2014 Annual report

"Understanding brain plasticity on body representations to promote their adaptive functions"

Program Director: Jun Ota (The University of Tokyo)

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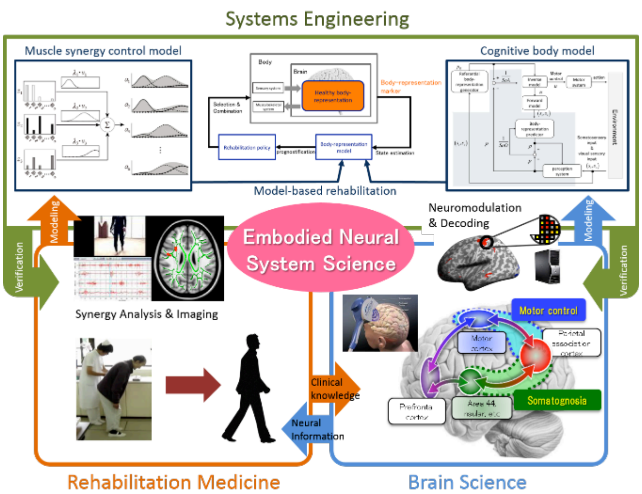
Program Overview and Activities of Steering Committee

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

I. Purpose of the Research program

As the Japanese society ages rapidly, we are experiencing a sharp increase in the number of cases of motor paralysis and other dysfunctions resulting from motor dysfunction, stroke, and neurodegenerative diseases. Thus, establishing effective rehabilitation techniques to overcome these motor dysfunctions is of paramount importance. The key to achieving this is to elucidate the mechanisms by which the brain adapts to changes in body functions. However, abnormalities in somatognosia can occur even in diseases that do not cause motor dysfunction. This indicates that we create and maintain a model of the body in the brain (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).

The purpose of this research program is to elucidate the neural mechanisms of the body representation in the brain 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 nine research projects (A01-03, B01-03, C01-03). In research projects A01/02, we will conduct experiments on humans and monkeys 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/B02, we will 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/C02, we will 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. The research projects A03, B03, and C03 are those for subscribed research groups.

III. Expected Research Achievements and Scientific Significance

Organically combining brain science and rehabilitation medicine by using systems engineering can be anticipated to yield the following three results:

1. By identifying the markers that reflect the moment-to-moment status and long-term changes in body representation in the brain, which govern somatognosia and motor control, it will be possible to quantitatively evaluate the effects of rehabilitation intervention.
2. By elucidating the slow dynamics of body representation in the brain and developing techniques that can be used to intervene in those dynamics, we will work toward developing innovative model-based rehabilitative techniques that permit predictions of prognosis.
3. We will describe the mechanisms of the important brain functions that are essential to the existence of somatognosia and motor control and pursue the computational principles of the brain that are shared by these functions.

IV. MEMBERS

We organize a management group for steering the research program (steering committee). Members of the management group are shown as follows:

X00 Comprehensive research management for understanding the plasticity mechanism of body representations in brain

Principal Investigator: Jun Ota (Univ of Tokyo). Funded Co-Investigator: Eiichi Naito (NICT), Shin-ichi Izumi (Tohoku Univ), Toshiyuki Kondo (TUAT). Co-Investigator: Hiroshi Imamizu (ATR), Kazuhiko Seki (NCNP), Kaoru Takakusaki (Asahikawa Medical Univ), Hajime Asama (Univ of Tokyo), Nobuhiko Haga (Univ of Tokyo), Akira Murata (Kinki Univ), Tetsuya Inamura (NII), Takashi Hanakawa (NCNP). Research Collaborator: Yoshiaki Iwamura (Ueno Gakuen Univ).

V. ACTIVITIES

Following events were held in the first year of the research program.

Kickoff meeting

Date and Time: Monday, July 31, 2014, 13:00-19:00. Tuesday, August 1, 2014, 9:00-12:00

Place: Meeting room, 4th floor, RIEC, Tohoku Univ.

Attendees: 30 in total (members only)

Contents: presentations by members about research plan, general discussion

Kickoff symposium

Date: Monday, September 29, 2014, 13:30-17:40

Place: Ito Memorial Hall, Hongo Campus, Univ of Tokyo

Attendees: 190 in total including members

Contents: presentations by program director, principal investigators, and two representative researchers, and briefing for how to apply subscribed research.

1st General meeting

Date: Monday March 9, 2015, 13:30～Wednesday, March 11, 2015, 12:00

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

Attendees: 70 in total (members only)

Contents: presentation about annual report by program director, PI of each planned research project, special invited talks by three emeritus professors (Prof. Shinoda, Prof. Ito, and Prof. Tsuchiya), and poster session by attendees.

1st Steering committee meeting

Date: Monday, September 29, 2014, 11:30-13:00

Place: meeting room at ITO Memorial Hall, Hongo Campus, Univ of Tokyo

Attendees: 18

Contents: General discussion on steering of the program, research plan, events, publicity, etc.

2nd Steering committee meeting

Date: Wednesday, March 11, 2015, 12:00-13:00

Place: Hotel Senshu-kaku, Hanamaki Onsen

Attendees: 18

Contents: General discussion on steering of the program, research plan, events, publicity, etc.

Activities in academic society (Organized Session proposal)

(1) Symposium on Systems and Information 2014 (SSI2014)
Date: Friday, November 21, 2014
Place: Tsushima campus, Okayama Univ.
Contents: 10 presentations by members and their collaborators.

(2) 27th Symposium on Distributed Autonomous System
Date: Friday, January 23, 2015
Place: Kagura Campus, Science Univ of Tokyo
Contents: eight presentations by members and their collaborators.

(3) 20th Robotics Symposia
Date and Time: Sunday, March 15, 2015
Place: Karuizawa Prince Hotel West
Contents: four presentations by members and their collaborators.

Website of the research program

Japanese version of the website for the research program (http://embodied-brain.org) was developed and released on August 19, 2014. Furthermore, English version of the website (http://embodied-brain.org/eng/) was presented on October 31, 2014.

VI. FUTURE EVENTS

In the next year, members of subscribed research groups will join the program. To encourage research collaboration between the planned and the subscribed research groups, general meeting will be held at an early date. In addition, we will plan workshops in related international conferences for public relation of the program.

Planned activities are follows:

(1) Organized session in ROBOMECH2015, May, 2015, Kyoto
(2) 2nd General meeting, Saturday, July 4, 2015, Kyorin University
(3) Plenary and workshop lecturers recommendation in 21th SICE Emergent Systems Sympoium 2015, August 31-September 2, 2015, Tokyo Univ of Science, Suwa
(4) International workshop in IROS2015, October, 2015
(5) 1st Public symposium, October, 2015, Tokyo area
(6) 3rd General meeting, March, 2016, Meeting room, Hotel Senshu-kaku, Hanamaki Onsen

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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. In 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.

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.

III. ACTIVITIES

(1)Kickoff meeting
Date and Time: July 31, 2014, 13:00-19:00. August 1, 2014, 9:00-12:00
Place: RIEC, Tohoku Univ.
Attendees: 30 in total (members only)
Contents: presentations by members about research plan, general discussion. We made an agreement as follows: (1) Research project A01 shares a technique of manipulating bodily awareness in a virtual reality environment with B01 and C01, and provide possible markers which can evaluate the effect of rehabilitative interventions conducted in Research project C01. (2) Together with C02, Research project A02 contributes to build-up new rehabilitation method to directly restore internal representation of muscle synergy control.

(2)Research project A02 meeting
Date and Time: September 30, 2014, 9:00-17:00.
Place: NCNP
Attendees: 25 in total (A02 members + B02, C02 members)
Contents: All members in Research project A02 and also several members from B02 and C02 present what they are doing and what they are planning in the project. We decided to share a program (algorithm) in the analysis of muscle synergy across all 02 (A-C) research projects. This program was provided by the members of B02 project. By this strategy, we promoted inter-project interaction and collaboration.

(2)Research project A02 meeting
Date and Time: September 30, 2014, 9:00-17:00.

Place: NCNP
Attendees: 25 in total (A02 members + B02, C02 members)
Contents: All members in Research project A02 and also several members from B02 and C02 present what they are doing and what they are planning in the project. We decided to share a program (algorithm) in the analysis of muscle synergy across all 02 (A-C) research projects. This program was provided by the members of B02 project. By this strategy, we promoted inter-project interaction and collaboration.

(3)Research project A01 meeting (Research project 01 (across A-C) meeting)
Date and Time: November 2, 2014, 14:00-17:00.
Place: Univ of Tokyo. Grad. Sch. of Engineering
Attendees: 20 in total (A01 members + B01, C01 members)
Contents: All members in Research project A01 and also members from B01 and C01 presented computational model of bodily awareness and change of sense of agency in schizophrenia patient, and discuss future collaboration across project A-C. After this meeting, Yano (B01), Imamizu and Maeda (A01) have started collaborative work to model the change of sense of agency in schizophrenia patient in the Bayesian frame work.

(4)Research project A01/02 meeting
Date and Time: January 16, 2015, 14:00-19:00.
Place: Univ of Tokyo. Medical hospital
Attendees: 30 in total (A01/02 members + B01/02, C01/C02 members)
Contents: On behalf of A01, first Imamizu showed their results that healthy participants can adapt temporal-spatial gaps between their own movements and avatar's movements in a virtual reality environment, and explain how to estimate change in the sense of agency and body ownership by using decoding technique. Second, Murata demonstrated importance of inferior parietal cortex (IPL) in the formation of sense of agency and body ownership. He found that IPL neurons not only react to monkey's own arm movements but also fires when monkeys merely looked at the play-back of their arm movements. Thus, he showed IPL activity can be a marker that reflects change in bodily awareness. On behalf of A02, first young Co-Investigator Hirashima (NICT) pointed out that definition of muscle synergy differs between brain science and engineering science and clarified the definition of muscle synergy to promote future collaborative works between research projects A and B. Second, young Co-Investigator Hirose (NICT) made a progress report about the ongoing project to identify neuronal substrates allowing muscle synergy control in humans using 7T MRI.

Future investigations

We reported details of 2014 research outcomes and activities in reports from each research project. In the FY2015, in the research project A01, they will start experiments to estimate change in the sense of agency and body ownership by using decoding technique, with a view to apply this technique to rehabilitation. In the research project A02-01, they will conduct electrophysiological experiments on monkeys how central motor system change its body representation when they manipulate physical states of animal's musculoskeletal system. Also, in humans they will identify neuronal substrates allowing muscle synergy control using high-tesla fMRI. Finally, in the research project A02-02, they shall conduct electrophysiological experiments on monkeys and cats to identify changes in animal's body representations when monkeys start performing bipedal walking and cats prepare walking. We share all of research outcomes and knowledge across all research projects (A-C). Furthermore, Research project A01 also investigates change in internal representation of patient's body in collaboration with C01. Research project A02, also together with C02, contributes to build-up new rehabilitation method to restore internal representation related to muscle synergy control.

Annual report of research project A01

Hiroshi Imamizu
Advanced Telecommunications Research Institute, Cognitive Mechanisms Laboratories

***Abstract*—Our research project aims to find neural correlates of bodily self-consciousness (senses of movement agency and body ownership), and neural mechanisms in which changes in bodily self-consciousness lead to changes in body representations in the brain. Based on these results, we are planning to develop a method for intervention and manipulation of the bodily self-consciousness. In this fiscal year, we developed experimental paradigms and analysis methods for quantitative evaluation of the bodily self-consciousness. We also succeeded in finding a part of the body representations in the monkey brains by using electrophysiological methods.**

I. INTRODUCTION

Appropriate body representations in the brain are essential for rapid and smooth control of the bodies. When injury and aging change our bodies, the representation must be adaptively modified in accordance with the changes. However, the body representation sometimes fails in adaptive changes, and is dissociated from the actual state of the body. In such cases, people suffer from movement disorders even after recovery of physical functions of the body, or from a phantom-limb pain caused by the illusory body representation. Because little is known about neural processes corresponding to changes in the body representation, we currently have no effective methods for cures of the dissociation between the brain and body. The purpose of our project is to develop a basic technology for the curing methods based on investigation of how the bodily self-consciousness induces changes in the body representation.

II. AIM OF THE PROJECT

We aim to identify neural correlates of the bodily self-consciousness, which consists of senses of agency ("I am moving this body") and body ownership ("This is my body"). Based on the identified neural mechanisms, we investigate slow processes in which changes in bodily self-consciousness lead to change in the body representation, and develop effective methods for promoting adaptive changes in the body representation. 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. Development of basic technology for objective indicies for somatognosia

A group of the principal investigator conducted researches on the two topics for objective evaluation of the bodily self-consciousness.

1) Neural correlates of "intentional binding" as an index of 'sense of agency.' It is known that a subjective timing between action (e.g., button press) and its consequence (e.g., flash) is compressed from the actual timing when the action is initiated by the own intention ("intentional binding"). This compression is a possible candidate for an objective marker of 'sense of agency'. We investigated relationships between the intentional binding and brain activity. Specifically, by using magnetoencephalography (MEG), we measured brain activity when human subjects voluntary presses a button and lit a flash. We examined if the readiness potential before button press shifts towards the timing of the delayed flash. In this fiscal year, we developed a method for identification of readiness potentials in MEG activity, and quantitative estimation of shift in the identified readiness potentials.

2) Development of basic technology for decoding the bodily self-consciousness. We developed decoding methods for prediction of human behaviors from brain activity: these methods are essential for decoding and reconstruction of the bodily self-consciousness from brain activity. Concretely, by using a machine learning technique, we succeeded in prediction of results of training on working memory from pre-training resting-state brain activity with a high prediction accuracy (coefficient of determination: 73%) [1]. We are planning to apply this method, which can extract neural information on subjective experiences, to decoding the bodily self-consciousness in the next fiscal year. Regarding psychophysical approaches to the bodily self-consciousness, Tomohisa Asai (co-investigator) identified tagging systems of own actions in memory [2], mechanisms for automatic compensation of movements based on body ownership [3] and mechanisms in which sense of agency elicits body ownership [4].

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

Yukari Ohki (funded co-investigator, Kyorin University) and her colleagues has developed a virtual reality system, to intervene senses of ownership and agency, and performed experiments with normal human subjects [5-8]. In the system, subjects moved their invisible right arms for 2 minutes to manipulate a virtual "hand" made by computer graphics (CG), while location and time delay between real and CG movement could be varied. After the interventions, some subjects could feel senses of ownership and agency for the virtual "hand", which were evaluated by a Likert rating-scale questionnaire. However, sense of ownership was influenced by similarity of the CG image to the real hand, while sense of agency was deteriorated by increasing the time delay. In the experiments, they also examined several objective parameters (visual position judgment of the real hand, bilateral hand position matching, target-reaching movement, and accuracy and stability of the movement). Among them, bilateral hand position matching and movement stability were partly associated with senses of ownership and agency, respectively. When subjects manipulated the virtual "hand" for a longer time (ca. 2 hours), their senses of ownership and agency were improved gradually, even in the subjects who did not feel them during the shorter time intervention. Thus, they concluded that the system was useful to induce and evaluate long-term changes in bodily self-consciousness.

C. Physiological mechanisms of body representation in the monkey brain

To study neural mechanism for encoding own body state, Akira Murata's group (funded co-investigator, Kinki University) recorded hand manipulation-related neurons and mirror neurons from area AIP and PFG from the monkey inferior parietal cortex [9-12]. It was revealed that these neurons responded to visual image of hand during grasping action, encoding visual kinematics of hand action. These results have been reported on the J. Cognitive Neuroscience [13]. The group is now going to record single unit activity of somatosensory cortex during execution of movement to investigate neural mechanisms that calculate prediction error between corollary discharge and actual sensory feedback.

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. They expanded their sense of agency studies into clinical rehabilitation, neuroimaging, and human engineering as below.

1) Maeda published a review article on a methodological advantage of the Keio method for studying 'subjective experience' such as sense of agency in the field of neuroscience [14].
2) They newly developed the temporal order judgment task (Keio method) in order to evaluate simple time perception in milliseconds time range. This task examines time-perception impairments of patients and excludes their contamination from sense-of-agency data.
3) They have published an fMRI study using the Keio Method, indicating that specific brain areas including default mode networks contribute to sense of agency. Based on this study, they have started functional imaging of patients with schizophrenia.
4) Using behavioral data from experiments using Keio method, they and co-researcher Yamashia in NCNP started simulation approach to emergence of sense of agency using neural networks.
5) They started mathematical modeling of behavioral data obtained by the Keio-method experiment. This study aims to investigate Bayesian inference processes in agency judgment, and provide the interpretation of neuroimaging data.
6) They also started basic researches enhancing self-agency for remote-controlled robotics with Hajime Asama (B01). This study aims to contribute to decommissioning of nuclear reactor in the Fukushima Nuclear Power Plant.
7) From the clinical standpoint in psychiatry, they tried to establish rehabilitation method to normalize sense of agency in schizophrenia, based on reinforcement learning methods.

IV. Future Perspective

In this fiscal year, we prepared experimental paradigms, analysis tools, and frameworks of computational modeling for investigation of the bodily self-consciousness. Especially, we made efforts for finding methods for developing objective evaluations of bodily self-consciousness (experiments on shift of readiness potentials, intervention of the bodily self-consciousness using CG, and experiments in which schizophrenic patients can participate), and developing decoding methods of neural information that can be applied to reconstruction of the bodily self-consciousness. Moreover, we succeeded in identification of the body representation, which encodes own body state, in the monkey brains. We started collaboration with computational group (Group B) with respects to computational models. During the above researches, we published the original articles in international journals [1][2-4][13]. Base on these results, we will establish objective indices of the bodily self-consciousness, and start investigation of neural correlates of the bodily self-consciousness and experiments on long-term changes in the body representation.

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Annual report of research project A02-01

Kazuhiko SEKI
National Institute of Neuroscience, NCNP

Abstract*—In the FY2014, 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 are based on three major Neuroscience hub in japan (NCNP, NICT, TMIMS) and include 16 scientists. Through frequent collaboration and discussion, we would like to establish the neural correlates of muscle synergy in microscopic and macroscopic levels.

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

A. A development of prototype of muscle synergy detector

As a collaborative project in all 02 group, we developed a prototype of muscle synergy detector using LabView based PC system.

B. Establishment of white-matter stroke model in monkey[1]

White matter (WM) impairment and motor deficit after stroke are directly related. However, WM injury mechanisms and its relation to motor disturbances are still poorly understood. In humans, the anterior choroidal artery (AChA) irrigates the internal capsule (IC), and stroke to this region can induce isolated motor impairment. The goal of this study was to analyze whether AChA occlusion can injure the IC in the marmoset monkey. The vascular distribution of the marmoset brain was examined by colored latex perfusion and revealed high resemblance to the human brain anatomy. Next, a new approach to electrocoagulate the AChA was developed and chronic experiments showed infarction compromising the IC on MRI scanning (day 4) and histology (day 11). Behavioral analysis was performed using a neurologic score previously developed and our own scoring method. Marmosets showed a decreased score that was still evident at day 10 after AChA electrocoagulation. We developed a new approach able to induce damage to the marmoset IC that may be useful for the detailed study of WM impairment and behavioral changes after stroke in the nonhuman primate. The AChAO method in marmoset monkeys established in this study will allow us to perform a detailed examination of motor dysfunction and recovery using previously reported behavioral evaluations (Marshall and Ridley, 2003; Freret et al., 2008) and additional evaluations such as gait pattern, pressure distribution and muscular synergy alterations after WM stroke. Additionally, showing the physiological mechanism for damaged IC compensation by other descending or cortical and subcortical networks will have a crucial implication on the establishment of novel rehabilitation strategies in human stroke patients. This model will be shared with Group 02 (A,B,C) to test if the prospective biomarker of neural representation of muscle synergy could be applied in the rehabilitation strategy from Stroke.

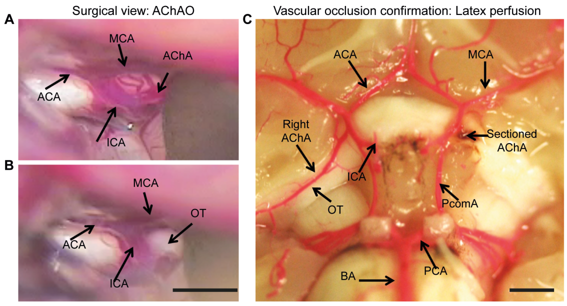

Figure 1 Surgical view of the anterior choroidal artery (AChA) of common marmoset

C. Investigation of fast and slow dynamics in human body cognition and motor control, and development of new fMRI decoding method

In the Naito's (CiNet/NICT) group, we have obtained the following research outcomes related to human body cognition and motor control. One of the goals in the Embodied-Brain project is to elucidate how motor network and fronto-parietal network in the brain interact and corporate each other to achieve cognitive and motor functions. In this aspect, Ikegami et al. focused on the mirror neuron system in the fronto-parietal network, and showed that when dart experts observed poor performance of novices, their performance significantly deteriorated [2]. This provided an evidence that understanding and recognition of other's motor performance directly affects one's one motor control process. Another important goal of the Embodied-Brain project is to describe fast and slow dynamics in human body cognition and motor control. In terms of this aspect, Ganesh et al. clearly showed the existence of these two systems when the brain incorporates a tool into our body which has been assumed a function of left fronto-parietal network in humans. When people made a reaching movement while they hold a long tool with their hands, the brain immediately perceived as their arms are shrinking as if the brain compensates the "functional" elongation of their arms due to the holding of the tool (fast dynamics). However, as people repeated this task, the brain gradually perceive as if their arms are elongating (slow dynamics) [3]. These findings clearly demonstrated the existence of fast and slow dynamics in the fronto-parietal embodiment process. Furthermore, Naito&Hirose provided a valuable evidence of slow dynamics in motor network in Brazilian soccer player "Neymar". Neymar recruited very limited and focal neural resources in foot motor regions when he rotated his right ankle, when compared with other professional footballers and Olympic swimmers (Figure 1). This research made big waves across countries all over the world [4, 5].

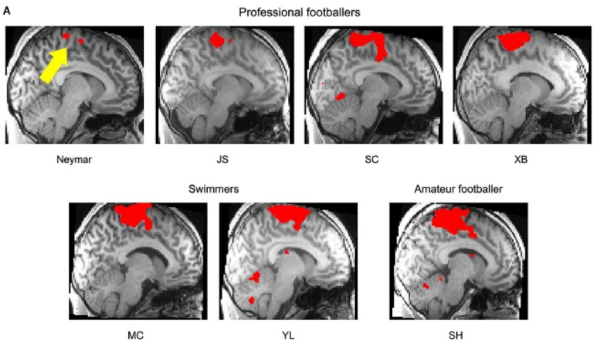

Figure 2 Small and focal brain activations in Neymar's brain during foot movement

Generally speaking, to elucidate what kind of information is being represented in human brain activation, it is necessary to develop a decoding method, which can extract brain information from the patterns of brain activities. Hirose et al. have developed new fMRI decoding algorithm called iSLR [6]. A conventional decoding method (SLR) had a problem of over-pruning where the algorithm fails to depict many brain activities that should have important information. Hirose et al. solved this problem by developing new decoding algorithm (iSLR) and showed that iSLR allows us to segregate focal motor representations for index and middle fingers, which was very difficult with conventional brain mapping methods.

D. *Releasing dentate nucleus cells from Purkinje cell inhibition generates output from the cerebrocerebellum (Kakei)*

The cerebellum generates its vast amount of output to the cerebral cortex through the dentate nucleus (DN) that is essential for precise limb movements in primates. Nuclear cells in DN generate burst activity prior to limb movement, and inactivation of DN results in cerebellar ataxia. The question is how DN cells become active under intensive inhibitory drive from Purkinje cells (PCs). There are two excitatory inputs to DN, mossy fiber and climbing fiber collaterals, but neither of them appears to have sufficient strength for generation of burst activity in DN. Therefore, we can assume two possible mechanisms: post-inhibitory rebound excitation and disinhibition. If rebound excitation works, phasic excitation of PCs and a concomitant inhibition of DN cells should precede the excitation of DN cells. On the other hand, if disinhibition plays a primary role, phasic suppression of PCs and activation of DN cells should be observed at the same timing. To examine these two hypotheses, we compared the activity patterns of PCs in the cerebrocerebellum and DN cells during step-tracking wrist movements in three Japanese monkeys. As a result, we found that the majority of wrist-movement-related PCs were suppressed prior to movement onset and the majority of wrist-movement-related DN cells showed concurrent burst activity without prior suppression. In a minority of PCs and DN cells, movement-related increases and decreases in activity, respectively, developed later. These activity patterns suggest that the initial burst activity in DN cells is generated by reduced inhibition from PCs, i.e., by disinhibition [7,8]. Our results indicate that suppression of PCs, which has been considered secondary to facilitation, plays the primary role in generating outputs from DN. Our findings provide a new perspective on the mechanisms used by PCs to influence limb motor control and on the plastic changes that underlie motor learning in the cerebrocerebellum.

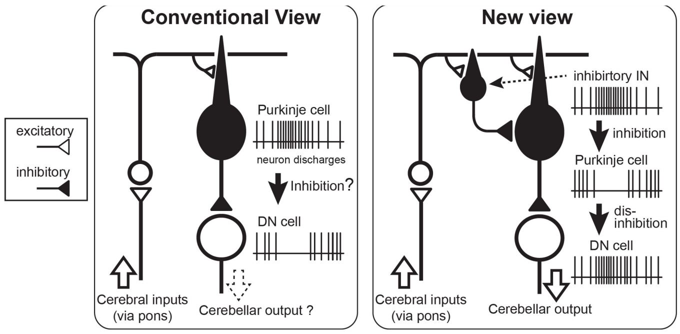

Fig. 3. Output mechanism of the cerebellum. Left: conventional view. Right: New view.

III. 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 four years.

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Annual report of research project A02-02

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***Abstract* - The present study 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. For this purpose, electrophysiological techniques combined with genetic and pharmacological approaches are employed in animal experimentation (cats and monkeys). Results will clarify neural substrates representing illusive postural body scheme in the fronto-parietal network that contributes to the adaptive postural and locomotor control.**

I. INTRODUCTION

In most mammals including humans, body is built up by a set of assembled segments, such as the head, trunk, fore (upper) limbs and hind (lower) limbs, which are linked together by flexible joints and muscles. The posture is constructed by the relative positioning of these body segments with respect to each other and to the gravitational environment (*postural orientation*) [1]. In quietly standing animals, the gravity force acting on the body's center of mass (Fig. 1, downward arrow) and the ground reaction force under the foot (upward arrow) are balanced so that the body tends to stay in the desired position (*static equilibrium*).

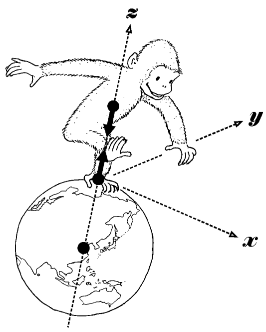

Fig. 1. Postural control in the geocentric reference frame : Postural orientation (rerelative positioning of the body segments with respect to each other and to the environment) and postural equilibrium.

The term "posture" encompasses not only the configuration of the whole body stably maintained in space, but also the configuration of a part of the body stabilized during voluntary movement (*dynamic equilibrium*) [1]. When a subject is reaching for an apple on the table, the focal movement of an upper limb is likely to destabilize the equilibrium of the body's center of mass. To prevent such imbalance ahead, the rest of body segments apart from the prime mover are repositioned to construct their new configuration, which provides a stable body platform for the efficient execution of reaching movement. Alternatively, during locomotion, each of the Frankfort plane (a plane passing through the left orbit and bilateral auditory meatus) and the truncal axis is maintained at a constant angle with respect to vertical, while each of the four limbs are moved back and forth, rhythmically [2]. Such a complementary relationship between posture and movement is compared to an iceberg; the apparent being the movement and the hidden part, which is often the most important, the posture [3].

Postural control is the process of sensorimotor coordination so as to successfully achieve two main behavioral goals such as postural orientation and postural equilibrium. Multisensory (visual, vestibular and somatosensory) signals are integrated to provide the geocentric reference frame for the CNS. These inputs are also served to form an internal representation of the body and its environment, often called as "*the body schema*" that may be party determined genetically and partly acquired through learning [4].

In either forelimb reaching or locomotion, onset of the purposeful movements is always preceded by postural control that is the most suitably adjusted. This process is called as "anticipatory postural adjustment (APA)". Because the APA is disturbed in patients with lesions in the CNS [3], it is essential to elucidate the mechanisms of the APA to reestablish adaptive physical capability in these patients. However, there is no substantial evidence how the program of APA is generated and what descending pathways are utilized to evoke APA.

II. AIM OF THE RESEARCH AND WORKING HYPOTHESES

The purpose of this project is to elucidate cortical and sub-cortical mechanisms of sensorimotor integration of bodily information that enable to perform adaptive postural-locomotor strategies. Then, we offer following working hypotheses. The first hypothesis is that the multimodal sensory signals will be integrated at the parietal cortex such as the parieto-insular vestibular cortex (PIVC) in the primates [5, 6] so that internal bodily information (body schema) can be produced. Second is that the information will be transmitted to the Brodmann's area 6 (supplementary motor area, SMA and dorsal premotor cortex, PMd) of the frontal lobe. The fronto-parietal network may play crucial role for generating motor programs. The third is that the motor programs of APA can be conveyed to the spinal cord via the cortico-reticular projection [7] and the reticulospinal tract. The fourth is that the operation of the fronto-parietal network is critical to the short-term and long-term alteration of postural-locomotor strategies.

III. RESEARCH THEME

This project involves three lines of experiments using different animals (monkey and cat). Electrophysiological techniques are combined with pharmacological, genetic and imaging approaches.

A. *Cortical mehcniams of postural-locomotor synergies in monkeys*

Unrestrained Japanese monkeys are trained to walk on the treadmill and to transform their locomotor patterns from quadrupedal (Qp) to bipedal (Bp) and vice versa. Such transformation drastically alters the postural orientation of all body segments in space (Fig. 2).

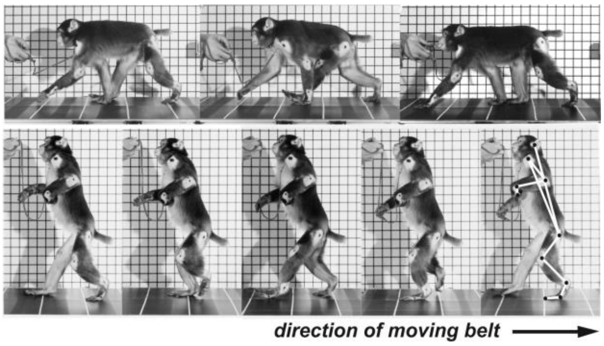

Fig. 2. Quadrupedal (top) and bipedal locomotion (bottom) exerted by a single monkey.

In this model, following studies will be performed. The first is to elucidate how internal bodily information is produced in the parietal cortex such as the PIVC. Single-unit activities are recorded from the PIVC to examine whether they receive multimodal sensory inputs and how they alter firing pattern in conjunction with the alteration between Bp and Qp. In the second, we test how the PIVC contribute to the changes in postural-locomotor strategies. For this, muscimol, $GABA_A$ agonist, is injected into the PIVC and examine the dynamics (by recording EMGs of trunk and limbs) and kinematics (by monitoring with a use of high-speed cameras) during walking. The third is how parieto-frontal projections contribute to motor programs. Activities of SMA/PMd neurons are recorded to examine convergent inputs from the PIVC. Firing properties of these neurons are then recorded in conjunction with the APA in obstacle clearance task. These studies will help understanding the short-term or fast-adaptive cortical mechanisms of embodyment alteration during postural-locomotor strategies.

B. *Imaging study of fronto-parietal network relating to the development of postural-locomotor strategies in monkey.*

This collaborating study with a Group A02-01 will examine the changes in the activity of fronto-parietal network of the monkey using 7T-fMRI in relation to the acquisition of Bp walking from Qp following training. This analysis may show the long-term or plastic changes in the fronto-parietal network involved in the alteration of postural-locomotor strategies.

C. *Cortical and subcortical mechiansms of APA during forelimb reaching task in the cat*

Cats are trained to make a discrete reaching movement with either forelimb and to retrieve a morsel of food while standing with each paw on a force platform (Fig. 3A). The reaching movements are expected to be preceded by an APA that will be characterized by a loading of the reaching forelimb (Fig. 3B, top) and shifting the position of the body's center of mass (Fig. 2B, bottom). When cats are well-trained, we will record activities of either the motor cortical neurons or reticulospinal neurons together with EMGs of limb and axial muscles, and ground reactive forces of all limbs during reaching task. In these analyses, we will elucidate dynamic properties of the cortico-reticulospinal system in conjunction with the APA during voluntary reaching movements.

Next, we will perform a lesion experiment on the same animal. The double infection of virus vectors [8] will be used to selectively interrupt the transmission through the cortico-reticular projection arising from the area 6. The impairment of an APA produced by this transient blockade will be investigated throughout the acute and recovery phases.

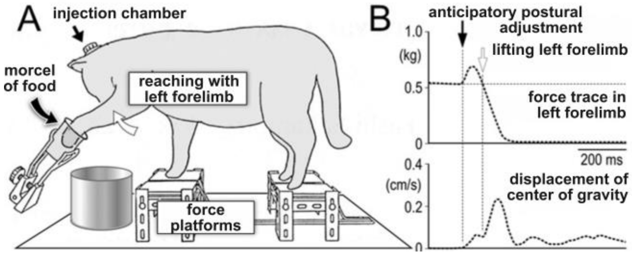

Fig. 3. A: a reaching task in the cat. B: changes in ground reactive force and center of gravity in anticipatory postural adjustment during food-reaching task.

IV. Progress and Future Perspective

In this first year, Takakusaki (principal investigator) and Funakoshi (co-investigator) in Asahikawa Medical University are preparing an experimental setup for cat experimentation. Nakajima (co-investigator) in Kinki University has started recording of motor cortical neurons in monkey, and observe that SMA neurons in the trunk/leg regions are quite dependent on postural orientation during locomotion. Some displayed selective activity in transition from Qp to Bp, as is strikingly different from activities in M1 neurons [9].

Next year, we will perform experimentation in accordance with the original plans for the final goal, i.e., to successfully probe electrophysiological, kinetic or kinematic parameters that are clinically applicable and give concrete expression to the "*plastic*" representation of body schema.

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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 within the brain, influenced by fast dynamics. We dealt with fast dynamics in our "Mobiligence" government-supported program between 2005 and 2009. Understanding slow dynamics will be the key to rehabilitation therapy, which have been central to research.

Group B is consisted of two projects (Project B01 and Project B02) as shown in Figure 1.

Aim of Project B01 is creation of "cognitive body model" of the body representations in the brain, which gives rise to body consciousness (sense of agency and sense of ownership). We assume that the body representations in the brain are kind of filters that modifies sensory data and sometimes deforms it. We are going to clarify how generation and renewal of the body representations are influenced by sensory experience and sense of ownership, on sense of agency, intention to move and on prediction of movement and sensory feedback.

Aim of Project B02 is creation of "muscle synergy control model" of the body representations in the brain, which modulates muscle synergy in response to the environment, etc. We used a treadmill with left and right belts, whose speed could be controlled separately to create an artificially asymmetrical walking environment. Also, we will create models of the posture control needed when a person maintains a standing position.

Models in the above two projects 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.

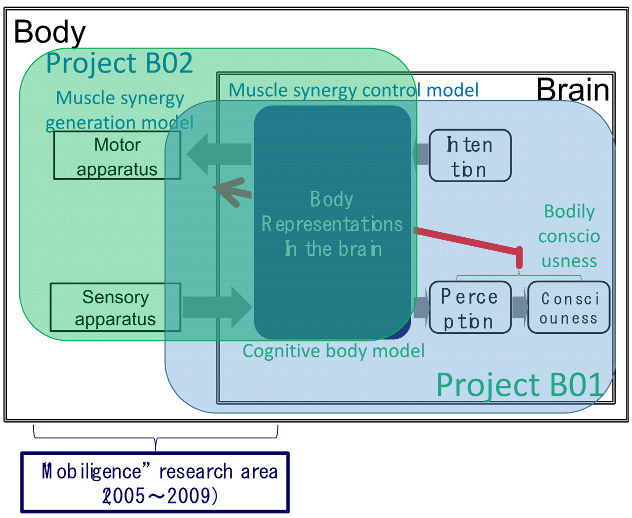

Figure 1 Relationship between topics in Group B

II. Group Members

Members in the two projects are shown as follows:
Group leader: Jun Ota (The Univ. of Tokyo)

<u>Project B01: Modeling of slow dynamics on body representations in brain</u>
Principal Investigator: Hajime Asama (Univ of Tokyo). Funded Co-Investigator: Toshiyuki Kondo (Tokyo Univ of Agriculture and Technology), Hirokazu Tanaka (JAIST), Shiro Yano (Ritsumeikan Univ.). Co-Investigator: Atsushi Yamashita (Univ of Tokyo), Jun Izawa (Univ of Tsukuba), Masafumi Yano (Tohoku Univ).

<u>Project B02: Modeling of motor control that alters body representations in brain</u>
Principal Investigator: Jun Ota (Univ of Tokyo). Funded Co-Investigator: Shinya Aoi (Kyoto Univ), Ryosuke Chiba (Asahikawa Medical University). Co-Investigator: Taiki Ogata (Univ of Tokyo), Tetsuro Funato (Univ of Electro-Communications), Dai Yanagihara (Univ of Tokyo), Kazuo Tsuchiya (Kyoto Univ).

III. Group Meeting

The following group meeting was held in Group B.
<u>Date and Time:</u> Monday, December 22, 2014, 15:00～18:00
<u>Place:</u> Room 713, 7th floor, Faculty of Engineering Building No.14, Hongo Campus, The Univ. of Tokyo.
<u>Attendees:</u> 20 in total including group members
<u>Contents:</u> four presentations by members about research plan and progress, general discussion.

Small scale meetings within Projects B01/B02 and joint meetings with members of Group A and C were also conducted. Group members discussed their research issues in several organized sessions in conferences.

As a future plan, group meetings will be held about twice a year and discussion will be held between members of planned research groups and those of subscribed research groups.

Annual report of research project B01

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. Figure 1 shows the structure of research group B01 to achieve the objectives.

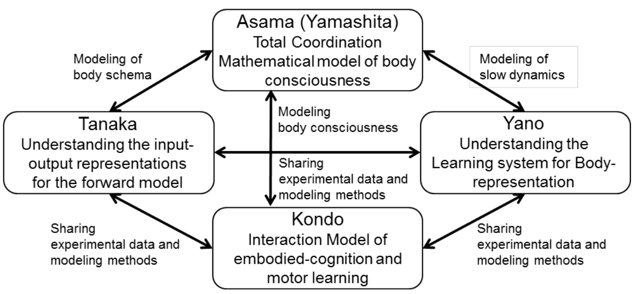

Fig. 1 Structure of research group B01

III. RESEARCH TOPICS

A. *Mathematical Model of Body Consciousness*

Asama's group (The University of Tokyo) examined how high-level cognitive processes, such as performance based inference and goal based expectation, influence the sense of agency. According to previous research, the comparison of motor signal and actual feedback has been confirmed to be critical to the generation of sense of agency. However, the influence of high-level cognitive processes have received fewer attention relative to the low-level processes (i.e., the comparing processes). According to our research, we found that participants reported higher sense of agency when their performance was raised by computer's assistance, although their actual control was weakened by the assistance[1]. Moreover, we also found that when there is a specific goal for someone's action, it is more difficult to produce the sense of agency because expectation for achievement of the goal negatively influenced the sense of agency. We concluded that the high-level cognitive processes are important for the sense of agency, besides the comparing processes, which are highlighted in the previous research.

The group examined the effect of power of action on the sense of agency. The group evaluated the sense of agency in different power condition. Pushing force was modulated by changing the hardness of button, which we used during the task. The group found that action with strong power enhances sense of agency in 700ms time delay when the attribute to self becomes ambiguous, which is shown in figure 2[2].

The group assumes that human judge sense of agency or sense of ownership from comparison between feedback from sensory organ and body representations, and also adjust or update body representations in that process. We attempt basic modelization in reference to data from previous research about simple arm movement.

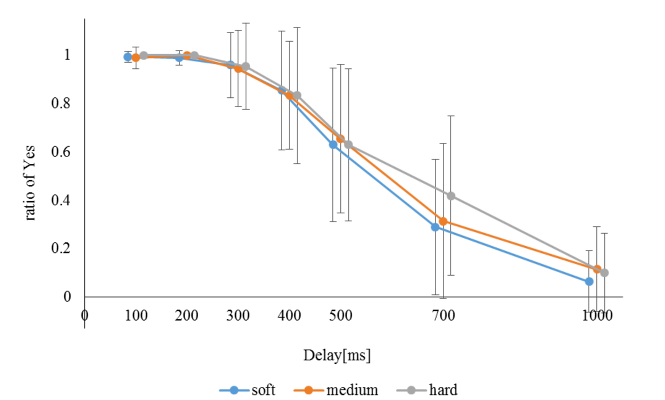

Fig. 2 Sense of Agency affected by pushing force difference

B. *Interaction Model of embodied-cognition and motor learning*

To clarify the relationship between embodied-cognition 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 visual/somatosensory stimuli on the neurofeedback training of motor imagery (MI) based BCI, and 2) the functional connectivity analysis of NIRS data during rubber hand illusion experiments.

In the former study, the group found that watching an instructive visual stimulus that includes a video clip of someone's hand grasping movements from first person point of view is significantly effective to improve MI-based BCI skill after a 4-days neurofeedback training[3], whereas providing somatosensory stimulus during MI training showed no significant improvement.

In the latter study, the group developed a visuo-tactile stimulator for the automation of RHI experiments to improve reproducibility and reliability of the experiments. Using the device, we recorded NIRS data from 20 regions (channels), which covers premotor/primary motor areas and intraparietal sulcus during RHI experiments. We evaluated functional connectivity between arbitrary two channels of NIRS by Granger causality analysis. The result suggests that the functional connectivity changes according to the synchronous/asynchronous stimulation condition that is related to the state of sense of ownership. Especially we found significant causality from right prefrontal area to ipsilateral premotor area under the synchronous stimulation condition.

C. Understanding the input-output representations for the forward model

Toward the goal of understanding the input-output representations for forward models, Tanaka's group (JAIST) formulated a computational model of human motor adaptation[4]. One type of motor adaptation is kinematic adaptation in which visual feedback of body is manipulated, and another is dynamic adaptation in which body dynamics is perturbed. Generally the two types of adaptation are thought to correspond to distinct neural substrates, given the distinct results of motor interference and motor generalization. The group extended our previous work that proposed vector cross products as a representation in the motor cortex, and built a computational model of visuomotor transformation with the cross-product bases. While adaptation to visuomotor rotation and force field generalize in an extrinsic and an intrinsic coordinate, respectively, our model could explain the psychophysical results using a single basis of cross products. This is the first modeling study that unifies the two types of adaptation in a unified way.

The group also proposed a computational model of how the cross-product representation is computed in the parieto-frontal motor network[5]. The model proposes that the parietal reach region (PRR) represents visual location of a movement target, the premotor area in the frontal lobe spatial vectors of limb segments, and the primary motor cortex computes vector cross products. Given motor control signals in the motor areas, the parietal area 5d estimates the body state as an internal forward model. This proposed model generally describes the nenurophysiological findings in the motor network.

D. Understanding the Learning system for Body-representation

Toward the goal of understanding the learning system for Body-representation, Yano's group (Ritsumeikan Univ.), at first, formulated a computational model of Sense of Agency which is accountable both for schizophrenia subjects and normal subjects. It is known the Asperger subject's recognition about the active degree of freedom of his own body becomes very few. It is also known that physically-injured subject's recognition about that becomes large, which is known as "phantom limb". Schizophrenia also acquires similar recognition about his degree of freedom, and researches about schizo suggest the possible cause as the sense of agency.

The group proposed the computational model about Sense of Agency which is able to explain the SoA both of schizophrenia and normal subjects equally well. The model is based on the Quartic exponential(QE) distribution which is the function of the prediction error and the natural extension of past study known as "comparator model". We are now analyzing the model to predict the new phenomena relevant to SoA for identifying the brain region responsible for SoA.

To consider the learning process about the Body-representation as acquiring the state space model from the visual information and body sensory information, it is unavoidable to align the start point and end point of experienced set of data. The SoA would perform this role, so the group are developing and integrating the computational model for the learning system now.

IV. Future Perspective

In this year, process in which body consciousness such as sense of agency and sense of ownership is generated, updated, and transformed was investigated as well as the factors that affect it, and the methods to model the slow dynamics of body representation in brain related to body consciousness were discussed. After the next year, slow dynamics model are implemented, and verification and evaluation of consistency of the models to the findings obtained by physiological research are investigated as well as application to rehabilitation including development of methods to intervene to body representation in brain by collaboration with A01 and C01.

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Annual report of research project B02

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***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 the synergy structure. As the start of this project in this year, we developed experimental systems for investigating posture and locomotion controls in humans and rats, and a calculation tool of muscle synergy for collaboration with brain and rehabilitation research groups.**

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

In this year, we started studies of posture and locomotion controls of humans and rats, and developed a tool for the analysis of muscle synergy.

A. Studies of posture control

1) Human compensatory posture control alteration

There are two kinds of well-known strategies for the human compensatory posture control to keep a certain posture for the disturbances; ankle strategy (AS) and hip strategy (HS). At the AS, humans keep the standing posture with the torque of the ankles while keeping the extended posture of the knees. On the other hand, at the HS, humans keep the standing posture with the torque of both ankles and knees. Past studies report that humans switch these strategies depending on the magnitude of the disturbance. We construct a model focusing on these posture controls through the experiments to change sensing inputs, environments, body conditions as well as the disturbance. In this first year, we prepared the experimental equipment and made a preliminary experiment. The strategy switching was observed depending on the degree of inclined floor, when subjects kept the standing posture on the moving inclined floor using the same magnitude of the disturbance without depending on the floor inclination. It can be consider that the environmental changes induced the changes of the posture control strategy.

2) Posture control simulator with muscular skeletal model

To verify the validity of the control models above mentioned, we develop a human posture control simulator with a muscular skeletal model as a neuromusculoskeletal model. Using the simulator, we simulate the standing motion and estimate the cause of a posture disease by changing parameters, such as muscular strength, delay of nerve response, and sensory information. In this year, for a neuromusculoskeletal model, we utilized the muscular skeletal simulator, OpenSim, and constructed a PD controller which controls the human standing posture in 100ms delay with feedforward control corresponding to muscular tonus[1]. Although the 100ms delay was so large to keep standing for the musculoskeletal model, we found the appropriate gains of PD controller with an optimization to keep standing of the model. From this result, it may be possible to simulate several diseases concerning with the muscular tonus control (e.g. Parkinson's disease).

3) Bipedal standing of rats

Human standing is characterized by a slow body sway, whose property alters by neurological disorders. We focus on the body sway to clarify the underlying mechanism in the alteration of posture control due to disorders. In this year, we developed an experimental system for rats to stand bipedally by their hindlimbs. We successfully measured steady bipedal standing of intact rats over 200 s. We identified their posture control system using measured positions of center of pressure and our previous nonlinear PID control model for human standing. The result showed that rats and humans have similar characteristics in the governing dynamics of posture control.

B. Studies of locomotion control

1) Hindlimb split-belt treadmill walking of rats

Split-belt treadmills, which have two parallel belts controlled independently, have been often used to investigate adaptive motor control in locomotion. Walking on this special environment shows characteristic short-term and long-term adaptations, which alter by neurological disorders, especially in the long-term adaptation. To clarify the underlying mechanism in the alteration of adaptations, we developed an experimental system for rats to walk bipedally by their hindlimbs on a split-treadmill. We successfully measured split-belt treadmill walking of intact rats, which showed similar short-term adaptation to humans and cats. In addition, we performed computer simulation of split-belt treadmill walking of our previous hindlimb neuromusculoskeletal model of rats, which showed similar short-term adaptation to measured rats. We also started to construct a neuromusculoskeletal model of rats with four legs.

2) Gait and posture analysis of decerebellate rats

Cerebellar dysfunction is one of the main causes of motion disorder. It is known that cerebellum has a site specificity of function. We evaluate and model the effect of site specificity of cerebellar motor dysfunction of partially decerebellate rats. We conducted experiments where we made rats, whose medial area or lateral area of cerebellum has been removed. We measured the angles of their knees and ankles during walking on a treadmill. The rats which have removal of medial area showed significant decrease of the movement of both angles, but rats which have removal of bilateral area showed no significant decrease. These results indicate that the medial area of cerebellum may control the muscular tonus for posture and gait.

3) Human walking and running gaits

Low dimensional structures, such as kinematic and muscle synergies, give meaningful insight to clarify the adaptation mechanism in motor control for generating and changing walking and running gaits in humans. We revealed common and specific spatiotemporal structures in kinematic synergy for these gaits from measured kinematic data. In addition, we started to construct a neuromusculoskeletal model for human walking and running gaits based on muscle synergy.

These results were presented at the special session of the embodied-brain systems science at SICE System and Information Division (SICE SSI2014) at Okayama University on 21-23, November, 2014 and at the organized session of the embodied-brain systems science at SICE Symposium on Decentralized Autonomous Systems at Tokyo University of Science on 22-23, January, 2015.

C. Tool developement for muscle synergy analysis

Toward the collaboration with the brain and rehabilitation research groups, we developed a GUI tool that displays the muscle synergy structure calculated from measured muscle activities. We demonstrated experiments at group meeting and the tool has been used by the brain and rehabilitation research groups.

IV. Future Perspective

As the start of this project in this year, we introduced the concept of this project and developed experimental systems for investigating posture and locomotion controls in humans and rats, and a calculation tool of muscle synergy for collaboration with brain and rehabilitation research groups. From these results, we obtained the fast dynamics model to generate the muscle activities for the posture and locomotion control to discuss the underlying mechanisms.

As future works, we continue the above mentioned experiments and construct more sophisticated fast dynamics models. Based on the experimental results and fast dynamics models, we construct a slow dynamics model. Furthermore, we collaborate with brain and rehabilitation research groups by providing analysis tools and receiving experimental data to improve modeling of the slow dynamics of the body representation in brain.

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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 on 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 : 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 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 propose a new neurorehabilitation for motor impairment after brain damage aimed at correcting the distorted body representation by maladaptive change.

C02 : Rehabilitation for postural/movement impairments using sensory intervention

In postural/motor control, we assume that muscle synergy is a marker for neural body representation. The aim of our project is to quantify the abnormality of muscle synergy in various movement disorders. Furthermore, we verify how muscle synergy improves through sensory intervention. We propose new theories for rehabilitation medicine focusing on the aspects of postural/motor control of neural body representation.

II. MEMBERS

Research Project C01

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)

Research Project C02

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)

III. RESEARCH ACCOMPLISHMENT

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

C01 : Neurorehabilitation based upon brain plasticity on body representations

The team in Tohoku university conducted an experiment to measure the response time to visual target appearing on real or fake body surface in order to describe the difference in attentional density in the space on the body or not. The Inamura's team in NII improved virtual reality system to apply for rehabilitation use.

C02 : Rehabilitation for postural/movement impairments using sensory intervention

This was the first year for this project, and we established the instruments to measure muscle synergy. Furthermore, we developed the devices for sensory intervention and applied them to some patients as a pilot study.

IV. ACTIVITIES

・ General meeting, Symposium

Kickoff meeting

Date and Time: Monday, July 31, 2014, 13:00-19:00. Tuesday, August 1, 2014, 9:00-12:00

Place: Meeting room, 4th floor, RIEC, Tohoku Univ. Attendees: 30 in total (members only)

Contents: presentations by members about research plan, general discussion

Kickoff symposium

Date: Monday, September 29, 2014, 13:30-17:40

Place: Ito Memorial Hall, Hongo Campus, Univ of Tokyo

Attendees: 190 in total including members

Contents: presentations by program director, principal investigators, and two representative researchers, and briefing for how to apply subscribed research.

1st General meeting

Date: Monday March 9, 2015, 13:30～Wednesday, March 11, 2015, 12:00

Place: Meeting room, Hotel Senshu-kaku, Hanamaki Onsen Attendees: 70 in total (members only)

Contents: presentation about annual report by program director, PI of each planned research project, special invited talks by three emeritus professors (Prof. Shinoda, Prof. Ito, and Prof. Tsuchiya), and poster session by attendees.

・ Group meeting

1st A01, B01, C01 group meeting

Date: Oct. 27. 2014

Place：University of Tokyo

Attendants：10 group members

Contents: Discussion on joint research among groups

Research project C02 meeting

Date: Dec. 1. 2014

Place：university hospital in university of Tokyo.

Attendants：8 group members

Contents: Research progress report

2nd A01, B01, C01 meeting

Date: Jan. 5. 2015

Place：University of Tokyo

Attendants：9 group members

Contents: Discussion on joint research among different group members

C group meeting

Date: Jan. 28. 2015

Place：Tohoku university

Attendants：15 group members

Contents: Research progress reports

・ Workshop

Observing meeting of rehabilitation in the acute stage

Date: Oct. 6. 2014

Place：hospital in university of Tokyo

Attendants：3 members

Contents: 3 members in engineering observed the clinical rehabilitation in the acute stage in the department of Physical medicine and rehabilitation in the university hospital in university of Tokyo.

Joint research meeting in Prof. Ohki's lab (A01) and Prof. Izumi lab (C01)

Date: Oct. 16. 2014

Place：Tohoku university

Attendants : 20 members and graduate students in Izumis's lab.

Contents: Assistant prof. Nakashima in Ohki's lab reported joint research on spinal cord injury.

A01, B01, C01 group meeting

Date: Nov. 2. 2014

Place：University of Tokyo

Attendants: 7 group members

Contents: Dr. Yano in B01 proposed a new model (preliminary) on body representation, and Assistant Prof. Maeda in A01 reported sense of agency (SoA) in schizophrenia.

Annual report of research project C01

Shinichi Izumi
Graduate School of Biomedical Engineering, Tohoku University

I. Introduction

To control our body as we desire, to know the state of the body, such as the position of the limb, is crucial. This information on the state of body, which is the internal representation stored in the brain, is utilized to generate a motor program when we move a body part. Although this internal representation has been considered as an important key to understand motor control in human so far, it is difficult to 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 propose a new neurorehabilitation for motor impairment after brain damage by the way of correcting 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 hand, 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.

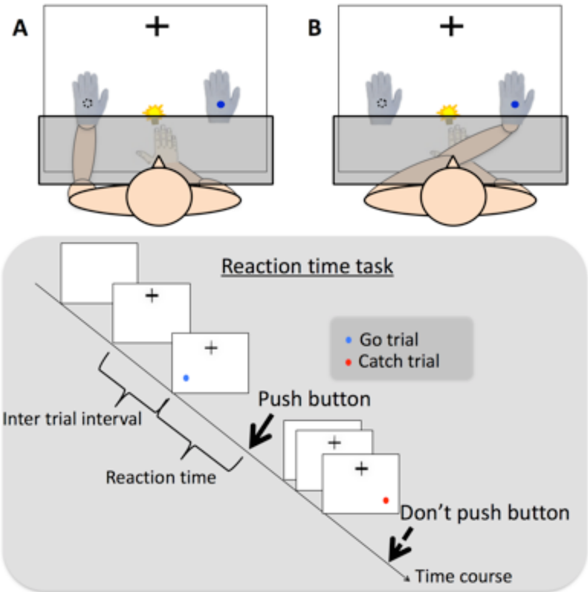

Fig. 1. The design of reaction time task.

B. Development of Virtual Reality Simulator for neurorehabilitation

In rehabilitation for motor impairment in hemiparesis, it is important to correct the distorted body representation of paretic limb caused by maladaptive plasticity in order for the patients to control the paretic limb based on the body representation. Patients with hemiparesis also have abnormality in perception of body axis and decline of attention to the paretic limb, because their body representations are distorted by the inconsistency in communication between brain and effector (limb). The Inamura's group in National Institute of Informatics, funded Co-investigator of research project C01, proposed a new model-based approach in neurorehabilitation utilizing virtual-reality simulator. In most of the current approaches, fixed movie recorded in advance is presented to the patients; on the contrary, our new approach aims at presenting visual materials suitable for each patient in terms of the severity of motor impairment with the virtual reality simulator by monitoring body representation of the patient. This VR system can be applied to the therapy for various symptoms related to body representation, such as phantom limb pain after amputation, abnormal gravity perception of body axis in pusher syndrome. For wide range of clinical use, this VR system has been improved to change various parameters of visual materials, for example, changing the length of arm or leg, and the perspective of visual materials, in order for a viewer to have the stronger body consciousness like body ownership and self-agency for the observing body part in this VR system.

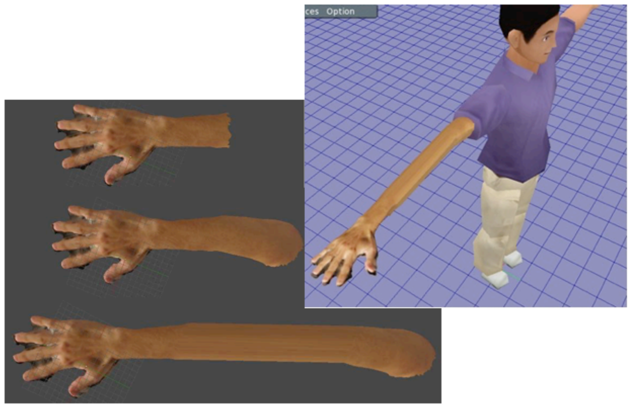

Fig. 2. The sample of arms with various length.

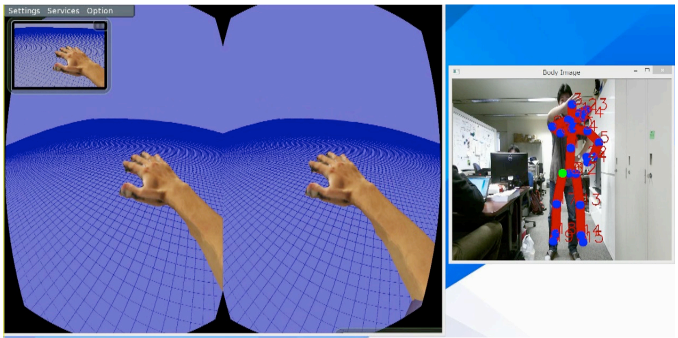

Fig. 3. The demonstration of movie from HMD.

IV. Future Perspective

In this current year, as we have been building up experiment setup for visual detection task to measure attentional density in peri-personal space, our experiment plan has been approved by the ethical committee in Tohoku university. We started to recruit the patients with hemiparesis or with limb amputation for our clinical experiment, especially the experiment to examine the effect of imitation therapy combined with the VR system.

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Annual report of research project C02

Nobuhiko Haga
The University of Tokyo Hospital

I. Introduction

Japan has become a super-aged society, in which more than 5 million people need to be cared. Most of them need care due to motor impairment. 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, but also related to sensory problems. Therefore, it may be possible to actually improve motor impairment 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. In this project, the process of real-time muscle synergy control is referred to as “fast dynamics”, while the process in which synergy control is altered (aggravated) by a disease or modified (improved) through long-term rehabilitation is referred to as “slow dynamics”.

It is not fully understood how muscle synergy control is altered in motor disorders. Moreover, while day-to-day rehabilitation is an intervention for fast dynamics, it remains to be elucidated what interventions make slow dynamics more efficient. This project aims to elucidate these unknown principles of muscle synergy control and to propose new theories for rehabilitation medicine.

II. Objectives

The objective of this research project is to propose a new type of rehabilitation through an understanding of muscle synergy control. The specific aims are as follows:

1) To identify neural body representation markers that reflect the functions of muscle synergy controllers using electromyography and functional brain imaging. To capture changes in markers with motor impairments.
2) To elucidate how sensory interventions for fast dynamics in muscle synergy control alter in the long-term (slow dynamics).
3) To propose and validate a novel model-based rehabilitation that efficiently brings about the functional recovery of motor impairment based on a mathematical model constructed through medical-engineering collaboration.

III. Research Description and Outcomes

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

The group of the principal investigators (Haga/Yozu) study patients with sensory nerve impairments including those with congenital insensitivity to pain. Congenital insensitivity to pain, which belongs to hereditary sensory/autonomic neuropathy type IV/V, involves a congenital abnormality in pain and thermal sensation. The investigators have already reported on abnormalities in gait in patients with congenital insensitivity to pain [1]. Present project intends to determine whether there is an abnormality in muscle synergy control during walking. If an abnormality in muscle synergy control is found, the study will further test whether muscle synergy control can be improved through a sensory intervention to replace the sensory disturbance. Specifically, an orthosis that converts foot pressure to sound will be developed in collaboration with the Owaki/Ishiguro group, and the changes of muscle synergy control by auditory feedback will be studied.

This year, the investigators set up equipments for muscle synergy measurement. Moreover, the foot pressure-auditory feedback orthosis developed in collaboration with the Owaki/Ishiguro group has been tested on four patients as a pilot study, and opinions were collected from the patients and their family members. As a result, points for improvement were identified with regards to cable layout, sheet properties, sound type, and main unit/sound source structure. Opinions regarding possible methods of use and learning included using sound as a simple alarm and learning together with parents.

B. Study on patients with motor impairments due to neurological diseases.

The Hanakawa and Kita group studies patients with Parkinson's disease and dystonia. These investigators have been conducting multimodal functional brain imaging studies [2], which may clarify pathophysiology underlying motor disturbance in patients with Parkinson's disease and its related disorders. In the present project, abnormalities in muscle synergy control during standing and walking will be studied in Parkinson's disease patients, and abnormalities in muscle synergy control during hand movements will be studied in dystonia patients. The effects of sensory interventions such as lidocaine injection on muscle synergy control will also be investigated.

This year, for Parkinson's disease, the group has shown that abnormal contraction of the external abdominal oblique muscle is involved in upper camptocormia, and abnormal contraction of the psoas major muscle may be involved in lower camptocormia [3]. Furthermore, a few white matter sites have been identified to associated with freezing of gait in patients with ischemic white-matter damage [5]. Instruments for quantitative assessment of freezing of gait were also introduced. For dystonia, the group conducted behavioral experiments and fMRI studies on the neural basis of musicians' dystonia, and showed that activities in the cerebellum were potentially related to dystonia symptoms [4].

C. Study on patients with motor impairments due to stroke.

The group of Yokoi and Sugi studies patients with stroke. These investigators have been conducting studies on BMI for upper limb paralysis and activating brain with functional electrical stimuli on muscle [6]. Present project intends to reveal abnormalities in muscle synergy control associated with stroke. Furthermore, interventions by active sensory feedback with electrical stimuli are performed, and their effects on the synergy control will be verified.

This year, the group studied what stimulation parameters promote knee extension and what stimulation parameters facilitate brain activities in FES to knee extensor muscles. The group clarified that the two do not necessarily match.

D. Development and application of sensory converting orthosis.

The group of Owaki and Ishiguro develops a sensory converting orthosis and examines the clinical effect in cooperation with the Haga/Yozu group and C01 group. Specifically, an orthosis that converts foot pressure during walking to sounds will be developed.

This year, a prototype orthosis equipped with five pressure sensors has been developed. A test in a hemiplegic patient has demonstrated that the orthosis improves hyperextension of the knee and the position of the center of pressure shifts backward when it is set to emit a sound with the heel sensor.

IV. Conclusions

This was the first year for this project, and all the four groups focused on establishing instruments for the measurement of muscle synergy control and devices for sensory interventions to fast dynamics. In the next year, research will advance to full-scale measurements and address how long-term sensory interventions can change muscle synergy control (slow dynamics).

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Research Project A01: Neural mechanisms inducing plasticity on body representations

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Research Project A02-02: Adaptive embodied-brain function due to alteration of the postural-locomotor synergies

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

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

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

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