeminal subnucleus caudalis (Sp5C) through the trigeminal nerve. This information then ascends directly or indirectly to higher brain regions, including the lateral parabrachial nucleus (LPBN). It has been reported that descending projections from the IC are found in the Sp5C and LPBN. However, the role of each projection is still poorly understood. We examined the effect of IC projections to the Sp5C and LPBN neurons using optogenetics and chemogenetics. Selective activation of descending inputs from the IC induced larger excitatory synaptic inputs to glutamatergic neurons in comparison to those to GABAergic/glycinergic neurons in both Sp5C and LPBN. In addition, IC inputs induced just faint IPSCs in these neurons. We next performed behavioral experiments that evaluated physiological functions of IC projections to the Sp5C and LPBN. We found that activation of IC projections to the Sp5C decreased the threshold of the head-withdrawal reflex induced by mechanical and thermal stimuli. Similarly, activation of IC projections to the LPBN increased a face wiping behavior responding to chemical stimuli to the whisker pad and decreased the threshold of the head-withdrawal reflex induced by mechanical stimuli. These results suggest that activation of the descending projections from the IC to both the Sp5C and PBN facilitate facial pain.

Keywords: insular cortex, parabrachial nucleus, trigeminal subnucleus caudalis, pain

Session 1: Short talk 1

Involvement of hypoxia inducible factor in intraoral pain caused by chronic intermittent hypoxia during sleep in ovariectomized rat

Sho Katsura[1, 2], Ayano Katagiri[1], Narikazu Uzawa[2], Takafumi Kato[1]

[1] Department of Oral Physiology, Graduate School of Dentistry, Osaka University, Suita, Japan
[2] Department of Oral & Maxillofacial Oncology and Surgery, Graduate School of Dentistry, Osaka University, Suita, Japan

Obstructive sleep apnea (OSA) is characterized by intermittent hypoxia (IH) during sleep caused by upper airway obstruction. The incidence in women drastically increases after menopause. OSA is reportedly a robust risk factor for intraoral pain, such as burning mouth syndrome (BMS), in postmenopausal women. Patients with BMS exhibit hypersensitivity of the intraoral mucosa to capsaicin stimulation. However, the neural mechanism by which IH during sleep induces BMS remains unknown. Therefore, we hypothesized that chronic IH (CIH) during sleep increases hypoxia inducible factor-1α (HIF-1α) in the peripheral nervous system, which induces intraoral pain in ovariectomized (OVX) rats.

OVX rats were exposed to CIH (nadir O_2 5%, 6-min cycles, 6 h/day, 14 days), and intraoral pain was assessed using a two-bottle preference drinking test with a capsaicin solution. Capsaicin consumption was significantly lower in the OVX-CIH group than that in the control group. OVX-CIH rats exhibited a significantly higher number of TRPV1-positive, HIF-1α-positive, and TRPV1+HIF-1α co-positive cells in the trigeminal ganglion. Furthermore, administration of HIF-1α inhibitor to the trigeminal ganglion of OVX-CIH rats alleviated intraoral sensitivity to capsaicin.

These findings suggest that CIH-induced stabilization of HIF-1α in the trigeminal ganglion contributes BMS-like intraoral pain through increased TRPV1.

Keywords: hypoxia inducible factor, chronic intermittent hypoxia, intraoral pain

Session 1: Short talk 2

Impact of inescapable footshock stress on masticatory muscle activity during sleep-wake cycle.

Yiwen Zhu[1], Ayano Katagiri[1], Hiroki Toyoda[1], Takafumi Kato[1]

1. Department of Oral Physiology, Graduate School of Dentistry, Osaka University.

Inescapable footshock (IFS) has been shown to induce stress/anxiety conditions manifested as sleep disruption and increase in sympathetic activity which are the potential factors of masticatory muscle activity (MMA) fluctuation during sleep-wake states.

In ten male Sprague-Dawley rats, electrodes were implanted for electroencephalogram (EEG), electromyogram (EMG) of the neck and left masseter muscle (MasL), and electrocardiogram (ECG) to monitor sleep, MMA, and heart rate (HR). Sleep recordings were conducted on two days during the dark phase (10:00–22:00). On day one, rats were placed in the IFS box for 30 minutes without stimulation, followed by recording from 11:00 to 14:00. On day two, IFS was applied at 1.0 mA for 0.5 s with 30-s intervals, followed by recording. Data were analyzed in 10-second epochs, with vigilance states (wakefulness [W], non-rapid eye movement [NREM] sleep, and rapid eye movement [REM] sleep) were manually scored. Arousals during NREM sleep were detected as no more than 3 consecutive W epochs. Delta EEG power during NREM sleep was calculated using Fast Fourier transform. HR was assessed by R-wave counts. Integrated EMG activity was normalized during chewing after baseline artifact subtraction. Cluster analysis was conducted for EMG further analysis, and two components were identified as cluster 1 (muscle contraction) and cluster 2 (muscle tone).

After IFS, sleep was suppressed, and the ratio of delta power significantly decreased during NREM sleep. HR during W and NREM sleep significantly increased. MMA significantly increased during sleep-wake cycles. Furthermore, the mean value of cluster 1 and 2 during W and NREM sleep increased significantly.

Keywords: Stress, sleep, masticatory muscle activity.

Session 2: Mini-review 3

Evaluation of food texture perception in rats

Chihiro Nakatomi

Division of Physiology, Department of Health promotion, Kyushu Dental University

Food texture refers to sensory expressions of physical properties of foods, which are commonly expressed using onomatopoeic terms such as "crunchy," "chewy," and "smooth". Sensation of food texture plays a crucial role in mastication, swallowing, and food preference. However, due to the lack of established animal experimental systems, the details of the physiological mechanism underlying texture sensation and perception have not been elucidated. A major challenge in studying texture perception in laboratory animals is that rodents can detect the flavors of additives used to modify physical properties of foods. To address this issue, we have developed evaluation systems for food texture perception in rats, eliminating the influence of taste and flavor. Using conditioned aversion tests, we found that rats can detect a low viscosity of 3.6 mPa･s (equivalent to Worcestershire sauce) and differences in springiness and hardness of agar gel. In addition, conditioned preference tests revealed that rats can detect the presence of cellulose microparticles approximately 1.5 μm in diameter. The evaluation of texture perception using rodents is a novel approach on a global scale. By integrating these experimental systems with genetically modified animal models and brain disruption experiments, it will be possible to elucidate the molecular and neurological mechanisms underlying texture perception.

Keywords: Food texture, Oral tactile sensation, Rat behavioral tests

Session 2: Mini-review 4

The neural circuit mechanism underlying the synergistic effect between different tastes

Takaaki Ozawa[1] Yoshinobu Oyama[1], Tomohiro Shibata[1], Mayuka Abe[1], Hinano Yonemaru[1], Yuma Matsumoto[1], Ryotaro Iwamoto[1], Koki Sakurai[1], Macpherson Tom[1], Takatoshi Hikida[1]

[1] Laboratory for Advanced Brain Functions, Institute for Protein Research, Osaka University. Osaka, JAPAN

Salt is not only a vital nutrient for maintaining health but also an essential seasoning for our rich dietary lifestyle. On the other hand, it has been suggested that overconsumption of salt can be a serious risk factor for high blood pressure, a trigger for stroke and heart attack. Human studies have suggested that umami substances enhance the palatability of salty food, and are useful in reducing sodium intake without compromising the palatability of our daily meals. However, the biological mechanism underlying umami's effect has not been investigated. In the present study, we investigated the roles of frontal cortex and neurotransmitter dopamine, which are known to play an important role in reward-seeking behavior, in the regulation of salt-seeking and umami's enhancing effect by using behavioral analysis, fluorescent imaging, and neural silencing. In this presentation, current datasets supporting their regulatory roles will be shown. Our results provide new evidence for the effectiveness of umami substances in sustainable salt intake reduction in our dietary lifestyle.

Keywords: Taste, Frontal cortex, Dopamine

Session 2: Short talk 3

A Study on Taste Disturbances in Cancer Chemotherapy: The Effect of S-1 Administration on Taste-Related Genes Expressions.

Karen Yamauchi Miyamoto [1], Yusuke Yokota [1], Chizuko Inui-Yamamoto [2], Namiki Kishigami [3], Emiko Tanaka Isomura [1], Shinsuke Ohba [2], Susumu Tanaka [1]

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[2] Department of Tissue and Developmental Biology, Graduate School of Dentistry, The University of Osaka, Osaka, Japan
[3] Department of Dentistry and Oral Surgery, Teramoto Kinen Hospital, Osaka, Japan

Objective: Taste disorders are frequently observed in patients undergoing cancer chemotherapy. They could lead to decreased appetite and oral intake, resulting in nutritional deterioration, which may ultimately hinder the continuation of cancer treatment. However, the mechanisms remain largely unknown. In this study, we conducted behavioral and genetic studies on taste preference alterations in rats administered S-1 to investigate the pathogenesis.

Methods: Male and female Sprague-Dawley (SD) rats were orally administered S-1 (15 mg/kg) for two cycles (one cycle: 14 days, followed by a 7-day drug-free interval). At first, we conducted a brief access test (BAT) to assess taste sensitivity before and after S-1 administration, using the following tastants: sweet (sodium saccharin), bitter (quinine hydrochloride), umami (monosodium glutamate), salty (sodium chloride), and sour (citric acid). After two cycles of S-1 administration, circumvallate (CV) and fungiform papillae (FF) were collected under deep anesthesia. The mRNA expression levels of taste-related genes (T1R1, T1R2, T1R3, PLCβ2, T2R107, Grm4, PKD2L1, and Car4) were analyzed using RT-qPCR.

Results: In BAT, compared to before S-1 administration, rats showed an increased intake rate for sweetness and sourness after administration. The results of RT-qPCR exhibited that the expression level of T1R2, a subunit of the sweet taste receptor, was significantly higher than that of the control group in both the CV and FF. Additionally, in the FF, the level of Car4, an enzyme related to sweet and sour taste perception, was significantly increased.

Conclusion: The behavioral changes in sweet taste perception aligned with alterations in taste-related-gene expression, suggesting that S-1 modulates peripheral taste receptor gene expression to affect taste sensitivity.

Keywords: S-1, taste disorders, taste receptor

Session 2: Short talk 4

Maternal hypothyroidism during fetal and neonatal periods causes ADHD-like behavior in mouse offspring

Shiho Mima[1,2], Atsuko Hayata-Takano[1,3,4], Shunsuke Tomita[5], Misaki Iwasaki[1,3,4], Keishi Ishida[5], Daisuke Matsumaru[5], Tsuyoshi Nakanishi[5], Kazuhiro Takuma[1,3,4]

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[4] United Graduate School of Child Development, Molecular Research Center for Children's Mental Development, Osaka University, Suita, Japan
[5] Laboratory Hygienic Chemistry and Molecular Toxicology, Gifu Pharmaceutical University, Gifu, Japan

Thyroid hormones are known to have an important role in brain development and neuronal maturation. The early embryo/fetus depends on a maternal supply of thyroid hormones as the thyroid gland has not fully developed. Thus, maternal hypothyroidism may be associated with the etiology of neurodevelopmental disorders in offspring. However, the underlying mechanisms are still unclear. In this study, we examined whether drug-induced maternal hypothyroidism affects emotional behavior and neuronal morphology in mouse offspring. Pregnant ICR mice were fed diet powder with or without an antithyroid drug propylthiouracil (PTU) at 250 ppm from embryonic day 6 (E6) to postnatal day 12 (P12), and the amount of PTU was reduced to 125 ppm from P13 to P21. The offspring were subjected to behavioral experiments at 4 (juvenile) and 8 weeks (adult) of age. We found that the total distance traveled significantly increased in the PTU-treated mice compared with control at both 4 and 8 weeks of age in the open field test. On the other hand, the time spent in the center zone of the PTU-treated mice did not change compared with control at both 4 and 8 weeks of age in the open-field test. Interestingly, Golgi staining study revealed an increase in the number of dendritic spines in layer 5 pyramidal neurons of the medial prefrontal cortex of the PTU-treated mice at 9 weeks of age. These findings indicated that maternal hypothyroidism may cause attention deficit hyperactivity disorder (ADHD)-like symptoms and disrupt dendritic spine formation in mouse offspring.

Keywords: Hypothyroidism / Attention Deficit Hyperactivity Disorder (ADHD) / Neuronal morphology