2015 Annual report

“Understanding brain plasticity on body representations to promote their adaptive functions”

Program Director: Jun Ota (The University of Tokyo)

Systems engineering

Brain science

Rehabilitation medicine

Embodied-Brain

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Area No. 4603
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http://embodied-brain.prg

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Program Overview and Activities of Steering Committee

Jun Ota
Research into Artifacts, Center for Engineering (RACE), The University of Tokyo

I. Purpose of the Research Program

The purpose of this research program is to elucidate the neural mechanisms of the body representation in the brain (internal representation of the body. Indicators of posture and body structure that are updated moment-to-moment by a wide range of sensory inputs that are related to motor performance) and the mechanism of the long-term changes in this representation and to apply these findings to rehabilitation interventions. In order to do this, we will attempt to combine brain science and rehabilitation medicine by using systems engineering (Fig. 1). We thereby intend to gain an integrated understanding of motor control and somatognosia in order to create a new academic discipline that is known as embodied-brain systems science.

II. Content of the Research Program

In order to achieve the above-mentioned goals of this study, we will establish eleven research projects (A01-03, B01-03, C01-03, X00, and Y00). In research projects A01-03, we conduct experiments on humans, monkeys and rats by using methods that are based on interventional neuroscience in an attempt to understand the neural mechanisms of the body representation in the brain and the process by which it changes with respect to somatognosia (sense of agency, sense of ownership) and motor control (muscle synergy control, anticipatory postural control). We will use neural decoding and virus vector technology to investigate markers that reflect changes in the body representation in the brain. In research projects B01-B03, we create dynamic models of the differing time constants of the fast dynamics and slow dynamics of the body representation in the brain based on neurophysiological experimental data and clinical data from patients undergoing rehabilitation. In research projects C01-C03, we attempt to quantify the rehabilitative effects with the markers. By integrating this with a model of the body representation in the brain, we will implement model-based rehabilitation and create predictions of prognosis for intervention. General group X00 Group is responsible for strategic planning of the program and support the research projects. International group Y00 promotes international collaboration of the members in the program.

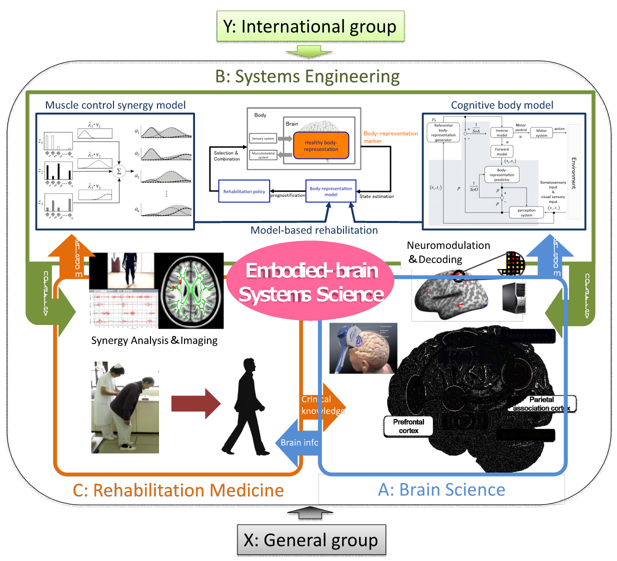

Fig. 1 Overview of Embodied-brain program

III. Activities

Following events were held in the research program.

1st lecture meeting on Embodied-brain systems science
- Date: Thursday, March 19, 2015.
- Place: Kyotanabe campus, Doshisha University
- Attendees: 30
- Contents: two talks on predictive control and feedback control and discussion

2nd General meeting
- Date: Saturday, July 4, 2015, 10:00-18:10
- Place: Mitaka campus, Kyorin University
- Attendees: 100 in total (member only)
- Contents: presentation by program director and group leaders, and PI of each subscribed research project.

1st Steering committee meeting in 2015 fiscal year
- Date: Saturday, July 4, 2015, 12:00-13:00
- Place: meeting room, Mitaka campus, Kyorin University
- Attendees: 19
- Contents: general discussion on steering of the program, research plan, events, publicity, etc.

1st Public symposium
- Date: Sunday, October 25, 2015, 10:20-18:00
- Place: Takeda Hall, University of Tokyo
- Attendees: 191
- Contents: presentations for general participants by project members including program director, group leaders, and a representative researcher (Prof. Saito), and panel discussion by the presenters.

2nd Steering committee meeting in 2015 fiscal year
- Date: Sunday, October 25, 2015, 12:00-13:30
- Place: meeting room, Takeda Hall, University of Tokyo

Attendees: 18
Contents: general discussion on steering of the program, research plan, events, publicity, etc.

3rd General meeting

Date: Monday March 7, 2016 13:30～Wednesday, March 9, 2016, 12:00
Place: Hanamaki, Iwate
Attendees: 100 in total (member only)
Contents: presentation about annual report by program director, PI of each research project, special invited talk by a emeritus professor (Prof. Iwamura), and poster session by attendees.

3rd Steering committee meeting in 2015 fiscal year

Date: Wednesday, March 9, 2016, 12:00-13:30
Place: Hanamaki, Iwate
Attendees: about 20
Contents: general discussion on steering of the program, research plan, events, publicity, etc.

Activities in academic society (Workshop proposal)

(1) IEEE/EMBS EMBC2015 Workshop
Date: Tuesday, August 25, 2015, 13:30-17:30
Place: Milano international conference center, Milano, Italy
Contents: 10 presentations by program members and invited international collaborators.

(2) IEEE/RSJ IROS2015 Workshop
Date: Monday, September 28, 2015, 8:30-12:30
Place: Hamburg international conference center, Hamburg, Germany
Contents: nine presentations by program members and invited international collaborators.

(3) Research collaboration in Sweden: activity of group Y00
Date: Monday, February 8, 2016～Sunday, February 14, 2016
Place: Chalmers University of Technology, Karolinska Institute
Contents: lab tours, presentation and discussion. Six attendees from the program.

Activities in academic society (Organized session proposal)

(1) SICE Annual Conference 2015
Date: Tuesday, July 28, 2015
Place: InterContinental Hangzhou Hotel, Hangzhou, China
Contents: six presentations by program members and their collaborators.

(2) MHS2015
Date: Tuesday, November 24, 2015
Place: Noyori memorial hall, Nagoya University
Contents: six presentations and five posters by the program members and their collaborators.

(3) 28th SICE-DAS symposium
Date: Thursday, January 21, 2016
Place: Hiroshima University
Contents: nine presentations by the program members and their collaborators.

(4) Special issue in Neuroscience Research journal
Volume: Vol 104 (March 2016)
Contents: published Special Issue "Body representation in the brain" (Guest Editors: Eiichi Naito, Akira Murata, Jun Ota). 14 review articles.

IV. Transdisciplinary Research in the Program

In this program, it is important to conduct transdisciplinary research by researchers from different rgroups. Followings are part of products in the program:

- Six articles among total 14 articles in Neuroscience Research journal have been written by authors from several (not one) research groups.
- Transdisciplinary studies among different research groups are now conducted or planned on the research issues such as upper limb rehabilitation, gait rehabilitation and somatognosia.

V. Activites by Young Researchers

This program promotes activities of young researchers. The followings are the list of them:

A. 2nd symposium on Embodied-brain systems science was jointly organized with the Japanese Society for Motor Control (JSfMC) from June 25, 2016 to June 27, 2016. The theme was "New trends in the perceptual motor learning." About 50 audiences joined with active discussion. There are three speakers: Hiroshi Ouchida (Tohoku Univ.), Kenji Ogawa (Hokkaido Univ.), and Shiro Yano (Tokyo Univ. of Agriculture and Technology).

B. 3rd symposium on Embodied-brain systems science was conducted at The Univ. of Tokyo on August 21, 2016. The theme was "Researches on Model based walking support system and clinical effects" with a wide range of topics from the model-based analysis on motor control to the robotics applications for rehabilitation aid. There are three speakers: Tetsuro Funato (The Univ. of Electro-Communications), Hideki Kadone (Tsukuba Univ.) and Mitsuhiro Hayashibe (Institut National de Recherche en Informatique et en Automatique)

VI. Future Events

Planned activities are follows:

(1) May 8 to May 9, 2016: 1st International Symposium on Embodied-Brain Systems Science (EmboSS 2016) at Tokyo. http://embodied-brain.org/conf/
(2) July 2016: organized session at IAS-14 conferece.
(3) August 2016: workshop at EMBC2016
(4) October 2016: workshop at IROS2016）
(5) March 2017: 4th general meeting
(6) Marcy 2017: Special issue at Journal of the Society of Instrument and Control Engineers

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Activities of Group A (Brain Science)

Eiichi Naito
Center for Information and Neural Networks (CiNet), National Institute of Information and communications technology (NICT)

I. Purpose of the research projects A01/A02

In research projects A01/02, we aim to elucidate neural substrates of body representation in the brain and to identify markers that reflect changes in the body representation. Here, we focus on three topics: (1) bodily awareness (sense of agency and body ownership), (2) muscle synergy control and (3) anticipatory posture adjustment, and we conduct manipulative (interventional) neuroscience to investigate how changes in the body representation cause changes in bodily perception and motor control vice versa. We conduct experiments on humans and animals (monkeys). By using electrophysiology and neuroimaging techniques, we elucidate how body representation changes (1) when we manipulate subject's bodily awareness in a virtual reality environment, (2) when we manipulate physical states of musculoskeletal system and (3) when monkeys start performing bipedal walking. To elucidate markers reflecting changes in the body representation, we use neuronal decoding techniques. Here we identify brain regions where the activities contain important information to predict contents of changes in bodily perception and motor control. By sharing the knowledge about causal relationship between internal body representation and bodily perception and motor control, and about dynamics in the change of neuronal representation of body with research projects B and C, we help constructing a model and contribute to reveal a principle of neuro-rehabilitation. In addition to research projects A01/02, other 7 groups, which have different experimental methods and approaches, have joined this project since this fiscal year. By doing so, we could facilitate the researches which was less covered by the A01/02 members and promoted inter-group collaborations for better understanding of wide range of body representations in the brain.

II. Members

We organize three groups in the research projects A01/A02. Members are shown as follows:

<u>Research project A01 Neural mechanisms inducing plasticity on body representations</u>
Principal Investigator: Hiroshi Imamizu (ATR). Funded Co-Investigator: Akira Murata (KinKi Univ), Yukari Ohki (Kyorin Univ), Takaki Maeda (Keio Univ). Other 4 Co-Investigators.
They conduct electrophysiological and neuroimaging experiments on humans and monkeys to identify neuronal substrates associated with bodily awareness (sense of agency and body ownership) when they manipulate subject's bodily awareness in a virtual reality environment.

<u>Research project A02-01 Neural adaptive mechanism for physical change</u>
Principal Investigator: Kazuhiko Seki (NCNP). Funded Co-Investigator: Eiichi Naito (NICT), Shinji Kakehi (Tokyo Metropolitan Institute). Other 13 Co-Investigators.
They conduct electrophysiological and neuroimaging experiments on humans and monkeys to identify neuronal substrates allowing muscle synergy control. In particular, they examine how the brain adapts and changes its body representations when they manipulate physical states of musculoskeletal system.

<u>Research project A02-02 Adaptive embodied-brain function due to alteration of the postural-locomotor synergies</u>
Principal Investigator: Kaoru Takakusaki (Asahikawa Med Univ). Funded Co-Investigator: Katsumi Nakajima (KinKi Univ), Other 1 Co-Investigator.
They conduct electrophysiological and virus vector experiments on animals (monkeys and cats) to identify neuronal substrates allowing anticipatory posture adjustment. In particular, they examine how the brain adapts and changes its body representations when monkeys start performing bipedal walking.

In addition to research projects A01/A02, other 7 groups have joined this project since this fiscal year. Members are shown as follows:

<u>Research project A03-1 Investigation of functional dynamics by hybrid techniques and real-time processing</u>
Principal Investigator: Kyousuke Kamata (Asahikawa Med Univ).
They measure human brain activity with ECoG and restore human motor functions through decoding techniques.

<u>Research project A03-2 Visualizing human body representations associated with hand movements with EEG</u>
Principal Investigator: Natsue Yoshimura (Tokyo Tech). Other 1 Co-Investigator.
They measure human brain activity associated with hand movements with EEG and estimate EEG sources. By using this brain activity, they reconstruct muscle activity and develop a method to intuitively control a power-assist robot.

<u>Research project A03-3 Investigation of change of body representation in basal ganglia due to chronic dopamine lacking and its manipulation</u>

Principal Investigator: Kouichi Nakamura (Kyoto Univ). Other 2 Co-Investigators.
They record beta-oscillation from animal's thalamic nuclei that are targeted by basal ganglia and try to prove that this is one of the body representation markers for Parkinson disease.

Research project A03-4 Investigation of change of body representation using direct recoding and stimulus intervention of human brain
Principal Investigator: Riki Matsumoto (Kyoto Univ). Other 5 Co-Investigators.
They measure brain activity with ECoG from human fronto-parietal cortices and evaluate slow dynamics of internal body representations associated with body cognition and motor control (grasping, tool-use, pantomiming) through clinical treatment.

Research project A03-5 Visualization and manipulation of change of internal body representation by peripheral nerve damage
Principal Investigator: Mariko Miyata (Tokyo Women's Medical Univ). Other 3 Co-Investigators.
They try to visualize change of internal body representation by peripheral nerve damage in rats and develop the methods to manipulate the representation.

Research project A03-6 Body and space in monkeys with hemi-spatial neglect
Principal Investigator: Masatoshi Yoshida (NIPS). Other 1 Co-Investigator.
They examine the change of internal body representation mainly in the ventral attentional network in monkeys with hemi-spatial neglect.

Research project A03-7 Change in internal body representation associated with recovery of grasping ability after the brain stroke: A mokey model study
Principal Investigator: Yumi Murata (AIST). Other 4 Co-Investigators.
They examine the neural mechanisms associated with functional recovery from internal capsule damage in monkeys and develop its computational model.

III. Activities

Entire group A meeting

Date and Time: January 21, 2016, 13:00-18:00. January 22, 2016, 9:00-13:00.
Place: Kinki Daigaku Kaikan. 5th floor
Attendees: 27 in total
Contents: 23 Group A members and 4 C02 members joined this meeting. Main purpose of this meeting was to confirm and facilitate inter-group collaboration between A01/A02 and A03 groups. From A03 groups, Yoshimura (Tokyo Tech), Murata (AIST), Makamura (Kyoto Univ), Matsumoto (Kyoto Univ) and Yoshida (NIPS) reported the progresses on their researches and discussed collaboration with group A01 and A02. From research projects A01 and A02, Murata (Kindai Univ) talked about efference copy and internal body representation, and Takakusaki (Asahikawa Med Univ) presented the data associated with muscle synergy control by reticular formation on the first day (Jan 21th). On the second day, Seki (NCNP) organized a session entitled "muscle synergy and body representation", and young researchers of Hirashima (NICT) and Oya (NCNP) reported the current status of their researches in collaboration with Group B02 and C02. In addition, Nakajima (Kindai Univ) and other young researchers of Hirose (NICT), Togo (ATR) and Yozu (Univ of Tokyo a member of C02) reported the progress of their projects and this information was shared by the all attendees.

Finally

We reported details of 2015 research outcomes and activities in reports from each research project. We had some of major outcomes in the FY2015. For example, Imamizu group made a first success on visualization of fast and slow dynamics associated with visuo-motor transformation learning in human brain, and Naito's group has revealed the hidden function of human right cerebral hemisphere by showing that the right inferior fronto-parietal SLF III network is deeply involved in the formation of human body image. In addition to these research outcomes, A02 in collaboration with B02 and C02 is trying to develop new rehabilitation method where we feedback current state of muscle synergy control of patients to themselves, and A01 in collaboration with C01 is now developing new rehabilitation method where we can make effective intervention to patient's internal body representation through patient's control of an avatar. These are ongoing inter-group collaborations, where we expect outcomes in next fiscal year.

Annual report of research project A01-1

Hiroshi Imamizu
Graduate school of Humanity and Sociologies, The University of Tokyo

***Abstract*—Our research project aims to find neural correlates of bodily self-consciousness, and neural mechanisms in which changes in bodily self-consciousness lead to changes in body representations in the brain. Based on these results, we will develop a method for intervention and manipulation of the bodily self-consciousness. In this fiscal year, we made significant advances in investigation of fast and slow dynamics in body representations, decoding bodily self-consciousness, and finding a cause of abnormality in bodily self-consciousness in schizophrenia. We also developed a new experimental paradigm for online electroencephalogram (EEG) measurement of bodily self-consciousness and for electroneurophysiological study on corollary discharge.**

I. Introduction

We assume that bodily self-consciousness consists of sense of agency ("I am moving this body") and sense of body ownership ("This is my body"). Our project mainly investigates bodily self-consciousness as cognitive process of body representation in the brain.

II. Aim of the Project

We aim to identify neural correlates of senses of agency and body ownership. Based on the identified neural mechanisms, we investigate how fast process related to bodily self-consciousness lead to change in slow process of the body representation. We will develop effective methods for promoting adaptive changes in the body representation for rehabilitation purpose. We take multiple approaches to these aims, including behavioral and brain imaging experiments with normal human subjects and schizophrenic patients, decoding methods of neural information, and electrophysiological experiments on monkeys.

III. Research Topics

A. Investigation of changing process in body representation and decoding bodily self-consciousness

A group of the principal investigator conducted researches on the two topics for change in body representation and bodily self-consciousness. First, they identified neural correlates of fast and slow processes using fMRI combined with computational models. Second, they succeeded in decoding self- or other-attribution of movements, which supports sense of agency.

1) Identification of neural correlates of fast and slow dynamics for change in body representation: They investigated brain activity when human subjects learned to manipulate a joystick in a specific direction. By fitting computational model to human behaviors, they identified time courses of change in fast and slow dynamics in body representation. They conducted multiple regression analysis of brain activity using the identified time courses as regressors. As a result, they found that the fronto-parietal network corresponds to fast process while the limited parietal region and the cerebellum correspond to slow process [1].

2) Decoding bodily self-consciousness: We started a project to use a decoding technique to develop a marker of body representation (bodily self consciousness). As the initial step, we succeeded in decoding self- or other-attribution of movement by human subjects. Subjects manipulated a joystick in an fMRI scanner while movement of other parson was blended into the joystick movement to variable degrees. This experimental manipulation elicited various subjective rating of self-attribution of movements. We constructed a decoder that can predict the rating from regional brain activity in the fronto-parietal network at statistically significant level. This is the first study on decoding bodily self-consciousness. This method will be utilized as one of objective indices for bodily self-consciousness. Several articles on psychophysical studies related to this experiment were published in international journals [2, 3].

B. Development of a virtual reality system to induce and measure changes in somatognosia

Yukari Ohki (funded co-investigator, Kyorin University) and her colleagues are approaching to identify neural substrates relating to the sense of body ownership, i.e., experiencing body parts as one's own. The data are essential to evaluate and modify body representations in the brain. For that purpose, Ohki's group is using a rubber hand illusion (RHI, Botvinick & Cohen, 1998): simultaneous stroking of an invisible real hand and a visible fake hand leads to strong sensation of illusory touch on the fake hand and body ownership over it. There have already been several studies, in which brain activities were examined during the RHI. However, there are at least two problems in the original RHI; it is difficult to 1) compare brain activities with and without RHI otherwise under the same conditions, and 2) evaluate instantaneous subjective states. Thus, they developed a modified RHI paradigm. In the paradigm, participants' invisible real and the visible fake hands are simultaneously stroked twice with paint brushes, and participants judge whether they sensed touch on the fake hand or not. To vary the subjective state, the fake hand is sometimes moved, because it was reported that the RHI is influenced by the distance between two hands (Lloyd, 2007). Ohki and colleagues observed that even short-duration visuo-tactile stimuli (2 strokes) could elicit mislocalization of touch toward the fake hand. By varying the distance between two hands systematically, two subjective states (with and without RHI) could be obtained at the same distance in each participant. By using the paradigm, Ohki's group is now examining brain activities reflecting the RHI with 64-channel EEG system. Preliminary results were reported in meetings [4].

Ohki's group is also collaborating with members from different research projects. Frist, they are collaborating with B01 research project to clarify how information about body parts is altered in virtual reality (VR). They found that active movements, or movement-related brain activities, are important to alter body representations effectively [5]. Secondly, they are cooperating with C02 to improve an immersive reality system (SIGVerse). Thus far, they have changed the system to be adjusted by subjects' physical sizes, which improves subjects' sense of immersion [6]. By using the system, they plan to alter body representations in patients with phantom limb pain.

C. Physiological mechanisms of body representation in the monkey brain

To study neural mechanism for encoding own body, Akira Murata's group (funded co-investigator, Kinki University) investigated effect of corollary discharge for neuronal activity in the parietal cortex in the monkey. The term of corollary discharge corresponds to efference copy, that is known as a copy of motor signal that is integrated with sensory reafferent signal or modulates it. It has been thought that corollary discharge is one of important factor for body consciousness or discharge in the parietal cortex by recording neuronal activity reflect sensory attenuation [7,8]. Murata's group replicated an apparatus of self-tickling same as Blakemore's experiment and are trying to record neurons in primary somatosensory cortex (SI) of the monkey during tickling by the monkey itself.

D. Methodology for studying aberrant sense of agency in schizophrenia, and its mathematical modeling

Takaki Maeda (funded co-investigator) and his colleagues have originally developed the sense of agency task (Keio method) for studying schizophrenia. In this fiscal year, their works have progressed in understanding for pathophysiology of aberrant SoA in schizophrenia thorough behavioral and brain imaging studies.

1) They applied for a patent for Keio method [9].

2) By using a modified version of Keio method, they found that 50 msec delay of prediction signal (efference copy and corollary discharge) issued by a forward model in schizophrenic patients [10]. This finding supports a disconnection hypothesis on schizophrenia.

3) They measured brain activity in schizophrenic patients and found that abnormal activity in inferior parietal lobe (IPL), insula, posterior cingulate cortex (PPC) and precuneus. Furthermore, functional connectivity between a part of IPL and the caudate nucleus on the left side is decreased in the patients.

4) To study computational account for sense of agency, they employed a humanoid robot driven by a recurrent neural network (RNN). The RNN is often used for modeling temporal sequence learning. The network was trained through capturing sense of agency behavioral data of healthy control in the Keio method. They studied another computational approach in order to investigate pathophysiological mechanisms of schizophrenia from the standpoint of working memory paradigm [11].

5) They published a review article on slow dynamics in body representation in collaboration with the B01 project [12].

IV. Future Perspective

In this fiscal year, we made significant advances in revealing neural correlates for bodily self-consciousness. Specifically, we identified neural correlates for fast and slow dynamics in body representation [1], succeeded in decoding of self- and other-attribution of movements, and found a reason for abnormality of sense of agency in schizophrenic patients (i.e., 50-msec delay in prediction of sensory consequence) [11]. These studies promoted new ideas and concepts, which led us to publication of several review articles [13, 14]. We developed a new experimental paradigm for online EEG measurement of sense of body owner ship, which will lead to manipulation and intervention of bodily self-consciousness. Electrophysiological experiments on corollary discharge in monkeys were prepared, and recording of neuronal activity was started. This experiment will advance our understanding neurophysiological basis of the bodily self-consciousness. We will combine these studies with functional neuroimaging studies on humans to reveal neural correlates of bodily self-consciousness. Based on these studies, we will develop methods for manipulation, induction and repair of bodily self-consciousness.

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Annual report of research project A02-1

Kazuhiko SEKI
National Institute of Neuroscience, NCNP

Abstract*—In the FY2015, we established 1) Stroke model using common marmoset, 2) *understanding the fast and slow dynamics in human body cognition and motor control, and development of new fMRI decoding method, and 3) understanding on the mechanisms used by Purkinje cells to influence limb motor control and on the plastic changes that underlie motor learning in the cerebrocerebellum.

I. Introduction

Our research group is based on three major Neuroscience hub in japan (NCNP, NICT, TMIMS) and include 18 scientists. Through frequent collaboration and discussion, we would like to find how the embodied brain control our body.

II. Aim of the Group

Aim of our collaborative study is to know the neural organization of muscle synergy generator and controller using electrophysiology and functional Brain imaging and propose the biomarker of brain plasticity on body representation. Research Topics

III. Research Topics

A. Neural adaptation in response to change in the musculoskeletal system

The musculoskeletal system can change over time (e.g. development or aging) or by injuries. After limb amputation or traumatic injury, somatosensory and motor cortical areas, as well as subcortical areas are reportedly subject to substantial reorganization, accompanied by an alternative (compensatory) motor coordination. However, so far, only little information is available about the cortical and subcortical adaptations to this physically modified body and its underlying mechanisms. By changing a primate's body using tendon cross-union of two forearm muscles, Seki's group seek to study the physiological adaptations on cortical and subcortical level as well as the time course with which those changes occur within and between cortical structures. This animal model will specifically be useful for neural description of both fast and slow dynamics of adaptation. We trained monkeys to perform a simple grasping task with two different objects (power grip and precision grip). Behavioural observations as well as chronic EMG (electromyographic) recordings from different forelimb muscles were used to evaluate the recovery and functional performance of the monkey. In this FY, we have been focused on a single tendon transfer (wrist muscle to finger muscle) in one monkey. We found that the monkey fully recovered and fed himself at day 1 after surgery and performed a power and precision grip with its modified arm. Secondly, movement and hold times recovered within only a few weeks after an initial increase and decrease, respectively, after the surgery. And lastly, the recorded EMG revealed continuous changes toward the pattern required for new function after tendon transfer. These result suggest that our tendon transfer model is useful to evaluate fast (single or a few days) and slow (a few weeks) dynamics of the neural adaptation to the altered body.

B. Relationship between the two modes of the cerebellar output and cerebellar ataxia

To understand the cerebellar contribution to the internal representation of the body and its update, Kakei's group tried to provide a systematic explanation of the various symptoms of cerebellar ataxia (Holmes 1917) in terms of the two output modes of the cerebellum (Ishikawa et al. PLoS ONE, 2014).

Our recent physiological findings explain well and systematically the two overlooked Holmes' clinical signs of cerebellar ataxia: *asthenia* and *adventitiousness*. We found that during wrist movement of monkeys, a large proportion of Purkinje cells (PCs), with somatosensory receptive fields (RFs) in the distal arm, was strongly suppressed before movement onset, while the majority of dentate cells (DNs) with the same RFs showed concurrent burst of activity. In contrast, PCs with RFs in the proximal arm demonstrated marked and simultaneous increase in activity, while DNs with the same RFs were strongly suppressed (Ishikawa et al. PLoS ONE, 2014; [5,6]). Our observation suggests that activation of DNs generated by reduced inhibition from PCs, i.e., disinhibition, facilitates the execution of wrist movement, while suppression of the DNs by increased PC activity contributes to the stabilization of proximal muscles and improves task performance. Thus, deficits of disinhibition and inhibition of DNs could be the physiological counterparts of *asthenia* and *adventitiousness,* respectively. In conclusion, it is most likely that *asthenia* and *adventitiousness* reflect deficits in the control of disinhibition and inhibition that determines the strength of cerebellar outputs. Thus, these Holmes' overlooked clinical signs could be clinically utilized as "*elements"* underlying ataxia [7]. Overall, it is possible to explain the body representation in the cerebellum as an aggregate of the cerebellar micro-complexes (i.e. PC-DN linkages) whose activities are changing dynamically between two modes.

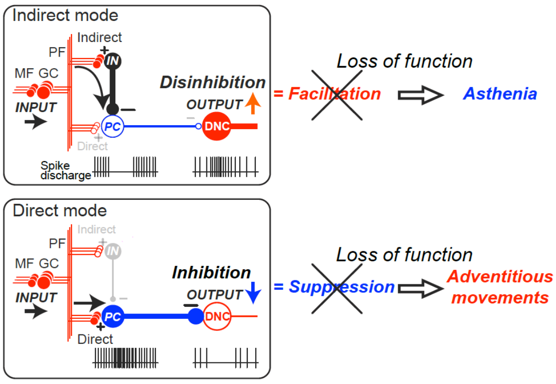

Figure 1. Relationship between breakdown of two modes of dentate nucleus cell (DNC) output and asthenia (top) and adventitious movements (bottom).

C. Body representations associated with hand/finger movements and neuronal substrates associated with formation of human body schema and body image

In the Naito's (CiNet/NICT) group, we have developed a new fMRI decoding algorithm called iSLR in the last fiscal year (Hirose et al. 2015). This method has solved a problem of a conventional decoding method (SLR) and has allowed us to segregate focal motor representations for index and middle fingers, which was very difficult with conventional brain mapping methods. In this fiscal year, using fMRI decoding technique, we have made a success to predict (classify) a type of forthcoming hand/finger movement to be performed from the preparatory brain activity of human secondary motor areas [1]. Many previous studies have shown that broader range of cortical and subcortical motor areas and fronto-parietal cortices are active during preparatory period. But this study, for the first time, clearly demonstrated that more concrete information about the content of motor program, which likely contributes the successful decoding, is represented not in the fronto-parietal cortices but in the supplementary motor area and dorsal premotor area contralateral to the hand. Furthermore, in collaboration with C02, we are identifying neural entity of maladaptive hand\finger representations in musician's dystonia with iSLR. So far, we have raised the possibility that overlapping representations for affected fingers in human primary sensory-motor cortices are the maladaptive neural entity of musician's dystonia. We are planning to intensively examine neuronal representations for muscle synergy using iSLR. In this fiscal year, Hirashima and Oya have pointed out a risk that synergy-like pattern can be analytically identified from muscle activity [2].

As for body cognition, using kinesthetic illusion where people can experience displacement of a vibrated immobile limb, Amemiya and Naito have revealed that activity of the inferior fronto (area 44)-parietal (area PF) network in the right hemisphere connected by the inferior branch of superior longitudinal fasciculus fiber tract (SLF III) is essential when people perceive change of their limb configuration (body image) [3]. In addition, we also summarized a series of our fMRI studies using various types of kinesthetic illusions, and came to a conclusion that activity in motor network during illusion, which may receive and process muscle afferents and efficiently transform them into motor commands, can be considered to be associated with the formation of human body schema (Fig. 1), whereas activity of the right inferior fronto-parietal SLF III network during illusion, which reflects the percept of one's own postural change, is likely involved in the formation of human body image [4].

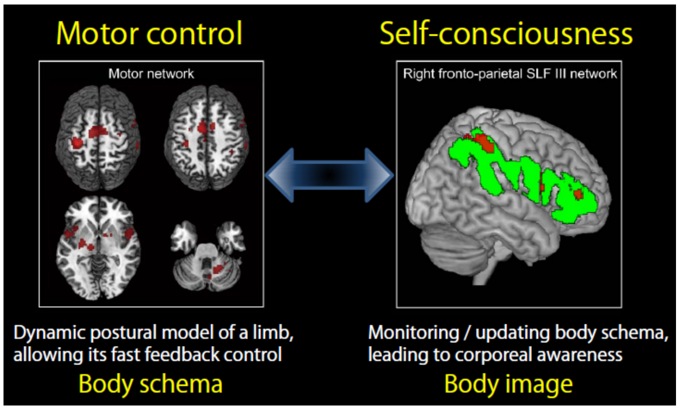

Fig. 2 Brain activity during kinesthetic illusion. It is conceivable that activity in motor network is associated with the formation of human body schema (left panel), whereas activity of the right inferior fronto-parietal SLF III network is involved in the formation of body image (right panel). Modified from ref [4].

IV. Future Perspective

Achievement of this FY will be a foundation of collaborative research within A02-01 and among A02, B02 and C02 group for upcoming years.

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Annual report of research project A02-2

Kaoru Takakusaki,
Research Center of Brain Function and Medical Engineering, Asahikawa Medical University

Abstract **- The present project is designed to examine cortical and subcortical mechanisms involved in the sensorimotor integration underlying anticipatory postural adjustments (APA) that precede the initiation and execution of voluntary movements. In the 2nd year of this project, experimentation in human beings and animals (monkeys and cats) have been performed. Following findings were obtained. First, APA was a feed-forward control process of controlling posture that requires motor programs and bodily information generated by fronto-parietal cortical network. Second, both the firing rate of the supplementary motor area (SMA) neurons and the contraction of paravertebral and leg muscles were higher during locomotion by biped than quadruped in the monkey. Third, reticulospinal neurons (RSNs) located in the ventral part of the pontomedullary reticular formation (PMRF), where cortico-reticular neurons abundantly projected from the motor cortical area that was relevant to the SMA in primates, were involved in the increase in the contraction of antigravity muscles of the cat. These results support our hypothesis that cortico-reticulospinal projections, arising from the SMA-ventral PMRF to the spinal cord, may have capability of the execution of APA.**

I. Introduction

An increase in the incidence of falling of elder people is one of the world-wide serious problems. This can be due not only to deficiency of skeletal and muscular function but to deterioration of higher-order brain functions [1]. However, such a consideration has not been well established, because there has been little neurophysiological evidence how higher-order brain function contribute to the postural control during gait. Particularly, it has been difficult to examine neuronal mechanisms of posture and gait in bipedal animals because of the absence of animal models. To overcome such a difficulty, we have developed bipedal-walking monkey model who can intentionally alter one's posture-gait patterns from quadruped to biped and vice versa. Also we have taken tactics to extract a common mechanism of controlling posture-gait synergy in human (biped) and quadruped animals, that is, anticipatory postural adjustment (APA) [2]. The APA is a preparatory postural control process which is optimized to adjust any types of voluntary movements, and we examined the mechanisms underlying this process in both human beings and animals.

Based on the above reason, we conducted following studies in this year (2015). First, we elucidated whether APA for gait initiation was feed-forward process depending on motor programs which utilized bodily-spatial information. Second, we recorded activities of neurons in the supplementary motor area (SMA), which is involved in motor programming, during locomotion in biped and quadruped in monkey. Then we examined how the firing property of the SMA neurons altered changes during alteration of the posture-gait pattern. Third, we examined whether pontomedullary reticular formation (PMRF), which receive massive input from the SMA, had a capability of regulating postural muscle tone.

II. Resluts

1. APA of gait initiation in human beings

Representative APA accompanied by gait initiation is shown in Fig.1. A subject, who stood on plates which enabled to measure ground reactive force (GRF; Fig.1A), started to walk with desirable stride by left leg. Changes in the GRF exerted on force plates under right and left feet following the stride length with 30 cm, 50 cm, and 70 cm are shown upper and lower panels in Fig.1B, respectively. Gait onset was indicated by abrupt decrease in the GRF in the left GRF. However, such an increase in the left GRF was observed approximately 100 ms preceding the onset of each step with different stride length. Moreover, the GRF was augmented in accordance with an increase in stride length, indicating that the changes in the GRF reflected the prediction of postural changes, i.e., APA, which could be induced by goal-directed intentional gait control. Accordingly, APA is feed-forward postural control process in conjunction with purposeful movements. Consequently, APA can be generated by motor programs that require higher-order brain functions.

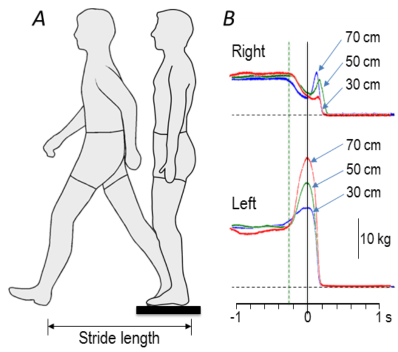

Figure 1. APA in gait onset

Placing one's foot on the desired position for avoiding obstacles, as well as forearm reaching, is a goal-directed movement that requires attention with precise visuo-motor processing. Visuo-motor pathways arise from the visual cortex to the prefrontal and premotor cortices including the premotor area (PM) and SMA via the parietal cortex. The fronto-parietal network may code bodily information such as the "body schema" constructed by temporal and spatial interactions between one's body and surroundings. Because motor programming utilizes such a bodily information, APA can be one of "markers of body representation". The motor programming also requires an activation of motor loops constructed by networks among the motor cortical areas, basal ganglia and cerebellum. Failure in APA is therefore observed in patients with damages in the cerebral cortex (paresis), basal ganglia (Parkinson's disease) and cerebellum (cerebellar ataxia). Consequently these patients have abnormality in posture-gait synergy and have a risk of falling.

2. **Role of SMA in the control of posture-gait synergy**

Changes in posture-gait synergy in Japanese monkey are shown in Fig.2 where the monkey was trained to walk with quadruped (Qp; upper column) and biped (Bp; lower column) on the moving treadmill. Truncal axis altered from horizontal to upright during the transition period from quadruped to biped (middle column). Such a postural alteration may require the augmentation of muscle contractions of antigravity muscles such as paravertebral and leg extensor muscles. Then attempts were made to record the activity of cortical neurons in the trunk and leg areas of the SMA so that we could elucidate whether the SMA coded information relevant to the alteration of posture-gait synergy.

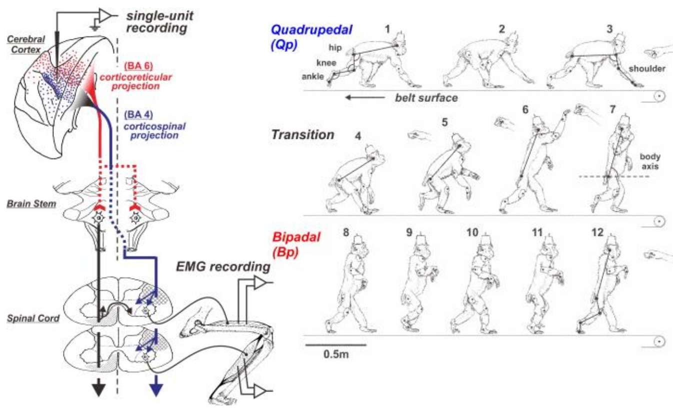

Figure 2. Expeerimental design and posture-gait synergy in monly walking

Activity of SMA neuron was classified into 3 patterns such as phasic, tonic and transient. The phasic firing corresponded to step cycles of walking. In both phasic and tonic neurons, firing rates were started to increase during transition period from Qp to Bp, and the augmented activity lasted during Bp walking. Moreover the changes in the firing rates well reflected the changes in the augmentation of antigravity muscles. On the other hand, a group of SMA neurons displayed transient burst firing (transient type) which was appeared preceding the transition from Qp to Bp and vice versa.

Motor cortical area neurons have descending projections to spinal cord with direct (corticospinal projection) and indirect (cortico-reticulospinal projection) connections (a left schema in Fig.2). The corticospinal projection mainly arises from primary motor cortex (M1) and contribute to local precise movements according to somatotopographical representation. On the other hand, descending neurons in the SMA and PM send massive fibers to the PMRF in addition to spinal cord [3], indicating that tonic firing neurons can be involved in postural control by modulating the activity of antigravity muscles via the cortico-reticulospinal projection. In addition we favor the idea that the transient firing neurons contribute to APA for transition of alternating posture-gait synergy.

3. **Role of the reticulospinal tract in the control of posture**

Because the SMA has massive projection to the ventral part of the PMRF [4], there is a need to examine whether RSNs in the ventral PMRF contributes to the control the contraction of antigravity muscles. For this, we employed acute decerebrate cat preparation where muscle tone was developed due to decerebrate rigidity (Fig.3Aa).

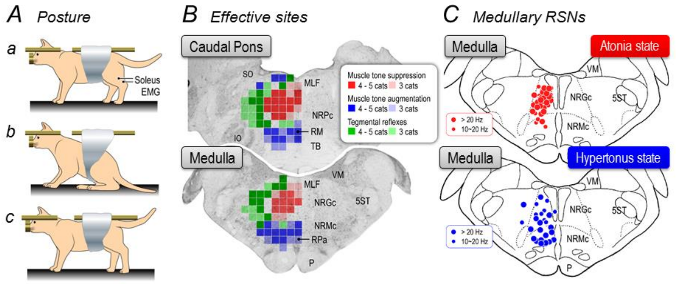

Figure 3. Reticulospinal control of antigravity muscles in decerebrate cats

When repetitive electrical stimulation (20-40 μA, 50 Hz) was applied to the medial part of the PMRF (marked by red in Fig.3B), postural muscle tone of the decerebrate cats was suppressed (Fig.3Ab). However, stimulation of the ventral part of the PMRF (marked by blue) increased the level of muscle tone and decerebrate rigidity was enhanced (Fig.3Ac). On the other hand, stimuli applied to the lateral part of the PMRF induced tegmental reflex or asymmetrical torsion posture which was characterized by the combination of leg flexion of one side and leg extension of the other side (marked by green). Next, firing rates of the medullary RSNs were examined during rigidity state and atonia state which was induced by injecting cholinergic agent into the pontine reticular formation [4]. It was observed that hypertonus-related RSNs (blue) were mainly located in the ventral part of the medulla (upper in Fig.3C). However, atonia-related RSNs (red) were located in the dorsomedial part of the medullary reticular formation (lower in Fig.3C).

III. Discussion and Future Perspective

The cat 6Aβ area corresponds to SMA in primates. Cortical neurons in the 6Aβ have dense projections to the ventral part of the PMRF [5]. It is now considered that cortico-reticulospinal projection in monkey and human beings is responsible for the control of posture-gait synergy [4]. Consequently, the present study may satisfy necessary condition of our hypothesis that body representation constructed by frontoparietal network contribute to APA via activation of cortico-reticulospinal projection arising from the SMA.

Further basic and clinical studies will be required to validate the hypothesis, and to test whether APA can be utilized as a maker of body representation.

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Annual report of research project A03-1

Kyousuke Kamada
Neurosurgery, Asahikawa Medical University

Abstract*— A brain-computer-interface (BCI) allows the user to control a device or software with brain activity. Many BCIs rely on dynamics of brain oscillations related to semantic and motor-imaginary tasks in the electroencephalogram (EEG). Derived electrocorticographic (ECoG) signals allow the investigation of spatially highly focused task-related activation within the high gamma activity (HGA), making the discrimination of individual finger movements, complex grasping or semantic tasks possible. Common spatial patterns (CSP) are used for BCI systems and provide a powerful tool for feature optimization and dimensionality reduction. This work focused on the discrimination of (i) three complex hand movements, as well as (ii) hand movement and idle state. Two subjects S1 and S2 performed single 'open', 'peace' and 'fist' hand poses in multiple trials and three subjects S1-S3 controlled a humanoid in the remote place. (iii) Four patients with subdural grids and 20 healthy subjects participated in a online BCI experiment with invasive (ECoG) and non-invasive (EEG) recordings, respectively. Signals in the high-gamma frequency range between 100 and 500 Hz were spatially filtered based on a CSP algorithm for all expedients. A multi-class linear discriminant analysis (LDA) showed for (i) an error rate of 7.22 % and 1.17 % for S1 and S2 using CSP selected features. For motor-imaginary to remotely control the humanoid, (ii) S1-S3 was able to perform such control over 4 sessions: They were performed consecutively over one day and the last session was performed two days afterwards. After each session, the performance of the classifier improved, reaching about 90% in the end. This experiment showed that ECoG-based motor imagery performed well despite a short training period. (iii) The average accuracy for all EEG and ECoG runs was 76.0 % and 94.6 %, respectively. Compared to EEG signals, the ECoG provided significant better accuracy in motor imaginary tasks

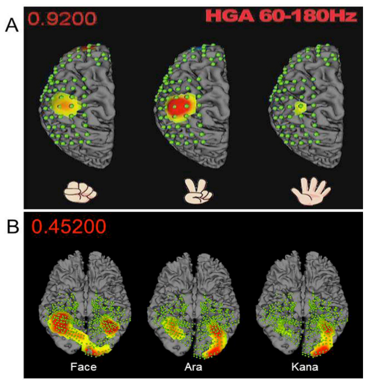
I. INTRODUCTION

BCI is a direct communication pathway between the brain and an external device. BCIs are often directed at assisting, augmenting, or repairing human cognitive or sensory-motor functions. Most of them rely on processed electroencepharogram (EEG) data containing event-related potentials (ERP) or oscillations showing event-related desynchronization/ synchronization (ERD/ERS). The EEG is widely spread in this area because of its low cost and easy setup, as well as its high temporal resolution. However, the low spatial resolution and signal-to-noise ratio are limiting factors in many BCI applications.

Electrocorticogram (ECoG) with subdural electrodes is more sensitive to both radial and tangential dipoles since electrodes are directly placed on the brain surface. In order to capture functional dynamics of neurophysiologcal phenomenon, this report explains electrophysiological characteristics of ECoG related to different motor tasks for brain signal decoding and BCI development.

In previous our study of off-line ECoG analysis, we demonstrated ECoG profiles related to motor execution and visual recognition by normalizing ECoG electrodes of 20 patients on a template brain. This normalization technique clearly delineated characteristic increase in band-power in frequencies above 40 Hz, which is called high-gamma activation (HGA). On the basis of the off-line analysis, we were confident that HGA patterns would contributed to decoding different tasks (Figure 1).

Figure 1 Different dynamics of high gamma activity (HGA) related to motor-executions (A) and visual recognitions (B). Upper left corner shows latency from visual ques. (A) The hand pose of peace sign demonstrated stronger and wider HGA than others. (B) Kana reading activated only the left temporal base. Face recognition showed the right temporal activation with wider HGA than other tasks[1].



This report provided us hints to adapt ECoG classifications for real-time processing. In this report, we focused on tasks related HGA on specific cortical regions for brain signal decoding. In addition, we demonstrated controlling a robot hand and a humanoid online to show future possibility for clinical practice.

Materials and Methods

We recorded ECoG in four patients with intractable epilepsy, who underwent implantation of subdural electrodes for diagnostic purposes at Asahikawa Medical University hospital between June 2014 and January 2016. During the ECoG recording, we instructed the patients to perform motor-execution of 3 hand poses and imaginary tasks of 2 hand poses All the patients had subdural electrodes (Unique Medical, Tokyo) implanted over the primary motor and somatosensory cortices. The used platinum electrodes had an inter-electrode distance of 5mm and an exposure diameter of 1.5 mm, which indicated high-resolution compared to the routine ECoG electrodes. Table 1 show more details of the patients.

Table 1. Demographic data of three patients

Subject	Gender	Age	Dominant hemisphere	Number of electrodes
S1	Female	35	Right	96
S2	Male	22	Left	60
S3	Female	54	Left	76
S4	Female	32	left	118

II. RESEARCH TOPICS

ECoG data processing: All analysis of the ECoG data was performed using custom software written in Matlab R2008b. The hand motion was monitored by 5DT monitor gloves (Fifth dimensional technologies, India). Common Spatial Patterns (CSPs) are a standard method for ECoG data to extract optimal discriminant features in movement (or movement imagination) tasks. The CSP weight matrix calculated with the optimal window size was then used to spatially filter the ECoG signals, and the four most discriminant feature channels were selected per decision pair (two largest eigenvalues from each side of the spectrum). Based on those features a two-class linear discriminant analysis (LDA) for the case 'movement' vs. 'idle', or a 3-class multi-class LDA (MLDA) for the hand poses decryption was calculated.

I) **Discrimination of Hand Poses**

Using the manual feature selection, the subjects S1 and S2 showed a minimal detection error for the three different hand poses of 13.89 % and 18.42 %, respectively. In contrast, the CSP based features led to a minimal classification error of 'fist', 'peace', and 'open' hand poses of 7.22 % and 1.17 % for S1 and S2, respectively. The shaded areas in Fig. 2 represent the 95 % (dark gray) respectively the 99 % (light gray) significance level for the McNemar test in all three test statistics[2].

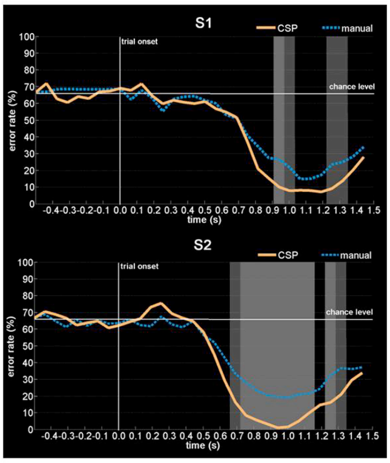


Figure 2 Averaged 3-class detection error for a single trial using manual (blue dotted lines) and CSP (red solid lines) feature extraction. The vertical line represents the time point of the visual stimulus that showed the subject which hand pose to perform. The gray bars represent the areas of significant differences between the two feature extraction method means; dark gray indicates $p < 0.05$ and light gray $p < 0.01$

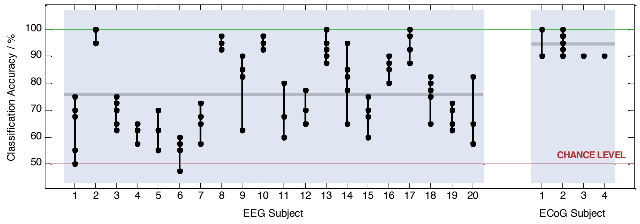
II) **Controlling the robot arm and the humanoid**

Mean training times to control the robot arm with motor-excursion of 3 hand poses and imaginary tasks of two hand poses were 58.2 and 25.4 min for all patients, respectively. In general, training session of EEG-based BCI needed more than 12 hours. Depending on motor-excursion, the maximum power and distribution were significantly different among hand poses according to our previous work, that made decoding hand poses much easier. For motor-imaginary to remotely control the humanoid, the patient was able to perform such control over 4 sessions: Three of those were performed consecutively over one day and the last one was performed two days afterwards. After each session, the performance of the classifier improved, reaching about 90% in the end. This experiment showed that ECoG-based motor imagery performed well despite a short training period compared to similar paradigms in EEG-based BCI.

III) **Online Accuracy of Invasive and Non-invasive BCI**

Signals were further epoched and spatially filtered by CSPs determined from the most discriminative time window. A linear classifier was then trained based on the variance of the four most prominent CSP features, computed by means of a sliding window of 1.0 s. Several runs were executed for each subject, where successive data sets were used for training and test (e.g. classifier determined from data set n was tested with data set n+1). As illustrated in Fig.3, the average accuracy for all EEG and ECoG runs is 76.0 % and 94.6 %, respectively[3].

Figure 3. Online accuracy of the BCI with classification feedback. A filled circle represents the accuracy over 40 trials in total.



III. FUTURE PERSPECTIVE

1, Futrher validation woudl be needed.

2, Identification of frequency coupling and functional connectivity would contribute to decoding.

3, It would be important to clarify not only motor systems, but also language or higher brain functions to understand whole brain systems.

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Annual report of research project A03-2

Natsue Yoshimura
Tokyo Institute of Technology

***Abstract*—This research project aims to visualize neural signaling and muscle synergies during hand or foot movements, using non-invasive brain activity signal recording methods. The visualizing technique could establish effective rehabilitation programs by visualizing transformation of neural signaling and muscle synergy organization by short and long-term motor learning. As the first step toward the aim, in the academic year 2015, we estimated muscle synergies using electromyography (EMG) signals and compared the difference of the synergies between healthy and disabled participants, and between different exercise intensities. As the second step, we estimated muscle activity signals relating to the ankle movements using electroencephalography (EEG) signals, which could be a method to associate brain activity signals with muscle synergies. Furthermore, we established a technique to render functional connectivity between EEG cortical current sources to visualize neural signaling.**

I. Introduction

The project representative Yoshimura has succeeded to reconstruct 2 muscle activity signals relating to the wrist flexion and extension movements using EEG signals by estimating signals of EEG cortical current sources that were randomly allocated on the surface of the cortex [1]. We expect that this technique can reveal neural representations of muscle synergies by comparing muscle synergies being estimated using the reconstructed muscle activity signals to contributive brain regions for the reconstruction.

II. Aim of the Group

Using EEG and functional magnetic resonance imaging (fMRI), our project aims to visualize neural signaling during flexion and extension movements of the hand or foot and to reveal neural representation of muscle synergies relating to the movements.

III. Research Topics

A. *Comparison of muscle synergies between healty and disabled people using EMG signals [2]*

Six healthy and 7 hemiplegia (Fugel-Meyer scores for upper limb: 19-58) participants moved cylinder-shaped small pegs on a desk. Their EMG signals were recorded from 8 muscles: the anterior deltoid (DeltA), the medial deltoid (DeltM), the upper trapezius (TrapUp), the rhomboid (Rhom), the biceps (Biceps), the triceps (Triceps), the flexor carpi radialis (FCR), and the extensor carpi radialis (ECR). We estimated their muscle synergies using a non-negative matrix factorization method (NMF) [3] from their EMG signals, and further classified the synergies using a hierarchical clustering analysis.

The raw EMG signals were high-pass filtered with cut-off frequency of 10 Hz, rectified, down-sampled from 1500 Hz to 50 Hz, and normalized to set standard deviation of respective EMG signals as 1. The processed signals were considered as muscle activity signals and used to estimate individual muscle synergies using a NMF. The number of muscle synergies was 4.5 ± 0.5 (mean $\pm$ S.D) for healthy participants and 4.0 ± 1.2, which were comparable to results of upper limb movements published in existing articles.

When the muscle synergies of all participants were classified into 7 clusters and 14 sub-clusters using an agglomerative hierarchical clustering analysis [4], we obtained several sub-clusters that showed different characteristics between the healthy and hemiplegia participants. Figure 1 illustrated 2 sub-clusters that consisted of muscle synergies relating to the wrist joint. It was found that Synergy 1-1 was used by both healthy and hemiplegia participants, whereas Synergy 1-2 that showed high co-contraction of agonist and antagonist muscles was used mainly by hemiplegia participants. The activity signal patterns of the synergies were different between healthy (blue) and hemiplegia (red) participants, suggesting that strategies of adjusting muscle activities tend to be different depending on pegs even their synergy patterns were similar.

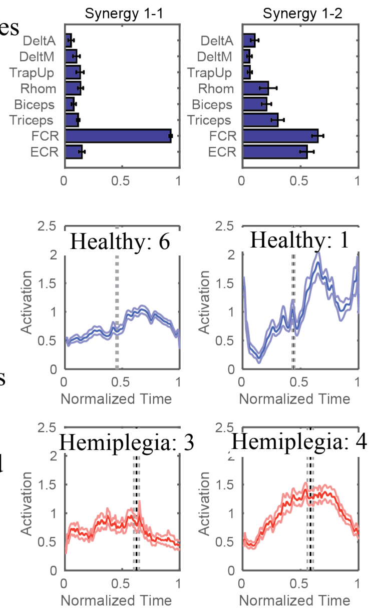

Fig. 1. Muscle synergies for the wrist joints and comparison between healthy and hemiplegia people.

B. *Comparison of muscle synergies between different exercise intensities using EMG signals of healthy people [5]*

In this project, we use vertical jump tasks to find the possibility of muscle synergy data as an effective coaching or training method that can be utilized in sports and rehabilitation fields. We plan to compare muscle synergies between novices and skilled people, but this academic year we estimated muscle synergies for 1 participant and compared his synergy patterns between jumping low and high. As shown in Fig. 2, the synergy patterns were almost the same between the two conditions, whereas Synergy 2 that showed high contribution of calf-side muscles showed differences in synergy pattern signals of rising moment before taking-off.

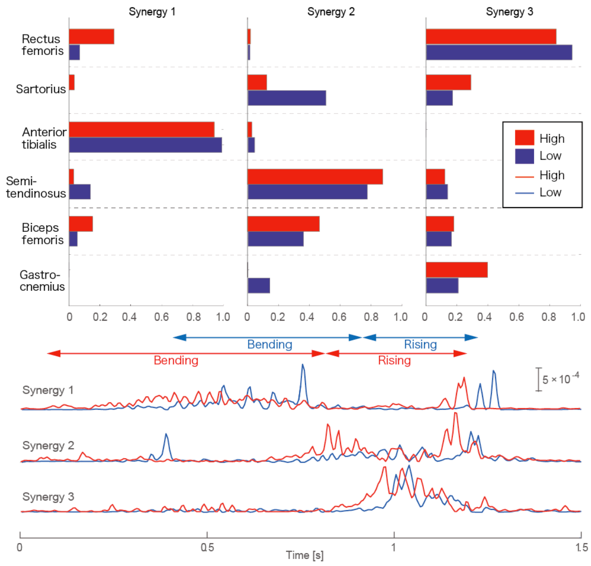

Fig. 2. Synergy pattern difference depending on jumping high and low.

C. *Muscle activity signal reconstruction from EEG signals during the ankle flexion and extension movements*

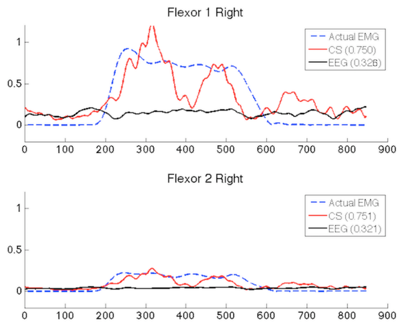

Fig. 3. Examples of reconstructed muscle activity signals during right ankle flexion movement. Upper: Anterior tibialis, Lower: Extensor hallucis brevis, Blue dotted lines represent actual muscle activity signals, red lines represent reconstructed signals using current sources signals, and black lines represent results using EEG sensor signals.

This project aims to extract brain biomarkers relating to gait for rehabilitation and establishing prosthetics to support gait. In the past experiments, we succeeded to reconstruct 2 muscle activity signals. To estimate muscle synergy, more muscle signals need to be reconstructed. Therefore, in this project, we aim to reconstruct 8 muscle activity signals during ankle flexion and extension movement tasks: right and left anterior tibialis, extensor hallucis brevis, gastrocnemis, and soleus. Using the same method as our previous experiments, a hierarchical Bayesian method [1,6] estimated EEG cortical current source signals, and a sparse regression method [7] reconstructed muscle activity signals. We have conducted fMRI experiments for 12 participants and EEG experiments for 6 participants in this academic year. Figure 3 shows examples of reconstructed muscle activity signals. At the moment, we obtained a similar tendency that EEG cortical current signals showed higher reconstruction accuracies than EEG sensor signals.

D. *A technique for visualizing functional connectivity of EEG cortical current sources*

We found a solution for visualizing relationship between EEG cortical current sources and muscle synergies. Figure 4 shows an example of language tasks. Balls in the figures are cortical current sources relating to language imagery, and the ball sizes are bigger if their contributions of imagery tasks are higher. Then, a seed current source and other current sources that showed high correlation coefficient with the seed are connected with lines.

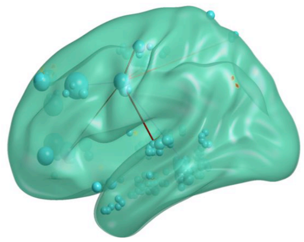

Fig. 4. An example of visualization of current sources and their functional connectivity. These current sources were related to language imagery tasks.

IV. Future Perspective

We established three fundamental techniques of muscle synergy estimation using EMG signals, muscle activity signal reconstruction from EEG signals, and visualization tool for EEG cortical current sources. In the next academic year, we are going to move on the third step of our project. Specifically, we are going to estimate muscle synergies using muscle activity signals reconstructed from EEG signals, and to find neural representation of muscle synergies by associating muscle synergies with current sources that highly contributed for the reconstruction.

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Annual report of research project A03-3

Kouichi C. Nakamura
Graduate School of Medicine, Kyoto University

***Abstract*—This research project utilizes the exaggerated beta oscillations in rat model of Parkinson's disease as an index of loss of body representation in the parkinsonian brain due to excessively synchronized oscillations of neuronal activities therein. We aim to determine the temporal and spatial distributions of the exaggerated beta oscillations and to examine the causal relationship between the exaggerated beta oscillations and movement difficulties in the parkinsonian brain. In this fiscal year, A. we established temporal properties of the exaggerated beta oscillations in the substantia nigra pars reticulata (SNr) of parkinsonian rats, B. we developed a system for combining electrophysiological and anatomical data for mapping, and C. we determined the properties of beta oscillations in thalamic and nigral LFPs in parkinsonian rats.**

I. Introduction

Movement difficulties in Parkinson's disease (PD), including akinesia and bradykinesia, can be considered due to abnormalities in internal representation of body; chronic loss of dopamine alters muscle synergy control in the brain, leading to akinesia/bradykinesia. Indeed, the globus pallidus and motor thalamic nuclei lose fine somatotopic representations in primate model of PD [1], illustrating the 'slow dynamics' of body representation in pathological PD. The widely accepted 'firing rate model' of PD maintains that the loss of dopamine leads to hypoactivity of the thalamus, which in turn causes hypoactivity of motor cortex, ultimately leading to akinesia/bradykinesia. However, with regard to the mean spontaneous firing rates of neurons in the motor thalamus and the output nuclei of the basal ganglia (the internal segment of globus pallidus [GPi] and the substantia nigra pars reticulata [SNr]), available literature is highly controversial and our own data from parkinsonian rats prepared by unilateral 6-OHDA injection did not support the model either. Instead, exaggerated beta (15–30 Hz) oscillations that emerge in the cortex and basal ganglia of both PD patients and animal models have attracted much attention [2], since it could account for akinesia/bradykinesia. During the exaggerated beta oscillations, functional body representations within the basal ganglia and the related circuits may be lost due to information loss by excessively synchronized firing of neurons, and hence the exaggerated beta oscillations could be useful as 'a negative marker of body representation in the brain'. In order to elucidate the routes by which the pathological beta oscillations prevail, it is particularly important to determine temporal and spatial distributions of beta oscillations at the thalamus and output nuclei of the basal ganglia. Furthermore, to understand the slow dynamics of body representations in the brain, it is imperative to validate the causal relationship of the exaggerated beta oscillations and movement difficulties by manipulating beta oscillations to recover normal movements.

II. Aims of the Group

The aims of this research group are to determine temporal and spatial distributions of the exaggerated beta oscillations and to examine the causality between the exaggerated beta oscillations and movement difficulties by using rat model of Parkinson's disease.

III. Research Topics

A. Establishment of temporal properties of the exaggerated beta oscillations in the SNr of parkinsonian rats.

The motor thalamic nuclei consist of the basal ganglia-recipient zone (BZ, corresponding to the VA and VM nuclei) and cerebellar-recipient zone (CZ, equivalent to the VL nucleus) [3]. Before the commencement of this research project, We had already found that BZ neurons, but not CZ neurons, show exaggerated beta oscillations in parkinsonian rats. In order to gain insights on the effect of the basal ganglia afferents on the genesis of thalamic beta oscillations, we examined the firing propensities of single unit activities in the SNr of parkinsonian rats [4,5,6].

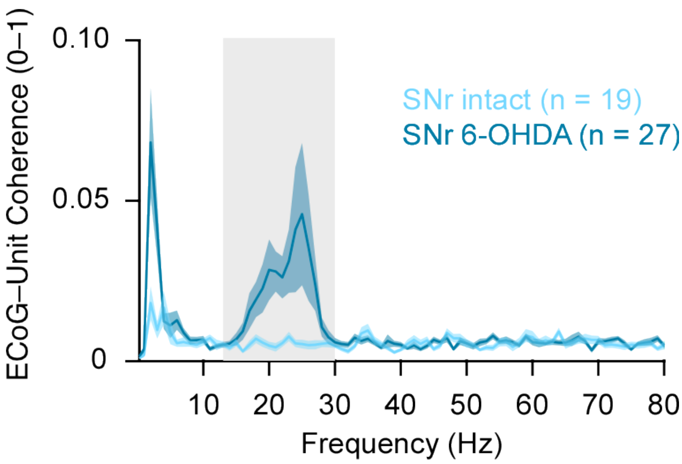

Fig. 1. Coherence spectra between spike trains of SNr neurons and ECoG indicate exaggerated beta oscillations in SNr.

In parkinsonian rats, while spike trains of thalamic BZ neurons showed distinctive beta power, power spectra of spike trains of SNr neurons did not show a peak within the beta frequency band. Nevertheless, spike trains of SNr neurons were evidently coherent to electrocorticograms (ECoGs) in the motor cortex in the beta band (Fig. 1). The low beta power thereof might be due to the highly rhythmic and tonic firing propensities of SNr neurons with relatively high mean firing rates (~25 Hz), which may jointly make them resistant to entrainment to beta rhythm.

Furthermore, while BZ neurons in parkinsonian rats prefer to fire before the troughs of cortical beta oscillations, SNr neurons slightly increase the firing probability after the troughs. Thus, in terms of cortical beta cycle, SNr neurons and thalamic BZ neurons are quite well apart by ~280˚, reflecting the inhibitory nature of nigro-thalamic projection.

B. Development of a system for creating the map of distribution of beta oscillations

So far we have found that the exaggerated beta oscillations are localized in the BZ but not CZ of the motor thalamus of PD model rats. However, the thalamic recipient of the basal ganglia afferent is not only the BZ of the motor thalamus but also includes mediodorsal (MD) nucleus, the caudal intralaminar nuclei (i.e. the parafascicular (PF) nucleus) and the rostral intralaminar nuclei (i.e. the central lateral (CL), paracentral (PC) and central medial (CM) nuclei). Since these thalamic nuclei are strikingly different in their cortical and striatal projection patterns, their influence on cortico-basal ganglia-thalamocortical loop circuit is predicted to be divergent. Hence, it is important to elucidate the distribution of the exaggerated beta oscillations outside of the motor thalamus as well. This year we focused on development of a system that combines electrophysiological data and anatomical data. Combination of DiI-labeling of penetration tracks of silicon probes and immunohistochemistry to GAD67, VGluT2, and GlyT2 allows us to extrapolate each recording site in the thalamus with a good accuracy. This integration allows us to map the magnitude of the beta oscillations (spectral power or coherence to ECoGs) in the virtual standard planes of the thalamus. To this end, we built a system with Excel, Python and MATLAB to extract the coordinates of recording sites from EPS graphic files that are exported from a graphic software and import the coordinates into MATLAB data files.

C. Analyses of exaggerated beta oscillations in the local field potentials (LFPs) in the thalamus and SNr

While action potentials are the output signal of single neurons, local field potentials (LFPs) are considered summation of postsynaptic potentials of nearby neurons and thus can be used as the indicator of synchronized input to local cell ensemble. Recordings with linear silicon probes provide stable LFPs from all the 16 channels. We analyzed power spectra of LFPs from the motor thalamus and SNr. The power of beta oscillations was weaker than that of spike trains of single neurons therein. Furthermore, although the peak frequency of the exaggerated beta oscillations were ~20 Hz for ECoGs and spike trains of single neurons, that of the beta oscillations in thalamic or nigral LFPs were lower in frequency (~15 Hz). Possibly due to this discrepancy in frequencies, the coherence between thalamic or nigral LFPs and ECoGs in the beta frequency band was not different between the dopamine-intact and parkinsonian rats, indicating that synchrony between LFP and ECoG beta oscillations was weak.

IV. Future Perspective

This year, we identified the temporal features of the exaggerated beta oscillations in the SNr of parkinsonian rats, developed a system for integrating electrophysiological and anatomical data for mapping the distribution of beta oscillations, and found the frequency discrepancies in between the beta oscillations in thalamic or nigral spike trains and those in LFPs therein. From next fiscal year onward, we will further advance the distribution of beta oscillations, with collaboration with A01 and A03 groups, establish the recording system for awake head-restrained animals with optogenetics.

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Annual report of research project A03-4

Riki Matsumoto

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

Abstract—**The implantation of subdural electrode grids over the parieto-frontal area for the presurgical assessment of patients with partial epilepsy offers the rare opportunities to record neural activities with wide-band ECoG, and apply 50 Hz (cortical mapping) and 1 Hz (connectivity mapping) electrical stimulation to delineate the parieto-frontal network for praxis. The praxis-related area was localized in the anterior part of SMG, mostly in PF. Transient functional impairment (fast dynamics) was specific to the tool use pantomime. Within the praxis network (PMv-PF), functional differentiation was observed between the interconnected PMv (negative motor response) and PF.**

I. Introduction

For epilepsy surgery, it is important to fully resect the epileptic focus to cure the disease. At the same time, it is also important to preserve the brain functions around the epileptic focus. As a part of presurgical evaluations for intractable partial epilepsy, patients undergo chronic implantation of subdural electrodes when the focus is not well determined by non-invasive evaluations or the focus is located at or around the important functional cortices such as language. In order to map the brain functions, we usually record neural activities (e.g., ERPs, high gamma activities) while patients complete a task (e.g., naming) and stimulate the functionally identified regions to evaluate the necessity of these areas in a particular brain function [1]. In contrast to neuroimaging activation studies, electrical cortical stimulation can delineate the cortex responsible for a particular task by making functional impairment. The functional interference is temporary (~5 s), discretely focal (～1cm) [fast dynamics], and in sharp contrast to chronic stroke lesions that are relatively large and usually associated with cortical plastic compensation [slow dynamics].

In order to elucidate the neural mechanisms of the body representation in the brain and the mechanism of the short and long-term changes in this representation, we first need to understand the underlying physiological neural mechanisms of the body representation in the brain with regards to somatognosia and motor control. In the research group A03-4, our objective is to map the fronto-parietal network related with the body representation, probe the neural biomarkers, and clarify the fast dynamics by means of invasive presurgical evaluation with direct neural recording from electrocorticogram (ECoG) and interventions by electrical stimulation. We hope to apply these findings to presurgical evaluation of functional neurosurgery and rehabilitation interventions.

II. Aim of the Group

Subjects are patients with intractable partial epilepsy who underwent chronic subdural electrode implantation in the parietal & frontal areas for presurgical evaluations (IRB#C533, 443). By means of ECoG recorded with wide-band frequencies, we probe neural activities related with tool use, reaching, grasping and fine hand movements. We use an electrical tracing method (1 Hz electrical stimulation) of cortico-cortical evoked potential (CCEP), which we originally developed [2] to probe interareal connections in the fronto-parietal network. Based upon the direct neural recording and connectivity findings, we define the core fronto-parietal network for body representation/motor control, and extract the neural marker representing praxis movements such as tool-use and reach-to-grasp behavior. We then apply 50 Hz electrical stimulation to the praxis-related fronto-parietal network (either to single or dual node of the network) during praxic tasks to elucidate the transient functional alternation, namely, fast dynamics alternation of the motor control and somatognosia.

III. Research Topics

We have carried out four research topics and review the their outlines here.

A. Left fronto-parietal netwrok for tool-use and its alternation (fast dynamics) by high frequency electrical stimulation

Subjects are 5 patients with intractable left partial epilepsy. They underwent subdural electrode implantation in the left, language-dominant, parietal & frontal areas for presurgical evaluations. In addition to routine clinical functional mapping by 50Hz electrical stimulation, we performed the tool-use pantomime task to explore the praxis-related function in the inferior parietal lobe. In all 5 patients, 50 Hz stimulation was performed in 54 electrodes in the left, language-dominant, inferior parietal lobe. In 22 % of electrodes (12 electrodes), stimulation elicited inability to pantomime the tool use. Patients' introspection implicated impairment in the retrieval of stored gesture representations for planning/execution of the praxic movements. In all 'tool use pantomime' electrodes, patients were able to use the tools actually and name the tools during stimulation. Finger tapping, reaching and precision grip were not impaired either in all electrodes. Anatomically, these 'tool use pantomime' electrodes were clustered on the left anterior division of supramarginal gyrus (SMG), mostly at PF in the Jülich cytoarchitectonic atlas. CCEP investigation revealed site-specific connections from SMG to PMv, where stimulation elicited negative motor response, suggesting functional differentiation within the praxis-related PMv-PF network. Different from the arcuate fasciculus for the dorsal language network (connecting the pars orbitalis and triangularis to the posterior superior and middle temporal gyri by CCEP connectivity [3]), probabilistic diffusion tractography revealed SLF III as the underlying white matter pathway for the praxis-related network [4].

In the latter part of FYI 2015, we have started recording of neural activities with wide-band ECoG during several praxic movements, and attempt to define their neural marker by integrating findings of 50 Hz (fast dynamics alternation) and 1 Hz (functional connectivity) electrical stimulation. We also started the quantitative assessment of transient alternation of motor control by the 3D motion capture system we introduced by this grant.

B. Human dorsal parieto-frontal connectivity map by using CCEP

Fronto-parietal network is essential for sensorimotor integration in various complex behaviors, and its disruption is associated with pathophysiology of apraxia, visuo-spatial disorders and asomatognosia. Despite advances in knowledge regarding specialized cortical areas for various sensorimotor transformations, little is known about the underlying cortico-cortical connectivity in humans, partly because we cannot directly apply findings of non-human primate tracer studies due to development of association cortices such as Brodmann's Area 39, 40. We have applied CCEP methodology for clinically mapping functionally relevant networks [2, 5] and also investigated the fronto-parietal functional connectivity [6]. This work, however, focused more on the ventral pathway because of the limited participants. In the present study, we recruited more patients to study the functional connectivity for the dorsal/medial parietal and frontal areas. The superior parietal lobule (SPL) connected to the dorsal premotor area and dorsal precentral gyrus. Within the parietal lobe, SPL had bidirectioinal connections to the medial parietal areas (the precuneus and posterior cingulate) [7].

C. Right fronto-parietal netwrok for corporeal awareness and its alternation (fast dynamics) by high frequency electrical stimulation

We have recently started the collaborative research with the research group A02-1 (Dr. Naito). Applying the same methodology of the research topic A, namely, wide-band ECoG recording during tasks, intervention with 50&1 Hz stimulation, we aim at delineating the right fronto-parietal network for corporeal awareness and self identification, their neural markers, and fast dynamics to the transient intervention.

D. Transition from fast to slow dynamics for plastic compensation of sense of agency: a brain surgery case series study

In close cooperation with Dr. Takeharu Kunieda (co-investigator at the Department of Neurosurgery, Kyoto Unviersity Hospital), we have recently started a collaborative research with the research group A01-1 (Drs. Imamizu, Ohki, and Maeda). We recruit patients with brain tumor who are planned to resect the non-dominant (right) temporo-parietal junction. We sequentially perform the sense of agency task before and after surgery to quantitate how the sense of agency changes in the acute to subacute postoperative periods. We focus on these periods in order to elucidate the transition from fast to slow dynamics for plastic compensation of sense of agency.

IV. Future Perspective

In the FYI 2015, we have delineated the ventral fronto-parietal network for tool-use and its transient alternation (fast dynamics) by means of 50 Hz and 1 Hz stimulation. We also probed the dorsal fronto-parietal connectivity map using CCEP. In the FYI 2016, we will focus on the following topics.

1) Quantitative assessment of the fast dynamics alternation by applying 50 Hz stimulation to the single or dual node of the praxic network

2) Elucidation of the neural markers for praxis by integrating direct wide-band ECoG recording, 50 Hz (fast dynamics alternation) and 1 Hz (connectivity mapping) stimulation.

3) Close collaboration with the research group A01-1&A02-1 to elucidate the right fronto-parietal network for human body representation in the brain, identify the markers reflecting this phenomenon, and transition from fast to slow dynamics for plastic compensation.

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A03-5 Visualization and manipulation of pathway-specific brain plasticity on the body representation following the sensory nerve injury

Hironobu Osaki, Yoshifumi Ueta, Mariko Miyata
Tokyo Women's Medical University, School of Medicine

Abstract— Peripheral nerve injury causes rewiring of the neural circuit in the brain. Recently we have demonstrated that transection of the whisker sensory nerve newly recruits multiple afferent fibers onto a relay neuron in the whisker sensory thalamus (V2 VPm) of mice within a week [Takeuchi Y. *et al*. (2012) J Neurosci 32: 6917]. In this project, we tried to reveal that origins of the newly recruited afferent fibers using transgenic mice whose all whisker-origin lemniscal fibers are visualized with td-tomato expression. We revealed that origins of the newly recruited fibers include non-whisker-sensory brainstem nuclei such as the mandibular (V3) subregions of trigeminal nuclei and the dorsal column nuclei, which normally represent body parts rather than whiskers. Furthermore, V2 VPm neurons after the transection occasionally had ectopic receptive fields representing non-V2 body parts, such as the lower jaw (V3 region) and the back. We also found that V2 VPm neurons in the transected group fired in a much more bursty manner than those in the control group. These results indicate that the peripheral nerve transection induces large-scale somatotopic reorganization, accompanied with bursty neural firing in the thalamus.

I. Introduction

In central nervous system, plastic changes, such as somatotopic reorganization occurs in response to the peripheral nerve injury.

In the mouse V2 VPm, mature single fiber innervation of lemniscal fiber to a V2 VPm neuron forms via developmental synapse elimination (Arsenault and Zhang, 2006, Takeuchi et al., 2014). Recently we have reported that complete transection of the primary whisker sensory nerve of mice causes functional remodeling of lemniscal fiber; newly multiple lemniscal fibers are recruited onto a VPm neuron (Takeuchi et al., 2012). Based on evidence accumulated *in vivo* studies, we hypothesized that the newly recruited lemniscal fibers contain multiple origins other than the whisker sensory principle trigeminal nucleus (PrV2), which leads to somatotopic reorganization. To reveal this, we tried to visualize whisker related somatotopic information, which is carried by lemniscal fibers using the transgenic mouse, and investigate how somatotopic representation changes on somatosensory pathway following whisker nerve injury.

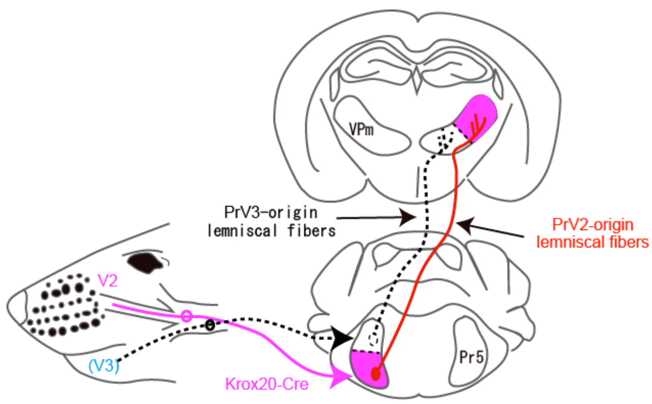
II. Aim of the Group

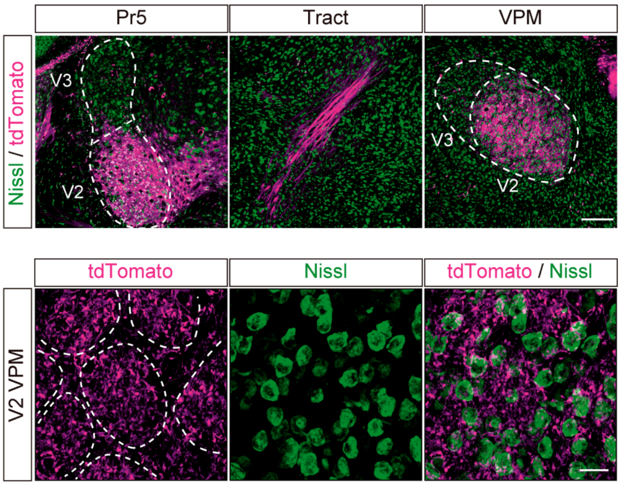
Our group uses anatomical and physiological techniques to study the neuronal circuit mechanism underlies the somatotopic reorganization after the nerve injury. Especially, the aim of this project is to visualize and/ or stimulate the specific neural circuit which appears injured-induced remodeling underlie somatotopic reorganization. We hope these findings will help us to understand neuropathic pain that is currently difficult to treat in human.

III. Research Topics

A. Visualization of somatotopic specific pathway using genetic tecnique in the mouse.

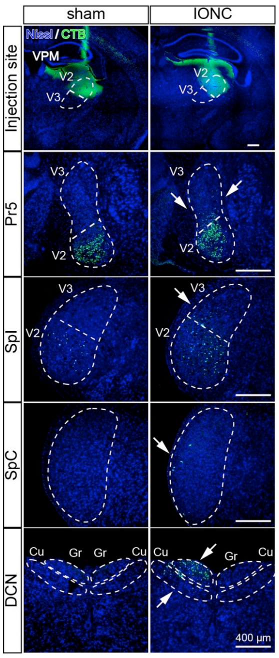
First, we tried to establish the visualization of somatotopic information on afferent fibers to the somatosensory thalamus. Using transgenic mice: Krox20 floxed ×Ai14 (td tomato reporter) mouse whose neurons (more than 90%) in the whisker sensory principle trigeminal nucleus (PrV2) was specifically labeled. Furthermore, lemniscal fibers and those terminals originated from PrV2 in the transgenic mice were clearly labeled with td-tomato.





B. *Visualization of somatotopic reorganization after the nerve injury in the mouse VPM.*

Second, we found that the whisker nerve transection caused the retraction of PrV2-originating lemniscal fibers and invasion of those not originating from PrV2 to the V2 VPM. This anatomical remodeling with somatotopic reorganization was highly correlated with the functional remodeling of lemniscal fibers. Using retorograde tracer , CTB, which was injected into theV2 VPM, origins of the non-PrV2 lemniscal fibers included the mandibular (V3) subregions of trigeminal nuclei and the dorsal column nuclei, which normally represent body parts other than whiskers.



IONC: infraorbital nerve cut (Whisker nerve transection)
Pr5: PrV, SpI: spinothalamic interpolaris, SpC spinal trigeminal nucleus caudalis, DCN, dorsal column nuclei

C. *Reorganization of receptive fields of V2 VPm neurons after the transection.*

We mapped receptive fields of V2 VPm neurons after the transection. Consistent with results from anatomical remodeling (Topics *B*), V2 VPm neurons in the transected group occasionally had ectopic receptive fields representing non-V2 body parts, such as the lower jaw (V3 region) and the back. On the other hand, receptive fields of V2 VPm neurons in control mice were confined to the V2 region on the face. Furthermore we also found that V2 VPm neurons in the transected group fired in a much more bursty manner than those in the control group.

IV. Future Perspective

We revealed that the nerve injury causes somatotopic reorganization in the thalamus. It remains unclear how this reorganization affects higher order network, such as the thalamo-cortical connection. To address this issue, we have been developed new tools. First, we have developed intrinsic-signal optical imaging system, by which we can visualize the cortical somatotopic map. Second, we have established a new transgenic mouse, whose all whisker-origin lemniscal fibers express channelrhodopsin-2 (ChR2), to manipulate the neural activity of lemniscal pathway optogenetically. By combining these tools, we could visualize the cortical somatotopic map reorganization and manipulate the injured neural pathway specifically. We also try to reveal molecular mechanism underlie thalamic somatotopic reorganization as a biomarker.

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Annual report of research project A03-6

Masatoshi Yoshida
National Institute for Physiological Sciences, Okazaki, Japan

I. Introduction

Spatial neglect is a symptom in which the (mainly) right side of the brain damages reduces or abolishes responses to the sensory stimuli in the contralateral to the lesion. Spatial neglect is a cognitive deficit that cannot be explained merely primary sensory deficits or motor deficits. Recent studies on human brain imaging suggests that spatial neglect is not caused by single brain area but rather by disintegration of the dorsal and ventral pathway for attention [1].

II. Aim of the Group

To understand the neural mechanisms of a certain neurological disease, it is indispensable to establish an animal model of the disease. However, the animal model of spatial neglect is not yet established. Recent studies on homology between human and non-human primates revealed that macaque monkeys also have the dorsal and ventral network for attention [2], [3]. The aim of the group is 1) to establish an animal model of spatial neglect by making a lesion in monkeys, to brain regions which is thought to be homologous to the dorsal and ventral pathway for attention and by evaluating behavior of the monkeys, 2) to investigate how the animal model of spatial neglect process information of retinal- and head-centered coordinates, by measuring gaze and head movement and 3) to understand the brain mechanisms of the deficits and recovery using functional brain imaging.

III. Research Topics

A. *Animal model of spatial neglect by making a lesion to the attention networks*

First, the research group conducted experiments in which the right superior temporal gyrus (STG) was surgically removed in two monkeys, so that the ventral attention network is disconnected.

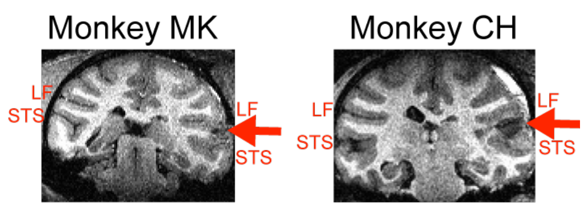

Fig. 1. MR structural images on the center of the lesion site in two monkeys. iemens Allegra 3T, MPRAGE3D, 0.5mm * 0.5mm * 0.5mm voxel. LF: lateral fissure, STS: superior temporal sulcus.

We used two Japanese monkeys (monkey MK, male, 8.2kg bw; monkey CH, male, 7.2kg bw). After training with behavioral task (described later), the right STG was surgically ablated by aspiration under isoflurane anesthesia. The lesion site was determined so that it does not include area MT posteriorly, and primary auditory cortex anteriorly. MR structural images taken 1week after the lesion demonstrates that the lesion site was confined in the right STG (Fig.1).

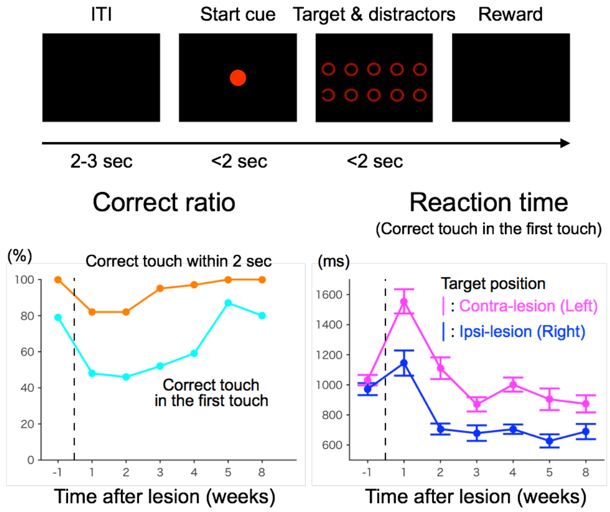

Fig. 2. The results of target-choice task in Monkey MK. (Top) The task sequence for the target-choice task. The target in this case is the flipped 'C' pattern on the left. (Bottom) Behaviral resutls. Correct ratio (left) nad reaction time (right) was calculated and plotted across time before and after the lesion.

To evaluate the behavior before and after the lesion, we devised a 'target-choice task', which was designed to mimic the line cancellation task used for evaluating human spatial neglect subjects (Fig.2). In this task, under head-unrestrained condition, monkeys chose the target among distractors by touching the target and get a reward. The correct ratio of Monkey MK decreased 1-2 weeks after the lesion but recovered to the normal level after that (Fig.2. lower left). On the other hand, reaction time to the target (Fig.2. lower right) was longer in the target in the contralateral to the lesion (the left half of the display; magenta line) than in the targets in the ipsilateral to the lesion (the right half of the display; blue line). A similar result was obtained from Monkey CH (experiment ongoing). These results suggest that spatial neglect is maintained for 2 months after the right STG lesion.

B. *Eye- and head-tracking*

We also examined the effect of the lesion on eye movements and head movements. It is already reported that the gaze and head movements in human spatial neglect subjects is biased to the ipsilateral to the lesion, during free-viewing of static and dynamic images [4]. We examined whether this is observed in the monkeys after the lesion. We used Tobii's TX300 for eye- and head-tracking. Tx300 is a remote-type eye tracker that can measure gaze position (where the subject is looking at) and eye position (eyeballs in the head, that is, head direction) in 300Hz sampling rate without head restraint.

The monkeys were tested with a free-viewing task. In this task, we measured gaze and eye positions during the monkeys sat on a monkey chair and view static images on the display with head-unrestrained. The monkeys were reinforced to view the images on the screen by giving juice reward while monkeys view the display. The monkeys were not reinforced to view specific items on the display. We calculated the distribution of gaze positions and plotted histograms before and after the lesion (Fig,3 left). We found that the gaze positions of Monkey MK was biased toward ipsilateral to the lesion 1-2 weeks after the lesion. A similar result was obtained from Monkey CH (experiments ongoing).

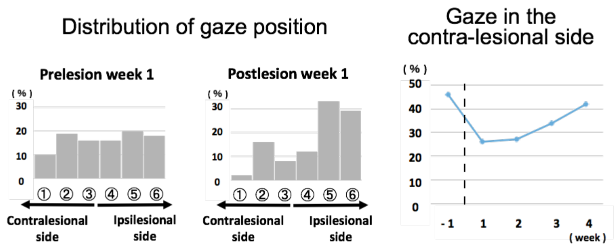

Fig. 3. The results of eye-tracking in Monkey MK. (Left) Distribution of gaze positions. (Right) Ratio of gaze in the contralateral to the lesion is plotted across the time after the lesion.

These results suggest that rSTG lesion induce spatial neglect in eye movements. Preliminary analysis of head-tracking data suggests that head direction is also biased toward ipsilateral to the lesion.

C. Functional brain imaging

The research group collaborated with Prof. Fukunaga in the National Institute for Physiological Science to measure brain activity of the monkeys before and after the lesion. We measured BOLD activity of the monkeys under 1% isoflurane anesthesia [5] by the echo-planaer imaging method. To quantify the functional connectivity of the attentional network in the brain, we put the seed on the frontal eye field, FEF and calculated correlation coefficients between the temporal fluctuation of the BOLD activity in the seed and that of the other brain regions.

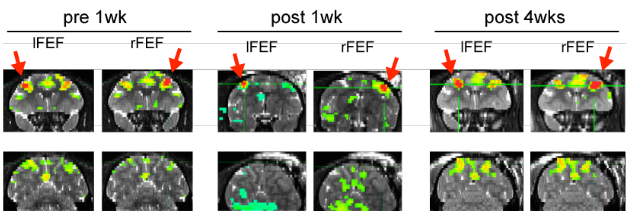

Fig. 4. rsfMRI in Monkey MK. (Top) Coronal slice containg FEF as the seed regions (indicated as a red arrow). (Bottom) Coronal slice containing LIP. The color indicates correlation coefficients. In post-lesion 1st week, the threshold for color representation is reduced. TR=2000ms; 1.25mm * 1.25mm * 1.60mm.

We found strong correlation between the BOLD activities of FEF and LIP (Fig.4, left) and those of FEF and STG. The former can be interpreted as the activity related to the dorsal network for attention and the latter can be interpreted as the activity related to the ventral network for attention. The correlation between the BOLD activity of FEF and LIP reduced 1 week after the lesion but the correlation 4 weeks after the lesion recovered to the value similar to the pre-lesion (Fig.4, middle and right). These results suggest that the damage in the part of the ventral attention network (rSTG) affected the functional connectivity in the dorsal attention network.

IV. Future Perspective

The damage to the part of the ventral attention network (rSTG) induced spatial neglect in the monkeys after 1-2 weeks after the lesion. Relatively mild deficits was sustained more than two months after the lesion. In parallel with this behavioral deficits and recovery, the functional connectivity in the dorsal attention network was reduced and recovered. To replicate these findings, we are going to test other monkeys. We are also going to model how body schema is affected in the monkeys by analyzing eye- and head-tracking data. We are also going to integrate these findings with the data form functional brain imaging so that we can elucidate the brain mechanism of body schema in general.

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Annual report of research project A03-7

Yumi Murata
Human Informatics Research Institute,
National Institute of Advanced Industrial Science and Technology (AIST)

***Abstract*— We have investigated the mechanisms of functional recovery using a monkey model of cortical lesion, in which a focal lesion is induced in the primary motor cortex (M1). Brain imaging of M1-lesioned monkeys using positron emission tomography revealed overactivity of the PMv during the recovery period. The causal role in motor recovery was confirmed by means of pharmacological inactivation by muscimol, indicating that the remaining cortical area compensates for the motor deficit caused by the M1 lesion. This functional reorganization may be based on axonal and synaptic reorganization as indicated by the increased gene expression of growth-associated protein-43 in PMv. Moreover, as the first step to understand functional recovery mechanisms in a clinically more relevant model, we induce a focal stroke in the internal capsule, an area susceptible in human stroke patients. Gross movement such as reaching and power gripping improved, whereas impairment of dexterous hand movements remained until 3 months after stroke induction. The result is in contrast to that observed in our M1-lesion model, in which drastic recovery of dexterous movements was observed during the first month, suggesting that the compensatory mechanism after internal capsule stroke is different from that after cortical lesion.**

I. Introduction

Damage to the brain results in functional deficit; however some functions recover following brain damage. Based on clinical observations, appropriate rehabilitative training is thought to facilitate the recovery of functional deficits caused by brain damage. However, it remains largely unclear how rehabilitative training promotes functional recovery. We previously conducted behavioral analyses using a macaque monkey model of brain damage, and reported that motor training after primary motor cortex (M1) lesion promotes recovery of precision grip (prehension of a small object with finger-to-thumb opposition) [1].

II. Aim of the Group

The aim of the present study is to investigate the brain regions of the macaque monkey, which are involved in functional compensation during the recovery of precision grip after lesioning the digit area in M1. In addition, to identify the cortical areas and pathways where neuritic or synaptic remodeling occurs during recovery after a lesion of M1, we focused on temporal changes in the gene expression of growth-associated protein-43 (GAP-43), the expression of which has been shown to be related to axonal sprouting and structural alteration of synapses. Moreover, we made a new brain damage model using macaque monkeys, in which a focal stroke was induced in the internal capsule, an area susceptible in human stroke patients.

III. Research Topics

A. Neural plasticity underlying the training-induced recovery of precison grip after primary motor cortex lesion in macaque monkeys

Before M1 lesion, all of the monkeys smoothly performed the precision grip task. Immediately after a lesion of the hand digit area in M1 by ibotenic acid injection (Fig.1), the monkeys could not perform a small-object retrieval task because of hand paralysis, including a complete loss of digit movement. Functional recovery of hand movements was observed during the course of daily post-lesion motor training. Specifically, the number of successful trials in the precision grip task progressively increased during the first month after the lesion.

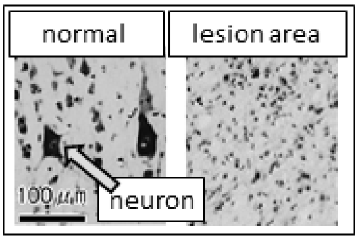

Fig. 1. The normal intact and lesion areas of the primary motor cortex

We measured regional cerebral blood flow as an index of brain activity during performance of precision grip by using $H_2{}^{15}O$-positron emission tomography (PET), and measured brain activity patterns during the functional recovery period after a lesion of the M1 digit area. The PET analysis showed that the regional cerebral blood flow during the precision grip task increased in the ipsilesional ventral premotor area (PMv) during the functional recovery (Fig.2) [2]. We then evaluated the contribution of the ipsilesional PMv to functional compensation using a pharmacological inactivation experiment by microinjections of muscimol, a $GABA_A$ receptor agonist. Muscimol injection into the ipsilesional PMv after recovery of precision grip impaired the recovered precision grip in affected hand, while the muscimol-induced inactivation of the same region had a small effect before lesion. This result suggests that the recovery of precision grip depends on increased activity of the ipsilesional PMv. Moreover, we investigated the plastic changes of neurons during the functional recovery using histochemical analysis of a plasticity-related protein (GAP-43), which may mediate axonal sprouting and structural alteration of synapses. In situ hybridization histochemistry revealed the increased gene expression of GAP-43 in the ipsilesional PMv during the recovery phase after M1 lesion [3]. The results of the present study may indicate that structural changes of neurons in the ipsilesional PMv are involved in functional compensation of precision grip after M1 lesion.

Fig. 2. A brain activity change that occurs during rehabilitative training-induced recovery in brain-lesioned animal.

B. Development and characterization of a monkey model of internal capsular stroke.

M1 lesions specifically impair motor function, leaving sensory and cognitive functions intact; they are therefore suitable for investigating changes in neural structure and function that are associated with deficits and recovery of motor behavior. However, in human stroke patients, the severity and outcome of motor impairments depend on the degree of damage to the white matter, especially that in the posterior internal capsule, an area susceptible in human stroke patients. Thus, to bridge the gap between the results obtained in M1-lesioned macaques and the development of clinical intervention strategies, it is important to establish a non-human primate model of focal stroke at the posterior internal capsule.

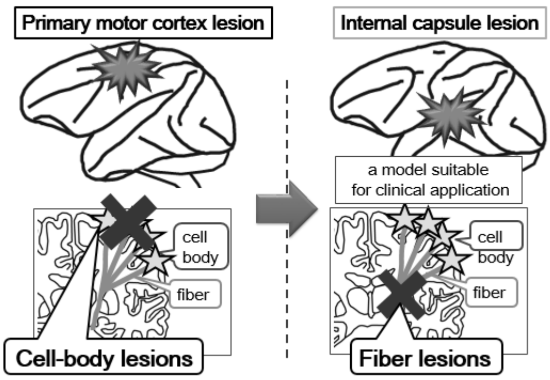

Fig. 3. The schema of two models

An anatomical MRI scan was performed on Japanese monkeys to identify the part of the internal capsule in which descending motor tracts from the hand digit area of M1 pass though. Endthelin-1, a vasoconstrictor peptide, was then injected into the identified part of the inner capsule (1.5 μL/μg; 15 tracks, 120 μl in total). The lesion was evaluated using a T2-weighted anatomical MRI scan after injection; the areas of increased T2 signal were observed around the injected area from 3 days to 1 week, then they gradually disappeared within 1 month after lesion.

Motor deficit occurred in the contralesional upper limb, as was shown by a decrease in the success rate of a small-object retrieval task, in which monkeys retrieve a small food morsel from a narrow tube. Recovery of gross movements such as reach and power grip occurred during the first week after lesion, while little recovery of dexterous movements including precision grip was observed even at 3 month after lesion. The result is in contrast to that observed in our M1-lesion model, in which drastic recovery of dexterous movements was observed during the first month, suggesting that the compensatory mechanism after internal capsule stroke is different from that after cortical lesion. We believe that the present model is useful not only for studying neurological changes underlying deficits and recovery but also for testing therapeutic interventions after stroke in the internal capsule of primates.

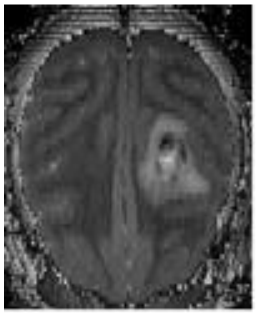

Fig. 4. A brain anatomical MRI after stroke in the internal capsule.

IV. Future Perspective

We will investigate the mechanism of the functional recovery after brain damage, using both M1-lesion model and capsular stroke model monkeys. Especially, we will focus on how anatomical changes of neuronal projection underlie functional recovery after brain damage.

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Activities of Group B (Systems Engineering)

Jun OTA
Research into Artifacts, Center for Engineering (RACE), The University of Tokyo

I. Research Plan

The systems engineering group (Group B) constructs mathematical models of the "slow dynamics" alteration of the body representation in the brain, influenced by fast dynamics. Understanding slow dynamics will be the key to rehabilitation therapy, which have been central to research. Group B consists of three projects (B01, B02 and B03) as shown in Fig. 1.

II. Research Results

Project B01 is a planned research project and the aim of the project is creation of "cognitive body model" of the body representations in the brain. Members (only the principal investigator and are funded co-investigators) as follows: Principal Investigator: Prof. Hajime Asama (Univ of Tokyo). Funded Co-Investigators: Prof. Toshiyuki Kondo (Tokyo Univ of Agriculture and Technology), Prof. Hirokazu Tanaka (JAIST), Prof. Shiro Yano (Ritsumeikan Univ.), and Jun Izawa (Tsukuba Univ.).

In this year, Project B01 executed psychophysical experiments to investigate the effect of multi-sensory integration and attention on body consciousness (sense of ownership, sense of agency) toward the modeling of them. This group also evaluated the electroencephalogram (EEG) features (e.g., current source estimation, readiness potential, and event-related de-synchronization) as a candidate of the marker to quantify motor intention, body schema, and body consciousness. Moreover, the group developed computational models of neural activities in motor area and schizophrenia.

Project B02 is a planned research project and the aim of the project is creation of "muscle synergy control model" of the body representations in the brain. Members are as follows: Principal Investigator: Prof. Jun Ota (Univ of Tokyo). Funded Co-Investigators: Prof. Shinya Aoi (Kyoto Univ), and Prof. Ryosuke Chiba (Asahikawa Medical University).

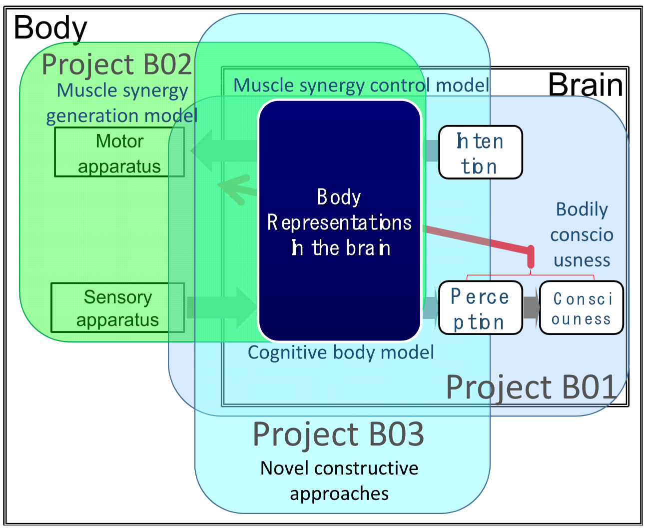

Figure 1 Relationship between projects in Group B

In this year, Project B02 developed experimental settings and results. From these results, we constructed fast and slow dynamics. We proposed fast dynamics model for postural control, which was verified in movable floor experiments and musculoskeletal simulations, and fast and slow dynamics models for locomotion, which was verified by split-belt treadmill walking of a biped robot and a rat neuromusculoskeletal model.

Project B03 is a subscribed research project and the aim of the project is to create the model of body representation in the brain, with novel constructive approaches.

In B03-01 (principal investigator: Prof. Tetsuro Funato (Univ. of Electro-Communications)), they approached the design principle of muscle synergy as follows: (1) kinematic synergy reflecting the COM motion was found in bipedally standing rat, (2) muscle synergy of walking rat was analyzed, and (3) posture control model that could represent the ataxic variation of motion was proposed.

In B03-02 (principal investigator: Prof. Yasuhisa Hasegawa (Nagoya Univ.)), they have developed robotic thumb with three DOFs and almost same workspace as human thumb. The interface device measures motions of human thumb and gives a tactile feedback to fingertip of the thumb using electric stimulation.

In B03-03 (principal investigator: Prof. Koh Hosoda (Osaka Univ.)), they have developed a muscular-skeletal robotic platform for constructive experiment of body image. We have also investigated a brain-inspiredarchitecture for building body image. Several prototypes of master-slave hand were developed for collaboration with other research groups in the project.

In B03-04 (principal investigator: Prof. Tadahiro Taniguchi (Ritsumeikan Univ.)), to construct a computational model of the formation process of body schema in the human central nervous system, they proposed an unsupervised machine learning method that can estimate a topology of tactile sensor distribution and the number of limbs, i.e., body parts, sequentially and automatically from high dimensional tactile sensor data using a Dirichlet process Gaussian mixture model.

III. Present Achievement of Group B

Followings are the present achievement of three projects:

In Project B1, they model body consciousness in relation to body cognition. With several experiments including rubber hand experiments, they estimate the model structure (which parameters influence the value of body consciousness), formulation, and correspondence with real data.

In Project B2, they model sensory-motor control process with respect to stance control and biped locomotion. They deal with the problems of various sensor inputs and muscle outputs with weighting and reweighting of muscle synergies and sensor feedback loops.

In Project B3, they model (a) generation process of body representation in the brain and (b) change of body configuration, by using constructive approach.

IV. GROUP MEETING

The following group meeting was held in Group B.
Date and Time: Tuesday, November 24, 2015, 10:00-12:00
Place: seminar room, VBL 4th floor, Nagoya University.
Attendees: 19 in total including group members.
Contents: Three presentations about research plan and progress by subscribed research group members, and general discussion.

Moreover, group members discussed their research issues in the following organized sessions in the related conferences.
(1) Sunday, March 15, 2015, 20th Robotics Symposia, 4 presentations.
(2) Tuesday, July 28, 2015, SICE Annual Conference 2015, 6 presentations.
(3) Tuesday, November 24, 2015, IEEE MHS2015, 5 presentations.
Small-scale meetings within Group B and joint meetings with members of Group A and C were also conducted.

V. FUTURE PLAN

Group meetings will be held and discussion will be conducted between members of planned research projects and those of subscribed research projects.

Models in the three projects of Group B share the body representations in the brain that changes slowly expressed as slow dynamics. We aim to construct mathematical models of humans who work on the environment, recognize the environment and the body through the body representations in the brain. Group B aims to contribute to Group A with modeling on the relationship between body cognition and motor control, and contribute to Group C with modeling for model-based rehabilitation.

Annual report of research project B01-1

Hajime Asama
The University of Tokyo

***Abstract*— Body consciousness such as sense of agency and sense of ownership is generated in real time based on the body representation in brain. This process can be called "fast dynamics." On the other hand, the body representation is created, updated and transformed through perceptional and motion experience, which can be called "slow dynamics." In this group, these dynamics on the process creating and updating body representation in brain related to body consciousness are investigated and modelled mathematically.**

I. Introduction

Body consciousness such as sense of agency and sense of ownership is generated in real time based on the body representation in brain. This process can be called "fast dynamics." On the other hand, the body representation is created, updated and transformed through perceptional and motion experience, which can be called "slow dynamics." In this group, these dynamics on the process creating and updating body representation in brain related to body consciousness are investigated and modelled mathematically.

II. Aim of the Group

The concrete objectives of B01 research group are mathematical modeling of creation of body consciousness and transformation of body representation of brain, verification of cognition-body mapping model, and examination of its application to model-based rehabilitation.

III. Research Topics

Fig. 1 shows the conception of body representation generation basing on body consciousness and the group structure.

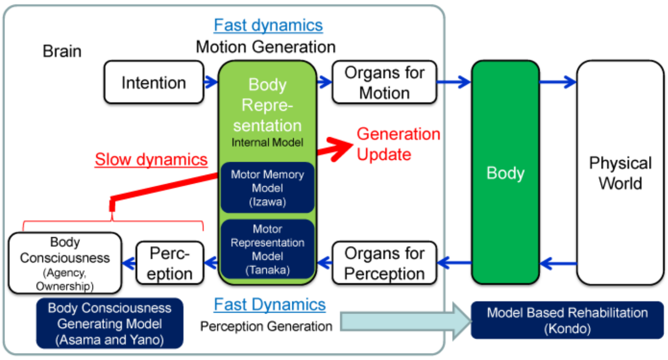

Fig. 1 Generating processes of body representation basing on body consciousness

Our research topics are as follows:

A. *Body Consciousness Generation Model*

(1) Understanding of body consciousness that influences slow dynamics

Asama's group (University of Tokyo) examined the role of high-level cognitive processes and the interaction with perceptual processes in body consciousness. We found that the comparison between an overarching goal and feedback of goal-attainment is critical for sense of agency, as the comparison between prediction basing on motor signal and sensory feedback [1, 2]. Further, we also found that goal and feedback of goal-attainment enhance updating of body representation via sense of agency [3]. Moreover, we found that the dominances of the two types of processes underlying body consciousness could change when processes resources or arousal of attention change [4, 5]. These findings are important for underlying human behaviors involving body consciousness, and provide important knowledge for construction of mathematical model of body consciousness.

Further, we examined neural activities during arising of sense of agency with electroencephalogram. We found that when the participants had stronger belief in their agency, the readiness potential, which usually occur before actions, started earlier and had larger amplitude comparing with the condition in which the participants' beliefs in agency was determined [6].

(2) Slow dynamics model of body representation updating basing on body consciousness

Asama's group examined kinematical model that represents slow dynamics of body representation updating accompany with changing of body consciousness. Specifically, we described the changing dynamics of arm length during a reaching task.

(3) Stochastic model of body consciousness

Toward the goal of understanding the learning system for Body-representation, Yano's group (Tokyo University of Agriculture and Technology) proposed the new and general point of view that the SoA corresponds to the likelihood of predictive distribution, which is the term commonly used in the statistical learning theory. This view enables us to derive a variety of hypotheses for experimental researches on the SoA [7]. As a practical matter, we derived a hypothesis for the Keio task, which is the experimental task to measure one's SoA, that examinee gradually becomes to feel the highest SoA at the average time of the event with the stochastic time delay. We got some experimental supports for this hypothesis.

We also proposed the theoretical idea that the initial behavior of the generalization error becomes slow [8]. The generalization error is an important value in the statistical learning theory, which evaluates the distance between the predictive distribution and the true distribution. Based on this idea, we proposed the hypothesis that the examinee in the Keio task shows slow learning when his or her prior belief is too strict. This hypothesis is experimentally supported [7, 8]. This theoretical idea also gives us the way to quicken the learning speed of examinee. It would be helpful for the motor learning tasks.

B. Embodied-brain Motor Representation Model

Understanding how body movements are represented in the brain is indispensable for understanding of body consciousness. Toward the goal of understanding the input-output representations for forward models, Tanaka's group (JAIST) made a detailed comparison among computational models of motor cortex that have been proposed [9]. Computational models fall broadly into (1) optimality models, (2) neural network models, and (3) spatial dynamics models. We argued the computational principles and the predictions made by these models and clarified issues for future studies. In addition, with the Kakei group, we discussed how dynamics computation are modeled in the cerebellar cortex and the cerebellar nuclei and the cerebellar loops with motor cortex and premotor cortex.

Furthermore, we performed a simultaneous recording of high-density EEG and body motion from humans performing a reaching task [10]. We obtained 19 subject data and localized brain sources by applying signal processing methods such as artifact subspace reconstruction, independent component analysis, dipole source localization and Granger-causality analysis. We found that those sources exhibited response properties modulated by movement directions (directional tuning) and its posture dependence. By exploiting the high temporal resolution of EEG, we demonstrate, during the movement task, how directional tuning evolved dynamically with a time scale of a few milliseconds. These results indicate that it is possible to investigate representations of body movements and body consciousness noninvasively using high-density EEG.

C. Motor Memory Model

Izawa(Univ. Tsukuba) developed the general computational framework of the motor adaptation that was composed of the following two dynamics: the memory update (fast) and the meta learning (slow) [11]. Based on the motor learning model, he proposed the model-based diagnostic approach through developing the computational neuroanatomical model of the brain disease where the deformation of the specific computational function may generates the motor dysfunctions [12]. This model was further extended to explain a computational mechanism of the neuro-rehabilitation that was composed of the dopaminergic reward-based action selection (fast dynamism) and the use-dependent recovery of the body schema (slow dynamics) [13]. It was suggested that balancing two dynamics was critical for a stable motor recovery.

D. Model based Rehabilitation

To clarify the relationship between body consciousness (i.e., sense of agency/ownership) and motor learning, and to find quantitative biomarkers reflecting plastic change of the body representation in brain, Kondo's group (Tokyo University of Agriculture and Technology) investigated 1) the effects of passive visuomotor experience on the change of body schema [14], 2) the functional connectivity analysis of NIRS data during rubber hand illusion [15], and 3) development of an immersive VR system for analyzing how these visual interventions modulate body consciousness and effect on the neurofeedback training of motor imagery-based BCI.

In the first topic, this group executed visuomotor learning experiment, and compared psychometric functions of estimated hand direction (body schema) between before and after the motor learning. They found that even passive motor experience leads to limited but actual compensation of body schema. In the second topic, they evaluated functional connectivity of NIRS data under RHI by using Granger causality analysis. They found that significant causality from right prefrontal area to ipsilateral premotor area under the synchronous stimulation condition. This may be related to the sense of ownership. In the third topic, they confirmed that immersive VR system enables subjects to have strong body consciousness and it would be promising markers of body representation in brain.

IV. Future Perspective

In this year, we constructed models of body representation generating processes (slow dynamics) basing on body consciousness. After the next year, we will collaborate with A01 and C01 groups, examining underlying physiological models and clarifying validity of our model based rehabilitation.

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Annual report of research project B02-1

Jun Ota
Research into Artifacts, Center for Engineering (RACE), The University of Tokyo

***Abstract*— To elucidate mechanisms of the body representation in brain for adaptive motor control, we aim to construct fast and slow dynamics models by focusing on muscle synergy. We assume that the alteration of muscle synergy structure reflects the alteration of the body representation in brain, and we clarify the contribution of the body representation in brain through modeling the fast and slow dynamics of synergy structure. In this year, we proposed fast dynamics model for postural control and fast and slow dynamics models for locomotion. The postural control model was verified in movable floor experiments and musculoskeletal simulations. The locomotion model was verified by split-belt treadmill walking of a biped robot and a rat neuromusculoskeletal model. These results give much consideration of the body representation in brain for adaptive motor control.**

I. Introduction

Body representation in brain plays an important role for the generation of adaptive motor functions (fast dynamics), while it gradually alters to adapt to the changes of several conditions by brain plasticity (slow dynamics). Meanwhile, muscle activities are represented by low dimensional structure composed of characteristic spatiotemporal patterns depending on tasks. This structure is well-known as muscle synergy and viewed as a neural strategy for simplifying the control of multiple degrees of freedom in biological systems.

In this project, to elucidate mechanisms of the body representation in brain for adaptive motor control, we aim to construct fast and slow dynamics models by focusing on muscle synergy. We assume that the alteration of muscle synergy structure reflects the alteration of the body representation in brain, and we clarify the contribution of the body representation in brain through modeling the fast and slow dynamics of the synergy structure.

II. Aim of the Group

The aim of our research project is as follows;

1. Modeling of generation of muscle activities (fast dynamics) based on muscle synergy generator and controller.
2. Modeling of alteration of muscle synergy controller (slow dynamics), which may reflect the alteration of body representations in brain.
3. Estimation of muscle synergy controller and its application for rehabilitation.

III. Research Topics

A. *Modeling of fast dynamics for postural control*

Ota’s (The University of Tokyo) and Chiba’s (Asahikawa Medical University) group aims to construct models focusing on fast and slow dynamics in postural controls to keep upright standing in collaboration with Takakusaki group (A02-2, Asahikawa Medical University). The model will reveal mechanism of the body representation in brain corresponding to human motion.

In this year, we made some experiments to investigate the fast dynamics in postural control on a flat and an inclined floor with outer force. The experiments was that subject keeps standing posture on the movable floor which slides and stops to back direction of the subject. We investigated difference of the postural controls with restraints of knees of subject. We measured the muscle activities at legs and trunk and analyzed the controls by muscle synergy model. The muscle activities were divided into 3 and 4groups on the flat and inclined floor movement without the restraint of knee, respectively. However, the number of groups was the same in flat and inclined floor with the restraints of knees. We considered that the same control of flat and inclined floor is abnormal in human and the control alteration could be fast dynamics in alteration of muscle synergy controller [1].

To verify the validity of the control models above mentioned, we developed a human posture controller which is combined with feedforward and feedback controls. And the controller was applied to musculoskeletal simulator to verify whether the controller can keep upright standing. With optimization of parameters in the controller, the human model could keep standing posture in 100 (ms) delay. From this result, the tonus control is important for standing posture and we can simulate various conditions of human [2].

We also investigated cerebellum functions of rats with medial or lateral cerebellar ablation. The ablations to the medial cerebellar cortex significantly decrease the ratio of the muscle tonus. However, the tonus could be recovered with the nucleus [3]. We find that the sensory inputs play important roles in motion generation and, currently, we try to make postural experiments with sensory inhibition and models for fast and slow dynamics of sensorimotor integration.

B. *Modeling of slow dyanmics for locomotion*

Aoi’s group (Kyoto University) aims to clarify the adaptation mechanism via fast, slow dynamics in motor control in locomotion of humans and rats in collaboration with Funato's group (B03-1, The University of Electro-

Communications). In this research project, we conduct the analysis of measured data during their locomotion and simulation studies using mathematical models of the neuromusculoskeletal systems. In this year, we improved a rat hindlimb walking model, which we have developed to model fast dynamics in locomotion including the reflexive control of temporal pattern of muscle synergies based on foot contact information, to incorporate slow dynamics.

Physiological studies have suggested that foot contact timing is predicted during locomotion and that the error induces compensatory motor behavior. In this study, we incorporated the prediction of foot contact timing and the modulation of the temporal pattern of muscle synergies through learning of the foot contact timing based on the error for slow dynamics model. More specifically, for the control input of muscle synergies $\sum w_i(m) \cdot v_i(\phi)$ ($w_i(m)$: spatial pattern (m: muscle), $v_i(\phi)$: temporal pattern (ϕ: phase)), we used

$$\dot{\phi} = \omega + (\hat{\phi} - \phi)\delta(t - t^C)$$

$$\hat{\phi}_{n+1} = \hat{\phi}_n + \gamma \frac{\partial V(\hat{\phi}_n)}{\partial \hat{\phi}_n}$$

where ω is basic frequency for locomotion, $\hat{\phi}$ is the prediction of foot contact timing, t^C is the foot contact time, V is the estimation function of foot contact timing error, and γ is the learning rate. This means that different time constants between the fast dynamics of immediate manipulation of muscle synergies and the slow dynamics of gradual modulation through the prediction and learning produce adaptive motor behavior in locomotion.

To evaluate the fast, slow dynamics models, we focused on the split-belt treadmill walking. In this special locomotor environment, the interlimb coordination shows fast and slow adaptations depending on the environmental situation. In particular, neural diseases impede the slow adaptive behavior. In this study, we first used a biped robot and a low-dimensional control system based on the kinematic synergy instead of muscle synergy and showed that the robot produced fast and slow adaptive behaviors on a split-belt treadmill, which were similar to those observed in humans [4]. Furthermore, we conducted computer simulation of split-belt treadmill walking of the rat hindlimb model with the muscle synergy-based controller and showed that the model produced fast and slow adaptive behaviors. We now started the measurement of rats to verify such adaptive behaviors in rats, especially in their muscle synergy structure [5].

These results were presented at the workshop “Embodied-Brain Systems Sciences” at 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC2015) at Milan, Italy on 25-29, August, 2015 and at 2015 IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS2015) at Hamburg, Germany on 28 September-2, October, 2015, at the general session “Embodied-brain Systems Science” at SICE System and Information Division (SICE SSI2015) at Hakodate Arena on 18-20, November, 2015, at the organized session “Embodied-Brain Systems Science” at 26th 2015 International Symposium on Micro-NanoMechatronics and Human Science (MHS2015) at Noyori Memorial Hall, Nagoya University on 23-25, November, 2015 [2, 6], and at the organized session “Embodied-brain Systems Science” at SICE Symposium on Decentralized Autonomous Systems at Hiroshima University on 21-22, January, 2016. In addition, we contributed to Special issue “Body representation in the brain” in Neuroscience Research [7, 8].

IV. Future Perspective

As 2nd year of this project, we developed the experimental setting and results and from these results we construct fast and slow dynamics. We proposed fast dynamics model for postural control, which was verified in movable floor experiments and musculoskeletal simulations, and fast and slow dynamics models for locomotion, which was verified by split-belt treadmill walking of a biped robot and a rat neuromusculo-skeletal model. These results give much consideration of the body representation in brain for adaptive motor control.

As future works, we continue the above mentioned experiments and construct more sophisticated fast and slow dynamics models. We will carry out experiments to evaluate the proposed models. Furthermore, we collaborate with brain research groups to find out biological substantiations and rehabilitation research groups to apply our models to monitor states of patients. We feed back the results to our models and improve modeling of the slow dynamics of the body representation in brain.

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Annual report of research project B03-1

Tetsuro Funato
The University of Electro-communications

***Abstract*—The coordination of movement: synergy provides a simple model of the body for managing a complex neuro-muscloskeletal system, and it is considered to reflect the body scheme. In order to approach the construction principle of the synergy, this group studies the functional role of the synergy using the animals with neural ataxia. In this year, we analyzed the synergy of healthy rats with standing and walking, and developed the experimental environment for the synergy of rats with neural ataxia. As the result of the analyses, standing and walking motions of rats were found to have similar characteristic of those of humans, and fundamental data for analyzing the change of synergy due to neural ataxia were obtained.**

I. Introduction

When human and animals perform a whole body movement such as walking or standing, coordination of multiple segments or muscles called synergy is observed. Such a coordination of motor elements provides a simple representation of complex and redundant neuro-muscloskeletal system, and thus it is considered to reflects the body scheme.

Muscle synergy, coordination of muscular activities, has a robust structure against different velocity or direction of walking. In the meanwhile, this structure is reported to be changed by some neural diseases. Synergies are reported to unify soon after stroke and they slowly divided [1]. Moreover, the coordination of knee, trunk and arm movement (kinematic synergy) in standing is reported to be weaken by spinocerebellar ataxia [2].

This research group approaches the construction and functional mechanism of synergy by the analysis of movement with neural ataxia, and aim for the construction of rehabilitation method using synergy analysis.

II. Aim of the Group

The aim of our research group is as follows.

1) Elucidation of the role of kinematic synergy on posture control: analysis of the kinematic synergy and dynamics of the standing rats with cerebellar dysfunctions.
2) Elucidation of the changing mechanism of muscle synergy: analysis of the muscle synergy of the walking rats after stroke. (collaboration with B02 group)
3) Construction of the synergy analysis system on clinical cite. (collaboration with C02 group)

III. Research Topics

In this year, we analyzed the synergies of standing and walking of healthy rats, and constructed a dynamical model for analyzing their functional roles. Moreover, we developed a system for synergy analysis on clinical cite, and constructed the experimental environment for patients with congenital insensitivity to pain with anhidrosis (CIPA).

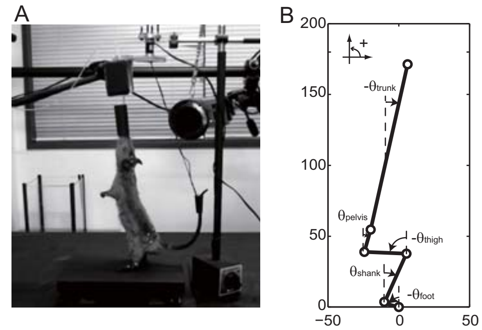

Fig. 1. Measurement of the motion of a standing rat

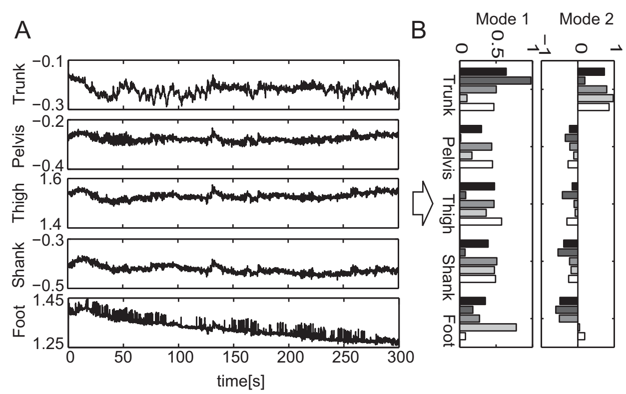

Fig. 2. Intersegmental coordination of a standing rat

A. Evaluation of kinematic synergy and posture control of rats

1) Analysis of kinematic synergy: In order to study the coordination of segments (kinematic synergy) in the posture control of rats, we measured the standing motion of rats using motion capture system (Fig. 1A), and extracted correlated motions among measured angles of 5 segments: trunk, pelvis, thigh, shank and foot (Fig. 1B, Fig. 2A, [3]).

As a result, motions of 5 segments were found to be composed of 2 coordinated motions for over 90 % (fig. 2B), where over 60 % was Mode 1 and 30 % was Mode 2. Then we compared these Modes with the Jacobian of the center of mass (COM) and trunk motion, and found that Mode 1 reflected COM motion and Mode 2 reflected trunk motion.

These results were similar to that had reported for human motion [4], implying that the posture control of rats was similar to that of human. Moreover, the motion of Mode 1 and Mode 2 corresponded to the motion of 1-link and 2-link inverted pendulum, respectively, and this provided the mathematical foundation of dynamical model of rat body.

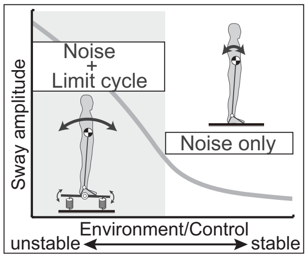

Fig. 3. Characteristic of the proposed posture control model

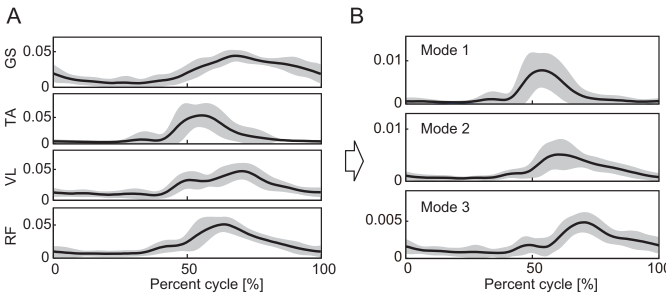

Fig. 4. Muscle synergy of a walking rat

2) Posture control model and evaluation of rat motion: Based on the body sway of human standing, we constructed a posture control model [5]. During standing, human body is not fixed but is continuously swaying. At that time, if the stability of standing floor is lowered, the amplitude of sway apparently increases. We proposed a 1-link inverted pendulum with nonlinear PID for explaining this phenomenon, and we found that human posture control used "fixed state" (sway generated by noise) and "rhythm state" (sway generated as limit cycle) depending on the stability of floors (Fig. 3, [5]).

We evaluated the posture control of rats using the same model, and found the control state (control gain) of standing rats was maintained around the center of the "fixed state" and "rhythm state" as in the humans [6].

From these researches, the evaluation method of posture control of rats was obtained. In the next study, change in kinematic synergy due to cerebellar dysfunction is analyzed for discussing the role of the synergy for control function.

B. Environment for synergy analysis of rats with stroke

In order to investigate changes in muscle synergy due to stroke, the environment for producing rats with stroke using Photothrombosis method was constructed and muscle synergy of walking rats was analyzed. The walking motion of rats on the treadmill was measured by a collaboration with B02 group. 4 activities of muscles were measured from Gastrocnemius, Tibialis Anterior, Vastus Lateralis and Rectus Femoris (Fig. 4A). By performing non-negative matrix factorization (NMF) for the measured activities, 3 muscle synergies shown in Fig. 4B were obtained.

As a result, the experimental environment for analyzing the muscle synergies of walking rats with stoke were constructed.

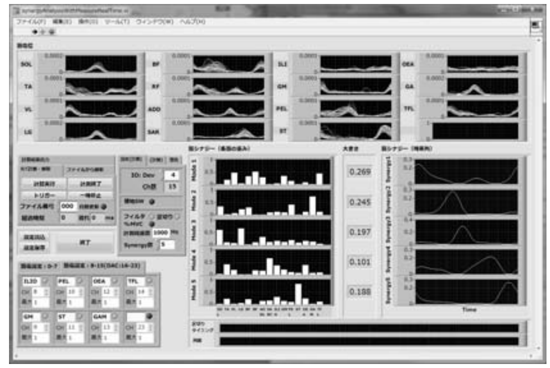

Fig. 5. Developed software for realtime synergy analysis

C. Construction of synergy analysis system and measurement of congenital insensitivity to pain with anhidrosis (CIPA)

We developed a system for analyzing muscle synergies on clinical cite, aiming to feedback the muscle synergy to patients (Fig. 5). Moreover, by collaboration with C02 group, we constructed the measurement environment of CIPA.

Muscle synergy of walking is known to change depending on the growth; the number of synergy increases between the newborn and child, and then synergy patterns change so that they match the touch-down and lift-off timing [7]. Here, the patients with CIPA cannot obtain the sensory information, and thus their synergies are potentially different from those of healthy adults. In the future research, we compare their synergy with healthy synergy, and try to modify the synergy by providing outer stimuli like sounds. Through these research, we construct the rehabilitation method using synergy analysis.

IV. Future Perspective

In this year, we performed synergy and dynamical analysis of healthy rats, and constructed the environment for measuring the rats with neural ataxia and patients with CIPA. Results of synergy analysis of rats were similar to those of humans. In the next year, we analyzes the motion of rats with cerebellar dysfunction and stoke, and patients with CIPA for elucidating the construction principle of synergy.

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Annual report of research project B03-2

Yasuhisa Hasegawa
Dept. of Micro-Nano Systems Engineering, Nagoya University

***Abstract*—Experimental devices, a robotic thumb and its operation interface device, are developed for a challenge that induces embodiment of the robotic thumb operated by a contralateral hand. The robotic thumb which has three active DOFs and the same workspace as a human thumb is attached on a palm of the left hand. The interface device on a left hand operates fingertip position of the robotic thumb, measuring position of the left thumb. The device gives a tactile feedback to fingertip of the left thumb using electric stimulation. A performance of the robotic thumb against a picking task is measured through some experiments with or without the tactile feedback so that we could evaluate importance of the feedback for the task and the embodiment of the robotic thumb.**

I. Introduction

An extra robotic arm attracts active attention from robotic researchers. In MIT, extra robotic fingers and arms are investigated [1], [2]. The fingers or the arms are however artificial devices and are not involved into operator's sense of agency and ownership. Embodiment of a tool is important to improve its utility. In the same way, embodiment of a robotic system is also a key to upgrade its operability. A pseudo-sensory feedback that imitates actual somatosensory feedback is often used in order to embody the robotic system including a prosthesis of an amputee. Nishio et al. used a vibration feedback to perceive a position of a robot arm [3]. Four vibration modes present angles of the robot arm, but perceptible angle resolution is not high, because four modes are not enough to present the angle. Sugiyama et al. used an electrical stimulation feedback to give tactile feeling of the virtual hand in a monitor [4]. As a basic study, aim of our study is to clarify factors and transition procedure of embody of an actuated robotic system through some training tasks. Out approach to organize the sense of agency and ownership about the robotic system is a temporal shift of the sense of agency and ownership of a part of own body.

II. Research topics

In this study, we focus on a robotic finger as a part of human body. Actually, our challenge is to shift sense of agency and ownership of the right thumb to a robotic thumb on the left hand through training. Electrical stimulation is used to prepare two cases: with a tactile feedback to the human body and w/o the tactile feedback. The right thumb is stimulated by the electrical stimulation device according to the tactile force measured by a tactile sensor equipped on the tip of the robotic thumb. A bolt pick-and-place experiment is conducted using the robotic thumb. We use time required to complete the task and failure count as task performance. The shift of the sense is evaluated based on the task performance and questionnaire. The more embodiment of the robotic finger is organized, the higher task performance is promising. The questionnaire is used to ask subjects about position of the right thumb, synchronizing motion of left finger and right thumb and so on.

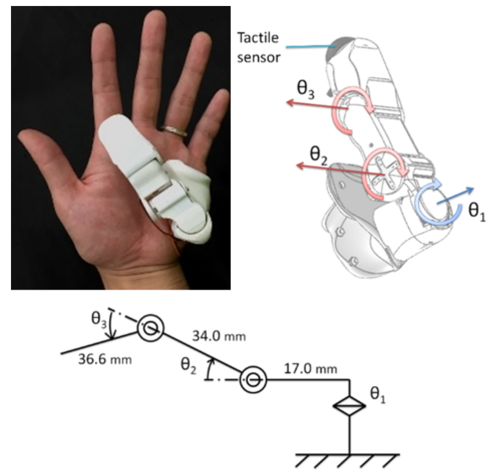

Fig. 1. Extra Robotic Thumb

TABLE I
Specifications of the robotic thumb

Length×Width×Thickness	87.6×28.2×23.0 [mm]
Weight	61 [g]
Degree of freedom	3
Max velocity of fingrobotic thumbip	130 [cm/s]
Grip force	2.0-3.2 [N]

III. Achievements

A. Robotic thumb with three DOFs

Figure 1 shows the robotic thumb and its axial composition. It is almost the same size as human thumb and has 3 active joints (1 yaw and 2 roll). It is attached on a palm of left hand, opposing with four fingers: index, middle, ring and little fingers. A tactile sensor which measures grasping force(0-40 [N] in z-axial force) is equipped on the tip of the robotic thumb.

B. Interface device for robotic thumb operation

The robotic thumb on the left hand is operated by the right thumb. A position of the right thumb is measured by an operation interface shown in Fig. 2. A position of the right thumb is calculated using forward kinematics based on outputs of four rotary encoders on the interface. The thumb position is send to the robotic thumb so that the robotic thumb could move in the same way as the right thumb.

A tactile information measured by the tactile sensor equipped on the robotic thumb is send to the electrical stimulation device [5]. Measured tactile force (0-6 N) is discretized into 255. The electrodes attached on the right thumb stimulate ball of the thumb. Waveform of the electrical stimulation is 50 Hz pulse wave whose duty ratio is 1 %.

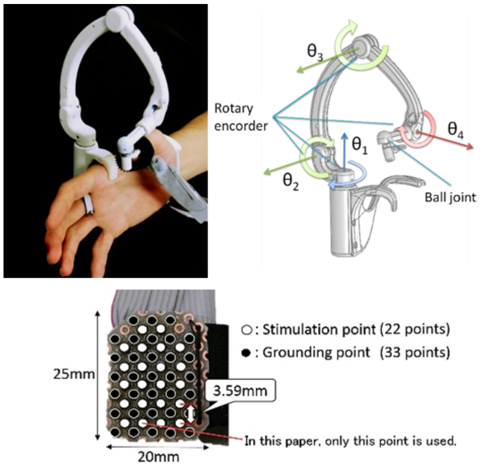

Fig. 2. Manipulation interface for robotic thumb

C. Evaluation of task performance under sensory feedback

The nine bolts pick-and-place experiment is conducted using the robotic thumb. Experimental environment is shown in Fig. 3. The task is to pick a bold on the table with the robotic finger, ring and little fingers and then to place it at a target position one by one. The trial runs through ten times with the tactile feedback and 10 times without the feedback. Time spent for the task and a failure count are used as a performance index. The required time and the failure count are shown in the table. II. The tactile feedback shortened 7.2 % of the required time and all subjects did not fail the picking task when the tactile feedback was given. The table III shows the questionnaire of the subjects. All subjects felt “The tactile feedback made the finger operation easier.” In addition, there are some reports: “After removing the devices, the left fingers moved automatically when I tried to move the right thumb,” “I felt that the right thumb transferred to the left hand,” and “I felt that the right arm disappeared during experiments.” All of these comments are limited to the case of “with tactile feedback”, not case of “w/o feedback.” This result implies contributions of the tactile feedback of the right thumb to transfer of body schema and image of the right finger.

IV. Future Perspective

We found that the developed robotic thumb has potential to transfer either of both the sense of agency and ownership of right thumb through experiments. As the next experiment, we will evaluate drift and its transition of proprioceptive sensation of the right thumb through training.

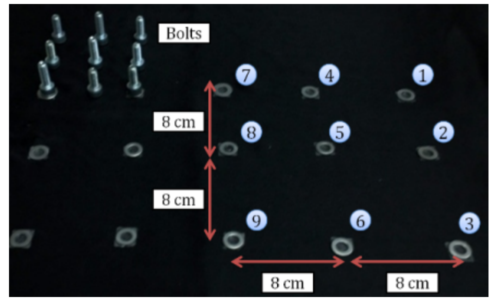

Fig. 3. Arrangement of items

TABLE II
Required time and failure counts

Subject		Required time [s]	Failure count
Subject A	With feedback	28.8	0
	Without feedback	33.1	3
Subject B	With feedback	24.9	0
	Without feedback	25.5	1
Subject C	With feedback	19.8	0
	Without feedback	20.6	2
Mean	**With feedback**	**24.5**	**0**
	Without feedback	**26.4**	**2**

TABLE III
Questionnaire results

Question item	Average point 1:Disagree∼5:Agree
I felt that the right thumb transfered to the left hand.	3.7
The robotic thumb was able to follow the right thumb.	4.3
The strength of ES was appropriate.	4.7
I got strange feeling about the size or shape of the bolts.	1
The operation was easy.	5
The tactile feedback made the operation easier.	5
I got strange feeling after I removed devices.	5
The ES was perceived like tactile.	4.7

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Annual report of research project B03-3

Koh Hosoda
Graduate School of Engineering Science, Osaka University

***Abstract*— this research proposal studies on the body image of a human, which can be obtained through the relation between image of the body in the vision and output from proprioceptive receptors of the muscles. We use a muscular-skeletal humanoid robot and brain-like neuron model to construct the system.**

I. Introduction

This research project studies how and where a human build body image and how a human learns the relation between the body image and information acquired through proprioceptors, by a constructive approach using a humanoid robot with human-like muscular skeletal system and brain-like neuron model (Academic year 2015-2016).

II. Aim of the Group

Volume of the body and/or the positon and orientation of the hand should be expressed in a certain space, whose axes are typically those of proprioceptive sensors in various modalities and ego-centric space. The body image is a function of the states of our muscles (- proprioceptive sensors), and can be utilized for structuring effects on the environment and can realize adaptive behavior against the change of the environment. This research project studies how and where a human build body image and how a human learns the relation between the body image and information acquired through proprioceptors, by a constructive approach using a humanoid robot with human-like muscular skeletal system and brain-like neuron model. The first dynamics and the slow dynamics can be modeled as adaptive behavior of the humanoid robot and the dynamics of the brain model, respectively. As a result, we can expect (1) adaptive behavior of the humanoid robot utilizing human's body image model, (1) validation of the brain model, and (3) a new method for rehabilitation by utilizing obtained generated scheme.

III. Research Topics

A. *Development of proprioceptive sensor board for pneumantic artificial muscles*

For investigating who the body image can be formed and modified, the project will build a humanoid robot platform that has similar muscular skeletal system as a human. For this purpose, we need a proprioceptive sensor board for pneumatic artificial muscles.

A human has reflex neural circuits going around spinal cord from muscle spindles and Gorge tendon organs through Ia and II fibers, to motot neuron to drive the muscles. This path is a fundamental block to move our body by the muscles. Existing work of modeling body image of the robot through interaction mostly utilizes joint angles as proprioceptors, and learning the image by the relation between the effectors position in its vision and the angles. However, a real human does not have joint sensors; it obtains information about its muscles though muscle spindles and Gorge tendon mechanism. It is hardly imagined that the articular capsule gives information about the joint angle. If we assume that a human can observe information about the muscles instead of joint angles, constructive knowledge about our body image will change drastically. Moreover, the construction of the body image has a strong correlation with the fundamental stretch reflexes. The project will build a realistic human-like muscular skeletal humanoid robot that may change the existing knowledge about constructive body image.

In this year, the research team developed a proprioceptive sensor board for pneumatic artificial muscles for realizing artificial spinal cord reflexes (Fig. 1). The sensor board obtains length information from the magnet sensor and pressure information from the pressure sensor, and emulate Ia and II fiber outputs taking the virtual dynamics of the muscle spindle into account. Emulated output of the Ia fiber is shown in Fig. 2.

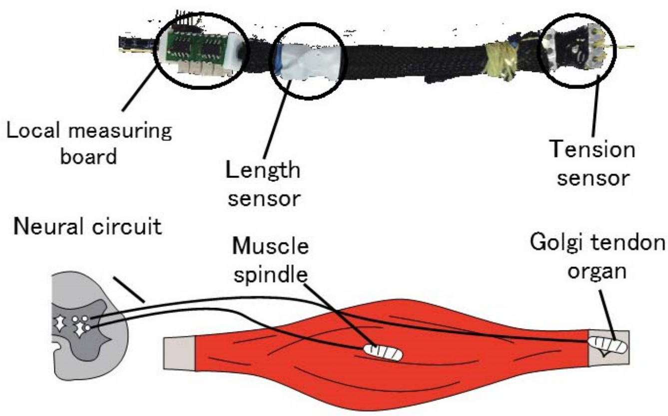


Fig. 1 Proprioceptive sensor board for pneumatic artificial muscles.

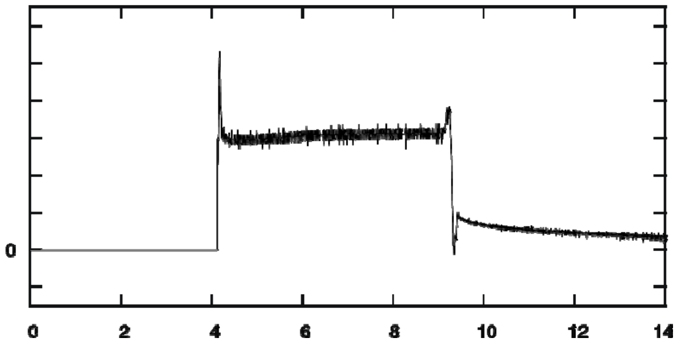
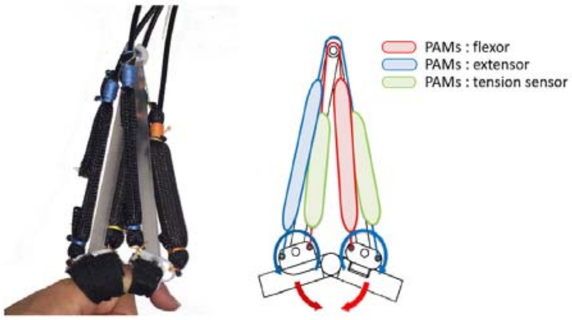


Fig. 2 Emulated output of the Ia fiber

B. Development of a master-slave finger exoskeleton driven by pneumatic artificial muscles

This year, the research project team has developed a master-slave finger exoskeleton that allows brain activity measurement by functional magnetic resonance imaging (fMRI). The MRI environment requires the device to be free from metal components and strongly immobilized, which can reduce the device's versatility and ease of setup (Fig. 3). To overcome these limitations, we designed a finger exoskeleton using pneumatic artificial muscles, which can be made metal-free and used for not only actuators but also sensors. We also proposed a symmetric, bilateral control method for the device and experimentally validated device performance and its control method.



(a) Overview of the developed finger exoskeleton

(b) Movement of the finger exoskeleton

Fig. 3 Master-slave finger exoskeleton driven by pneumatic artificial muslces

IV. Future Perspective

This year, we have developed a proprioceptive sensor board for pneumatic artificial muscles which will be used as a component of a muscular-skeletal humanoid robot for constructive study on the body image. We have programmed the board to emulate the output the fibers for spinal cord reflexes. We have also developed a master-slave finger exoskeleton driven by pneumatic artificial muscles for the collaboration with Research Project A02. In the next year, we conduct experiments of the equipment and generate hypothesis on the body image.

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Annual report of research project B03-4

Tadahiro Taniguchi
Ritsumeikan University

***Abstract*—To construct a computational model of the formation process of body schema in the human central nervous system. We proposed an unsupervised machine learning method that can estimate a topology of tactile sensor distribution and the number of limbs, i.e., body parts, sequentially and automatically from high dimensional tactile sensor data using a Dirichlet process Gaussian mixture model.**

I. Introduction

Our goal of this research project is to develop a generative Bayesian model of a latent tree structure for slow dynamics of body schema. When we formalize the dynamics of human body movement, we often use multi-link representations for modeling the human body system. Because the representation is adequate and useful to describe human kinematics and kinetics, it has been widely used in the context of robotics. At the same time, it is also considered that human brain system has an internal model using multi-link representation. Many studies related to human behaviors and cognitions have been performed on the basis of the assumption. a

However, it is difficult to estimate the state space of multi-link system itself from sensory information, e.g., haptic, visual, auditory, and proprioception. It has not been clarified how a human can form the state space of multi-link system itself. If we assume that a human has the right multi-link state space by nature and it is fixed, to explain our lifelong adaptation of body schema becomes difficult. For example, we can change our body schema when we grow and when we lose our some body parts. Phantom limb is an interesting phenomenon that shows human adaptable characteristics of body schema [1].

It is important to develop a computational model that can reproduce the slow dynamics of the body schema, i.e., a multi-link state space, to clarify the relationship between multimodal sensory information and the slow dynamics of body schema in human brain system.

A graph representation of an ordinal body skeleton structure does not have a closed circuit. Therefore, in our study, we assume that multi-link structure of human body can be represented by a tree structure, and develop a probabilistic generative model of the tree structure representing multi-link body system. We assume that human brain forms body schema by inferring latent variables of the probabilistic generative model from multimodal sensory information using Bayesian inference procedure, and the process of Bayesian inference corresponds to slow dynamics of body schema. Based on this assumption, we attempt to clarify the slow dynamics from the computational point of view (Figure 1).

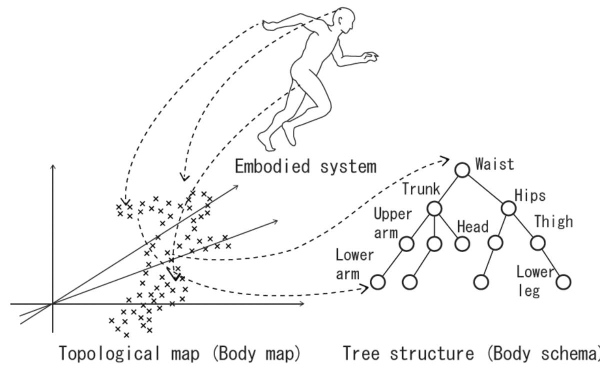

Fig. 1. Body map and body schema

II. Aim of the project

The goal of this project is to develop a Bayesian model that can infer multi-link body structure automatically from multi-modal sensory-motor information. The obtained model and its inference procedure can be interpreted as a model of slow dynamics of human body schema. The computational model will be able to be used for obtaining new understanding of remedy for phantom limbs and developing a new rehabilitation training methods.

The procedure of the research project is as follows:

1) Development of a Bayesian generative model of latent tree structure for a multi-link body system
   - 1-1 Development of a method for forming low-dimensional representation of a body map
   - 1-2 Development of a clustering method that can estimate latent tree structure of a body map
   - 1-3 Development of an inference method of body schema using a Bayesian generative model of latent tree structure
2) Evaluation of a Bayesian generative model of latent tree structure using an agent simulator
3) Experiment of body schema learning using a humanoid robot

In this year, we mainly coped with the first topic, and obtained several results.

III. Achievement

This year's achievement is summarized as follows.

A. Building simulation experiment environment for body map learning

We built a simulation experiment environment for body map learning by following Mori et al. [2] to a certain extent. Figure 2 shows an overview of the developed simulation environment. An agent with a multi-link body structure has

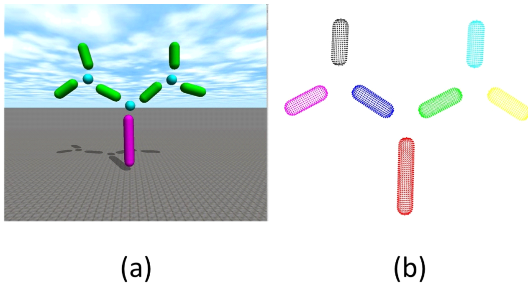

Fig. 2. Artificial agent with tree structure in simulation experiment

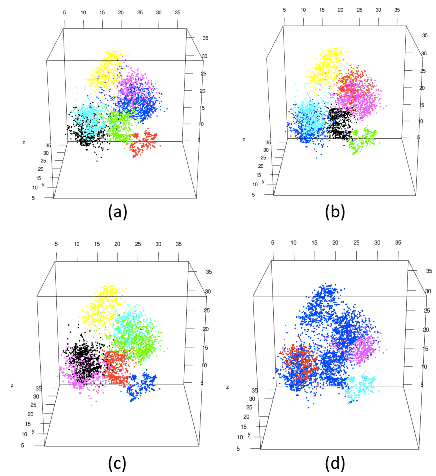

Fig. 3. Result (a) Ward's method (b) K-means (c) GMM (d) DPGMM (proposal)

many tactile sensors on each body part, and each body part is connected using a universal joint with each other. The simulation space is filled with liquid, and each tactile sensor obtains pressure information depending on the agent's body movement. The agent is a model of a fetus in womb showing general movement.

B. Automatic estimation of the number of limbs from tactile information

We developed a method inspired by Olsson et al. [3] that can form a low-dimensional feature space in which the topological relationship between tactile sensors can be reconstructed. The method uses similarity measure that calculates difference between time series data obtained from different tactile sensors and projects positions of tactile sensors in the feature space representing a body map. We showed that the method could reconstruct topological relationship of tactile sensors on the agent's body (Figure 3). In addition, we showed that Dirichlet process Gaussian mixture model (DPGMM), which is a nonparametric Bayesian clustering method, could estimate the number of limbs and the relations between tactile sensors and limbs almost perfectly (Table I). We reported this result in a conference [4].

C. Linked Gaussian Mixture Model

By extending DPGMM, we developed a new clustering method called linked Gaussian mixture model (Linked GMM). The linked GMM can estimate not only clusters of data, but also the links between the nodes automatically under the

TABLE I
RESULTS OF CLUSTERING TACTILE SENSORS ON BODY MAP

Clustering methods	ARI (3 dimensional)	ARI (9 dimensional)
K-means	0.9313	0.7728
Ward's method	0.8843	0.9988
GMM	0.9252	0.9972
DPGMM	0.2674	0.9988

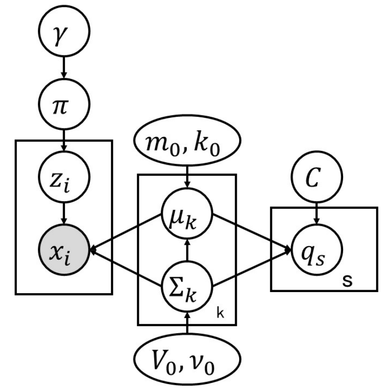

Fig. 4. Graphical model of linked GMM

constraint that the latent graph which consists of the nodes and the links is a tree structure. We evaluated the Linked GMM using synthetic data.

IV. CONCLUSION AND FUTURE PERSPECTIVE

In this year, we coped with the estimation problem of the link structure of an agent. In the problem setting, the agent can only obtain information about its tactile sensors while it moves randomly like a fetus in a womb. We developed a method for forming a feature space that can reconstruct the topological relationship between tactile sensors, and applied DPGMM to the estimated tactile sensor distribution in the feature space. The method could determine the number of limbs and the relations between tactile sensors and limbs almost perfectly.

Our future directions are as follows. The method developed in this year is not a generative process that integrates latent a tree model and multimodal sensory information directly. Besides, the probabilistic model does not involve motor information. To develop an integrative generative model for body schema and derive efficient inference procedure is our future work. Especially, considering visual information is important for understanding a popular remedy for phantom limb. Developing a computational model of slow dynamics of body schema that involves visual and tactile information simultaneously is also our future work.

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Activities of Group C (Rehabilitation medicine)

Shinichi Izumi
Graduate School of Biomedical Engineering, Tohoku University

I. PURPOSE OF THE RESEARCH

In the group C, our aim is to measure the effect of rehabilitation to motor impairment after brain damage by using the biomarker of the body representation. We will provide a model-based neurorehabilitation based upon the body representation and will predict a prognosis for improvement by our method in motor impairment of the patients with hemiparesis. To achieve these goals, we set 2 research projects below.

C01-1 : Neurorehabilitation based upon brain plasticity on body representations

The body representation stored in our brain cannot be seen by outside person objectively and thus, we alternatively try to visualize and reveal the representation of body in psychophysiological way by focusing on the phantom limb, which is the vivid sensation of existing lost limb after limb amputation, because this phantom limb is a subjective experience coming not from actual sense but non-updated internal representation of body stored in the brain. By this approach, we understand the representation of body and purpose a new neurorehabilitation for motor impairment after brain damaged aimed at correcting the distorted body representation by maladaptive change.

C02-1 : Rehabilitation for postural/movement impairments using sensory intervention

In posture/movement impairments, the temporal and spatial activity patterns of systemic muscles are impaired, and muscle synergy control may have abnormalities. This project aims to elucidate abnormal muscle synergy control in motor impairment and to propose new theories for rehabilitation using sensory intervention.

II. MEMBERS

Research Project C01-1

Principal Investigator : Shin-ichi Izumi (Tohoku University)

Funded Co-Investigator : Tetsunari Inamura (National Institute of Informatics)

Co-Investigator : Naofumi Tanaka (Tohoku University)

Co-Investigator : Yutaka Oouchida (Tohoku University)

Co-Investigator: Kazumichi Matumiya (Tohoku University)

Co-Investigator: Yusuke Sekiguchi (Tohoku University)

Co-Investigator: Hiroaki Abe (Konan Hospital)

Research Project C02-1

Principal Investigator: Nobuhiko Haga (The University of Tokyo)

Funded Co-Investigator: Takashi Hanakawa (NCNP)

Funded Co-Investigator: Hiroshi Yokoi (The University of Electro-Communications)

Funded Co-Investigator: Dai Owaki (Tohoku University)

Co-Investigator: Akio Ishiguro (Tohoku University)

Co-Investigator: Arito Yozu (The University of Tokyo)

Co-Investigator: Masao Sugi (The University of Electro-Communications)

Co-Investigator: Kahori Kita (Chiba University)

Co-Investigator: Shin-ichi Furuya (Sofia University)

Co-Investigator: Kazumasa Uehara (NCNP)

III. RESEARCH ACCOMPLISHMENT

In this section, summary of group C will be reported.

C01-1 : Neurorehabilitation based upon brain plasticity on body representations

The team in Tohoku University conducted experiments to examine the relationship between the superiority effect of attention to body and the frequency in the use of hand by the reaction time task measuring the response time to visual target presented either on actual or fake hand surface. The Inamura's team in NII has been being built a database system collecting the data on effective movements for motor rehabilitation of paretic limb in the stroke patients using Virtual Reality system.

C02-1 : Rehabilitation for postural/movement impairments using sensory intervention

By this year, groups in our project have established measurement systems for muscle synergy control, and constructed integrated system for brain function analyses. They have prepared and partially started measurement in patients with congenital insensitivity to pain, Parkinson disease, and stroke. They have also analyzed the usefulness of transcranial direct current stimulation and functional electric stimulation as intervention. Moreover, as sensory intervention, they started to use novel biofeedback prostheses as pilot study.

IV. Activities

・ General meeting, Symposium

National Institute of Informatics, OPEN HOUSE 2015

Date and Time: Friday, June 12, 2015.14:30-15:50

Place: Special Conference Room, 1F

Attendees: 80 in total including members

Contents: presentations by program director and members about research.

The 9th International Conference on Complex Medical Engineering (CME2015) OS: Neurorehabilitation

Date: Friday, June 19, 2015. 8:30-10:00

Place: Okayama Convention Center

Attendees: 20 in total including members

Contents: presentations by program director and members about research.

2nd General meeting

Date: Saturday, July 4, 2015.

Place: Mitaka Campus, Kyorin University

Attendees: 100 in total (members only)

Contents: presentation by program director, PI of each planned research project and new project members.

IEEE EMBC 2015 Half-day Workshop on Embodied-Brain Systems Science, Milan, Italy

Date: August 25, 2015. 13:30-17:30

Place: MiCo, Milan Conference Center, Milan, Italy

Attendees: 50 in total including members

Contents: presentations by program director and members about research.

IEEE/RSJ IROS 2015 Half-day Workshop on Embodied-Brain Systems Sciences, Hamburg, Germany

Date: September 28, 2015. 8:30-12:30

Place: Congress Center Hamburg, Hamburg, Germany

Attendees: 30 in total including members

Contents: presentations by program director and members about research.

1st Symposium on Embodied-Brain Systems Science

Date: October 25, 2015.

Place: Takeda Hall, Univ. of Tokyo

Attendees: 190 in total including members

Contents: presentations by program director and members about research.

2nd General meeting

Date: Monday, March 7, 2016. - Wednesday, March 9, 2016.

Place: Meeting room, Hotel Senshu-kaku, Hanamaki Onsen

Attendees: 80 in total (members only)

Contents: presentation about annual report by program director, PI of each planned research project, special invited talks, and poster session by attendees.

・ Group meeting

1st C group meeting

Date: Jul. 23. 2015

Place：Tohoku university

Attendants：34 group members

Contents: Research progress reports

2nd C group meeting

Date: Jan. 28. 2016

Place：Tohoku university

Attendants：15 group members

Contents: Research progress reports

・ Workshop

Meeting for muscle synergy in diseases (Research Project C02)

Date: Aug 18, 2015

Place：The University of Tokyo Hospital

Attendants：4 members

Contents: Setting-up of measurement systems for muscle synergy control.

Annual report of research project C01-1

Shin-ichi Izumi
Graduate School of Biomedical Engineering, Tohoku University

I. Introduction

It is difficult know directly what the internal representation of body in our brain is. We alternatively try to visualize and reveal the representation of body in psychophysiological way by focusing on the phantom limb, which is the vivid sensation of existing lost limb after amputation, because this phantom limb is a subjective experience coming not from actual sense but non-updated internal representation of body stored in the brain. By this approach, we aim to understand the representation of body and purpose a new neurorehabilitation for motor impairment after brain damage by the way of normalizing the distorted body representation by maladaptive change.

II. Aim of the Group

The number of those who have disorder in brain function, motor and sensory functions after stroke, has been rising because the number of stroke survivors is increased owing to the advance of clinical medicine. This situation creates a great need for effective rehabilitation for motor impairment and many types of rehabilitative approaches have been produced. Although some techniques improve temporally motor impairment immediately after intervention, the patients with hemiparesis tend not to use a paretic limb gradually in everyday life, because they cannot control their paretic limb as they intend. This is because the current rehabilitation approaches are not enough for a paretic limb to be a functional limb, which is a limb the patients want to use for some purpose in daily living. To make a paretic limb functional one is not only that the paretic limb is improved in function but also that brain can recognize a paretic limb as an own body part and send an appropriate motor command to the paretic limb.

For this purpose, we hypothesized that there would be the cognitive mapper of body, which is a neural mechanism for estimating the body state and the environment neighboring to body utilizing the information from sensory and motor information. The states in body parts including paretic limb of the patients with hemiparesis would be coded in this mapper in the brain and this mapper could bring the body consciousness, such as body ownership and self-agency, to us when we move a body part. According to previous studies, because this mapper seems to be very flexible to the change in the body and environments, the body consciousness generated by the mapper also change when this mapper change. Thus, although it is natural that we could access the cognitive mapper of body in the brain through the body consciousness, we have no way to know and measure the change of the mapper by an intervention to body consciousness. Firstly, in our group we focus on the two unique phenomena; the abnormality in perception of gravity in body after brain damage and abnormal sensation of amputated limb. For a new approach in neurorehabilitation, we try to measure and visualize this mapper in the patients with abnormal body representation by psychophysical method and to correct the mapper.

III. Research Topics

2 major topics will be reported below.

A. *Psychophysical experiments for visualizing and measuring body representation*

Our group started the psychophysical experiments to measure response time to visual stimulus appearing on bodily space (body surface) and the peripersonal space (neighboring space to body), in order to visualize attentional density in 2 dimensional space, which include bodily space and peripersonal space, because the response time to visual stimulus get shorter when visual stimulus appear in the place at which more attention is directed. It is known that more attention tends to be directed at the space around body, which is called as “nearby-hand effect” and thus in the space near and, the response time to the visual stimulus would be shorter than the space far from body. Utilizing this attentional effect, we tried to measure the amount of attention directed to paretic limb after stroke and phantom limb after amputation. This 2 dimensional map of attentional density reflect what they perceive subjectively their paretic and phantom limb are and can be a score for body ownership for their affected limb.

We measured the attention to the paretic limb with this paradigm in stroke patients without higher cognitive deficit in order to compare with the data of the healthy volunteers. In this task, the participants were required to response to a visual stimulus presented randomly either on the paretic hand or a dummy hand as soon as possible and response time was measured. There were two experimental conditions; one was named as Hand-L and the participants were asked to straightening out their paretic hands on the desk, the other was named as Hand-R they put their paretic hands crossing the midline of the body. In the healthy volunteers, they responded to the visual stimulus on their hand faster than the one on the dummy hand in both conditions, on the contrary, in the stroke patients, significant difference was not found in response time between Hand-L and Hand-R conditions. The correlation analysis between the reaction time and patient’s characters reported the significant correlation of the severity of finger function and time since onset with the response time. These results suggest that the stroke patients directed less attention to their paretic hands than the healthy volunteers to their hands and that this decline of attention to the paretic limb was caused by not only brain damage but also the disuse of their paretic limb.

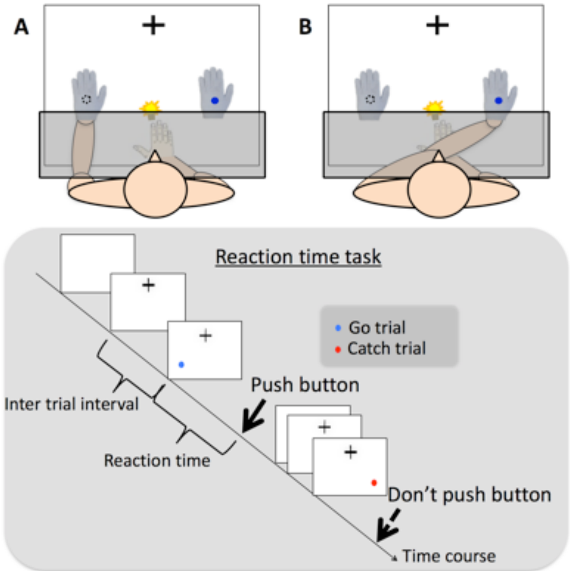

Fig. 1. The design of reaction time task.

B. Development of VR platform for neurorehabilitation and cloud-based motion database

In the last year (2015), we have proposed a prototype of VR platform for neurorehabilitation in which body configurations of patient avatar can be changed. For example, the length of the arm can be modified according to a subjective sense of patients as shown in the Fig.2. In this year (2016), we improved the prototype system for VR interface and process speed. Regarding the VR interface, plugin software for the latest motion measurement device (Kinect V2) and head mounted display (Oculus DK2) is developed. Additionally, display function of avatar's body has been updated in order to reduce the display delay time from about 200-300[ms] to less than 100[ms]. The response time from subject's motion and visual feedback to the subject is strongly influenced for the sense of agency. It has been investigated that the 100[ms] delay almost doesn't have any negative influences for the sense of agency. Therefore, the latest system realized a good performance for neurorehabilitation avoiding the bad effect on the sense of agency.

We have started a primitive experiment using this system with members of A01 team. In the experiment, we are collecting suitable target motions from healthy subjects towards real clinical rehabilitation for patients. As the first step, we are investigating the effect of change of avatar's body appearance on the sense of agency and body representation in the brain. We have confirmed that the length of avatar's arm has influence on the body representation in the brain, and it almost doesn't have any influence the sense of agency.

We also developed a cloud-based motion database for imitation therapy. In the imitation therapy, the relationship between target motions which are shown to a patient and response motion by the patient is important information to design the rehabilitation program. This database system deal with the both of motions for the imitation therapy. Since the database system is connected to the VR platform, it is easy to collect both of the motions. Additionally, since the system is already working on a server at NII with MySQL database server, everyone can access to the database through the Internet. Total length of the recordable motion is 810 days, and improvement of HDD enables the database quantity larger than now. Additionally, this system has flexibility to record not only motion data but also arbitrary biological signals such as pulse rate, EMG and so on. Using this flexibility, we'd like to consider the future collaboration with other teams to support research on extraction of maker of body representation in the brain.

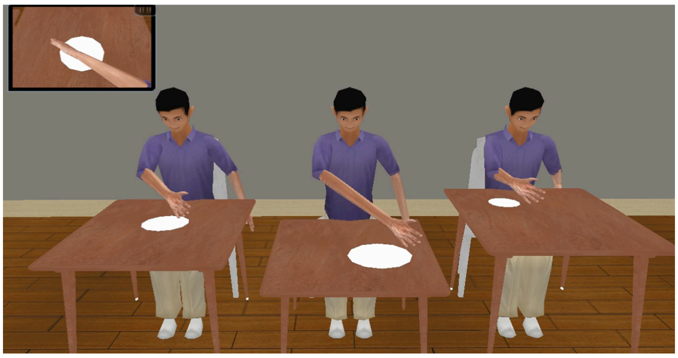

Fig. 2. The demonstration of movie with various length of arm

IV. Future Perspective

We found the decline of attention to paretic limb of the stroke patients by visual stimulus detection task. This suggests that body representation of the paretic limb in the stroke patients alter by the disuse of the paretic limb. We will reveal the relationship between the improvement of motor function and decline of the attention to the paretic limb and will introduce VR simulator to our experiment in order to examine the alteration of body representation by perceptual change of body in VR system.

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[3] T. Inamura: Immersive virtual reality system towards cloud based neurorehabilitation, IEEE/RSJ IROS 2015 Half-day Workshop on Embodied-Brain Systems Sciences, Hamburg, Germany, 2015

[4] N. Aizu, T. Sudo, Y. Oouchida, S. Izumi. "The effect of illusory ownership on imitation of finger movements with chronic phase stroke hemiplegia" (in prep)

Annual report of research project C02-1

Nobuhiko Haga
The University of Tokyo Hospital

I. Introduction

To perform motion properly, various types of sensory input must be reflected in posture/motor control prior to or concomitantly with the motion. Thus, the motor impairment is not just a musculoskeletal problem and related to sensory problems. Therefore, motor impairment can be improved through sensory intervention. In posture/movement impairments, the temporal and spatial activity patterns of systemic muscles are impaired, and muscle synergy control may have abnormalities. It is not fully understood how muscle synergy control is altered in motor disorders. Moreover, while daily rehabilitation is an intervention for fast dynamics (FD), it remains to be elucidated what interventions provoke slow dynamics (SD) efficiently. This project aims to elucidate abnormal muscle synergy control in motor impairment and to propose new theories for rehabilitation.

II. Aim of the Group

The aims of Haga/Yozu group are to clarify gait abnormality in patients with congenital insensitivity to pain from the aspect of muscle synergy control, and to reveal whether the abnormality could be improved by interventions that compensate sensory disturbance.

The aims of Hanakawa group are to clarify changes of body representations associated with dystonia and Parkinson's disease, thereby developing methods to monitor biomarkers of movement disorders. They will also try to develop neuro-rehabilitation on the basis of knowledge about changes of body representations in movement disorders.

The aims of Yokoi/Sugi group are to clarify abnormality in muscle synergy control as SD of stroke patients, and to conduct intervention in muscle synergy control as FD by using functional electric stimulation. The analytical method based on fMRI, fNIRS, and EEG measurement is proposed for detecting neuroplasticity produced in motion of limbs induced by muscle synergy control as FD.

The aims of Owaki/Ishiguro group are to verify the short-term and long-term effects of a novel biofeedback prosthetics, that transforms weak or deficient kinesthetic feedback into an alternative sensory modality, for patients with sensory impairments and to elucidate brain plasticity on body representation during the intervention process.

III. Research Topics

A. Study on patients with motor impairments due to sensory disturbance

Haga/Yozu group has already reported on gait abnormalities in patients with congenital insensitivity to pain [1]. The present project intends to determine whether an abnormality in muscle synergy control exists during gait, and will investigate whether muscle synergy control can be improved through a sensory intervention to replace their disturbed pain sensation, using prostheses that converts foot pressure to sound, developed by Owaki/Ishiguro group. This year, the investigators reviewed the literature and made the up-to-date summary of the congenital insensitivity to pain [2]. The investigators also developed a measurement system for muscle synergy of gait in collaboration with Owaki/Ishiguro and Funato groups, and it can measure motion and muscle synergy concurrently [3]. Patients with congenital insensitivity to pain will be investigated with this system, and the efficacy of the auditory feedback orthosis will be examined.

B. Changes of body representations in movement disorders

In collaboration with Owaki/Funato group, Hanakawa group has started to measure synergistic abnormalities in Parkinsonian gait, especially freezing of gait. Resting-state fMRI is used to capture associated body representational changes. A prototype system for assessing kinematics and dynamics during walking has been established, and measurements in patients have been started. Furthermore, in collaboration with Drs Furuya and Kita, Hanakawa group has started to collect multi-disciplinary data (MRI and transcranial magnetic stimulation) in patients with musician's dystonia [4]. In collaboration with Drs Hirose and Naito, the group has also started a decoding study of body representations in patients with dystonia. The development of neuro-rehabilitation using transcranial direct current stimulation has been commenced as well. Based on the preliminary results and considerations, the group has published several review articles [5-7].

C. Study on patients with motor impairments due to stroke

Yokoi/Sugi group, in order to realize intervention in muscle synergy control as FD by using FES, developed a multi-spot stimulating electrode device for FES system, and confirmed the device is able to induce a variety of hand postures. For the purpose of clarifying the effect of multi-spot stimulation, pattern analysis is applied and they have derived the relationship between muscle synergy control of simple hand postures and multi-spot stimulation. Also, the visualization approach of brain activity is started for construction and trial utilization of fNIRS measurement system to explore analyzability of SD in the brain by simultaneous use of FES device and fNIRS instrument. To confirm the usability of the system, leg press training test is applied for healthy persons for three months with intervention in muscle synergy control as FD by using FES, and analyzed SD induced by the training. Furthermore, for the evaluation of muscle synergy under rehabilitation of hemiplegia, the cycling exercise system has been produced. This system is constituted both of measurement of muscle activities and analysis of exercise quantities. Muscle activities are measured by using electromyography and ultrasonography. The exercise quantities are measured by using goniometer, tread force detection devices, and a crank angle detection device. The analysis of exercise quantities is described by transfer entropy of statistical valiance of those sensor values. The experimental result shows that transfer entropy is useful for evaluating variation of SD. For the next step, the FES feedback system coordinating with foot pressure is producing for the verification of training system [8,9].

D. Efficacy of prosthetics transforming sensory modalities

Owaki/Ishiguro group improved their prosthetics transforming sensory modalities, called *Auditory Foot* [10,11], which transforms cutaneous plantar sensation to auditory feedback signals during walking and examined the clinical effect in cooperation with C01 group. They recruited 10 stroke patients with hemiplegia, and compared their walking among four conditions with the use of two pressure sensors on heel and fifth metatarsal: (i) Without auditory feedback (with prosthetics); (ii) Auditory feedback from only heel sensor; (iii) Auditory feedback from only fifth metatarsal sensor; and (iv) Auditory feedback from both heel and fifth metatarsal sensors. We confirmed significant difference between the conditions (i) and (iv) in maximum hip extension angle of the affected side at the middle stance phase and the end of stance phase for 7 patients. Moreover, we analyzed data of one patient with the SIAS score for sensory function (Touch/Position) = 0. We confirmed the following results: (i) Enhancing the peak-to-peak value of ground reaction force in the longitudinal direction; (ii) Effective dynamic joint stiffness profile during stance phase, in which the stiffness became smaller at the beginning of stance phase leading to shock absorbing and loading on the heel, whereas the stiffness became larger at the end of stance phase leading to effective push-off the ground; and finally, (iii) Effect on the temporal patterns of "kinetic synergy", i.e., the coordination between joint moments [12-17] Furthermore, they contributed to the establishment of measurement system for patients with congenital insensitivity to pain in Haga/Yozu group [2,3].

IV. Future Perspective

Until this year, groups in C02 project have prepared for and partially started measuring muscle synergy in various motor impairments, discussing and collaborating members in groups A and B. Interventions such as prostheses transforming sensory modalities have also started. During the following years, our project continue measurements, clarify changes in FD and SD by interventions, and aim at proposing new theories for rehabilitation.

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Annual report of research project C03-1

Masashi Hamada

Department of Neurology, the University of Tokyo

***Abstract*—The aim of this research project is to improve motor deficit/impairment by means of non-invasive brain stimulation (NIBS). We firstly showed that the effects of quadripulse stimulation (QPS), a new powerful neuromodulation technique, are less variable than other NIBS plasticity inducing protocols. We also tested the effects of NIBS induced plasticity on gain adaptation task. Finally, in order to gain some insight into a possible effect of NIBS on gait, we started gait analysis using pressure sensor system.**

I. Introduction

Non-invasive brain stimulation (NIBS) has been used in variety of neuroscience fields as well as clinical setting. This is because some NIBS protocols, such as repetitive transcranial magnetic stimulation (rTMS), appear to have after-effects on the excitability of the stimulated area that outlast the period of stimulation by minutes or even hours. At least some of these effects depend on activity in NMDA receptors and therefore it has been assumed that they might represent an analog of early stages of synaptic plasticity. Given that maladaptive process of synaptic plasticity involve motor deficit/impairment in neurological disorders, rTMS might be an effective neuromodulatory strategy to improve such motor deficit. However, evidence suggest that NIBS can have a moderate benefit in terms of motor recovery and hence the technique is not yet ready for broad clinical use. There are several possible reason for this disappointing results. First, the major issue of any NIBS protocols is that the after-effects of NIBS are highly variable. Second, the effects of NIBS are usually measured by motor evoked potential (MEP), since MEP measurement is easy and convenient. Given MEP mainly represents the excitability of corticospinal neurons, it is possible that the effects on behaviour and motor learning, which involve pyramidal neurons as well as other stimulated neurons, might be different from those measured by MEP. It is hence important to measure not only MEP but also behaviour in order to assess the effects of rTMS/NIBS.

II. Aim of the Group

The aim of this research project is to improve motor deficit/impairment by means of NIBS. For this purpose, we used quadripulse stimulation (QPS) for NIBS protocol. Depending on the interval of four monophasic magnetic pulses, QPS at short interval (i.e. 5ms) can induce long lasting increase of MEP, while QPS at long interval (i.e. 50 ms) is able to induce lasting decrease of MEP [1,2]. Based on our personal experience, we thought that QPS is a powerful neuromodulation technique, compared with other NIBS protocols, because most of the subjects we had been tested showed expected response. However, there is no study showing how the after-effects of QPS are variable and therefore, we assessed the variability of QPS in 35 subjects.

We also tested the effects of rTMS on motor learning. We employed gain adaptation task, one type of cerebellar learning paradigm. Finally in order to gain some insight into a possible effect of NIBS on gait, we started gait analysis using pressure sensor system.

III. Research Topics

A. *Variability of QPS*

First, our group tested excitatory QPS at 5 ms (QPS5) and inhibitory QPS at 50 ms (QPS50) in 35 healthy volunteers. After baseline measurements of MEP, QPS was applied to the hand area of primary motor cortex, followed by MEP measurements for 30 min. Figure 1 showed the time course of each QPS and response profile.

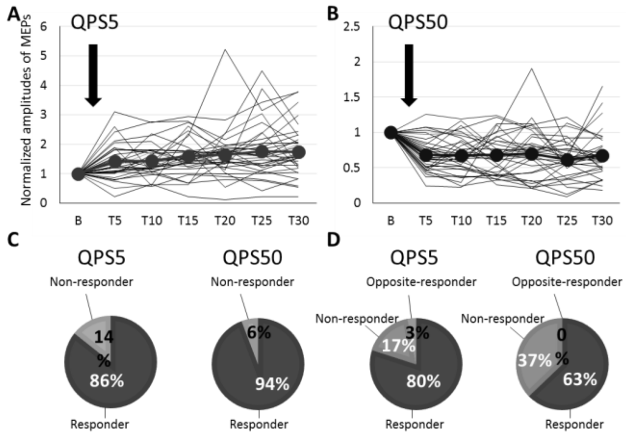

Fig. 1. Time course of QPS and response profile.

Although there was a large variation in response between individuals, it seems that not many subjects respond to QPS in the opposite way. On average there was a potentiating effect of excitatory QPS5 and a depressive effect of inhibitory QPS50, consistent with the original reports [1,2] (one way ANOVA, $P<0.001$). Over 80% of participants increased their response after excitatory QPS-5 (86%) and decreased it after inhibitory QPS-50 (94%). The present results show that the response to QPS protocol is mostly predictable and not much variable at least in this cohort. This value suggests that QPS should be less variable than other plasticity protocols in which about 50% of participants fail to respond in the “canonical” manner [3]. Surprisingly, there are very few opposite responders to excitatory QPS5 (3%) and no opposite responders to inhibitory QPS50. The main conclusion is that the after-effect of this type of QPS on corticospinal excitability is relatively consistent and hence QPS might be better option to obtain consistent clinical outcome when NIBS is used in clinical settings. This study was published in Brain Stimulation [4].

B. *Gain adaptation task and paired asscociative stimulation (PAS)*

Although TMS clearly lacks the focality to stimulate isolated synaptic inputs to corticospinal neurons, it is well known that activation of corticospinal neurons in the hand are of motor cortex is influenced by the direction of the induced current in the brain. A TMS-induced electric current that flows posterior-to-anterior across central sulcus preferentially activates monosynaptic inputs to corticospinal neurons (PA-inputs), whereas, the anterior-to-posterior current activates oligosynaptic inputs (AP-inputs), which are different from monosynptic PA inputs. In the previous report [5], we showed the evidence that PA-inputs are responsible for PAS21.5, but not PAS25, while AP-inputs are responsible for PAS25, but not PAS21.5. Furthermore PAS25 are affected by cerebellar activity modulation and also interfered with cerebellar gain adaptation task. We therefore concluded that AP-inputs involves model-based learning [5]. In this context, not only PAS25, but also PAS25 with AP current may be more effective to interfere gain adaptation task. We therefore tested the effects of PAS at 21.5 or 25 ms with PA or AP current during slight contraction of targeted muscle on gain adaptation task. The results showed that irrespective of current direction, PAS25 interfered with gain adaptation, while PAS21.5 was not. Furthermore, only PAS25 with AP current increased MEP size. In contrast to our initial hypothesis, the results indicate that the effects on gain adaptation task depend on timing of PAS but not on the current induced in the brain and that MEP increase did not necessarily associate the outcome of motor learning.

C. *Gait analysis using pressure sensor sheet*

Third, in collaboration with C02 group, we have started to measure gait using pressure sensor sheet. The primary aim of this particular project is to evaluate gait accurately in neurological disorders because several recent studies suggest that NIBS over motor related area may possibly improve gait and balance, but again the effects may be very subtle. We employed pressure sensor sheet system (Walk Way MW-1000, Anima co ltd, 120 x 480 cm). The advantage of our system is that in addition to usual gait variables (stride, step, center of pressure, etc), we can also measure directional shift because of larger sheet area than conventional system. Figure 2 showed the example of healthy control and Parkinsonian patient.

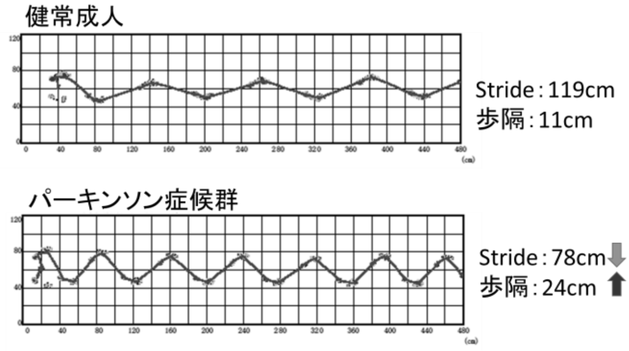

Figure 2. Gait analysis in healthy and Parkinsonian patient

Stride was smaller and step width was larger in patient compared with healthy subject.

IV. Future Perspective

We firstly showed that the effects of quadripulse stimulation (QPS), a new powerful neuromodulation technique, are less variable than other NIBS plasticity inducing protocols. We also tested the effects of NIBS induced plasticity on gain adaptation task. Finally, in order to gain some insight into a possible effect of NIBS on gait, we started gait analysis using pressure sensor system. There are several implication from the results obtained this year. First, the effects of QPS are less variable so that it might be better to use this technique to improve motor deficit/impairment in neurological patients. Second implication is that MEP changes do not necessarily associated with the outcome of motor learning, consistent with the previous study. The new finding is that even without MEP changes (by PAS25 with PA current), gain adaptation is impaired. Because NIBS may activate bunch of the neurons in the stimulated area, we suggest that MEP change may represent only small part of corticospinal excitability, so that the effects of NIBS on motor learning may be completely independent from MEP changes, given that neurons other than corticospinal neurons may deeply involve several types of motor learning, such as gain adaptation. Finally, using our gait analysis system, we will investigate potential therapeutic effects of NIBS next year.

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Annual report of research project C03-2

Keisuke Shima
Faculty of Engineering, Yokohama National University

***Abstract*—Hemiplegics and other people with physical impairments require intensive physiotherapy to address the difficulties they experience in generating natural joint motion based on voluntary and coordinated multi-muscle contraction. Against such a background, the author proposes a new human-human interface design involving the classification of patterns in multi-channel electromyograms (EMGs) and controlled electrical stimulation on a multi-channel basis. In 2015, the following achivements were made: 1) development of a novel neural network with anomaly detection for accurate motion classification from biosignals such as electromyograms (EMGs); 2) proposal of a current-joint angle model for control of joint motion through functional electrical stimulation (FES); and 3) implementation of a novel method for the communication of joint movement and muscle contraction patterns between two subjects based on EMG classification and FES control. The outcomes of this research are expected to form the basis of a support method for motor skill training.**

I. Introduction

Natural human movement requires appropriate coordinated contraction patterns involving multiple muscles; without this coordination, such movement cannot be achieved. In the motor function rehabilitation, therapists must evaluate multi-muscle cooperation during motion via inspection and palpation, and must provide instruction on such cooperation by touching or tapping the skin near the relevant muscles. However, it is difficult to provide accurate evaluation and instruction using only verbal communication and palpation for large numbers of muscles and to conduct effective training based on the results of muscle condition evaluation [1]. Against such a background, an effective method is needed to support the evaluation and communication of muscle contraction patterns and joint motions between therapists and patients in motor skill training.

This study was conducted toward the development of a novel rehabilitation method based on a combination of functional electrical stimulation and pattern classification to support the evaluation and control of muscle contraction patterns for patients with hemiplegia caused by stroke or spinal cord injury. The technique is designed to eliminate misclassification and erroneous communication of data on movements with the inclusion of a neural network with anomaly detection to support accurate classification of related patterns. Using this approach, patterns of muscle coordination can be communicated from person to person (for example, between a therapist and a patient) during the movement of joints, allowing mutual exchanges of information on collaborative muscle contraction. The technique can be considered potentially beneficial in areas such as rehabilitation for EMG-based motor function and training in EMG-based complex skills (Fig. 1).

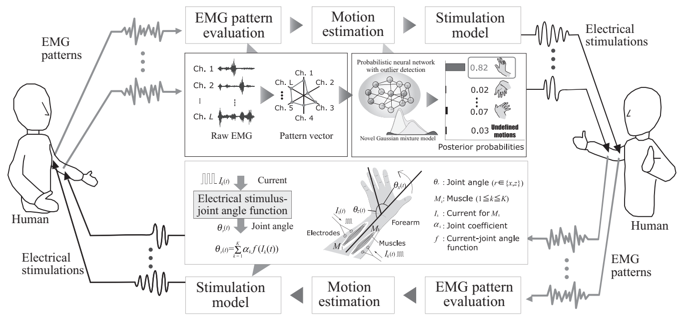


Fig. 1. Concept of the proposed EMG-based human-human interface using FES

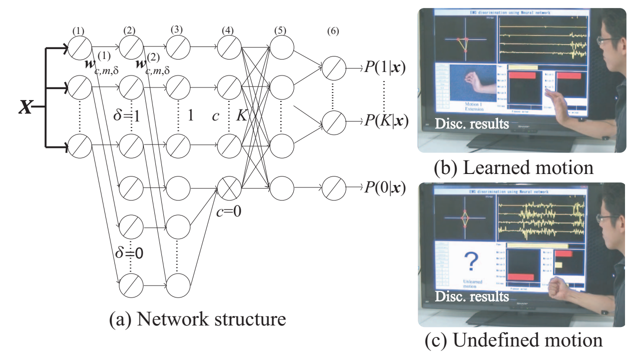


Fig. 2. Probabilistic neural network structure with anomaly detection [2]

II. Achievements

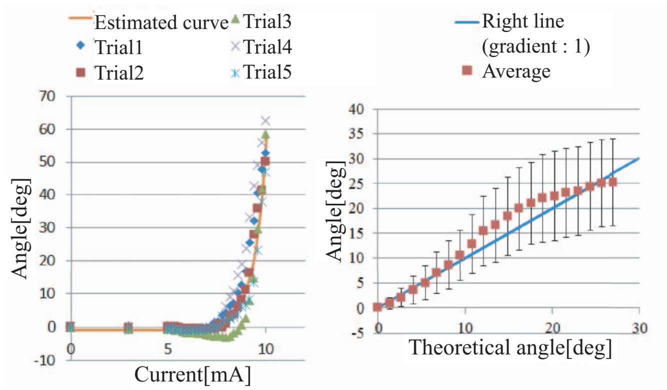
A. Development of a novel neural network enabling accurate classification and anomaly detection

FES-based communication is impaired by unexpected stimulation of the subject's muscles if EMG patterns are misclassified by the learning machine. Accordingly, a method of accurately determining the user's intended motion from EMG patterns is needed in addition to anomalous-data identification.

This study involved the investigation of a novel neural network [2] based on a newly defined Gaussian mixture model [3] that incorporates a probability density function for complementary classes. The accuracy of discrimination for EMG patterns measured from users' forearm motions was also evaluated (Fig. 2). The proposed approach enables accurate identification of undefined data as a complementary class in addition to learned data (average discrimination rate: 91.0 ± 17.8[%].

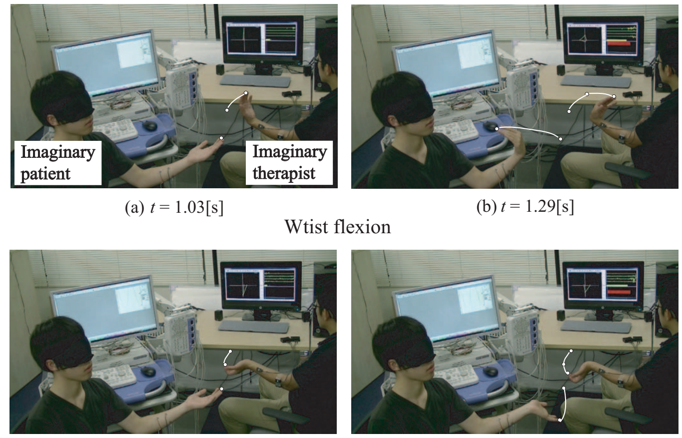
B. Creation of an electrical stimulation model for expression of current-joint angle characteristics

Figure 3(a) shows stimulation results for the subject's flexor carpi radialis. It can be seen that the wrist angles increase



(a) (b)

Fig. 3. Characteristics of the joint angle and the current [4]



(a) $t = 1.03$[s] (b) $t = 1.29$[s]

Wtist flexion

(c) $t = 7.10$[s] (d) $t = 8.03$[s]

Wrist extension

Fig. 4. A series of photos during motion control experiments in human–human condition [4]

exponentially with the electrical stimulus values. These outcomes indicate that the proposed method supported definition of the relationships between joint angle and stimuli as the exponential function shown below (where a, b, c and d are real variables computed using the least squares method), and that the joint angle can be controlled using the inverse function of Eq. (1) via electrical stimulation (coefficient of correlation between desired and measured angles: 0.995) [4].

$$\theta(t) = ae^{b(I(t)-c)} + d \tag{1}$$

C. C. Establishment of a motion communication method based on EMG classification and FES

To verify the validity of the proposed method, evaluation experiments with four conditions were conducted: 1) communication of information on muscle contraction patterns from Subject A to Subject B (human-human condition); 2) communication of information on patterns from the unaffected side to the affected side (mirror condition); 3) enhancement of information on patterns and joint-motion based on intended motion (enhancement condition); and 4) communication of information on complex tasks (object pinching and moving) from human to human (teleoperation task). The electrodes used for EMG measurement and electrical stimulation were attached to the users' forearm and/or upper arm. The discrimination motions were wrist flexion, wrist extension, ulnar flexion, pinching motion, elbow flexion, and elbow extension. Simulation electrode placement was based on the outcomes of preliminary experiments.

Figure 4 shows experimental results for the human-human condition (1). It can be seen that wrist motions conducted by the imaginary therapist were classified accurately from EMG patterns, and that electrical stimulation allowed the imaginary patient to mirror these motions. These results indicate successful communication of muscle contraction information between two subjects using EMGs and electrical stimuli [4]–[6].

III. Future perspectives

This report outlines a novel rehabilitation support method enabling the communication of muscle contraction patterns and joint movements between two subjects (such as a therapist and a patient). The outcomes of testing performed to verify the applicability of the approach indicate the capacity for the transfer of patterns in motion and muscle contraction between individuals. In future work, the author plans to investigate the effectiveness of motor skill training using the proposed method and to discuss how the training may influence motor and brain functions. Collaborative research must also be considered to support the study of brain systems.

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Annual Report of Research Project C03-3

Masahiko Mukaino, Ryoma Sassa, Fumihiro Matsuda
Department of Rehabilitation Medicine I, Fujita Health University, School of Medicine
Department of Rehabilitation, Fujita Health University Hospital
Faculty of Rehabilitation, School of Health Science, Fujita Health University

Abstract—**Recent clinical studies have shown the complexity of the system for balance maintenance. Understanding of this system is still limited, especially for dynamic balance function, which might due to the lack of objective measurement of dynamic balance ability. Thus, the purpose of the present study was to develop an objective method to quantify dynamic balance ability. In this preliminary study, we attempted to develop an index for the objective measurement of dynamic balance function from the relationship between center of gravity (COG) and center of pressure (COP). The subjects comprised nine hemiparetic post-stroke patients and five healthy subjects. Simultaneous measurement of COG and COP was performed using a three-dimensional motion analysis system (Kinematracer, KisseiComtec, Japan) combined with force plate system. As indices to evaluate dynamic balance function, the latency of COP passing COG after heel contact (LCP) and the averaged |COP|−|COG| subtraction value during stance phase (ASV) were calculated. In order to evaluate the validity of the measurement, the Berg Balance Scale (BBS), a frequently used clinical balance scale, was used. The results showed significant differences (0.13±0.02s vs 0.29±0.23s) between the healthy subjects and patients in LCP, and large but not significant differences (4.3±0.5cm vs 2.7±2.0cm) in ASV. The ASV was strongly correlated with BBS. A strong correlation was observed between COG acceleration and ASV, except for one patient with severe balance disorder. These results indicate the need for further investigation into the feasibility of COP-COG measurements for evaluation of balance ability.**

I. Introduction

In previous clinical studies, the balance function has been explained as a system consisting of multiple factors [1]. Accordingly, efforts have been made to understand balance disorders as an impaired system; however, this attempt at constructing a model is based on clinical observations, might be left insufficient due to the lack of objective measurement. Especially, the ability to maintain balance during movement is mostly evaluated only by clinical scales, which limits understanding of the mechanism.

The purpose of this study is to develop the system to measure dynamic balance ability using a kinematic and kinetic methodology, which may contribute to the understanding of the systems employed to maintain balance during movement.

II. Aim of the Group

The aim of the group was to establish an objective measurement system for the dynamic balance function, which will contribute to understanding of the system for maintaining balance. In the present study, we developed a simultaneous measurement system for center of gravity (COG) and center of pressure (COP) to quantify the response of foot pressure to trunk movement, which we assume to represent dynamic balance function.

III. Research Topics

A. Establishment of Measurement Systems

Our group firstly developed simultaneous measuring systems for COG and COP. Previous studies have shown that COG acceleration in the anterior-posterior axis and lateral-medial axis is closely correlated with the gap in the displacement of COG and COP [2]. Our plan was to use this gap to make an index for dynamic balance ability.

The simultaneous measurement of COG and COP was performed using a three-dimensional motion analysis system (Kinematracer, KisseiComtec, Japan) combined with force plate system (Tech Gihan, Japan). For the calculation of COG, markers were attached to 10 landmark sites on the body bilaterally: the acromion processes, the hip joints (one third of the distance between the greater trochanter and the anterior superior iliac spine), the knee joints (midpoint of the lateral epicondyle of the femur), the lateral malleoli, and the fifth metatarsal heads. The virtual COG was calculated using a software that estimated the equation of Ehara and Yamamoto [3]. Briefly, the centers of seven segments (trunk, bilateral thighs, bilateral lower thighs, and bilateral feet) were defined from the markers. The mass ratios of each segment were hypothesized to be as follows: trunk 0.66, thigh 0.1, lower thigh 0.05, and foot 0.02. COG was then calculated as the composition center of the seven segments.

The task for measurement was for subjects to step on the force plate 10 times, so that we could see the dynamic balance ability in lateral axis. Before and after the task, subjects remained standing for 5 s. While stepping, subjects were instructed to keep both feet no more than 35 cm apart; this was intended to reduce compensation by foot position.

The acceleration of COG in the medial direction (braking followed by acceleration in the other direction) is necessary for maintaining balance during stepping. When COG moves laterally, the leg in the direction of movement is the main source of power for “braking.” Therefore, the data for the bilateral heel contact (HC) were used for the present analysis. Acceleration in the medial direction is produced when COP is placed laterally to COG. Therefore, the averaged |COP|−|COG| subtraction value (ASV) were developed for an index for balance evaluation.

B. Preliminary Study with Stroke Patients

Next, we performed a preliminary study for stroke patients and healthy subjects using the method, in order to investigate the feasibility of this measurement.

Methods

The subjects comprised nine hemiparetic post-stroke patients and five healthy subjects. The inclusion criteria for the patients were (1) able to stand and step five times, and (2) not dependent on either the assistance of another person or assisting devices (e.g., handrail, canes, and orthotics). The subjects numbered six males and three females (six with right hemiplegia and three with left hemiplegia) with a mean age of 57±9 years. The mean total score of the Stroke Impairment Assessment Set (SIAS) motor test was 9±1. In this study, firstly the COG-COP gap in displacement was calculated and compared with the COG acceleration. The ASV, the index for the COG-COP gap in displacement, was then calculated, and to investigate the validity of the index, the Berg balance scale (BBS) [4], which is a frequently used scale for evaluating balance function, was employed for comparative measurement.

Results and Discussion

As in the previous studies [2], the COP-COG gap and COG acceleration closely correlated with each other, except in one patient who presented with a low BBS score (Table 1). ASV was extremely low in the patients with low BBS. These results may imply that patients with low balance ability maintain balance by a strategy other than the COP-COG relationship; a more detailed analysis of the strategy of patients with low balance function is thus necessary for a better understanding of the system for balance maintenance employed by people with a balance disorder.

In this preliminary investigation, ASV was strongly correlated with BBS (Figure 1). This may imply the high validity of this index for objective balance measurement. Further study with a larger population should be performed.

IV. Future Perspective

In this preliminary study, we performed the simultaneous measurement of body movement and foot pressure, to estimate dynamic balance function. The index developed from the lateral displacement of COP and COG was strongly correlated with BBS.

For further development of this study, we will collect more data to investigate the validity of this measurement, and we will extensively develop the indices in order to investigate various aspects of the balance function. These indices will be used to develop models for balance disorder that can be used in predicting recovery and simulating the effect of interventions, in collaboration with the specialists in the field of system engineering. This may be a strong basis for future collaboration with brain science.

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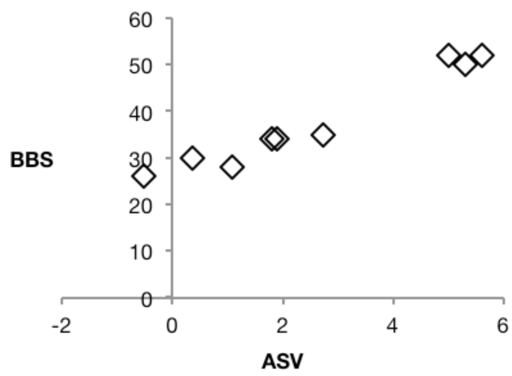
Table1 Correlation between COG acceleration and COP-COG subtraction value

	Correlation coefficient	*BBS*
Pt 1	−0.49	26
Pt 2	−0.85	28
Pt 3	−0.84	30
Pt 4	−0.94	34
Pt 5	−0.93	34
Pt 6	−0.94	35
Pt 7	−0.96	50
Pt 8	−0.91	52
Pt 9	−0.90	52
Hs 1	−0.91	
Hs 2	−0.86	
Hs 3	−0.90	
Hs 4	−0.92	
Hs 5	−0.93	

Fig. 1 Correlation between BBS and ASV



Annual report of research project C03-4

Shu Morioka
Department of Health Science, Kio University

***Abstract*— We quantitatively evaluated the distorted sense of body ownership and agency in asomatognosia and apraxia, using a visual feedback delay system. We found a specific dysfunction in the efference copy for agency in apraxia. Furthermore, our results revealed that sensorimotor incongruence promoted distorted bodily consciousness as well as a change of muscle activation patterns during periodic movement.**

I. Introduction

It has been suggested that disownership and/or disagency occurs in asomatognosia, apraxia and hemiplegia after stroke. However, there have as yet been no objective and quantitative evaluations with regard to the symptoms of disownership and disagency in these disorders.

II. Aim of the Study

We performed two studies, A and B. The purpose of study A was the objective and quantitative evaluation of disownership and disagency in asomatognosia and apraxia, using a visual feedback delay system. The purpose of study B was quantifying distorted bodily consciousness kinematically by analyzing changes in muscle activation patterns.

III. Research Topics

A. *Quantitative evaluation of distorted bodily consciousness (disownership and disagency) in asomatognosia and apraxia*

We tested 19 patients following stroke. Patients experienced tactile inputs, passive movements or active movements under conditions of delayed visual feedback (33–594 ms) and judged whether an observed hand image was delayed with respect to the true felt hand location (Figure 1). To examine the differences in judgment curve shape between tactile stimulations and passive or active movements, logistic curves were fitted to the patients' responses in the incongruent judgment task. The point of subjective equality (PSE) and steepness *a* were calculated using a judgment curve, where PSE represents the delay length where congruent and incongruent judgment probabilities are equal (50%). In addition, we evaluated patients' motor and sensory function, asomatognosia and apraxia. Motor and sensory function were evaluated using the stroke impairment assessment set (SIAS), while asomatognosia was evaluated using the verbal asomatognosia and somatoparaphrenia assessment, and sense of body ownership was evaluated using a 7-point Likert scale. Apraxia was evaluated using the TURIA (AST) screening criteria.

The analysis for PSE and *a* of each condition was performed by comparing the within-symptom group and also between each symptom groups, as well as determining the correlation between PSE/*a* and the severity of symptoms.

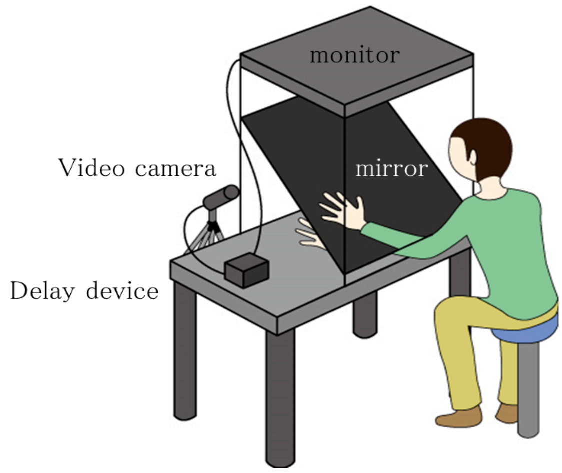


Fig. 1 Visual feedback delay system

The results showed that PSE and *a* were not significantly different between normal motor-sensory function and dysfunction, and there was no significant correlation between PSE/*a* and severity of motor-sensory dysfunction. However, *a* in all conditions in the low ownership group was lower than that in the normal ownership group. Interestingly, only the PSE in the active movement condition in the apraxia group was more delayed than that in the non-apraxia group (false and non-apraxia), but other conditions' PSEs were not different. Also, the severity of apraxia showed a significant correlation with the PSE of the active movement condition. This result suggests a specific dysfunction in the efference copy in apraxia. (Figures 2 & 3)

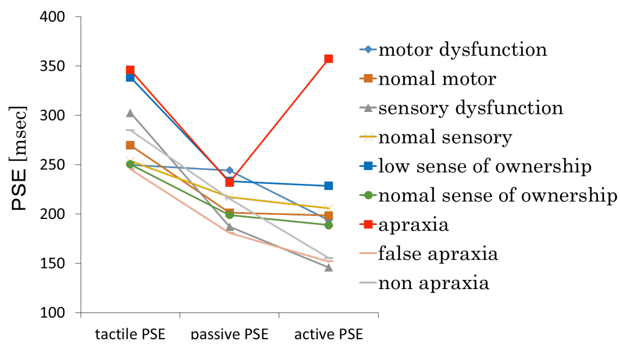


Fig. 2 PSE of each condition for each group

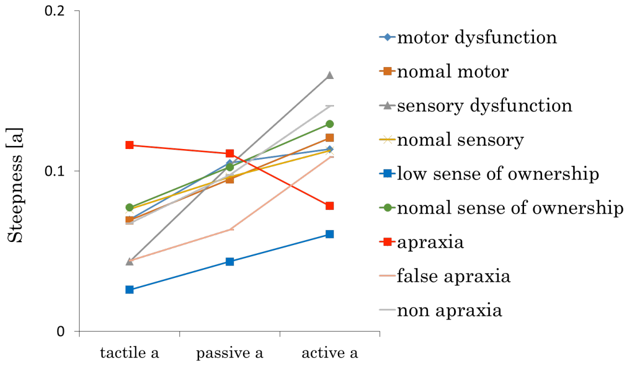


Fig. 3 Steepness (a) of each condition for each group

B. Effect of conflict between motor intention and sensory feedback on periodic movement and subjective perception

The conflict between motor intention and sensory feedback produces abnormal perception (i.e., heaviness and an abnormal sense of ownership). Our group has investigated the relationship between distortions of periodic movement that are produced by sensorimotor incongruence and subjective perception.

Forty healthy participants were enrolled. A visual feedback delay system (Shimada et al. 2009, 2010, 2014) was used to evoke participants' sensorimotor incongruence. Participants periodically flexed and extended their wrist while seeing a delayed image of their hand (varying from 0 to 600 ms). Five delay conditions (0, 150, 250, 350, 600 ms) were tested for each participant. During wrist movement, electromyographic (EMG) activities in flexor and extensor carpi radialis (FCR and ECR, respectively) were recorded. Also, to analyze the change in EMG activity and movement rhythm, the values of integral and peak frequency were calculated. To record changes in subjective perception, each participant used a 7-point Likert scale from –3 (strongly disagree) to +3 (strongly agree) to rate the following two statements: "I felt that my hand was another hand" and "I felt heaviness during movement".

We found that EMG activity decreased and that movement rhythm became slower with extended delay (Fig. 4).

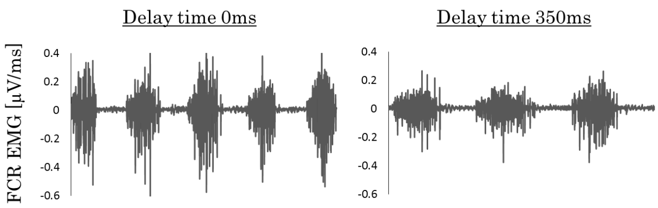


Fig. 4 The EMG activity and rhythm

Further, we divided participants into two subgroups with cluster analysis. The results showed that the peak frequency of participants in subgroup B decreased more than that in subgroup A. The movement rhythm of subgroup B became slower with extended delay, and a logistic regression curve showed that participants in subgroup B felt heaviness more than those in subgroup A (Fig. 5).

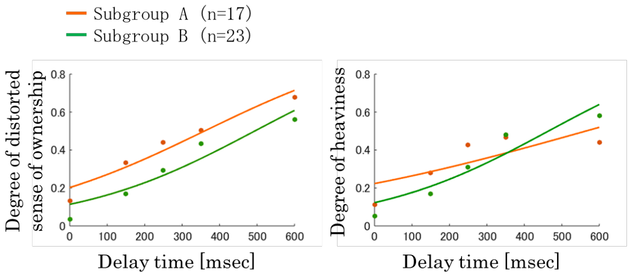


Fig. 5 The change of subjective perception

We suggest that the sense of heaviness, which was evoked in hemiplegic patients, might result from the disturbance of movement rhythm caused by sensorimotor incongruence. We aim to reveal kinematic markers that are related to this change in subjective perception.

IV. Future Perspectives

We quantified the distorted efference copy in apraxia psychophysically using a visual feedback delay system. We also revealed the muscle patterns related to distorted bodily consciousness. From these results, we explored the possibility of quantifying distorted bodily consciousness. In future, to validate the reliability of this evaluation using a visual feedback delay system, we will continue to record data from patients with a distorted sense of ownership and agency. In parallel, we will consider rehabilitation methods to improve distorted bodily consciousness.

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38. H. Imamizu: Neural mechanisms inducing plasticity on body representation, IEEE/RSJ IROS 2015 Half-day Workshop on Embodied-Brain Systems Sciences, Hamburg, Germany, 2015
39. H. Asama: Modeling of slow dynamics on body representations in brain, IEEE/RSJ IROS 2015 Half-day Workshop on Embodied-Brain Systems Sciences, Hamburg, Germany, 2015
40. T. Inamura: Immersive virtual reality system towards cloud based neurorehabilitation, IEEE/RSJ IROS 2015 Half-day Workshop on Embodied-Brain Systems Sciences, Hamburg, Germany, 2015
41. K. Seki: Muscle synergy as a foundation of embodied brain, IEEE/RSJ IROS 2015 Half-day Workshop on Embodied-Brain Systems Sciences, Hamburg, Germany, 2015
42. R. Chiba: Motion Dynamics Analysis and Modeling for Body Representation in Brain, IEEE/RSJ IROS 2015 Half-day Workshop on Embodied-Brain Systems Sciences, Hamburg, Germany, 2015
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44. Tanaka H: How motor cortex represents body movements: Optimality, recurrent neural networks and spatial dynamics, IEEE The 24th International Symposium on Robot and Human Interactive Communication (RO-MAN) Kobe, Japan, 2015
45. Tanaka H, Miyakoshi M, Makeig S: Coordinate Systems in the Motor System: Computational Modeling and EEG experiment, The 5th International Conference on Cognitive Neurodynamics, Sanya, China, 2015
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47. Y. Ohki: Neural mechanisms inducing plasticity on body representation, IEEE EMBC 2015 Half-day Workshop on Embodied-Brain Systems Science, Milan, Italy, 2015
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49. T. Inamura, and Y. Oouchida: Neurorehabilitation based upon plasticity on body representations, IEEE EMBC 2015 Half-day Workshop on Embodied-Brain Systems Science, Milan, Italy, 2015
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53. E. Naito: Neuronal representation of human body schema and its essential contribution for motor control and self-consciousness, IEEE EMBC 2015 Half-day Workshop on Embodied-Brain Systems Science, Milan, Italy, 2015
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72. Akira Murata: Self and other's body in the parietal mirror neuron system, Japan-China Joint Symposium for Understanding Cortical Cognitive Functions, Kyoto, Japan 2015
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Member List

Steering Committee (X00): Comprehensive research management for understanding the plasticity mechanism of body representations in brain

Principal Investigator	Jun Ota (Professor, The University of Tokyo)
Funded Co-investigator	Eiichi Naito (Research Manager, NICT)
Funded Co-investigator	Shin-ichi Izumi (Professor, Tohoku University)
Funded Co-investigator	Toshiyuki Kondo (Professor, Tokyo University of Agriculture and Technology)
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Co-investigator	Kazuhiko Seki (Director, NCNP)
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Research Project A01-1: Neural mechanisms inducing plasticity on body representations

Principal Investigator	Hiroshi Imamizu (Professor, The University of Tokyo)
Funded Co-investigator	Akira Murata (Associate Professor, Kinki University)
Funded Co-investigator	Yukari Ohki (Professor, Kyorin University)
Funded Co-investigator	Takaki Maeda (Assistant Professor, Keio University)
Co-investigator	Satoshi Shibuya (Assistant Professor, Kyorin University)
Co-investigator	Kenji Ogawa (Associate Professor, Hokkaido University)
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Co-investigator	Masahiro Yamashita (Researcher, ATR)

Research Project A02-1: Neural adaptative mechanism for physical changes

Principal Investigator	Kazuhiko Seki (Director, NCNP)
Funded Co-investigator	Eiichi Naito (Research Manager, NICT)
Funded Co-investigator	Shinji Kakei (Project Leader, Tokyo Metropolitan Institute of Medical Science)
Co-investigator	Ken-ichi Inoue (Assistant Professor, Kyoto University)
Co-investigator	Naomichi Ogihara (Assosiate Professor, Keio University)
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Co-investigator	Takeru Honda (Researcher, Tokyo Metropolitan Institute of Medical Science)

Research Project A02-2: Adaptive embodied-brain function due to alteration of the postural- locomotor synergies

Principal Investigator	Kaoru Takakusaki (Professor, Asahikawa Medical University)
Funded Co-investigator	Katsumi Nakajima (Lecturer, Kinki University)
Co-investigator	Hiroshi Funakoshi (Professor, Asahikawa Medical University)
Co-investigator	Yuriko Sugiuchi (Associate Professor, Tokyo Medical and Dental University)
Co-investigator	Yasuo Higurashi (Researcher, Kinki University)

Research Project A03-1: Interpretation of Functional Dynamics by Hybrid Imaging Technique and Real-time Data Processing

Principal Investigator	Kyosuke Kamada (Professor, Asahikawa Medical University)

Research Project A03-2: Research for visualizing neural representation of the wrist movement using electroencephalography

Principal Investigator	Natsue Yoshimura (Associate Professor, Tokyo Institute of Technology)
Co-investigator	Hiroyuki Kambara (Assistant Professor, Tokyo Institute of Technology)

Research Project A03-3: Alterations and control of body representation in the basal ganglia circuit after chronic dopamine loss

Principal Investigator	Kouichi C. Nakamura (Assistant Professor, Kyoto University)
Co-investigator	Hiroyuki Hioki (Assistant Professor, Kyoro University)
Co-investigator	Takuma Tanaka (Assistant Professor, Tokyo Institute of Technology)

Research Project A03-4: Neural basis of human body representation: a direct electrocorticographic recording and stimulation study

Principal Investigator	Riki Matsumoto (Associate Professor, Kyoto University)
Co-investigator	Akio Ikeda (Professor, Kyoto University)
Co-investigator	Takeharu Kunieda (Lecturer, Kyoto University)
Co-investigator	Masao Matsuhashi (Associate Professor, Kyoto University)
Co-investigator	Akihiro Shimotake (Assistant Professor, Kyoto University)
Co-investigator	Moritoo Inouchi (Assistant Professor, Kyoto University)

Research Project A03-5: Visualization and manipulation of pathway-specific brain plasticity on the body representation following the sensory nerve injury

Principal Investigator	Mariko Miyata (Professor, Tokyo Women's Medical University)
Co-investigator	Hironobu Osaki (Assistant Professor, Tokyo Women's Medical University)
Co-investigator	Yoshifumi Ueta (Assistant Professor, Tokyo Women's Medical University)
Co-investigator	Goichi Miyoshi (Assistant Professor, Tokyo Women's Medical University)

Research Project A03-6: Body and Space in the animal model of spatial neglect

Principal Investigator	Masatoshi Yoshida (Assistant Professor, NIPS)
Co-investigator	Masaki Fukunaga (Associate Professor, NIPS)

Research Project A03-7: Body representation changes in macaque brain during motor recovery after internal capsular stroke

Principal Investigator	Yumi Murata (Researcher, AIST)
Co-investigator	Tomoyuki Ueno (Lecturer, University of Tsukuba)
Co-investigator	Tatsuya Yamamoto (Assistant Professor, Tsukuba International University)
Co-investigator	Takuya Hayashi (Unit Leader, RIKEN)
Co-investigator	Noriyuki Higo (Chief Scientist, AIST)

Research Project B01-1: Modeling of slow dynamics on body representations in brain

Principal Investigator	Hajime Asama (Professor, The University of Tokyo)
Funded Co-investigator	Toshiyuki Kondo (Professor, Tokyo University of Agriculture and Technology)
Funded Co-investigator	Hirokazu Tanaka (Associate Professor, JAIST)
Funded Co-investigator	Shiro Yano (Researcher, Ritsumeikan University)
Funded Co-investigator	Jun Izawa (Associate Professor, University of Tsukuba)
Co-investigator	Atsushi Yamashita (Associate Professor, The University of Tokyo)
Co-investigator	Masafumi Yano (Emeritus Professor, Tohoku University)
Co-investigator	Qi An (Research Assistant Professor, The University of Tokyo)
Co-investigator	Wen Wen (Researcher, The University of Tokyo)

Research Project B02-1: Modeling of motor control that alters body representations in brain

Principal Investigator	Jun Ota (Professor, The University of Tokyo)
Funded Co-investigator	Shinya Aoi (Lecturer, Kyoto University)
Funded Co-investigator	Ryosuke Chiba (Associate Professor, Asahikawa Medical University)
Co-investigator	Taiki Ogata (Assistant Professor, The University of Tokyo)
Co-investigator	Dai Yanagihara (Associate Professor, The University of Tokyo)
Co-investigator	Kazuo Tsuchiya (Emeritus Professor, Kyoto University)
Co-investigator	Toshio Aoyagi (Professor, Kyoto University)

Research Project B03-1:

Principal Investigator	Tetsuro Funato (Assistant Professor, The University of Electro-Communications)

Research Project B03-2:

Principal Investigator	Yasuhisa Hasegawa (Professor, Nagoya University)

Research Project B03-3:

Principal Investigator	Koh Hosoda (Professor, Osaka University)
Co-investigator	Ichiro Tsuda (Professor, Hokkaido University)
Co-investigator	Hideo Kubo (Professor, Hokkaido University)
Co-investigator	Shuhei Ikemoto (Assistant Professor, Osaka University)

Research Project B03-4:

Principal Investigator	Tadahiro Taniguchi (Associate Professor, Ritsumeikan University)
Co-investigator	Yoshinobu Hagiwara (Assistant Professor, Ritsumeikan University)

Research Project C01-1: Neurorehabilitation based upon brain plasticity on body representations

Principal Investigator	Shin-ichi Izumi (Professor, Tohoku University)
Funded Co-investigator	Tetsunari Inamura (Associate Professor, NII)
Co-investigator	Naofumi Tanaka (Associate Professor, Tohoku University)
Co-investigator	Yutaka Ouchida (Assistant Professor, Tohoku University)
Co-investigator	Kazumichi Matsumiya (Associate Professor, Tohoku University)
Co-investigator	Hiroaki Abe (Lecturer, Kohnan Hospital)
Co-investigator	Yusuke Sekiguchi (Lecturer, Tohoku University)

Research Project C02-1: Rehabilitation for postural/movement impairments using sensory intervention

Principal Investigator	Nobuhiko Haga (Professor, The University of Tokyo)
Funded Co-investigator	Takashi Hanakawa (Director, NCNP)
Funded Co-investigator	Hiroshi Yokoi (Professor, The University of Electro-Communications)
Funded Co-investigator	Dai Owaki (Assistant Professor, Tohoku University)
Co-investigator	Akio Ishiguro (Professor, Tohoku University)
Co-investigator	Arito Yozu (Assistant Professor, The University of Tokyo)
Co-investigator	Masao Sugi (Associate Professor, The University of Electro-Communications)
Co-investigator	Kahori Kita (Assistant Professor, Chiba University)
Co-investigator	Shin-ichi Furuya (Associate Professor, Sophia University)
Co-investigator	Kazumasa Uehara (JSPS PD, NCNP)

Research Project C03-1: Developing a new therapeutic application of neuromodulation

Principal Investigator	Masashi Hamada (Assistant Professor, The University of Tokyo)

Research Project C03-2: Muscle Contraction Pattern-Based Direct Rehabilitation Using Motion Estimation And Functional Electrical Stimulation

Principal Investigator	Keisuke Shima (Associate Professor, Yokohama National University)
Co-investigator	Koji Shimatani (Associate Professor, Prefectural University of Hiroshima)
Co-investigator	Hideki Nakano (Researcher, Kio University)
Co-investigator	Atsushi Tasaka (Lecturer, Osaka Yukioka College of Health Science)

Research Project C03-3: Development of a clinical tool for measuring dynamic balance function

Principal Investigator	Masahiko Mukaino (Lecturer, Fujita Health University)
Co-investigator	Fumihiro Matsuda (Assistant Professor, Fujita Health University)

Research Project C03-4: Elucidation of distortion of sense of agency and ownership in asomatognosia and apraxia and development of neurorehabilitation method

Principal Investigator	Shu Morioka (Professor, Kio University)
Co-investigator	Sotaro Shimada (Professor, Meiji University)
Co-investigator	Atsushi Matsuo (Professor, Kio University)
Co-investigator	Makoto Hiyamizu (Associate Professor, Kio University)
Co-investigator	Yohei Okada (Assistant Professor, Kio University)
Co-investigator	Hiroshi Maeoka (Assistant Professor, Kio University)
Co-investigator	Satoshi Nobusako (Assistant Professor, Kio University)
Co-investigator	Michihiro Osumi (Assistant Professor, Kio University)