

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 2015

> > 2015年8月

<表紙の言葉>

表紙のデザインは,波形様の曲線と異なる色彩からなります.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, which may remind you of brain waveforms and different frequencies. Hoping to enjoy EEG wave surfing.

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Preface

Since one year has past after we have issued the first annual report of the Department of Epilepsy, Movement Disorders and Physiology, Kyoto University Graduate School of Medicine in 2014, it is again my great honor and pleasure that we could issue the second annual report. We appreciate very much all of you who kindly gave the very important comments and suggestion, upon the first annual reports from all over the place.

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 Human Brain Research Center (Prof. Hidenao Fukuyama) 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.

Upon the completion of the second 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 strong support to our activity. Without their support, 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.

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 2015

With my best wishes,

& Abeda

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

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To begin with

The details of the annual report in each aspect are shown in the following pages as done in the first annul 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 sate for epilepsy
- 2) "Oscillology": Launching of the new research field in Japan
- 3) EEG/ Epilepsy fellowship in Kyoto University Hospital
- 4) Teaching session
- 5) Innovated EEG: "New wine, what you put into new leather bag"
- 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 for better understanding of epilepsy, it is now recognized one of the most representative disorders of clinical neuroscience for both neurology and neuropsychiatry. It is 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/
- 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 great help of Department of Neurology (Prof. Takahashi), and 1-2 fellows have been always employed so far. As for clinical care in the second year, more than that of the first year, we tried to contribute to the activity of the Kyoto University Hospital and Graduate School of Medicine, as much as possible, by conduct 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 Japanese Society of Epilepsy.
- 5) "New wine, what you put into new leather bag". Clinical EEG has the history of more than 80 years since the clinical application after the first recording from humans by Prof. Hans Berger in 1920s. In the 21st century, clinical EEG is now in the era of "wide band EEG" to record from extremely low or even DC shifts to extremely fast activity by means of technological advancement, in the daily clinical situation from patents. It could delineate or reflect the activity of glia as well as at least partly action potentials, respectively. It was by no means imagined in the last century as the clinical EEG. It is also the same for CCEPs. By keeping the basic concept that EEG reflects the neuronal (and glial) electrophysiological activity from cellular level to system level, EEG will provide us with essential information by employing the new methods and techniques constantly.

Namely, "New wine (= evolutionally new findings), what you put into new leather bag (=new technology and methodology)." (It may be similar to the Japanese concept hidden in the tradition of "Regular Shrine Removal.")

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



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 neurphysiological 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 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.

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Members of this Department and Affiliated Persons

Members of Department of Epilepsy, Movement Disorders and Physiology

Professor Associate Professor Secretary

Akio Ikeda, M.D., Ph.D. Riki Matsumoto, M.D., Ph.D.

Miki Watanabe

Visiting Scientist

Kiyohide Usami, M.D. (Dept. of Neurology, Rakuwakai Otowa Hospital, Nov. 2014-) Tomoyuki Fumuro, Ph.D. (Dept. of Medical Technology and Sciences, School of Health Sciences at Fukuoka, International University of Health and Welfare, Mar. 2015-)

Affiliated members from Department of Neurology

Assistant Professor Akihiro Shimotake, M.D., Ph.D. Medical Staff Katsuya Kobayashi, M.D., Ph.D.

Graduate Students (Doctoral course)

- D4 B. Bayasgalan T. Sakurai D3 M. Ota
- Kei Sato
 - H. Takeyama

D2 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, Apr. 2015 -)

D1 Kazuaki Sato (Apr. 2015 -) K. Tanioka (Apr. 2015 -) M. Togo (Apr. 2015 -) M. Sakamoto (May 2015 -) Graduate Student (Master's course) M1 Shamima Sultana (Apr. 2015 -)

EEG/Epilepsy fellowship T. Inoue (Apr. 2013 -) D. Fujii (Sep. 2014 - Nov. 2014) H. Yoshimura (Jul. 2015 - Sep. 2015)

Affiliated members Department of Neurosurgery Senior Lecturer T. Kunieda, 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.





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 system 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), Bereitscheftspotentials (BPs), cortico-cortical network, movement disorders, sleep disorders, autoimmune epilepsy, wideband EEG

Unique key words: ictal DC shifts, cortico-cortical evoked potentials (CCEP), cortical tremor, ictal apraxia, ictal paresis

1) Pathophysiology of medically intractable epilepsy and its treatment

a) Shaping presurgical evaluations for intractable epilepsy

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.

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. We have extensively made multidisciplinary approaches with MEG, EEG-fMRI 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 (wideband EEG), ranging from direct current shifts (DC shifts) to high frequency oscillation (HFO). In our recent report, several features of ictal DC shifts and HFOs were extracted in 16 patients who underwent chronic intracranial recording below (Fig. 1) (Kanazawa et al., 2014).

- 1) Sensitivity and reproducibility: Ictal DC shifts were identified in 12 out of 16 patients. In these 12 patients, ictal DC shifts occurred in 71.3% of all seizures on average.
- 2) Temporal profile: Out of seven patients with ictal DC shifts and HFOs together, five patients showed DC shifts preceding HFOs with statistical significance.
- 3) Spatial profile: In 15 patients with conventional ictal pattern, 12 patients showed DC shifts and/or HFOs. Among them, DC shifts and HFOs were observed in more restricted area than conventional ictal pattern. Mean number of electrodes showing DC, HFO and conventional ictal pattern were 9.0±11.5, 10.4±8.4 and 16.3±17.2, respectively. In one patient, DC shifts were recorded from the depth electrode in the white matter, but HFOs were not recorded.
- 4) Relevance to pathological findings: DC shifts were identified in ① 75% (3/4) of glioma, ② 77.8% (7/9) of cortical dysplasia and ④ 50% (1/2) of hippocampal sclerosis. On the other hand, HFOs were in ① 50% (2/4), ② 44.4% (4/9), ③ 50% (1/2).

We have been applying such a wideband EEG technology (ictal/interictal DC shift and HFO) to further localize the



Figure 1. Onset times of ictal DC shifts (red) and HFOs (black) relative to conventional change. Patient 3 showed no conventional ictal change, and ictal DC shift onsets are plotted relative to HFO onsets, which are set to time 0. Ictal DC shifts tended to occur earlier than HFOs. In five out of seven patients with both ictal DC shifts and HFOs, the onset difference was statistically significant (Kanazawa et al., 2015)

core epileptogenic zone for epilepsy surgery.

An *in vivo* electrical tract tracing method by cortico-cortical evoked potentials (CCEPs) is an exciting new technique for presurgical cortical mapping developed in Cleveland Clinic and Kyoto University. By means of subdural electrodes implanted for presurgical evaluation, electrical pulses (0.3-ms duration, frequency of 1 Hz, alternating polarity, 1–10 mA) are directly delivered to the cortex, 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 for treatment of epilepsy

As described above, EEG-fMRI could evaluate the whole brain including the subcortical structures. Using this technique, we have been studying the pathological basis of praxis-induced epilepsies and symptomatic epilepsy caused by hypothalamic hamartoma, a model of subcortical epilepsy and epileptic encephalopathy.

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 means of comprehensive study such as video-EEG monitoring (VEEG), neuropsychological tests, FDG-PET and MRI, we have revealed the smoldering nature of the autoimmune limbic encephalitis (Fig. 2). 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).

Interestingly, LGI1 antibody and *LGI1* gene mutation present different phenotypes: LGI1 antibody could mediate autoimmune limbic encephalitis whereas *LGI1* is the causative gene for autosomal dominant lateral temporal lobe epilepsy (ADLTE). We established *Lgi1* heterozygous mutant rats (*Lgi1*^{L385R/+}) as an animal model of ADLTE in close cooperation with the Institute of Laboratory Animals, and are currently promoting the project with Prof. Ono's lab in Osaka University of Pharmaceutical Sciences.

In collaboration with the Department of Pharmacy in Kyoto University Hospital, we have extensively investigated the effect of the gene polymorphism to tailor dosage of antiepileptic medication, such as CYP2C19 polymorphism for efficacy of clobazam.



Figure 2. A patient with autoimmune encephalitis (positive for anti-VGKC complex antibodies) in our institute. Imaging: Initial MRI and FDG-PET revealed abnormal intensity/swelling and hypermetabolism in the bilateral mesial temporal lobes, respectively (arrow heads). Later, the bilateral mesial temporal lobes had become atrophic on MRI and showed improved hypermetabolism on FDG-PET gradually (top). Clinical course: the symptoms fluctuated and prolonged despite of infrequent clinical seizure (middle). Subclinical EEG seizure pattern: rhythmic activities evolve into lower frequency in the right temporal area (bottom). The occurrence rate of EEG seizure patterns corresponded to activity of encephalitis. (Kanazawa et al., 2014)

As an interventional neurophysiology, we have introduced neuro-feedback therapy for patients with intractable epilepsy. Using the DC-EEG machine, we have performed clinical trials in which the patients learn to regulate their slow cortical potential (SCP) and thereby decrease their cortical excitability. The neuro-feedback therapy is side-effect free and regarded as one of the promising alternative therapies.

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

We now try to elucidate the mechanism of vagus nerve stimulation for seizure reduction in collaboration with Kinki University (Prof. Kato) and Hiroshima University (Prof. Iida).

c) Advanced EEG analysis

EEG now has a history of more than 80 years for evaluation of brain functions and diagnosis of brain diseases,

III. Activity report Research activities

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.

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, semantic cognition, motor control) 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 (\sim 5 s), discretely focal (\sim 1 cm²), and in sharp contrast to chronic stroke lesions those 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 event-related potential, Bereitschaftspotential (BP) and high frequency oscillation/activity. Recently, we investigated the role of the basal temporal language area (BTLA) using a comprehensive approach (Shimotake et al., 2014). Discrete local field potentials were observed in BTLA while participants completed semantic tasks. Electrical stimulation 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 (Fig. 3). Furthermore, high frequency electrical stimulation to the area is also related to semantic processing of humor (Yamao et al., 2014).

We incorporate cortico-cortical evoked potentials (CCEPs) to probe inter-areal functional connectivity in order to perform 'system mapping.' For example, in close collaboration with the Department of Neurosurgery, we have applied CCEP intraoperatively to monitor the integrity of the dorsal language pathway. In this novel approach, we first define the anterior perisylvian language area (AL) according to presurgical anatomical/functional neuroimaging findings and CCEP connectivity patterns under general anesthesia. We then monitor the integrity of the language network by stimulating AL and by recording CCEPs from the posterior perisylvian language area consecutively during resection of the tumor in the vicinity of the arcuate fasciculus (Yamao et al., Hum Brain Mapp 2014, selected as the Editor's Choice Award 2014). 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. This year, by comparing neural oscillations (high frequency activities, HFA >80 Hz) induced either by direct single-pulse cortical stimulation or peripheral median nerve stimulation, we elucidated that different propagation modes and/or different terminal layers determine HFA frequency bands (Kobayashi et al., 2015).

We have demonstrated the central mechanisms and functional alteration under pathological condition relevant to i) the motor control (conflict processing, negative motor phenomena, praxis and reaching), 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 evaluations (functional MRI, diffusion tractography, MEG, neuropsychology). Additionally, we are now tackling with decoding of complex neural signals during various tasks in



Figure 3. Comprehensive mapping of the basal temporal language/semantic area

A. Language mapping with conventional, gualitative high frequency cortical stimulation. In this representative case, high frequency cortical stimulation was delivered to the left basal temporal lobe while the patient completed various language tasks. Impairment of the tasks (arrest or slowing) was investigated during stimulation. The black oval denotes the core region of the basal temporal language areas (BTLA) defined by high frequency electrical stimulation and local field potentials obtained during naming. B. The six spheres in different colors on the ventral view of the left hemisphere of standard MNI space shows the each core region of BTLA in six patients (upper figure). Note their locations are consistent with activation areas in semantic functional neuroimaging studies of normal volunteers (lower figure). The representative local field potential (Patient 4) shows the clear positive activity for synonym judgment (its processing supposedly requires access to semantic memory) while no apparent activity for the control task of number size judgment. C. Quantitive assessment by cortical stimulation. Electrical cortical stimulation with weaker intensity was delivered to the same core region of BTLA, time-locked to the task. It produced significant slowing in synonym judgment and picture naming tasks where semantic processing was required. In contrast, the reaction time of the number size judgment task was not affected. Taken together with the local field potential recording, the finding of quantitative electrical cortical stimulation suggest the active role of BTLA in semantic processing. (modified from Shimotake et al., 2014 with permission)

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 4-year activity of international/domestic neural oscillation conference led to launching 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). Under the leadership of Prof. Atsushi Nambu at the National Institute for Physiological Sciences, Professor Ikeda will manage the research project A01 on "the Direct Recording of Human Neural Oscillations".

3) Pathogenesis of movement disorders and its treatment

We have investigated movement disorders, mainly myoclonus and myoclonus epilepsy, by way of epidemiological, genetical 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,

III. Activity report Research activities

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 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. 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 (Fig. 4: right).

Unverricht-Lundborg disease (ULD) is the most common form of progressive myoclonus epilepsy syndrome (PME)



Figure 4. Regional distribution of PME and BAFME in Japan investigated by the nationwide questionnaire. There is no regional clustering in both diseases.



Figure 5. Correlation between the age at SEP recording and its amplitudes in 7 ULD patients. Values of P25 and N35, and the gradients of their temporal changes drawn by calculating the averaged value of the ages and amplitudes between previous and present SEP recordings (black lines) in 7 patients are compared with linear regression curves of 19 healthy subjects (gray lines). P25 and N35 amplitudes were larger in ULD patients. As for the components associated with giant SEP (i.e., P25 and N35), 7 ULD patients showed a tendency of slight decrease in amplitude during the follow-up period, and the degree of its tendency was even lower than that of healthy subjects.

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 (Fig. 5) (Kobayashi et al., 2014). Similar to BAFME, PME including ULD also presented no regional clustering in Japan (Fig. 4: left).

Collaborators

Affiliation: Nishi-Niigata Chuo National Hospital

Position: Honorary hospital director

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 Affiliation: INS - Institut de Neurosciences des Systèmes, UMR INSERM 1106, Aix-Marseille Université Position: Team leader Dr. Marco Catani, M.D., Ph.D. Affiliation: Natbrain lab, Department of Forensic and Neurod evelopmental Sciences, Institute of Psychiatry, King's College London Position: Clinical Senior Lecturer and Honorary Consultant Psychiatrist Dr. Nathan Earl Crone, M.D. Affiliation: Department of Neurology, Johns Hopkins University School of Medicine Position: Associate Professor Prof. Mattew A. Lambon-Ralph, FRSLT (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 [Domestic] Dr. Koji lida, M.D., Ph.D. Affiliation: Department of Neurosurgery, Hiroshima University Hospital Position: Lecturer 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.

III. Activity report Research activities

Prof. Amami Kato, M.D., Ph.D. Affiliation: Department of Neurosurgery, Kinki University Hospital Position: Professor

Prof. Takashi Nagamine Affiliation: Department of Systems Neuroscience, Sapporo Medical University School of Medicine 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 Conputational neuroscience Labs Position: Department Head

Dr. Satoru Saito, Ph.D. Affiliation: Division of Cognitive Psychology in Education, Kyoto University Graduate School of Education Position: Associate Professor

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

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 Pharmacy, Kyoto University Hospital Position: Deputy director of pharmacy/Associate professor

(Listed in the alphabetical order of their family names)

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 2014, we saw 1092 outpatients. 103 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 2014, we examined 35 patients in the EMU (subdural/depth electrode implantation: 4, presugical evaluation: 24, evaluation of limbic encephalitis: 6, diagnosis of epilepsy: 11).

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 1265 patients (including 906 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 2014, our team performed epilepsy surgery in 14 patients (4 with chronic intracranial electrode implantation) and awake brain surgery about 60 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.



Neuropsychological assessment of semantic memory

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. Three adult neurologists and one pediatric neurologist 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) Current Trainee of EEG/Epilepsy fellowship Takeshi Inoue (from April 2013 -) Hajime Yoshimura (from July 2015 - September 2015)

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 2014, our department produced 5 board-certified epileptologists (JES), and 1 board-certified neurophysiologist (EEG part, Japanese Society of Clinical Neurophysiology).

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. We also have provided educational activities by complying the request of lectures nationwidely (please refer to the achievements for details). Both staffs regularly teach EEG reading and epileptology at the affiliated hospitals.

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

EEG reading room (Department of Neurology)

Lecture for medical staffs in the Neurology clinic



Recruitment of EEG/Epilepsy fellowship



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 Principal investigator: Akio Ikeda Subject number: 15H05874

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

Fiscal years of 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

Fiscal years 2014 - 2015 Grant-in-Aid for Exploratory Research Principal investigator: Riki Matsumoto Subject number: 26560465

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 of 2015 - 2017 Co-investigator: Akio Ikeda Subject number: 15ek0109120h0001

Others

The Japan Epilepsy Research Foundation Fellowship Grant 2015 Kiyohide Usami

Kyoto University Educational & Research Promotion Foundation Fellowship Grant 2015 Kiyohide Usami

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

Riki MatsumotoNov, 2014Encouragement Award (Japan Society of Clinical Neurophysiology)Riki MatsumotoMay, 2015Excellent Teacher (Japan Neurology Society)

Prize-awarded essay Jun 15th, 2015 Human Brain Mapping Editor's Choice Award 2014 Intraoperative dorsal language network mapping by using single-pulse electrical stimulation. Hum Brain Mapp, 2014. 35(9): 4345-61. doi: 10.1002/hbm.22479. Y. Yamao, R. Matsumoto*, T. Kunieda*, Y. Arakawa, K. Kobayashi, K. Usami, S. Shibata, T. Kikuchi, N. Sawamoto, N. Mikuni, A. Ikeda, H. Fukuyama and S. Miyamoto (* co-corresponding authors)

V Attached materials

Conference on Neural Oscillation 2015 and Kick-off of the Grant-in-Aid for Scientific Research on Innovative Areas: The Non-linear Neuro-oscillology - Towards Integrative Understanding of Human Nature.

Since its launch 4 years ago at the Okazaki Conference Center in National Institute of Natural Sciences, the 4th conference on Neural Oscillation was held at Kyoto University as a joint-conference with the 9th Motor Control Conference. The purpose of this conference is to create a new unitary framework for understanding the functional relevance of neural oscillations from single neuron recording and animal models to human non-invasive studies. In this conference, a special lecture or symposiums were arranged for 1) Grounded theory for analyzing neural oscillation data, 2) Kuramoto-model and non-linear oscillators, and 3) Probing motor and higher brain functions from human electrocorticogram: insights from wide-band EEG oscillation. More than 250 researchers participated this year. Young researchers and postgraduate students presented their posters and enjoyed discussion with senior participants.

We are proud to announce that our 4-year collaborative activity in a multidisciplinary group from all over the country led to the launch of the 5-year research fund from the Ministry of Education, Culture, Sports, Science and Technology (MEXT). The Grant-in-Aid for Scientific Research on Innovative Areas: The Non-linear Neuro-Oscillology-Towards Integrative Understanding of Human Nature has been recently launched under the leadership of Prof. Atsushi Nambu at the National Institute for Physiological Sciences (NIPS). In this collaborative framework, 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).

第9回 Motor Control 研究会サテライト国際シンポジウム

神経オシレーションカンファレンス 2015

場所:京都大学時計台講堂国際交流ホール 日程:平成27年6月25日(木)AM10:00-

開催趣旨:

本カンファレンスでは基礎と臨床の研究者が一堂に会して、神経機能の発現に関わるオシレーションの作動原理 について、単一細胞レベルからシステムレベル、理論やモデルまで広く各分野の研究者の方々にご講演いただき、 広く議論して解明していく事を目的としています。神経活動の時間的なパターン解析や、神経細胞の集合的活動 (ニューラルアンサンブル)、空間的に離れた複数の神経活動間の共振やコヒーレンス、脳情報の分散コーディング など多彩な研究手法の中身を知る良い機会でもあり、またてんかん・パーキンソン病・統合失調症など精神神経 疾患の病態生理と神経オシレーションの異常(ディスリズミア)における臨床的応用の可能性も探っていきます。

講演の他にポスター発表も開催し、トラベルグラントも予定しています。これまでオシレーションの研究に触れた ことのない方や学生の参加も歓迎いたします。多数の研究者の皆様の参加をお待ちしております。

・シンポジウム1「オシレーションのデータ対話型理論に向けて」

講演者北野勝則(立命館大学) 藤澤 茂義(理化学研究所) 伊藤浩之(京都産業大学)

・シンポジウム2「Probing motor and higher brain functions from human electrocorticogram: insights from wide-band EEG oscillation」

 講演者
 池田
 昭夫(京都大学)
 鎌田
 恭輔(旭川医科大学)

 Josef Parvizi (スタンフォード大学)
 YuanYuan Chen (マンチェスター大学)

・特別講演 「リズム現象と縮約理論」

蔵本 由紀(京都大学名誉教授)

(時間・発表は変更の場合があります)

企画者:池田昭夫(京都大学) 南部篤(生理学研究所) 美馬達哉(京都大学) 松橋眞生(京都大学)
 Web サイト http://hbrc.kuhp.kyoto-u.ac.jp/NeuralOscillation
 E-mail (事務局) neuroscillation@bpp2.kuhp.kyoto-u.ac.jp



Conference on Neural Oscillation 2015 V. Attached materials



HOME ご挨拶	領域体制	計画研究研究成果活動情報	関連リンク	
- 計画研究			計画研究	
A03 ヒト脳発	振現象の直接記	録	A班: 新規の集団発振現象を探索	
ヒト脳機能は多次元・	多階層の発振現象の非線	形的相	A01	
互作用により発現する。 動原理の根本は共通し、	、一方、脳機能の異常発 、てんかんは、自律的な	現在17F 広周波帯域解析 単発皮質電気刺激によるヒト機能結合地 脳ネッ ^{成人物調要てんかん} 皮質・皮質用 CCEP 単発電気	8 A02	
「ネットワーク病」と	マの次元・喧唐で回剰元 足えられる。本研究計画		A03	
よび広域の集団発振現	止不服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			
空間的観点からは、局がで、発達過程の観点からの物理	所神経回路(細胞外多電極 らは、ヒトの乳児・小児 モデルを構築し、正常短	記録)からシステムレベル(皮質脳波、頭皮上脳波、脳磁・ ・成人脳および動物モデルで比較検討する。B班と連携し	B班: データ対話的な数理モデル 構築 expan	
空間的観点からは、局 で、発達過程の観点か 記録データからの数理 を目指す。C班と連携し による多次元・多階層	所神経回路(細胞外多電極 らは、ヒトの乳児・小児 モデルを構築し、正常振 ノ、外的および内的な振動の での生理的・病的振動の	記録)からシステムレベル(皮質脳波、頭皮上脳波、脳磁 ・成人脳および動物モデルで比較検討する。B班と連携し 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 助制御の手法を用いて、突発性振動異常の制御を試み、f 変容機構を明らかにする。	BPU: データ対話的な数理モデル 構築 解明 下入 介入による発振制御と 臨床応用	
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HP: http://epilepsy.med.kyoto-u.ac.jp/

EEG&EMG seminar

\sim For those who start learning EEG&EMG \sim

To meet the demands of skill-learning of EEG&EMG in the Kansai region, the Kansai EEG&EMG society was founded at 2008 (representative: Dr. Shuji Hashimoto). The 8th EEG&EMG seminar was held in this February, and more than 160 young doctors and technologists gathered from all over the Kansai region. Our department, in close cooperation with the Department of Neurology, has served as the secretary office of this seminar to organize the seminar and revise the program contents based upon the feedback from the audience. The skilled clinical neurophysiologists from all over the Kansai region gather together to provide talks and hands-on lectures to educate young doctors and technologists for enhancement of the quality of EEG&EMG in this region.



Visiting physician

[Overseas]

December 3, 2014 Dr. Steven Z. Rapcsak, M.D. Affiliation: Neurology, Psychology, and Speech, Language, & Hearing Science, University of Arizona Position: Professor

December 4, 2014 Dr. Meng-Fai Kuo, M.D., Ph.D. Affiliation: Division of Pediatric Neurosurgery, Department of Neurosurgery, National Taiwan University Children's Hospital Position: Chief and Associate Professor

Dr. Shih-Hung yang, M.D., Ph.D. Affiliation: Division of Pediatric Neurosurgery, Department of Neurosurgery, National Taiwan University Children's Hospital Position: Assistant Professor

Dr. Wen-Ching Wong, M.D. Affiliation: Department of Pediatric Neurology, National Taiwan University Children's Hospital Position: Lecturer

Dr. Ming-Kai Pan, M.D., Ph.D. Affiliation: Department of Neurology, National Taiwan University Hospital

Li-May Sung, Ph.D. Affiliation: Graduate Institute of Linguistics, National Taiwan University Position: Director and Associate Professor

Chia-Rung Lu, Ph.D. Affiliation: Graduate Institute of Linguistics, National Taiwan University Position: Assistant Professor

Bo-Cheng Kuo, Ph.D. Affiliation: Graduate Institute of Linguistics, National Taiwan University Position: Assistant Professor

April 1, 2015 Dr. Yue-Loong Hsin, M.D. Affiliation: Department of Neurology, Chung Shan Medical University Hospital Position: Chief

V. Attached materials Visiting physician

June 24-26, 2015 Yuanyuan Chen, Ph.D. Affiliation: Neuroscience and Aphasia Research Unit, University of Manchester Position: Research Associate

June 24-26, 2015 Dr. Josef Parvizi, M.D., Ph.D. Affiliation: Stanford Human Intracranial Cognitive Electrophysiology Program (SHICEP), Stanford Program for Intractable Epilepsy, Stanford University Position: Associate Professor, Director

[Domestic]

July 7, 2014 Dr. Rei Enatsu, M.D., Ph.D. Affiliation: Department of Neurosurgery, Sapporo Medical University Position: Assistant Professor

March 25, 2015 Dr. Kiyohito Terada, M.D., Ph.D. Affiliation: Shizuoka Institute of Epilepsy and Neurological Disorders Position: Chief Medical Staff

July 15, 2015 Keiichi Kitajo, Ph.D. Affiliation: Rhythm-based Brain Information Processing Unit, RIKEN BSI-TOYOTA Collaboration Center, RIKEN Brain Science Institute Position: Unit leader

Yuka Okazaki, Ph.D. Affiliation: Rhythm-based Brain Information Processing Unit, RIKEN BSI-TOYOTA Collaboration Center, RIKEN Brain Science Institute Position: Research Scientist

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

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