



京都大学大学院医学研究科
てんかん・運動異常生理学講座

Department of Epilepsy, Movement Disorders and Physiology
Kyoto University Graduate School of Medicine

年次報告書
Annual Report 2016

2016年8月

<表紙の言葉>

表紙のデザインは、波形様の曲線と、てんかんキャンペーンの紫と多彩な色からなります。脳波の波形と周波数を想像させます。脳波のサーフィンがもっと上手になることを目指して。

<Front cover>

Design of the cover page is the slow waveforms with different colors including purple, which may remind you of brain waveforms and different frequencies. Hoping all of you to enjoy EEG wave surfing.

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Preface



Since two years have past after we have the issued the first and second annual reports of the Department of Epilepsy, Movement Disorders and Physiology, Kyoto University Graduate School of Medicine, it is again my great honor and pleasure that we could issue the third annual report. We appreciate very much all of you who kindly gave the very important comments and suggestion, upon the previous annual reports from other places and fields.

First of all, since the establishment of this department in August 2013, we have been supported, as the endowed department, by GlaxoSmithKline K.K., Niho Kohden Co., Otsuka Pharmaceutical Co., and UCB Japan Co. Ltd. Within the Kyoto University, we greatly appreciate the warmest and continuous support by the Department of Neurology (chaired by Prof. Ryosuke Takahashi), and also by the Departments of Neurosurgery (Prof. Susumu Miyamoto), Psychiatry (Prof. Toshiya Murai), Pediatrics (Prof. Toshio Heike), and Diagnostic Imaging & Nuclear Medicine (Prof. Kaori Togashi).

Based on or in addition to the daily clinical practice for patients with epilepsy and movement disorders in the Kyoto University Hospital, the aim of this Department was originally planned as follows.

- 1) Clinical Research: To solve pathophysiology of epilepsy and movement disorders, and to develop new treatments that could lead to the advanced medical care. We also aim at standardizing it in clinical practice.
- 2) Translatable and Translational Research: To promote clinical practice and research of clinical neurophysiology on epilepsy and movement disorders and its clinical application, because basic- and clinical epileptology and movement disorders are very closely related to neurophysiological knowledge and methods.
- 3) Education: To provide the integrated teaching opportunity for training of physician-scientists, clinical specialists and leaders of related fields internationally.
- 4) Industry-academia collaboration under the appropriate COI management

Upon the completion of the third year, we again greatly appreciate all of the Departments of Kyoto University Graduate School of Medicine and all of the Clinical Divisions of the Kyoto University Hospital for their warmest and sincere support to our activity. Without this supports, we could not complete any of them by all means that were reported in this annual report. It was also strongly supported by so many collaborators, researchers and friends in Japan and also internationally.

In this annual report, we are also very pleased to report the outcome and the current state of industry-academia collaboration. We hope that it may represent a positive face of endowment department in general and that it may help industry partners understand the significance of the endowment department in the future plan.

We again tried to summarize what we could do and not, which help us analyze and understand the situation, and then help us improve and modify the current condition, and also start the new concerns. We would greatly appreciate your any feedback to us that is very helpful for our future contribution to the patients close to or distant from us.

At the end of my preface, I thank all of our friends very much whoever kindly worked hard to make and edit this annual report.

August 2016

With my best wishes,



Akio IKEDA, MD, PhD
Chairman and Professor
Department of Epilepsy, Movement Disorders and Physiology
Kyoto University Graduate School of Medicine

Congratulatory remarks



On behalf of the Vice President of International League Against Epilepsy (ILAE), I want to congratulate Professor Akio Ikeda, for his 3rd year Anniversary Remark of Department of Epilepsy, Movement Disorders and Physiology, Kyoto University Graduate School of Medicine. First of all, I also want to congratulate Professor Akio Ikeda, for his great efforts to realize and perform such outstanding programs, for clinical and basic researches, education, administration, as well as clinical treatments for patients with neurological disorders.

Professor Akio Ikeda is outstanding neurologist and epileptologist not only in Japan and Asian friend countries but also in all over the world-wide countries.

In ILAE, publication of the research articles for Official Journal (Epilepsia) is one of the most important activities. Professor Akio Ikeda was nominated as an Associate Editor of the Epilepsia since 2013, and he not only organized and controlled many reviewers with his amazing abilities but also he reviewed many articles whether to accept or reject for Epilepsia with his sharp decision. I am very happy to see his contribution because I heard many reputations of his good work from ILAE Executive members. I can always remember his earnest but strict attitude for clinical and basic researches.

Recently, World Health Organization (WHO) approved 'Global burden of Epilepsy and the need for coordinate action at the country level to address its health, social and public knowledge implications', at WHO General assembly in Geneva, in February 2015. This decision is now a world-wide movement for epilepsy to introduce and implement national health care plans of action for epilepsy management, aiming to overcome inequalities and inequities in health, social and other related services including Japan. I am sure that Professor Akio Ikeda can further develop this important resolution for patients with epilepsy in coming next step in his department.

With my best wishes,



Tatsuya Tanaka, MD., DMSc.
Vice President, ILAE 2009-2017
Past President, Japan Epilepsy Society
Professor Emeritus, Asahikawa Medical College
Honorary Director, Yamabiko Medical Welfare Center

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I Introduction

To begin with

The details of the annual report in each aspect are shown in the following pages as done in the second annual report last time, and thus as the essence of general message directly related to our Department, I am briefly listing them which occurred or appeared in the last year. I would greatly appreciate your comment and feedback.

- 1) Evolutional changes in the social state for epilepsy
 - 2) "Oscillology": the new research field including epilepsy in Japan
 - 3) EEG/ Epilepsy fellowship in Kyoto University Hospital
 - 4) Teaching session
 - 5) Epilepsy should be approached based on the broad scope of general neurology and clinical neuroscience.
-
- 1) Epilepsy used to be recognized as a neuropsychiatric disease in Japan historically. Once recently the genetic study, neurophysiological analysis and pathological approach have advanced better understanding of epilepsy, it is now recognized one of the most representative disorders of clinical neuroscience for both neurology and neuropsychiatry. As shown by the fact that World Health Assembly closes, passing resolutions on epilepsy. <http://www.who.int/mediacentre/news/releases/2015/wha-26-may-2015/en/>. It has aided in improving clinical care in epilepsy in Japan as follows. Insurance reimbursement in epilepsy has greatly improved since last April 2016 by the National Healthcare System for prolonged-video EEG monitoring, remote reading system of digital EEG and EEG reading service.
 - 2) With regard to clinical and translatability research, we have been appointed as the member of Grant-in-Aid for Scientific Research on Innovative Areas (Research in a proposed research area): Non-linear Neuro-Oscillology - Towards Integrative Understanding of Human Nature. We will aim at exploring novel multi-dimensional oscillatory phenomena, working mainly on primate/rodent models, direct recordings of human brain activity, and advanced measurements of human brain systems. (<http://www.nips.ac.jp/oscillology>)
 - 3) We have provided the special EEG/ Epilepsy fellowship as the joint activity with the Department of Neurology (Prof. Takahashi), and 1-3 fellows have been always employed so far. As for clinical care in the third year, more than that of the first and second year, we tried to contribute to the activity of the Kyoto University Hospital and Graduate School of Medicine, as much as possible, by conducting our initial purposes.
 - 4) We also tried to contribute to the region of Kyoto and Kansai directly by patient care, and also tried to provide the teaching seminars in the field of clinical EEG, clinical epilepsy, and clinical neurophysiology by means of many medical societies, i.e., Japanese Society of Neurology, Japanese Society of Clinical Neurophysiology, and Japan Epilepsy Society.
 - 5) Epilepsy should be approached based on the broad scope of general neurology and clinical neuroscience. So-called autoimmune epilepsy is one of the most important topics in clinical care and research in epilepsy, and neuroimmunological approaches are very important from general neurology's point of view. Glia has also been regarded very important for both neurodegenerative disorders and epilepsy. Epilepsy is one of the commonest neurological disorders, and thus approaches to epilepsy in patient's care, research and teaching should be done based on the broad scope of general neurology and clinical neuroscience.

I. Introduction

In the last, for young people, we very much welcome all of you who are interested in this field from any places, and we hope to work and learn together.

With my best wishes,

Akio IKEDA, MD, PhD

Outline

Funding prospects

Establishment	June 1st, 2013
Arrival of staffs	August 1st, 2013

Name of the Endowed Department

Department of Epilepsy, Movement of Disorders and Physiology
Kyoto University Graduate School of Medicine

Founding vision

- 1) As an academic department in the university hospital, we promote researches and clinical applications of clinical neurophysiology, which is essential for elucidating the pathophysiology and developing the treatment of clinical epileptology.
- 2) It is our mission to elucidate the pathophysiology and develop the treatment of epilepsy and movement disorders so as to develop the highly advanced medicine for its application to clinical practice. We also make best efforts to offer opportunities of trainings and educations to young physicians both from Japan and abroad to foster the specialists and physician-scientists in the field of epilepsy.

Research vision

In close collaboration with the Department of Neurology, we aim at achieving the following projects in a comprehensive, efficient and multidisciplinary manner.

1. Development of medical devices for wide-band EEG recording&analysis, and its application to elucidation of epileptogenicity
2. Promotion of epilepsy surgery and research on higher brain functions&its plasticity under epileptic conditions
3. Combined imaging and neurophysiological researches on the pathophysiology of the epileptic focus
4. Research on the pathophysiology and treatment of movement disorders
5. iPS (induced pluripotent stem) cell research and animal model research on epileptogenesis
6. Establishment of the training programs for the advanced specialists in the related fields
7. Promote collaborative researches with basic and mathematical scientists to understand neural oscillations underlying both physiological brain functions and pathology

Companies of endowment (in alphabetical order)

GlaxoSmithKline K.K.
NIHON KOHDEN CORPORATION
Otsuka Pharmaceutical Co., Ltd.
UCB Japan Co., Ltd.

Contact address

URL: <http://epilepsy.med.kyoto-u.ac.jp>
E-mail: epilepsy@kuhp.kyoto-u.ac.jp (Secretary)
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TEL: (+81)-75-751-3662
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Members of this Department and Affiliated Persons

<Members of Department of Epilepsy, Movement Disorders and Physiology>

Professor: Akio Ikeda, M.D., Ph.D. Associate Professor: Riki Matsumoto, M.D., Ph.D. (- Jul. 2016)
Secretary: Miki Watanabe Medical assistant technician: Makiko Matsushita (Apr. 2016 -)
Visiting Scientist: Kiyohide Usami, M.D., Ph.D. (Dept. of Neurology, Rakuwakai Otowa Hospital, Nov. 2014 - Sep. 2015)
Tomoyuki Fumuro, Ph.D. (Dept. of Medical Technology and Sciences, School of Health Sciences at Fukuoka, International University of Health and Welfare, Mar. 2015 -)
Research support personnel: Takeshi Inoue M.D. (Dept. of Pediatric Neurology, Osaka city general hospital, May 2016 -)

<Affiliated members from Department of Neurology>

Associate Professor: Riki Matsumoto, M.D., Ph.D.
(Aug. 2016 -)
Assistant Professor: Akihiro Shimotake, M.D., Ph.D.
Katsuya Kobayashi, M.D., Ph.D.

Graduate Students (Doctoral course):

M. Ota, Kei. Sato, H. Takeyama, M. Daifu-Kobayashi,
M. Kinboshi (from Wakayama Medical University), T. Murai,
M. Nakatani (from Juntendo University School of Medicine),
J. Togawa, K. Yoshinaga, S. Neshige (from Hiroshima
University School of Medicine), Kazuaki. Sato, K. Tanioka,
M. Togo, M. Sakamoto

Graduate Student (Master's course): Shamima Sultana

EEG/Epilepsy fellowship:

T. Inoue (Apr. 2013 – Mar. 2016)
H. Yoshimura (Jul. 2015 – Sep. 2015)
T. Tsukada (Oct. 2015 – Mar. 2016)
D. Fujii (Feb. 2016 -)
M. Honda (Apr. 2016 -)

Research student and undergraduate student:

B. Bayasgalan (Apr. 2016 -)
R. Kurauchi
(Department of Human Health Sciences, Apr. 2016 -)

<Affiliated members>

Department of Neurosurgery

Senior Lecturer: T. Kunieda, M.D., Ph.D.
(- Apr. 2016, Ehime University)
K. Yoshida, M.D., Ph.D.
Assistant Professor: T. Kikuchi, M.D., Ph.D.

Human Brain Research Center Research and Educational Unit of Leaders for Integrated Medical System

Program-specific Associate Professor:
M. Matsuhashi, M.D., Ph.D.

Department of Clinical Laboratory Medicine

Assistant Professor: T. Hitomi, M.D., Ph.D.

Department of Respiratory Care and Sleep Control Medicine

Assistant Professor: M. Inouchi, M.D., Ph.D.





Activity report

Research activities

Our main goal is to solve so-called "clinical questions", which have been raised in the daily clinical activity, and have remained unsolved yet.

Based on the concept of systems neuroscience, by means of established and newly developed various methods, many clinical and basic researches are conducted as follows.

KEY WORDS

General key words: epilepsy, epilepsy surgery, higher cortical function (motor control, praxis, language, semantic cognition, vision, will), Bereitschaftspotential (BP), cortico-cortical network, movement disorders, sleep disorders, autoimmune epilepsy

Unique key words: ictal DC shift, high frequency oscillation (HFO), cortico-cortical evoked potential (CCEP), cortical tremor, ictal apraxia, ictal paresis, wide-band EEG

1) Pathophysiology of medically intractable epilepsy and its treatment

a) Unraveling pathophysiology for intractable partial epilepsy

Epilepsy surgery has been established as an option for treatment of intractable partial epilepsy. The epileptogenic lesions, such as hippocampal sclerosis, cavernous angioma, and brain tumor, are the most common candidates for the one-stage surgery. It is still a challenge to localize the epileptic focus in 'MRI-negative' patients, who show no (apparent) lesion by clinical MRI studies. We have extensively made multidisciplinary approaches with video-EEG monitoring, MEG and FDG-PET to 'visualize' the epileptic focus in these MRI-negative patients for possible treatment with epilepsy surgery. Especially in the MRI-negative cases, we occasionally need invasive evaluation with intracranial electrodes to precisely delineate the epileptic focus and map the eloquent cortices at and around the epileptic focus. In addition to the conventional frequency band (Berger rhythm: 0.3-70 Hz), advancement in medical engineering has enabled us to record electrocorticogram with a broader frequency band (wide-band EEG), ranging from direct current shifts (DC shifts) to high frequency oscillations (HFOs). In our recent report, several features of ictal DC shifts and HFOs were extracted in 16 patients who underwent chronic intracranial recording as follows; 1) high occurrence rates of DC shifts during ictal period, 2) DC shifts preceded HFOs with statistically significance in most patients, 3) DC shifts and HFOs were observed in more restricted area than conventional ictal pattern, 4) higher occurrence rate in focal cortical dysplasia than hippocampal sclerosis (Kanazawa et al., 2014). We have been applying this wide-band EEG technology (ictal/interictal DC shift and HFOs) to further localize the core epileptogenic zone for epilepsy surgery. Furthermore, we started collaborative studies with Osaka University of Pharmaceutical Sciences to elucidate generation mechanisms of DC shifts and HFOs by means of wide-band EEG analysis and multi-unit recording in epilepsy model animals.

It has been known that epileptic discharges can spread to the other areas through intercortical networks. Thus, in addition to epileptic foci, it would be important to understand an epileptic network formulated by epileptic foci, propagating areas and connecting white matters. MRI tractography is a method evaluating anatomical networks. By combination with MR tractography and FDG-PET, we delineated decreased integrity of seizure propagation tracts in MTLE patients (Imamura et al., 2016). We recruited 18 patients with MTLE and 18 healthy subjects. In the patients, the remote functional deficit zone was defined using FDG-PET as an extratemporal region showing glucose hypometabolism. Using diffusion MRI tractography, we defined a seizure propagation tract (PT) that connects the focus with a remote functional deficit zone. We also used the corticospinal tract (CST) and inferior longitudinal fasciculus (ILF) as control tracts. Fractional anisotropy (FA), mean diffusivity (MD), and volume of the tracts were compared among PT, CST, and ILF. Tractographic analysis identified the uncinate fasciculus, arcuate fasciculus, and fornix as PTs. A decrease in FA was found in MTLE patients compared with healthy subjects in all tracts, but

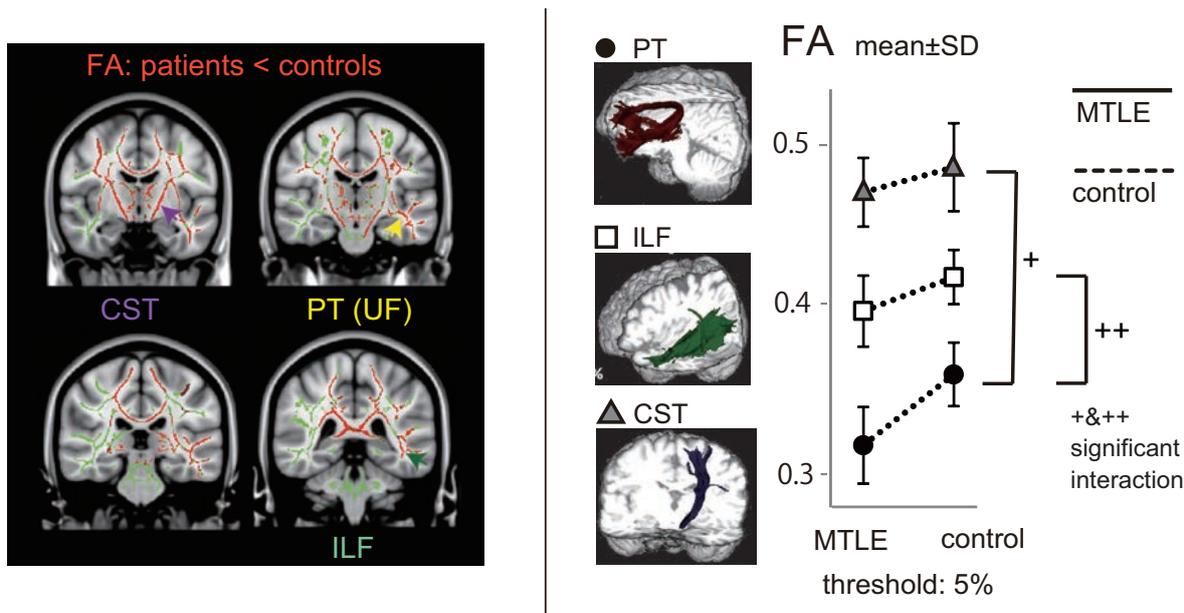


Figure 1. (Center) We delineated a seizure propagation tract (PT) that connects the focus with a remote functional deficit zone. PT goes through mainly uncinate fasciculus (UF). We also used the corticospinal tract (CST) and inferior longitudinal fasciculus (ILF) as control tracts. (Left) Whole brain analysis using TBSS delineated a widespread decreased FA in the MTLE patient group, which involved the PT, ILF and CST. (Right) A decrease in FA was found in MTLE patients compared with healthy subjects in all tracts, but PTs showed a more significant decrease in FA than did the two control tracts (modified from Imamura et al., 2016).

PTs showed a more significant decrease in FA than two control tracts (Fig. 1). Although white-matter damage was observed in all candidate tracts examined, the integrity of white matter was most significantly decreased in PTs in MTLE. The present findings demonstrate that epileptic activity impairs not only the focus, but also the whole network (the focus - the propagation tract - the remote functional deficit zone).

Cortico-cortical evoked potential, CCEP, is an *in vivo* electrical tract tracing method for presurgical evaluation, developed in Cleveland Clinic and Kyoto University (Matsumoto et al., Brain 2004). By means of subdural electrodes, electrical pulses (0.3-ms duration, frequency of 1 Hz, alternating polarity, 1–10 mA) are directly delivered to a part of the cortices, and CCEPs are obtained from adjacent and remote cortical regions by averaging the electrocorticogram time-locked to the stimulus onset. It promises to refine our understanding of surgical candidacy, first through a more precise and tailored evaluation of the seizure network in each individual patient, and second through greater understanding of the functional systems of the brain involved. Both are important for improving our ability to identify patients at high risk for poor surgical outcomes across multiple outcome measures.

b) Unraveling pathophysiology and treatment for various epilepsy syndrome

Even in the 21st century, electroencephalography (EEG) remains essential in the diagnosis of “epileptogenicity”. Simultaneous recording of EEG and fMRI (EEG-fMRI) is a new technique that takes advantages of both modalities and complements each other to delineate both the cortical and subcortical structures related with epileptic activities. We for the first time introduced this technique to Japan to investigate the epileptic network and underlying pathophysiology in various types of epileptic syndromes such as praxis-induced epilepsy and hypothalamic hamartoma (HH). Recently, we demonstrated epileptic networks of HH by means of EEG-fMRI (Usami et al., 2016). Eight patients with HH were recruited, and underwent EEG-fMRI. A general linear model was utilized for analyzing fMRI, using time-shift models designed by timing at and around spikes (from -8 sec to + 4 sec) convolved with hemodynamic response function. Any BOLD responses were observed in all patients, and six out of eight patients

presented BOLD responses at/around the hypothalamus ipsilateral to attachment of the hamartoma. In group analysis, activations included the ipsilateral hypothalamus, brainstem tegmentum, bilateral precune, lateral parietal lobes and the contralateral dominant bilateral cerebellum, and deactivations included the ipsilateral cuneus, bilateral caudate nuclei, thalami, hippocampi, and a part of default mode network (DMN) (Fig. 2). Based on the results, hypothalamus, brainstem, cerebellum and cerebral cortices would be a network generating epileptic activities, and DMN and hippocampi might be relevant to loss of awareness during seizures and epileptic encephalopathy in HH patients.

Recently the role of autoimmunity has been highlighted for a subset of encephalitis and epileptic seizures. Nowadays, high-resolution MRI can depict subtle structural changes in the medial temporal lobe, such as hippocampus and amygdala, which are often the main inflammatory foci in autoimmune limbic encephalitis. By

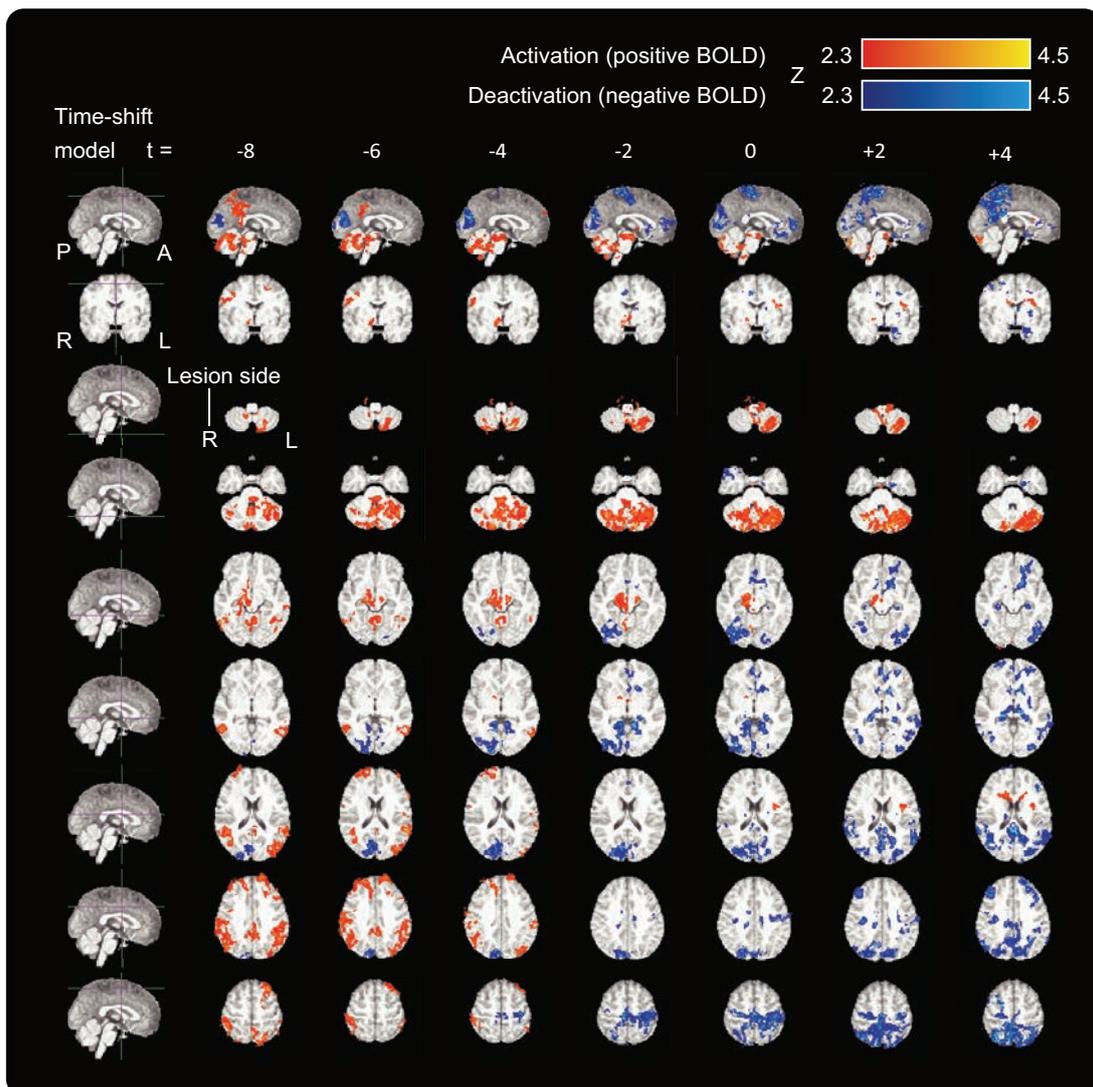


Figure 2. Group analysis of EEG-fMRI. Group analysis of seven patients revealed the common epileptic network associated with epilepsy with HH. Before group analysis, MRI images were flipped in the left-right dimension so that the right hemisphere shows the side of attachment (unilateral attachment) or that of predominant hypothalamic activation (bilateral attachment). The voxels with significant activation/deactivation by cluster-level statistics ($p < 0.007$ after Bonferroni correction) are overlaid on the group mean anatomical image in the MNI standard space. Activations included the ipsilateral hypothalamus, brainstem tegmentum, bilateral precune, and lateral parietal lobes, mainly with early time-shift models, and the contralateral dominant bilateral cerebellum (contralateral dominant) with later time-shift models. Deactivations included the ipsilateral cuneus, bilateral caudate nuclei, thalami, hippocampi, precune, and lateral parietal lobes (Usami et al., 2016).

means of comprehensive study such as video-EEG monitoring (VEEG), neuropsychological test, FDG-PET and MRI, we have revealed the smoldering nature of the autoimmune limbic encephalitis. We have been utilizing multidisciplinary approach (VEEG, FDG-PET and 3T MRI) for offering tailor-made immunotherapy for patients with autoimmune epilepsy. Additionally, we reported that autoimmune mechanism could underlie in an epileptic patient with atypical clinical picture (triple pathology in a patient with parietal tumor) (Matsumoto et al., 2015). Now we attempt to make diagnostic criteria of autoimmune epilepsy, based on both clinical picture and various examinations (Sakamoto et al., 57th annual meeting of Japan Society of Neurology).

We started conducting collaborative researches in epilepsy by means of iPS cells with Prof. Haruhisa Inoue (Center for iPS Cell Research and Application: CiRA).

c) Advanced EEG analysis

EEG now has a history of more than 80 years for evaluation of brain functions and diagnosis of brain diseases, ranging from brain death, coma to epilepsy. Medico-engineering collaboration between Prof. Shibasaki's group (Kyoto University School of Medicine, Neurology, Human Brain Research Center) and Prof. Nakamura's group (Saga University, Faculty of Science and Engineering) has been done to develop the automatic EEG interpretation system, and it is currently under clinical investigation. Now we plan to establish a remote EEG viewing system in collaboration with the department of Neurology of Kobe City Medical Center General Hospital and Takeda General Hospital, and Nihon Kohden, aiming at improvement in quality about clinical practice of epilepsy and a close intermural link. In addition, we started a collaborative study with National Cerebral and Cardiovascular Center in order to establish the diagnostic criteria and treatment for the post-stroke epilepsy patients.

2) Mapping higher functions/network and elucidating its functional alteration under pathological condition

In epilepsy surgery, it is important to map cortical functions to preserve eloquent cortices in addition to the localization of the epileptic focus. Therefore, we need to perform comprehensive 'system mapping' to help neurosurgeons to make strategy of surgery for individual patients. We have made vigorous attempts at developing various techniques for mapping higher cortical functions (e.g., language, motor control etc.) and their network for clinical application.

Functional neuroimaging tells us if specific brain regions are active during certain tasks, but activation by itself does not demonstrate the necessity of those areas. In contrast, electrical cortical stimulation, a gold standard method since mid-20th century, can delineate the cortex responsible for a particular task by making functional impairment. The functional interference is temporary (~ 5 s), discretely focal (~ 1 cm²), and in sharp contrast to chronic stroke lesions that are relatively large and usually associated with cortical plastic compensation.

However, high frequency electrical stimulation often results in afterdischarges that delay functional mapping and harbor a risk of seizure induction. Recent technical advances have enabled us to record the cortical activities relevant to higher cortical functions with wideband EEG technology - from infraslow to high gamma activities. In our institute, in addition to the gold standard method of high frequency electrical stimulation, we perform comprehensive mapping of higher cortical functions by recording epicortical infraslow and high frequency oscillation/activity during motor or cognitive tasks. Recently, we investigated the role of the basal temporal language area (BTLA) using a comprehensive approach. Discrete local field potentials were observed in BTLA while participants completed semantic tasks. Electrical stimulation (lower stimulus intensity & duration) to the area evoked semantic paraphasia and prolonged reaction time selectively during the semantic tasks. The study demonstrated that the BTLA is crucial for semantic processing especially among language functions (Shimotake et al. 2015). In some researchers, it has been considered that the basal anterior temporal lobe is the 'visual' language area. To identify whether this area has visual or semantic function, we, for the first time, applied the representational similarity analysis (RSA), one of the novel decoding methods, to ECoG data (epicortical event related potentials recorded during picture naming task). We could demonstrate that ventral anterior temporal lobe selectively coded semantic processing rather than the visual

or phonological processing (Fig. 3) (Chen, Shimotake et al. 2016). Furthermore, high frequency electrical stimulation to the area and its adjacent areas sometimes induced mirth or laughter, suggesting that this area is also related to semantic processing of humor (Yamao et al., 2016).

We incorporate cortico-cortical evoked potentials (CCEPs) to probe inter-areal functional connectivity in order to perform 'system mapping'. CCEP is an *in vivo* electrical tract tracing method developed in Cleveland and Kyoto (Matsumoto et al., 2004). Single electrical stimulation (1 Hz) is applied to a part of the cortices and cortical evoked potentials, i.e., CCEPs, were recorded from adjacent and remote cortical activities through cortico-cortical connections. With this CCEP method, we can probe cortico-cortical networks involved in functional brain systems and seizure network in each individual patient. Furthermore, by gathering data of cortical functions and networks from many patients in various physiological and pathological states and analyzing them as a group, we attempt to feedback this valuable information into the system neuroscience by providing functional/connectivity references for non-invasive researches.

We can also use induced evoked potential (CCEP) and high frequency activities (HFA) as a dynamic marker of cortical connectivity and excitability since it can "snapshot" the connectivity and excitability within 20-30 trials (< 1 min). We applied this method to awake and sleep cycle and found that cortical connectivity and excitability are different between wakefulness and non-REM (rapid eye movement) sleep, with REM sleep being the intermediate state among them. Increase of neuronal excitability, as reflected in induced HFA, was immediately followed by intense inhibition during non-REM sleep. It was only the frontal lobe that showed rebounded hypersynchrony after intense inhibition during non-REM sleep. These sleep-induced dynamic changes or properties would underlie unconsciousness during sleep and frequent nocturnal seizures in frontal lobe epilepsy.

HFAs consist of physiological HFAs related to various brain functions and pathological (epileptic) HFAs or high frequency oscillations (HFOs). Factors regulating HFA frequency have not been well elucidated in humans. We focused on the primary somatosensory cortex (SI) since physiological HFAs overriding somatosensory evoked potentials have

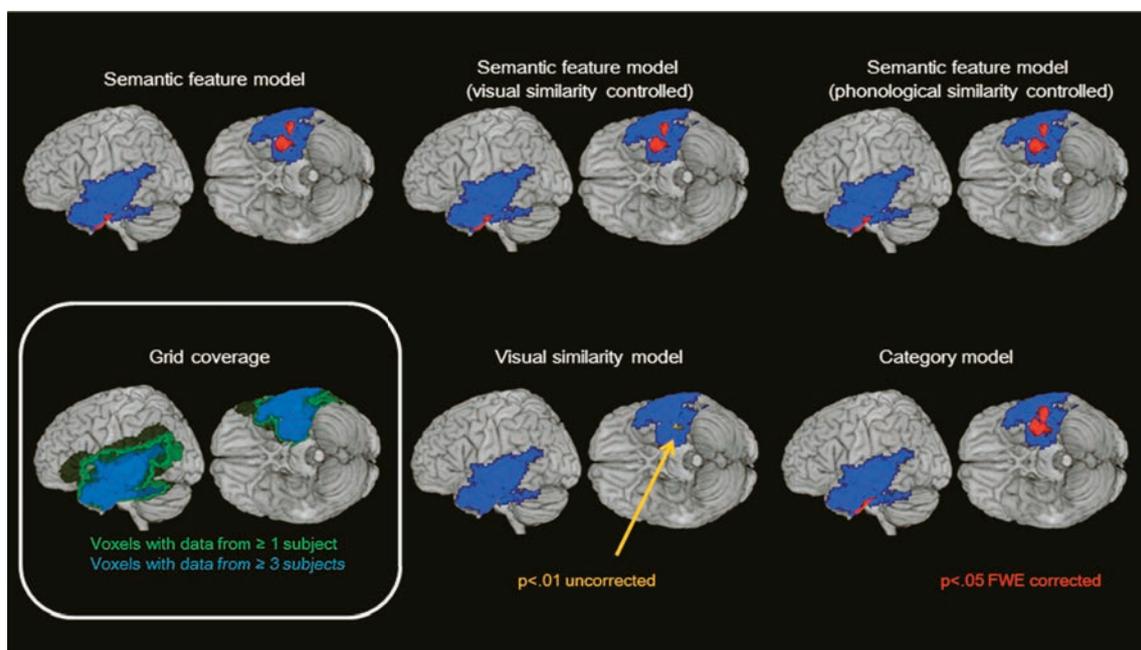


Figure 3. Representational similarity analysis (RSA) applied to the cortical event related potential

We used representational similarity analysis (RSA) to the cortical event related evoked potential during picture naming task performed in ten patients with subdural electrodes covering ventral and lateral anterior temporal regions.

We compared the obtained neural activity with the pre-defined theoretical semantic, visual and phonological models. Neural activity selectively coded the semantic representation in the ventral anterior temporal subregion. (Modified from Chen, Shimotake et al., 2016 with permission)

been extensively studied in humans. We, in the SI, compared HFAs induced by median nerve stimulation with those induced by electrical stimulation (HFAs overriding CCEPs) of the cortex connecting to SI. We clarified that different propagation modes and/or different terminal layers seemed to determine HFA frequency, and that since HFAs overriding CCEPs and HFA induced during various brain functions share a similar broadband profile of the power spectrum, cortico-cortical horizontal propagation seems to represent common mode of neural transmission for processing these functions (Kobayashi et al., 2015).

We have demonstrated the central mechanisms and functional alteration under pathological condition relevant to i) the motor control (negative motor phenomena, praxis, reaching, conflict processing and response inhibition), ii) language (dorsal and ventral language networks with emphasis on semantic cognition) and iii) visual functions (retinotopic mapping by functional MRI), combined with non-invasive evaluation (functional MRI, diffusion tractography, MEG, neuropsychology). Additionally, we are now tackling with decoding of complex neural signals during various tasks in cooperation with seasoned researchers in and out of the Kyoto University (Graduate School of Informatics, Dr. Satoshi Tsujimoto; Advanced Telecommunications Research Institute International, Dr. Rieko Osu; School of Psychological Sciences, the University of Manchester, Prof. Matthew Lambon-Ralph). Finally, we are pleased to announce that our group (A03 “the Direct Recording of Human Neural Oscillations”, Prof. Ikeda as PI) engages in the national research group of “Neuro-Oscillology” which is funded by Grant-in-Aid for Scientific Research on Innovative Areas from the Ministry of Education, Culture, Sports, Science and Technology (MEXT). We also have taken part in the ‘Embodied-Brain Systems Science’ funded by another grant from MEXT (A03-4, Dr. Riki Matsumoto as PI), in order to reveal the motor control and the mechanism of body representations especially in the fronto-parietal network.

3) Pathogenesis of movement disorders and its treatment

We have investigated movement disorders, mainly myoclonus and myoclonus epilepsy, by way of epidemiological, genetic and electrophysiological methods. BAFME (benign adult onset familial myoclonus epilepsy) has been investigated mainly in Japan and European countries for 20 years. The clinical pictures are as follows: i) adult onset, ii) autosomal dominant (unknown causative gene), iii) cortical (myoclonic) tremor (tremulous myoclonus), iv) infrequent generalized seizure, v) cortical reflex myoclonus disclosed by electrophysiological study. We have also been studying BAFME since it was first reported in 1990. As its name suggests, BAFME was considered to present no progression

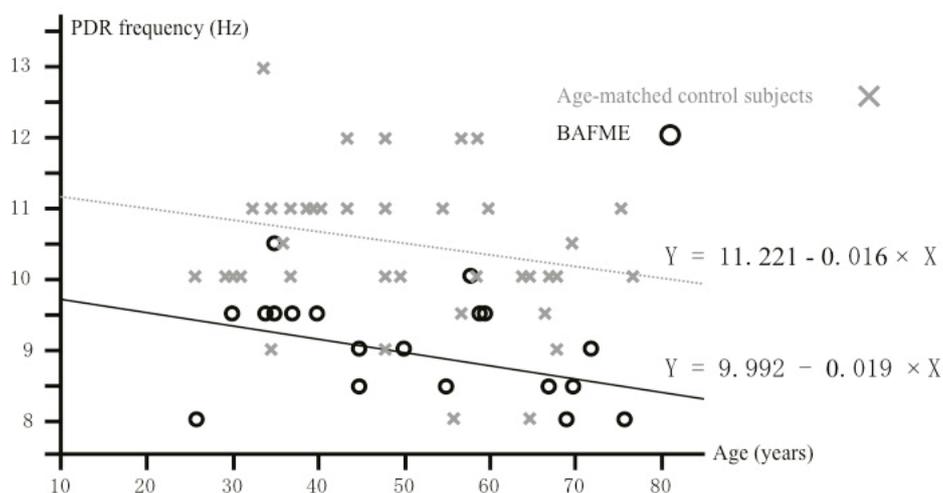


Figure 4. Linear regression analysis between age at the time of EEG recording and frequency of PDR in 19 BAFME patients and 38 age-matched control subjects. A simple regression curve for BAFME patients is represented by the black line, and for age-matched control subjects by the grey dotted line. Open circles indicate BAFME patients and crosses indicate age-matched control subjects. There was a non-significant tendency for a slowing of PDR with age in both BAFME and age-matched control subjects. Comparison of the gradients corresponding to PDR frequency relative to age between the two groups revealed no significant difference.

and good prognosis. However, cortical myoclonic tremor has been proved to worsen with aging. Recently, we demonstrated slow progression of the disease, based on the electrophysiological evidence. Namely, the amplitude of somatosensory evoked potential, reflecting the cortical excitability in the primary sensori-motor cortices, more exaggerated with aging in BAFME patients than normal volunteers. We also demonstrated clinical anticipation in BAFME, in which the onset of generalized seizure and cortical (myoclonic) tremor became earlier in the next generation. The anticipation in BAFME was more apparent in patients with maternal transmission. By comparing the EEG posterior dominant rhythms (PDRs) between patients with BAFME and age-matched control subjects, we showed mild diffuse encephalopathy in BAFME. By means of cortico-muscular coherence, we clarified that hyperexcitability of primary sensorimotor cortex and the subcortical structures such as basal ganglia and cerebellum would be involved in the generator mechanisms of cortical tremor in BAFME (in preparation). These findings would be helpful to search a causative gene of BAFME. In addition, the nationwide questionnaire for neurologists and epileptologists in Japan revealed that BAFME patients were found diffusely without regional accumulation. The further survey based on the detailed clinical information of about 100 BAFME patients showed that the clinical core symptoms were rather homogeneous for BAFME in Japan (in preparation).

Unverricht-Lundborg disease (ULD) is the most common form of progressive myoclonus epilepsy syndrome (PME) in the world, but mainly reported from Baltic and Mediterranean region. The symptoms consist of epileptic seizure, myoclonus, ataxia and cognitive impairment and are gradually deteriorated. We reported ULD cases in Japan, in some of which the development of symptoms and increase of SEP amplitude became very subtle for long-term follow-up. Similar to BAFME, PME including ULD also presented no regional clustering in Japan.

Besides epilepsy patients, we reported a case of elderly woman with exaggerated startle reflex and unconsciousness drop attack including the analysis of electromyography polygraph.

Collaborators

We have been collaborating closely with the Departments that officially support our department. Other collaborators are listed below.

[Overseas]

Dr. Stéphanie Baulac, Ph.D.

Affiliation: Institut du Cerveau et de la Moelle épinière (ICM), Epilepsy Unit

Position: Research Director

Dr. Christophe Bernard, Ph.D.

Affiliation: INS - Institut de Neurosciences des Systèmes, UMR INSERM 1106, Aix-Marseille Université

Position: Team leader

Prof. Marco Catani, M.D., Ph.D.

Affiliation: Natbrain lab, Department of Forensic and Neurodevelopmental Sciences, Institute of Psychiatry, King's College London

Position: Head of the Natbrainlab, Clinical Senior Lecturer and Honorary Consultant Psychiatrist

Prof. Nathan Earl Crone, M.D.

Affiliation: Department of Neurology, Johns Hopkins University School of Medicine

Position: Professor

Prof. Matthew A. Lambon-Ralph, FRCSLT (hons), FBPSS

Affiliation: School of Psychological Sciences, University of Manchester

Position: Professor of Cognitive Neuroscience & Associate Vice-President (Research)

Dr. Dileep R. Nair, M.D.

Affiliation: Epilepsy Center, Cleveland Clinic

Position: The Section Head of Adult Epilepsy and Director of Intraoperative Neurophysiologic monitoring

Prof. Angela Vincent, Ph.D.

Affiliation: University of Oxford

Position: Emeritus professor

Dr. Marco de Curtis, M.D.

Affiliation: Fondazione IRCCS Istituto Neurologico Carlo Besta

Position: Head of Epileptology and Experimental Neurophysiology Unit, Head of Pre-clinical Neuroscience Laboratories

[Domestic]

Dr. Koji Iida, M.D., Ph.D.

Affiliation: Department of Neurosurgery, Hiroshima University Hospital

Position: Associate Professor

Dr. Yushi Inoue, M.D., Ph.D.

Affiliation: Shizuoka Institute of Epilepsy and Neurological Disorders, National Epilepsy Center, Department of Clinical Research

Position: Hospital director

Prof. Shigeki Kameyama, M.D., Ph.D.

Affiliation: Nishi-Niigata Chuo National Hospital

Position: Honorary hospital director

Prof. Amami Kato, M.D., Ph.D.

Affiliation: Department of Neurosurgery, Kinki University Hospital

Position: Professor

Prof. Masatoshi Nakamura, Ph.D.

Affiliation: Research Institute of Systems Control, Institute for Advanced Research and Education, Saga University

Position: Emeritus professor

Prof. Shigeto Nishida, Ph.D.

Affiliation: Department of Information and Communication Engineering, Faculty of Information Engineering, Fukuoka Institute of Technology

Position: Professor

Dr. Teiichi Onuma, M.D., Ph.D.

Affiliation: Musashino Kokubunji Clinic

Position: Honorary hospital director

Dr. Rieko Osu, Ph.D.

Affiliation: Department of Motor Control and Rehabilitation, ATR Computational neuroscience Labs

Position: Department Head

Dr. Satoru Saito, Ph.D.

Affiliation: Division of Cognitive Psychology in Education, Kyoto University Graduate School of Education

Position: Professor

Prof. Yoshio Sakurai, Ph.D.

Affiliation: Laboratory of Neural Information, Graduate School of Brain Science, Doshisha University

Position: Professor

Dr. Hiroshi Shibasaki, M.D., Ph.D.

Affiliation: Kyoto University

Position: Professor Emeritus

Dr. Takenao Sugi, Ph.D.

Affiliation: Institute of Ocean Energy, Saga University

Position: Associate professor

Prof. Shoji Tsuji, M.D., Ph.D.

Affiliation: Department of Neurology, The University of Tokyo Hospital

Position: Professor

Dr. Satoshi Tsujimoto, Ph.D.

Affiliation: Department of Intelligence Science and Technology, Graduate School of Informatics, Kyoto University

Position: Associate professor

Dr. Hiroki Yamamoto, Ph.D.

Affiliation: Graduate School of Human and Environmental Studies, Kyoto University

Position: Assistant professor

Dr. Ikuko Yano, Ph.D.

Affiliation: Department of Pharmacokinetics and Pharmaceutics, Kobe University Graduate School of Medicine

Position: Associate professor

(Listed in the alphabetical order of their family names)

Direct recording of the neural oscillation in human brain

(Grant-in-Aid for Scientific Research on Innovative Areas from the Ministry of Education, Culture, Sports, Science and Technology, Japan: Non-linear Neuro-oscillology: Towards Integrative Understanding of Human Nature)

Prof. Ichiro Tsuda, Ph.D.

Affiliation: Department of Mathematics, Faculty of Science, Hokkaido University

Position: Professor

Dr. Keiichi Kitajo, Ph.D.

Affiliation: Rhythm-based Brain Information Processing Unit, RIKEN Brain Science Institute

Position: Unit Leader

Prof. Katsunori Kitano, Ph.D.

Affiliation: Department of Human and Computer Intelligence, Ritsumeikan University

Position: Professor

Prof. Toshio Aoyagi, Ph.D.

Affiliation: Department of Applied Analysis and Complex Dynamical Systems, Kyoto University Graduate School of Informatics

Position: Professor

Prof. Tatsuya Mima, M.D., Ph.D.

Affiliation: The Graduate School of Core Ethics and Frontier Sciences, Ritsumeikan University

Position: Professor

Dr. Hiroaki Wagatsuma, Ph.D.

Affiliation: Graduate School of Life Science and Systems Engineering, Kyushu Institute of Technology

Position: Associate Professor

Prof. Katsuhiko Kobayashi, M.D., Ph.D.

Affiliation: Department of Child Neurology, Okayama University Graduate School of Medicine

Position: Professor

Prof. Takashi Nagamine, M.D., Ph.D.

Affiliation: Department of Systems Neuroscience, Sapporo Medical University School of Medicine

Position: Professor

**Neural basis of human body representation: a direct electrocorticographic recording and stimulation study.
(Grant-in-Aid for Scientific Research on Innovative Areas from the Ministry of Education, Culture, Sports, Science and Technology, Japan: Understanding brain plasticity on body representations to promote their adaptive functions
("Embodied-Brain"))**

Dr. Eiichi Naito, Ph.D.

Affiliation: Center for Information and Neural Networks (CiNet), National Institute of Information and Communications Technology (NICT)

Position: Research Manager

Prof. Hiroshi Imamizu, Ph.D.

Affiliation: Department of Intelligence Science and Technology, Graduate School of Informatics, Kyoto University

Position: Professor

Dr. Takaki Maeda, M.D., Ph.D.

Affiliation: Department of Neuropsychiatry, Keio University School of Medicine

Position: Senior Lecturer

**The elucidation of glial function in intractable epilepsy and standardization of clinical practice guidelines.
(Japan Agency for Medical Research and Development (AMED): Practical Research Project for Rare Diseases)**

Prof. Taketoshi Maehara, M.D., Ph.D.

Affiliation: Department of Neurosurgery, Tokyo Medical and Dental University

Position: Professor

Prof. Akiyoshi Kakita, M.D., Ph.D.

Affiliation: Department of Pathology, Brain Research Institute, Niigata University

Position: Professor

Prof. Yukihiro Ohno, Ph.D.

Affiliation: Laboratory of Pharmacology, Osaka University of Pharmaceutical Sciences

Position: Professor

**The establishment of diagnostic criteria and treatment for post-stroke epilepsy patients.
(AMED: Practical Research Project for Life-Style related Diseases including Cardiovascular Diseases and Diabetes Mellitus)**

Dr. Masafumi Ihara, M.D., Ph.D.

Affiliation: Department of Stroke and Cerebrovascular Diseases, National Cerebral and Cardiovascular Center

Position: Director, Cerebrovascular Medicine and Neurology

Clinical activities

1) Outpatient Epilepsy Clinic. Promoting cooperation between hospitals and clinics for epilepsy care

As a team of specialists, we have made full efforts to provide the best care to patients suffering from epilepsy or movement disorders. Until recently, epilepsy has been recognized as a childhood-onset disease. However, with the advent of a superaging society, epilepsy that develops in the middle-aged or elderly has become a current problem in Japan. In addition, the number of the hospitals and physicians that can offer the epilepsy care is not adequate. Moreover, it is unclear which department, neurology, neurosurgery, or psychiatry, is in charge for the adult epilepsy service. In order to offer the optimal epilepsy care, it is very important to establish the cooperation model among general physicians and epilepsy specialists for epilepsy care like that in European and North American countries. As a tertiary care institute for epilepsy in Kyoto, we have led cooperation among primary, secondary and tertiary facilities in the Kinki district (esp. in Kyoto-Shiga region) to provide a comprehensive epilepsy service with a dedicated team of neurologists, neurosurgeons, pediatricians and psychiatrists.

In the fiscal year 2015, we saw 1008 outpatients. 299 patients were newly consulted from other hospitals and clinics in the Kinki district. We promoted hospital-clinic cooperation by returning the referral patients to their local clinics and hospitals.

2) Inpatient evaluation and treatment for epilepsy (including video-EEG monitoring)

Since 1991, we have been running the epilepsy monitoring unit (EMU) in the Neurology Ward for evaluation of patients with epilepsy. We now have two dedicated rooms for EMU, equipped with the digital video-EEG system.

By capturing seizures with simultaneous video and EEG recording, we can perform

- i) An accurate diagnosis of epilepsy: To determine whether the seizure is epileptic or non-epileptic, including movement or psychogenic disorders,
- ii) Identification of epileptic focus: To locate the epileptic focus for epilepsy surgery in patients with medically intractable epilepsy.

In the fiscal year 2015, we examined 40 patients in the EMU (subdural/depth electrode implantation: 3, presurgical evaluation: 15, evaluation of limbic encephalitis: 5, diagnosis of epilepsy: 17).

In addition, we provide patients with multidisciplinary studies for comprehensive evaluation, such as 3 tesla MRI, routine EEG, FDG-PET/SPECT, MEG and neuropsychological testing. Routine EEGs were performed in 1231 patients (including 869 outpatients) in this fiscal year.

3) Epilepsy Surgery

We have established an epilepsy surgery program with close collaboration with the Department of Neurosurgery since 1991. Since the first epilepsy surgery in 1992, we have performed more than 190 epilepsy surgeries, with the majority of patients having seizure freedom or substantial decrease leading to better QOL. We provide each patient with the individually tailored surgery plan by incorporating the findings of the multimodal studies (see below) as well as the Wada test. The patients may proceed to the invasive presurgical evaluation with intracranial electrodes (subdural and/or depth electrodes) when the epileptic focus cannot be precisely localized (such as in cases with non-lesional MRI) or the focus is located at or around the functionally important areas such as motor or language cortices. In such cases, the patients undergo the first surgery for implantation of intracranial electrodes. After electrode implantation, the patients are evaluated for the epileptic focus (by recording seizures) and the functional cortical areas (by incorporating the state-of-art mapping techniques) for 1-2 weeks. Then, the patients undergo the second surgery for resection of the epileptic focus. The patients may undergo the awake brain surgery, where the patients wake up from anesthesia if necessary. Awake surgery has the advantage to evaluate the brain functions such as motor and language during resection and monitor the 'natural' epileptic spikes without any influence from anesthetics. In the fiscal 2015, our team performed epilepsy surgery in 8 patients (3 with chronic intracranial electrode implantation) and awake brain surgery about 24 patients (including non-epilepsy cases).

4) Examinations for epilepsy

As the tertiary care epilepsy facility, we provide patients with the state-of-arts studies for the evaluation of epilepsy. As the comprehensive epilepsy program in the national university hospital, we incorporate the leading techniques as clinical research studies (IRB approved) for the optimal presurgical evaluations.

- Electroencephalography (EEG)
- Magnetoencephalography (MEG)
- FDG-PET (18F-fluorodeoxyglucose positron emission tomography)
SPECT (Single photon emission computed tomography) including ictal SPECT
- 3 tesla MRI
- functional MRI (fMRI)
- EEG-fMRI (simultaneous EEG and functional MRI recording)
- Neuropsychological testing (WAIS-III, WMS-R, WAB, semantic batteries and Kanji/Kana related tasks)
- invasive EEG monitoring with intracranial electrodes

Recently, autoimmune epilepsy is regarded as one of the important cause of epilepsy. Following tests are diagnostic for autoimmune epilepsy.

- Cerebrospinal fluid / serum antibody test

5) Development of novel treatments for epilepsy

- i) Interventional Neurophysiology: Recently, neurophysiology has been highlighted for its application to treatment of various neurological diseases. In our hospital, we apply a novel interventional neurophysiology method, neurofeedback treatment, to medically intractable patients in whom epilepsy surgery is not applicable. Patients train themselves to control the brain activity (by adjusting slow EEG potentials) to suppress epileptic seizure activity. Our preliminary study shows a good efficacy as comparable to that for the Vagus Nerve Stimulation.
- ii) Promoting the clinical trials for new anti-epileptic drugs.

6) Diagnosis and treatment for movement disorders

It is also our mission to provide the optimal care for patients with movement disorders. We provide precise diagnosis using advanced diagnostic tools for better treatment of movement disorders such as tremor, myoclonus, dystonia and other involuntary movements.

The pathophysiology of movement disorders, however, is not fully understood. We have been investigating their pathophysiology and treatment in close collaboration with the Department of Neurology and Human Brain Research Center (HBRC).

7) Simulation training of brain death determination

Since Organ Transplant Law went into force in 1997, we, in close collaboration with the affiliated departments, have been regularly practicing the course 'Simulation-based training in brain death determination'. In this course, we simulate the management about how and what to do when the donor is found and until organs are taken. The training is highly practical for those in charge of brain death determination in our hospital. In the fiscal 2015, we participated in the first case of brain death determination of Kyoto University Hospital in close collaboration with many affiliated departments.



京都大学大学院医学研究科 / 京都大学医学部附属病院神経内科 寄附講座

てんかん・運動異常生理学講座

Department of Epilepsy, Movement Disorders and Physiology

HOME | サイトマップ

English

検索



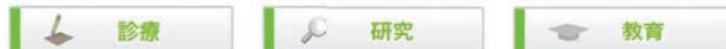
- HOME
- ご挨拶
- 診療内容
- メンバー
- 研究
- 業績
- 教育
- 年次報告書 Annual Report
- リンク



てんかん・運動異常生理学講座の御紹介

本講座では、以下を設置理由および目的として、京都大学医学研究科に寄附講座として、平成25年8月1日に設立されました。本学の臨床神経学講座(高橋良輔教授)より支援講座としての御支援をうけながら、以下を目指します、

- 1) 集学的立場から、てんかんおよび運動異常症の病態解明と治療の開発、高度先進医療の推進、実践医療としての確立と普及を目指す。同時に、将来の本分野の担い手となる専門医と臨床研究者の養成と教育機会を国内外に広く提供します。
- 2) 臨床てんかん学の病態と治療と常に表裏一体関係である生理学の研究と臨床応用の発展を、大学病院の立場から推進します。



お知らせ

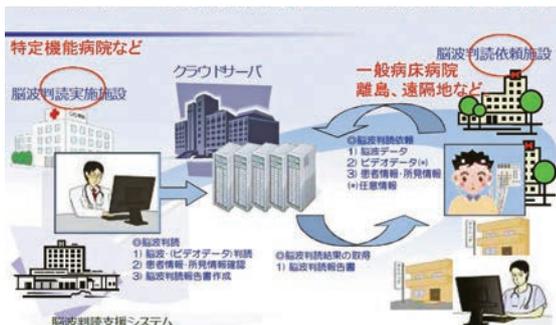
Video EEG monitoring room



EEG conference



デジタル脳波判読の遠隔診断
データ通信での判読、患者負担なし、正確な診断と迅速な対応



(reprint permission from Nihon Koden)

Annual course 'Simulation-based training in brain death determination' in Kyoto University Hospital



Educational activities

1) Offering the optimal education and research to Japanese and foreign physicians

■ EEG/Epilepsy fellowship

With great support by the Department of Neurology, we have set up the EEG/Epilepsy fellowship for training young neurologists, neurosurgeons, pediatricians, and psychiatrists. Four adult neurologists, one pediatric neurologist, and one neurosurgeon have already completed this fellowship. Our education covers various fields of epileptology with a focus on clinical neurophysiology. We plan to welcome foreign young doctors for fellowship training as well.

Contents of the fellowship program are listed as follows;

- 1) Training of routine EEG reading (emergency EEG as well)
- 2) Analysis of the long-term video-EEG monitoring for diagnosis and presurgical evaluation
- 3) Clinical practice of adult epilepsy
- 4) Training of medical treatment with anti-epileptic drugs

Graduates of EEG/Epilepsy fellowship

Reiko Tsuda (from June 2011 to August 2011)

Daiki Fujii (from September 2014 to November 2014)

Takeshi Inoue (from April 2013 to March 2016)

Hajime Yoshimura (from July 2015 to September 2015)

Tsuyoshi Tsukada (from October 2015 to March 2016)

Current Trainee of EEG/Epilepsy fellowship

Daiki Fujii (from February 2016 -)

Masayuki Honda (from April 2016 -)

■ Intramural, multidisciplinary monthly case conference

In cooperation of the Departments of Neurology, Neurosurgery, Pediatrics, Diagnostic Radiology, Psychiatry, Rehabilitation, and Clinical Laboratory Medicine, and Human Brain Research Center, we have been holding the intramural, multidisciplinary monthly case conference for more than a decade. In the conference, we discuss the diagnosis and surgical indication of epilepsy patients for comprehensive epilepsy practice as a tertiary epilepsy special facility. The numbers of participants and the discussion cases are getting larger. As a training facility certified by Japan Epilepsy Society (JES), this conference is open for doctors outside the hospital to discuss their problem case or to obtain the credit to apply board examination of JES-certified epileptologist.

■ EEG conferences and so on

For our graduate students and EEG/Epilepsy fellows, we have been offering multifaceted educational and research trainings, such as EEG reading skills in EEG conferences twice a week, seeing outpatients and inpatients with staffs, and epilepsy/clinical neurophysiology researches. One EEG conference and research conference are held in English for training skills in English presentation. The other conference is held in Japanese and open for the in-hospital technicians and out-hospital doctors for providing them with training opportunities for the practical basic EEG reading skills (about 30-40 participants).

■ Specialist training

In the fiscal year 2015, our department produced one board-certified epileptologist (JES).

■ Extramural workshops

Regarding educational activities outside the institute, as the secretary office in general, we have organized the district EEG & EMG teaching course for the young doctors and technicians in Kansai (Kansai EEG & EMG workshop) every year since 2008. In 2015, we newly founded and organized the EEG seminar advanced course for the purpose of acquisition of specialized knowledge and reading skills in clinical EEG sponsored by the Japanese Society of Clinical Neurophysiology. We also have provided educational activities by complying the request of lectures nationwide (please refer to the achievements for details). Both staffs regularly teach EEG reading and epileptology at the affiliated hospitals.

■ EEG/Epilepsy lecture series

We have been holding the intensive lecture series of the basics of EEG and epileptology for EEG/Epilepsy fellows and young doctors.

2) Offering medical staffs' education for caring of epilepsy patients

In the Kyoto University Hospital, we have offered education for epilepsy and related disorders to doctors and medical staffs. For the medical staffs in the Neurology clinic and ward, we hold comprehensive monthly lectures about pathophysiology of epilepsy, seizure semiology, and medical care of patients living with epilepsy.

3) Providing patients, family and society with valuable information

We have responded to the request by the patients, family, and society in cooperation with Japan Epilepsy Association. For example, we have joined the lectures sponsored by Japan Epilepsy Association for the public, and also the continuing medical education lectures for physicians by Japan Medical Association.

Interdisciplinary monthly case conference



Interdisciplinary monthly case conference



EEG/Epilepsy lecture series



EEG reading room (Department of Neurology)



Recruitment of EEG/Epilepsy fellowship



京都大学神経内科
EEG/Epilepsy Fellowship 募集

- 1.対象 卒後4年目以降の段階の神経内科、脳外科、小児科、精神科等の若手医師
- 2.専門研修内容
 - i. 幅広い脳波判読の研修と経験
 - ii. 長時間ビデオ脳波モニターの解析
 - iii. てんかんの診療
 - iv. 各種抗てんかん薬の臨床研修
- 3.期間 単年度単位で1年間（より短期研修も希望に応じて可能）
- 4.処遇 非常勤医師待遇

少しでも興味がある方は、一度是非ご連絡ください

連絡先：京都大学神経内科事務室、担当：松本理器、池田昭夫
tel: 075-751-3771, fax: 075-751-3265, email: neuroofc@kuhp.kyoto-u.ac.jp

Research grants obtained from extramural sources & awards

The ministry of Education, Culture, Sports, Science and Technology of Japan Grant-in-Aids for Scientific Research (KAKENHI)

Fiscal years 2015 – 2019
Grant-in-Aid for Scientific Research on Innovative Areas (Non-linear Oscillology)
Principal investigator: Akio Ikeda
Subject number: 15H05874

Fiscal years 2015 – 2016
Grant-in-Aid for Scientific Research on Innovative Areas (Embodied Brain Systems Science)
Principal investigator: Riki Matsumoto
Subject number: 15H01664

Fiscal years 2014 – 2016
Grant-in-Aid for Scientific Research (B)
Principal investigator: Akio Ikeda
Subject number: 26293209

Fiscal years 2014 – 2017
Grant-in-Aid for Scientific Research (B)
Principal investigator: Riki Matsumoto
Subject number: 26282218

Health Labour Sciences Research Grant

Fiscal years 2014 – 2016
Principal investigator: Yushi Inoue
Co-investigator: Akio Ikeda
Subject number: H26 - 難治等 - 一般 - 051

Japan Agency for Medical Research and Development (AMED)

Fiscal years 2015 – 2017
Co-investigator: Akio Ikeda
Subject number: 15ek0109120h0001

Fiscal years 2016 – 2017
Co-investigator: Akio Ikeda
Subject number: 16ek0210057h0001

Others

The Japan Epilepsy Research Foundation Research Grant
Fiscal years 2014 – 2016
Principal investigator: Riki Matsumoto

The Japan Epilepsy Research Foundation Research Grant
Fiscal years 2014 – 2016
Principal investigator: Tomoyuki Fumuro

Awards

Akio Ikeda: Masakazu Seino Memorial Lecture
The 11th Asian & Oceanian Epilepsy Congress (AOEC), Hong Kong, May 2016

Riki Matsumoto, Takeharu Kunieda: The Japan Epilepsy Research Foundation Research Award 2016



Society-academia collaboration

As society-academia collaboration, both collaborative study and teaching seminar were conducted. All activities were conducted with the companies under the regulation of Kyoto University Graduate School of Medicine and University Hospital and under the regulation of Japanese law. Therefore, the detailed English version was not made, and please refer to the Japanese part of this report in details.

Only the name of company and the content of collaboration were listed as follows.

1) Collaborative study

GlaxoSmithKline K.K.

Clinical study of drug exchange from Valproic acid to Lamotrigine

NIHON KOHDEN CORPORATION

- 1) Analysis system of wide-band EEG in clinical EEG
- 2) Clinical and technical establishment of remote reading system of digital EEG in Japan
- 3) Optimal condition of high frequency cortical stimulation in cortical mapping

UCB Japan Co., Ltd.

Phase III clinical trial of Lacosamide

2) Teaching seminars

UCB Japan Co., Ltd.

Clinical epilepsy seminar in Kinki district area: a whole day course in 2014 and 2015

VI Attached materials

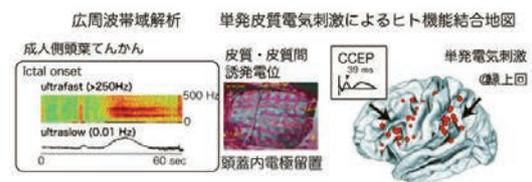
Collaborative research activity in the Grant-in-Aid for Scientific Research on Innovative Areas: Non-linear Neuro-oscillology - Towards Integrative Understanding of Human Nature.

This five-year innovative research program is led by Prof. Atsushi Nambu (National Institute for Physiological Sciences, Division of System Neurophysiology) and aims to create a new academic field of Neuro-oscillology, which enables us to understand human nature. We will devote ourselves to researches on wideband-EEG oscillations to understand the human nature and network diseases such as epilepsy (Research Project A03: Principal Investigator Akio Ikeda) and to collaboration with the researchers of other fields including mathematical modeling, intervention and Exploration groups.

Homepage: <http://www.nips.ac.jp/oscillology/>

A03 ヒト脳発振現象の直接記録

ヒト脳機能は多次元・多階層の発振現象の非線形相互作用により発現する。一方、脳機能の異常発現も作動原理の根本は共通し、てんかんは、自律的な脳ネットワークが突発的に種々の次元・階層で過剰発振する「ネットワーク病」と捉えられる。本研究計画では、正常脳機能およびてんかん発作発現にかかわる局所および広域の集団発振現象をヒト脳からの直接記録で探索する。



空間的観点からは、局所神経回路(細胞外多電極記録)からシステムレベル(皮質脳波、頭皮上脳波、脳磁図)で、発達過程の観点からは、ヒトの乳児・小児・成人脳および動物モデルで比較検討する。B班と連携し、記録データからの数理モデルを構築し、正常振動現象および病態下の異常発振の作動原理と制御機構の解明を目指す。C班と連携し、外的および内的な振動制御の手法を用いて、突発性振動異常の制御を試み、介入による多次元・多階層での生理的・病的振動の変容機構を明らかにする。



研究代表者	池田 昭夫 京都大学大学院 医学研究科 てんかん運動異常生理学
研究分担者	小林 勝弘 岡山大学 医学部 小児神経学
	長峯 隆 札幌医科大学 医学部 神経科学
	松本 理器 京都大学大学院 医学研究科 てんかん運動異常生理学
	國枝 武治 京都大学大学院 医学研究科 脳神経外科学
研究協力者	小林勝哉 京都大学大学院 医学研究科 臨床神経学

HP: <http://epilepsy.med.kyoto-u.ac.jp/>



2nd group meeting (June 27th-28th, 2016, Sapporo)

9th electroencephalography (EEG) and electromyography (EMG) seminar

January 30th, 2016, Kyoto University

The 1st EEG and EMG seminar was held in February 2008 in Kyoto in order to acquire and improve the basic knowledge and techniques of clinical neurophysiological studies. From the 2nd EEG and EMG seminar, this seminar became a training session related to Japanese Society of Clinical Neurophysiology. Since then, the seminar has been held every winter in Kyoto. Our department served as the secretary office of this seminar. About 150 participants attended comprehensive lectures and hands-on about clinical neurophysiological studies.



1st advance course of electroencephalography (EEG) seminar

August 8th-9th, 2015, Shirankaikan and Shirankaikan Annex

The advance course of electroencephalography (EEG) seminar was founded by Japanese Society of Clinical Neurophysiology (A committee of advance course of electroencephalography (EEG) seminar: Chair Akio Ikeda) in order to acquire specialized knowledge and technique about clinical EEG. The seminar adopted ANZAN (Australian-New Zealand Association of Neurology) style which consists of 8 sessions, and each session consists of lecture (30 min) followed by practical hands-on related to lecture (60 min). About 50 participants deepened their knowledge about recording and reading of clinical EEG.

EEG samples were prepared by the courtesy of ANZAN (Prof. Andrew Bleasel, Prof. Earnest Somerville, Prof. John W. Dunne, and Prof. Nicholas Lawn).



104th Kinki Regional Division of Japanese Society of Neurology

March 6th, 2016, Senri Life Science Center, President Akio Ikeda



Epilepsy Lectures in Autumn 2015, Kyoto

October 26th, 2015, Shirankaikan Annex

We invited Prof. Solomon Moshé (Albert Einstein College of Medicine, ILAE past president) and Prof. Gary Mathern (UCLA, Epilepsia Chief Editor) to give special lectures before the annual meeting of the Japan Epilepsy Society.



5th Masakazu Seino Memorial Lecture

May 13th, 2016, Hong Kong

Prof. Akio Ikeda gave Masakazu Seino Memorial Lecture in the 11th Asian & Oceanian Epilepsy Congress (AOEC).

5th Masakazu Seino Memorial Lecture



Lecturer:

Prof Akio Ikeda

Kyoto, Japan

*"Exploring the mysteries of EEG:
can infraslow and DC shift
improve epilepsy treatment?"*

Chairman:

Dr Shih-Hui Lim

Singapore



Visiting physicians

[Overseas]

October 26th, 2015

Prof. Gary Mathern (Epilepsia, Chief editor)

Affiliation: Neurological Surgery, UCLA-David Geffen School of Medicine

Position: Professor

Prof. Solomon Moshé (ILAE, past president)

Affiliation: Charles Frost Chair In Neurosurgery and Neurology

Professor of Neurology, Neuroscience & Pediatrics

Vice-Chair, Dept. of Neurology

Director Pediatric Neurology

Director Clinical Neurophysiology

Albert Einstein College of Medicine and Montefiore Medical Center

January 20th, 2016

Prof. Matthew A. Lambon-Ralph, FRSLT (hons), FBPsS

Affiliation: The University of Manchester

Position: Professor of Cognitive Neuroscience & Associate Vice-President (Research)

February 22nd, 2016

Dr. Junji Ito

Affiliation: Institute of Neuroscience and Medicine, Computational and Systems Neuroscience & Institute for Advanced Simulation, Theoretical Neuroscience, Research Centre Jülich, Germany

Position: PostDoc

Prof. Sonja Gruen

Affiliation: Institute of Neuroscience and Medicine, Computational and Systems Neuroscience & Institute for Advanced Simulation, Theoretical Neuroscience, Research Centre Jülich, Germany

Position: Professor

July 20th, 2016

Prof. Michel Thiebaut de Schotten, PhD, CR2 CNRS

Affiliation: Brain Connectivity and Behaviour Group

FrontLab, Brain and Spine Institute

ICM, Hôpital Pitié-Salpêtrière, Paris, FRANCE

Position: Associate Professor

[Domestic]

December 21st, 2015

Yoshio Sakurai, Ph.D

Affiliation: Laboratory of Neural Information, Graduate School of Brain Science, Doshisha University

Position: Professor

February 3rd, 2016

Hiroshi Imamizu, M.D., Ph.D.

Affiliation: Department of Psychology, The University of Tokyo

Position: Professor

March 15th – 16th, 2016

Prof. Ichiro Tsuda, Ph.D.

Affiliation: Department of Mathematics, Hokkaido University

Position: Professor

Prof. Toshio Aoyagi, Ph.D.

Affiliation: Department of Applied Analysis and Complex Dynamical Systems, Kyoto University

Position: Professor

Dr. Keiichi Kitajo, Ph.D.

Affiliation: Rhythm-based Brain Information Processing Unit, BTCC

Position: Unit Leader

Prof. Katsunori Kitano, Ph.D.

Affiliation: Department of Human and Computer Intelligence, Ritsumeikan University

Position: Professor

Yutaka Yamaguti, Ph.D.

Affiliation: Fukuoka Institute of Technology

Position: Assistant Professor

Takao Namiki, Ph.D.

Affiliation: Department of Mathematics, Hokkaido University

Position: Associate Professor

Jiro Okuda, Ph.D.

Affiliation: Department of Intelligent Systems, Faculty of Computer Science and Engineering, Kyoto Sangyo University

Position: Professor

Akihiro Yamaguchi, Ph.D.

Affiliation: Fukuoka Institute of Technology

Position: Associate Professor

Satoru Tadokoro

Affiliation: Department of Mathematics, Hokkaido University

Position: Research Fellow

Keiko Usui, M.D., Ph.D.

Affiliation: Department of Systems Neuroscience, Sapporo Medical University

Position: Lecturer

March 30th, 2016

Kouichi Nakamura, Ph.D.

Affiliation: Department of Morphological Brain Science, Graduate School of Medicine, Kyoto University

Position: Assistant Professor

March 31st, 2016

Kohei Nakajima, Ph.D.

Affiliation: The Hakubi Center for Advanced Research & Graduate School of Informatics, Kyoto University

Position: Assistant Professor

April 6th, 2016

Eiichi Naito, Ph.D.

Affiliation: Brain Networks and Communication Laboratory, Center for Information and Neural Networks (CiNet), National Institute of Information and Communications Technology (NICT)

Position: Research Manager

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Department of Epilepsy, Movement Disorders and Physiology
Kyoto University Graduate School of Medicine

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