筋・骨格系の痛みの神経機構に関する国際ワークショップ

International Workshop on the Neural Mechanism of Musculoskeletal Pain

Date: Dec. 4 & 5, 2004
Venue: Noyori Conference Center
(Nagoya University, Nagoya, Japan)

日時：平成１６年１２月 ４日(土)～５日(日)
場所：名古屋大学野依記念学術交流館

Organizing Committee for the International Workshop on the Neural Mechanism of Musculoskeletal Pain

筋・骨格系の痛みの神経機構に関する
国際ワークショップ組織委員会

Purpose and Goal of This Workshop

Musculoskeletal pain such as low back pain, knee pain and rheumatoid arthritis afflicts many people, and its prevalence is rising as societies age. While great progress has been made in understanding the neural mechanisms of pain over the past decades, the main focus has been on pain from the skin. In contrast, experimental research on the neural mechanisms of musculoskeletal pain has been quite limited both in Japan and other countries; it is the area of pain research that is conspicuously lagging. This workshop will provide an opportunity for participants to hear about recent progress in this field from major researchers from throughout the world. In addition, the organizers have recently received research assistances from the Ministry of Health, Labour and Welfare, and Japan Foundation for Aging and Health, and we will present and discuss the results of our joint studies with the aim of exploring directions for the next steps to take this field forward. There will also be lectures and poster presentations on recent developments in the general neural mechanisms of pain, making this an excellent opportunity to consider musculoskeletal pain from a broad range of perspectives.

Organizing Committee
International Workshop on the Neural
Mechanism of Musculoskeletal Pain

本ワークショップの目的と意義

腰痛・膝痛・関節リウマチをはじめとした筋・関節の痛みは非常に頻度が高く、かつ 高齢化社会の進展に伴い増大しつつあります。痛みの神経機構の理解は皮膚の痛みを中心として大きく進歩しましたが、関節や筋の痛みの神経機構についての実験的研究は国内外ともに極めて少なく、疼痛研究領域のなかでもその研究は特に遅れています。本ワークショップでは世界におけるこの分野の代表的研究者から最近の研究成果を聞き、また、最近オーガナイザーらが厚生科学研究費や長寿科学振興財団の研究助成を受けて共同で進めてきたこの分野の研究成果を発表して討論し、次のステップへの方向性を探ることを目的としています。また、疼痛の神経機構一般についての最近の展開についての講演やポスター発表の場も作り、広い視点から筋骨格系の痛みを考える場としたいと考えております。

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Program

(Oral: 2F Conference Hall
Poster: 1F Meeting Room)

December 4 (Sat.)

9:50-10:00 Opening remarks: Kazue Mizumura
(Research Institute of Environmental Medicine, Nagoya University)

Session I. Muscular pain models and function of primary afferents (Chair: Hans-Georg Schaible, Takao Kumazawa)

10:00-10:40 Lars Arendt-Nielsen (Arborg University, Denmark)
Muscular pain models and function of primary afferents

10:40-11:05 Kenji Kawakita, Kaoru Okada, Kazunori Itoh
(Meiji University of Oriental Medicine)
Experimental trigger point models induced by repetitive eccentric exercises in humans, rabbits and rats

11:05-11:30 Kazue Mizumura, Toru Taguchi, Ryoko Tamura, Jun Sato
(Research Institute of Environmental Medicine, Nagoya University)
Muscular mechanical hyperalgesia and alteration of C-fiber muscular afferent activities in the rat model of delayed onset muscle soreness

11:30-12:10 Siegfried Mense, Ulrich Hoheisel (Heidelberg University, Germany)
Novel agents involved in the mediation of muscle pain at the peripheral and central level

12:10-13:00 Lunch and poster

Session II. Poster

13:00-14:00 Oral presentation of posters by young researchers
(Chair: Maria A. Giamberardino, Jun Sato)

14:00-15:30 Poster presentation

Session III. **Peripheral mechanism of hyperalgesia**
(Chair: Siegfried Mense, Makoto Tominaga)

15:30-16:10 Kathleen A. Sluka (University of Iowa, USA)
Animal models of musculoskeletal pain. Similarities and differences, and specifics associated with ASIC3 channels.

16:10-16:50 Gerald F. Gebhart (University of Iowa, USA)
Visceral nociceptors and hypersensitivity

16:50-17:15 Keiji Naruse, QiongyaoTang, Masahiro Sokabe
(Graduate School of Medicine, Nagoya University)
Mechanosensitive Ion Channel: molecules of mechanotransduction

17:15-17:40 Makoto Tominaga (National Institute of Natural Sciences)
TRP channels and nociception

18:00- Social (Universal Club, Nagoya University Symposion)

December 5 (Sun.)

Session IV-I. **Central mechanism of hyperalgesia and analgesia-I**
(Chair: Kathleen A. Sluka, Megumu Yoshimura)

9:00- 9:25 Yasuo Sugiura (Graduate School of Medicine, Nagoya University)
Spinal termination of the unmyelinated afferent fibers from skin, muscle and visceral organs

9:25- 9:50 Koichi Obata, Koichi Noguchi (Hyogo College of Medicine)
MAP kinases and the role in neuropathic and flammatory/arthritic pain

9:50-10:15 Kazuhide Inoue, Makoto Tsuda (National Institute of Health Sciences)
The neural mechanism of pain sensation through ATP receptors

10:15-10:55 Hans-Georg Schaible (Jena University, Germany)
The role of spinal prostaglandins in arthritis-evoked spinal hyperexcitability

10:55-11:15 **Break**

Session IV-II. Central mechanism of hyperalgesia and analgesia-II
(Chair: Gerald F. Gebhart, Kazuhide Inoue)

11:15-11:40 Megumu Yoshimura, Go Kato, Hidemasa Furue, Toshiharu Yasaka, Toshihiko Katafuchi (Graduate School of Medical Sciences, Kyushu University)
Functional significance of the descending serotonergic system on the spinal sensory transmission revealed by an in vivo patch-clamp recording

11:40-12:05 Ryusuke Kakigi, Yohei Tamura (National Institute of Natural Sciences)
Effects of repetitive transcranial magnetic stimulation (rTMS) on acute pain

12:05-13:20 Lunch and Poster

Session V. Factors modifying pain (aging, weather, etc.)
(Chair: Lars Arendt-Nielsen, Yasushi Kuraishi)

13:20-13:45 Shinichi Konno, Shinichi Kikuchi (Fukushima Medical University)
Low back pain related model

13:45-14:25 Maria Adele Giamberardino (G. D'Annunzio" University of Chieti, Italy)
Muscle pain and aging

14:25-14:50 Yasushi Kuraishi (Toyama Medical and Pharmaceutical University)
Factors increasing the incidence of postherpetic pain in mice

14:50-15:15 Jun Sato, Morihiko Aoyama, Masahiro Yamazaki, Ken Takahashi, Megumi Funakubo, Kazue Mizumura
(Research Institute of Environmental Medicine, Nagoya University)
Weather and arthritis pain: influences of simulated meteorological changes on pain-related behaviors in arthritic rats

15:15 Closing remarks: Yasuo Sugiura
(Graduate School of Medicine, Nagoya University)

List of poster presentations

Board No. Title/Authors/Affiliations

1. **Changes in skeletal muscle and spinal cord induced by downhill running**
   Hisako Urai[1], Katsuya Kami[1], Emiko Senba[2]
   [1]Department of Health Sciences, Osaka University of Health and Sport Sciences, [2]Department of Anatomy & Neurobiology, Wakayama Medical University

2. **Muscular tenderness revealed by behavioral pain test and c-Fos protein expression in the spinal dorsal horn following eccentric contraction in rats**
   Toru Taguchi, Ryoko Tamura, Jun Sato, Kazue Mizumura
   Dept, Neural Reg., Res. Inst. Environ. Med., Nagoya University

3. **Mechanical, chemical, and thermal responses of the C-fiber sensory receptors recorded from rat muscle-nerve preparations *in vitro* after eccentric contraction**
   Toru Taguchi, Jun Sato, Kazue Mizumura
   Dept, Neural Reg., Res. Inst. Environ. Med., Nagoya University

4. **Measuring the muscle pain using a transcutaneous pressure: simulation and experimental studies**
   Takahashi K[1, 2], Taguchi T[2], Itoh K[3], Nishimura N[3], Morisada M[3], Okada K[3], Kawakita K[3], Mizumura K[2]
   [1]Japan Foundation for Aging and Health, [2] Res. Inst. Environ. Med., Nagoya Univ., Nagoya, Japan, [3] Meiji-Univ. Oriental Medicine

5. **Autonomic nervous function tests in an experimental model for chronic pain**
   Hiroki Sakurai[1], Tatsuyuiki Hashimoto[1], Yusuke Ohmichi[1], Kouhei Harimoto[1], Takahiko Yoshimoto[1], Kunihiro Eguchi[1,2], Yoshiko Yamaguchi[1], and Takao Kumazawa[1]
   [1] Department of Algesiology, School of Medicine, Aichi Medical University, [2] Department of Physiology, School of Dentistry, Aichi Gakuin University

6. **Chronic pain initiated by muscle injuries in the rats**
   Tatsuyuki Hashimoto[1], Hiroki Sakurai[1], Yusuke Ohmichi[1], Kohei Harimoto[1] Takahiko Yosimoto[1], Kunihiro Eguchi[1, 2], Yoshiko Yamaguchi[1] and Takao Kumazawa[1]
   [1]Department of Algesiology, Aichi Medical University, [2]Department of Physiology, School of Dentistry, Aichi Gakuin University

7. **Attempt to establish an experimental model of the chronic muscle pain in rats**

Itoh Kazunori[1], Okada Kaoru[2], Kawakita Kenji[2]
Department of [1]Clinical Acupuncture and Moxibustion, [2]Physiolgy, Meiji University of Oriental Medicine

8. **Wind-up-like facilitation of the flexor reflex induced by focal electrical stimulation of the gastrocnemius-soleus muscle after eccentric exercise under ischemia in rats**

Itoh Kazunori[1], Okada Kaoru[2], Kawakita Kenji[2]
Department of [1]Clinical Acupuncture and Moxibustion, [2]Physiolgy, Meiji University of Oriental Medicine

9. **Effect of local ischemia on eccentric exercise-induced localized sensitive region in rabbit**

Itoh Kazunori[1], Okada Kaoru[2], Kawakita Kenji[2]
Department of [1]Clinical Acupuncture and Moxibustion, Physiolgy[2], Meiji University of Oriental Medicine

10. **Comparison of three different acupuncture procedures on the chronic low back pain in aged patients.**

Itoh Kazunori[1], Katsumi Yasukazu[2], Hirota Satoko[2], Kawakita Kenji[3]
Department of [1]Clinical Acupuncture and Moxibustion, [2]Orthopaedic Surgery, [3]Physiolgy, Meiji University of Oriental Medicine

11. **Changes in the response property of rat dorsal horn neurons after carrageenan myositis**

Okada K[2], Morisada M[2], Itoh K[2], Kawakita K[1],
Department of [1]Physiology, [2]Clinical Acupuncture and Moxibustion, Meiji University of Oriental Medicine

12. **Tramadol treatment for Fibromyalgia and Myofascial pain.**

Kenji Miki, Osamu Akahori, Tomio Yamamoto, Masao Yukioka
Dept. of Orthopaedic surgery, Amagasaki Central Hospital.
Dept. of Rheumatology, Yukioka Hospital

13. **Blockade of central 5HT3 receptor subtype reduces neural activity in the rat Vc/C2 junction region following temporomandibular joint inflammation**

Keiichiro Okamoto[1,2], Akihisa Kimura[1], Tomohiro Donishi[1], Yasuhiko Tamai[1]
Emiko Senba[2]

Department of [1]Physiology, [2]Anatomy and Neurobiology, Wakayama Medical University

14. **p38 activation in intact DRG contributes to heat hyperalgesia after spinal nerve ligation**

Koichi Obata and Koichi Noguchi
Department of Anatomy and Neuroscience, Hyogo College of Medicine

15. **p38 MAP kinase is up-regulated in spinal microglia and peripheral Schwann cells, mediating pain, and inducing motor dysfunction and hypoalgesia in rat models of lumbar disc herniation and lumbar spinal canal stenosis respectively**

T. Ito, Ohtori, G. Inoue, H. Doya, T. Ozawa, T. Saito, H. Moriya, K. Takahashi,
Department of Orthopedic Surgery, Graduate School of Medicine, Chiba University

16. **ERK MAP kinase activation in the dorsal root ganglion (DRG) following the DRG injury in rats**

[1,2]H. Douya, [1]S. Ohtori, [1]K. Takahashi, [1,2]Y. Aoki, [2]H. Ino, [1]Y. Takahashi,
[1]T. Ozawa, [1,2]T. Saito, [1]H. Moriya, [2]T. Yamashita
[1]Dept. of Orthopedic Surgery and [2]Dept of Neurobiology, Chiba University, Japan

17. **Sensory nerve ingrowth into the inner part of annulus fibrosus following exposure of nucleus pulposus in lumbar intervertebral disc in rats**

Gen Inoue , Seiji Ohtori, Yasuchika Aoki, Tomoyuki Ozawa, Hideo Doya,
Tomoko Saito, Toshinori Ito, Hideshige Moriya, Kazuhisa Takahashi
Department of Orthopedic Surgery, Graduate School of Medicine, Chiba University

18. **Blocking antibody to the p75 neurotrophin receptor prevent NGF-mediated sensitization of sensory neurons**

Tomoko Saito[1,2], Masashi Fujitani[2], Seiji Ohtori[1], Tomoyuki Ozawa[1], Hideo Doya[1,2], Gen Inoue[1], Toshinori Ito[1], Hideshige Moriya[1], Kazuhisa Takahashi[1], Toshihide Yamashita[2]
Department of [1]Orthopedic Surgery, [2]Neurobiology, Graduate School of Medicine, Chiba University

19. **The human lumbar intervertebral disc is innervated primarily by small-diameter-sized peptide containing nerve fibers**

Tomoyuki Ozawa, Seiji Ohtori, Yasuchika Aoki, Tomoko Saito, Gen Inoue, Toshinori Ito, Hideo Douya, Hideshige Moriya, Kazuhisa Takahashi.

Department of Orthopedic Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan.

20. **Heat and mechanical hyperalgesia in mice model of cancer pain.**

Hideaki Asai [1] , Masamichi Shinoda [2] , Kenjiro Nagamine [1] ,
Noriyuki Ozaki [2] , Iwai Tohnai1,Minoru Ueda [1] , Yasuo Sugiura [2]

[1] Department of Oral and Maxillofacial Surgery, [2] Department of Functional Anatomy and Neuroscience, Nagoya University Graduate School of Medicine

21. **Thermal and mechanical hyperalgesia induced by experimental squamous cell carcinoma of the lower gingiva in rats**

Kenjiro Nagamine [1], Noriyuki Ozaki [2], Masamichi Shinoda [2], Hideaki Asai [1], Iwai Tonai [1], Minoru Ueda [1], Yasuo Sugiura [2]

[1] Department of Oral and Maxillofacial Surgery, Nagoya University Graduate School of Medicine, [2] Department of Functional Anatomy and Neuroscience, Nagoya University Graduate School of Medicine

22. **Role of nerve growth factor in gastric hyperalgesia induced by experimental ulcer in the rat**

Noriyuki Ozaki, Chikako Ito, Masamichi Shinoda, Yasuo Sugiura
Dept Func Anat & Neurosci, Nagoya Univ Grad Sch Med

23. **Alteration of $P2X_3$ receptor expression in trigeminal ganglia following monoarthritis of temporomandibular joint in the rats**

Masamichi Shinoda[1], Noriyuki Ozaki[1], Hideaki Asai[1,2], Kenjiro Nagamine[1,2], Yasuo Sugiura[1]

[1]Department of Functional Anatomy and Neuroscience, [2]Department of Oral and Maxillofacial Surgery, Nagoya Univ. Graduate School of Medicine

24. **Mediators expression in sensory neurons following carrageenan induced muscle hyperalgesia**

Yuko Fujii, Noriyuki Ozaki, Yasuo Sugiura
Department of Functional Anatomy and Neuroscience, Nagoya University Graduate School of Medicine

25. **Modulation of paratrigeminal neuronal activity following temporomandibular joint inflammation**

Yoko Yamazaki[1], Junichi Kitagawa[2], Asako Shima[2], Hiroshi Kamo[2], Yoshiyuki Oi[1], Koichi Iwata[2]

Departments of [1]Anesthegiology and [2]Physiology, Nihon University School of Dentistry

26. **Behavioral study of intra-articular high-dose lidocaine in chronic arthritis rat.**

Motohiro Kawasaki, Takahiro Ushida, Hiroyuki Watanabe, Tatsunori Ikemoto, Toshikazu Tani

Department of Orthopaedic surgery, Kochi Medical Shool

27. **A vicious cycle of pain via peripheral glutamate receptors**

Narihito Iwashita, Natsu Koyama

Department of Physiology, Shiga University of Medical Science

28. **Unilateral chronic pain distorts visuospatial perception**

Masahiko Sumitani[1], Satoru Miyauchi[2], Gaku Sakaue[1], Takaya Inoue[1], Yoichi Matsuda[1], Masahiko Shibata[1], Takashi Mashimo[1]

[1] Department of Acute Critical Medicine (Anesthesiology), Osaka University Graduate School of Medicine, [2] Brain Information Group, Kansai Advanced Research Center, Communications Research Laboratory

29. **Functional roles of TTX-sensitive and TTX-resistant sodium channels in action potential generation of the mouse dorsal root ganglion neurons**

Tomoya Matsutomi, Chizumi Nakamoto, Taixing Zheng, Jun-ichi Kakimura, Nobukuni Ogata

Department of Neurophysiology, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan

30. **Cellular mechanism regulating the upregulation of $Na_V1.9$, a TTX-resistant Na channel, in mouse doral root ganglion neurons**

Jun-ichi Kakimura, Tomoya Matsutomi, Taixing Zheng, Chizumi Nakamoto, Nobukuni Ogata

Department of Neurophysiology, Graduate School of Biomedical Sciences, Hiroshima University

31. **Metabotropic 5-HT receptor activation modulates capsaicin receptor function in mouse colon DRG neurons**

Takeshi Sugiura, Gerald F. Gebhart

Dept. Anesthesiology & Medical Crisis Management, Nagoya City University Graduate School Medical Sciences, Dept. Pharmacology, The University of Iowa

32. **ASIC3 can generate sustained current by small pH drops**

J. Yagi[1,2], H.N. Wenk[2], L.A. Naves[2,3], E.W. McCleskey[2]

[1] Dept of Integrative Physiol, Kyorin Univ Sch Med, [2] Vollum Inst, Oregon Hlth & Sci Univ, Portland, OR, USA, [3] Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

33. **Co-expression of TRPV2 with TrkC in the developing and adult dorsal root ganglia**

Shinobu Tamura, Yoshihiro Morikawa, Emiko Senba

Department of Anatomy and Neurobiology, Wakayama Medical University

34. **Molecular basis of congenital insensitivity to pain with anhidrosis (CIPA): mutations in *TRKA (NTRK1)* gene encoding the receptor tyrosine kinase for nerve growth factor (NGF)**

Yasuhiro Indo

Department of Pediatrics, Kumamoto University School of Medicine

35. **Functional interaction of TRPV1 with EP_1: peripheral nociceptive mechanism of prostaglandins E_2**

Tomoko Moriyama[1,2], Tomohiro Higashi[2,3], Kazuya Togashi[2,3], Tohko Iida[1], Eri Segi[4], Yukihiko Sugimoto[5], Tomoko Tominaga[2,3], Shuh Narumiya[4] and Makoto Tominaga[2,3]

[1]Dept. of Cell. and Molec. Physiol., Mie Univ. Sch. of Med., [2]Sect. of Cell Signaling, Okazaki Inst. for Integrative Biosci, Natl Inst of Natural Sci,. [3]Dept. of Physiol. Sci., the Grad. Univ. for Advanced Studies, [4]Dept.of Pharmacol., Kyoto Univ., Fac. of Medicine, [5]Dept. of Physiol. Chem., Grad. sch. of Pharmaceu. Sci.,

36. **Modulation of TRPV1 activity by prostaglandin I_2**

Tomohiro Higashi[1,2], Tomoko Moriyama[1,3], Kazuya Togashi[1,2], Eri Segi[4], Tohko Iida[3], Tomoko Tominaga[1,2], Yukihiko Sugimoto[5],Shuh Narumiya[4] and Makoto Tominaga[1,2]

[1]Section of Cell Signaling, Okazaki Institute for Integrative Bioscience, National Institutes of National Sciences, [2]Dept. of Physiological Sciences, The Graduate University for Advanced Studies, [3]Dept. of Molecullar and Cell Physiology, Mie University School of Medicine, [4]Dept. of Phamacology, Kyoto University Faculty of Medicine, [5]Dept. of Physiological Chemistry, Graduated School of Pharmaseutical Sciences, Kyoto University

37. **Functional analysis of anti-phosphorylated TRPV1 antibody**

Namie Murayama[1,2], Mitsuko Numazaki[3], Makoto Tominaga[1,2]

[1]Sec. of Cell Signaling, Okazaki Inst. for Integrative Biosci., Natl. Inst. of Natural Sci., [2]Dept. of Physiol. Sci., the Graduate Univ. for Advanced Studies, [3]Dept Cell and Molec Physiol , Mie Univ Sch of Med.

38. **The role of TRPV1 in the bradykinin-evoked nociceptive responses**

Kimiaki Katanosaka[1], Ratan K Banik[1,3], Giron Rocio[1], Tomohiro Higashi[2], Makoto Tominaga[2], Kazue Mizumura[1]

[1]Research Institute of Environmental Medicine, Nagoya University, [2] Okazaki Institute for Integrative Bioscience, [3] College of Medicine, University of Iowa

39. **Prostaglandin EP3 receptors (EP3R)-mediated attenuation of desensitization in intracellular calcium ($[Ca^{2+}]_i$) increase induced by bradykinin (BK)**

Yasuko Kozaki, Fukushi Kambe, Yoshitaka Hayashi, Sachiko Ohmori, Hisao Seo, Takao Kumazawa, Kazue Mizumura

Research Institute of Environmental Medicine, Nagoya University