Program & Abstract

Challenge to Intractable Oral Diseases

This symposium is partly supported by a Grant-in-Aid "Challenge to Intractable Oral Disease" from Osaka University Graduate School of Dentistry

Oral Neuroscience 2016

Program & Abstract

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Organizer: Satoshi Wakisaka (Osaka University)

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Osaka University Graduate School of Dentistry

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This symposium is partly supported by a Grant-Aid “Challenge to Intractable Oral disease” from Osaka University Graduate School of Dentistry.

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Access:

Oral Session: Lecture Hall (Building D, 4F)
Poster session: Lecture room (Building D, 4F)
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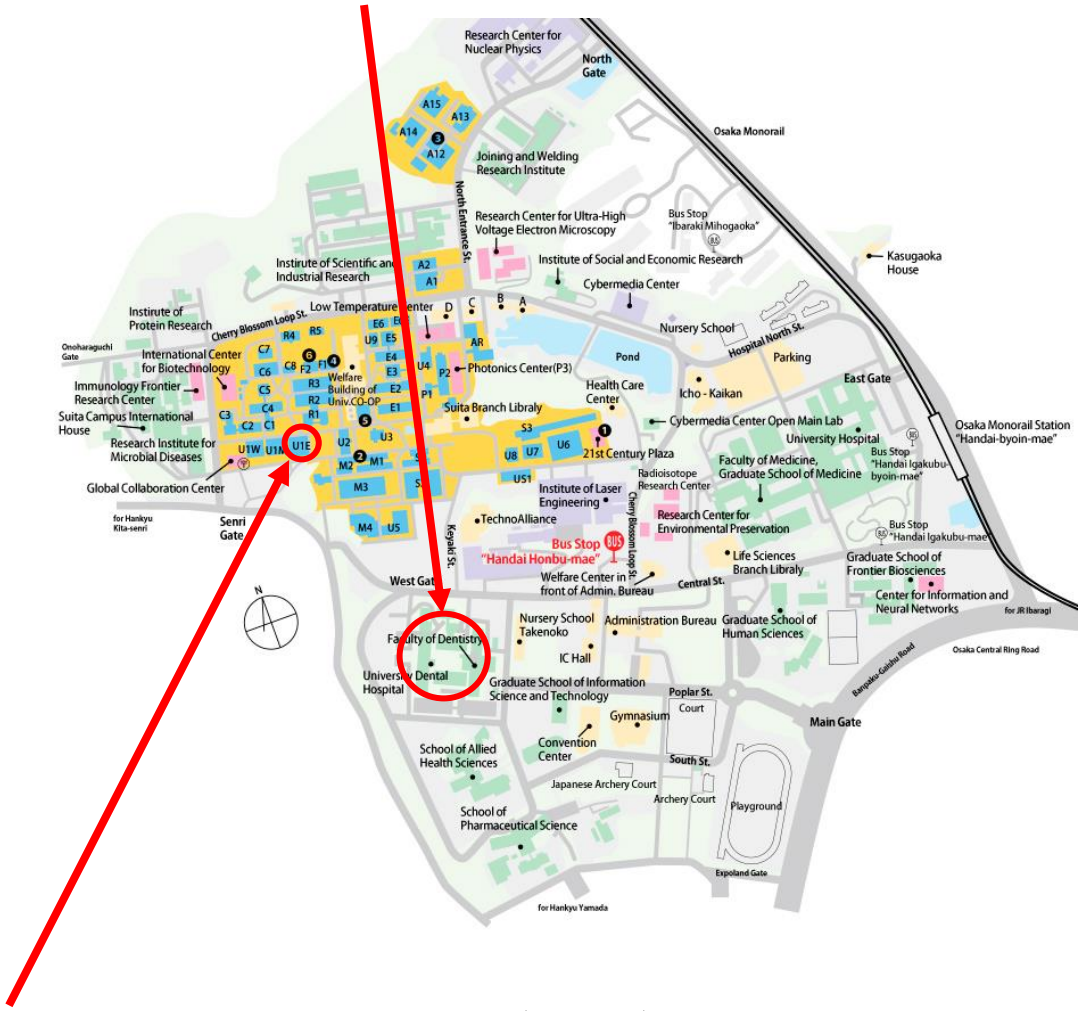

Information exchange meetings (18:00~):
La Scena, Faculty of Engineering, GSE Common East 15F
(about five minutes' walk from the Faculty of Dentistry)

Oral Neuroscience 2016

Oral Session: Lecture Hall (Building D, 4F)

1000 Opening Remarks Satoshi Wakisaka

Session 1	Chair	Mikihiko Kogo Atsushi Yoshida

1005- [L-1] **Chemosensory stimuli modulate feeding patterns and glucose kinetics after glucose-loading**

Tadataka Tsuji (Graduate School of Dentistry, Osaka University)

1035- [L-2] **Brain mechanisms of conditioned taste aversion: Role of limbic and reward systems**

Tadashi Inui (Graduate School of Human Sciences, Osaka University)

1105- [L-3] **Pathophysiological considerations of sleep bruxism from human and animal studies**

Takafumi Kato (Graduate School of Dentistry, Osaka University)

1135- [L-4] **Schizophrenia risk from impairment of sorting nexin-mediated intracellular protein trafficking**

Takanobu Nakazawa (Graduate School of Dentistry, Osaka University)

1205- [L-5] **Integration of sensory and motor function in the orofacial region**

Junichi Kitagawa (School of Dentistry, Matsumoto Dental University)

Lunch and Poster Session (1235-1400)

Session 2	Chair	Koichi Iwata Satoshi Wakisaka

1400- [L-6] **Approaching the migraine pathophysiology through the perspective of the dentistry**

Chiho Kudo (Graduate School of Dentistry, Osaka University)

1430- [L-7] **Mechanisms of orofacial nociception and neuropathic pain**

Ryuji Terayama (Graduate School of Medicine, Dentistry and Pharmaceutical Science, Okayama University)

1500- [L-8] **Mechanisms underlying extraterritorial orofacial pain associated with trigeminal nerve injury and inflammation**

Koichi Iwata (School of Dentistry, Nihon University)

Coffee Break and Poster Session (1545-1630)

Special Lecture	Chair	Satoshi Wakisaka

1630- **The role of adenosine neurotransmission in peripheral neuropathy**

Gary J Bennett (Adjunct Professor, University of California San Diego & COE, BioIntervene Inc)

1730- Closing Remarks Mikihiko Kogo

1800- Information exchange meetings at the La Scena, GSE Common East 15F

Poster presentations:

[P-01] **The role of the periodontal ligament cells in neuronal differentiation induced by mechanical stimuli**

Kaori Takahashi, Takashi Yoshida and Minoru Wakamori
Tohoku University graduate School of Dentistry

[P-02] **Post-translational modifications of water channel aquaporin-5 in salivary gland cells**

Takahiro Hasegawa, Chenjuan Yao, Tetsuya Akamatsu, and Hiroshi Yoshimura
Tokushima University Graduate School

[P-03] **TRPV1 and TRPM8 channels expression and activity in the superior laryngeal nerve innervating the laryngopharynx and associated laryngeal regions: an immunohistochemical and electrophysiological study**

Mohammad Zakir Hossain, Hiroshi Ando, Shumpei Unno, Yuji Masuda
and Junichi Kitagawa
Matsumoto Dental University

[P-04] **Protein kinase A regulates long term potentiation of intrinsic excitability in neonatal trigeminal motoneurons**

Bakhshishayan Sanam[1], Enomoto Akifumi[1,2], Tsuji Tadataka[1,3], Tanaka Susumu[1], Yamanishi Tadashi[1,4], Kogo Mikihiko[1]
[1]Graduate School of Dentistry, Osaka University,
[2]Kinki University School of Medicine,
[3]Saiseikai Matsusaka General Hospital,
[4]Osaka Medical Center and Research Institute for Maternal and Child Health

[P-05] **Hyperpolarization-activated current in mesencephalic trigeminal nucleus neurons affected by the activity of locus coeruleus neurons**

Yin, D., Sato, H., Toyoda, H. & Kang, Y.
Osaka University Graduate School of Dentistry

[P-06] **Mapping jaw motor responses to electrical stimulation in amygdala in guinea pigs**

Yoshio Ueno, Takafumi Kato, Hiroshi Yano, MD Sams Sazzad Ali, Hiroyuki Yano, Makoto Higashiyama, Fumihiko Sato, Atsushi Yoshida
Osaka University Graduate School of Dentistry

[P-07] **Depression of GABAergic synaptic transmission in the insular cortex of the capsaicin-treated rats**

Shota Murayama and Masayuki Kobayashi
Nihon University School of Dentistry

[P-08] **Role of anandamide-induced network oscillation in the insular cortex in causing taste-driven feeding**

Sato, H., Yin, D., Toyoda, H. & Kang, Y.
Osaka University Graduate School of Dentistry

[P-09] **The effect of continuous casein restriction on development of taste tissue**

Katsura Ueda[1], Yoshihumi Matsuda[1], Chizuko Inui-Yamamoto[2], Michiko Nakatsuka[1], Shunji Kumabe[1], Isao Tamura[1]
[1]Osaka Dental University
[2]Osaka University Graduate School of Dentistry

[P-10] **Effects of zinc deficiency on the membrane excitabilities in mesencephalic trigeminal neurons**

Saori Yamada[1], Susumu Tanaka[1], Soju Seki[1], Kumiko Kida[1], Tadataka Tsuji [1,2], Mikihiko Kogo[1]
[1]Graduate School of Dentistry, Osaka University
[2]Saiseikai Matsusaka General Hospital

[P-11] **Effects of zinc deficiency on proliferation and apoptosis in rat circumvallate papillae**

Akiyo Kawano[1], Shiho Honma[1, 2], Hitoshi Niwa[1] and Satoshi Wakisaka[1]
[1]Osaka University Graduate School of Dentistry
[2]Baika Women's University

[P-12] **Chronic treatment with ADHD drugs improves autism-like behaviors in mice prenatally exposed to valproic acid**

Shigeru Hasebe[1], Yuta Hara[2], Momoko Higuchi[2], Yukio Ago[2], Takanobu Nakazawa[1,2], Hitoshi Hashimoto[2, 3], Toshio Matsuda[2], Kazuhiro Takuma[1, 3]

[1]Graduate School of Dentistry, Osaka University

[2]Graduate School of Pharmaceutical Sciences, Osaka University

[3]United Graduate School of Child Development, Osaka University

[P-13] **Effects of food preference on masticatory muscles activity and autonomic nerve activities during mastication**

Shiho Honma[1,2], Satoshi Wakisaka[1]

[1]Osaka University Graduate School of Dentistry

[2]BAIKA Women's University

[P-14] **Effect of denture wearing on BOLD signal induced by jaw tapping**

Hideyuki Fukami and Yoshinori Sahara

Iwate Medical University School of Dentistry

[P-15] **Serotonin enhances NMDA receptor-mediated responses via 5-HT2A receptors in the dendrites of rat jaw-closing motoneurons**

Inoue T, Dantsuji M, Nakamura S, Mochizuki A, Nakayama K, Kiyomoto M, Ozeki M.

Showa University School of Dentistry

[P-16] **The formation of mandibular condyle in rats fed with unpalatable chow**

Chizuko Inui-Yamamoto[1], Tadashi Inui[2], Shiho Honma[1,3], Makoto Abe[1], Satoshi Wakisaka[1]

[1]Osaka University Graduate School of Dentistry

[2]Osaka University Graduate School of Human Sciences

[3]BAIKA Women's University

Abstract
Oral Session

Special Lecture

The role of adenosinergic neurotransmission in peripheral neuropathy

Gary J. Bennett, PhD
Adjunct Professor, Dept. Anesthesiology, University of California San Diego
and
CEO, BioIntervene Inc.

Current treatments for neuropathic pain are inadequate. Adenosine and its four cognate GPCR receptors (A1AR, A2AAR, A2BAR, and A3AR) have important roles in physiological and pathophysiological states. Studies in patients with neuropathic pain have shown that intravenous infusions of adenosine have extraordinary analgesic properties, but adenosine itself can not be used as a medicine because it has a plasma half-life of only seconds. Animal studies show that agonists with selectivity for the A1AR and A2AAR subtypes are analgescis, but their use is limited by cardiovascular and renal side-effects. In contrast, kidney and cardiovascular tissues express very low levels of the A3AR subtype. Our laboratory and others have shown that agonists selective for the A3AR are potent analgesics in every animal model of neuropathic pain tested to date. Complete analgesic effects are seen with doses that have no detectable side-effects, no analgesic tolerance develops, and the mechanism of action does not involve the opioid cannabinoid systems. A3AR agonists have several potential mechanisms of action, including stimulation of astrocytes to release IL-10 and an effect on neuronal mitochondria that promotes energy production. In summary, data collected to date indicate that A3AR selective agonists may provide safe and effective pain relief in patients suffering with chronic neuropathic pain.

Invited Lectures (L-1)

Chemosensory stimuli modulate feeding patterns and glucose kinetics after glucose-loading

Tadataka Tsuji
The First Department of Oral and Maxillofacial Surgery,
Osaka University Graduate School of Dentistry, Suita, Osaka
Department of Oral and Maxillofacial Surgery, Saiseikai Matsusaka General Hospital,
Matsuzaka, Mie, Japan

Chemosensory stimuli including tastes and odors modulate various physiological activities related to energy homeostasis. We suggested the importance of these chemical senses in glucose kinetics by imposing interventions during glucose intake in humans. The specific odor stimuli, Osmanthus fragrans, directly affect the levels of feeding-related neuropeptides in the hypothalamus in rats, resulting in the changes in the masticatory pattern. The aim of this study was to examine how any interventions associated with odor during and/or before ingestion affect feeding behavior and blood glucose (BG) after ingestion. We thereby recorded the feeding pattern with electromyography (EMG) activities of the masticatory muscles in the anosmic rats and applied the conventional glucose tolerance test to rats through disruption and various stimulation of these chemical senses. After the anosmic treatment, the feeding time was shortened with a longer latency to the start of eating and the cumulative food intake over 4hrs was decreased compared to those before the treatment. EMG analyses of the masticatory muscles during feeding pellets showed that the EMG bursts, which correspond to rhythmical jaw movements, became larger. These behavioral changes indicate fast eating with powerfully gnawing and chewing after the anosmic treatment. The experimentally-impaired olfactory function induced an evident downward shift in the BG curve together with changing of sweet palatability by two-bottle preference test, consistent with the previous reports. Addiction of grapefruit odor stimuli before ingestion, a representative flavor of enhanced sympathetic nerve, dramatically changed the BG curve. More specifically, the effect of grapefruit odor was due to neural message from nasal cavity, consistent with that of limonene odor. These results suggest that favorable chemical senses before and during ingestion are the important factors to maintain BG after ingestion as well as feeding pattern. An attractive fragrance could be utilized as a fascinating means of BG control.

Invited Lectures (L-2)

Brain mechanisms of conditioned taste aversion: the role of the amygdala and reward systems

Tadashi Inui and Tsuyoshi Shimura
Division of Behavioral Physiology, Department of Behavioral Sciences
Graduate School of Human Sciences, Osaka University

Taste sensation signals us whether a food is edible or not. A palatable taste means nutritious, while aversive one indicates toxic. An experience of visceral malaise after food consumption induces the establishment of aversion to a taste of the food. This phenomenon, referred to as conditioned taste aversion (CTA), is caused by an association between the taste and visceral inputs. To elucidate the neural mechanisms of CTA, we have investigated the role of the amygdala and the brain reward system on CTA. The basolateral amygdala (BLA) has anatomical connections with taste-related brain regions. We examined the effects of the pharmacological inactivation of the BLA on rat's behaviors to a saccharin solution as a conditioned stimulus (CS) after the establishment of CTA. The BLA inactivation caused decrease in aversion and reduction of hesitation to lick the CS. We next explored the activation of the neural projections from the BLA on the CTA retrieval, using the manganese-enhanced MRI. It showed that the projections from the BLA to the nucleus accumbens (NAc), the bed nucleus of the stria terminalis (BNST), and central amygdala (CeA) are activated on the CTA retrieval. Then, we further investigated the involvement of the projections from the NAc to ventral pallidum (VP), which are known to be GABAergic. The CS presentation significantly increased the GABA efflux in the VP. We also tested the effects of microinjections of $GABA_A$ receptors antagonist bicuculline into the VP on the CTA retrieval. The bicuculline injections decreased the aversion to the CS. Our recent study has demonstrated that the microinjections of $GABA_A$ receptor agonist muscimol into the BNST reduce the hesitation to lick the CS. These results suggest that the neural projections from the BLA have discrete roles on the CTA retrieval: The BLA-NAc-VP plays a role in the aversion to the CS, whereas the BLA-BNST is involved in the approach behavior.

Invited Lectures (L-3)

Pathophysiological considerations of sleep bruxism from human and animal studies

Takafumi Kato[1,2,3]
1:Department of Oral Anatomy and Neurobiology,
Osaka University Graduate School of Dentistry,
2: Osaka University Hospital Sleep Medicine Center
3: Osaka University United Graduate School of Child Development

Sleep bruxism (SB) is a common sleep related disorder characterized by rhythmic jaw-closing muscle contractions during sleep, with a prevalence of 6-10% in the adult population. It has been recognized as a clinical relevant problem in dentistry since it is often associated with orodental consequences. However, neurophysiological mechanisms of sleep bruxism remain unknown. Polysomnographic studies in humans have shown that patients reporting tooth grinding noise exhibit an increased number of rhythmic masticatory muscle activity (RMMA) during NREM sleep, and that the occurrence of RMMA is related to transient arousal under sleep processes and autonomic activities. To further understand the neurophysiological mechanisms of SB, the jaw motor activities in the naturally sleeping animals (guinea pigs) are currently being investigated. EMG activity level of the jaw-closing and -opening muscles exhibits similar stage-dependent changes while the temporal fluctuations of activity level were not correlated between two muscles. In addition, EMG bursts of the jaw muscles are generally of a low activity level and inhomogeneous for the duration, amplitude and intervals during sleep periods. Nonetheless, rhythmic or repetitive jaw muscle bursts occurred occasionally during sleep. The patterns of rhythmic jaw muscles differed between NREM and REM sleep. When repetitive electrical micro-stimulations to cortico-bulbar tract were given during sleep, the responses of jaw-closing and -opening muscles to stimulation differed between NREM and REM sleep. Therefore, there finding suggest that the distinct combinations of neural modules contributing to masticatory rhythm and pattern generations can be activated during distinct sleep periods, which may underlie the pathophysiological variations of SB. Moreover, animal model can be a useful research option for investigating the mechanisms of sleep related movements such as SB.

Invited Lectures (L-4)

Schizophrenia risk from impairment of sorting nexin-mediated intracellular protein trafficking

Takanobu Nakazawa, Shigeru Hasebe, and Kazuhiro Takuma
Department of Pharmacology, Graduate School of Dentistry, Osaka University

Schizophrenia is a complex disorder characterized by profound disturbances of cognitive, emotional, and social functioning. While schizophrenia is highly heritable, the genetics are complex and clear interpretation of genetic data is difficult. Accordingly, diagnosis and categorization of schizophrenia are based entirely on clinical phenomenology without sufficient information on underlying biological mechanisms. Intracellular trafficking of proteins is essential for the function of highly polarized cells including neurons. Since altered intracellular trafficking results in impaired synaptic function, it may also be related to the pathophysiology of schizophrenia. However, there is little molecular evidence for the involvement of intracellular trafficking in schizophrenia. Here we demonstrate that a deficit in intracellular protein trafficking mediated by sorting nexins is a new molecular pathophysiology of schizophrenia. We identified a genetic association of a brain-enriched sorting nexin, *ARHGAP33*, with schizophrenia. Patients with the risk allele of *ARHGAP33* had regional reductions in brain volume. ARHGAP33 interacted with SORT1 to cooperatively regulate TrkB trafficking to synapses. Consistent with this finding, *ARHGAP33* knockout mice had significantly decreased synaptic TrkB expression. Importantly, *ARHGAP33* knockout mice exhibited impaired development of dendritic spines and schizophrenia-like behavioral abnormalities, both of which were effectively rescued by pharmacological enhancement of TrkB signaling in adulthood. Furthermore, we found a strongly correlated decrease in *ARHGAP33* and *SORT1* expression in peripheral lymphocytes of schizophrenia patients. These results suggest that ARHGAP33/SORT1-mediated trafficking of TrkB could be a promising therapeutic target and a novel biomarker for diagnosis of schizophrenia.

Invited Lectures (L-5)

Integration of sensory and motor function in the orofacial region

Junichi Kitagawa, DDS, PhD
Department of Oral Physiology, School of Dentistry, Matsumoto Dental University

The sensory-motor integration in orofacial motor functions has been an interesting area of research which has not been fully understood in details. In our recent researches we have put some light on how sensory input during orofacial pain conditions modulate orofacial motor activities. In addition, we have also been studied the sensory-motor integration of swallowing.

Recently, we have studied the involvement of astroglial glutamate-glutamine shuttle in modulation of the jaw-opening reflex (JOR) following chronic constriction injury of the infraorbital nerve (ION-CCI). The hyperactive astroglial cells increased in the trigeminal motor nucleus (motV) after ION-CCI. This was associated with enhanced JOR. Microinjection of glutamine synthetase blocker methionine sulfoximine in the motV suppressed the JOR-amplitude. In addition, the JOR-amplitude gradually returned to the control level after glutamine microinjection in the motV. The findings suggest that astroglial glutamate-glutamine shuttle in the motV is involved in the modulation of the excitability of the trigeminal moto-neurons affecting the various jaw reflexes associated with trigeminal nerve injury. Besides, we have been studying the swallowing reflex that is an important reflex in feeding behavior. In our previous studies we reported that sequential swallowing reflex were initiated by electrical stimulation of the pharyngeal branch of the glossopharyngeal (GPN-ph) nerve and superior laryngeal branch (SLN) of vagus nerve. The stimulus frequency and the latency of the GPN-ph nerve stimulated reflex swallowing was approximately the same as that for the SLN. The findings indicated that the GPN-ph plays a major role in the initiation of reflex swallowing from the pharynx in rats. We also found that sour taste stimuli on the pharyngo-laryngeal region facilitate reflex swallowing in comparison with water or other taste stimuli. In addition, very recently we demonstrates that cannabinoids facilitate the swallowing reflex elicited by SLN stimulation. Sensation in the pharynx and larynx is considered to play significant roles in controlling food intake.

Invited Lectures (L-6)

Approaching the migraine pathophysiology through the perspective of the dentistry

Chiho Kudo
Department of Dental Anesthesiology,
Osaka University Graduate School of Dentistry and Osaka University Dental Hospital

Migraine is an episodic neurological disorder by recurrent, severe unilateral pulsating headache, with an associated morbidity of up to 15% worldwide. The clinical characteristics of migraine, in addition to severe headache, include photophobia, phonophobia or autonomic nervous symptoms, such as nausea and vomiting. Although migraine is not life threatening, it has a significant impact on migraine patient's quality of life. Many researchers have tried to elucidate the mechanism of the migraine pathophysiology using experimental animal models, by the stimulation of the dura mater with capsaicin, mustard oil or inflammatory soup, to directly activate the trigeminovascular system or by cortical spreading depression induced by mechanical, chemical or electrical stimulation. But the exact mechanism has not been fully understood so far. It has recently been reported that migraine patients are often suffering from headache attacks accompanying with the cutaneous allodynia in the craniocervical region, and this allodynia is supported to be a risk factor for migraine chronification. In addition, migraine patients sometimes complain of atypical pain in regions innervated by the 2nd (V2) or 3rd (V3) division of the trigeminal nerve (TN) instead of headache during the migraine attack period, such as non-odontogenic toothache or lower-half facial migraine, which situations sometimes lead a misdiagnosis and an improper treatment by dentists. These clinical findings may be caused by interaction and sensitization among divisions of TN. Recently, our group demonstrated that the sensitization of V2 by the loose ligation enhances responses in a migraine animal model. It suggests that the sensitization of V2 could influence the activation and the sensitization of 1st division of TN in the trigeminocervical complex as the central sensitization, subsequently exacerbating pain sensation and pain-related behaviors of migraine. Here, I review the potential mechanism of migraine pathophysiology and show our recent experimental data for the knowledge necessary to the clinical practice for dentistry.

Invited Lectures (L-7)

Mechanisms of orofacial nociception and neuropathic pain

Ryuji Terayama
Department of Oral Function and Anatomy
Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

Orofacial somatosensory information is conveyed to the primary relay sites within the trigeminal sensory nuclear complex (TSNC) of brainstem via afferent components of the trigeminal nerve. From rostral to caudal, the TSNC consists of the trigeminal principal sensory nucleus (PrV) and three subdivisions of the trigeminal spinal tract nucleus, namely, the subnucleus oralis (Vo), subnucleus interpolaris (Vi) and subnucleus caudalis (Vc). The most caudal component of the TSNC, the Vc, has been generally considered to play an essential role in orofacial pain transmission and to represent the trigeminal homologue of the spinal dorsal horn. It has also been documented that trigeminal nerve injury induces hyperexcitability of Vc neurons and is responsible for development of neuropathic pain state. Lines of evidence, however, suggest implication of the rostral subdivisions of the TSNC in the processing of orofacial pain sensations. Therefore, the rostral subdivisions of the TSNC as well as the subnucleus caudalis have some roles in the neuropathic pain state. In this presentation, I will show the structure and function of the TSNC involved in orofacial pain sensations and summarize some of our recent findings about pathological pain conditions after peripheral nerve injuries including 1) activation of MAP kinases and glial cells in the TSNC after injury to the lingual nerve, 2) changes in excitability of Vo and Vc neurons examined with c-Fos expression induced by electrical stimulation of the lingual nerve after injury to the lingual nerve or the inferior alveolar nerve, and 3) convergent nociceptive input to Vc neurons after injury to the inferior alveolar nerve.

Invited Lectures (L-8)

Mechanisms underlying extraterritorial orofacial pain associated with trigeminal nerve injury and inflammation

Koichi Iwata, Masamichi Shinoda and Ayano Katagiri
Department of Physiology, School of Dentistry, Nihon University Tokyo Japan

This presentation will focus on activation of satellite glial cells as well as neurons in the trigeminal ganglion (TG) in association with trigeminal nerve injury or orofacial inflammation, and presents recent data indicating that functional interactions between neurons and satellite glial cells within the TG are involved in orofacial extraterritorial pain spread. We have recently shown increased excitability of TG neurons innervating the trigeminal 2nd branch (V2) region following inferior alveolar nerve (V3) transection or lower lip (V3) inflammation. V3 nerve injury also resulted in significantly reduced potassium channel activity in TG neurons innervating the V2 region, resulting in hyperexcitability of uninjured TG neurons. Various molecular changes were also evident in neurons and satellite glial cells in the TG in association with trigeminal nerve injury or orofacial inflammation. The expressions of P2Y12 in satellite glial cells and nitric oxide in neurons were significantly increased in the V2 region of the TG following lingual nerve injury or inferior alveolar nerve transection, and the expression of NGF also spread to neurons in the V2 region of the TG following lower lip (V3) inflammation, suggesting that changes in the expression of these molecules may be involved in extraterritorial orofacial pain. Also, over-expression of connexin 43 is also thought to participate in the spread of the activation of satellite glial cells, and indeed we recently observed that the expression of connexin 43 protein was strongly enhanced in satellite glial cells in association with inferior alveolar nerve transection. These findings suggest that functional interactions between connexin 43 and satellite glial cells play a pivotal role in the spread of neuronal hyperexcitability within the TG, resulting in sensitization of TG neurons innervating uninjured or uninflamed orofacial areas.

Abstract
Poster Session

Poster session (P-01)

The role of the periodontal ligament cells in neuronal differentiation induced by mechanical stimuli

Kaori Takahashi, Takashi Yoshida and Minoru Wakamori
Div. of Mol. Pharmacol. & Cell Biophys. Tohoku Univ. Grad. Sch. of Dent.

Recently, a dental implant treatment is becoming common, but cannot regenerate the periodontal membrane including periodontal ligaments (PDL), nerves and blood vessels. Particularly, the nerve differentiation mechanisms in the periodontal membrane are not clear. It has been reported that branches of Ruffini endings, mechanoreceptors, are not formed without mechanical stimuli in the rat PDL [(1)]. On the other hand, PC12 cells are differentiated by co-culture with human PDL cells without mechanical stimulation [(2)]. These findings suggest that the mechanical stimuli are important for the nerve induction into periodontal membrane and that hPDL cells produce neurotrophic factors. However, effects of PDL mechanical stimulation on nerve induction remains unknown. We focused on the time-dependent changes of types and amounts of neurotrophic factors produced by the PDL cells during mechanical stimulation. And we examined the neurite growth after adding supernatant medium of rat PDL cells loaded with mechanical stimulation.

Primary cultured rat PDL cells were seeded on silicon chamber, and loaded with periodic mechanical stimulation for 0, 24, 48 and 72hrs. The mRNA levels of growth factors were analyzed using real-time PCR method. The supernatant medium of the rat PDL cells with or without mechanical stimulation was added to mouse neuroblastoma cell line, Neuro-2a. The mRNA levels of BDNF and NT-4, except NGF, produced by rPDL cells were increased depending on the duration of mechanical stimulation. The significant neurite growth was observed in Neuro-2a cells by addition of the supernatant medium of rat PDL cells loaded with mechanical stimulation for over 48 hrs.

Taken together, these results suggest that nerve induction is accelerated by the mechanical stimulation via increase of released neurotrophic factors, such as BDNF and NT-4, released from the PDL cells.

(1) Shi et al. *Arch. Histol. Cytol.*, 68, 289-299, 2005
(2) Tomokiyo et al. *J. Cell Physiol.*, 227, 2040-2050, 2012

Key Words : neurotrophic factor, periodontal ligament, mechanical stimulation

Poster session (P-02)

Post-translational modifications of water channel aquaporin-5 in salivary gland cells

Takahiro Hasegawa, Chenjuan Yao, Tetsuya Akamatsu, and Hiroshi Yoshimura
Department of Molecular Oral Physiology, Institute of Biomedical Sciences,
Tokushima University Graduate School, Tokushima, Japan

Aquaporin-5 (AQP5), a water channels protein, plays an important role in the saliva secretions. We found that two types of post-translational modifications, phosphorylation and ubiquitination, of AQP5 are induced by autonomic agents in the salivary gland cells.

Phosphorylation of AQP5 was rapidly and transiently induced by the injection of isoproterenol, an adrenergic beta receptor agonist, in the mouse salivary glands and by the treatment of forskolin and cAMP analogues in human submandibular gland (HSG) cells transfected with AQP5. The treatment of H-89, a protein kinase A inhibitor, and mutant analyses in the HSG cells revealed that AQP5 is phosphorylated at its threonine-259 by protein kinase A through the cAMP signaling pathway. In addition, transient emergence of phosphorylated AQP5 at plasma membrane and similar localization between wild type and non-phosphorylated type of AQP5 suggest that AQP5 is phosphorylated at plasma membrane and that this phosphorylation does not contribute to AQP5 trafficking in the salivary gland cells.

Short-ubiquitination of AQP5 was rapidly and transiently induced by the injection of pilocarpine and carbachol, muscarinic acetylcholine receptor agonists, in the mouse salivary glands and by the treatment of calcium-mobilizing agents such as thapsigargin, an inhibitor of endoplasmic reticular Ca^{2+}-ATPase, and A23187 calcium ionophore in the HSG cells. The induction of AQP5 ubiquitination was inhibited by the chelation of the extracellular calcium ions in the HSG cells. These results suggest that AQP5 is ubiquitinated through the Ca^{2+} signaling pathway required Ca^{2+} influx.

Taken together, AQP5 is phosphorylated and ubiquitinated in the salivary gland cells through the cAMP- and Ca^{2+}-signaling pathway, respectively. Although the individual roles and the relationships of these modifications are still unclear at present, both the post-translational modifications of AQP5 possibly involves in a process of the saliva secretions.

Key Words : Aquaporin-5, salivary gland, post-translational modification

Poster session (P-03)

TRPV1 and TRPM8 channels expression and activity in the superior laryngeal nerve innervating the laryngopharynx and associated laryngeal regions: an immunohistochemical and electrophysiological study

Mohammad Zakir Hossain[1], Hiroshi Ando[2], Shumpei Unno[1], Yuji Masuda[3] and Junichi Kitagawa[1]

[1]Department of Oral Physiology, [2]Department of Biology, [3]Institute for Oral Science, Matsumoto Dental University, 1780 Gobara, Hirooka, Shiojiri, Nagano 399-0781, Japan.

The laryngopharynx and associated laryngeal regions are important areas for swallowing and respiration. The sensory nerves innervating these areas have been reported to respond to chemical stimuli like sour, salt, acids etc.. Transient receptor potential (TRP) channels present in these areas may be activated by chemical stimulations in these regions. In the present study, we investigated the expression of TRPV1 and TRPM8 channels in the nodose-petrosal ganglionic complex (NPc) containing the cell bodies of the afferent nerves from the superior laryngeal nerve (SLN) innervating the laryngopharynx and associated laryngeal regions. We also recorded the whole nerve activity of the SLN during chemical stimulation by capsaicin and menthol in these regions. The cell bodies stained by a neuronal retrograde tracer fluoro-gold (FG) were observed scattered in all of the NPc following the FG-injection to the regions. The number of cells positive to both FG and TRPV1 in the nodose ganglion (NG) was lessor than that in the petrosal ganglion (PG). The number of cells positive to both FG and TRPM8 was indifferent between the NG and PG. Approximately, half of the TRPM8-positive cells showed TRPV1-immunoreactivity. In addition, most of the TRPV1- and TRPM8-positive cells were expressed on NF-200-negative cells indicating their presence in non-myelinated neurons. Whole nerve recording of the SLN revealed dose depended response to both capsaicin and menthol. The background activity of SLN increased during passing of the capsaicin solution through the laryngopharynx and associated laryngeal regions. Menthol causes initial increase followed by decrease of SLN activity. The present study demonstrated the electrophysiological characteristics and evidence of attribution of TRPV1 and TRPM8 channels to the chemical responses of the SLN. The findings suggest the involvement of TRPV1 and TRPM8 channels in regulating food palatability and reflex swallowing.

Key Words : TRPV1 and TRPM8 channels, Superior laryngeal nerve, food palatability.

Poster session (P-04)

Protein kinase A regulates long term potentiation of intrinsic excitability in neonatal trigeminal motoneurons

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Synaptic plasticity is an intrinsic feature of neuronal activity that mostly has been studied in the field of learning and memory. However, the intracellular mechanisms underlying plasticity at motor nuclei, influencing motor behavior, are less studied. Trigeminal motoneurons (TMNs) send the final signal outputs to the muscles which control the jaw movements such as mastication, suckling and swallowing. Long-term potentiation (LTP) is a long-lasting enhancement of synaptic effectiveness that follows tetanic electrical stimulation. LTP is activity-dependent form of synaptic plasticity which has been reported in various types of neurons in the central nervous system. However, the mechanisms of plasticity in the trigeminal system have been remained unexplained.

In the present study we investigated the mechanisms of intrinsic excitability of LTP (LTP-IE) in TMNs and its dependence to calcium influx. Experiments were performed on neonatal rats using whole-cell patch-clamp recording to assess the intrinsic excitability of motoneurons. Excitability in TMNs was characterized by a leftward shift in frequency-current curves, whereas resting membrane potential and input resistance exhibited no remarkable changes. To characterize the calcium dependence of LTP-IE, first the extracellular calcium during induction protocol was blocked, then intracellular calcium was buffered with bis-(*o*-aminophenoxy)-*N,N,N',N'*-tetraacetic acid. Under both conditions LTP-IE was prevented. Finally, effects of protein kinase A (PKA) on LTP-IE were studied. Blocking PKA prevented LTP-IE, whereas pharmacological activation of PKA both mimicked and occluded that phenomenon. This suggests that LTP-IE occurs through postsynaptic calcium influx and subsequent activation of PKA.

Key Words : Trigeminal motoneuron, Long-term potentiation, protein kinase

Poster session (P-05)

Hyperpolarization-activated current in mesencephalic trigeminal nucleus neurons affected by the activity of locus coeruleus neurons

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Locus coeruleus (LC) is a small population of noradrenergic neurons located in the ventrolateral side of the fourth ventricle in the rostral pons. LC neurons widely project to the central nervous system and thereby involve in multiple brain functions such as arousal, attention stress and emotion. Noradrenaline (NA) released from the nerve terminal of LC neurons contributes to about 70% of the total extracellular NA in the brain. NA release from soma of LC neurons may have the characteristics of autoinhibition by α2-adrenergic autoreceptor. First of all, we investigated the electrophysiological properties of the LC neurons and the effect of α2-adrenergic receptor antagonist, atipamezole, on the LC neurons using whole-cell current-clamp recordings. We found that the LC neurons show voltage-dependently inactivating K^+ currents, low-threshold Ca^{2+} spikes and autoinhibition by α2-adrenergic autoreceptor. The proprioceptive sensory neurons innervating jaw-closing muscles are exceptionally located in the mesencephalic trigeminal nucleus (MTN), which medially adjoins or intermingles with the LC nucleus. It has been reported that the MTN neurons receive synaptic inputs from the LC neurons. However, it has not been addressed in detail whether and how neural activity in LC effect on that in MTN. We investigated whether hyperpolarization-activated current (I_h) in MTN neurons would be affected by the activity of LC neurons. The MTN neurons can display two distinct firing patterns by either relaying spike trains arising from muscle spindles or generating bursts in response to synaptic inputs. The MTN neurons express I_h, which can decrease glutamate receptor current, thereby suppressing bursts. We found that the activation of α2-adrenergic receptors caused I_h inhibition in MTN neurons. The activation of single LC neuron by current injection could successfully cause I_h inhibition in MTN neurons. We are currently investigating the mechanism of synchronization among LC neurons by using dual whole-cell patch-clamp recording.

Key Words：Locus coeruleus, Mesencephalic trigeminal nucleus, Hyperpolarization-activated current

Poster session (P-06)

Mapping jaw motor responses to electrical stimulation in amygdala in guinea pigs

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Aim: Rhythmic jaw movements can be induced by stimulating various brain structures in experimental animals. Jaw motor representations within the amygdala remain to be clarified. This study aimed to investigate the areas of amygdala contributing to the jaw movements in anesthetized guinea pigs.

Methods: Experiments were performed using four Hartley guinea pigs placed in the stereotaxic apparatus under anesthesia with ketamine and xylazine. Electromyographic activities from masseter and digastric muscles were recorded. Jaw movements were recorded using an optoelectronic recording apparatus. The short-train (pulse duration: 200 μs; frequency: 500 Hz; 3 pulses) and long-train (pulse duration: 200 μs; frequency: 30 Hz; 180 pulses) electrical microstimulations were given to the rostral half of amygdala through the glass coated stainless electrodes. Stimulating sites were spaced in rostrocaudal and mediolateral steps of 0.5 mm and in dorsoventral steps of 0.2 mm within each site. After the experiments, the sites where the stimulation induced jaw movements were histologically identified.

Results: Short-train stimulations induced short-latency responses in bilateral masseter and/or digastric muscles. Within the stimulus sites where short-latency responses were evoked, long-train stimulations induced three patterns of jaw movements, i.e., tonic jaw opening movements and rhythmic jaw open-close movements with or without lateral jaw shifts. Histological analysis revealed that the stimulating sites with short-latency responses and the above patterns of jaw movements were distributed within the ventral part of amygdala, which covered the medial, basal and cortical nuclei, while those with rhythmic jaw movements with lateral jaw shifts were more localized to the cortical nucleus.

Conclusion: These results suggest that the ventral part of amygdala can play a role for controlling jaw movements and that the patterns of induced jaw movements differed within this part.

Key Words : Amygdala, Rhythmic jaw movements, Electrical microstimulations

Poster session (P-07)

Depression of GABAergic synaptic transmission in the insular cortex of the capsaicin-treated rats

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Trigeminal nociceptive information is corded as firing patterns of the peripheral nerves that project to the second sensory neurons in the trigeminal spinal nucleus caudalis. This information is mediated by unmyelinated C fibers and myelinated Aδ fibers, which process slow and fast pain, respectively, and thus, the primary sensory neurons play an important role in nociceptive signaling. A model rat with ablation of unmyelinated C fibers shows an elevation of nociceptive threshold and is likely to exhibit low excitability of the cerebral cortex. In this study, we performed whole-cell patch-clamp recording to explore cortical inhibitory local network in the model rat whose C fibers were ablated by capsaicin (CAP, 100 mg/kg) injection 1-2 days after birth. Whole-cell patch-clamp recording from layers II/III pyramidal (Pyr) and fast-spiking neurons (FS) in the insular cortical slice preparation were obtained 20-25 days after CAP treatment.

Miniature IPSCs (mIPSCs) recorded under application of CNQX (20 μM) and tetrodotoxin (1 μM) showed smaller amplitude of mIPSCs without changing their frequency both in Pyr and FS of the model rat than those in control. This finding suggests that GABAergic transmission is down regulated in the CAP-treated rat via postsynaptic mechanisms. To confirm this idea, we next recorded unitary IPSC (uIPSC), and the variance-mean analysis was performed by changing extracellular calcium concentration from 1 mM to 4 mM. Our V-M analysis showed that quantal size of GABA release is smaller in the CAP model in comparison to that of control. These results suggest that C fiber elimination induces depression of GABAergic synaptic transmission in the insular cortex, where nociceptive information is integrated.

Key Words：insular cortex, nociception, GABA

Poster session (P-08)

Role of anandamide-induced network oscillation in the insular cortex in causing taste-driven feeding

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Blood concentration levels of anandamide (AEA) and N-oleoylethanolamine (OEA), which are released from enteroendocrine cells in the gastrointestinal tract, inversely change depending on hunger or satiety. AEA increases food intake via activation of cannabinoid type 1 receptors (CB1Rs) in various brain regions, while OEA decreases food intake via activation of G-protein coupled receptor 119 (GPR119). In the rat insular cortex where CB1Rs are expressed, the primary gustatory insula (Gu-I) that processes chemo-sensory information from the tongue caudally adjoins the gastrointestinal region of the autonomic insula (GI-Au-I) that processes mechano- and chemo-sensory information from the gastrointestinal tract. Neuronal activity in the GI-Au-I increases in the hunger state, causing appetite sensation while umami and sweet taste sensations produced in the Gu-I enhances appetite sensation produced in the GI-Au-I. It may then be possible that an activation of CB1R by AEA causes a neuronal interaction or coordination between the Gu-I and GI-Au-I, which may play an important role in the control of taste-driven feeding. However, these possibilities have not been addressed.

Here, we show with optical recording that the application of AEA induces theta-rhythm oscillatory coordination between the Gu-I and GI-Au-I. This coordination was modulated by GABAB receptor (GABABR)-mediated feed-forward inhibition and was abolished by AM251, an antagonist of CB1R, or OEA. We propose a novel brain mechanism in which taste-driven feeding is regulated by the neural coordination between the Gu-I and GI-Au-I through the opposing activities between CB1R and GPR119. This mechanism is consistent with the inverse changes in the blood concentration levels of AEA and OEA, depending on the state of hunger or satiety. In contrast to the known involvement of the hypothalamus in the regulation of food intake as nutrients, our results provide new insight into the higher-order brain mechanism responsible for emotional feeding behavior caused by taste recognition.

Key Words：Oscillation, Insular cortex, Anandamide

Poster session (P-09)

The effect of continuous casein restriction on development of taste tissue

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Sufficient nutrient intake in developmental and growth stages make our life rich and healthy. If we cannot take enough nourishment in early stage, several unfavorable affections are induced in various regions of our bodies including taste tissues. Previously, we presented that continuous dietary sodium restriction during developmental stage brought some changes in taste preference and the properties of taste cells in constructing taste buds. Needless to say that deficiency of other nutrient have possibilities to alter the development of taste tissues, but the effects of each nutrients on developing taste organs are not clear in detail.

In this study, we bred the rats exposed to continuous dietary casein restriction, fed by casein-restricted food (including 5% casein) from embryonic day 3 through developmental stage to adulthood (DCR rats) to investigate the relationship between continuous dietary casein restriction and development of taste organ. Two-bottle taste preference test for the solutions of basic tastes against distilled water on DCR rats was performed to reveal the alteration of sensitivity for each basic taste stimuli. We could not find obvious alteration in the preference for salty taste between DCR and wild type rats. On the other hand, we found some difference in the preference for saccharin and sodium inosinate (IMP), in spite of the preference for sucrose and monosodium glutamate do not show apparent difference between two groups.

We also carried out immunohistochemistry against the molecules specifically distributing in peripheral taste cells (PLC β2, G-α gustducin and NCAM) on taste buds in circumvallate papillae of wild type and DCR rats. The size of taste buds seems to be reduced by DCR rats compared with wild type rats, but immunoreaction for these molecules do not show apparent alteration between two groups.

Key Words: taste preference, taste bud, development

Poster session (P-10)

Effects of zinc deficiency on the membrane excitabilities in mesencephalic trigeminal neurons

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Zinc is essential to maintain healthy immune system and its deficiency leads to impairments such as growth restriction accompanying by reduced food intake, taste disturbance, and disrupted learning and memory. Our recent study has revealed that zinc deficiency with reduced mastication impairs spatial memory in young adult mice (Kida et al., 2015). It remains to be clarified, however, how zinc deficiency could influence on the neuronal excitabilities in trigeminal neurons related to rhythmical oral motor output. Mesencephalic trigeminal neurons (MTN), as primary sensory neurons, are critically involved in the genesis and control of oral-motor activities (Tanaka et al., 2003). In the present study, we investigated the effects of zinc deficiency on the membrane properties involving spike discharge characteristics in MTN using whole-cell patch clamp recording techniques.

Sprague-Dawley neonatal rats were employed and assigned into control and zinc deficient (ZD) groups, which were fed by normal or zinc deficient diet from postnatal day 1, respectively. The body weight of each diet group was monitored daily and serum zinc level was examined at the age of postnatal day 12. Whole-cell configuration was obtained from coronal brain slices through the mesencephalic trigeminal nucleus prepared from p8-17 rats. ZD group showed poor weight growth and electrical recordings from P8-12 neurons demonstrated smaller value of cell capacitance, depolarized resting membrane potential which was accompanied by an increase in input resistance in comparison with normal condition. In addition, action potential properties did not show significant differences between two groups, while the rheobasic current for maintained minimum discharge was smaller and 1st ISI or mean spike frequency in repetitive firing activities were higher in ZD group than those in control. Further experiments showed that NPY, one of orexigenic agents, became less effective on spike discharge characteristics in ZD group.

Key Words: Mesencephalic trigeminal neurons, Zinc deficiency, neuromodulation

Poster session (P-11)

Effects of zinc deficiency on proliferation and apoptosis in rat circumvallate papillae

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Low zinc is one of the reasons to cause taste disorder. Previous studies have shown that the turnover of taste cells is delayed in zinc-deficient rats. In the present study, we examined proliferation and apoptosis of taste buds in circumvallate papillae of zinc-deficient rats. Furthermore, we investigated whether the changes of zinc-deficient rats were rescued after feeding a normal diet.

Rats were divided into three groups: fed a normal diet for 8 weeks (normal rats); fed a zinc-deficient diet for 4 weeks (zinc-deficient rats); fed a zinc-deficient diet for 4 weeks, followed by a normal diet for 4 weeks (rescued rats).

The number of taste cells in the taste buds of normal rat and zinc-deficient rat is no significant difference. The positive rate of proliferating cell nuclear antigen (PCNA), a marker of proliferating cells, was significantly decreased from 17.5% in the taste buds of normal rats to 10.7% in those of zinc-deficient rats. The positive rate of Bcl-2-assosiated X protein (Bax), a marker of apoptotic cells, was significantly decreased from 29.4% in the taste buds of normal rats to 20.9% in those of zinc-deficient rats. In rescued rats, both the PCNA and Bax-positive rate returned to that observed in normal rats.

The present results indicate that low-zinc caused the prolonged life span of taste bud cells, and that these changes in zinc-deficient rats were rescued after feeding normal diet.

Key Words: Zinc deficiency, taste bud cells, PCNA

Poster session (P-12)

Chronic treatment with ADHD drugs improves autism-like behaviors in mice prenatally exposed to valproic acid

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Taking antiepileptic drugs, most especially valproic acid (VPA), during pregnancy has been reported to increase the risk of autism in children. We have recently demonstrated that mice prenatally exposed to VPA on embryonic day 12.5 display autism-like behaviors and are useful as an autism mouse model (Kataoka et al., Int. J. Neuropsychopharmacol., 2013; Takuma et al., Pharmacol. Biochem. Behav., 2014; Hara et al., Behav. Brain Res., 2015). In the present study, we examined the effects of attention deficit/hyperactivity disorder (ADHD) drugs methylphenidate and atomoxetine, which increase the extracellular dopamine and noradrenaline levels in the prefrontal cortex of mice (Koda et al., J. Neurochem., 2010), on the autism-like behaviors and decrease in cortical dendritic spine density in mice prenatally exposed to VPA. Pregnant ICR mice were intraperitoneally injected with either 500 mg/kg of VPA or saline on day 12.5 of gestation. After birth, the offspring were weaned, and then the male offspring were subjected to experiments at 8 weeks of age. Acute treatment with methylphenidate (3 mg/kg) or atomoxetine (1 mg/kg) did not affect social interaction deficits and recognition memory impairment in mice prenatally exposed to VPA, although it increased prefrontal dopamine and noradrenaline release. In contrast, chronic treatment with methylphenidate or atomoxetine for 2 weeks improved the autism-like behaviors and decrease in dendritic spine density in the prefrontal cortex of mice prenatally exposed to VPA. The ameliorative effects of these drugs on behaviors and dendritic spine morphology were antagonized by concomitant treatments with the dopamine-D_1 receptor antagonist SCH39166 or the dopamine-D_2 receptor antagonist raclopride, but not by the α_2-adrenoceptor antagonist idazoxan. These findings suggest that chronic treatment with ADHD drugs ameliorates abnormal behaviors and declined dendritic spine density in the prenatal VPA-exposed autism mouse model via continuous activation of prefrontal dopaminergic system (Hara et al., Autism Res., 2016).

Key Words: autism, valproic acid, ADHD drugs

Poster session (P-13)

Effects of food preference on masticatory muscles activity and autonomic nerve activities during mastication

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Ingestion behavior, which is comprised of chewing and swallowing, is an important factor controlling quality of life. Many studies revealed that the characters of foods, such as texture, taste and flavor, affect the chewing and swallowing. A little is known, however, on the effects of preference of flavor on the ingestion behavior. In the present study, we examine the effects of preference of flavor on autonomic nervous activity and chewing pattern ingestion behavior by monitoring the electorocardiogram (ECG) and the surface electromyogram (EMG).

We investigated chewing behavior during ingestion of the two types of gum, favorable flavor gum and unfavorable flavor gum in adult male human subjects (age; 25-35 years old). ECG was monitored autonomic nerve activity from heart rate variability (HRV) analyzing R-R intervals, and surface EMG was monitored for masticatory muscle movements. The experiments are approved by the Ethics Committee of the Osaka University Graduate School of Dentistry.

Specifically we focused on the autonomic nervous activity during post-chewing stage and correlated it to individual chewing patterns. Four types of autonomic nervous activity were observed; 1; sympathetic nervous activity was getting dominant. 2; parasympathetic nervous activity was getting dominant. 3; both sympathetic and parasympathetic nervous activities were shown as almost the same degree. 4; hard to analyze because of the behavior was shown randomly. In group 1, masticatory muscles activity tend to increase, however some subjects and some parameters in the chewing patterns was decreased. In group 2, masticatory muscles activity tend to decrease. In group 3, both increasing and decreasing muscle activities were observed. In group 4, we could not find the definitive alterations of autonomic nervous activity and mastication activity.

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Key Words: Mastication, EMG, HRV analysis

Poster session (P-14)

Effect of denture wearing on BOLD signal induced by jaw tapping

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Animal research indicates that there are unique characteristics of the orofacial motor system such that many orofacial movements (*e.g.,* chewing, swallowing) necessitate exquisite motor control processes to coordinate the activity of the vast array of muscles in the orofacial region, the sensory input, the peripheral effector organs, and central nervous control. The use of noninvasive visualizing techniques (e.g., PET, MRI, MEG) proved to be an important asset in studying such processes as it afforded a way to confirm basic findings characterized in nonhuman animal studies. We used functional magnetic resonance imaging to examine human brain activities during a simple jaw movement, namely, denture tapping. The major activated areas during tapping in the young dentulous group were the primary motor and somatosensory cortices, while in the elderly dentulous group, the parietal and temporal association cortices, thalamus, and basal ganglia were the major activated areas. Areas of activation during tapping tasks with and without occlusal contact differed greatly. During tapping without occlusal contact, the activation area in the primary motor and somatosensory cortices was relatively broader. In the elderly edentulous group, the tapping task significantly activated the primary motor and somatosensory cortices; prefrontal, parietal, temporal, and occipital association areas; and the cerebellum. Denture wear caused more extensive activation of the thalamus and basal ganglia. These suggest that further comparison of BOLD task-evoked activation patterns would discriminate the functional disturbances and recovery from functional deficits, and could identify networks and measure individual or group differences in network integration and activity.

Key Words: fMRI, denture tapping, aging

Poster session (P-15)

Serotonin enhances NMDA receptor-mediated responses via 5-HT2A receptors in the dendrites of rat jaw-closing motoneurons

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Masseter motoneurons (MMNs) have the well-developed dendrites where MMNs receive huge and diverse inputs. MMNs have been reported to receive both glutamatergic and serotonergic inputs in the dendrites; however it is unclear how two inputs affect each other. In this study the experiments were performed with the brainstem slice preparations from postnatal day 2-5 rats. We made whole-cell patch clamp recordings from retrogradely-labeled MMN by dextran-tetramethylrhodamine-lysine. MNI-caged glutamate (300 or 1000 μM) was added to the bathing solution, and focal photolysis of caged glutamate was accomplished using a 365 nm nitrogen-pulsed laser or 730 nm two photon laser systems. Bath application of 5-HT increased the amplitude of the laser-evoked depolarizing responses in the dendrites of the MMNs in dose-dependent manner, in addition to induction of membrane potential depolarization. 5-HT-induced enhancement of the laser-evoked responses was mimicked by application of the 5-HT_{2A} receptor agonist TCB-2 and was reduced by the 5-$HT_{2A/2C}$ receptor antagonist Ketanserin. Application of NMDA receptor antagonist APV suppressed the 5-HT-induced enhancement, whereas application of the AMPA receptor antagonist CNQX did not affect the 5-HT-induced enhancement. Immunoelectron microscopy revealed that both NMDA receptors and 5-HT_{2A} receptors were located in the dendrites. Pretreatment of Src kinase inhibitor PP2 reduced the 5-HT-induce enhancement of the glutamate responses in MMNs, whereas Ca^{2+} chelator BAPTA and PLC inhibitor U73122 did not affect the 5-HT-induced enhancement of the glutamate responses. The phosphorylation of Src was increased by the treatment with 5-HT. Furthermore, 5-HT enhanced the glutamate responses even in Mg^{2+} free Ringer. These results suggest that activation of 5-HT_{2A} receptors enhanced the NMDA receptor-mediated glutamate responses in the dendrites of the MMNs at least in part through the Src kinase pathway. Such enhancement of glutamate responses by 5-HT may contribute to appropriate control of the jaw motor function.

Key Words: Jaw-closing motoneuron, 5-HT_{2A} receptor, NMDA receptor

Poster session (P-16)

The formation of mandibular condyle in rats fed with unpalatable chow

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The mandibular condyle plays a critical role in masticatory movement, and its formation is affected by feeding of the difference food qualities, for example, soft or hard chow on development stage. Although food preference cause changes in the masticatory movement, whether the role of food preference in the formation of mandibular condyle still remain unclear. Therefore, we analyzed the relationships between feeding behaviors and the morphologies of mandibular condyle of the rats fed with denatonium (DEN), sucralose (SUC), low-sodium (LOS), or normal chow (NOR) from 3 to 11 wks. In the behavioral test, we measured the complete time to finish eating a chow (3.0 g), and counted the number of “holding” and “feeding” during eating it, after overnight food deprivation. The amount of food intake in the DEN and LOS groups were lower than that in the NOR group. The number of “holding” and “feeding” in the DEN group were larger than that in other groups. The rats of the DEN group ate a chow bit by bit during feeding a piece of denatonium chow. The feeding pattern in the DEN group or LOS group was largely different from the NOR or SUC group. The body mass indices in the DEN or LOS group at 11 wks were smaller than that in the NOR group. But, the height of the neck of mandible and the width of the right-left line of the mandibular condyle in the DEN group were larger than that in other groups. The width of the rostral-caudal line in the LOS group was larger than that in the NOR group. These results indicate that the feeding of a denatonium or a low sodium chow changes the formation of the mandibular condyle. It is possible that food preference affects the changes in the morphologies of the mandibular condyle.

Key Words: food preference, mandibular condyle, feeding pattern