2016 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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Contents

Project overview and Activities of Steering Committee

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I. Objective of this program

With coming of a super-aged society in Japan, many disorder accompanying aging, such as motor paralysis due to stroke / cerebral degeneration disease, are rapidly increasing. Establishment of an effective rehabilitation method to overcome these motor disabilities is an urgent task. In order to deal with this problem, it is indispensable to elucidate the mechanism of brain adaptation to changes in body function. For example, an increase in fall due to age suggests that brain adaptation is not associated with a decrease in motor function. Conversely, even in a disease state without any dysfunction in the locomotorium, abnormality may occur in the body perception. These facts indicate that an internal model of the body (we call this “body representation in the brain”) is constructed and maintained in our brain, and when abnormality occurs in the body representation in the brain, it means serious dysfunctions to the sensory system and motor system occur. In the embodied-brain systems science area, we aim to clarify the neural mechanism of the body representation in the brain and its long-term change mechanism and apply it to rehabilitation intervention. For this reason, we try to integrate brain science and rehabilitation medicine with the intermediation of system engineering which can consistently describe the behavior of human as a mathematical model. By doing this, we aim to create a new academic area of "Embodied-brain Systems Science" that comprehensively understands body cognition and motion control, and establishes a truly effective rehabilitation method.

II. Activities of the program

During two years from the start of the program until 7 February 2017, the program has over 361 journal papers (including 248 international journals), over 251 international conference presentations, and over 530 domestic oral presentations. From the second year onwards, we publish transdisciplinary research papers steadily and publish special issue papers on interdisciplinary research promoted in this area to international journals. Specific research results include the research that identifies activity dynamics with multiple time frequencies in the brain by using machine learning technique from fMRI measurement data (Brain science group), the research that obtains muscle synergy in walking / upper limb movement with a novel statistical data analysis method (Systems engineering group), development of rehabilitation system that activates physical Illusion with Immersive VR and analysis of degree of intervention to the body representation in the brain (Rehabilitation medicine group) . In addition to these, top-level researchers also participated in subscribed research groups. Several research projects could get excellent research results than expected when this project started The outcomes of this area are widely outreached to more than 13,000 people. Young researchers association is also organized, and the training to the next generation researchers is carried out to undertake excellent studies on interdisciplinary research field.

III. Activities of the project

Here we will describe from three categories: activities as the project, activities in academic societies, and interim evaluation to the project.

A. *Activities as the project*

- 1st international conference on embodied-brain systems science (EmboSS 2016)
Date: May 8-10, 2016
Place: Tokyo
Contents: 2 day conference and 1 day evaluation meeting. Invited talks (Prof. Trevor Drew, Dr. Calogero M. Oddo, Prof. Paulus Walter). Presentation by the area organizer and principal investigators. Poster session by researchers.
- Lecture meeting and call-for-proposal meeting for subscribed research groups
Date: September 15, 2016
Place: Tokyo
Contents: Presentations by the area organizer and group leaders. Two presentations by area members
- 4th project meeting
Date：February 27 – March 1, 2017
Place: Kagoshima
Contents: Invited talk. Oral and poster presentations by area members. Discussion.

B. *Actuvities in academic societies*

- The 10th ICME International Conference on Complex Medical Engineering (CME 2016)
Date: August 4-6, 2016
Place: Tochigi
Contents: Organized session
- 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC 2016)
Date: August 16-20, 2016
Place: United States

Contents: Workshop , Three invited talks from oversea researchers. Presentations by area members. About 30 attendees.

- 10th Motor control research symposium

Date: September 1-3, 2016
Place: Tokyo
Contents: Sponsorship

- MHS 2016 (Micro-NanoMechatronics and Human Science)

Date : November 29, 2016
Place: Aichi
Contents: Organized session. Plenary talk by Prof. Ueda (Georgia Tech), Keynote talk by an area member

We have conducted new scheme this fiscal year for enhancing collaboration among trans-group members, they are, trans-group meetings: A (brain science) -02 (motor control) transdisciplinary meeting (member of group A, B02, C02 and other members attended) and C (rehabilitation medicine) – 01 (body consciousness) meeting (members of group C, A01,B01 and other members attended).

-A-02 meeting
Date : November 24-25, 2016
Place: Tokyo
Contents: oral/poster presentations and discussion

-C-01 meeting
Date: December 13-14, 2016
Place: Miyagi
Contents: presentation and discussion

C. *Interim evaluation*

The term of Grant-in-Aid for Scientific Research on Innovative Areas is five years. Interim evaluation is conducted three year after the start of the project, and final evaluation is conducted on the next year of the final year of the project [1]. This year is that of the interim evaluation. The evaluation is based on the discussion among member of the evaluation board with documents and presentation. The evaluation result of this area is A (In accordance with the purpose of the research area, the progress is just as expected). The concrete comments is shown in [3].

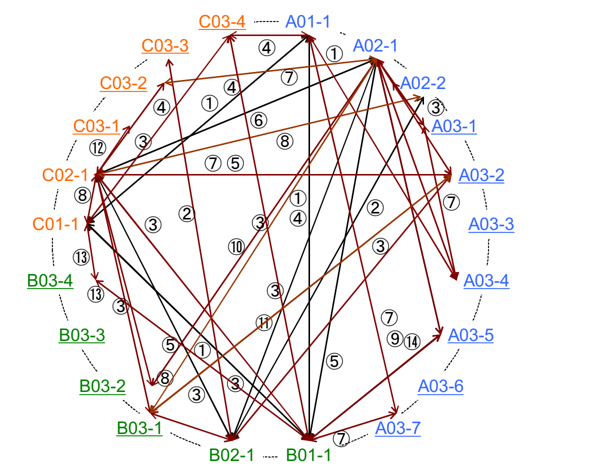

Fig. 1 Trans-area collaboration

IV. Collaboration among groups

In this area, we have promoted trans-group studies from the start of the area. At this moment, we can see many collaboration among area members, including those in subscribed research group members. The topics in collaboration are shown in Fig. 1. Here, meaning of the numbers in Fig. 1 is shown as follows: (1) sense of agency, (2) posture control, (3)muscle synergies, (4)sense of ownership, (5)upper-body movement, (6) dystonia, (7) brain imaging, (8) locomotion, (9) grasping, (10) artificial thumb, (11) soft touch, (12) crawling, (13) body schema, and (14) neural plasticity.

V. Activities of young researchers

We run the Associates of Young Researchers of Embodied-Brain Systems Science to develop interdisciplinary research methods and young members. Currently we have 44 members.

In this year, we held journal clubs, research symposiums, and tutorials, two times. We hosted organized sessions three times in academic conferences, and submitted a glossary of technical terms for an academic journal.

We held journal clubs in May and November. The speakers were Associate Prof. H. Tanaka (JAIST), Assistant Prof. A. Yozu (Univ. Tokyo), Associate Prof. A. Murata (Kindai Univ.) and Associate Prof. R. Chiba (Asahikawa Medical Univ.). We held research symposiums in August and December. The speakers were Dr. Giulia Cisotto (University of Padova), Assistant Prof. Y. Ouchida (Tohoku Univ.) and Dr. H. Abe (Konan Hospital). In January, we held a tutorial of theory and applications of signal processing. Speaker was Associate Prof. H. Tanaka (JAIST).

We hosted organized sessions in three conferences: SICE-LE 2016, SICE-SSI 2016, and SICE-DAS 2016. We issued glossary of this field and submitted it to Journal of the Society of Instrument and Control Engineers.

VI. Future plan

The plan in 2017fiscal year is shown as follows:

- July, 2017: 5th Area meeting (for area members only)
  Contents: discussion with new subscribed research group members
- October to December, 2017: 2nd symposium on embodied-brain systems science (for open)
- March, 2018: 5th Area meeting (for area members only)

References

[1] Interim and final evaluation for Grant-in-Aid for Scientific Research on Innovative Areas, http://www.mext.go.jp/a_menu/shinkou/hojyo/1381026.htm, in Japanese,

[2]List of research areas for interim evaluation in 2016, http://www.mext.go.jp/a_menu/shinkou/hojyo/1381028.htm in Japanese

[3] Report from area organizers for Interim and final evaluation for Grant-in-Aid for Scientific Research on Innovative Areas and comments from evaluation board, http://www.mext.go.jp/component/a_menu/science/detail/__icsFiles/afieldfile/2017/01/13/1381078_1_1_1.pdf, in Japanese.

Annual report of international activity support group

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I. AIM OF THE GROUP

The international activity support group is a planned research to support the international activities within the scientific research on innovative areas. The research program on embodied-brain systems science aims to realize model-based rehabilitation based on the concept of biomarkers and models of body representation in the brain. For this aim, the group sets up core-projects that integrate Group A (brain science), Group B (system engineering), and Group C (rehabilitation medicine), and promotes their fusion research as the international collaboration.

Specifically, two core-projects: "bodily self-consciousness core" and "synergy-based control core" are designed. The former is organized by 01 research projects group, which focuses on body consciousness and related symptom such as phantom limb/paralysis, while the latter is organized by 02 research projects group, which is investigating upper and lower limbs rehabilitation focusing on the mechanism of synergy-based control. Moreover, members of 03 research projects group (subscribed research projects) also participated in the both core-projects.

This group has three purposes; 1) to increase publication of international joint research through the activities promoting international joint research and building researcher network, 2) to feedback the outcomes of the international collaboration to the research program, and 3) to increase international visibility of the research program. Every year, the group calls for the proposal of international activities from researchers in the research program, and decides the activities to be supported in the following fiscal year based on the above criteria. After the end of the international activity, the group asks the accepted proposers not only to submit their activity report but also to present their outcomes to the members of the research program at the end of the year meeting.

II. SUPPORTED INTERNATIONAL ACTIVITIES IN FY2016

International activities supported by the grant in FY2016 are listed below.

1	Type: Invitation of outstanding researcher Applicant: A02-1 E.Naito, K.Amemiya Content: In July, the applicant invited Dr. Michel Thiebaut de Schotten (Institut du Cerveau et de la Moelle Epinière), who is an outstanding researcher in bodily self-consciousness core, and discussed with him about fMRI brain imaging methodology.
2	Type: Invitation of outstanding researcher Applicant: ：A01-1 Y.Ohki, C01-1 S.Izumi, and others Content: The applicants invited Dr. Max Ortiz Catalan (Chalmers University of Technology), who is an outstanding researcher in bodily self-consciousness core, and discussed with him about treatment methodology for phantom limb pain.
3	Type: Invitation of outstanding researcher Applicant: ：A03-7 Y. Murata, A01-1 H.Imamizu, B01-1 J.Izawa, and others Content: The applicants invited Dr. Nicolas Schweighofer (University of South California), who is an outstanding researcher in bodily self-consciousness core, and discussed with him about mathematical modeling of motor rehabilitation.
4	Type: Invitation of outstanding researcher Applicant: ：A02-1 E.Naito, and T.Ikegami Content: The applicants invited Dr. Flavia Filmon (Max Planck Institute for Human Development), who is an outstanding researcher in bodily self-consciousness core, and discussed with him about fMRI brain imaging methodology.
5	Type: Invitation of outstanding researcher Applicant: ：B01-1 T.Kondo Content: The applicants invited Dr. Yoshikatsu Hayashi (University of Reading), who is an outstanding researcher in bodily self-consciousness core, and discussed with him about BCI neurorehabilitation.
6	Type: Dispatch of young scientist Applicant: ：C03-2 K.Shima Content: The applicant dispatched a young scientist in synergy-based control core to Prof. P.G.Morasso's laboratory in Italian Institute Technology, and asked him to conduct international collaboration about posture control.
7	Type: Dispatch of young scientist Applicant: ：B02-1 J.Ota, A02-1 K.Seki, and others Content: The applicants dispatched six young scientists in synergy-based control core to Fondazione Santa Lucia, University of Messina, University of Padova, and Taormina. In each base, they held international workshop on posture and locomotion control.
8	Type: Invitation of outstanding researcher Applicant: ：B01-1 T.Kondo Content: ：In November, the applicant invited Prof. Jun Ueda (Georgia Institute of Technology), who is an outstanding researcher in robot rehabilitation, and asked him to give plenary talk at IEEE MHS 2016. The

	applicant and many researchers in the research program discussed with Prof. Ueda at the conference.
9	Type: Invitation of outstanding researcher Applicant: : A01-1 Y.Ohki, C01-1 S.Izumi, and others Content: In May, the applicants invited three outstanding researchers: Dr. Max Ortiz-Catalan (Chalmers University of Technology), Dr. Nicolas Schweighofer (University of Southern Calfornia), and Dr. Marco Santello (Arizona State University) to the international workshop in IEEE EMBC2016. Many researchers in the research program discussed with the invited researchers at the conference.
10	Type: Invitation of outstanding researcher Applicant: : C02-1 T.Hanakawa Content: The applicant invited Dr. Giulia Cisotto (University of Padova), who is an outstanding researcher in synergy-based control core, and discussed with her about writer's cramp (focal hand dystonia).
11	Type: Dispatch of young scientist Applicant: : A02-2 K.Takakusaki Content: The applicant dispatched a young scientist in synergy-based control core to Prof. Trevor Drew's laboratory in University of Montreal, and asked him to conduct international collaboration about posture control.

III. Future Perspective

In this year, the group supported 11 international activities within the research program. Through these activities, novel international collaboration research has begun, and international visibility of our research program increased.

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 in Group A

In research projects of Group A, we are aiming to elucidate neural substrates of body representations in the brain and to identify biomarkers that reflect changes in the body representations. Here, we have been focusing on three topics: (1) bodily awareness (sense of agency and body ownership), (2) muscle synergy control and (3) anticipatory posture adjustment, and we have been conducting manipulative (interventional) neuroscience to investigate how changes in the body representation cause changes in bodily perception and motor control vice versa. We are conducting experiments both in humans and in animals (monkeys, cats and rats). By using electrophysiological and neuroimaging techniques, we have been revealing how body representations change (1) when we manipulate participant'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 biomarkers that reflect changes in the body representations, 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 with research projects B and C, we help them to construct a model and also contribute to reveal a principle of neuro-rehabilitation. In this fiscal year, we have intensively facilitated inter-group and inter-project collaborations not only within Group A (A01, A02-1, A02-2 and seven A03 projects) but also between the projects across Groups A, B and C.

II. Members

We have promoted the inter-group and inter-project collaborations based on the following research team organization.

<u>Research project A01: Neural mechanisms inducing plasticity on body representations</u>
Principal Investigator: Hiroshi Imamizu (Univ of Tokyo). Funded Co-Investigator: Akira Murata (Kindai Univ), Yukari Ohki (Kyorin Univ), Takaki Maeda (Keio Univ). Other 10 Co-Investigators.

<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 14 Co-Investigators.

<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 (Kindai Univ), Other 7 Co-Investigator.

<u>Research project A03-1: Investigation of functional dynamics by hybrid techniques and real-time processing</u>
Principal Investigator: Kyousuke Kamata (Asahikawa Med Univ).

<u>Research project A03-2: Visualizing human body representations associated with hand movements with EEG</u>
Principal Investigator: Natsue Yoshimura (Tokyo Tech). Other 2 Co-Investigators.

<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.
Declination in this fiscal year

<u>Research project A03-4: Investigation of change of body representation using direct recoding and stimulus intervention of human brain</u>
Principal Investigator: Riki Matsumoto (Kyoto Univ). Other 5 Co-Investigators.

<u>Research project A03-5: Visualization and manipulation of change of internal body representation by peripheral nerve damage</u>
Principal Investigator: Mariko Miyata (Tokyo Women's Medical Univ). Other 3 Co-Investigators.

<u>Research project A03-6: Body and space in monkeys with hemi-spatial neglect</u>
Principal Investigator: Masatoshi Yoshida (NIPS). Other 1 Co-Investigator.

<u>Research project A03-7: Change in internal body representation associated with recovery of grasping ability after the brain stroke: A mokey model study</u>
Principal Investigator: Yumi Murata (AIST). Other 4 Co-Investigators.

III. Activities

A joint meeting across A01, A02, A03, B02 and C02 projects
Date and Time: November 24, 2016, 13:00-18:00. November

25, 2016, 9:00-13:00.
Place: Tokyo Metropolitan Institute of Medial Science (〒156-8506 2-1-6 Kami-kitazawa Setagaya Tokyo)
Local organizer: Shinji Kakehi
Attendees: 45 in total
Contents: 30 Group A members, 7 Group B members and 8 Group C members participated in this meeting. Main purpose of this meeting was to grasp and promote current status of inter-group and inter-project collaborations not only within Group A (A01, A02-1, A02-2 and seven A03 projects) but also between the projects across Groups A, B and C in particular for 02 projects. The present research situations and outcomes were reported by 22 members. We had active and fruitful discussions.
On the first day (Nov 24th), first, the program director, Jun Ota reported about the interim evaluation for entire projects of Embodied-Brain Systems Science held on Oct 5th. After this report, we started the following four sessions.

1. Body representations in human cerebral cortex, chaired by Hiroshi Imamizu (A01: Univ Tokyo) Presenters: Ryu Oohata (A01: Univ Tokyo) and Eiichi Naito (A02-1: NICT)
2. Body representations for postural and motor control, chaired by Kaoru Takakusaki (A02-2: Asahikawa Med Univ) Presenters: Katsumi Nakajima, Yasuo Higurashi (A02-2: Kindai Univ) and Kaoru Takakusaki (A02-2: Asahikawa Med Univ)
3. From neural activity to body representations, chaired by Takashi Hanakawa (C02: NCNP) Presenters: Saeka Tomatsu (A02-1: NCNP), Kyosuke Kamata (A03-1: Asahikawa Med Univ), Riki Matsumoto (A03-4: Kyoto Univ) and Kei Mochizuki (A01: Kindai Univ)
4. Compensation of body representations after nerve and brain damages, chaired by Shinji Kakehi (A02-1: Tokyo Metropolitan Institute) Presenters: Masatoshi Yoshida (A03-6: NIPS), Yumi Murata (A03-7: AIST) and Hironobu Ozaki (A03-5: Tokyo Women's Medical Univ)

On the second day (Nov 25th), we had the following three more sessions.

5. The cerebellum and its related functions, chaired by Shinji Kakehi (A02-1: Tokyo Metropolitan Institute) Presenters: Kahori Kita (C02: Chiba Univ), Tetsuro Funato (B02: UEC Tokyo) and Takahiro Ishikawa (A02-1: Tokyo Metropolitan Institute)
6. Neuro-rehabilitation based on sensory manipulations, chaired by Akira Murata (A01: Kindai Univ) Presenters: Arito Yozu (C02: Univ Tokyo), Dai Oowaki (C02: Tohoku Univ) and Masao Sugi (C02: UEC Tokyo)
7. Identification of muscle synergy and its modelling, chaired by Katsumi Nakajima (A02-2: Kindai Univ) Presenters: Shinya Aoi (B02: Kyoto Univ), Ryusuke Chiba (B02: Asahikawa Med Univ) and Natsue Yoshimura (A03-2: Tokyo Tech)

In addition to these oral sessions, we had poster sessions. We discussed and exchanged opinions and views in front of the posters mainly during coffee break periods.

Finally

The interim evaluation for entire projects of Embodied-Brain Systems Science was done on Oct 5th in this fiscal year. We got score A in this evaluation. In this fiscal year, we have made a success to increase the number of inter-group and inter-project collaborations and to enhance cross-project researches. We reported details of 2016 research outcomes and activities for each research project separately. Overall, when compared to the initial phase of this Embodied-Brain Systems Science project, we have revealed many new aspects about neural substrates of body representations and promoted the understanding of the body representations in the brain. In the inter-project collaborations across A02, B02 and C02, we have started trials in some rehabilitation hospitals in order to develop a new rehabilitation method based on feedback about a current status of muscle synergy of a patient. Furthermore, in the manipulative sensory rehabilitation, we have confirmed the effectiveness of auditory feedback that can replace somatosensory feedback and developed this basic system.

Annual report of research project A01-1

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Abstract—**Our research project mainly examines the bodily self-consciousness, which is a perceptual expression of the embodied brain system. More specifically, we aim 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 findings, we develop methods to make intervention and manipulation on the bodily self-consciousness. In this fiscal year, we have accomplished to refine decoding techniques for the manipulation, and to analyze EEG signals for clinical use. In addition, we succeeded in finding neuronal activities reflecting the corollary discharge in monkey studies, which is a clue to neuronal networks underlying the bodily self-consciousness.**

I. Introduction

Healthy humans feel the bodily self-consciousness, which includes senses of agency (SoA; "I am moving this body") and body ownership (SoO; "This is my body"). Our research project mainly examines the bodily self-consciousness, which is a perceptual expression of the embodied brain system.

II. Aim of the Project

We aim to identify neural correlates of SoA and SoO. Based on the identified correlates, we investigate neural mechanisms in which changes in bodily self-consciousness lead to long-term changes in body representations in the brain. Furthermore, we establish methods to make intervention and manipulation on the bodily self-consciousness by using the findings. Finally, we will develop effective methods for promoting adaptive changes in the body representation, to reflect body states properly. We take multiple approaches to these aims, including behavioral and brain-activity recording experiments with normal human subjects and schizophrenic patients, decoding methods of neural information, and electrophysiological experiments on monkeys.

III. Research Topics

Below, we will specifically describe and outline our four accomplishments in this year.

A. *Decoding bodily self-consciousness as a basis for manipualtion of bodily self-conciousness*

A group of the principal investigator developed basic methods for extracting bodily self-consciousness from brain activity by using decoding methods.

1) <u>Decoding attribution of movements to self or others</u>: Since the last fiscal year, they have been involved in delpoment of methods for decoding self or other attribution of movements, which is basis for SoA. In our experiments, human 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. The research group constructed a decoder that can predict the rating from regional brain activity. In this fiscal year, we increased number of subjects and reliability of our mehtods. Moreover, they investigated relationship bewteen prediciton error of movement and sefl-attribution. Sepcifically, they investigated brain regions where prediciton error can be decoded. As a result, such region is only a small part of regions where the attribution can be decoded. This means that the prediction error is importnat but not decisive information for the movement attibution, and that it is important to understand intermediate processes between prediction error and conscious attribution of movements. Several articles on psychophysical studies related to this experiment were published in international journals [1, 2]. They also succeeded in decoding internal models of tools independent of effectors (hands) as a development of brain signal decoders [3].

2) <u>Predition of reaction time from MEG brain activity in a signle trial</u>: For onlie-manipulation of bodiliy self-consciouness, it is necessary to extract brain information from neuronal activity with high temporal resolusion. We succeded in development of a technique that predictis reaction time from pre-movement MEG brain activiy and published it in international journal [4]

B. *Mechanisms of body representation in the human brain and clinical applications*

Yukari Ohki (funded co-investigator, Kyorin University) and her colleagues are approaching to identify neural substrates relating to SoO in humans. In the past years, they have already revealed that multiple brain areas are related to SoO [5]. In this year, they performed experiments described below.

1) They made 64-channel EEG recordings, to clarify neural basis for SoO. For that purpose, they performed a modified rubber hand illusion paradigm, which they have developed to induce the rubber hand illusion by short-term stimulation. To compare brain activities with and without illusion, they performed the event-related spectrum perturbation analysis, and detected brain areas that show differences between the two conditions. Especially, there are differences around bilateral sensori-motor areas in an α range, and around right parietal cortex in θ and β ranges.

2) They investigated whether movement-related brain activities can be induced by observing other's hand movements, if subjects feel SoO to the hand. For that purpose, they brushed invisible subjects' and visible other's hands simultaneously or alternatively. Subjects reported SoO to the other's hand only during the simultaneous condition. When subjects observed the hand movements, their hand was sometimes moved

involuntarily and μ suppression was observed in EEG, which was stronger and longer under the simultaneous condition. Strength of the μ suppression was correlated with the strength of SoO. This study was done with Shimada et al (C03-4).

3) They collaborate with members of C01 research group, to develop a new rehabilitation method by using SIGVerse, which is a cloud-based virtual reality (VR) system made by Inamura. In the system, subjects manipulated an avatar whose arm shows different length. After the manipulation, subjects feel SoO to the avatar, and indicate different proprioceptive drift, depending on the length of avatar's arm. Thus, SIGVerse can be useful for immersive rehabilitation therapy.

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. It has been thought that corollary discharge is one of important factor for body consciousness or body schema [6]. In this year, Murata's group has tried to investigate sensory attenuation which reflect influence of corollary discharge in the somatosensory cortex during voluntary movement). In the experiment, the monkey applied tactile stimulations to his left hand with a brush controlled by a lever manipulated with the right hand. The brush followed the lever movement synchronously or with temporal delays. Furthermore, the passive tactile stimulation without any lever movement was also introduced. Single units were recorded from somatosensory cortex and area 5 of one monkey. It was found that certain proportion of neurons showed less activity during synchronous tactile stimulation comparing with delay condition, consistent with sensory attenuation for predicted sensory feedback. Furthermore, there were other neurons showing weaker activation to the stimuli with large delays comparing with synchronous stimulation, possibly coding the accuracy of sensory prediction by corollary discharge. These results suggest that the predicted and actual sensory feedbacks are compared and interact with each other in relatively early stages of cortical somatosensory processing. It was also found that some neurons area 5 showed activity corresponded with lever movement, suggesting proprioceptive input from right hand or corollary discharge from motor area. It is necessary more precise study.

D. Methodology for studying aberrant sense of agency in schizophrenia, and its underlying pathophysiology

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 neural basis of SoA thorough behavioral and physiological studies.

1) They applied for an international patent for Keio method based on PCT: Patent Cooperation Treaty [7].

2) By using a modified version of Keio method, they found that strong intentional effort promotes judgments of self-attribution when the causal relationship between actions and effects is uncertain. This study may contribute to the understanding of the underlying mechanisms of SoA [8].

3) They demonstrated that the state of anticipation for the feedback affected the readiness potential(RP) onset and amplitude in the ERP study. Earlier and larger RP was observed when the feedback-anticipation was inconsistent in relative with the consistent condition.

4) They have started a post-surgical operation study on SoA. The influence of resection around insula or inferior parietal lobe could provide critical roles of those areas for SoA. Moreover, they have also introduced a stereo-EEG in order to clarify the neuro-physiological roles of those area.

5) They measured brain activity in schizophrenic patients and found that decreased functional connectivity between supra-marginal gyrus in the inferior parietal lobe and the caudate nucleus.

6) They provide the evidence that subjects employ a Bayesian update as the reinforce learning algorithm in the Keio method, and hypothesized that aberrant SoA in schizophrenia could be due to malfunction of the learning processes.

IV. Future Perspective

In this fiscal year, we have accomplished to refine decoding techniques, intervention and manipulation on the bodily self-consciousness. We have also identified multiple sources in EEG activities, reflecting the bodily self-consciousness. We are now collaborating with the rehabilitation group (C01), to apply the EEG signals in clinical use combined with VR. Even in terms of basic science, we have obtained a clue for how the brain forms the bodily self-consciousness. Our accomplishments make it possible to approach the bodily self-consciousness and embodied brain system from cross-sectional and multifaceted perspectives. In the coming years, we will develop methods to interfere with and manipulate the bodily self-consciousness, based on the achievements.

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Annual report of research project A02-1

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***Abstract*—In the FY2016, we established 1) Animal model and optogenetic tool to explore embodied brain, 2) *Mechanism underlying improvement of cerebellar ataxia with induced plasticity, and 3)* body representations associated with hand/finger movements.**

I. INTRODUCTION

Our research group is based on three major Neuroscience hubs in Japan (NCNP, NICT, TMIMS) and includes 18 scientists. Through frequent collaboration and discussion, we would like to find how the embodied brain controls 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 adaptations of the central nervous system to this physically modified body and its underlying mechanisms.

Seki's group (NCNP) conducted experiments using rats and monkeys to establish two animal models that allow us to examine this mechanism. Two lines of experiments are on-going within this group.

First, we aimed to establish a tendon-transfer model using the forearm muscles of macaque monkeys and evaluate the adaptation of their neural control by means of behaviour and EMG (electromyographic) measurement. We trained a monkey to perform a simple grasping task (power-and precision grip). Behavioural observations as well as chronic EMG recordings from different forelimb muscles were used to evaluate the performance of the grasping task. After this training, we surgically cut the tendon of one extrinsic finger flexor (Flexor digitorum profundus, FDP), and one wrist-elbow flexor (Brachioradialis, BRD), both at wrist level. The distal end of BRD was then joined with the FDP tendon. We found that the monkey fully recovered, fed himself at day 1 post-surgery and performed a power and precision grip with its modified arm using BRD to effectively flex the digits within a few weeks. Furthermore, movement and hold times recovered within weeks. And lastly, recorded EMG's revealed continuous changes in the BRD activity profile stabilizing after some weeks and resembling roughly the activity profile of an extrinsic finger flexor muscle.

In subsequent experiments an actual tendon cross-union was performed between EDC (Extensor digitorum Communis) & FDS (Flexor digitorum superficialis) in two monkeys one of which performing in a flexion-extension task rather than a grasping task. We can show that the temporal activity profiles of FDS and EDC continuously changed over time eventually reaching a new equilibrium with FDS peaking earlier and EDC later with respect to the pre-surgery activity profile. We furthermore found first evidence for an early and late adaptation period in showing that the muscle activity first changed rather drastically but eventually adopts a new equilibrium lying between the initial 'extreme state' after surgery and its original activity pattern.

Second, we are establishing a method to manipulate somatosensory feedback to the CNS in alert animals and examine how the bodily representation in the CNS may be affected. For this purpose we investigated the efficacy of gene transfer by AAV6 and 9 into small- and large diameter DRG cells in the adult common marmoset. We injected the AAV6 or AAV9 containing green fluorescent protein gene (GFP) into the left sciatic nerve (n=4 for each) using glass capillary under anesthesia. Four weeks after the injection, each animal was sacrificed and DRG (L5-7) was extracted for histological analysis. For quantification of transduction efficiency, GFP-positive neurons were defined as cells with the fluorescence intensity greater than average background fluorescence plus 2 standard deviations of neurons in a section from a naïve tissue with no viral vector injection. Every fourth DRG section was selected from consecutive serial sections (3 to 6 sections for each DRG), and in each selected section, the number of GFP labeled cells was counted and transduction efficiency was expressed as the percentage of total neuronal profiles revealed by NewN staining. Overall efficacy of gene delivery was not different by AAV 6 or 9. For example, GFP-positive cells were found in 10.5 % (AAV6) or 12.3 % (AAV9) of DRG neurons. However, the efficacy of transduction into small, medium and large sized DRG cells were remarkably different between AAV6 and AAV9. For example, the distribution of the GFP-positive cells in the small, medium, and large-sized DRG cells was 30.8, 53.0, and 16.1% for AAV6, but 8.7, 48.5, and 42.6% for the AAV9.

B. Improvement of cerebellar ataxia with induced plasiticity

Climbing fiber (CF) inputs to the cerebellar cortex are known to induce LTD in parallel fiber (PF)-Purkinje cell synapses and LTP in PF-Basket cell synapses (Jörntell & Ekerot, 2002; Ishikawa et al. PLoS ONE, 2014)[2]. On the other hand, CF activities are rather low (~1Hz) and its modulation is small and unreliable even in awake behaving animals. Therefore, in a physiological condition, the gain of CF-induced plasticity in the cerebellum is estimated to be rather small. Our recent surprising observation is that it is possible to activate CFs and induce complex spikes (CSs) in Purkinje cells almost securely (~100%) by simply applying electrical stimulation to peripheral nerves (Fig. 1). This observation hinted us an idea to induce plastic changes in the cerebellar neuron circuitry with electrical stimulation. In fact, in our previous collaboration with Naito's group (Uehara et al. PLoS ONE, 2011) we observed a stimulus-induced stabilizing effect for finger movements that lasted days in healthy control subjects. Indeed, in a trial experiment, we observed that electrical stimulation to the axillary nerve showed a significant stabilizing effect for whole arm movements in a patient with spinocerebellar degeneration. We are currently planning a larger clinical experiment.

C. Body representations that generates variability and abnormality in human hand/finger movements

Naito's (CiNet/NICT) group conducted fMRI experiments in human participants. Elaborate hand/finger movements require muscle synergy control. In this fiscal year, we mainly investigated (1) neuronal substrates that generate variability in well-trained hand/finger movements and (2) maladaptive changes of hand/finger representations in the motor cortex in musician's dystonic patients (pianists). Performance of a hand/finger motor task fluctuates trial by trial even when people well-trained the task. In the present study, using the

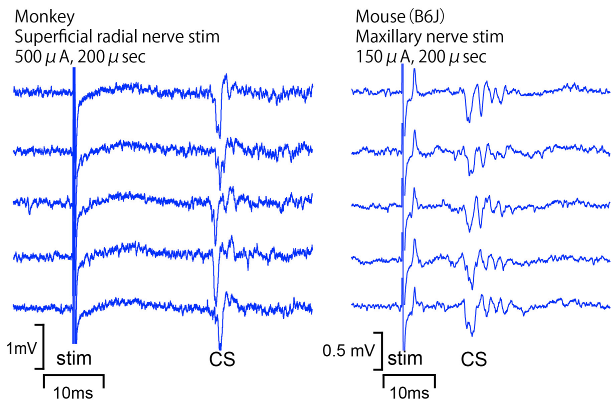

Fig.1. Induced CSs in monkey and mouse

very well-trained motor task, we showed that fluctuation of brain activity in a broader range of frontoparietal cortices (does not belong to motor network) is associated with variability of the task performance. We further showed that the variability becomes even greater when we augmented the brain activity in the frontoparietal network by using transcranial direct current stimulation, which indicates the caudal relationship between the frontoparietal activity and the variability in performance [1]. We also examined maladaptive changes of hand/finger representations in the motor cortex of dystonic pianists, in collaboration with C02 project. Here we analyzed hand\finger representations in the motor and somatosensory cortices by using an fMRI decoding technique (iSLR) developed by our group (Hirose et al. 2015). We got a series of decoding results indicating that each finger representation considerably overlaps spatially in the motor cortex of the dystonic pianists when compared with normal pianists (left panel in Fig. 2), and that such considerable overlap was not robust in the somatosensory cortex (right panel in Fig. 2). This indicates that maladaptive changes of hand/finger representations in dystonic pianists mainly occur in the motor cortex. Now we are preparing a manuscript.

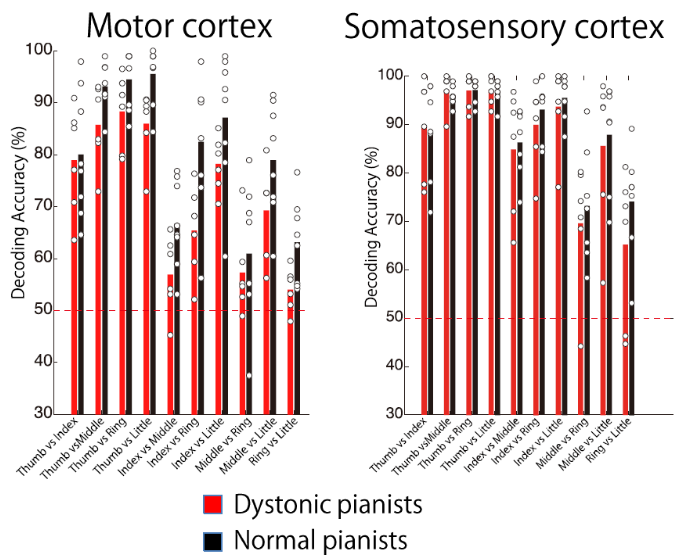

Fig.2 Decoding accuracy (vertical) when we identified a finger used from each pair of fingers (horizontal) based on the activity in the motor cortex (left) and in the somatosensory cortex (right) during finger movements. In every pair of fingers, dystonic pianists showed lower accuracy in the motor cortex (left), which was not robust in the somatosensory cortex (right), indicating that each finger representation considerably overlaps spatially in the motor cortex of the dystonic pianists as compared to normal pianists.

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

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***Abstract* – Voluntary movements associate with postural control that depends on cognitive information of one's body interacting with surrounding space. The cognitive information is required to produce body schema, which is further utilized to maintain upright posture against to the gravitational force and to produce motor programs of anticipatory postural adjustment (APA) and the goal-directed movements. The motor programs are then converted to synergistic contractions of postural muscles as well as those for purposeful movements. The present project is designed to explore cortical and subcortical mechanisms underlying these processes. In this year (2016), following two studies were performed in animals. First, firing property of neurons in the supplementary motor area (SMA) was examined in relation to the changes in kinematics and dynamics during alteration of posture-gait strategies from quadrupedal locomotion (QL) to bipedal locomotion (BL) in monkeys. Emphasis can be placed in the role of elector spine muscles, one of the major antigravity muscles in the trunk, in BL with upright posture. Firing property of most SMA neurons well reflected EMG patterns of trunk-limb muscles, particularly elector spine muscles, during locomotion, indicating that the SMA plays critical role for generating muscle synergies during posture-gait control. In the second study, kinematics and dynamics during forelimb reaching in cats. It was observed that center of vertical pressure (CVP) at reaching to the target was precedingly determined when forelimb was lifted from the floor, indicating that the APA is achieved by the motor program including forward-model of posture. All these results support our hypothesis that the cognitive postural control process generates synergistic contractions of postural muscles so that purposeful action can be achieved.**

I. Introduction

Standing and walking, reaching arm and grasping the door knob, and opening the door. Such daily behaviors are affected in patients with damages in the central nervous system due to cerebrovascular disorders and degenerative disorders including Parkinson's disease and Alzheimer's disease. One of serious problems in these patients is falling that is mostly ascribed to disturbance of postural control. Thorough understanding the neuronal mechanisms underlying postural control is therefore essential for developing strategy to regain or functional recover these motor functions.

II. Aim of the Group

Because body balance is altered by movements, postural control that precedes the purposeful action should be achieved so that falling can be prevented. Such a feed-forward postural control may require motor programs which anticipate interactions between one's body and surroundings caused by the movements [1]. The motor program may essentially fulfill two purposes such as anticipatory postural adjustment (APA) and upright posture against the gravitational force [2-3].

However, knowledge is still insufficient to develop strategy for recovery of motor function after brain damages. Particularly, critical questions as follows are remained unsolved. First, how frontoparietal network constructs motor programs based on cognitive information of body-space interaction. Second, what descending pathways from the cerebral cortex to spinal cord achieve APA and upright posture. Therefore, the aim of this research project (A02-2) is to understand cortical and subcortical mechanisms of such a cognitive postural control.

III. Research Topics

To understand the mechanisms of how motor programs achieve postural control associating with voluntary movements, following studies using animals were performed in this year (2016). First, firing property of neurons in the supplementary motor area (SMA) was examined in relation to the changes in kinematics and dynamics during posture-gait alteration from quadrupedal (QL) to biped locomotion (BL) in unrestrained Japanese monkeys. Second, mechanisms of APA following forelimb reaching movements was examined in cat with unrestrained conditions. Based on findings in these studies, role of bodily information in the modification of motor programs for postural control during voluntary movements is discussed.

1. Role of SMA in the control of posture-gait strategy during locomotion of the monkey

(1) Alteration of posture-gait synergy following the changes in posture-gait patterns from QL to BL.

Changes in the body-axis angle and EMG activities of trunk-limb muscles in the monkey were examined during treadmill locomotion by quadruped and biped. During QL, EMG activity of the elector spine muscles was low, because body weight was dispersed to four limbs. However, it became prominent during BL, particularly the period of stance phases of each hindlimb. Accordingly, control of elector spine muscles can be important to achieve BL with upright posture.

(2) Firing property of SMA neurons during QL and BL.

We reported last year that SMA neurons became more active during BL than QL, and some population of neurons displayed burst activity preceding the transition from QL to BL and vice versa. In this year, we further found populations of neurons that exhibited transient burst activity specific to either QL (Fig.1Aa) or BL (Fig.1Ab). Some population of neurons exhibited biphasic activities (both swing and stance phases) during BL (Fig.1B). Firing property of this neuron quite resembled to EMG activities of elector spine muscles. These findings suggest the presence of motor programs of various posture-gait synergies in the SMA. Because there are massive projections from the SMA to the pontomedullary reticular formation in addition to spinal cord [3], the motor programs in the SMA may be translated to motor command signals which produce various types of posture-gait patterns via the cortico-spinal and cortico-reticulospinal pathways.

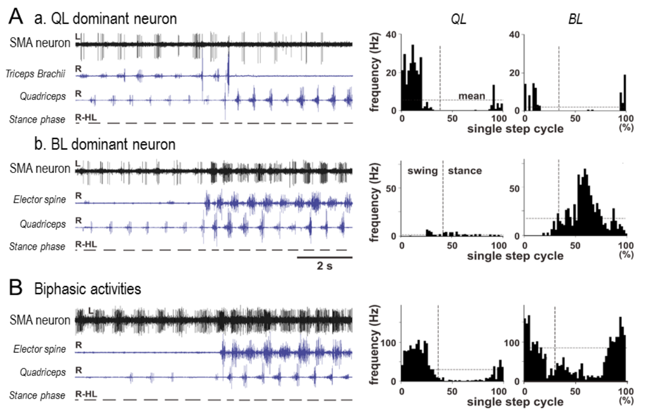

Fig. 1. Firing properties of SMA neurons and EMG activities during treadmill locomotion of unrestrained monkey

A. (a) Polygraphic recordings of the activity of QL-specific SMA neuron (top trace), EMG activities of triceps brachii (2nd trace) and quadriceps (3rd trace), and the periods of stance phase. Firing of the SMA neuron was reduced in accordance with EMG activities of triceps brachii by the transition from QL to BL. Histograms indicate that firing of this neuron was obvious during swing phase of QL (left) but it was greatly reduced during BL (right). (b) Polygraphic recordings of BL-specific SMA neuron. Arrangement of traces are moslty the same as (a) other than 2nd trace which shows EMG activity of elector spine muscles. Although the SMA neuron was silent during QL, it was active during BL. Histograms indicate obvious firing during stance phase of BL. B. This neuron was active both stance and swing phases during BL as can be seen in polygraphic recording and histograms.

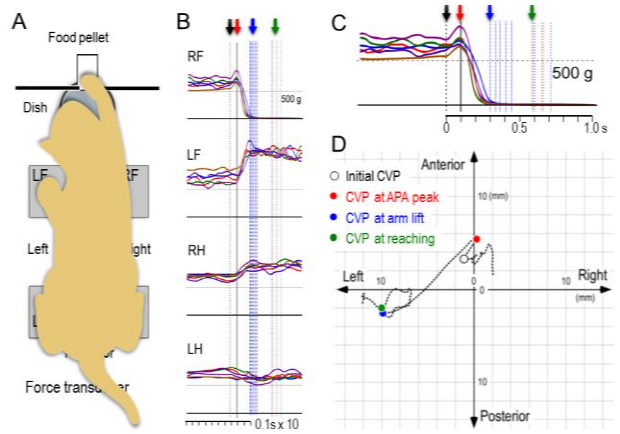

Fig. 2. Postural control during forelimb reaching movement

A. Schematic illustration of experiments. B. Changes in GRF exerted in each limb. Traces from 6 trials were superimposed. Black and red arrows indicate the onset and peal of APA. Blue and green arrows indicates the timing of arm lift from the floor and that of achivement of reaching. RF and LF; right and left forelimbs, RH and LH; right and left hindlimbs. C. GRF exerted in RF with large scales. D. Representative changes in CVP following reaching movement on the horizontal plane. Open and red circles are CVP positions of the onset and peak of APA, respectively. Blue and green circles indicate CVP positions at arm lift from the floor and at achievement of reaching, respectively. See text for further explanations.

2. **Postural control during forelimb reaching in the cat**

Postural control during forelimb reaching was examined by recording cat movements combined with ground reactive force (GRF) exerted in each limb (Fig.2A). An increase in the GRF exerted in the right forelimb (RF) was a sign of stating a series of reaching movement (an arrow in Fig.2B). The indicates the onset of APA. Then the GRF of RF was declined due to lift of the RF together with an increase in GRF of left forelimb (LF; Fig.2B). The onset of APA preceded to the onset of lifting the limb by 0.05-0.1 s. Approximately 0.3 s and 0.7 s after APA, the cat lifted forelimb and reached to the target (blue and green arrows in Fig.2B), respectively. Shift of the center of vertical pressure (CVP), which reflects position of center of gravity on horizontal plane, was calculated by the changes in GRF [5]. It was observed that the direction of CVP change following reaching movement (a green circle in Fig.2D) was opposite to that induced by APA (a red circle). Therefore, APA may code for direction of postural changes due to reaching movements. Moreover, the position of CVP induced by reaching (a green circle) was mostly equal to the CVP position which was induced by lifting the forelimb (a blue circle), indicating that APA was already accomplished until the cat lifted forelimb. Because the above characteristics was observed when spatial position of the target was altered, cognitive information of body-space interaction can be utilized to construct forward-model of posture and movements so that APA can achieved.

IV. Discussion & Future Perspective

Studies in monkey locomotion provided important findings that firing of SMA neurons represented activities of antigravity muscles such as elector spine and quadriceps muscles during BL with upright posture. A recent study using simulation model of monkey locomotion by Aoi's group (B02) further revealed the importance of the role of muscle synergy of antigravity muscles in alteration of posture-gait strategies from QP to BP [6]. Consequently, our tentative conclusion is that the motor program in the SMA may be engaged to synergistic control of posture-gait strategies against gravitational circum-stance. Results from the cat experiments showing that APA is a process of constructing forward model of posture associating with goal-directed action may greatly attribute to the advance of understanding cognitive postural control mechanisms. To facilitate these considerations, next stage of our studies aims to elucidate how cognitive body-space information is constructed by integrating multi-sensory signals which converges to the parieto-temporal cortices so that appropriate forward models of posture and movements can be constructed, and to explore what descending pathways attribute to APA.

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Annual report of research project A03-1

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***Abstract*—We have developed a novel functional mapping technique, which analyzes and visualizes induced high Gamma activity (HGA) by different tasks in real-time. This technique was utilized for brain tumor resection during awake craniotomy, skipping electrocotical stimulation (ECS), which was named as passive mapping. The sensitivity and specificity of passive HGA mapping were approximately 85%. In addition, we combined cortico-cortical evoked potentials (CCEP) with passive HGA mapping by passive story listening tasks to detect the temporal language area. Cortical stimulation with 1Hz to the identified language area demonstrated CCEPs on the frontal language area, which should have functional connections (Super-passive mapping). We applied passive HGA mapping to a case with intractable epilepsy due to focal cortical dysplasia. The case showed abnormal functional reorganization, that was inferior shift of hand/leg motor and expressive language functions. This was the first case, who proved functional reorganization by electrophysiological technique. Furthermore, we investigated four epilepsy cases, who had subdural grids on the temporal base and found functional localization related to visual perception of words, faces and non-words. We created each decoder depending on the stimuli by combining Common Spatial Pattern and Linear Discrimination Analysis, which enabled us to achieve decoding with high accuracy of more than 95% in real-time at bedside.**

Introduction

Rapid biosignal processing is an important tool to learn about motor and language processing in the human brain. To perform most tasks, different brain areas work in tandem with each other, resulting in complex functional networks. To visualize the functional dynamics across the whole brain, we plan to record electrical signals directly from the brain's surface. This approach, which is called electrocorticography (ECoG), is often used in neurosurgery for patients who need subdural grid implantation for diagnostic purposes and awake craniotomy. At bedside and in operation rooms, we performed real-time data processing of ECoG with motor- and language-related tasks. It was possible to visualize the functional dynamics of each patient and thus learn more about brain functions and pathology than conventional methods alone. In addition, we applied common spatial patterns (CSP) and linear discrimination analysis (LDA) to decode brain functions of visual perception. The classifiers with CSP and LDA perfectly discriminate the ECoG induced by visual stimuli such as "word", "face" and "blank"[1 3]

I Research Topics

A: Passive Mapping: In total, 22 patients (9 with epilepsy and 13 who underwent awake craniotomy) participated in this study. We recorded ECoG during hand motor and language tasks using subdural grids and obtained HGA (60–170 Hz) maps in real time. The patients underwent electrocortical stimulation (ECS) mapping to validate the suspected functional locations on HGA mapping. The sensitivity and specificity for the language area were 86.9% ± 21.9% and 87.6% ± 6.7%, respectively in the epilepsy group and 90.1% ± 11.2% and 90.0% ± 4.2%, respectively in the awake craniotomy group.

Figure 1: Passive mapping at bad-side

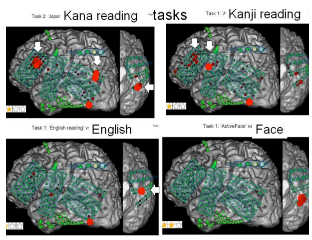
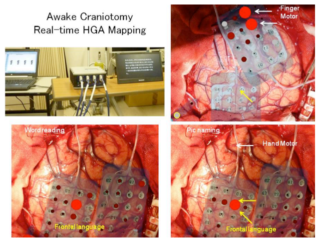


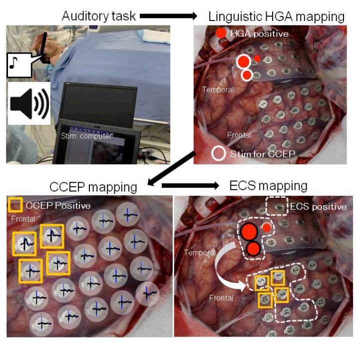
Figure 2: Passive mapping for awake craniotomy



Most HGA-positive areas were consistent with ECS positive regions in both the awake craniotomy and epilepsy groups and there were no statistical differences between two groups[2].

B Super-passive mapping: Five patients, each underwent resection of lesions harboring the language areas by "Super-passive" mapping. We performed functional localization of the receptive language area, using real-time HGA mapping with passive listening to linguistic sounds. Furthermore, single electric pulses were delivered to the identified receptive temporal language area to detect cortico-cortical evoked potentials (CCEP) on the frontal lobe. Linguistic HGA mapping quickly identified the language area on the temporal lobe. The combination of linguistic HGA and frontal CCEP (Fig.3) demonstrate language centers without any patient cooperation or effort. In this small case series, the sensitivity and specificity were 93.8% and 89%, respectively[3].

Figure 3: Super-passive mapping, demonstrating the temporal and frontal language areas by HGA and CCEP recording The patients under anesthesia did not need any cooperation or attention to stimuli.



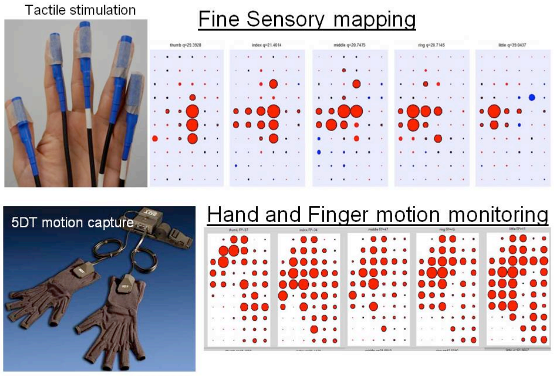
C Identification of Normal and Pathological Representations of Motor/Language Functions by Passive

Mapping.

We implanted subdual grids which covered primary motor / sensory areas in four patients and made precise functional mapping by motion-capture devices and tactile stimulations. We confirmed the functional representations by ECS and found high reliability of the passive mapping (Fig, 4).

Figure 4: Motor-sensory HGA mapping

In a pathology case, we investigated a 27 year-old patient suffering from intractable epilepsy due to focal cortical dysplasia (FCD: congenital disease). He suffered from frequent seizure and moderate right hemiparesis. MRI demonstrated the lesion just in the primary hand / leg motor areas. .Since ECS always evoked seizures, it did not work for mapping. Passive mapping clearly delineated HGA induced by hand-leg motor and word-reading and picture naming tasks and showed inferior shift of HGA accumulation. Passive mapping suggested that eloquent functions (red bubbles) and the lesion (blue circle) were separated due in the pathological condition. In addition, there was no HGA accumulation directly on the primary hand / leg areas. On the basis of passive mapping, we determine the resection border between FCD and shifted eloquent functional areas (Fig.5) . We resected the lesion including upper parts of motor and sensory cortices. and finally reached the midline (falx).The patient became seizure free with no neurological deteriolation.



This is the first case, who showed abnormal functional representations, which were confirmed by electrophysiological technique.

Figure 5: FCD and passive HGA mapping

We investigated four cases with intractable epilepsy and implanted subdural grids, which covered temporal base. In general, temporal base including fusiform and interior temporal gyri play major roles on visual perception. We did passive mapping with presentation of words, faces and non-words and black. Passive mapping showed 3-6 channels depending on visual stimuli (figure 6). We used CSP and selected the best 2 and worst 2 patterns of generated 40 CSP and achieve classification using LDA. Cases with grids in the right hemisphere showed high decoding accuracy for all visual stimuli. After the decoding training, we created real-time LDA classifiers, which perfectly classified face-and word-ECoG and showed the decoding results on the screen. Decoding for perception might have potentials to contribute to development of communication-BMI

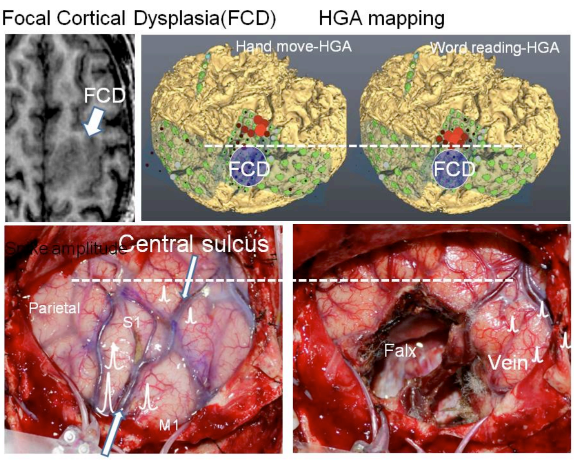
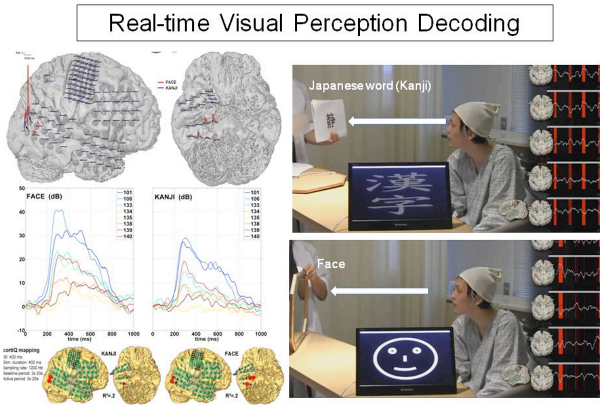


Figure 6 HGA mapping with visual stimuli and real-time decoding of visual stimuli by ECoG in real world.



I. Future Perspective

Passive mapping (Real-time HGA analysis) allowed simple and rapid detection of motor and language functional areas. ECoG with different visual stimuli were perfectly classified and apply this technique in three dimensional real world. For future studies, high resolution grids and high performance computers and sophisticated decoding programs would be invented and developed in a few years. In addition, real-time decoding and functional feedback would contribute to neuro-modulation and rehabilitation.

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Annual report for research project A03-2

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***Abstract*—The aim of this research project is to visualize neural signaling and muscle synergies during hand and foot movements using non-invasive recording methods. This technique could contribute to rehabilitation programs by allowing for visualization of changes over time in neural signaling and muscle synergy organization following short and long-term motor learning. In academic year 2016, through inter-group and international collaborations, we focused on finger movements which we found to be suitable for synergy analysis. Using electroencephalography (EEG) and electromyography (EMG) signals during finger movement tasks, we performed task decoding analysis based on EEG signals. We are currently working to establish a signal reconstruction method for finger muscle activity. For the finger muscle activity reconstruction, we are collaborating with the University of California, San Diego and are developing an MRI analysis toolbox, which we plan to publish as open source software.**

I. Introduction

The project representative and colleagues succeeded in reconstructing two muscle activity signals relating to wrist flexion and extension by estimating signals of EEG cortical current sources that were equidistantly distributed over the surface of the cortex [1]. We expect that this technique will allow us to identify neural representations of muscle synergies by associating brain activity signals with EMG signals.

II. Aim of the Group

Using EEG and functional magnetic resonance imaging (fMRI), we are investigating and aim to visualize neural representations of hand and foot movements and their relationships to muscle synergies. This academic year, after considering a variety of movements, complexities of muscle positions, and associated activities, we found finger movements to be suitable for our synergy analysis.

III. Research Topics

A. Analyses of EEG/EMG signals during finger movement tasks — an international collaboration with SCCN

Through an international collaboration with the Swartz Center for Computational Neuroscience (SCCN) at the University of California, San Diego, we recorded 128-channel EEG and 98-channel EMG signals simultaneously during finger movement tasks. Subjects were instructed to move a PC cursor to one of 8 targets on a PC screen using a trackpad with the index finger. EEG and EMG signals were recorded using Biosemi Active Two System with a sampling frequency of 2048 Hz. EMG was recorded by covering the arm with elastic bands which allowed equidistant positioning of the electrodes (Fig. 1).

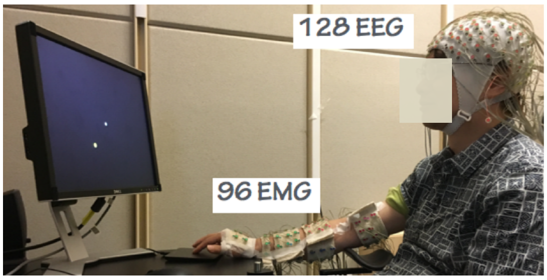
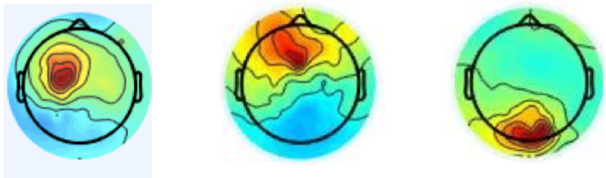


Fig. 1. Experimental setup



M1, RV: 5.24 SMA, RV: 6.21 Visual area, RV: 8.51

Fig. 2. EEG-ICs with low RV values

Signal preprocessing was performed using EEGLAB, a widely adopted EEG analysis application developed by SCCN [2]. We filtered the EEG signals with a 1-60 Hz band-pass filter, down-sampled the signals to 128 Hz, and applied common average referencing and Adaptive Mixture Independent Component Analysis (AMICA). We estimated precise locations of independent components, particularly those with low residual variance (RV) values, using the Neuroelectromagnetic Forward Head Modeling Toolbox (NFT), which provides a solution for the EEG inverse problem. Anatomical MRI was acquired using a General Electric Discovery MR750 3.0-T scanner installed at the Center for Functional MRI in UCSD. The ICs with low RV values were found in the primary motor area (M1), supplementary motor area (SMA), and visual area.

To determine if the recorded EEG and EMG contained enough information to represent muscle activities and synergy patterns, we performed a decoding analysis for movements in 8 directions using all estimated ICs. Sparse logistic regression showed significantly higher accuracy than chance level (12.5%) for the 8-class classification. Interestingly, the highest contributing IC for the classification was also an IC with a low RV value and located in the M1 hand area (Fig. 2, left). This suggests that the AMICA successfully extracted information relating to the movements, and made our attempt at synergy analysis described in the following section B feasible. We presented these results at the MoBI Workshop co-organized with the EEGLAB Workshop and held at SCCN on November 22, 2016.

The EMG signals were also pre-processed using EEGLAB. We applied a 20-200 Hz band-pass filter, down-sampling to 512 Hz, common average referencing, and AMICA to the signals. Some of the resultant ICs seemed to represent finger muscle differences. Using these results, we are working to solve an EMG inverse problem, as described in the next section B, using the same methods for EEG based on NFT.

B. *Solving an EMG inverse problem to estimate activation of finger muscles located deep inside the arm — an inter-group and international collaboration*

Since many finger muscles are located deep inside the arm, EMG signals recorded from skin surface electrodes contain many muscle activity signals other than that of the target muscle. To reconstruct finger muscle activity signals from EEG and perform finger muscle synergy analysis, it is necessary to extract each finger muscle activity. Therefore, we are attempting to solve an EMG inverse problem using high density EMG electrodes. This attempt is being carried out with other research groups: A02 (Drs. Seki, Oya, and Hirashima), B02 (Drs. Ota and Shirafuji), B03 (Dr. Funato), and C02 (Dr. Hanakawa).

To solve the EMG inverse problem, we need to create an arm model that specifies borders of skin, fat, muscles, and bones of the arm based on anatomical arm MRI (Fig. 3). We are working with group C02 in developing a high resolution T1-weighted MRI acquisition sequence for creating the arm model.

We also designed a MATLAB-based application that can combine series of MRI images of the forearm and upper arm, and position EMG electrodes on the skin in the combined arm image (Fig. 4). This application is going to be released as an EEGLAB plugin that will play a role similar to NFT but target muscles of the arm and leg.

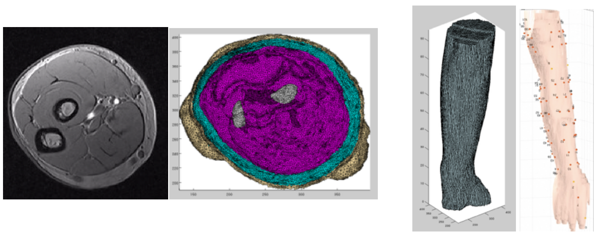


Fig. 3. High dimensional MRI and the arm model

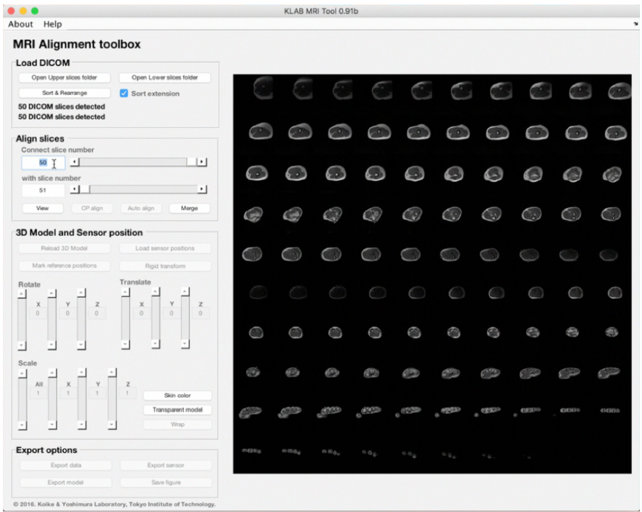


Fig. 4. Arm MRI processing toolbox

C. *Other achievements*

The following achievements of the academic year will lead to future projects in robot control and rehabilitation using synergy theory.

・Kawase T., Yoshimura N., Kambara H., and Koike Y., Controlling an electromyography-based power-assist device for the wrist using electroencephalography cortical currents, *Advanced Robotics*, Vol. 31(1-2), pp. 88-96, 2016.

・Minati L., Yoshimura N., and Koike Y., Hybrid control of a vision-guided robot arm by EOG, EMG, EEG biosignals and head movement acquired via a consumer-grade wearable device, *IEEE Access*, Vol. 4, pp. 9528-9541, 2017.

・Yoshimura N., Okushita R., Aikawa H., Kambara H., Hanakawa T., and Koike Y., Classifying force level of hand grasping and opening using electroencephalography cortical currents, International Brain-Computer Interface Meeting 2016, California, USA, June 1, 2016.

IV. Future Perspective

We have begun work on establishing a method for associating finger muscle synergies and brain activity signals. In the next year, after establishing the method, we will visualize the representation of synergies in the brain and investigate applications of the method in motor learning and rehabilitation.

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Annual report of research project A03-4

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Abstract—**The implantation of subdural electrode grids over the fronto-parietal area for the presurgical evaluations of patients with partial epilepsy offers the rare opportunities to record neural activities with wide-band ECoG, and apply electrical stimulation (cortical mapping and connectivity mapping) to delineate the parieto-frontal network through the SLF III. Within the left network, functional differentiation was identified between the PMv (negative motor response) and PF (tool use pantomime impairment). Within the right network, we have started to explore the neural activity for self-consciousness. We are also investigating the fast – slow dynamics for the sense of agency in the patients undergoing resection of the brain tumor in the right SLF III network.**

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. 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 around the important functional cortices. For functional mapping, we usually record neural activities (e.g., ERPs, high gamma activities) while patients complete a task and then locate the cortex responsible for a particular task by delineating functional impairment during electrical stimulation. The functional interference is temporary (~5 s), discretely focal (~2 cm^2) [fast dynamics], and in sharp contrast to chronic lesions usually associated with cortical plastic compensation.

In the FYI 2015, we delineated the fronto-parietal 'praxis' network by combining 50 Hz (fast dynamics alternation) and 1 Hz (functional connectivity) electrical stimulation. In the FYI 2016, by further developing collaboration with the research group A01-1 & A02-1, we were able to integrate our invasive neurophysiology methods with sophisticated neuropsychology, decoding and imaging techniques for comprehensive elucidation of the ventral fronto-parietal network for praxis (left hemisphere), corporeal awareness and sense of agency (right hemisphere). We aimed at i) identifying the surrogate markers reflecting these clinically relevant brain functions, and ii) revealing transition from fast to slow dynamics for plastic compensation.

II. AIM OF THE GROUP/METHODS

Subjects are patients with intractable partial epilepsy who underwent chronic subdural electrode implantation in the frontal & parietal areas for presurgical evaluations and gave written consent to the research protocols IRB#C533&443. By means of wide-band electrocorticogrphic (ECoG) recording, we probed neural activities in the ventral fronto-parietal network where the SLF III subserves the major white matter pathway. We focused on the functions related with "SLF III network" such as tool use, reaching, grasping and fine hand movements in the left hemisphere, and self-other face discrimination and kinesthetic illusory movement in the right hemisphere. We employed an electrical tract tracing method (1 Hz electrical stimulation) of cortico-cortical evoked potential (CCEP), which we originally developed [1], to probe cortico-cortical connections in the fronto-parietal network. Based upon the direct neural recording and connectivity findings, we extracted the neural surrogate marker representing the SLF III related functions. We then applied 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. We also recruited patients who underwent resection of the brain tumors in the right fronto-parietal network for the longitudinal neuropsychological assessment of the sense of agency (SoA) before and after the neurosurgery. We attempted to identify the cortex responsible for SoA and delineate the transition from the fast (functional impairment) to slow (plastic change, reorganization) dynamics alternation for SoA.

III. RESEARCH TOPICS

We have carried out the following three research projects.

A. Left fronto-parietal netwrok for tool-use and fine movements, and its fast dynamics alternation

In the FYI 2015, we performed the tool-use pantomime task to explore the praxis-related function in the inferior parietal lobe in 5 patients with intractable left partial epilepsy, who underwent subdural electrode implantation in the left frontal & parietal areas for presurgical evaluations. 50 Hz stimulation was performed in a total of 54 electrodes (across 5 patients) in the left inferior parietal lobe. In 22 % of electrodes (12 electrodes), stimulation elicited inability to pantomime the tool use. 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. Probabilistic diffusion tractography revealed SLF III as the underlying pathway for this network, which is discrete from the arcuate fasciculus (AF) for the dorsal language network [3]. In this FYI 2016, we have analyzed CCEP focusing on the connectivity between the SMG and temporal lobe. 3 of 5 patients showed the functional connectivity from the SMG to the lateral and ventral inferior temporal gyrus. Taken together with our recent intraoperative CCEP study that revealed semantic network between the rostral IFG (Pars Orbitalis and Triangularis) and inferior temporal cortices [4], this result clarified the direct link between the semantic and praxis networks for the access and retrieval of semantic memory during the praxis movement.

Thanks to the excellent S/N ratio of ECoG signals across wide-band frequencies, ECoG provides a rare but unique and valuable opportunity to decode neural activity on a single trial basis. We successfully decoded the ipsilateral upper limb movements from the high gamma activities recorded in the precentral motor cortex by using the support vector machine (SVM) [5]. By applying the Representation Similarity Analysis (RSA) to ECoG for the first time, we were able to compare the matrix of neural activities (LFP) with those of pre-defined theoretical models (semantic, visual and phonological) from the lateral and ventral temporal lobe and demonstrated that the ventral anterior temporal lobe coded the semantic representation per se [6]. Based on our decoding experiences, in close collaboration with A02-1 research group, we attempted to decode the types of praxis movements (tool use, non-meaningful gestures) from the high gamma activities in 4 patients by using SVM or sparse logistic regression (SLR). We are currently analyzing the weight information of the decoder together with the findings from low frequency (connectivity mapping) and high frequency (fast dynamics alternation) electrical stimulation to delineate the functional differentiation within the praxis network.

We recruited 3 patients and quantitatively evaluated the mode of impairment when stimulating the ventral premotor hub at lower intensity, where a negative motor response or the complete arrest of fine movements was elicited at higher intensity. We plan to elucidate the mode of alternation at the network level by stimulating simultaneously the two hub areas within the fronto-parietal network.

B. Right fronto-parietal netwrok for corporeal awareness and its alternation (fast dynamics)

We further developed the collaborative research with the research group A02-1 (Dr. Naito). Applying the same ECoG analyses, namely, wideband ECoG recording during tasks and intervention with 50&1 Hz stimulation, we aim at delineating the right fronto-parietal network for corporeal awareness and selfc identification by defining their neural surrogate markers and evaluating the fast dynamics alternation by electrical stimulation. We will further recruit patients with the subdural electrode implantation over the right fronto-parietal area for the self-other face discrimination and kinesthetic illusory movement tasks.

C. Transition from fast to slow dynamics for plastic compensation of sense of agency (SoA)

In close collaboration with Dr. Kazumichi Yoshida (co-investigator at the Department of Neurosurgery, Kyoto University Hospital), we continued a collaborative research with the research group A01-1 (Drs. Imamizu and Maeda). We recruited 4 patients with brain tumor who were planned to have the resection of the right parietal lobe or insula. We sequentially performed the sense of agency task (Keio method) before and after surgery to quantitate how the sense of agency changes in the acute to subacute postoperative periods. Preliminary results revealed dynamic change of SoA after the surgery, indicating the resected area as a responsible region for SoA. We plan to recruit more subjects and combine the longitudinal neuropsychology assessment with sequential resting-state fMRI (rsfMRI) evaluation in order to elucidate plastic compensation of sense of agency at a network level.

IV. Future Perspective

We will further develop the inter-group collaboration to establish a comprehensive approach (combining our invasive neurophysiology techniques with ECoG decoding, Keio SoA method, and sequential rsfMRI connectivity analysis) for elucidation of the left and right SLFIII network. We, in particular, focus on delineating the fast dynamic alternation (functional impairment) and its transition into slow dynamics alternation (plastic change, reorganization), so that these valuable findings can be translated into clinical neuroscience and finally into patient care. We believe our clinical system neuroscience findings contribute to the Embodied-brain System Science as important clinical reference data for the construction and verification of engineering models, and the elucidation of the long-term compensatory mechanism by rehabilitation.

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Annual report of research project A03-5

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***Abstract*—The mechanism of "Phantom-limb pain" is thought to be based on the remaining sensory pathway that lost its sensory input by transection of sensory nerve. Because selective stimulation of the remaining pathway is technically difficult, how the pathway changes in CNS after transection. In this study, we selectively stimulated the lemniscal pathway that lost the sensory input by using optogenetical technique and observed the thalamocortical network was robust even after the transection. We also found the molecular mechanism to maintain the matured neural network and the mathematical model that explains the way of maturation of the developing neural network in collaboration with Dr. Yano (B01 group). Furthermore, we revealed the pain related new cortical area that was activated when the sensory input was injured. These results may be responsible for the pathogenic mechanisms of "Phantom-limb pain".**

I. Introduction

Peripheral nerve injury caused by limb amputation induces the symptom called "Phantom-limb sensation" or "Phantom-limb pain". It is suggested that massive receptive field reorganization relates with "Phantom-limb pain" [1]. Because it is difficult to stimulate electively the injured sensory pathway, it is unknown that how the injured pathway changes and affects the reorganization. The aim of our research project is to understand the neural mechanisms that cause the receptive field reorganization by sensory nerve injury, and why the injury induces "Phantom-limb sensation" or "Phantom-limb-pain". To explore these, first, we selectively visualize and stimulate the injured neural pathway using optogenetics in transgenic mice. Second, we studied the molecular mechanisms to maintain matured neural network. Third, we explored whether the neural activity related with nociception increases following the sensory nerve injury.

II. Research Topics

A. Selective activation of the injured neural pathway

To study how the injured neural pathway modifies, we developed the tool to activate the injured pathway selectively. Weused transgenic mice expressing channel-rhodopsin 2 (ChR2) in whisker sensory related lemniscal fiber and stimulate selectively by laser *in vivo*. And then, the intrinsic signal imaging system *in vivo*. As the result, the injury of whisker sensory nerve fiber did not cause shrinkage of whisker sensory cortex known as barrel cortex (Fig. 1).

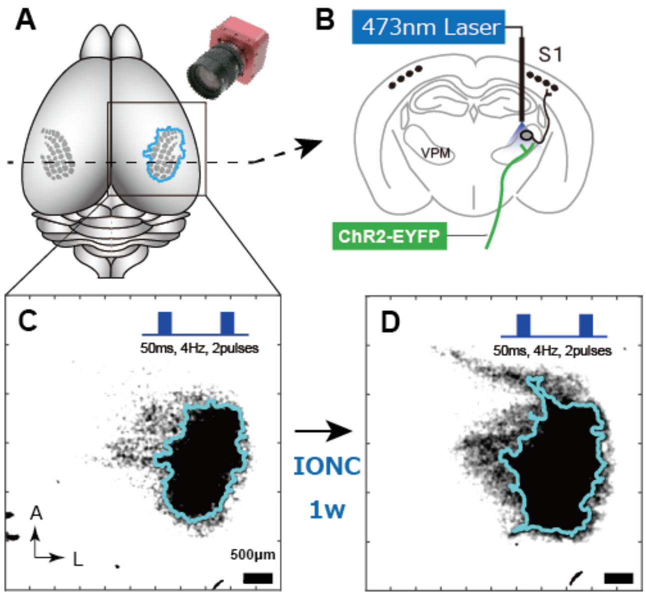

Fig. 1. Selective activation of whisker sensory related lemniscal fiber. **A**, The intrinsic signal was taken by a CMOS camera. **B**, Whisker sensory related lemniscal fiber, expressing Channel rhodopsin 2, was activated by 473nm laser. **C**, The area of whisker sensory cortical area known as barrel cortex was shown by blue line. **D**, The area of barrel cortex did not shrink after 1 week from whisker sensory nerve cut (infra-orbital nerve cut: IONC).

B. Molcular mechanism to maintain the matured synapses

The pruning and the strengthening synapses occur in the developing neural network, and the neural network matures. However, itremains unknown how the matured neural network is maintained. Our group found that metabotropic glutamate receptor 1 (mGluR1) is necessary for synaptic maintenance in matured neural network [2]. To explain the process of developing neural network mathematically, Dr. Yano (B01 group) and our group observed the morphological changes of synaptic terminal in whisker related lemniscal synapses in the developing thalamus, and explained these changes by simple mathematical model. The log scale of axon terminal volume fit with the normal distribution. We quantified the mean as the scale parameter and the standard distribution as the shape parameter (Fig. 2).

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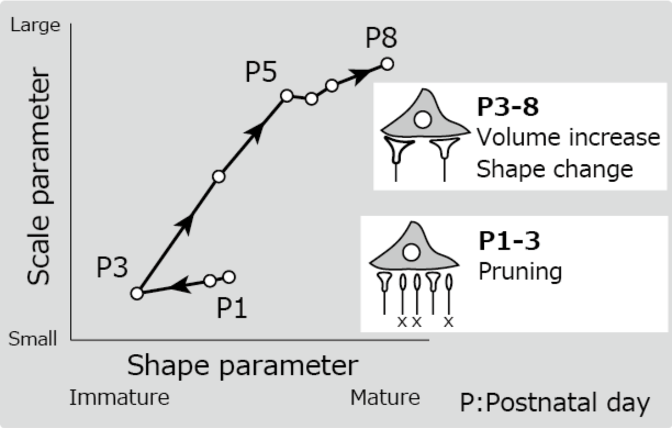

Fig. 2. Explanation of developing whisker related lemniscal fiber terminal from the mathematical model. In collatoration with Dr. Yano (B01)

C. Why does sensosry nerve injury induce pain?

It hold many mysteries that why phantom pain occurs after its main sensory input has lost. To address this issue, we observed morphological change of whisker sensory synapses in the VPM by sensory nerve injury. We found that whisker sensory nerve injury induced the invasion of other sensory input, such as lower jaw, into the whisker sensory area in the thalamus. This tendency was also observed *in vivo* electrophysiology; the neurons in the whisker sensory area in the thalamus became to respond to lower jaw stimuli. In addition, sensory nerve injury induced not only the sensory map reorganization but also extraterritorial pain behavior [3]. This suggests the sensory nerve injury increases activity in the pain related cortical area. To observe the increase activity in the pain related cortical area, we used the intrinsic signal imaging system *in vivo* and found that the increase of signal in the dysgranular area placed beside barrel cortex. The dysgranular area was also visualized by c-Fos signal to capsaicin injection into the whisker pad, which means this area is one of the "pain" related area in the cortex.

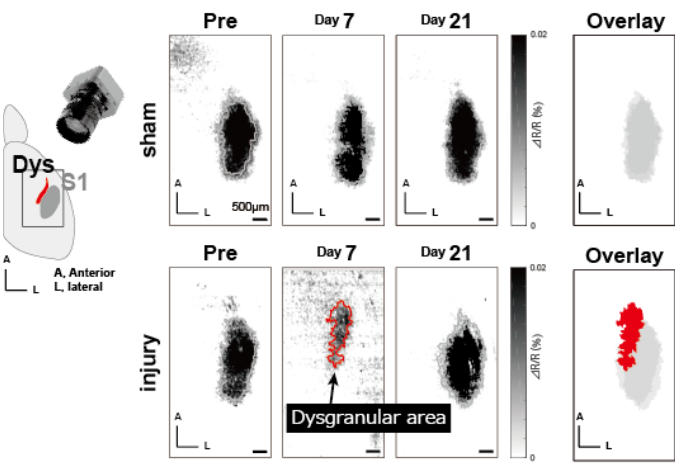

Fig. 3. Visualization of pain related area, dysgranular area, in whisker sensory nerve injured mice.

III. Future Perspective

From the study using optogenetics, we found that the neural pathway was reserved after losing sensory input. This suggests that the "Phantom-limb sensation" bases on the injured neural network is highly reserved after amputation. To explore the mechanisms how neural network is reserved after losing main sensory inputs will be helpful to understand the mechanism that induces "Phantom-limb sensation".

We found that the mGluR1 is a key molecular mechanism to maintain the mature neural network. This mechanism could be used to control the maintenance of the neural network that lost its main sensory input, and to recovery from the symptom "Phantom-limb-sensation".

The sensory nerve injury activates dysgranular area in mice. Because cytoarchitectonic features in mouse dysgranular area are similar to those in human area 3a [4], which receives nociceptive and proprioceptive information from somatosensory thalamus, our results are of help to understand the mechanisms of inducing "Phantom-limb pain" in human.

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Annual report of research project A03-6

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I. Introduction

Unilateral spatial neglect (USN) 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. USN is a cognitive deficit that cannot be explained merely primary sensory deficits or motor deficits. Recent studies on human brain imaging suggests that USN is caused by disintegration of the attention networks [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 USN is not yet established. Recent studies on homology between humans and non-human primates revealed that macaque monkeys also had the attention networks [2], [3]. The aims of our group are 1) to establish an animal model of USN by making a lesion in monkeys, to a brain region which is thought to be homologous to the ventral attention network (VAN), 2) to investigate how the animal model of USN process information in 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 four monkeys, so that VAN was disconnected. MR structural images taken after the lesion demonstrates that the lesion site was confined in the right STG (Fig.1).

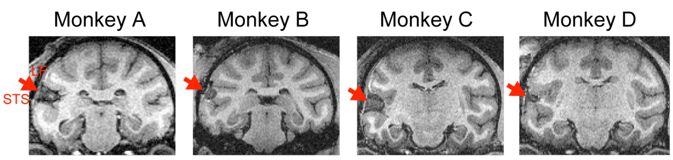

Fig. 1. MR structural images on the center of the lesion site in four monkeys. Siemens Allegra 3T, MPRAGE3D, 0.5mm * 0.5mm * 0.5mm voxel. LF: lateral fissure, STS: superior temporal sulcus.

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 evaluation of USN in humans (Fig.2). In this task, under head-unrestrained condition, monkeys chose the target among distractors by touching the target to get a reward (Fig.2A). The correct ratio was decreased for 1-2 weeks after the lesion but was recovered to the normal level after that (Fig.2B). On the other hand, the mean reaction times were longer in the target on the contra-lesional side (Fig.2C, light blue) than in the targets in the ipsi-lesional side (Fig.2C, orange blue). These results suggest that spatial neglect is maintained for 3 months after the right STG lesion.

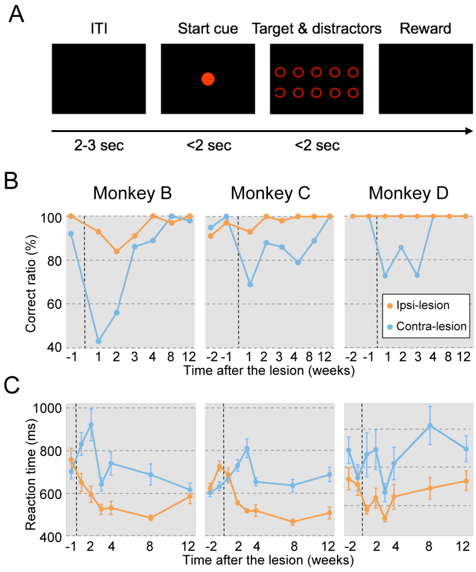

Fig. 2. The target-choice task. (A) The task sequence. The target in this case was the flipped 'C' pattern on the left. Correct ratio (B) nad reaction time (C) were plotted across time before and after the lesion.

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 USN subjects were biased to the ipsi-lesional side during free-viewing [4]. We examined whether this is observed in the monkeys after the lesion. We used Tobii's TX300 for eye- and head-tracking during free-viewing of natural images under head-unrestrained condition. Horizontal angles of the eyes were also calculated using a formula eye = gaze - head. Three monkeys were tested with a free-viewing task. The probabilities of gaze positions were calculated and were plotted across time before and after the lesion (Fig,3 left). We found that the gaze positions of Monkey B were biased toward ipsi-lesional side for three months (Fig.3, left). Head angles were biased toward ipsi-lesional side for three weeks after the lesion (Fig.3, middle). Head angles were biased toward ipsi-lesional side later than three weeks after the lesion (Fig.3, right). Similar results were obtained from other two monkeys.

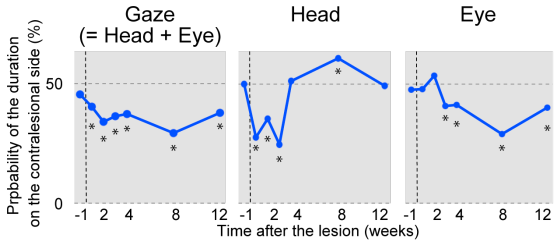

Fig. 3. Eye- and head-tracking in Monkey B. Probabilities of gaze positions (left), head angles (middle) and eye angles (right) on the contralesional side were plotted across time before and after the lesion.

These results suggest that the rSTG lesion affected eye-head coordination during the recovery stage of USN. This is an important finding that will have a big impact for building a computational model of body schema.

Taken together, the results in (A) and (B) suggests that the symptoms were observed irrespective of whether hands (A) or eyes (B) were evaluated. This meets the criteria for USN that the symptoms cannot be explained by primary motor deficits. Since both tasks were performed under a head-unrestrained condition, the symptoms cannot be explained by primary visual deficits. Thus, we conclude that we established a monkey model of USN by making a lesion in the right STG.

C. Functional brain imaging

The research group collaborated with Prof. Fukunaga in the National Institute for Physiological Science to measure brain activities of the monkeys before and after the lesion. We measured BOLD activity of the monkeys under 1% isoflurane anesthesia [5] using the echo-planar imaging sequence. To quantify the functional connectivity of the dorsal attentional network (DAN) in the brain, we calculated correlation coefficients between the temporal fluctuation of the BOLD activity in FEF and LIP.

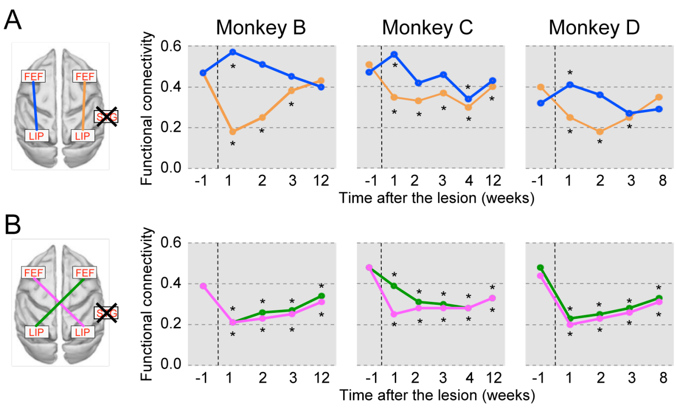

Fig. 4. Results of rsfMRI in three monkeys. Functional connectivity of DAN within hemisphere (A) and between hemispheres (B) were plotted across time before and after the lesion.

The functional connectivity between the ipsi-lesional FEF and the ipsi-lesional LIP was reduced for three weeks after the lesion but was recovered to the prelesion level after that (Fig.4A, orange). The functional connectivity between the contra-lesional FEF and the contra-lesional LIP was increased at one week after the lesion (Fig.4A, blue). The functional connectivity between the ipsi-lesional FEF and the contra-lesional LIP and the functional connectivity between the contra -lesional FEF and the ipsi-lesional LIP were decreased for three months after the lesion (Fig.4B). These results suggest that the acute stage of the lesion can be characterized by an imbalance between the connectivity within the ipsi-lesional DAN and the connectivity within the contra-lesional DAN (Fig.5, middle). On the other hand, the chronic stage of the lesion can be characterized by reduced inter-hemispheric interaction between the ipsi-lesional DAN and the contra-lesional DAN (Fig.5, right).

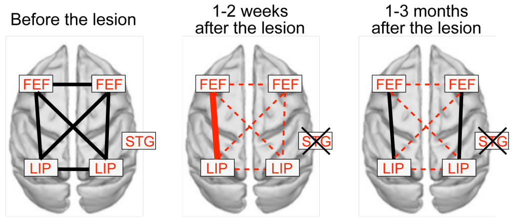

Fig. 5. Summary of rsfMRI experiments. A think red line denotes an incresed functional connectivity. Thin dotted red lnes denote decresed functional connectivities.

IV. Future Perspective

The damage to a part of VAN (rSTG) induced USN in monkeys. In parallel with the behavioral deficits and recovery, the functional connectivities in DAN were also affected. Future analysis will focus on investigating attentional function using the Posner paradigm [6] and analysis based on the saliency computational model [7] designed for monkeys. We will also examine the neural mechanism by using neurophysiological and pharmacological methods.

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Annual report of research project A03-7

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***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). In the study reported here, we performed diffusion tensor imaging to investigate plastic changes of neuronal tracts, and found an increased fractional anisotropy value at the white matter underlying the ipsi-lesional ventral premotor area (ip-PMv). An anatomical tracer study indicated the newly-formed projections from ip-PMv to the magnocellular red nucleus is involved in functional compensation after M1 lesion. We also established a neuro-computational model that simulates a relationship between temporal changes of grip strategy and rate of successful retrieval. Moreover, 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 improved, whereas impairment of dexterous hand movements remained until 3 months after stroke induction. A histological analysis indicated a decrease in the abundance of large neurons in M1 layer V, from which the descending motor tracts originate. Therefore, Wallerian degeneration and subsequent atrophy of M1 neurons may be involved in long-lasting impairment of dexterous movements including precision grip.**

I. Introduction

The brain has a capacity to recover function following the local damage. Appropriate rehabilitative training is thought to facilitate the process of recovery. However, it remains largely unclear how rehabilitative training promotes functional recovery. We have examined the process of functional recovery after brain injury in the macaque monkey, as it has cerebral and musculoskeletal structures being similar to those of humans. We induced an irreversible lesion in the primary motor area (M1) of the cerebral cortex, from which a large portion of the motor output projections to the spinal cord originate, and examined the recovery of motor function. Our behavioral analyses suggested that recovery after M1 lesions includes both training-dependent and training-independent processes, and that recovery of precision grip, grasping with the index fingertip and thumb tip in finger-to-thumb opposition, requires intensive postlesion training [1]. Moreover, our brain imaging analysis suggested that changes of brain activity occur in uninjured motor areas during recovery of precision grip after M1 lesions [2].

II. Aim of the Group

The aim of the present study is to investigate temporal changes behavior after lesioning of M1 and changes of neuronal structures that underlies functional recovery of precision grip. The additional aim of the study is to investigate changes in brain structure in the macaque monkeys in which a focal stroke was induced in the posterior internal capsule, an area susceptible in human stroke patients.

III. Research Topics

A. Rewiring of subcortical projections after primary motor cortex lesion in macaque monkeys

Using M1-lesioned macaque monkeys, we studied changes of connections from the motor cortex during motor recovery. After mapping the motor representation in M1 using intracortical microstimulation techniques, ibotenic acid was injected intracortically to destroy the hand area of M1. Immediately after lesion induction, paralysis, including complete loss of digit movements, was observed in the hand contralateral to the lesioned motor cortex. The diffusion tensor MR imaging was performed before and during motor recovery after M1 lesion, to investigate brain connectivity in each phase. An increased fractional anisotropy value in the white matter underlying the ventral premotor area of the ipsilesional hemisphere (ip-PMv) was associated with motor recovery, indicating that projections from ip-PMv were increased during motor recovery.

Moreover, we histologically investigated the subcortical connections of ip-PMv in the M1-lesioned monkeys after motor recovery in comparison with those in the intact animals, by using biotinylated dextran amine (BDA). A remarkable difference between the lesioned and intact monkeys was observed in the red nuclei: the BDA-labeled terminals were observed in the magnocellular nucleus as well as the parvocellular nucleus of the M1-lesioned monkeys, but were observed only the parvocellular nucleus of the intact monkeys. These results suggest that the newly-formed projections from ip-PMv to the magnocellular red nucleus is involved in functional compensation after M1 lesion. This study was performed in collaboration with Dr. T. Hayashi at RIKEN, Dr. T. Yamamoto at Tsukuba International University, and Dr. N. Higo at AIST.

B. A neuro-computational model to understand recovery of grasping movement after M1 lesion

Our behavioral analyses in M1-lesioned macaque monkeys showed that transfer from alternative grips to the precision grip occurred despite the transient decrease in rate of successful retrieval in a task involving retrieval of small food pellets from cylindrical wells in postlesion-trained monkeys [2]. We established a neuro-computational model that simulates this relationship between temporal changes of grip strategy and success rate, in collaboration with Dr. J. Izawa at University of Tsukuba.

We simulated activity of motor cortical neurons, and then removed a set of simulated neurons from the simulation, as a mimic of brain lesion. Recovery of grasping movements was simulated using a hybrid model that mixed supervised and unsupervised learning. In this simulation, alternative grips and the precision grip were represented by vectors in different directions. This simulation successfully reproduced recovery process after M1 lesion: a change from alternative grips to the precision grip during the transient decrease in success rate. Therefore, both supervised and unsupervised learnings may be involved in the recovery of grasping movements after M1 lesion.

In our previous analyses, grip forms were evaluated in the test session, in which pellets to be retrieved were placed into one of five different sized wells. In this year's survey, grip forms were also evaluated in the daily training session, in which the size of the training well was fixed. Consequently, we found that changes of grip forms occurred during the training session as well as the test session (Fig. 1).

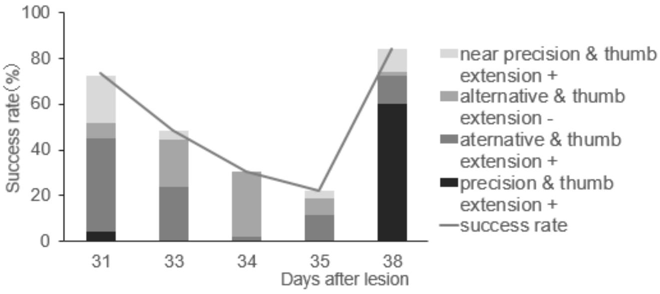

Fig. 1. Temporal changes of grip forms during training sessions

C. *Changes of neuronal structures in a monkey model of internal capsular stroke*

M1-lesioned macaque monkeys specifically impair motor function. Therefore, M1-lesion is 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, we established a macaque model of focal stroke at the posterior internal capsule [3].

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. 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 until the end of the behavioral evaluation at 3 month after lesion.

As a first step in investigating changes in brain structure induced by internal capsular stroke, we measured the size of neurons in layer V of M1. In the intact M1, there was an abundance of large neurons. In contrast, at 3 weeks after injection and beyond, there were fewer large neurons in layer V of M1 ipsilateral to the internal capsular stroke (ipsi-late in Fig. 2). No significant change in neuronal size was observed in the contralateral M1 or in the ipsilateral M1 2 weeks or earlier after stroke induction. These results suggest that Wallerian degeneration and subsequent atrophy of M1 neurons occurred over several weeks after ET-1 injection. A decrease in the abundance of large neurons in M1, from which the descending motor tracts originate, may be involved in long-lasting impairment of dexterous movements including precision grip.

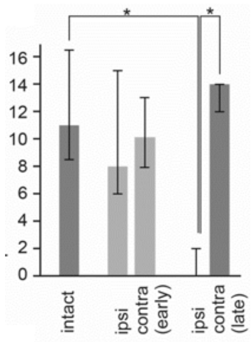

Fig. 2. The percentage of large pyramidal neurons (area >500 μm^2) in M1

IV. Future Perspective

We will further investigate the mechanism of the functional recovery after brain damage, using both M1-lesioned macaque monkeys and macaque monkeys with capsular stroke. Especially, we will intensively study how anatomical changes of neuronal projection underlie functional recovery after brain damage.

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Group B：Systems engineering

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I. Objective in Group B

Group B (systems engineering group) aims at establishing computational functional models of the body representation in the brain that realize sensor-motor association, through the integration of the knowledge of brain science (mainly obtained by researchers in Group A) and that of rehabilitation medicine (mainly obtained by researchers in Group C). Projects B01 and B02 construct the multi-time frequency dynamical model of the body representation in the brain with respect to its activities (fast dynamics) and its long-term changes (slow dynamics). The proposed models are verified with the experimental data from neurophysiology and the clinical data during rehabilitation treatments . Project B03 is for subscribed research projects. Members of the projects direct novel constructive approaches for modelling studies in embodied-brain systems science.

II. Research products in Group B

B01 is a planned research in systems engineering group directed to approaches from body cognition, which involves Hajime Asama (Univ. of Tokyo), Toshiyuki Kondo (Tokyo Univ. of Agriculture and Technology), Hirokazu Tanaka (JAIST), Shiro Yano (Tokyo Univ. of Agriculture and Technology), and Jun Izawa (University of Tsukuba).

In this team, mechanisms that multi-modal sensory information or motion intention modulates the body consciousness (i.e., sense of agency/ownership) and modeling of the body consciousness are investigated in constructive approaches as well as identification quantitative biomarkers. Moreover, motor control models are constructed, and methodologies for rehabilitation based on the models are studied.

Towards the modeling of body consciousness, the team has achieved several outcomes through psychological experiments investigating how multi-modal sensory integration (as in rubber hand illusion) and higher-level cognitive processes influence the body consciousness. These findings and actual data has been associated with the structure and formulation of the models. In addition, they verified that EEG features such as source current estimation, ERP, and ERD can be a biomarker for identifying body consciousness and body schema. Furthermore, they evaluated the validity of mathematical models of neural activities in motor cortex and a schizophrenia model based on statistical learning theory, then they verified the hypothesis derived from these models through psychological and brain imaging experiments.

B02 is a planned research in systems engineering group directed to approaches from motor control, which involves Jun Ota (Univ. of Tokyo), Shinya Aoi (Kyoto Univ.), and Ryosuke Chiba (Asahikawa Medical Univ.). This team aims to develop fast and slow dynamics models by focusing on muscle synergy to elucidate mechanisms of the body representation in brain for adaptive motor control under the assumption that the alteration of muscle synergy structure reflects the alteration of the body representation in brain.

For the fast dynamics of postural control, we have constructed a model with integration of multisensory inputs which alterations induce postural alterations. To verify the validity of the control model, we have developed the postural controller which is combined with feedforward and feedback controls which have been applied to musculoskeletal simulator to verify whether the controller can keep upright standing with optimization of parameters. In addition, we have developed fast and slow dynamics models for locomotion from the reflex and learning controls of muscle synergy generation based on the foot contact timing. We integrated these models with a musculoskeletal model of rat hindlimbs, and performed forward dynamic simulation of split-belt treadmill walking. We verified our fast and slow dynamics models for locomotion by comparing the simulation result and measured data of rats, and investigated roles of muscle synergies for adaptive motor control in locomotion.

Project B03 is a subscribed research group and deals with the problems in embodied-brain systems science from novel constructive approaches. The concrete issues are analysis of muscle synergy (Prof. Tetsuro Funato @ The Univ. of Electro-Communications, artificial thumb (Prof. Yasuhisa Hasegawa @ Nagoya Univ.), artificial muscles and tendons (Prof. Ko Hosoda @ Osaka Univ.), and virtual human body (Prof. Tadahiro Taniguchi @ Ritsumeikan Univ.).

Relationship between projects B01,B02,B03 are shown in Fig. 1

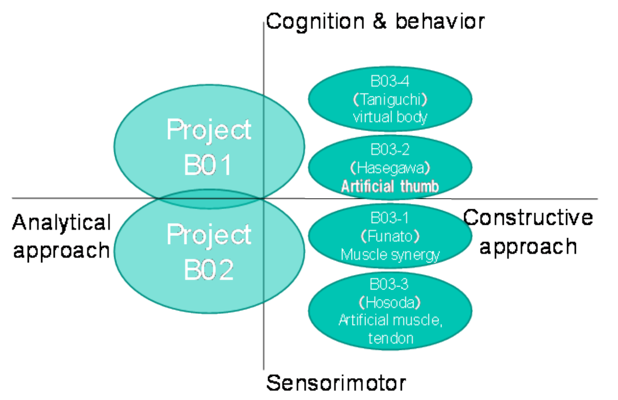

Fig. 1 Relationship between projects in Group B

III. Activities in Group B

Meetings of Group B and activities mainly organized by members in Group B are described as follows:

-22nd SICE Emergent system symposium
Date: August 24-26, 2016
Place: Nagano
Content: Endorsement. Plenary talk, lecturer at the workshop

-SICE Annual Conference 2016
Date: September 20-23, 2016
Place: Ibaraki
Content: organized session with SICE Technical Committee on Autonomous Decentralized Systems

-SICE life engineering symposium 2016（LE2016）
Date: November 3-5, 2016
Place: Osaka
Contents: Organized session

-Group B meeting
Date: November 29, 2016
Place: Aichi
Contents: report on interim evaluation, two presentations

-SICE systems and information symposium 2016（SSI2016）
Date: December 6-8, 2016
Place: Shiga
Contents: poster sessions

-29th SICE distributed autonomous system symposium
Date: January 30-31, 2017
Place: Tokyo
Contents: Organized session

-Group B meeting
Date: March, 2017
Place: Hokkaido
Contents: presentations and discussion

IV. Future plan

Group B is going to hold academic society activities in 2017 like 2016, such as SICE Emergent system symposium, SICE Annual Conference, SICE systems and information symposium, SICE distributed autonomous system symposium.

As for research direction in Group B from the viewpoint of modelling aspect, members of Group B deal with two problem: specification of state variables and formulation of slow dynamics. Figure 2 shows the schematic view of the approaches. As a future plan, we aim at integrating the two problems and modelling of the body representation in the brain depending on the tasks humans do.

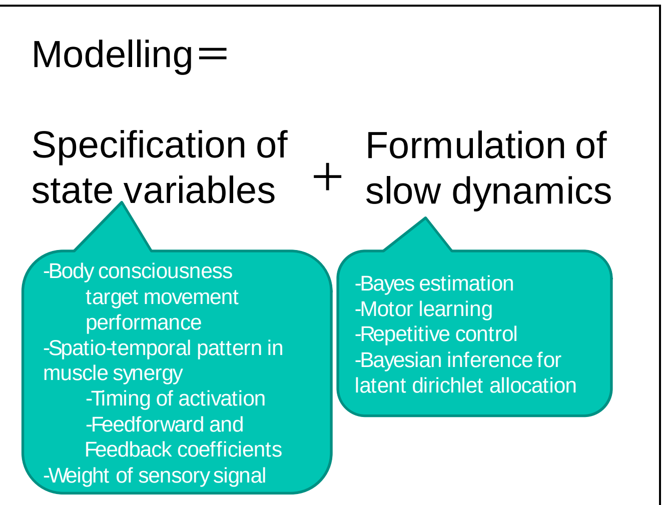

Fig.2 Modelling process in Group B

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

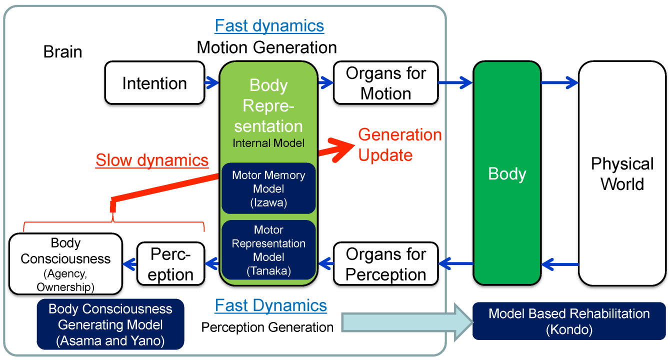

Fig. 1 Generating processes of body representation basing on body consciousness

III. Research Outcomes

Our research outcomes on each topic are summarized as follows:

A. Body Consciousness Generation Model

(1) Understanding of body consciousness that influences slow dynamics

Asama's group (University of Tokyo) examined perceptive processes underlying the body consciousness. First, we examined the influence of high-level cognitive processes on task performance on a low level perceptual processing of delay detection, and found task performance raised the threshold of delay perception, although the participants perceived the intervention of a third party. Second, we examined the attention allocation during the updating of body consciousness. We compared the attention allocation between the conditions when people gain the sense of control and when they lose the sense of control. As a result, we found that people are very sensitive to small reduction in control and strongly feel out of control with slight decrease in control. At last, we examined the brain activity during the preparation of motion during the fast dynamics updating of body consciousness [1]. We found that the readiness potential starts earlier and showed larger amplitude when people learned that their motion produces consistent and reliable consequence, in relative to the condition when the consequence of action is sometime absence These findings provide important knowledge to understand the updating of embodied-brain model in slow- and fast dynamics.

(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. It is considered that the body representation updating occurs based on visual or proprioceptive sense. To examine the dynamics of the body representation updating, we performed an experiment with participants on some conditions in which humans get different body consciousness with altered visual information. According to our results, we found that the body representation of hand, human move consciously, is updating with either sense of ownership or sense of agency. On the other hand, the body representation of elbow, human move subconsciously, is updating with only sense of agency. Additionally, we attempt basic modelization in reference to the result of experiment.

(3) Stochastic model of body consciousness

Yano (Tokyo University of Agriculture and Technology) engaged in comprehensive study on actual motor learning and sense of agency. Usually, generating sense of agency requires predictive model of actual sensory feedback [2]. However some kind of motor learning process doesn't require any kind of such predictive models. To resolve the incongruity, we proposed a reinforcement learning algorithm which belongs to direct policy search approach [3], and considered the relations between motor learning process and cognitive learning process. Understandings of these processes would contribute better motor rehabilitation methods.

Moreover, we experimentally validated the hypothesis that is from our past proposed mathematical model of sense of agency [4], in cooperation with Prof. Kondo group. The hypothesis is that the prior distribution becomes broader the learning process becomes faster. We can measure the speed of learning process in an indirect way by observing the sense of agency or sense of ownership. Our hypothesis is supported experimentally.

B. *Embodied-brain Motor Representation Model*

Toward understanding body consciousness, it is crucial to understand how the brain represents body movements. Tanaka's group (JAIST), in collaboration with Kakei's group (A02), discussed computational modeling of neural activities in cerebellar and cerebral cortices and dynamics of cerebral-cerebellar loops [5]. We hypothesized that the cerebellum approximates the recurrent network dynamics of cerebral cortex with the feedforward network dynamics of the cerebellar cortex, and discussed a possible neural network mechanism. Based on this hypothesis we are analyzing neural activities of mossy fibers, Purkinje cells and cerebellar nuclei.

Besides, we tackled the neural representations of body movements and body consciousness through high-density EEG and novel signal processing methods [6, 7]. First, movement directional tuning and its posture dependence, which have been reported in monkey electrophysiology, were examined by using high-density EEG during natural movements. Advanced signal processing methods revealed movement directional tuning in many EEG sources in a way comparable with monkey electrophysiological experiments. Next, we developed a novel signal processing method that extracts recurring wave patterns embedded in EEG. Compared to conventional methods, the proposed method without external timings for trial average is effective for cognitive functions that are not necessarily time-locked to external events (e.g., motor intention and body consciousness), and is being applied to the data from Imamizu's group (A01).

C. *Motor Memory Model*

Izawa(Univ. Tsukuba) developed the computational model of neurorehabilitation where the reward-based decision making and Hebbian learning play important role. Based on this model, the novel strategy of robotic rehabilitation was proposed [8]. Since this model includes a reinforcement learning architecture for selecting skills, he investigated the mechanism of reward/cost based learning for action selection and found that the motor costs significantly influenced our reward-based skill learning [9]. Also, he confirmed that the reward based motor learning and the learning to feel agency (sensory prediction error) are dissociable and found that tease two processes are mediated via two independent architectures[10]

D. *Model based Rehabilitation*

To clarify the relationship between bodily self-consciousness and motor learning, and to find quantitative biomarkers reflecting plastic change of the body representation in the brain, Kondo's group (Tokyo University of Agriculture and Technology) investigated (1) the effects of passive visuomotor experience on the change of body schema [11], (2) the functional connectivity analysis of brain activities (EEG and NIRS) during RHI [12], and (3) development of an immersive VR system for analyzing how the visual interventions modulate bodily self-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 learning. They found that passive motor experience leads to limited but actual compensation of body schema, even though it does not contribute to inverse model. In the second topic, they evaluated functional connectivity of NIRS and EEG 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 an amputee to have strong body consciousness and it would be a promising intervention for reducing phantom limb pain.

IV. Future Perspective

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

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Annual report of research project B02-1

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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 synergy structure. In this year, we proposed fast dynamics model for postural control and verified it in experiments with alterations of multisensory inputs and musculoskeletal simulations. In addition, we focused on split-belt treadmill walking of a rat and verified our fast and slow dynamics models for locomotion by comparing the results of forward dynamic simulation of a neuromusculoskeletal model and kinematic synergy analysis of measured data.**

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, to investigate the fast dynamics in postural control, we tried to construct a model for integration of multisensory inputs which alterations induce postural alterations. It is known that the multisensory inputs integrated in the process of motion generation and these alter those weights in the integration with depending on conditions. The experiments were that subject keeps standing posture with several changes of sensory inputs which were visual, vestibular and tactile inputs. We investigated the alterations of weights in an integration model with measurements of center of pressure. As a result, with eyes' closing, we could observe a proper reweighting. However, with caloric stimulation of an ear, the reweighting could not be observed. This indicated that standing strategy was altered by learning effect of sensory inputs.

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. As a result, the human model could keep standing posture with only somatosensory inputs in 100 (ms) delay [1]. Moreover, the standing posture could be kept with less muscular tonus when visual and vestibular feedback could be utilized. This result was very similar with human upright standing and indicated the importance of multisensory inputs [2]. Currently, we improve this to simulate the quiet standing against outer force.

We also investigated cerebellum functions of rats with medial or lateral cerebellar ablation. We constructed a model for initial diagnosis of cerebellar disease by the investigation. From the results of the investigation, we design the indexes to estimate impaired regions of cerebellum. By the model, we consider the role of cerebellum in motion generation [3].

B. *Modeling of fast, 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 the last year, we developed fast and slow dynamics models of motor control in locomotion from the reflex and learning controls of muscle synergy generation based on the foot contact timing. Through the integration with a musculoskeletal model of rat hindlimbs, we performed forward dynamic simulation of split-belt treadmill walking. As a result, our model showed rapid and slow adaptations in locomotor behavior depending on the environmental variations. In this year, we analyzed the measured data during the hindlimb split-belt treadmill walking of rats and compared the analysis result with the simulation result to verify the validity of our mathematical model. In particular, we investigated the kinematic synergy to find the coordination structure in the joint level. As a result, while the spatial pattern has almost no difference among various conditions of the locomotion environments, the temporal pattern has a crucial difference depending on the environment. In particular, the phase of the temporal pattern rapidly shifted in accordance with the speed discrepancy between the belts, and furthermore the phase shift slowly returned after the environment returned. There trends were observed in our simulation result and verified the validity of our mathematical model in the kinematic level.

Furthermore, in this year, we performed the measured data analysis and modeling study for quadrupedal and bipedal locomotion and gait transitions between them of Japanese monkeys in collaboration with Nakajima's group (A02-2, Kindai University). For the measured data analysis, we analyzed the EMG data measured from 11 muscles of one side including upperlimb, lowerlimb, and trunk muscles during quadrupedal and bipedal locomotion using the nonnegative matrix factorization. As a result, common and different characteristics in the spatiotemporal patterns of muscle synergies were clarified between these gaits. For the modeling study, we developed a motor control model for quadrupedal and bipedal locomotion based on muscle synergy hypothesis similarly to the rat hindlimb model above, although fast and slow dynamics were not yet incorporated. In addition, we modeled additional muscle synergy control for the gait transition from quadrupedal to bipedal locomotion. Through the integration with a musculoskeletal model of Japanese monkeys, we performed forward dynamic simulation of bipedal and quadrupedal locomotion and the gait transition. We compared the simulation results with the measured data to verify the validity of our mathematical model.

These results were presented at the organized session "Embodied-brain Systems Science" of SICE Life Engineering Symposium at Osaka International House on 3-5, November, 2016, and at the organized session "Embodied-brain Systems Science" of SICE Symposium on Decentralized Autonomous Systems at Chofu Creston Hotel on 30-31, January, 2017. In addition, Ota, Chiba, Aoi from B02-1 and other members visited the laboratories of Prof. Andrea d'Avella, Prof. Yuri Ivanenko, and Prof. Enrico Pagello in Fondazione Santa Lucia, University of Padova, and University of Messina and joined workshops to discuss future collaboration.

IV. Future Perspective

As 3rd year of this project, we developed the models of fast and slow dynamics by the results of several experiments and simulations. We proposed fast dynamics model for postural control, which was verified with alterations of multisensory inputs and musculoskeletal simulations, and fast and slow dynamics models for locomotion, which was verified by split-belt treadmill walking of rats and the neuromusculo-skeletal model. These results give much consideration of the body representation in brain for adaptive motor control.

As future works, we continue to 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

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The University of Electro-communications

Abstract—**In order to approach the mechanism of dysfunction due to neural ataxia and effective rehabilitation, this group studies the functional role of synergy and control system using animals and patients with neural ataxia. In this year, we analyzed the control system of rats with lesion in inferior olivary nuclei (IO), and analyzed the synergies of congenital insensitivity to pain (CIPA) and stroke patients. As a result, lesion in IO was found not to affect the synergy but affect the transmission of control torque to muscle, synergies of CIPA showed abnormality in activation duration and timing which can be modified by providing sensory information, and synergy of Fugl-Meyer Assesment (FMA) of stroke patients reflected the FMA score.**

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. Synergies has been reported to change characteristically by neural ataxia [1], thus the possible use of synergy for rehabilitation is expected. In this year, we performed (1) elucidation of the posture control of standing rat with lesion in cerebellar system (achievement A), and (2) synergy analysis of the congenital insensitivity to pain patients and stroke patients (achievement B, C).

II. Aim of the Group

The aims of this research group are (1) to approach the mechanism of motor dysfunction due to neural ataxia through the evaluation of motion and dynamical analysis, and (2) to construct the rehabilitation method by evaluation of motion and synergy analysis of patients with neural ataxia.

III. Research Topics

A. Posture control of rats with neural dysfunction

1) Standing experiment of rats with lesion in inferior olivary nuclei (IO): In order to consider the contribution of IO to posture control, standing motion of rat with lesion in IO (IO rats) were measured (collaboration research with B02). 4 Wistar rats became IO rats by injecting 3-Acetylpyridine after their healthy motion were measured. In the experiment, rats stood bipedally as in Fig. 1A, and their motion were measured using motion capturing system.

From the measured time series of joint position, 4 segmental angles defined as Fig. 1B were calculated. Then intersegmental coordination (kinematic synergy) was derived by singular value decomposition of the segmental angles, and the intersegmental coordination before and after lesion were compared. As a result, 2 intersegmental coordination contributed over

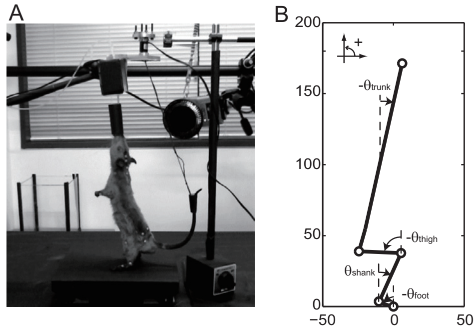

Fig. 1. Measurement of the motion of a standing rat

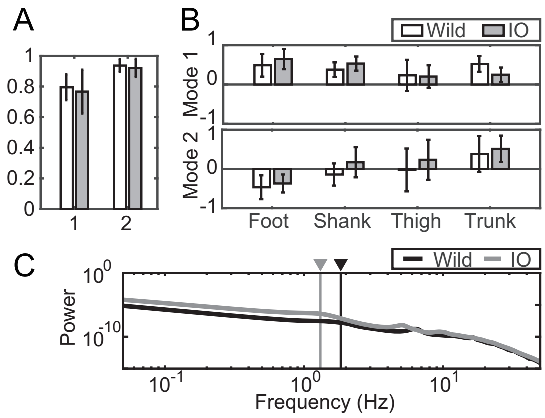

Fig. 2. Experimental results of standing rat. A: contribution ratio. B: intersegmental coordination. C: power spectrum. Results are those of rats with dysfunction in inferior olivary nuclei (IO) and wild type (wild).

0.8 of all the motion (Fig. 2A). Moreover, intersegmental coordination before and after lesion had similar pattern (Fig. 2B), and ANOVA failed to show significant difference by lesion. Therefore, lesion was considered not to affect to the intersegmental coordination.

From the measured motion, power spectrum of the center of mass (COM) was also calculated using maximum entropy method (MEM) (Fig. 2C). Calculated power spectrum (Fig. 2C) had peak around 1 Hz in both before and after lesion (triangles in the figure). These peak frequencies decreased after lesion, and power under the peak frequency increased.

Above all, experimental data showed that the lesion in IO did not affect to the intersegmental coordination, but affect to the peak frequency of power spectrum. Next subsection discusses the reason of these results through the evaluation of control system using dynamical model.

2) Evaluation of the control system with lesion in IO: The system model of standing rats was considered as shown in Fig.

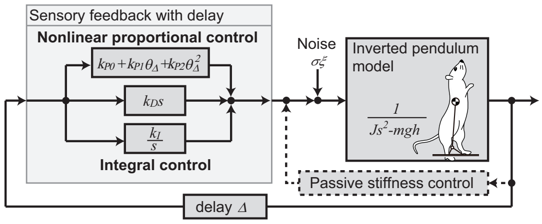

Fig. 3. System model of the standing rats.

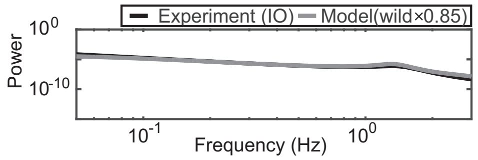

Fig. 4. Comparison of the measured power spectrum of IO rat (Experiment) and system model with wild parameters ×0.85 (Model).

3, and the effect of lesion in IO was investigated through the identification of control parameters. Here, θ_Δ is angle from ankle to COM, and delay τ is fixed (40 ms).

Identification was performed by searching parameters in which the power spectrum between system model and experiment matched. As a result, the identified parameters of IO rats were lower than those of healthy rats in similar rates (approx. 0.8) for every parameters. Then, we also calculated the power spectrum of the system model with control torque of 0.85 times that of the healthy rat, and we found that the power spectrum matched that of IO rats (Fig. 4).

These results indicated that the lesion in IO did not affect to each control system but affected to input torque, i.e., somewhere after generation of control torque to muscle input.

B. Muscle synergy of congenital insensitivity to pain (CIPA)

As a collaboration research with C02, walking motion of congenital insensitivity to pain (CIPA) patients was analyzed. Walking experiment was performed in normal condition and in a condition with a device that provides touch-down information developed by C02 group. Then, the motion between healthy and CIPA patients, and the motion with and without device were compared.

As a result, walking with touch-down information reduced the floor pressure at touch-down. This indicated the developed device functioned effectively for avoiding a dangerous walking with high touch-down pressure, typically found in CIPA patients. Moreover, muscle synergies of CIPA patients (Fig. 5) showed that (1) synergy activation extended than that of healthy subjects, and (2) peak timing of muscle synergy were different from touch-down and lift-off timing (Fig. 5A). These gaps were decreased by the developed device (Fig. 5B).

Gap in (2) indicated that the change in the peak timing contributed to the decrease in the touch-down pressure. Further analysis of walking motion of CIPA and neural mechanism related to the change in muscle synergy will connect to the construction of effective rehabilitation of CIPA patients.

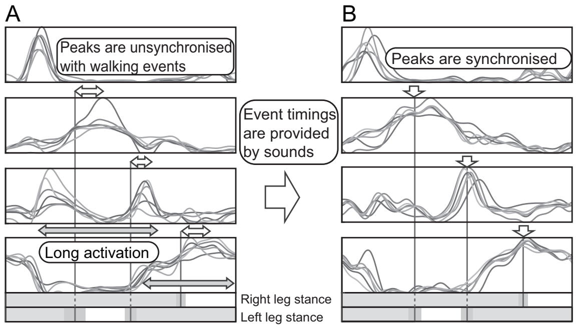

Fig. 5. Walking muscle synergies of congenital insensitivity to pain (CIPA).

C. Evaluation of post-stroke motion using muscle synergy

In order to investigate the possible use of muscle synergy for the evaluation of motor dysfunction due to stroke, muscle synergy of 7 stroke patients were analyzed (a collaboration research with A02, C02 and Morinomiya hospital). As an experiment, stroke patients performed a movement of Fugl-Meyer Assessment (FMA) with 37 tasks, such as rotation and bending of upper limbs, and 42 muscle activities around upper body and trunk were measured. FMA is an well-known evaluation method for rehabilitation judged by medical staff.

As a result, 4 synergies related to the whole arm motion, wrist rotation, pinching, and trunk rotation were extracted for each trials. Moreover, by calculating the correlation of synergies among subjects, the difference of correlation by trials were found to reflect the difference in the FMA score.

These results indicated that the data-based indices of muscle synergies could be used in the same manner with FMA score, and this expected the effective use of synergy for the evaluation of rehabilitation process.

IV. Conclusion

A) Experiment and dynamical analysis of standing rats with lesion in inferior olivary nuclei (IO) showed the lesion did not affect the coordination of body segments but affect the transmission of control torque [2].

B) Muscle synergies of congenital insensitivity to pain (CIPA) patients during walking were different from that of healthy subjects in two points: duration of activity and peak timing, and providing touch-down information could modify the walking pattern to safer one with lower floor reaction [3].

C) Evaluation of muscle synergies of stroke patients during Fugl-Meyer Assessment (FMA) showed that the difference in muscle synergy among patients reflected the difference in FMA score, indicating the possible use of synergy for the evaluation of rehabilitation.

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Annual report of research project B03-2

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***Abstract*—Our research purpose is to clarify an important feedback and a control method for embodiment of an extra robotic limb including a robotic thumb. In this year, we shift body representation and evaluate how body schema is modified after use of the robotic thumb. As a result, proprioceptive drifts and task performance improved when subjects controlled the robotic thumb without visual confirmation of its posture. We confirmed that body schema was modified after a grasping task execution with the the robotic thumb.**

I. Introduction

Extra robotic limbs that are developed to support an user as extra arms or fingers attract active attention from robotic researchers [1]. Embodiment of the robotic system is a key to upgrade its operability. Inclusion of an artifact's kinematics into his body representation is important for an user to use the robotic limb as a part of his body. Rubber hand illusion and tool embodiment imply that body representation can be transferred and extended [2] [3]. We aim to transfer body representation about right thumb to the robotic thumb (Fig. 1) on left hand by inducing body transfer illusion. Moreover, we try to construct an evaluation method of embodiment of an extra limb that has more complicated machinery than tools.

II. Research topics

In this research, our trials are to shift body representation and to evaluate how body schema is modified. We verified shift of body representation in a reaching fingertips experiment. Electric stimulation displays tactile information of the robotic thumb on right thumb similarly to rubber hand illusion. After the reaching task, we measured proprioceptive drifts and evaluate how body representation is shifted. To evaluate how body schema is modified, we focus on the difference of height of the arm trajectories before and after a grasping task.

III. Achievements

A. Inducement of proprioceptive drifts

In order to study how body representation can be transferred, we conducted a reaching fingertip experiment. The experimental task is to touch a target finger with the robotic thumb. The target finger is displayed on a monitor in front of a subject. Subjects perform this task for 30 seconds as a set and repeat it for ten sets. We divided subjects into two groups to investigate how visual feedback affects learning efficiency of the robotic thumb control. One group controls it with visual feedback and the other group controls it without visual feedback. As shown in Fig. 2, the learning efficiency improved faster and proprioceptive drifts increased more when subjects performed the task without visual feedback. The experimental results imply that control learning without visual feedback may form a forward model of the robotic thumb efficiently.

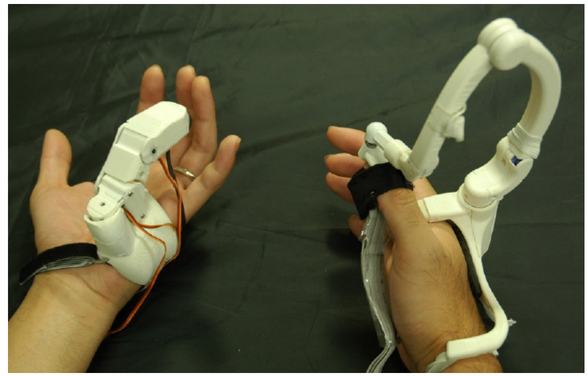

Fig. 1. Extra Robotic Thumb and Control Interface

B. Method to evaluate body schema modification

1) Modification of body representation after a grasping task: We proposed a method to evaluate that kinematics and dynamics models of an extra limb are embedded into body representation. Previous research proved that body representation was extended to tips of tools while using tools [4].

We conducted an object grasping experiment to verify a hypothesis that recovery level from a deviated state represents a degree of body schema modification. Subjects shuttle their arms over a partition grasping an object with the robotic thumb. Before and after this experiment, subjects perform the same task without the robotic thumb. We measured the height of the arm trajectories during the task. As shown in Fig. 3, the arm trajectories became more higher while using the robotic thumb. The height of the arm trajectories does not recover from the initial level after use of the robotic thumb. This anchoring of the arm trajectories implies that the subject plans the arm movement based on body schema including the robotic thumb's kinematics.

2) Recognition of the robotic thumb posture with somatosensory information: We conducted an arm moving experiment to verify that somatosensory information from right thumb enables to recognize a posture of the robotic thumb. Subjects are blindfolded and shuttle their arms over a partition keeping MP joint angle. We evaluate the height of the arm trajectories, keeping various MP joint angles. The experimental results (Fig. 5) prove that subjects can recognize the posture of the robotic thumb based on the somatosensory information through their right thumbs.

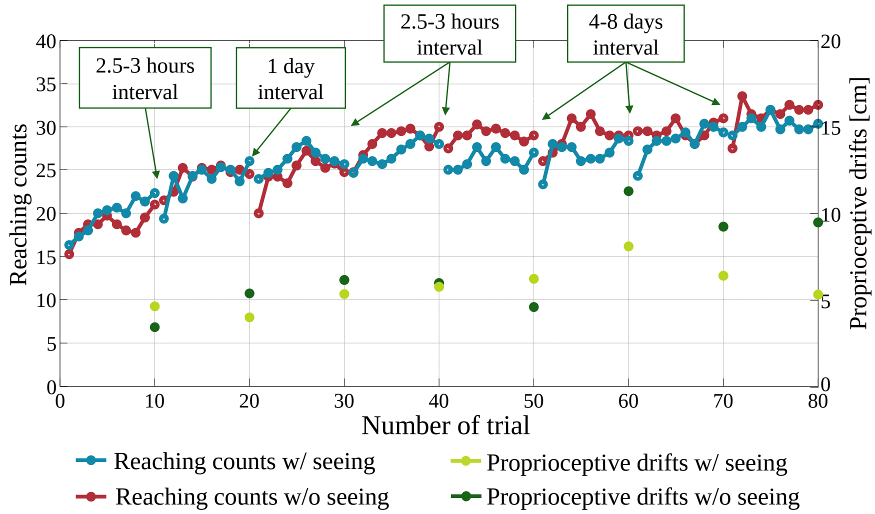

Fig. 2. Reaching counts and proprioceptive drifts

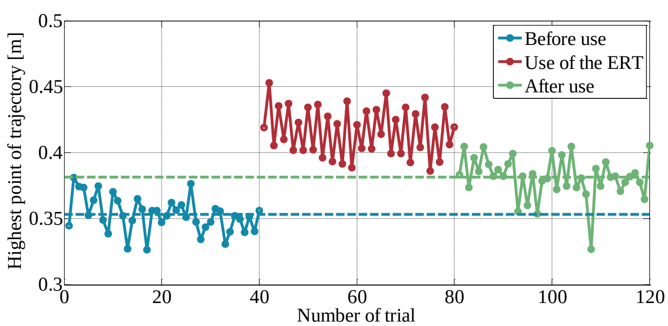

Fig. 3. The highest points of the arm trajectories while a subject performs the task in object handling experiment. Blue broken line represents the average height before use of the ERT and green one the average height after use of the ERT. The height of the arm trajectories after use is higher than one before use.

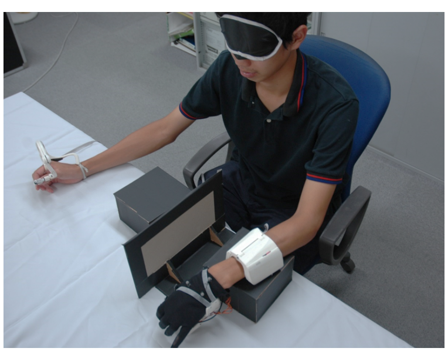

Fig. 4. A picture of arm moving experiment. A partition and two stands are put in front of a subject. Subjects are blindfolded and shuttle their arms over the partition with their palms facing down.

IV. Future perspective

In this year, we try to shift body representation, and evaluate how body schema is modified after use of the robotic thumb. As a result, learning efficiency improved faster and

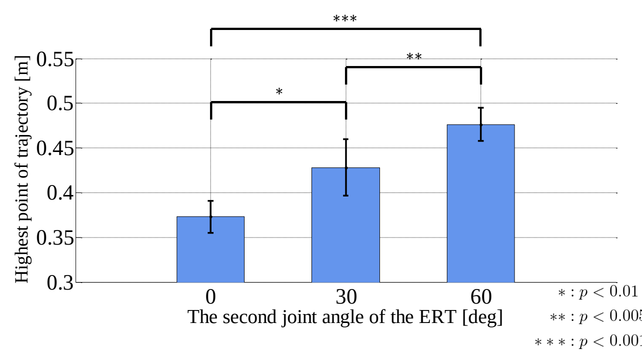

Fig. 5. The highest points of the arm trajectories while a subject performs the task in arm moving experiment without visual feedback. The subject changes the arm trajectories according to the ERT posture.

proprioceptive drifts increased more when subjects controlled the robotic thumb without visual confirmation of its posture. These experimental results imply that control learning without visual feedback forms a forward model of the robotic thumb efficiently. We confirmed body schema was modified after a grasping task using the robotic thumb. In the next year, we are going to compare an inner model of the robotic thumb that subjects learn its operability with or without visual feedback.

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Annual report of research project B03-3

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***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.

ve approach using a humanoid robot with human-like muscular skeletal system and brain-like neuron model (Academic year 2015-2016).

III. Research Topics

A. *Development of a humanoid robot experimental platform with anthropomorphic muscular-skeletal strucutre*

The research project has developed an anthropomorphic humanoid robot experimental platform that has similar muscular-skeletal structure as a human. The platform will be used for experiments of body image acquisition, and the roll of the muscular-skeletal structure will be investigated in a constructivistic viewpoint. The platform is shown in Fig. 1. It has shoulder, elbow, and wrist joints, and a 1 DOF hand. These joints are driven by 28 artificial muscles and 1 spring. The muscular structure is shown in Fig. 2.

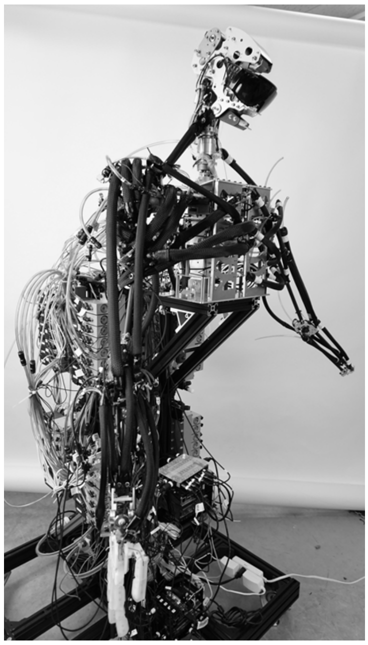

Fig. 1. Muscular-skeletal humanoid upper-body. *(The robot is equipped with 28 artificial pneumatic muscles and 1 spring. It has shoulder, elbow, an wrist joints, and a 1 DOF hand. The muscular structure is similar to that of a human.)*

Each muscle is equipped with pressure and tension sensors, and its state is observed. The length can be calculated from the pressure and tension, and this information can be utilized for generating reflexes.

B. *Preliminary simulation of body-image acquisition*

The project has proposed a framework for dynamical control of a robot based on visual information. The robot can estimate its state from its subjective view based on the convolutional neural network. Based on the estimated state, the robot can learn forward dynamics model, and this can be utilized for control the robot by model predictive control. The effectiveness of this framework is demonstrated by dynamic simulation of a 1 DOF robot arm.

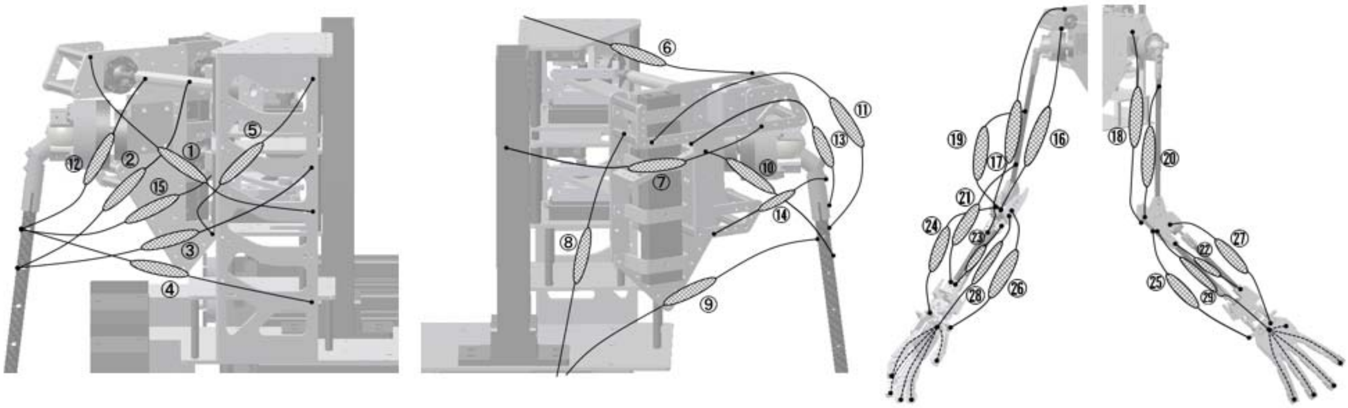

Fig. 2. Musces of the muscular-skeletal humanoid upper-body. (*The robot is equipped with 28 artificial pneumatic muscles and 1 spring: (1)pectoralis minor, (2) pectoralis major, (3) serratus anterior, (4) trapezius (upper), (5) trapezius (middle), (6) trapezius (lower), (7) latissimus dorsi, (8) deltoid (dorsal), (9) deltoid (middle), (10) deltoid (ventral), (11) supraspinatus, (12) infraspinatus, (13) subscapularis, (14) teres minor, (15) biceps brachii, (16) triceps brachii, (17) anconeus, (18) brachialis, (19) brachioradialis, (20) supinator, (21) pronator quadratus, (22) extensor carpi radialis longus, (23) extensor carpi ulnaris, (24) flexor carpi radialis, (25) extensor carpi radialis brevis, (26) flexor digitorum profundus, (27) extensor digitorum, (28) hand flexor, and (29) hand extensor spring*)

C. Constructive understanding of human behavior by using compliant muscular-skeletal humanoid robot

The project has formalized constructive understanding of human behavior by using compliant muscular-skeletal humanoid robot. This is written in the book, "Soft Humanoid Robotics" [1].

IV. FUTURE PERSPECTIVE

This year, the project has developed an experimental platform of an anthropomorphic muscular-skeletal humanoid robot. It also conducted basic simulation of the body-image acquisition based on convolutional neural network and model predictive control. The constructiveist viewpoint of understanding human intelligent behavior is formalized in the book [1].

Experiments will be conducted for understanding the acquisition of body image utilizing the experimental platform developed in this year, applying the local reflexes based on the local receptors of the artificial muscles. By these experiments, the process how the body-image is acquired, what kind of mechanism is needed, and change of the development of the body acquisition in the case of lacking some body parts will be investigated through the constructive approach. These issues cannot be investigated if we only observe the behavior of the real humans. The expected results will play a great role to understand how a human can utilize the body image and what kind of interaction between the slow and fast dynamics can be emerged.

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Annual report of research project B03-4

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***Abstract*— A human fetus/infant is considered to obtain its body schema through physical interaction with his/her environment before and after his/her birth. To obtain a computational understanding that can explain the process through which a fetus/infant estimates his/her body schema, especially its kinematic structure represented by a tree structure, we developed a computational model called Dirichlet process Gaussian mixture model with latent joints (DPGMM-LJ). 1) We showed that DPGMM-LJ could estimate a kinematic structure of an agent having a multi-link kinematic structure in a simulation environment automatically. 2) We also showed that the estimation success rate was high when the system has a certain degree of whole-body motor coordination. 3) To analyze the slow dynamics of phantom limb pain in a constructive approach, we examined the slow dynamics after the agent loses its several limbs in the simulation model using DPGMM-LJ. The comparative study showed that different settings about interpolated information about nervous signals for lost limbs produced different outcomes of body schema estimation.**

I. Introduction

Humans have body maps in motor cortex and somatosensory cortex. Furthermore, to control their body properly, it is important to have a representation of their body structure in the brain. When people develop a robot, they usually give kinematic model involving kinematic structure to the robot to control its body properly. Meanwhile, when researchers model human motor control mathematically, multi-link structure based on tree structure is commonly used to represent kinematic structure of a human body. Here, we call the body representation involving the kinematic structure of the human body, body schema.

To understand the adaptive dynamics of the state space model itself, i.e., kinematic structure, that is driven by multimodal sensorimotor information obtained from the sensorimotor system, it is necessary to clarify the slow dynamics of body schema. Normally, when the multi-link system of the body is described as a graph structure, it does not have a closed path. In this study, we assume that the multi-link structure of the body is a tree structure that is probabilistically generated from a probabilistic generative model. We assume that a human brain estimates its kinematic structure by estimating latent variables of the generative model using Bayesian inference based on sensory information (observations). The inference process is regarded as slow dynamics of body schema.

II. Aim of the Group

The goal of this research group is to construct a computational model that can simulate slow dynamics of body schema based on Bayesian latent tree structure generation process, and to show that the model can determine kinematic structure from multimodal sensorimotor information obtained by the system itself. By achieving this objective, we can obtain a model of slow dynamics of body schema in the brain that models the kinematic structure of the body. It will lead to the new computational interpretation of phantom limb treatment and the invention of new rehabilitation treatments.

In this study, we develop a machine learning method based on Bayesian nonparametrics and develop a probabilistic generative model that generates latent tree structures. By conducting simulation experiments in the virtual space using this computational model, we aim to understand the influence of various conditions about the learning period of the body schema and to obtain suggestions on the adaptation process of the body schema when body parts are injured.

III. Research Topics

Below are three concrete research topics of this fiscal year and explain each outline[1].

A. *DPGMM-LJ for body schema estimation using whole-body tactile information*

We aimed to construct a computational model of the slow dynamics through which fetuses and infants organize intracerebral representations of kinematic structures. Specifically, we proposed the Dirichlet process Gaussian mixture model with latent joints (DPGMM-LJ) as a machine learning method that can estimate the latent tree structure based on whole-body tactile information obtained through random movement [1].

In the previous fiscal year's research, we developed a simulation environment in which an agent having a multi-link body structure, i.e., a tree structure, moved randomly. The agent is regarded as a model qualitatively imitating the human fetus. The agent has many tactile sensors on its whole body and performs a random movement in the simulation environment. We showed that the number of body parts could

[1] In addition to these topics, research on simultaneous estimation of self position, map and body map was conducted. But, details are omitted in this report for the sake of space limitation [5].

be estimated by using Dirichlet Process Gaussian mixture model which is a conventional clustering method based on Bayesian nonparametrics from tactile sensor information alone [2,3]. In this fiscal year's research, we developed DPGMM-LJ, applied it to the same simulation environment, and showed its effectiveness. More specifically, by clustering observed time series data obtained from tactile sensors placed on the surface of a multi-link system, the proposed model could infer the tree structure of the agent's body in a probabilistic manner.

B. *Effect of motor coordination on body schema formation*

Human fetuses present random movements in the womb. The general movement is a characteristic random movement of the fetuses. Although the general movement is a voluntary random movement, a certain degree of correlation between body parts are observed. It is widely known that coordinated body movement, which is also observed in ordinal human behaviors, can be observed in human fetuses' general movement. We conducted an experiment aiming to clarify the influence of such coordinated random movement in the body schema formation process [1]. As an experimental result, when each joint operates independently or moves completely together, i.e., in a fully dependent manner, the estimation result was totally inaccurate. When each body parts moved in a moderately coordinated manner, the estimation result was improved. This suggests that coordinated structure in the in fetal general movement is important from the viewpoint of body schema learning, i.e., slow dynamics of body schema.

C. *Analysis of slow dyanamics of body schema*

We conducted a simulation study on slow dynamics of phantom limbs, which is one of the most important subjects in this research area, using the proposed model, i.e., DPGMM-LJ. Phantom limbs are symptoms that patients feel as if their body parts that were missing still exist even after the parts of their bodies are lost. This condition can be regarded as a situation in which the body schema formed in the brain cannot re-adapt to changed body structure, i.e., body structure without the lost body parts. Therefore, after the agent learn its body schema by using DPGMM-LJ, we broke some of body parts of the agent and observed the re-adaptation process about its kinematic structure estimation (Fig. 1). This means examining the slow dynamics of phantom limbs. As a result, it was observed that the dynamics of the re-adaptation differed greatly across the conditions about how to model the information obtained from the nerves involved in the lost site after the defect (Fig. 2) [4].

IV. Future Perspective

In this fiscal year 's research, we developed a Bayesian inference method of the body schema based on the latent tree structure generation process and verified its effectiveness by the simulation experiments. Also, we could obtain suggestions on the slow dynamics of body schema after the injury of its body using the constructive model.

Meanwhile, considering actual rehabilitation treatments, it is obvious that multimodal information, not only tactile information but also proprioceptive sensation and visual information, play important roles. One of the future studies is to construct a slow dynamics model of the body schema including this information to understand the rehabilitation method and to invent new rehabilitation treatments.

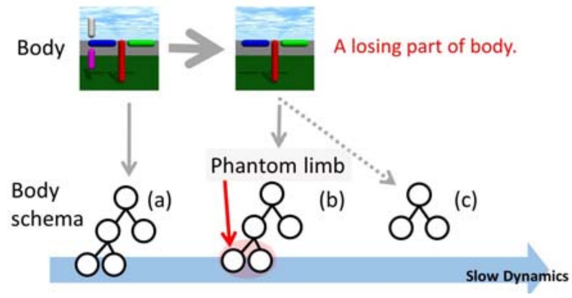

Fig. 1. Schematic description of the simulation experiment

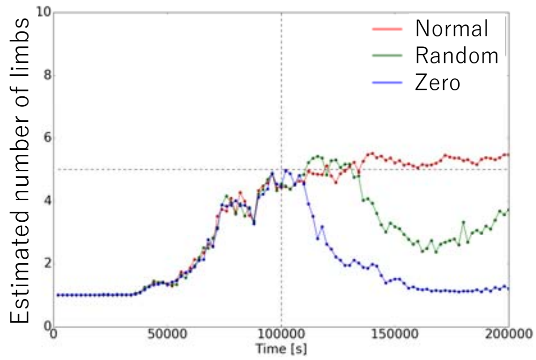

Fig. 2. Slow dynamics of the estimated number of limbs after the system lost its body parts

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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.

<u>C01：Neurorehabilitation based upon brain plasticity on body representations</u>

The body representation stored in the brain cannot be seen by outside person objectively and thus, we alternatively try to visualize and reveal the representation of body in psychophysical 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.

<u>C02：Rehabilitation for postural/movement impairments using sensory intervention</u>

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

<u>Research Project C01</u>

Principal Investigator : Shin-ichi Izumi (Tohoku University)

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

Co-Investigator : Naofumi Tanaka (Teikyo 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)

Co-Investigator: Masahiko Ayaki (Keio University)

Co-Investigator: Fuminari Kaneko (Sapporo Medical University)

<u>Research Project C02</u>

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)

<u>Research Project C03</u>

<u>C03-1</u> Developing a new therapeutic application of neuromodulation

Principal Investigator: Masashi Hamada (The University of Tokyo)

<u>C03-2</u> Muscle Contraction Pattern-Based Direct Rehabilitation Using Motion Estimation And Functional Electrical Stimulation

Principal Investigator: Keisuke Shima (Yokohama National University)

<u>C03-3</u> Development of a clinical tool for measuring dynamic balance function

Principal Investigator: Masahiko Mukaino (Fujita Health University)

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

Principal Investigator: Shu Morioka (Kio University)

III. ACTIVITIES

・ Workshop, Symposium

1st International Symposium on Embodied-Brain Systems Science (EmboSS 2016)

Date: May 8-9, 2016.

Place: Ito International Research Center, The University of Tokyo

Contents: Presentations by program director and members about research.

The 10th International Conference on Complex Medical Engineering (CME2016)

Date: Aug 4, 2016.

Place: Tochigi Convention Center

Contents: Presentations by program director and members about research.

IEEE EMBC 2016 Full-day Workshop on Embodied-Brain Systems Science

Date: Aug 16, 2016.

Place: Disney's Contemporary Resort, Florida, USA

Contents: Presentations by program director and members about research.

・ Group meeting

A and 02 group meeting

Date: Nov. 24-25. 2016

Place：Tokyo Metropolitan Institute of Medical Science

Contents: Research progress reports

C and 01 group meeting

Date: Dec. 13-14. 2016

Place：Tohoku university

Contents: Setting-up of database systems for model based rehabilitation.

・ General meeting

4th General meeting

Date: Feb. 27, 2017. - March 1, 2017.

Place: Meeting room, Kirishima Kokusai Hotel

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

Annual report of research project C01-1

Shin-ichi Izumi
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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

A. *Rehabilitation based on body representation with bodily consciousness*

It is known that a visual target in space near and on the body could be detected faster than that in the space far from the body, known to be “the Nearby hand effect”. This effect is induced by the attention directed to the body, which is called as “bodily attention” , because body continue to be directed by attention in order to monitor the configuration and state of it for body perception and motor control. Our group is aiming to visualize the body representation in the brain by describing the distribution of the bodily attention around the body with a visual detection task. The distribution of the bodily attention in the 2-dimensional space could reflect the body representation in the real environment, because bodily attention is directed in top-down manner to the space based on the body representation in the brain. We conducted some experiments to measure bodily attention to the paretic and intact hand in stroke patients, elucidating the relationship between the bodily attention and motor function, and further bodily consciousness.

1) Alteration of bodily attention resulted from improvement of motor function in paretic limb

Our data of the bodily attention in healthy and stroke patients showed that the bodily attention was not directed to the paretic limb as much as the intact limb of the stroke and healthy participants. To ensure the tight connection between bodily attention and motor function, we designed a longitudinal experiment to examine the alteration of the bodily attention to the paretic limb before and after the therapeutic intervention of paretic limb, including repetitive transcranial magnetic stimulation (rTMS) to the primary motor cortex in damaged hemisphere of the stroke patients followed by motor training. In this study, we measured the reaction times to visual stimulus on either the paretic or the fake-rubber hand before and after TMS intervention for 2 weeks with 600 stimulations followed by 1 hour’s intensive paretic limb exercise in a day, and evaluated the angle range of the metacarpophalangeal joint (MP) in the paretic hand in chronic stroke patients with hemiparesis. The results showed the statistically significant correlation between the change in the bodily attention to the paretic limb in the reaction time task and that in angle range of

MP joint before and after TMS. This strong connection of bodily attention to motor function of the paretic limb suggested that the bodily attention reflect body representation playing an important role in motor execution.

2) The relationship between motor function and body ownership of the paretic limb

According to the experiments by A01 group, the alteration of the body perception caused by making body ownership changed experimentally could affect the motor output of the limb of which body ownership was changed in healthy participants. Thus, we examined the effect of altering the body ownership of the paretic limb caused by the rubber hand illusion to the motor function of the limb in the chronic stroke patients. In this experiment, the patients were instructed to imitate the finger open-close cyclic movements displayed on the head-mounted display (HMD) with the angle of their MP joint recorded in the two situations where the hand displayed in the HMD had body ownership or not. To induce the body ownership toward the hand that the patients were observing in the HMD, before finger movement phase, the patients watched the movie of brushing a hand with a writing brush while either congruent or incongruent brushing in direction and timing was given to their real hands simultaneously. In the results, comparing the ranges of MP joint angle during imitating in the two situations where the observing hand was equipped with or without body ownership by the rubber hand illusion, the body ownership of the observing hand provided statistically significant improvement with their finger movements during imitating the hand movement in the HMD. This result suggests the link of the bodily consciousness to the motor function of the paretic limb in the chronic stroke patients and the possibility of operating bodily consciousness to facilitate motor learning and rehabilitation for motor impairment.

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

Inamura 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. A device named PerceptionNeuron, which can capture whole body motion and finger motion, has been adopted for rehabilitation with grasping motion.

We have started a primitive experiment using this system with members of A01 team. As the first step, we investigated the effect of change of avatar's body appearance on the sense of agency and body representation in the brain. Through an experiment on 12 healthy subjects, we have confirmed that the change of length of the avatar's arm has influence on the body representation in the brain[3]. Since sense of agency/ownership was not affected by the change of the length, it is confirmed that our system does not have any problem to apply to neurorehabilitation.

We also developed a cloud-based motion database for imitation therapy. The relationship between target motions, which are shown to a patient, and response motion by the patient is recorded at a cloud system as shown in Fig.1. The system is already working on a server at NII with MySQL database server. Additionally, this system has flexibility to record not only motion data but also arbitrary biological signals such as pulse rate, EMG and so on. We have already started a collaboration with Prof. Shimada (C03-4 group) about investigation of unconscious reaction for rubber hand illusion.

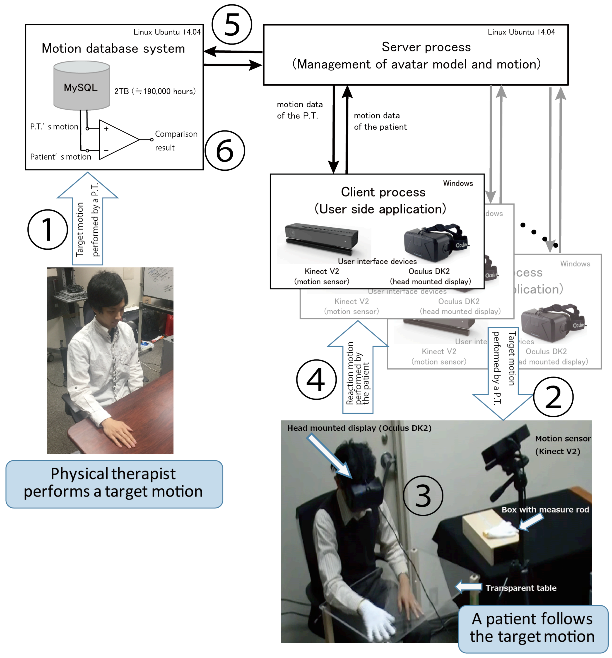

Fig. 1. A system configuration of the imitation therapy using the cloud based sensorimotor database

IV. Future Perspective

Our group are planning to develop the rehabilitation method to improve the bodily attention to the paretic limb, which reflected body representation in the brain. In addition, we will be exploring the way that maladaptive body representation in the stroke patients is reversed by operating body perception experimentally using the VR system.

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Annual report of research project C02-1

Nobuhiko Haga
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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, and 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 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 (CIP) from the aspect of muscle synergy control, and to reveal whether the abnormality could be improved by interventions that compensate sensory disturbance.

The aim of Hanakawa group is to develop new rehabilitation technique for motor disturbance in neurological disorders. The present study first aimed at finding imaging biomarkers in movement disorders. This year, we focused on the application of resting-state fMRI (rs-fMRI) technology to patients with musicians' dystonia (MD).

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 (FES). The analytical method based on fMRI, fNIRS, and EEG is proposed for detecting neuroplasticity produced in motion of limbs induced by muscle synergy control as FD.

The aim of Owaki/Ishiguro group is to verify the short- and long-term effects of a novel biofeedback prosthesis, in which the sensor prosthesis transforms plantar sensations to auditory feedback signals, for patients with sensory impairments and to elucidate brain plasticity on body representation during the rehabilitation process

III. RESEARCH TOPICS

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

Haga/Yozu group had made the up-to-date summary of CIP [1], and had reported on gait abnormalities in CIP patients [2]. Based on the assumption that the gait abnormalities come from abnormalities in muscle synergy control, the investigators had developed a measurement system for muscle synergy of gait in collaboration with Owaki/Ishiguro and Funato groups [3].

This year, the investigators measured two patients by using the above system, and five patients by using another system. The immediate effect of intervention that compensates sensory disturbance has been evaluated [4]. The data of one patient has been analyzed. There were improvements in kinematics and muscle synergy. The maximum plantar pressure during walking has reduced in this patient [5,6,7,8]. The investigators have also proposed new methodologies to express various types of gait [9,10,11].

B. Changes of body representations in movement disorders

Twenty-one patients with MD of the right hand and 34 healthy musicians participated in the study [12,13]. We acquired rs-fMRI during a visual fixation task at a 3T magnet. We also obtained MIDI information during piano playing, and used variability of inter-keystroke interval (IKI) as a measure of motor performance. After preprocessing of rs-fMRI data, we applied group-ICA analysis to retrieve resting-state networks (RSN) at a group level, and then performed a dual regression analysis using motor-related RSN as networks of interest. The results showed abnormally enhanced within-RNS functional connectivity in the basal ganglia for the patients with MD as compared with the control. Furthermore, the functional connectivity correlated with the variability of IKI (poorer the performance, higher the connectivity). This study suggests that rs-fMRI may provide a useful biomarker for MD.

C. Study on patients with motor impairments due to stroke

Yokoi/Sugi group studies muscle synergy control disorders due to brain strokes. In order to evaluate skill levels of inter-limb coordination tasks at the recovery of motor function after stroke, we have proposed a quantitative evaluation method based on transfer entropy. A walking task, often used in rehabilitation after stroke, is chosen as the target task. According to transfer entropy analysis between EMG data of lower limb muscles, we found that the difference of transfer entropy from left to right leg muscles and the one in reverse along the time delay t reflects the skill levels of inter-limb coordination [14]. Using this method, we can quantitatively evaluate the change of SD of patients in rehabilitation training.

In order to realize intervention in muscle synergy control FD by FES, we have also developed a FES system based on multiple stimulation electrodes and biphasic burst-modulated rectangular stimulation wave for hand and upper limb rehabilitation. This FES system has various tuning parameters, e.g. stimulation patterns (anode/cathode/neutral setting for each electrode), time intervals of stimulation between electrodes, and wave profiles, which are adjusted according to individual patient. In this context, we are now studying the following three topics; (1) quick search of appropriate stimulation pattern, (2) optimal time intervals of stimulation between electrodes that induces large concentric muscle contraction, and (3) stimulation wave profiles suitable for surface FES [15,16].

D. Efficacy of prosthetics transforming sensory modalities

Owaki/Ishiguro group, using their prosthetics transforming sensory modalities (Auditory Foot) [10,11], which transforms cutaneous plantar sensation to auditory feedback signals during walking, performed researches on short- and long-term effects on walking in stroke patients [17,18,19], and muscle synergy model-based rehabilitation for CIP patients [8].

In the former, we have investigated the clinical effect in collaboration with C01 group (Prof. Izumi and Dr. Sekiguchi). We compared four conditions: (i) Without auditory feedback (AF) (with prosthetics); (ii) AF from only heel sensor; (iii) AF from only fifth metatarsal sensor; and (iv) AF from both sensors. We recruited stroke patients with hemiplegia, and confirmed significant difference in the maximum hip extension angle and ankle plantar flexor moment of the affected side during stance phase between the conditions (i) and (iv) [8, 9]. Moreover, we performed walking rehabilitation for 1 month and have got and are analyzing the clinical and kinematics/ kinetics data for 10 patients before/during/after rehabilitation.

In the latter, we have established a novel rehabilitation system for "Muscle Synergy Model-based Rehabilitation", which can monitor muscle synergy as indirect marker of body representation in real-time and perform effective rehabilitation using Auditory Foot, in collaboration with B03-1 (Dr. Funato) and C02 (Dr. Yozu) Group. For a CIP patient, we found that auditory biofeedback signals reduced maximum plantar pressure during walking.

IV. Future Perspective

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

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Annual report of research project C03-1

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***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 [1]. For example, we have shown previously that expected response rate by theta burst stimulation (TBS) is about 50%. 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) [2,3] for NIBS protocol. We have shown last year that the effects of QPS are less variable than other NIBS protocols [4]. We have tested whether QPS has an impact on motor learning this year. Furthermore, using TBS, we have tried to identify the reason for huge variability of TBS.

Meanwhile, we also tested the effects of rTMS on motor learning last year. We developed 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. *Effect of QPS on motor learning*

First, our group tested the effects of excitatory QPS at 5 ms (QPS5) and inhibitory QPS at 50 ms (QPS50) on motor learning. Motor task used in this experiment is repetitive finger abduction task, which is often used as used dependent, model free learning. After baseline measurements of MEP, QPS was applied to the hand area of primary motor cortex, followed by finger abduction task. Figure showed the time course of acceleration of finger abduction.

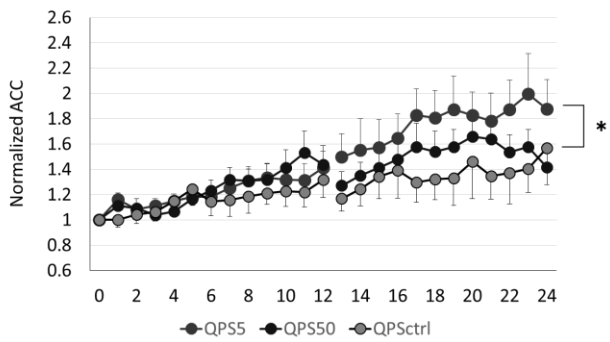

Fig. 1. Time course of finger abduction acceleration after QPS.

Compared to the control QPS condition, we found significant increase of acceleration after QPS5, but not after QPS50. We have shown previously that other NIBS protocol which increase the excitability of stimulated area can also increase acceleration of finger abduction task and that possible explanation would be that given this kind of repetitive movement where recruitment of cortico-spinal neurons (CSNs) projecting to target muscles would generate a burst of activity in synergistic muscles, increasing the excitability of CSNs may help to increase synergic activity during finger abduction task [5]. Likewise, since QPS5 indeed increase CSN excitability and thus helps to generate a burst of activity in synergistic muscles.

B. *The effects of stimulation intensity on TBS response*

We have shown previously that TBS effects rely on greater activation of later I-waves; people in whom late I-waves are recruited have “expected” responses to TBS, while people in whom early I-waves are recruited demonstrate the opposite responses [1]. The results indicate that depending on the difference in stimulated I-waves (early vs. late), the effects of TBS could be differ. We thus focused on the stimulation intensity of TBS, since the intensity itself substantially affect I-wave recruitment. Usually 80% active motor threshold is used for TBS. It is therefore possible to assume that the I-wave component would be differ substantially among different people using this "fixed" intensity. More specifically, we hypothesized that preferential activation of late I-wave cannot be obtained in non-responder of TBS, and thus opposite response is induced in these people.

We conducted the experiments using TBS with different stimulation intensity. The results showed that changing the intensity had a huge impact on TBS response. The non-responder became responder when we decreased the stimulation intensity and vice versa.

We conclude that TBS responses are dependent on stimulation intensity and that the ease of I-wave recruitment may implicated in our findings.

C. *Gait analysis using pressure sensor sheet*

Third, in collaboration with C02 group, we have started to measure gait using pressure sensor sheet last year. 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 patients.

Stride was smaller and step width was larger in patient compared with healthy subject. We have already tested 20 parkinsonian patients and age matched healthy participants this year.

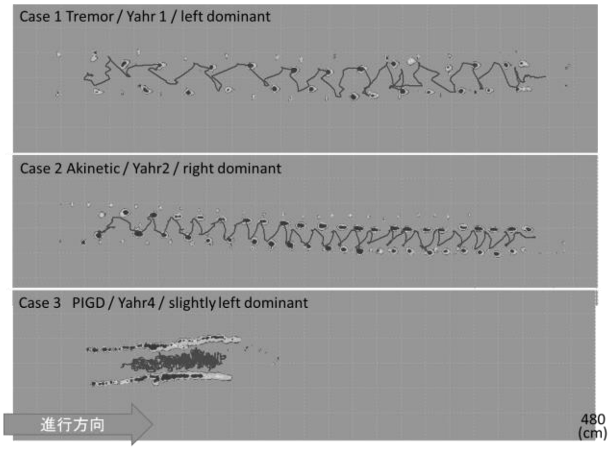

Figure 2. Gait analysis in healthy and Parkinsonian patient

IV. Future Perspective

We firstly showed that the effects of QPS on motor learning. We also revealed that stimulation intensity is an important determinant of NIBS protocols. 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, QPS has an impact on motor learning and therefore it might be better to use this technique to improve motor deficit/impairment in neurological patients. Second implication is that stimulation intensity, which substantially affect which neurons are more likely to be stimulated, is an important determinant of NIBS outcomes. Finally, using our gait analysis system, we will investigate potential therapeutic effects of NIBS in near future.

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Annual report of research project C03-2

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***Abstract*—The author proposed a new human-human interface design [1], [2] involving the classification of patterns in multi-channel electromyograms (EMGs) and controlled electrical stimulation on a multi-channel basis.**

In 2016, the following achievements were made: 1) development of a new electrode selection method for functional electrical stimulation; 2) proposal of a Bayesian classification method based on the new approximate GMM toward hardware implementation in order to realize pattern classification with high accuracy on a FPGA; 3) implementation of novel haptic equipment incorporating electrical and fingerpad stimulation as part of an applicable unit for virtual force generation; and 4) development of a training system based on a multi-class brain-computer interface (BCI) and usage of electrical stimulation. The outcomes of this research are expected to support effective motor skill training in clinical environments.

I. Introduction

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. 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.

II. Aim of the study

This study was conducted toward the development of a novel rehabilitation method based on a combination of functional electrical stimulation (FES) and electromyogram (EMG) pattern classification to support the evaluation and control of muscle contraction patterns for patients with hemiplegia caused by stroke or spinal cord injury. 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 [1], [2].

The technique is designed to enable the selection of effective electrode placement in FES-based rehabilitation based on current-joint angle characteristics. For efficient EMG pattern classification, a novel approximated static model and a neural network supporting hardware implementation are also proposed. A novel haptic device design based on electrical and mechanical stimulation of the fingertips and a BCI-based rehabilitation method are additionally considered. The technique can be considered potentially beneficial in areas such as rehabilitation for EMG-based motor function and training in EMG-based complex skills.

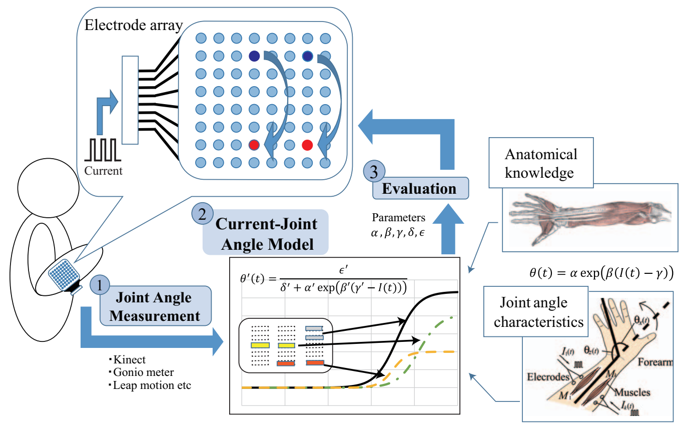


Fig. 1. Proposed electrode selection method

III. Research topics

A. Electrode positioning based on current-joint angle characteristics

Electrode positioning for efficient electrical stimulation is paramount in FES-based rehabilitation because stimulation in inappropriate locations places a physical burden on the subject. However, it is very difficult to locate the motor point of each muscle, and therapists must find appropriate positions through trial and error based on anatomical expertise in clinical environments.

This study involved the examination of a novel model for estimation of current and joint-angle characteristics in FES (defined as per Eq. (1)) and the development of an optimal channel selection method based on the parameters of a model for efficient stimulation (Fig. **??**).

$$\theta(t) = \frac{\epsilon'}{\delta' + \alpha' \exp(\beta'(\gamma' - I(t)))} , \quad (1)$$

where $\theta(t)$ is the joint angle measured from the subject, $I(t)$ is the current, and $\alpha', \beta', \gamma', \delta'$, and ϵ' are real coefficients estimated from measurement data using the least squares method. Sample current-joint angle characteristics and the estimation model are shown in Fig. **??**. The experimental results gave a motor point for stimulation as estimated on the basis of anatomical expertise and previous study, and indicated that more effective positions can be determined using a multi-channel electrode array (64 electrodes) with the proposed method [3].

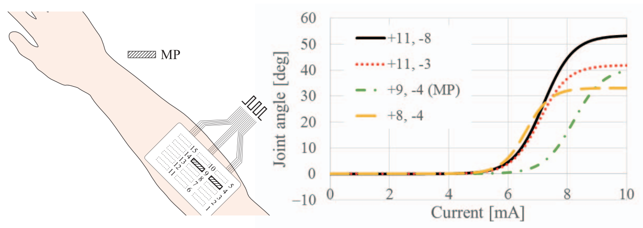
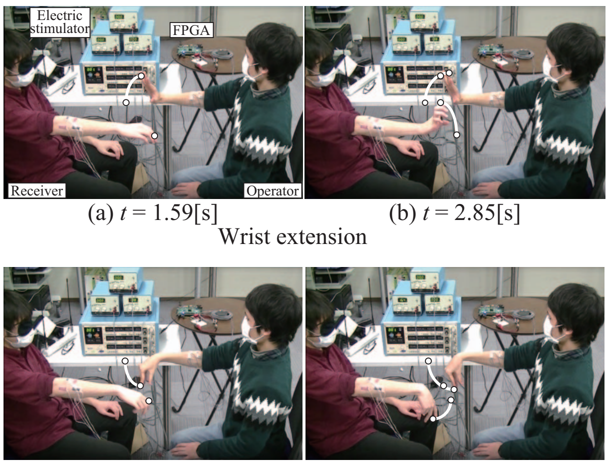


Fig. 2. An example of electrode selection experiments (current-joint angle characteristics)



(a) $t = 1.59$[s] (b) $t = 2.85$[s]
Wrist extension

(c) $t = 4.58$[s] (d) $t = 5.26$[s]
Wrist flexion

Fig. 3. FPGA-based human-human interface

B. Approximated GMM for EMG classification

To support effective rehabilitation based on the proposed method in clinical environments or at patients' homes, this study focused on the development of a new approximated Gaussian mixture model toward the implementation of hardware such as FPGAs. Incorporation of the proposed approximated GMM into a neural network structure enables GMM-based classification using arithmetic operations and shift units on hardware for EMG pattern classification with high accuracy [4]. Figure **??** shows experimental application of the proposed system with an FPGA. The proposed hardware model allows EMG and FES-based rehabilitation without a PC.

C. Haptic device design based on somatosensory stimuli

The study reported involved consideration of a novel design for haptic devices enabling the generation of virtual forces based on the curent-joint angle model. With this approach, a small-scale mechanical unit is used to deform fingerpads and fingertip position is controlled using electrical stimuli (Fig. **??**). These outcomes underline the feasibility of the approach for application with a wearable device for force feedback in a virtual reality system [5].

D. BCI-based rehabilitation system

For efficient rehabilitation based on neural motor commands, this study involved the consideration of a motor learning system based on multi-class pattern classification of

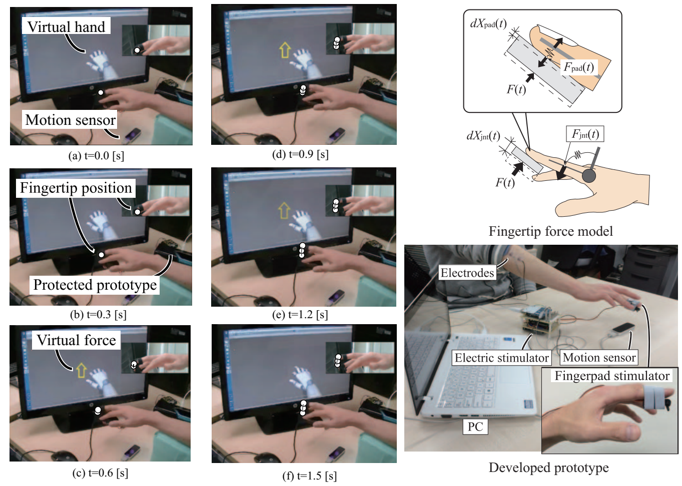
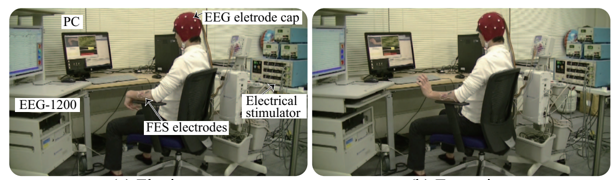


Fig. 4. Proposed wearable haptic system based on somatosensory superimposed stimuli [5]



(a) Flexion (b) Extension

Fig. 5. BCI-based rehabilitation system

electroencephalograms (EEGs) and FES. Examples of wrist flexion/extension training are shown in Fig. **??**.

IV. Future perspectives

This report outlines proposed methods enabling the communication of information on muscle contraction patterns and joint movements between two subjects (such as a therapist and a patient) based on high-accuracy classification of EMG and EEG signals. These approaches can be used to support rehabilitation tasks such as motor skill training in clinical environments or at home. In future work, the author plans to investigate the effectiveness of motor skill training using the proposed method and to discuss how training may influence motorneurone function based on collaborative research. Combinations of robot-based rehabilitation should be considered for more effective training

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Annual Report for Research Project C03-3

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I. Abstract

Recent clinical studies have revealed the complexity of the balance maintenance system. To accurately evaluate rehabilitation effects, objective monitoring is required to identify the balance maintenance mechanism and measure the effect of intervention, including its effect on daily activities. This study aims to develop an objective method for quantifying dynamic balance abilities and clarify the variable relationships, which may advance the current understanding of the neural and physical systems for balance maintenance. In this study, we attempted to develop several indices to objectively and simply measure dynamic balance function based on the relationship between the center of gravity (COG) and the center of pressure (COP), as well as investigate the relationships between these indices. The subjects comprised 29 hemiparetic post-stroke patients. Simultaneous COG and COP measurements were performed using a three-dimensional motion analysis system (Kinematracer, KisseiComtec, Japan) combined with a force plate system (Tech Gihan, Japan). For the indices for evaluating dynamic balance function, we calculated the average (|COP|−|COG|) difference during stance phase (ASV), COG and COP velocity, and the percentage of time that the COG and the COP directions matched (%match). According to the results, the correlation coefficient between the COG velocity at heel contact and the ASV was 0.85, suggesting that the COP-COG relationship could be a major driving force of COG movement during stepping. The multiple regression analysis with ASV as a dependent variable, and with these two variables as explanatory variables, showed a relatively good fit, with a determination coefficient of 0.75. These results indicate that the relationships between the indices could be used to explain the ability to control COG movement. We encourage further investigation into the feasibility of COP-COG measurements to evaluate balance ability.

II. Introduction

Previous studies have shown the importance of balance function for patients' gait and everyday activities. Thus, balance function has been one of a major rehabilitation target (1,2). To accurately evaluate rehabilitation effects, objective monitoring is required to identify the balance maintenance mechanism and measure the intervention's changes, including its effect on daily activities.

Previous studies have described the balance function as a multifaceted system, and clinical scales have been developed to selectively evaluate each of its aspects (3). These well-structured clinical scales, however, are not commonly used in clinics, possibly because they are time-consuming and have minimal impact on clinical decision-making. There are also large-scaled measurement systems to measure dynamic balance, however, such kinds of systems are not commonly used because the systems are very expensive and time-consuming. so it is still difficult to evaluate the multiple aspects of balance and how the body system maintains it in the daily clinics. Instead, clinical balance function is commonly evaluated using rather simple clinical screening scales, or posturography that examine center of foot pressure movement which can be used only to evaluate static balance function.

In this study, we developed a simplified measurement system for evaluating balance function that focuses on relationship between center of gravity (COG) and center of pressure (COP) during the stepping movement. This system makes detailed and dynamic balance function evaluation simpler and more clinically feasible.

III. Group Aim

This study aims to: 1) confirm the validity of the COG-COP movement measurement; 2) develop simplified indices for measuring balance functions; and 3) clarify the relationships between the indices to facilitate a better understanding of balance maintenance systems.

IV. Research Topics

Methods

The subjects comprised 29 hemiparetic post-stroke patients. Patients were included if they met the following criteria: (1) they were able to stand and step five times and (2) do so independent of assistance from others or devices (e.g., handrails, canes, and orthotics). The subjects included 18 males and 11 females with a mean age of 60±9 years. Of the 29 patients, 17 had right hemiplegia, and 12 had left hemiplegia.

The simultaneous COG and COP measurements were performed using a three-dimensional motion analysis system (Kinematracer, KisseiComtec, Japan) combined with a force plate system (Tech Gihan, Japan). To calculate the COG, markers were bilaterally attached to 10 landmark sites on the body: the acromion processes, the hip joints (one-third the distance between the greater trochanter and the anterior superior iliac spine), the knee joints (the femur's lateral epicondyle midpoint), the lateral malleoli, and the fifth metatarsal heads. The virtual COG was calculated using software that estimated measurements based on Ehara and Yamamoto's equation (4). The subjects were asked to step on the force plate 10 times, allowing us to measure the dynamic balance ability on the lateral axis. Before and after the task, she ubjects remained standing for five seconds. The following values, which are based on the COG-COP relationship, were calculated and averaged for each step: ASV, the average (|COP|-|COG|) difference, which measures the COG-COP displacement gap index; COGVhc, the COG velocity at heel contact; COPVmax, the maximum COP velocity during stepping; and %match, the percentage of time that the COG and COP directions matched. The Berg Balance Scale (BBS), which is frequently used to evaluate balance function, was also scored for its evaluation validity.

Results and Discussion

First, we investigated the correlation between the ASV and the BBS, which were shown to be highly correlated in the previous preliminary report. We found a correlation coefficient of 0.51, which is significantly lower than described in the previous report, in which the correlation coefficient was as high as 0.90. Since ASV can be influenced by the foot pressure control range, the partial correlation coefficient between the BBS and the ASV was calculated excluding the effect of step width, generating a value of 0.75. This can be interpreted as relatively high, thus showing that the ASV at least partially reflects balance ability.

The COG-COP relationship is known to be related to COG acceleration. Therefore, we examined the relationship between the ASV and COG velocity. The correlation coefficient between COG velocity at heel contact and the ASV was 0.85 (Figure 1).

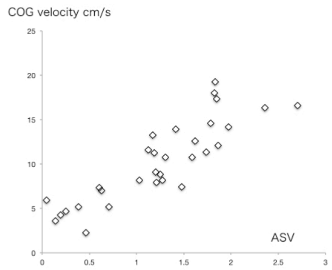

Figure 1 Correlation between COG velocity and ASV

In addition, we hypothesized that the ASV would be determined by the ability to control COP direction to follow COG movement, and by the ability to move the COP fast enough to overtake the COG. Thus, the percentage of time that the COG and COP directions matched (%match) and the COP maximum speed (COPvmax) were used as an index indicating the ability to quickly move the COP. The multiple regression analysis with ASV as a dependent variable and these two variables as explanatory variables showed a relatively good fit, with a determination coefficient of 0.74 (Table 1). Based on these results, Figure 2 shows the possible relationships between the variables.

Table 1 Multiple regression analysis results

Variables	partial regression coefficient	standardized partial regression coefficient	t	p
%match	0.039	0.729	7.49	<.0001*
COPVx max	0.003	0.384	3.95	0.0005*
Constant	-2.924		-6.18	<.0001*
adjusted R^2	0.740			

V. Future Perspective

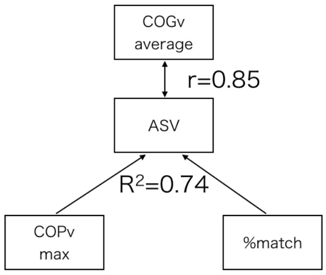

Figure 2 Relationships between variables

These results indicate that the relationship between the COG and the COP reflects balance function, as shown in the preliminary report. The COP velocity correlated with he ASV, and the ASV was majorly explained by the COP velocity and the ability to control the COP direction.

To further advance the comprehensive understanding of balance maintenance body systems, we propose the following research avenues: (1) the development of applicable parameters other than the step motion; (2) investigation into intervention effects on these parameters; (3) further investigation into the relationships between these indices and gait parameters; and (4) investigation into these parameters' relationships and those of other measurement methods, such as electromyograms and brain imaging.

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Annual report on research project C03-4

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Abstract— **We examined sensory integration in apraxia using delayed visual feedback methods. We found a specific impairment of motor predictions in apraxia. Furthermore, our results revealed that sensorimotor incongruence promoted distorted body consciousness as well as a change of muscle activation patterns during periodic movement. We also found that sensorimotor integration incongruence affects brain activity and motor performance, as well as motor learning.**

I. Introduction

It has been suggested that disownership and/or a loss of agency occurs in apraxia and hemiplegia after a stroke. However, there are no objective, quantitative evaluations of the symptoms of disownership and loss of agency that occur in these disorders. In addition, the influence of sensorimotor integration incongruence on muscle activity, brain activity, motor performance, and motor learning is not clear.

II. Aim of the Study

We performed four studies: A, B, C, and D.

The purpose of study A was to objectively and quantitatively evaluate disownership and loss of agency in apraxia using a visual feedback delay system.

The purpose of study B was to quantify distorted body consciousness and muscle and brain activation changes caused by visuomotor asynchrony. This was achieved using an electromyogram (EMG) and an electroencephalograph (EEG).

The purpose of study C was to investigate the effect of visuomotor temporal discrepancy on manual dexterity as well as the contribution of the contralateral limb reference to motor performance.

The purpose of study D was to investigate the adverse effects of visuomotor incongruence on motor learning using a visual feedback delay system. The neural mechanism of these effects was studied using near-infrared spectroscopy.

III. Research Topics

A. Quantitative evaluation of disownership and loss of agency in apraxia

This study used a task to detect delayed visual feedback (Shimada et al., 2009, 2010, 2014) in response to three types of stimulation (tactile stimulation, passive movement, and active movement) to examine the precision of multisensory integration in apraxia.

We found that the threshold for the detection of delayed visual feedback (DDT) was extended significantly when apraxic limbs were actively moved compared with when non-apraxic limbs were actively moved. The gradient of the probability curve for DDT (hereafter "steepness") was significantly flatter when apraxic limbs were actively moved compared with when non-apraxic limbs were actively moved. However, there were no differences in DDT or steepness from tactile stimulation or passive movement in apraxic or non-apraxic limbs. In addition, the severity of apraxia was significantly correlated with DDT and steepness during active movement (Fig. 1).

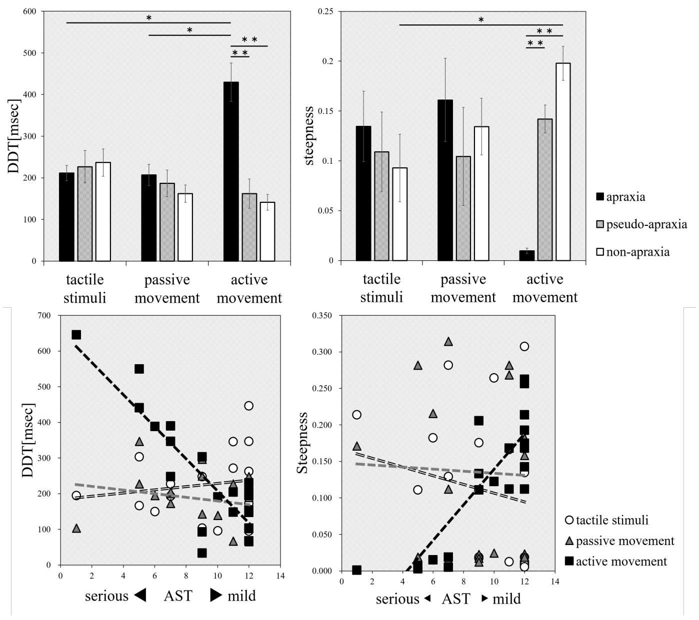

Figure 1 A comparison of the DDT and steepness of each group, and their correlation with apraxia severity

These results suggest that apraxia causes a deficit of motor predictions (efference copy, predicted sensory feedback) and an unconscious loss of agency of the sense of limbs.

To verify the impairment of motor predictions, we are currently investigating the motor-related potential of apraxic patients. As a preliminary study, we investigated the effect of sensorimotor discrepancy on motor-related potentials for healthy volunteers.

B. The relationships between sensorimotor incongruence and limb perception, EMG, and EEG activity

Visual feedback delay was introduced using a hardware device (EDS3305; Eletex, Osaka, Japan) connected between the video camera and the monitor. Five delay conditions (0, 150, 300, and 750 ms delays) between self-generated movement and visual feedback were used to induce sensorimotor incongruence. We evaluated limb perception and EMG activity as well as motor-related potentials, which were observed in the contralateral motor cortex. Our results showed that the sense of disownership and limb heaviness increased with increasing delay time, and movement rhythm and muscle activity were decreased with increasing delay time. Additionally, the latency of peak amplitude in motor-related potentials was delayed (Fig. 2).

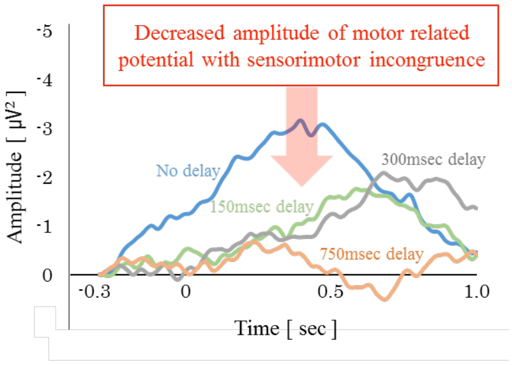

Figure 2 Attenuation of motor-related potential with sensorimotor incongruence

In the present study, the time delay between self-generated movement and visual feedback altered not only limb perception and movement rhythm, but also motor cortical activity. We therefore revealed that sensorimotor incongruence was able to distort the motor program. These results suggest a disease model for the distorted embodiment that occurs in patients with apraxia or hemiplegia. We plan to record motor-related potentials of clinical patients in the future.

C. The influence of visuomotor incongruence on motor control and the reference effect of the limb

These studies were performed on 20 right-handed, healthy volunteers using the visual feedback delay system during a peg board task. The conditions were 1) a "real-time condition", without video delay/reference; 2) "reference condition", with a 300 ms delay of the video; and 3) "no-reference condition". The contralateral limb was used as the reference. The subjective difficulty level under each condition was recorded on a 7-point Likert scale. Furthermore, brain activity at the time of performing each condition was measured using near-infrared spectroscopy (FOIRE 3000; Shimadzu Co., Ltd.). Effect size (ES) was used as an indicator.

In this study, performance was significantly decreased in the no-reference condition compared with the real-time and reference conditions. The subjective difficulty level of the no-reference condition was significantly higher compared with the real-time condition. Furthermore, the ES of the left parietal lobe of the reference condition was significantly increased compared with the no-reference condition. There was also a significant correlation between performance and the ES of the left parietal lobe.

This study thus showed that visuomotor discrepancy reduces manual dexterity, but performance is improved by the reference effect of the contralateral limb. Furthermore, the current results suggest that the reference effect of the body is related to the parietal lobe.

D. The influence of visuomotor temporal integration on motor learning

In this study, 30 right-handed, healthy volunteers were required to practice pegboard tasks under the video delay system, to investigate the effect of visual feedback delay on motor learning. The subjects were divided into three groups: 1) the practice group under real-time conditions (10 subjects), 2) the practice group with a visual delay of 300 ms (10 subjects), and 3) the practice group with a 600 ms delay (10 subjects). We conducted three trials of pegboard practice under each condition. Brain activity during practice was measured using near-infrared spectroscopy. According to our results, the real-time group and the 300-ms-delay group were significantly improved after practice compared with before practice. There was no change in performance in the 600-ms-delay group. In addition, the performance of the real-time group was significantly improved compared with the 600-ms-delay group. There was also a significant correlation between performance and the ES of the middle parietal region and left parietal lobe. This study showed that motor practice under visuomotor synchrony is more effective than motor practice under asynchrony. In addition, performance in the pegboard task was shown to be related to parietal lobe activity.

IV. FUTURE PERSPECTIVES

Future studies will attempt to elucidate motor prediction abnormalities in apraxic patients using electrophysiological methods. Future studies will also investigate the effects of interventions that may facilitate sensorimotor integration in disorders such as hemiplegia, apraxia, asomatognosia, and chronic pain.

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52. J. Ota: Embodied-brain Systems Science: Introduction and Overview Workshop on Embodied-Brain System Science and Robotics Engineering for Rehabilitation Padua, Italy 2016
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62. H. Imamizu: Change in brain activity during motor learning 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC2016): Workshop "Embodied-Brain Systems Science and Neurorehabilitation" Orlando, Florida, USA 2016
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72. T. Yamamoto, T. Hayashi, Y. Murata, H. Onoe, and N. Higo: Increased projections from ventral premotor cortex to deep cerebellar nucleus after primary motor cortex lesion in macaque monkeys, The 10th FENS Forum of Neuroscience Copenhagen, Kingdom of Denmark. 2016
73. T. Oya: Neural representation of muscle synergy in primate red nucleus and motor cortex Embodied-Brain: Perspectives from Motor Control and Muscle Synergies Taormina, Italy 2016
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78. Kamada. K: Stroke rehabilitation at Asahikawa University recoveriX and mindBEAGLE workshop Monterey USA 2016
79. Kamada. K, Tamura. Y, Ogawa. H, Anei. R: Novel passive language mapping with mild awake state for tumor surgery Osaka 2016
80. Kamada. K: Clinical Impact of Real-time passive mapping, 38th EMBC Workshops & Tutorials Orlando, USA 2016
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86. K. Shima and K. Shimatani: A New Approach to Direct Rehabilitation Based on Functional Electrical Stimulation and EMG Classification 2016 International Symposium on Micro-NanoMechatronics and Human Science Nagoya, Japan 2016
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89. Kamada. K: ECoG-based BCI for motor functions, BIOMAG 2016 Korea 2016
90. Kamada. K: Passive mapping and active monitoringof ECoG in brain pathology 11th International Workshop on Advances in Electrocorticography Texas, USA 2016
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92. Mohamad Arif Fahmi Bin Ismail, Sotaro Shimada: The Effect of Delayed Visual Feedback on 'Robot' HAnd Illsuion: a near-infrared spectroscopy study. The 20th Annual Meeting of Association for the Scientific Study of Consciousness Buenos Aires, Argentine Republic 2016
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104. H. Imamizu: Neural mechanisms underlying sense of agency 4th mini-symposium on Cognition, Decision- making and Social function RIKEN Brain Science Institute (BSI), Saitama, Japan 2016
105. A. Takai, T. Noda, G. Kisi, T. Teramae, H. Imamizu, and J. Morimoto: Learning arm movements instructed by a robotic system during motor imagery Society for Neuroscience 2016, San Diego, USA. 2016
106. M. Hamada: Plasticity of human motor and sensory cortices induced by non-invasive brain stimulation, The 10th ICME International Conference on Complex Medical engineering (CME2016), Utsunomiya Japan, 2016
107. M. Hamada: Determinants of the induction of cortical plasticity by theta burst stimulation 6th International Conference on Transcranial Brain Stimulation Goettingen, Germany 2016
108. M. Hamada: Current direction - Basic physiology and plasticity 2nd International Brain Stimulation Conference Barcelona, Spain 2017
109. T. Sasaki, S. Tokushige, N. Togashi, S. Terada, Y. Terao, Y. Ugawa, and M. Hamada: Effect of subthreshold paired associative stimulation during voluntary contraction on motor learning 2nd International Brain Stimulation Conference Barcelona, Spain, 2017
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111. M. Hamada: Deep Brain Stimulation and Neuromodulation of Neurodegenerative Disorders, Irvine, CA, USA 2016
112. M. Hamada: rTMS for Parkinson's Disease International Symposium on rTMS treatments Tokyo, Japan 2016
113. M. Hamada: Physiological Background of TMS and Repetitive TMS 13th NMG Practical Course Transcranial Magnetic and Electrical Stimulation Göttingen, Germany 2016
114. M. Hamada: A new therapeutic application of neuromodulation The 1st International Symposium on Embodied-Brain Systems Science (EmboSS 2016) Tokyo 2016
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120. J. Lee, S. Kakei: Development and clinical application of a novel system to make quantitative evaluation of motor function using wrist movement IGAKUKEN Summit for Japan and Korea Science Leaders 2016 Tokyo, Japan 2016
121. S. Izumi: A new system for exercise of upper extremity of patients after stroke with using peripheral nerve magnetic stimulation device Biomedical Engineering ecosstem symposium Kuangfu campus, Taiwan 2016
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126. A. Ikeda: Advanced techniques in HFO analysis. Workshop HFOs and the Epileptogenic Zone, 11th Asian & Oceanian Epilepsy Congress (AOEC) Hongkong, China 2016
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154. T. Inamura: Effect of flexible change of VR based self-body appearance for bodyrepresentation in the brain, 2016 EMBC workshop on embodied-brain Systems Science and rehabilitation Florida, USA, 2016
155. T. Inamura: A Cloud Based VR Platform for Sharing Embodied Experience in HRI The 2016 IEEE/RSJ International Conference on Intelligent Robots and Systems, Daejeon, Korea, 2016
156. T. Mimura, Y. Hagiwara, T. Taniguchi and T. Inamura: Clustering latent sensor distribution on body map for generating body schema, The 14th International Conference on Intelligent Autonomous Systems Shanghai, China 2016
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Member List

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

Principal Investigator	Jun Ota (Professor, The University of Tokyo)
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<u>Research Project A01-1: Neural mechanisms inducing plasticity on body representations</u>

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Co-investigator	Cai Chang (Researcher, ATR)
Co-investigator	Ryu Ohata (Researcher, The University of Tokyo)

<u>Research Project A02-1: Neural adaptative mechanism for physical changes</u>

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

Principal Investigator	Kaoru Takakusaki (Professor, Asahikawa Medical University)
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Co-investigator	Kazuhiro Obara (Assistant Professor, Asahikawa Medical University)
Co-investigator	Mirai Takahashi (Assistant Professor, Asahikawa Medical University)
Co-investigator	Seiji Matsumoto (Lecturer, Asahikawa Medical 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 A03-4: 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 (Professor, Ehime 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)
Co-investigator	Kazumichi Yoshida (Lecturer, 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)
Co-investigator	Soichiro Fujiki (Assistant Professor, The University of Tokyo)
Co-investigator	Shohei Shirafuji (Researcher, The University of Tokyo)

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)
Co-investigator	Masahiko Ayaki (Associate Professor, Keio University)
Co-investigator	Fuminari Kaneko (Associate Professor, Sapporo Medical 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 (Professor, Prefectural University of Hiroshima)
Co-investigator	Hideki Nakano (Assistant Professor, Kyoto Tachibana University)
Co-investigator	Atsushi Tasaka (Associate Professor, Osaka Health Science University)

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)