2017 Annual report

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

Program Director: Jun Ota (The University of Tokyo)

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http://embodied-brain.prg

Contents

Project overview and Activities of Steering Committee

Jun OTA
Research into Artifact, Center for Engineering (RACE), the University of Tokyo

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 three years from the start of the program until 10 January 2018, the program has over 401 journal papers (including 281 international journals), over 260 international conference presentations, and over 556 domestic oral presentations. From the third year onwards, we publish transdisciplinary research papers steadily and publish special issue papers on interdisciplinary research promoted in this area to international/domestic 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 14,000 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 two categories: activities as the project, activities in academic societies.

A. *Activities as the project*

- 5th project meeting
Date: Jun 20, 2017
Place: Tokyo
Contents: Presentation by the area organizer, group leaders, and principal investigators of the second period subscribed research groups.

- 2nd Public symposium
Date: October 14, 2017
Place: Tokyo
Attendees: 185
Contents: Presentations for general participants by program members including the area organizer, group leaders, and 6 representative researchers.

- 6th project meeting
Date：March 1 - 3, 2018
Place: Kagoshima
Contents: Invited talk. Oral and poster presentations by area members. Discussion.

B. *Actuvities in academic societies*

- AMAM2017
Date: Jun 27, 2017
Place: Sapporo
Contents: Special session (6 oral presentations)

- The 2017 IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS2017)
Date: September 28, 2017
Place: Vancouver, Canada
Contents: Workshop， 9 oral presentations including two international invited talks.
Attendees: 30

- SICE SSI 2017
Date: November 26, 2017
Place: Hamamatsu, Shizuoka
Contents: Special session (13 poster presentations)
- MHS 2017 (Micro-NanoMechatronics and Human Science)
Date：December 5, 2017
Place: Nagoya, Aichi
Contents: Organized session (5 oral and 3 poster presentations). Keynote talk by an area member.
- 30th SICE Symposium on Decentralized Autonomous Systems
Date: January 28-29, 2018
Place: Nagoya, Aichi
Contents: Presentation (6 presentations)

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 the first and the second periods 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 49 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.

Here is the list of activities in this year. We held two special sessions at the international conferences, one special issue in the academic journal, two workshops, and one symposium.

Followings are the details of the activities. We organized one special session of our project at The IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS 2017). We also organized another special session at The International Symposium on Adaptive Motion of Animals and Machines (AMAM2018) (also written in Subsection III.B). We organized the special issue about the project at the Journal of the Robotics Society of Japan (Vol. 35, No.7, 2017). We held two workshops about frontier researches about our project. Associate Professor Tetsuya Inamura (National Institute of Information, Japan) provided the topic about data-base projects related to recent data-driven sciences. Professor Shu Morioka (Kio University, Japan) provided the topic about body consciousness and clinical cases.

We hosted debate meeting in the 6th project meeting to unify philosophical concepts each researcher holds.

VI. Future Plan

The plan in 2018 fiscal year is shown as follows:

- Dec, 2018: 2nd International Symposium on Embodied-brain Systems Science (EmboSS 2018)
- March, 2019: 6th Area meeting (for area members only)

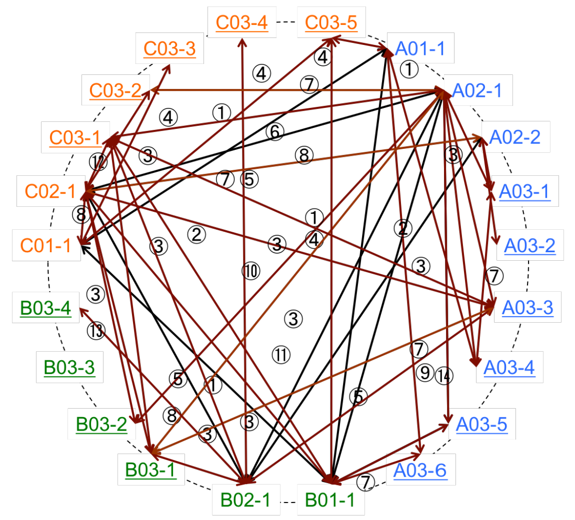

Fig. 1 Trans-area collaboration

Annual report of international activity support group

Jun OTA

Research into Artifacts, Center for Engineering (RACE), the University of Tokyo

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 FY2017

International activities supported by the grant in FY2017 are listed below.

1	Type: Dispatch of young scientist Applicant: B02-1 J.Ota Content: The applicant dispatched a young scientist in synergy-based control core to Prof. Y.Ivanenko's laboratory in Fondazione Santa Lucia, and asked him to conduct international collaboration about analysis and modeling of muscle synergy.
2	Type: Invitation of outstanding researcher Applicant: B02-1 J.Ota Content: The applicant invited Prof. Enrico Pagello (University of Padua), who is an outstanding researcher in synergy-based control core, and discussed with him about understanding the mechanism of human upper limb control and its application to intelligent robot design.
3	Type: Invitation of young scientist Applicant: B02-1 J.Ota Content: The applicant invited Prof. Enrico Piovanelli (University of Padua), who is a young researcher in synergy-based control core, and discussed with him about signal source estimation of forearm multi-channels EMG.
4	Type: Invitation of outstanding researcher Applicant: C02-1 D.Owaki Content: The applicant invited Prof. Dagmar Sternad (Northeastern University, Action Lab) to the international organized session in AMAM 2017, who is an outstanding researcher in synergy-based control core. Many researchers in the research program discussed with the invited researcher at the conference.
5	Type: Invitation of outstanding researcher Applicant: A02-1 K.Seki Content: The applicant invited Dr. Takei (Queen's University) to the workshop in JNSS 2017, who is an outstanding researcher in synergy-based control core. Many researchers in the research program discussed with him about posture control.
6	Type: Invitation of outstanding researcher Applicant: A02-2 K.Nakajima Content: The applicant invited Prof. Marc A Maier (Université Paris Descartes), who is an outstanding researcher in synergy-based control core, and conducted international collaboration about adaptive posture and locomotion control.
7	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).
8	Type: Invitation of outstanding researcher Applicant: B01-1 H.Asama Content: The applicant invited Prof. Giulio Sandini (Istituto Italiano di Technologia) and Prof. Paul Vershure (Universitat Pompeu Fabra) to international worksop in IROS 2017, who are outstanding researchers in bodily self-consciousness core. Many researchers in the research

	program discussed with the invited researchers at the conference.
9	Type: Invitation of outstanding researcher Applicant: C01-1 S.Izumi Content: The applicant 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.
10	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.
11	Type: Invitation of outstanding researcher Applicant: B01-1 J.Izawa Content: The applicant invited Dr. Nicolas Schweighofer (University of Southern California), who is an outstanding researcher in bodily self-consciousness core, and discussed with him about mathematical modeling of neuro-rehabilitation.
12	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.
13	Type: Invitation of outstanding researcher Applicant: B01-1 T.Kondo Content: The applicant invited Dr. Yoshikatsu Hayashi (University of Reading), who is an outstanding researcher in bodily self-consciousness core, and discussed with him about BCI neurorehabilitation.

III. FUTURE PERSPECTIVE

In this year, the group supported 13 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) in 2017

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, new A03 research members for 2nd period joined the project and we have intensively facilitated inter-group and inter-project collaborations not only within Group A (A01, A02-1, A02-2 and six 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 12 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 16 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: Visualization of brain functional dynamism by hybrid functional analysis with real-time feedback</u>
Principal Investigator: Kyousuke Kamata (Asahikawa Med Univ). Other 2 Co-Investigators.

<u>Research project A03-2: Neural basis for the reference frame and the functional synergies in controlling eye-head coordination</u>
Principal Investigator: Yuriko Sugiuchi (Tokyo Med Dent Univ). Other 1 Co-Investigator.

<u>Research project A03-3: Development of assistive technologies for rehabilitation by visualizing neural representation of muscle synergies using electroencephalography</u>
Principal Investigator: Natsue Yoshimura (Tokyo Tech). Other 3 Co-Investigators.

<u>Research project A03-4: Human fronto-parietal network for embodied-brain system: A combined electrocorticographic decoding, stimulation and lesion study</u>
Principal Investigator: Riki Matsumoto (Kyoto Univ). Other 5 Co-Investigators.

<u>Research project A03-5: Understanding the interaction between tactile and nociceptive information in the somatosensory cortex and controlling of nociception</u>
Principal Investigator: Hironobu Osaki (Tokyo Women's Medical Univ). Other 3 Co-Investigators.

<u>Research project A03-6: Body representation changes underlying motor recovery after internal capsular stroke in macaques</u>
Principal Investigator: Noriyuki Higo (AIST). Other 3 Co-Investigators.

III. Activities

A joint meeting across A01, A02, A03, B01 and C01 projects
Date and Time: January 22, 2018, 10:00-17:30.
Place: Center for Information and Neural Network, National

Institute of Information and Communications technology (〒565-0871 1-4 Yamadaoka, Suita-city, Osaka)

Local organizers: Eiichi Naito (NICT), Yutaka Oouchida (Tohoku UNiv)

Attendees: 17: Hiroshi Imamizu (A01:Univ of Tokyo), Yukari Ohki (A01:Kyorin Univ), Akira Murata, Kei Mochizuki (A01:Kindai Univ), Eiichi Naito, Kaoru Amemiya (A02-1:NICT), Riki Matumoto, Akihiro Shimotake, Masaya Togo, Tamaki Kobayashi (A03-4:Kyoto Univ), Hirokazu Takana (B01:JAIST), Shinichi Izumi, Yutaka Oocuhida (C01:Tohoku Univ), Fuminari Kaneko, Aimi Okawada (C03-3:Keio Univ), Shu Morioka (C03-5:Kio Univ), Sotaro Shimada (C03-5:Meiji Univ), Jun Ota (B02:Univ of Tokyo: cancelled due to the flu)

Contents: The seventeen members across A, B and C groups, who have been seriously working on the issues related to frontoparietal functions (the main topic of 01 project) joined the meeting and deeply discussed these issues. We first started with topic presentation session (see below), followed by over three-hours discussion session for each topic. The main purpose of this meeting was (1) Sharing most recent research outcomes by members, (2) Sorting and sharing most advanced international knowledge about these issues, (3) Achieving consensus for understanding of the frontoparietal functions and (4) Discussing future research direction about these topics. The program of the topic presentation session and presenters are as follows.

1. Understanding pathophysiological basis of asomatognosia and apraxia based on animal data. Presenter: Akira Murata (A01:Kindai Univ)
2. Neural basis of apraxia in the left cerebral hemisphere: comparison with body recognition in the right cerebral hemisphere. Presenters: Riki Matsumoto (A03-4: Kyoto Univ)
3. Pathophysiological and neural basis of asomatognosia, apraxia and spatial neglect. Presenter: Shu Morioka (C03-5: Kio Univ)
4. Importance of right inferior frotoparietal SLF III network for body and self recognition and its development. Presenter: Eiichi Naito (A02-1: NICT)

After this session, we had a discussion session chaired by Eiichi Naito (NICT). All the attendees deeply discussed mainly the following three points (1) functional differences between inferior frontal cortices (ventral premotor and area 44) and inferior parietal cortices and how to make a model of efference copy, (2) lateralized functions and interaction between human right and left cerebral hemispheres in terms of asomatognosia, spatial neglect, apraxia and language functions, (3) how the frontoparietal networks contribute motor control and motor learning and the direction of future researches related these issues and so on.

Finally

In this fiscal year, research articles related to slow dynamics of internal brain representations have begun to be published, which has been lesser until last year. As for a meeting, until last year, we had a meeting where many researchers presented their works in short time in order to share their research contents among project members. Since this has been effectively achieved by this year, in this fiscal year, we a meeting where we mainly focused on discussion based on strong demand from many members. For this purpose, we focused on the topic of frontoparietal network and somewhat limited the number of attendees. We got better feedback from the attendees and especially younger researchers reported that they have learned many things from this meeting. In this fiscal year, new A03 research members for 2nd period joined the project. However, their researches are highly compatible with those of core project (A01, A02-1, A02-2) members, so that we could seamlessly facilitate inter-group and inter-project collaborations. Finally, I have an impression that the Embodied-Brain Systems Science has been gradually expanded into the related fields due to the successive efforts by project members. I wish the Embodied-Brain Systems Science to be further deeply ingrained in the Japanese society.

Annual report of research project A01-1

Hiroshi Imamizu
Graduate school of Humanities and Sociology, The University of Tokyo

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 developed basic methods for manipulation of bodily self-consciousness by using behavioral and neurofeedback training. In addition, we continued our global decoding analysis in the human brain to investigate neural correlates of bodily self-consciousness at network level, and started to record Electrocorticography (ECoG) in a monkey neurophysiological study.**

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.

III. Research Topics

A. Development of basic techinques for manipualtion of bodily self-conciousness

A group of the principal investigator investigated neural processes underlying bodily self-consciousness (especially SoA), and developed basic methods for manipulation of SoA.

1) Neural processes underlying SoA: We continuted our decoding analysis of the fMRI data related to attribution of movements to self or others (as a basis for SoA). As a result, we found that subjective rating of the attribution can be decoded from motor-regions in the basal ganglia. This suggests that SoA is determiend by not only a post-dictive process after the movemenet but also accumulation of sensory-motor information during the movement. We also found that activity-patterns in regions near the right temporal-parietal junction (TPJ) can predict the subjective rating rather than the prediction error. These regions are probably involved in the final decision process of SoA. Separately from this study, our paper finding neural correlates for intentional binding, which has been establided as a sbjective mearure of SoA, was acceptted by NeuroImage [1].

2) Developmet of neurofeeback technique: we developed baisc methods for manipulation of SoA using a neurofeedback training. We obtained the following results:

(a) We developed a new neurofeedback method for chainging functional connectivity between brain regions in the intended direction (increment or decriment in connectivity) [2].

(b) We confirmed that SoA can be changed by biased feedback information at the behavioral level. This suggests possibility of SoA manipulation by the neurofeedback training.

(c) We developed an experimental paradigm that clearly activates the right TPJ, which is the target of the neurofeedback training, in individual subjects.

(d) We conducted a preliminary neurofeedback experiment manipulating activity in the right TPJ.

3) Empirical examination of independency of muscle synergies: In relationship to the long-term change in bodily self-consciousness, we experimentally examined if muscle synergies identified by computational models are voluntary and independently controlled [3]. This result validated an important but empirically-unexamined assumption in computational studies that the muscle synergies are the minimum units for voluntary control of movements.

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. Based on results obtained in the past years, they performed experiments described below.

1) They analyzed EEG recordings, to obtain instantaneous biomarkers that reflect SoO. For that purpose, they made 64-channel EEG recordings during a modified rubber hand illusion paradigm, which they have developed to induce the rubber hand illusion by short-term stimulation. This year, they analyzed the results further. They made recordings from 20 healthy volunteers under the paradigm. After each trial, the subjects answered if and how strong they feel SoO to the rubber hand. After rejecting trials contaminated by artifacts, they analyzed data from 10 subjects, from whom they got more than 70 trials both with and without SoO. To compare brain activities with and without SoO, they performed the event-related spectrum perturbation analysis, and detected brain areas that showed differences between the two conditions. Electrodes, which showed significant differences in powers of β and γ ranges, were lateral parts of frontal cortex, central sulcus, and parietal cortex, in addition to occipital cortex. They performed discriminant

analysis by using the powers at electrodes in these regions, and found that they can discriminate two conditions with 62.8 % accuracy, and with 70 % accuracy when only trials under high confidence were included. Thus, it is suggested that those signals can be used as a biomarker for SoS. Brain areas that showed the activities could be TPJ, SI, SII, PPC, PMv and iusula, which correspond well to the previous reports. However, they observed stronger activities in the left rather than the right hemisphere, which is different from the previous reports. The power increases might reflect embodiment of the external object. Activities in the occipital cortex most probably reflect attention around the rubber hand, as a result of SoO to the rubber hand.

2) In the last year, they observed movement-related brain activities (μ suppression) by observing other's hand movements, in case subjects feel SoO to the hand. This year, they wrote a paper based on the results [4]. Furthermore, they started new experiments related to the movement observation. In the experiments, they brushed invisible subjects' hand and visible other's hand on a monitor, and the subjects observed sudden movements by other's hand. Visual feedback on the monitor was delayed by 80, 280, and 480 ms. SoO was decreased when the delay is getting longer. In addition, amplitudes of the μ suppression was significantly greater under 80 than 280-480 ms delay. This means that the μ suppression can also be used as a biomarker for SoS. This study was done with Shimada et al (C03-4).

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. In the last year, to investigate neural activity related to sensory attenuation, we recorded single cell activity in somatosensory cortex, using a device by which tactile stimulations on the monkey left hand were applied with a brush controlled by a lever manipulated with monkey's right hand. As a result, it was found that activity of some number of neurons in the right somatosensory cortex were influenced by lever movement, showing less or higher activity compared with passive somatosensory stimulation [51]. This is likely due to corollary discharge accompanied by motor behavior of the right hand. However, it was not clear how the corollary discharge reached to the somatosensory cortex. To study this issue, ECoG recoding from motor cortex and somatosensory cortex is one of solutions. As a pilot experiment, we implanted ECoG electrodes on the left precentral and postcentral gyrus successfully. We learned some procedures of implantation of ECoG electrodes and recording. During of movement of right hand action, we found that some modulatory activity of ECoG of the postcentral electrode. This might be due to corollary discharge from motor cortex or proprioceptive input. In the next stage, it is necessary to record ECoG from bilateral precentral and postcentral gyrus simultaneously. Furthermore, with the same task, we are still recording of single cell activity in the somatosensory cortex of the second monkey to increase the number of neurons.

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, computational, neuroimaging and physiological studies.

1) They measured brain activity by resting-state fMRI in healthy subjects and compared with behavioral data of the Keio method. They analyzed functional connectivity in the whole brain for the normal emergence of SoA. This study will contribute to identification of target connectivity for the future neurofeedback training.

2) To study neuro-dynamical account for SoA behavior, they employ a humanoid robot driven by a recurrent neural network (RNN). The RNN model successfully reproduced the behavioral features of SoA task in the healthy controls. Moreover, the simulated lesion experiment illustrated that bidirectional changes of SoA (excessive and diminished SoA) could be induced by the temporal perturbations of signals in sensory-motor prediction process. The results support the proposed hypothesis that the aberrant SoA in schizophrenia may be due to the delayed prediction signals in sensory-motor control systems.

3) They have continued 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.

4) They studied repetition effects of the Keio method. This study could provide the learning algorithm of the Forward model for SoA from the perspective of slow dynamics.

5) They investigate that subjects employ a Bayesian update as the learning algorithm in the Keio method from the perspective of fast dynamics.

IV. Future Perspective

In this fiscal year, we have accomplished to prepare manipulation on the bodily self-consciousness and investigation at network level. We developed a new technique in neurofeedback training and obtained rich data suggesting the global brain mechanism contributing the bodily self-consciousness. We now have the outline of emergent process of the bodily self-consciousness. In the coming years, we will develop methods to interfere with and manipulate the bodily self-consciousness, based on the achievements in collaboration with the rehabilitation group.

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Annual report of research project A02-01

Kazuhiko SEKI
National Institute of Neuroscience, NCNP

***Abstract*—In the FY2017, we established 1) two types of tendon-transferred primate model, 2) *State prediction in the cerebro-cerebellum and fully-digitized evaluation of cerebellar ataxia, and 3)* plastic changes (slow dynamics) during development of human body representations**

I. INTRODUCTION

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

II. AIM OF THE GROUP

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

III. RESEARCH TOPICS

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

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. Behavioural observations and chronic EMG recordings from different forelimb muscles were used to evaluate the grasp performance. Subsequently, 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. The monkey fully recovered, fed himself at day 1 post-surgery and performed a precision grip using BRD successfully as finger flexor. Furthermore, movement and hold times recovered within weeks. Lastly, recorded EMG's revealed continuous changes in the BRD activity profile stabilising after some weeks and resembling the activity profile of an extrinsic finger flexor. In subsequent experiments actual tendon cross-unions were performed between the Extensor digitorum Communis and Flexor digitorum superficialis of the same monkey and two control monkeys. The subjects fully recovered and continuous changes in the EMG activity profile occurred including some muscles which were not part of the cross-union. Activity patterns were either reduced in EMG amplitude or adopted a new equilibrium (time of peak activity) between original and expected pattern. We suggest this unique time-course of adaptation may represent the slow dynamics of neural adaptation in response to the modification of musculoskeletal system. To further pursue this possibility, we just implanted the ECoG array over the sensorimotor cortex of a monkey. In the next FY, we are aiming to establish the indirect biomarker [1] of embodiment by analysing this signal.

Obviously, the slow-dynamics of adaptation could represents the dynamics of sensory input [2] during the adaptation. To assess this input directly, we are also establishing an animal model that may allow us to manipulate the somatosensory input during the adaptation. We already established the control experiment using rats. In the next FY, we will apply this paradigm into tendon-transferred monkeys.

B. State prediction in the cerebro-cerebellum and fully-digitized evaluation of cerebellar ataxia

B-1. State prediction in the cerebellum

Kakei's group, together with Tanaka's group in JAIST (B01), is working on a project to analyze the internal mechanism of the cerebellum as a synergy controller. Recent computational studies hypothesize that the cerebellum performs state prediction known as a forward model. To test the forward-model hypothesis, we analyzed relationship between activities of the three major groups of cerebellar neurons: mossy fibers (MFs) (inputs to the cerebellum, n=94), Purkinje cells (intermediate representation, n=83), and dentate cells (DCs) (output from the cerebellum, n=73) in the cerebro-cerebellum, all recorded from a monkey performing step-tracking movements of the wrist. Our analysis of these cerebellar activities demonstrated that the firing rates of MFs at time t+t_1 were well reconstructed from as a weighted sum of firing rates of DCs at time t, thereby proving that the DC activities contained predictive information about the future MF inputs thereby supporting the forward-model hypothesis of the cerebellum (Tanaka et al. in preparation).

B-2. Fully-digitized evaluation of cerebellar ataxia

To understand the complex mechanisms of the embodied brain system, it is essential to decode neural mechanisms of individual synergy controllers, as described above. On the other hand, it is equally important to develop a system to deconvolute the movement (phenotype of the embodied brain system) into components, each of which is originated from an individual synergy controller. In order to achieve this goal, Kakei's group, in collaboration with Kondo's group (B02), developed a motion evaluation system with Kinect v2 sensor (Fig. 1) [3]. This system provides dual modes of motion analysis: 1) movement of a small body part of interest (e.g. Fig. X, *red dot*); 2) movement of the whole body as a link of the bones (e.g. Fig. 1, white dots and lines). We are now working on a new project to use this system for analysis of contributions of different synergy controllers in patients with various neurological disorders.

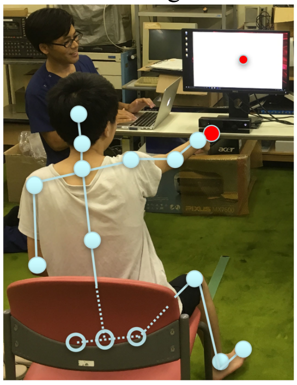

Fig. 1 A fully-digitized system to evaluate cerebellar ataxia with Kinect v2 sensor. Most clinical evaluations focus only on movements of small body parts (e.g.; red dot), while this system also provides a systematic description of different body parts or whole body (white dots and bones).

C. Investigation of plastic changes (slow dynamics) during development of human body representations

Naito's (CiNet/NICT) group is conducting fMRI experiments in humans. In this fiscal year, in order to promote connection between 01 and 02 projects, we investigated (1) how human motor network and inferior frontoparietal network connected by the inferior branch of the superior longitudinal fasciculus tract (SLF III) are involved in self-body recognition and (2) how functions of these networks develop during typical human development. As for self-body recognition tasks, we used a proprioceptive illusion task and a self-face recognition task (Figure). When we identified brain regions active during these tasks in adults, the inferior frontoparietal regions commonly activated during both tasks in a right-side dominant manner [4], indicating the importance of the right inferior frontoparietal network in human self-body recognition. The series of our previous studies (Naito et al. 2016) have shown that proprioceptive illusion activates not only the right inferior frontoparietal network but also motor network in adult brains. When we conducted proprioceptive illusion experiment in children, adolescents and adults, we found adult-like pattern of motor network activity in the motor cortex (M1) and the cerebellum already in children (M1 activity: green sections in upper row of Fig.2). On the other hand, we found bilateral inferior frontoparietal activity in children unlike adults, and that adult-like right-dominant use of this network emerged during adolescence (red sections in upper row of Fig.2) [5]. Interestingly, the emergence of right-side dominance during adolescence was due to suppression of activity in the left-side network especially in the left inferior parietal lobule (blue section in upper row of Fig.2) [5]. We also conducted self-face recognition experiment in the same children, adolescents and adults. We found children mainly used visual cortices (orange sections in lower row of Fig.2) without using inferior frontoparietal networks substantially [6]. The adult-like use of inferior frontoparietal network emerged during adolescence and its use showed right-side dominance as in proprioceptive illusion (red sections in lower row of Fig.2). The adult-like common use of right-side inferior parietal region between both tasks was observed in adolescents [6]. The series of results provided valuable knowledge in the development of human body representations.

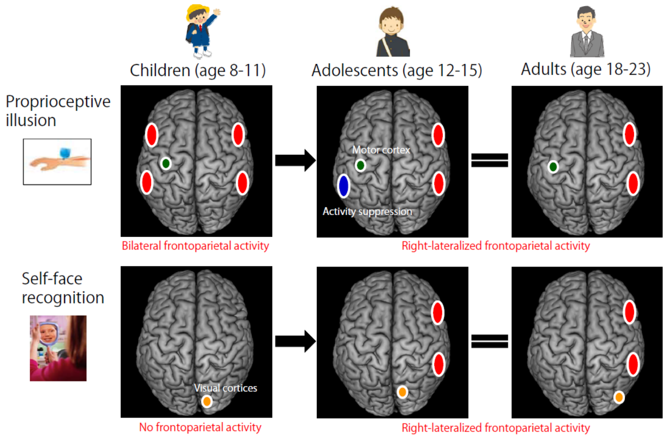

Figure 2. Upper row: Developmental change of brain activity in the motor cortex (green sections) and in the inferior frontoparietal network (red sections) during proprioceptive illusion task. Lower row: Developmental change of brain activity in the visual cortices (orange sections) and in the inferior frontoparietal network (red sections) during self-face recognition task. Blue section in the upper row indicates the left inferior parietal region where activity suppressed during illusion in adolescents.

IV. Future Perspective

These achievement has been published in the 6-original paper. Other project aiming to establish a new assessment of Stroke patient by using muscle synergy biomarker is also ongoing that will be published in the next FY.

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Annual report of embodied-brain project A02-2

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

Abstract - **Voluntary movements requires a sequence of postural control that is optimized to the purposeful actions. This process is organized by the prediction of body-circumstance interaction and motor programs that produce synergistic contractions of muscles. The aim of our research group is to understand the cortical and subcortical mechanisms involved in these processes. In this fiscal year, cognitive aspect of postural control was studied in animal models. In the monkey locomotor task, role of the fronto-parietal network (FPN) in the alteration of posture-gait synergy was examined. In the cat forelimb reaching task, changes in anticipatory postural adjustments in response to the alteration of target position were elucidated. Our findings suggest that cognitive postural control played by the FPN requires motor programs that rely on the sense of postural verticality which is constructed based on egocentric coordinates.**

I. Introduction

Postural control is disturbed by lesions in the brain such as cerebrovascular disorders and neurodegenerative disorders. Because postural control that is optimized to the purposeful actions is required to achieve movements under the relevant circumstance, understanding neuronal mechanisms of adaptive postural control is critical so that scenario of reconstructing motor function after brain damages is established [1].

II. Aim of the Group

The aim of our research group (A02-2) is to elucidate higher order mechanisms of postural control during voluntary movements. For this purpose, animal experimentation was performed to examine following two issues in this fiscal year. First, Japanese monkeys were employed to study information processing in the fronto-parietal network involved in postural control during bipedal and quadruped locomotion. Second, role of cognitive information in the alteration of APA during goal-directed forelimb reaching was examined in the cat.

III. Research Topics

1. Cortical control involved in the alteration of posture-gait strategy in the monkey

Nakajima and Higurashi at Kindai University investigated (1) synergy patterns of postural muscles and (2) cortical mechanisms of sensorimotor integration during locomotion in Japanese monkeys. Professor Marc A. Maier, FR3636, CNRS and Université Paris Descartes in Paris, participated in these studies operated by International Activities Supporting Group.

(1) Changes in postural muscle synergies following alteration of gait patterns from quadrupedal to bipedal locomotion

As shown in Fig. 1, electro-myographic (EMG) activities of trunk and proximal leg muscles were increased during bipedal locomotion (BpL) compared to quadrupedal locomotion (QpL). The monkey also exhibited postural sway in the left (dashed lines) and right (solid lines) directions which synchronized with left-right steps. Because the postural sway was symmetric against to the vertical axis, such a postural synergy during BpL may contribute to stabilization of upright posture under the gravitational circumstance.

(2) Activity of dorsal premotor cortex (PMd) neurons during locomotion

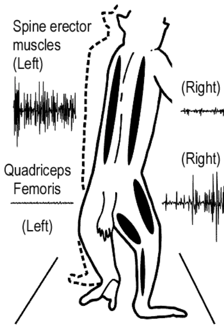

Figure 1 Trunk-limb muscle synergy during bipedal locomotion

The activity of 44 PMd neurons was examined. While they exhibited common patterns in BpL and QpL in relation to step cycles, one-third of them reduced firing rates during BpL compared to QpL.

In the previous study [2], activity of supplementary motor area (SMA) neurons reflected synergistic contractions of trunk and leg muscles during locomotion, indicating that the SMA could dexterously control the dynamic trunk posture as well as stepping limb movements. Moreover, their activity was higher during BpL than QpL. Similarly, neurons in the primary motor cortex (M1) exhibited higher activity during BpL. However, they rather reflected accurate leg muscle contractions. These findings suggest the presence of functional topography in the motor cortical areas in relation to the posture-gait control.

(3) Effects of muscimol injection into vestibular areas of the parietal lobe on locomotor behaviors.

Because the SMA receives projections from the parietal lobe including the parieto-insular vestibular cortex and primary somatosensory cortex (S1) [3] where bodily information can be reserved [4]. Muscimol, a $GABA_A$-receptor agonist, was then injected into the leg area of the S1 so that changes in posture-gait control was examined. As shown in Fig. 2, the right leg, which was contralateral to the injection side, missed stepping on the platform. This resembles to motor disturbance due to

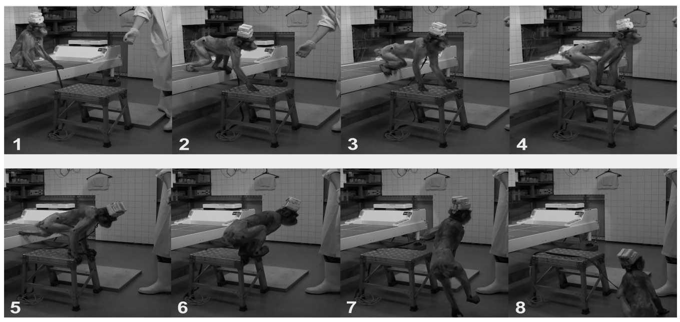

Figure 2. Effects of muscimol injection into the left S1 on posture-gait control. While both hands and right foot precisely stepped on the platoform (1-4), the left foot slipped it, resulting in falling (8).

damages in thalamus and posterior crus of the internal capsule. In addition, gait disturbance with slapping impact of the right foot [5] was observed. The crude locomotor pattern resembles to the symptom observed in ataxic gait patients with cerebellar lesion and peripheral sensory disturbance.

2. APA of forelimb target reaching in the cat

Takakusaki, Nakajima and Takahashi at Asahikawa Medical University have investigated neuronal mechanisms of APA in human and animals. In this fiscal year, we examined how spatial information of the target was reflected in APA of forelimb reaching in the cat. Trevor Drew, a professor in the Montreal University, participated in this research operated by International Activities Supporting Group.

The cat learned forelimb reaching to the food pellets in the barrel of the front panel. Center of vertical pressure (CVP), a parameter of center of gravity, was calculated from the ground reactive force exerted in each foot (Fig. 3A-B). CVP positions when the cat gazed at the target were indicated by black circles. Then, CVP transiently moved to the left just before lifting the left forelimb and it rapidly shifted to the right (open circles). Such a trajectory of CVP reflects the change in the center of gravity associated with APA. Thereafter, cat lifted left forelimb (filled squares) and reached to the target (open triangles). Note that the CVP positions at forelimb lifting and reaching were very close, indicating that APA is accomplished when cat lifts the forelimb. Then, how did APA code spatial information of the target? We examined the changes in CVP associated with reaching to the spatially different targets (Fig. 3C). When the position of target was moved to from center to the left and right, CVP positions at forelimb lifting and reaching were shifted to

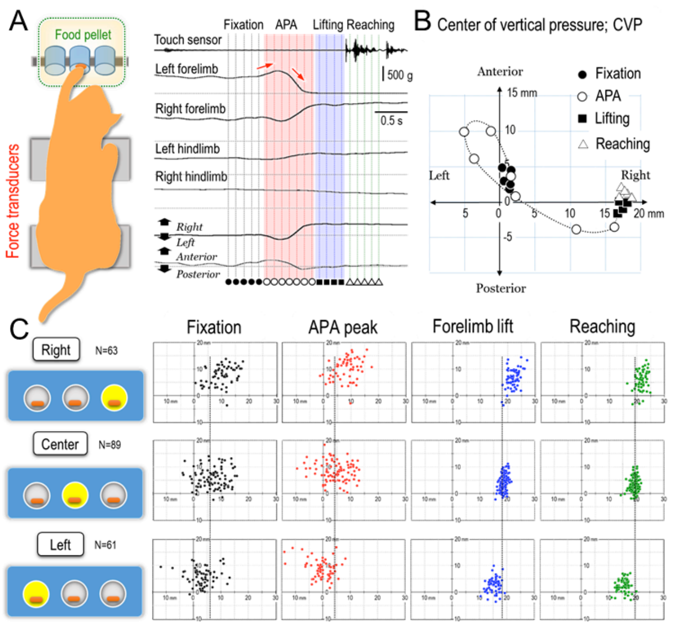

Figure 3. Changes in CVP during forelimb reaching in the cat.
A. Schematic illustration of the experiment (left) and chagens in the ground reactive force during reaching (right). B. Changes in CVP on the horizontal plane during reaching task by the left forelimb. Timing of reaching was monitored by the sensor attached to the front panel. C. CVP altered in response to the changes in the location of the target. Note that CVP positions of forelimb lift and reaching were very close.

the left and right, respectively.

These results suggest that the motor programs of postural control as well as precise limb movements require cognitive information of the relationship between one's body and targets.

IV. Summary and Future perspective

Findings over the past 4 years are summarized as following 3 points. First, there is a functional organization in the motor cortical areas in relation to posture-gait control of the monkey. Specifically. M1, SMA and PMd contribute to the control of precise movements, posture and step cycles during locomotion, respectively. Second, cortico-reticulospinal pathway arising from the SMA may contribute to APA [6], which requires motor programs based on spatial cognitive information between self-body and circumstance. Third, bodily information including the sense of postural verticality may be particularly important for motor postural control programs so that upright posture is maintained (without falling) during movements.

There are two objectives of the final year of this project. The first objective is to obtain more specific findings indicating that the fronto-parietal network contributes to the cognitive information processing at the parietal cortex and motor programing at the motor cortex for posture-gait control in the monkey using pharmacological and electrophysiological techniques. The second objective is to elucidate the role of cortico-reticulospinal pathway in APA during forelimb reaching task in the cat using genetically-manipulated techniques combined with neuroanatomy and electrophysiology.

We expect that results of our project lead to (1) understanding pathophysiological mechanisms of posture-gait disturbance due to brain damages, (2) progress of functional reconstruction method and technology, and (3) development of "bio-maker of higher-order brain function" based on the mechanisms of APA.

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Annual report of embodied-brain project A03-1

Kyousuke Kamada
Asahikawa Medial University

Abstract—**Recent neuroimaging studies suggest that intractable epilepsy involves pathological functional networks as well as strong epileptogenic foci. Combined cortico-cortical evoked potential (CCEP) recording and tractography is a useful strategy for mapping functional connectivity in normal and pathological networks. In this report, we demonstrate the efficacy of preoperative combined CCEP, high gamma activity (HGA) mapping, and tractography for surgical planning and of intraoperative CCEP measures for confirmation of selective pathological network disconnection. Methods: We treated eight intractable epilepsy cases, all with subdural grid implantation, using presurgical CCEP, HGA, and diffusion tensor imaging (DTI)-based tractography analysis as well as continuous CCEP monitoring during resection surgery. Results: Four of eight patients had measurable pathological CCEPs. The mean N1 latency of normal CCEPs related to language functions was 22.2 ± 3.5(Mean ± SD) ms, while pathological CCEP latencies varied between 18.1 and 22.4 ms. Pathological CCEPs diminished after complete disconnection in four cases, with good postsurgical outcome (long-term postoperative seizure-free status), while the two patients with residual pathological CCEPs showed poorer seizure outcome. Significance: Combined CCEP measurement, HGA mapping, and tractography greatly facilitated targeted disconnection of pathological networks. Although CCEP recording requires technical expertise, it allows for assessment of pathological network involvement in intractable epilepsy and may improve seizure outcome**

Introduction: Intractable epilepsy may arise from multiple foci or low seizure threshold. In addition, there is growing evidence from neuroimaging studies that intractable epilepsy involves pathological networks that allow rapid spread of focal seizure activity [1 3] . High gamma activity (HGA) augmentation in the 60−170 Hz range is assumed to reflect cortical center functioning [7-8-6-9]. Physiological and pathological networks in epilepsy patients can also be mapped by measuring cortico-cortical evoked potentials (CCEPs) in response to stimulation of epileptic foci. Matsumoto et al. elucidated the pathophysiology of ictal motor semiology and rapid spread of epileptic discharges within the motor system. It has been speculated that spread of epileptic activity within such networks is predictive of relatively poor outcome following epilepsy surgery[4]. In this study, we combined CCEP, HGA, and diffusion tensor imaging (DTI)-based tractography allowed us to map patient-specific networks for surgical planning.

Patients and Methods: Eight patients suffering from intractable epilepsy underwent surgical treatment. Six patients were without gross structural brain abnormalities, such as mesial temporal sclerosis, tumors, or cortical dysplasia on anatomical MRI, Case 5 and 8 revealed a lesion in the primary-sensory area, and posterior temporal aspect on anatomical MRI.

Cortico-cortical evoked potential (CCEP) recording for functional connectivity: Based on seizure monitoring and functional mapping with electrocortical stimulation (ECS) and HGA, we measured CCEPs in response to stimulation of identified epileptogenic foci and eloquent areas for identification of functionally connected areas. The electrical stimulus was a constant current square wave pulse of 0.3 ms duration delivered at 1 Hz. Two adjacent channels were used as bipolar stimulating electrodes to apply localized current to the targeted cortical area. Stimulus polarity was alternated to reduce stimulus artifacts. In each session, we recorded CCEPs twice to confirm reproducibility and set the post-stimulus recording period as -100 ms to 800 ms. The Welch-test, a derived t-test for populations with different variances, was used to check for significant differences between the averaged baseline and CCEP waveforms. The significance threshold was set to $p < 0.05$ for a two-tailed t-distribution. We then validated the HGA-CCEP mapping results by ECS [10].

Results: Pathological network CCEPs: In the six cases with multiple foci, we used alternating square pulses to evoke pathological CCEPs in functionally connected areas. Four of six cases exhibited CCEPs at distant regions. Pathological CCEPs suggesting aberrant functional connectivity with the epileptogenic foci were found in four cases, while the two other multi-focal cases showed few detectable pathological CCEPs. The pathological CCEPs resembled normal responses in both directions but the profile was unique to each patient. Table 2 summarizes the number of CCEP-detecting electrodes and the response latencies.

Representative case: A 29-year-old right-handed male started having complex partial and generalized seizures with frequent absence seizures 10 years prior to surgery. Although he had multiple AED trials, he continued to experience more than five seizures daily. Neuroimaging by MRI demonstrated no structural pathology. Twenty-four hour video−EEG monitoring demonstrated frequent 3-Hz spikes and waves from bilateral frontal lobes but did not clearly distinguish the epileptogenic hemisphere. The ECoG electrodes covering bifrontal, bitemporal, and orbitofrontal cortices revealed frequent spikes and waves from bilateral frontal lobes (Fig. 1B). It was thus difficult to determine the seizure-onset hemisphere even on ECoG. Interictal bilateral spikes and waves and ictal spikes were randomly observed from both frontal lobes. Stimuli from electrodes 4, 5, and 6 on the right side evoked obvious pathological CCEPs from 7 channels (8, 9, 10, 13,14,15,18 and 19) of the contralateral hemisphere (Fig. 1). The first (N1) and second negative (N2) peaks were 24.4 ms and 55 ms after stimulation and ~100uV in amplitude (Fig.1B). We stimulated the non-functional frontal channels for reference, and CCEPs were not induced.

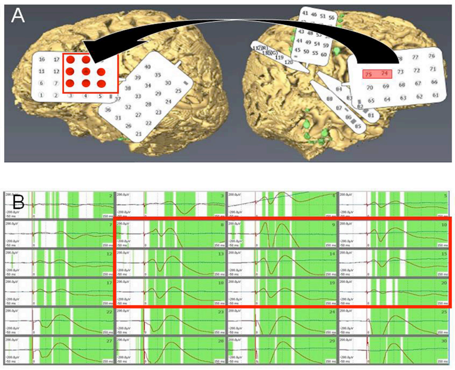
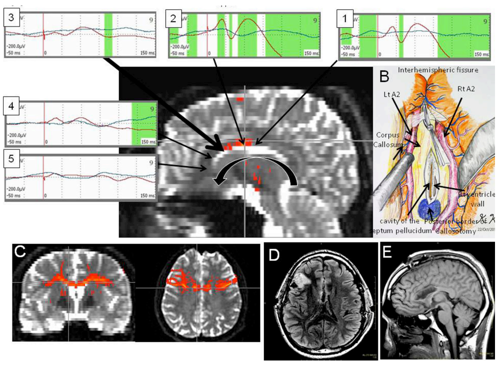


Fig.1 (A) Pathological CCEPs recorded from left frontal lobe (red square) of the case in response to stimulation of the right epileptogenic foci (red channels; 8, 9, 10, 13,14,15,18 and 19). (B) CCEP deflections in the red square over the right frontal channels. The CCEPs in this case consisted of two obvious deflections.

Combining tractography with the locations of positive ECoG channels and pathological CCEPs revealed a pathological network including the anterior corpus callosum (Fig. 2). In the operating room, tractography-integrated neuronavigation and monitoring of bifrontal pathological CCEPs identified seizure-propagating projections through the anterior corpus callosum (Fig. 2). We exposed the posterior border of the corpus callosum and started resection toward the anterior part with continuous CCEP monitoring. CCEP waveforms gradually decreased in amplitude with little latency change. When the resection reached the genu, CCEPs immediately disappeared (Fig.2). After resection, we recorded ECoG on the interhemispheric fissure and found no pathological activities. Real-time CCEP monitoring confirmed complete resection. Thirty-six months after operation, he has been seizure free with administration of 800 mg/day valproic acid and started to work.

Fig. 2 (A) Pathological CCEPs recorded from left frontal lobe (red square) of the case in response to stimulation of the right epileptogenic foci (red channels; 8, 9, 10, 13,14,15,18 and 19). (B) CCEP deflections in the red square over the right frontal channels. The CCEPs in this case consisted of two obvious deflections.



I. Research Topics

A.First topic: In patients with epielpsy, each has different normal and pathological network to visualize connectivity of epileptogenic foci.

B. Second topic: Dysconnecting and preserving pathological and normal networks improved functional prognoais of epilepsy.

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Annual report of research project A03-2

Yuriko Sugiuchi
Department of Systems Neurophysiology, Graduate School of Medicine, Tokyo Medical and Dental University

Abstract—When a rotational acceleration is given to the body and activates the semicircular canals, the head is turned in the opposite direction to compensate for the head movement [1]. This stereotyped head movement from the activated canal should be produced by contraction of a proper set of neck muscles in a specific spatial and temporal pattern. Since the vestibulospinal reflex is phylogenetically old, it may be the prototype of the motor control system in the central nervous system. This study was aimed at revealing the neural substrates for muscle synergies in the vestibulocollic reflex system. As the first step, the convergent input patterns from six semicircular canals to branchiomeric flexor muscles (sternomastoid and cleidomastoid muscles) were analyzed using an intracellular recording method in the cat, and compared with those of extensor neck muscles belonging to dorsal proper muscles. The results showed that the splenius of dorsal proper muscle origin, and sternomastoid and cleidomastoid muscles of branchiomeric muscle origin had a common pattern of input from the semicircular canals, and thus might form the same muscle synergy.

I. Introduction

It is generally accepted that the central nervous system (CNS) forms muscle synergies and decreases degree of freedom in order to simplify motor control of voluntary movements. Muscle synergies in daily activities in animals and humans were identified with a new non-negative matrix-factorization method. However, little is known about neural substrates for muscle synergies in the CNS. This study was aimed at revealing neural mechanisms of functional synergies of neck muscles using the vestibulospinal reflex system as a model of the motor control system. When the semicircular canals are activated by rotational acceleration, the eyes and head are turned in the opposite direction to compensate for the head movement. These reflexes are called vestibuloocular and vestibulocollic reflexes, respectively. During these reflexes, information from the activated canal should be distributed to a proper set of multiple eye and neck muscles. Since this set of muscles have the common function that rotates the eyes and head in the same plane of the stimulated canal, they are considered to form a muscle synergy.

The neural substrates of muscle synergies in the vestibuloocular reflex, whose system is composed of only six pairs of eye muscles, have been analyzed in detail, and it turned out that innervation patterns of single vestibuloocular neurons with their collateral branches on extraocular motoneurons determined the functional synergies of eye mucles in the vestibuloocular system. On the other hand, neural substrates of neck muscle synergies in the vesitbulocollic reflex are yet to be determined, because of the complexity of the neck movement system composed of many cervical vertebral bones and muscles. Since the vestibulospinal reflex is phylogenetically old, it may be the prototype of the motor control system in the CNS.

II. Purpose of the study

This study was aimed at revealing the neural substrates of muscle synergies in the vestibulocollic system by identifying a target group of neck muscles innervated by single vestibulospinal tract neurons. We determined the intraspinal locations of motoneurons of each neck muscle [2], and found that the borders between neighboring motor nuclei are interdigitated. Therefore, it is difficult to determine the target neck muscles merely based on the relative location of projection area of axons.

The early part of this study was aimed at analyzing properties of synaptic inputs from six semicircular canals to motoneurons of each neck muscle, i.e. the convergent input patterns from six semicircular canals onto motoneurons of each neck muscle. The results of these studies will reveal the group of muscles that receive excitatory or inhibitory input from each semicircular canal. Our working hypothesis is that such spatial patterns of neck muscles activated by single semicircular canals reside in spatial projection patterns of single vestibulospinal tract axons to motor nuclei of neck muscles. Therefore, before morphological analysis of projection patterns of single vestibulospinal axons that receive each semicircular canal input, which is the final goal of this study, the convergent input patterns from three pairs of semicircular canals to each neck muscle were examined by recording intracellular potentials from neck motoneurons.

We previously analyzed semicircular canal inputs to some neck muscles that belong to proper dorsal muscles [3, 4, 5]. Neck flexor muscles in mammals are originated from branchiomeric organs [2], and innervated by cranial nerves, which are very different from proper dorsal muscles originated from truncal muscles. Input patterns from the semicircular canals to these neck flexor muscles were examined and compared with those of neck extensor muscles of proper dorsal muscles [3, 4, 5]. The possibility of forming synergies among those neck muscles of different phylogenetic origins was discussed.

III. Research Topics

A. Muscle innervation by the spinal accessory nerve

Innervations of neck muscles by the spinal accessory nerve were examined by careful dissection. It innervated the cleidomastoid, sternomastoid and trapezius muscles in the cat. The cleidomastoid and sternomastoid muscles were separated in the cat, but correspond to the sternocleidomastoid muscle in humans.

B, Elimination of possible effect by current spread

Intracellular potentials were recorded from neck motoneurons in the upper cervical cord of chloralose-anesthetized cats. Motoneurons were identified by their antidromic spikes evoked by stimulation of each muscle nerve. Separate electric stimulation of six canal nerves was performed according to the method developed by Suzuki et al. [6]. Final electrode position was determined by observing a characteristic eye movement evoked by stimulation of each semicircular canal nerve. At the end of each experiment, the labyrinth was opened and positions of stimulating electrodes were examined in relation to individual semicircular canal nerves.

Since the semicircular canal nerves are very close to each other, it is crucial to eliminate the possibility of effect evoked by current spread to adjacent nerves arising from semicircular canals or the otolith organs. Motoneurons of obliquus capitis caudalis (OCA) muscle received excitatory, inhibitory and excitatory input from the ipsilateral anterior, lateral, and posterior canal nerves, respectively, and inhibitory, excitatory and inhibitory input from the contralateral semicircular canals, respectively [3]. In every preparation, synaptic inputs of opposite polarity from adjacent canals on one side in OCA motoneurons were considered to be indicators to eliminate the effect evoked by possible current spread to adjacent canal nerves.

C. Input pattern to the cleidomastoid and sternomastoid motoneurons

Intracellular recordings from cleidomastoid and sternomastoid motoneurons showed that stimulation of individual semicircular canal nerves evoked excitatory and inhibitory postsynaptic potentials in these motoneurons, and from their latencies, they were considered to be disynaptic via the vestibular nucleus. These motoneurons received inhibition from the ipsilateral three semicircular canal nerves, and excitation from the contralateral three semicircular canal nerves. This pattern of input was common to all motoneurons antidromically activated from the spinal accessory nerve.

D. Pathways from the six semicircular canal nerves to cleidomastoid and sternomastoid motoneurons

In order to determine the pathways conveying inputs from individual semicircular canals to cleidomastoid and sternomastoid motoneurons, the descending medial longitudinal fasciculus (MLF) was sectioned in the midline in the medulla. All inputs from the six semicircular canal nerves were abolished after the section, indicating that they were conveyed via the MLF, not via the lateral vestibulospinal tract. Therefore, they were medial vestibulospinal tract neurons. Further sectioning experiments showed that excitation from the contralateral canals and inhibition from the ipsilateral canals were mediated via the MLF ipsilateral to the recorded motoneurons.

IV. Future Perspective

Input pattern from the six semicircular canals to cleidomastoid and sternomastoid (flexors) motoneurons was the same as that to splenius (extensor) motoneurons. Neck extensor and flexors are arranged in a symmetrical location in relation to horizontal axis of the body, and their motoneurons receive the same pattern of input from the six canal nerves. Therefore, these neck muscles form a muscle synergy, so that ventro- and dorsiflexion are always cancelled by each other, and only lateral flexion of the head occurs. This finding indicates that forming a muscle synergy can create a novel functional unit beyond the function of each muscle level.

We are determining the convergent input patterns from six semicircular canal nerves to motoneurons of individual neck muscles in the present study. From these results, we could identify a muscle synergy of neck muscles activated by stimulation of a particular canal. Our working hypothesis is that this muscle synergy activated by a particular canal is determined by the branching pattern of single vestibulospinal axons in the cervical cord. Therefore, as the second step of this study, we will analyze the branching pattern of single vestibulospinal axons in the upper cervical cord. For that purpose, single vestibulospinal axons will be penetrated in the cervical cord, identified as to their semicircular canal input, and then intraaxonally-injected with horseradish peroxidase. The stained axons will be reconstructed three-dimentionally using serial sections, and their innervation patterns of neck motor nuclei will be compared with the present electrophysiological data.

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Annual report for research project A03-3

Natsue Yoshimura
Institute of Innovative Research, Tokyo Institute of Technology

***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 the academic year of 2017, we applied one of muscle synergy analysis method to electroencephalography (EEG) cortical current source (CS) signals and showed that the EEG-CS synergy signals could enhance decoding accuracies of 8 finger movement tasks. Especially, the accuracies of 8 finger joint movements (i.e., flexion, extension, etc.) drastically increased as well as those of 8 target directions, which means this method could extract information relating to internal motion coordinate frame much better than EEG sensor signals. This research was published by Scientific Report [1].**

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 [2]. 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 aim to visualize neural representations of hand and foot movements and to investigate their relationships to muscle synergies.

III. Research Topics

A. Decoding of 8 joint movements and movement directions using center-out finger reaching tasks [1]

As a part of international collaboration with Swartz Center for Computational Neuroscience (SCCN), University of California, San Diego, who is developing the most popularly used EEG analysis toolbox called EEGLAB [3], we performed simultaneous recording of 128-ch EEG and 96-ch electromyography (EMG) signals during an 8-direction finger reaching task. Participants moved a PC cursor from the center of the screen to one of 8 targets located radially from the center and distributed 45° apart on a 10-cm radius circle. The tasks were done in two different elbow posture (extending: 0° and bending: 90°, Fig. 1). The way of data acquisition with the two postures helps decoder training to extract brain activity signals specific to target directions or finger joint movements.

We estimated EEG-CS using Variational Bayesian multimodal encephalography (VBMEG) [4] and performed decoding analysis for 8 movement directions and joint movements using the estimated EEG-CS and Sparse Logistic Regression (SLR) [5].

EEG-CS showed significantly higher decoding accuracies than EEG sensor signals in joint movement decoding (Fig. 2, EEG vs. CS). In addition, when applying principal component analysis followed by independent component analysis (PCAICA) to EEG-CS, decoding accuracies drastically increased (Fig. 2, CS synergy). We named the signals as current source synergy (CS synergy) because the PCAICA method is used for muscle synergy analysis [6].

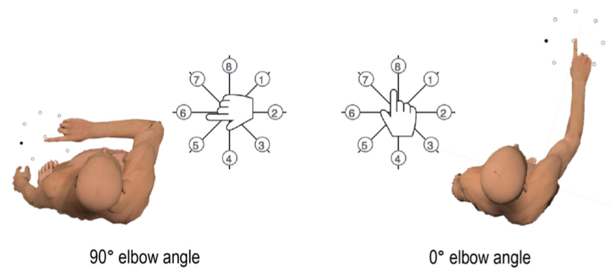

Fig. 1. Target directions and elbow angles. *(Reviced from Yoshimura et al., Scientific Reports, 2017)[1]*

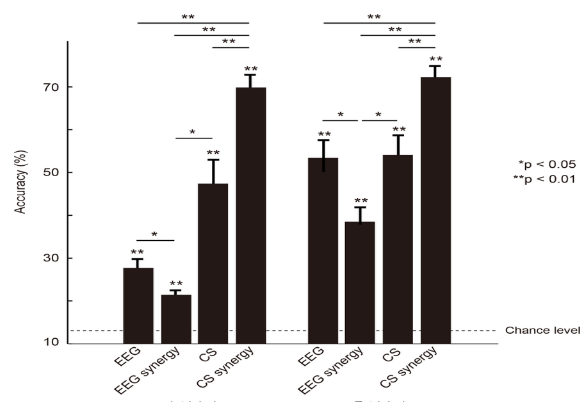

Fig. 2. Classification accuracies comparison among EEG sensor, EEG synergy, current source (CS), and CS synergy. *(Left group: finger joint movements decoding, Right group: target direction decoding. Yoshimura et al., Scientific Reports, 2017)[1]*

The increase by PCAICA was especially shown in joint movement decoding (Fig. 2. Left group). We further investigated CS synergies that were frequently selected by decoders of cross-validation analysis, and found that CS synergies that highly contributed to joint movement decoding had high spatial weight values for CSs located in the hand-knob area of the primary motor cortex. On the other hand, CS synergies that highly contributed to movement direction decoding had high spatial weight values for CSs located in the premotor area rather than the primary motor or the hand-knob areas (Fig. 3). These results suggested that PCAICA extracted information relating to joint movement exclusively from CS signals that included other information such as visual information. We therefore expect that this method can be applicable to find neural representation of muscle synergy.

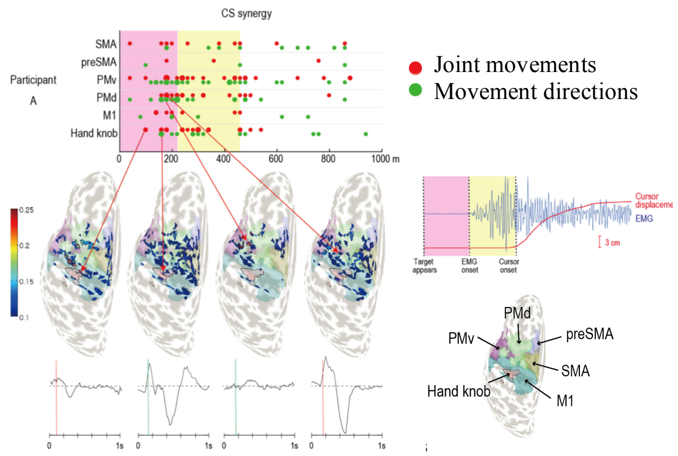

Fig. 3. Spatial and temporal features that contributed to decoding of movement directions (green) and joint movements (red).

Muscle synergies were estimated from the simultaneously recorded EMG signals using the most popular non-negative matrix factorization (NMF) method. As shown in Figs. 4 and 5, it was found that the 8 joint movements with the two elbow postures can be realized by 4 muscle synergies.

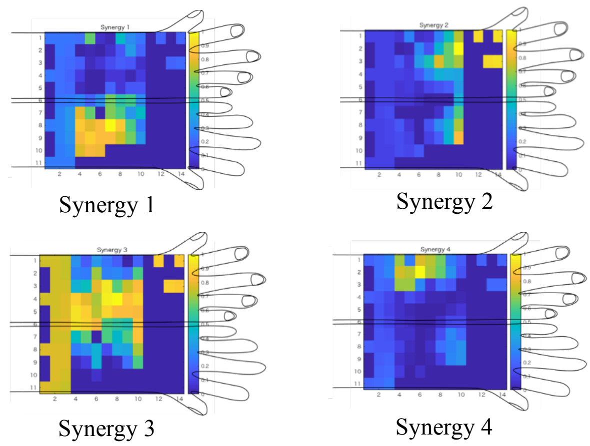

Fig. 4. Topological maps of the 4 estimated synergy weights on the arm. (*Yello represents hight weight and blue represents low weight values*).

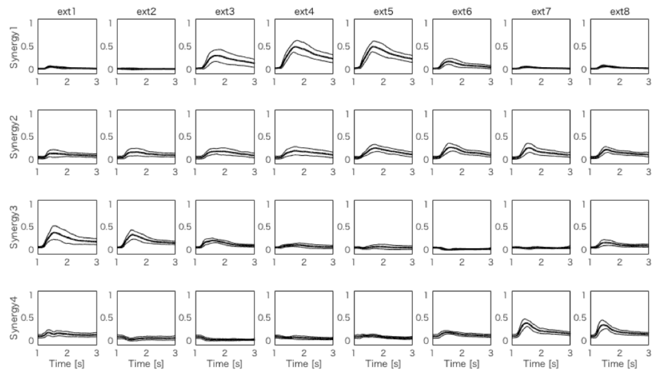

Fig. 5. Mean temporal patterns of the 4 estimated synergy for the 8 movements with extending elbow.

B. *Other achievements*

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

・A. Mejia Tobar, R. Hyoudou, K. Kita, T. Nakamura, H. Kambara, Y. Ogata, T. Hanakawa, Y. Koike and N. Yoshimura, "Decoding of ankle flexion and extension from cortical current sources estimated from non-invasive brain activity recording methods," *Frontiers in Neuroscience*, 11(733), pp. 1-12, 2018.

For the aim of developing Brain-machine interface for gait support, we decoded 9 ankle movements (flexion and extension of left and right ankles with two force levels, and no-motion) from EEG-CS.

・L. Minati, M. Frasca, N. Yoshimura, and Y. Koike, "Versatile locomotion control of a hexapod robot using a hierarchical network of non-linear oscillator circuits," *IEEE Access*, pp. 1-24, 2018.

We developed an ant-like robot that controlled by non-linear analog circuits, and oscillation patterns spontaneously generated by the circuits with only 5 hierarchical parameters realized versatile locomotion patterns that actually existed in ants.

IV. Future Perspective

We suggested CS synergy had a possibility to extract finger joint movement information effectively. In the next year, we will try to identify neural representation of muscle synergy in the brain through investigation of relationship between muscle synergy and CS synergy obtained by this experiment.

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Annual report of research project A03-4

Riki Matsumoto
Department of Neurology, Kyoto University Graduate School of Medicine

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 fronto-parietal network through the SLF III. Within the left network, functional differentiation in negative motor area was quantitatively evaluated by 3D motion capture system. Within the right network, we have explored the neural activity for self-consciousness and sense of agency. 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 2016, we delineated the fronto-parietal 'praxis' network by combining 50 Hz (fast dynamics alternation) and 1 Hz (functional connectivity) electrical stimulation. In the FYI 2017, 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 sense of agency (SoA) 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. In the patients with electrode implantation in the right fronto-parietal areas, we recorded the ECoG during the Keio method task for assessment of SoA. We also recruited patients who underwent resection of the brain tumors in the right fronto-parietal network for the longitudinal neuropsychological assessment of 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 : functional mapping and its fast dynamics alternation

We recruited 6 patients with intractable left partial epilepsy, who underwent subdural electrode implantation in the left frontal area for presurgical evaluations and quantitatively evaluated the mode of impairment when stimulating the precentral gyrus and the inferior frontal gyrus (IFG) at lower intensity, where a negative motor response or the complete arrest of fine movements was elicited at higher intensity. In 4 patients with the precentral negative motor area (NMA), the quantitative analysis revealed significant decrease of stroke in finger tapping and maximum aperture in grasping, while the reaching velocity, pantomime of tool-use did not change significantly. In the more rostral NMA (in caudal IFG and at its border to the precentral gyrus), quantitative analysis also showed significant decrease of stroke and aperture in finger tapping and grasping, respectively. In addition, reaching velocity was significantly decreased. The qualitative analysis showed arrest of tool-use pantomime in 1 out of 2 patients (IFG). Precentral NMA seems to play a more role in controlling elementary finger movements and could be responsible for limb-kinetic apraxia. More rostral NMA is likely associated with more complex movements and could be responsible for higher order apraxia [2]. We plan to elucidate the mode of alternation at the network level by stimulating simultaneously the two hub areas within the fronto-parietal network. 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. Based on our decoding experiences, we attempted to decode the types of praxis movements (tool use, non-meaningful gestures) from the high gamma activities, recorded from 7 patients. We are currently analyzing the weight information of the decoder to delineate the functional differentiation within the praxis network.

B. Fronto-parietal netwrok mapping by CCEP

In the FYI 2016, by means of electrical cortical stimulation, we revealed the functional connectivity and differentiation within the praxis-related PMv-PF network in 5 patients with intractable left partial epilepsy. In the FYI 2017, we have analyzed CCEP form SMG to the temporal lobe. 4 patients showed the functional connectivity from SMG to the lateral and ventral inferior temporal gyrus. This result clarified the direct link between the semantic and praxis networks for the access and retrieval of semantic memory during the praxis movement [3]. We have investigated the laterality of the connection between the frontal and temporo-parietal cortices by means of CCEP. The CCEP amplitudes were larger in the dominant hemisphere, suggesting the hypotheses regarding the relation-ship between language functions and the development of this network [4]. Using CCEP, we have also electrophysiologically investigated the frontal aslant tract (FAT), a deep frontal pathway connecting the superior frontal gyrus to Broca or caudal IFG [5]. Lastly, we recruited 9 patients to study the functional connectivity for the dorsal/medial parietal and frontal areas and delineated distinct connectivity patterns among the precuneus, the dorsal posterior cingulate cortex (dPCC) and the paracentral lobule (PCL): the precuneus connected more with the lateral convexity (e.g., dorsal premotor area, inferior parietal lobule), dPCC more with the medial area, and PCL mainly with pre- and post-central gyri. Within the parietal lobe, SPL had bidirectioinal connections to the medial parietal areas (the precuneus and dPCC) [6].

C. Right fronto-parietal network for corporeal awareness: transition from fast to slow dynamics

We further developed the collaborative research with the research group A02-1 (Dr. Naito). Applying wideband ECoG recording during tasks, we aim at delineating the right fronto-parietal network for self identification by defining their neural surrogate markers. 3 patients did tasks of self-other face discrimination and we recorded high gamma activity from intracranial electrodes. During the self-face judgment, 2 of 3 patients showed high gamma activation around the postcentral sulcus and IFG. We will further recruit patients with the intracranial electrode implantation and plan to decode the activity of SLF III network during self-other face discrimination by using a support vector machine.

In close collaboration with Dr. Kazumichi Yoshida (co-investigator at Kyoto Univ.), we continued a collaborative research with the research group A01-1 (Drs. Imamizu & Maeda). We recruited 11 patients with brain tumor who were planned to have the resection of the right parietal lobe or insula. We sequentially performed the SoA task (Keio method) before and after surgery to quantitate how the sense of agency changes in the acute to subacute postoperative periods. The results from patients with the insula lesion revealed dynamic change of SoA after surgery, indicating the resected area as a responsible region for SoA [7].

We have started a collaborative research with Dr Yano for the SoA estimation model. Based on this model which was established from the normal and patient data for Keio methods, we have analyzed quantitatively the postoperative dynamic alternation of SoA in the 11 brain tumor patients. In 2 cases from 11, who had intracranial electrode implantation in the right frontal lobe, we have successfully recorded the ECoG during the Keio method task. High gamma activity was observed from the right insula or premotor ventral area, implying the significance for SoA in these areas. We have also started the decoding analysis of the recorded ECoG. 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 SoA 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) for elucidation of the left and right SLF III 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

Hironobu Osaki
Department of Physiology I (Neurophysiology), School of Medicine, Tokyo Women's Medical University

***Abstract*— Peripheral nerve injury causes neuropathic pain. It is suggested that the neuropathic pain is based on not only the peripheral nerve but the central nervous system including the brain. However, representation of nociception in the primary somatosensory cortex (S1) is still poorly understood. In this research project, we focus on the representation of nociception in S1. By using c-Fos immunohistochemistry, intrinsic signal imaging and 32ch multi-unit extracellular recording *in vivo*, we found that the dysgranular area in S1 is nociceptive stimulus responsive area. For developing new method to control nociception, we used a focal infarction model and tested the effect on the input-output of the intact but connecting area. By combining these findings, we try to develop a network based method for controlling nociception.**

I. Introduction

When we feel pain, we sometimes touch and rub the painful body part to relieve the pain. This suggests that tactile information can suppress nociceptive information. Based on this phenomenon, Melzack and Wall proposed "Gate control theory", which tactile information from the skin conveyed through fast Aβ-fiber suppresses nociceptive information transmitted through slow c-fiber at the spinal cord[1].

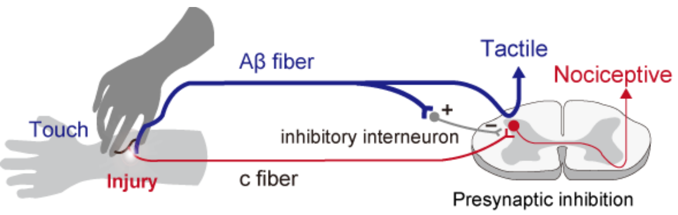

Fig. 1. Gate control theory.

Recently, the circuit supporting the gate control theory was found in the spinal cord[2]. However, the circuit based on the competition between tactile and nociceptive information within the central nervous system except the spinal cord remains to be unknown.

Some of the chronic pain condition, such as trigeminal neuralgia, sciatic neuralgia and phantom limb pain, are suggested to be based on not only the peripheral nerve but the central nervous system including the brain. For example, the severity of phantom limb pain is related with the degree of modification of the receptive field in the somatosensory cortex[3]. Therefore, we need to consider the role of higher order central nervous system for nociception. However, it remains unclear and to be still discussed about how the nociceptive information is processed within the primary somatosensory cortex (S1).

II. Aim of the Group

Our group focuses on the tactile and nociceptive thalamo-cortical pathway of mice, and explores the representation of nociceptive information in S1. We try to find the phenomenon that the competition between tactile and nociceptive information in S1 and use this competition to control nociception. For this, we explore ①the somatotopic map of nociception, ②the area of nociceptive and tactile processing area and ③pathway specific activation by optogenetics for competition of nociceptive and tactile information.

III. Research Topics

A. *Somatotopic map of nociception*

We have shown that the nociceptive information of whisker pad is processed in the dysgranular area next to the barrel field in S1 (Fig.2 upper). To determine whether the dysgranular area represents nociceptive information in somatotopic manner, we need to explore the representation of nociceptive information of other body parts in S1. For this we injected the 4% formaline into hindlimb (HL) of mice and perfused after 1 hour followed by c-Fos immunohistochemistry. As a result, we found that the c-Fos positive neurons were located within the dysgranular area surrounding tactile hindlimb area in S1. This suggests that layer 4 of dysgranular area in S1 represents nociceptive information in somatotopic manner[4].

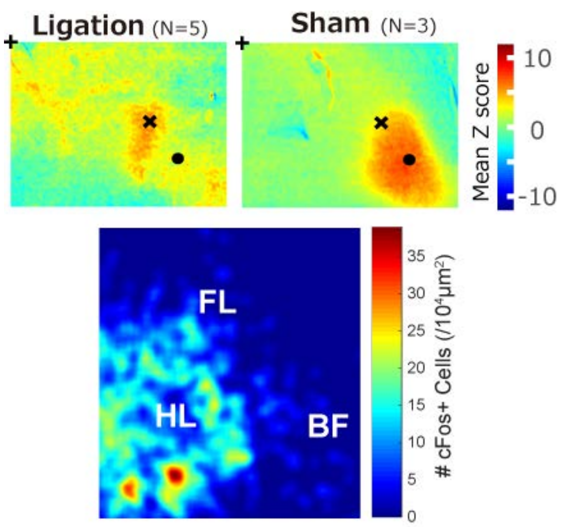

Fig. 2. Somatotopic arrangement of nociception in S1 dysgranular area.

B. *Nociceptive stimulus responsive neurons in S1*

Second, we developed the peltier heating device to produce noxious heat stimulus. By using 32ch extracellular recording system, we have successfully recorded the nociceptive neural response in S1 dysgranular area (Fig. 3).

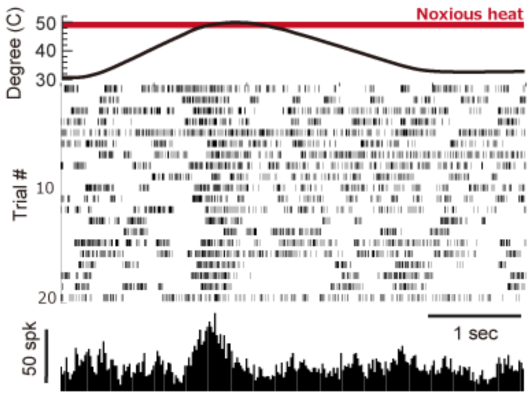

Fig. 3. Noxious heat responsive neurons in S1 dysgranular area.

C. *Developing galvo mirror controlled photoactivation*

We have found that the nociceptive information is represented within dysgranular area in S1 in somatotopic manner. If so, we might induce the nociceptive behavioral response according to the stimulated area in S1 dysgranular area. For this experiment, we are developing galvo mirror controlled laser stimulation system. By using the system, we can stimulate Channel rhodopsin 2 (ChR2) expressing neurons *in vivo* or *in vitro* according to the somatotopic map of nociception. This system will start to work at early next year.

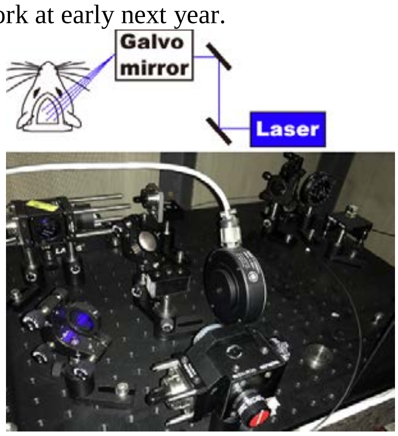

Fig. 4. Galvo mirror controlled photoactivation system.

D. *Focal infarction induced tactile response modification and laminar specific recovery*

Several cortical ablation studies were done to control nociception or pain, but the results were unsatisfactory. This is because we should consider the effect of focal ablation on the remaining connected area not only in acute phase but also in chronic phase when the nervous system shows homeostatic plasticity[5]. Therefore, we made focal infarction by using photo-thrombosis method in M1 vibrissa controlling area and recorded multi-unit neural activity in S1 barrel field. We found that M1 infarction induced hyper activity in S1 in acute phase (postoperative day 3) and this hyper activity returns to normal in chronic phase (postoperative day 14) except layer 5, which is input layer from M1. We also analyzed current-source density, which reflects afferent input modification, and found the loss of feedback input from M1 in acute phase[6].

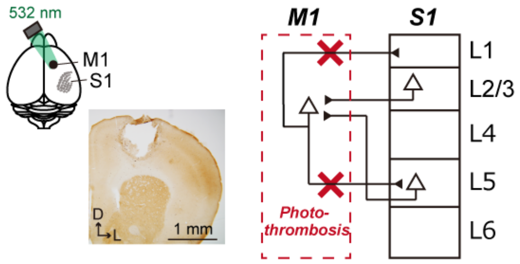

Fig. 5. Focal infarction affects connected area in layer specific manner.

IV. Future Perspective

The M1 focal infarction study suggests that we need to think about the neural network to modulate the neural activity when controlling nociception or pain. In the next year, we will use galvo mirror controlled photoactivation to modulate specific neural pathway according to the somatotopy and try to explore the competition between nociceptive and tactile information within S1 for developing a new method to control nociception.

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Annual report of research project A03-6

Noriyuki Higo
Human Informatics Research Institute,
National Institute of Advanced Industrial Science and Technology (AIST)

***Abstract*—We have investigated the mechanisms of functional recovery using a macaque model of brain lesion. In the study reported here, we investigated brain activity changes after recovery from focal infarcts induced in the posterior limb of internal capsule. At first, we established an fNIRS monitoring system to detect macaque cerebral motor activity during voluntary movements without head fixation. Using the system, we investigated brain activity changes after motor recovery from brain infarction. After recovery, increases in oxygenated Hb and decrease in deoxygenated Hb at the ipsilesional ventral premotor area contralateral to the hand used was more prominent than those before brain infarction. The causal role of the area in motor recovery was confirmed by means of the inactivation experiment. In additon, we developed and characterized a macaque model of central post-stroke pain, which is thought to be induced by maladaptive plasticity after brain damage. Further research will uncover plastic changes which underlie functional recovery as well as those which induce pathological outcomes such as pain.**

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 in similar to those of humans. Our behavioral analyses suggested that recovery of precision grip, grasping with the index fingertip and thumb tip in finger-to-thumb opposition, can be induced by 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 [1]. To bridge the gap between the results obtained in M1-lesioned macaques and the development of clinical intervention strategies, it is important to establish a non-human primate model of stroke at subcortical structures.

II. AIM OF THE GROUP

The aim of the present study is to investigate changes of neuronal functions and structures that underlies functional recovery and pathological outcomes after stroke at subcortical structures, using macaque monkeys as a model animal.

III. RESEARCH TOPICS

A. *fNIRS monitoring of macaque cerebral motor activity during voluntary movements without head fixation*

Several noninvasive methods are available for monitoring brain activity, including functional magnetic resonance image, positron emission tomography, and functional near-infrared spectroscopy (fNIRS). A current major limitation to these methods is that they require the head to be immobilized for reliably accurate measurements to be taken. Here we developed an fNIRS system capable of monitoring cerebral motor activity during voluntary movements of macaque monkeys without the need for head fixation. The fNIRS optode arrangement was customized for the present monkey study. Because the superficial layers such as the scalp and skull of the monkey head are thinner and the brain is smaller than those of humans, the optimal source–detector distance for measuring fNIRS signals from the monkey brain was presupposed to be smaller. We estimated the source–detector distance optimal for monkey brains through a calculation simulating light propagation in an optical model of the monkey head (Fig. 1).

We detected significant increases in oxygenated hemoglobin (Hb) and decrease in deoxygenated Hb in the primary motor area (M1) contralateral to the hand used in a reach-grasp-retrieval task. In more rostral and ventral regions in both hemispheres, the hemodynamic changes remained at similar levels regardless of which hand was used. Direct feeding to the subject's mouth eliminated activity in the hand M1 whereas that at bilateral ventral regions (mouth M1 area) remained. This system allows for the accurate and stable monitoring of motor activities in the motor areas of unrestrained, awake macaque monkeys.

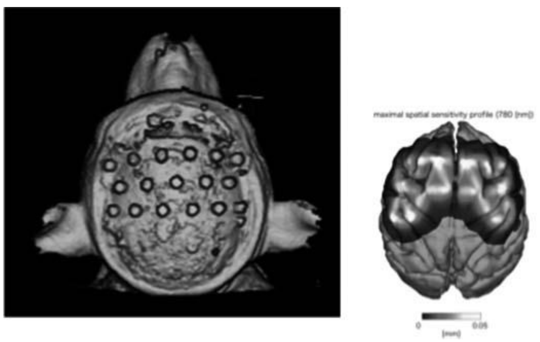

Fig. 1. Simulation of light propagation in the macaque motor cortex

B. Brain activity changes after motor recovery from brain infarction

Focal infarcts were induced in the posterior limb of internal capsule by injecting endothelin-1 (ET-1), a vasoconstrictor peptide. Immediately after ET-1 injection, paralysis was observed in the hand contralateral to the injected hemisphere, as we recently reported [3]. Thereafter, the hand movements were gradually recovered.When the hand movements were recovered almost to the level before infarction, brain activity during a reach-to-grasp movement was evaluated. fNIRS measurements were performed during the same task sessions as those conducted before ET-1 injection. Task-evoked fNIRS signals at the primary motor area (M1) in both hemispheres showed smaller amplitudes than those observed before ET-1 injection. After recovery, increases in oxygenated Hb and decrease in deoxygenated Hb was observed in additional region at the ipsilesional ventral premotor area contralateral to the hand used (Fig. 2).

The causal role of the area in motor recovery was confirmed by means of the inactivation experiment using muscimol. Our previous M1 lesion study reported the increase of activation in the ipsilateral premotor area after recovery [2]. The present result with internal capsular infarcts was similar to the previous finding. Thus, it suggested that some common mechanism in the compensatory neural change in motor cortex is involved in functional recovery in both cases. The present study also suggests that the fNIRS measurement is applicable to evaluate the brain activity change essentially occurred in the functional recovery induced by rehabilitative training.

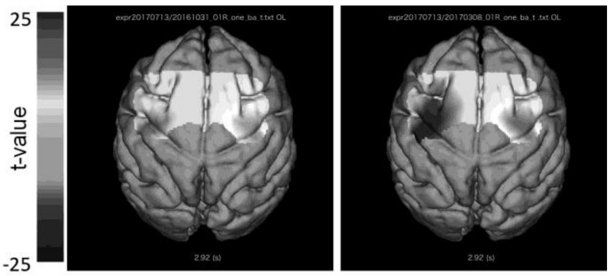

Fig. 2. Spatial mapping of activation before infarcts (left) and after motor recovery from infarcts

C. Establishment of a macaque model of central post-stroke pain

Central post-stroke pain (CPSP) can occur after a cerebrovascular accident in the ventral posterolateral nucleus of the thalamus. Developing therapeutic interventions for CPSP is difficult because the mechanism is unclear. Here we developed and characterized a macaque monkey model of CPSP [4]. The location of the ventral posterolateral nucleus was determined by magnetic resonance imaging (MRI) and extracellular recording of neuronal activity during tactile stimulation to the macaque’s hand. Thereafter, a hemorrhagic lesion was induced by injecting collagenase type IV. Histological analysis revealed that most of the lesion was localized within the ventral posterolateral nucleus. Several weeks after the injection, the macaques displayed behavioral changes that were interpreted as reflecting the development of both mechanical allodynia and thermal hyperalgesia (Fig. 3). Immunohistochemistry revealed that microglial and astrocytic activation in the perilesional areas lasted at least 3 months after injection. The present model faithfully reproduced the symptoms of patients suffering from CPSP because both mechanical allodynia and thermal hyperalgesia often develop several weeks after cerebrovascular accident. The long-lasting glial activation revealed here may be characteristic of primate brains following injury. The present model will be useful for examining the neurological changes underlying CPSP. Moreover, we believe that it will be useful for testing therapeutic interventions for CPSP. Brain activity, as measured by fMRI and fNIRS, in the macaque [5], combined with behavioral outcomes could be used to further understand the mechanism of CPSP.

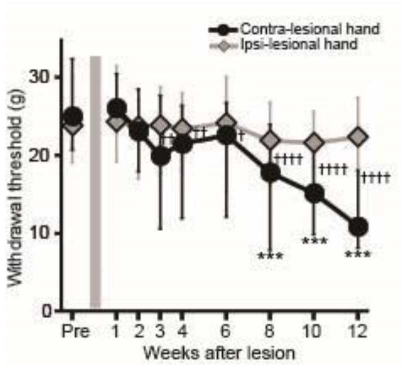

Fig.3. Weekly changes in the withdrawal response to mechanical stimulation.

IV. Future Perspective

Further research using anatomical and gene expression analyses will uncover plastic changes which underlie functional recovery as well as those which induce pathological outcomes in cellular and molecular levels.

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Group B : Systems engineering

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

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

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 (Univ. 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, Prof. Asama 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. Prof. Yano proposed that the variance of the prior distribution of body representation in the brain accelerates the learning convergence rate. He and his colleagues are currently trying to verify this hypothesis by the sense of agency and the sense of ownership tasks (with A01-1 and A03-4). Prof. Tanaka examined the activities mossy fibers (cerebellar inputs), Purkinje cells (output from the cerebellar cortex), and dentate cells (cerebellar outputs), and found that they are well described by linear models (with A02-1). Prof. Izawa identified the coordinate systems of body representation in the cortex, and found that PPC, PMd, S1, and M1 have different coordinate systems to represent the motor commands for wrist reaching movements by applying the machine learning to decode information buried under multivoxel pattern of BOLD signals taken from MRI (with A02-1). Prof. Kondo investigated the effects of target-directed motor imagery on an EEG-based BCI feature. In addition, he developed a diagnosis system for motor ataxia such as cerebellar disease using an RGB-D sensor (with A02-1), and proposed a software platform for model-based rehabilitation by combining an immersive VR and a cloud database system (with C01-1).

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.

Members of B02 constructed postural control model with muscle tonus controller by adding to conventional feedback controller. We verified necessity of the muscle tonus controller by using of detailed musculoskeletal simulations. And we obtained the results which similar to the human results in experiments of sliding platform. We also obtained a hypothesis that the muscle tonus control may increase body stiffness to reduce perturbation by experiments of multisensory alterations when there are errors between sensations. For the locomotion control model, we measured the hindlimb split-belt treadmill walking by rats to verify the fast and slow dynamics models proposed previously. In addition to the joint kinematics, we measured EMG data this year. We also investigated the muscle synergy structure from the muscles of the lower limbs, upper limbs, and trunk of Japanese macaques during bipedal and quadrupedal walking in collaboration with A02-2. We found common and specific spatio-temporal structures between the gait patterns.

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 finger movement (Dr. Natsuki Miyata @ AIST).

B03-1 (Funato), B03-1, in collaboration with C02-1 and C03-1, obtained new knowledge about muscle synergy in Congenital insensitivity to pain patients. Moreover, in collaboration with 02 groups, B03-1 revealed a relationship between muscle synergy and the efficiency of rehabilitation after stroke.

B03-2 (Hasegawa) investigated possibility of robotic finger's embodiment when the finger is controlled based on contraction of auricularis posterior muscles. The performances of the robotic finger were compared in two cases: the finger is controlled with or without vibration stimulation which could be a substitute of a deep sensation about finger position.

B03-3 (Hosoda) develops several kinds of sensors to observe the state of the pneumatic artificial muscles of a humanoid robot that has a human-comparative muscular-skeletal structure, for realizing reflex of the muscles. It studied on machine learning methods for learning kinematics/dynamics of a robot arm for acquiring the body image.

B03-4 (Miyata) studied the grasping strategy by the healthy hand with the artificially-disabled thumb in terms of joint range of motion. Taping technique was introduced to realize artificial disability and the grasps were analyzed focusing on contact regions.

III. Activities in Group B

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

-SICE systems and information symposium 2017（SSI2017）
Date: November 26, 2017
Place: Hamamatsu, Shizuoka
Contents: poster sessions: 13presentations

-Group B meeting
Date: December 4, 2017
Place: Aichi
Contents: two presentations (Yano and Fujiki)

-IEEE MHS 2017 (Micro-NanoMechatronics and Human Science)
Date: December, 5, 2017
Place: Aichi
Contents: Organized session（Oral Presentation: 5， Poster Presentation: 3）, Keynote speech (Chiba)

-29th SICE distributed autonomous system symposium
Date: January 28-29, 2018
Place: Aichi
Contents: 6 Presentations

IV. Future plan

Group B is going to hold academic society activities in 2018 like 2017.

As for research direction in Group B from the viewpoint of modelling aspect, members of Group B deal with two problems as a final year of the project: formulation of slow dynamics, and collaboration with Group A members and Group C members.

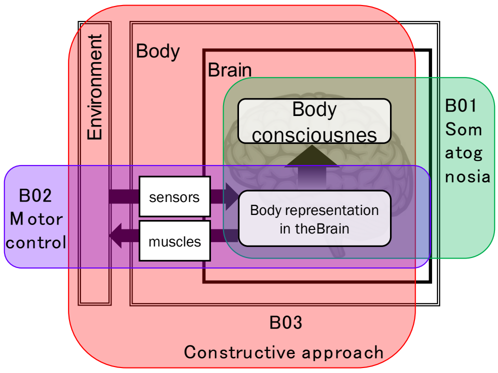

Fig. 1 Whole structure of Group B

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.

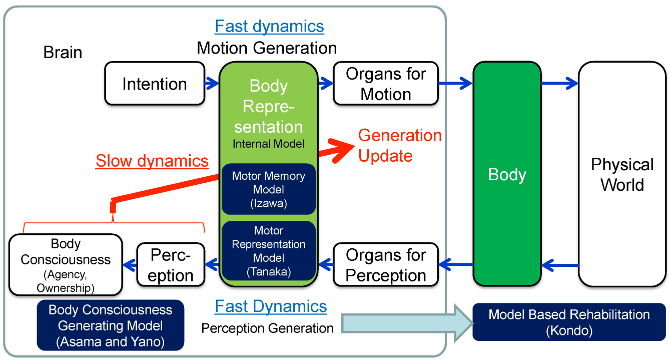

Fig. 1 Generating processes of body representation basing on body consciousness

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 attentional allocation directed by the sense of agency. We found that when people feel the sense of agency over objects, their attention is strongly attracted to the objects. More important, when people have initially acquired the sense of agency, a small loss of control also strongly attracts attention. These findings point toward careful perceptual monitoring of degree of one's own agentic control over external objects. We suggest that control has intrinsic cognitive value because perceptual systems are organized to detect it and, once it has been acquired, to maintain it [1].

Moreover, poor sense of agency is known to cause slow response, and it is important to maintain driver's sense of agency. This research investigated the driver's sense of agency under driving assistance. We found that driving experience might affect sense of agency under driving assistance. Also, we experimentally investigated the EEG indices related to driver's sense of agency, by measuring driver's alpha power. As a result, it was implied that the relationship between assisted driver's sense of agency and alpha power might differ by type of assistance, driving experience or driver's characteristics [2].

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

Asama's group conducted analysis of the changes in the body representation base on body consciousness. Specifically, we focused on the upper limb of human. To examine the dynamics of the body representation change, we performed an experiment with altered visual information. The participants were subjected to four conditions that differentially affect body consciousness. We measured body representation between before and after change quantitative and found that the structure of body representation of upper limb change with either sense of ownership or agency. Additionally, we attempt mathematical modeling of body representation change focused on the perceived finger position and introduced variable representing the body consciousness. The model is premised on that body representation of human change based on feedback from visual or somatic sense [3].

(3) Stochastic model of body consciousness

Yano (Tokyo University of Agriculture and Technology) engaged in mathematical modeling both of the sense of agency and the sense of ownership. Throughout these modeling, he formulated the relationship between fast-slow dynamics and these senses. He also proposed testable experiments and rehabilitation methods based on these models [4]. The test of these experiments is currently ongoing collaboration with A01 Imamizu Group, Maeda Group, A03 Matsumoto Group, and B01 Kondo Group.

By integrating the past researches, like comparator model and Bayesian causal inference model, he employed statistical inference approach to formulate the mathematical model. Then, based on the relationship between Bayesian inference and Mirror descent algorithm [5], he clarified which parameter determines the time constant of the dynamics related to them.

His model proposes that the variance of the prior distribution accelerates the learning convergence rate. His group are currently trying to verify this hypothesis by the sense of agency task and the sense of ownership task.

B. Embodied-brain Motor Representation Model

Toward understanding body consciousness, it is crucial to understand how the brain represents body movements [6]. Tanaka's group (JAIST), in collaboration with Kakei's group (A02), analyzed cerebellar neural activities of monkey during wrist movements for understanding input-output representations of a forward model [7, 8]. We examined the activities mossy fibers (cerebellar inputs), Purkinje cells (output from the cerebellar cortex), and dentate cells (cerebellar outputs), and found that they are well described by linear models. Also, we found that the activities of dentate cells at time t could predict the activities of mossy fibers at time t+t1. This finding suggests that the current cerebellar output is predictive for the future cerebellar inputs, a hallmark of a forward model. This work is now in preparation for submission.

Besides, we tackled the neural representations of body movements and body consciousness through high-density EEG and novel signal processing methods. We developed a novel signal processing method that extracts recurring wave patterns embedded in EEG. Our new method optimizes trial onsets on a trial-by-trial basis to obtain components that are not time-locked to external timings. The proposed method was successfully applied to mismatch-negativity data. Also, the method was extended for a group analysis and successfully applied to steady-state-visual-evoked-potential data. This work was already submitted for publication.

C. Motor Memory Model

Izawa (Univ. Tsukuba) identified the coordinate systems of body representation in the cortex and found that PPC, PMd, S1, and M1 have different coordinate systems to represent the motor commands for wrist reaching movements by applying the machine learning to decode information buried under multi-voxel pattern of BOLD signals taken from MRI while the subjects performs motor task with manipulating the handle of MRI-compatible force sensor developed also by the authors [9]. This study is collaboration with Dr. Kakei in the group A who previously identified the coordinate systems of motor commands in primate's brain.

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 target-directed motor imagery on an EEG-based BCI feature [10], and (2) developed a diagnosis system for motor ataxia using an RGB-depth sensor [11], and (3) an immersive VR system for analyzing how the visual interventions modulate bodily self-consciousness, and they applied the VR system for a patient with phantom limb pain [12].

In the first topic, this group executed EEG measurement experiments, and found that target-directed motor imagery enhances event-related desynchronization (ERD) compared with the non-target condition. This implies that it will be a promising BCI training method. In the second topic, they developed a simple diagnosis system for motor ataxia using Microsoft Kinect v2 sensor, and verified its usefulness by more than 100 participants. In the third topic, they developed an immersive VR system which enables an amputee to have strong body self-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 A and C 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

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

***Abstract*— To elucidate mechanisms of the body representation in brain for adaptive motor control, we aim to construct fast and slow dynamics models by focusing on muscle synergy. We assume that the alteration of muscle synergy structure reflects the alteration of the body representation in brain, and we clarify the contribution of the body representation in brain through modeling the fast and slow dynamics of synergy structure. In this year, we proposed fast dynamics model for postural control and verified it in movable floor experiments and musculoskeletal simulations. In addition, we measured EMG data from rats walking on a split-belt treadmill by their hindlimbs to verify our proposed fast and slow dynamics models in locomotion.**

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. To observe alterations of human posture by alterations of multisensory inputs, we experimented with manipulating of visual, vestibular and proprioceptive sensations by closed-eyes, Galvanic vestibular stimulation (GVS) and vibration on tibialis anterior tendon respectively [1]. We measured Center of Pressure (CoP) and Electromyogram (EMG) in the experiments. From the results of the experiments, we observed valid alterations of posture by the manipulations of the sensations physiologically. In the experiments, the deviation of CoP increased with closed-eyes. This indicates that "reweighting" on multisensory integration was observed in this condition. On the other hand, with GVS and vibration, we observed no reweighting but tendency of tonus increasing from EMG results. As the result of experiments, we obtained the relationships between sensory inputs, reweighting and muscle tonus outputs. These observations bring us some progress to estimate human postural controller.

To verify validity of the postural control and sensory integration models, we developed a simulator with musculoskeletal model and we observed the postural control simulations [2]. The postural controller was proposed last year, in which feedback and feedforward control were combined. The musculoskeletal model included 15 DoFs of 7 joins and 70 muscles and the controller dealt with activities of all muscle to keep upright posture. In the simulations, we added perturbations which were sliding platforms to 12 directions at every 30 deg. We can obtaine proper controllers with adjusted muscle tonus to keep upright standing on moving platform. Also, we observed that the controlled muscle activities in the simulations were very similar to experimental results. These indicate that our neuromusculoskeletal model is valid and we can estimate the fast dynamics of postural control. We also considered that muscle tonus control plays very important role in postural control as mentioned in physiology.

Currently, we collaborate with groups of C03-1 and C03-4 to investigate slow dynamics in postural control. We are designing experiments to construct a model of postural alterations in long term with patients of neurological disorders such as stroke. As our approach, slow dynamics will be modeled by comparing with experimental results and simulated results which will be obtained with parameterized muscle weakness and/or sensory weakness.

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 in collaboration with Funato's group (B03-1, The University of Electro-Communications). In this research project, we conduct the analysis of measured data of animals and simulation studies using mathematical models of the neuromusculoskeletal system. 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 structure. 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 produced rapid and slow adaptations in locomotor behavior depending on the environmental variations. Furthermore, we measured kinematic data during hindlimb split-belt treadmill walking of rats and found that the temporal pattern of the kinematic synergy showed a rapid phase shift after the environmental change, and furthermore it slowly returned after the rapid change. There trends were observed in our simulation result and verified the validity of our mathematical model in the kinematic level. In this year, we further measured EMG data during hindlimb split-belt treadmill walking of rats and found rapid changes in the EMG data, which suggests the validity of our model in the motor control level.

Furthermore, in this year, we investigated the muscle synergy structure of the Japanese macaque during bipedal and quadrupedal walking in collaboration with Nakajima's group (A02-2, Iwate Medical University). We analyzed measured EMG data of nine muscles from the lower limbs, upper limbs, and trunk of two bipedally trained Japanese macaques by using non-negative matrix factorization. We found common and specific spatio-temporal structures of the muscle synergies between the gait patterns. In particular, the linear combination of four spatial and temporal patterns can explain most of the EMG data irrespective of the individual and gait pattern. The lower-limb muscles are responsible for the three among the four patterns. The trunk muscles and upper-limb muscles are coordinated with the lower-limb muscles depending on the gait pattern. These will improve the understanding of motor control strategy for different gaits in the Japanese macaque.

These results were presented at the special session "Embodied-Brain Systems" of the 8th International Symposium on Adaptive Motion of Animals and Machines (AMAM2017) at Clark Memorial Student Center, Hokkaido University on 27-30, June, 2017 [3, 4].

IV. Future Perspective

As the 4th year of this project, we developed 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 in locomotion, which were verified by forward dynamic simulation of a neuromusculoskeletal model and measurement of kinematic and EMG data for split-belt treadmill walking of rats. These results will improve the understanding 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 with rehabilitation research groups to apply our models to monitor states of patients. We feed back the results to our models and improve modeling of the slow dynamics of the body representation in brain.

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Annual report of research project B03-1

Tetsuro Funato
The University of Electro-communications

***Abstract*—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 of patients with neural ataxia. This year, we analyzed the posture control of patients with congenital insensitivity to pain (CIPA), and analyzed synergies of stroke patients. As a result, posture control of CIPA patients showed decreasing in motion component of feedfoward control. Synergy of stroke patients showed unification of common synergies of healthy subjects, and this unification of synergies was more frequently observed in severe stroke patients than in light stroke patients.**

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 (A) an analysis of the posture control of patients with congenital insensitivity to pain (CIPA), and (B) synergy analysis of the stroke patients for synergy-based rehabilitation.

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 through the evaluation in motion and synergy analysis of patients with neural ataxia.

III. Research Topics

A. Analysis of posture control in CIPA patients

CIPA patients walk with strong impact at touch-down due to their lack in pain sensitivity. In previous study, our group, in collaboration with C group, analyzed the walking motion of CIPA patients, and found the extended activity of muscle synergy compared to healthy subjects. In order to investigate the reason of such an effect of CIPA on control system, this year, we analyzed the posture control of CIPA patients.

In the experiment, COM motion during standing was measured for 4 CIPA patients. As standing conditions, eye-closed condition and eye-open condition were alternately measured. Measurement of 60 s was performed 11 trials for 3 patients and that of 30 s was performed 4 trials for 1 patient.

Figs. 1A show the body sway of CIPA patients. From Fig. 1A, COM moved for approx. 20 mm for both sagittal and lateral direction. This behavior is almost same with that reported in healthy subjects.

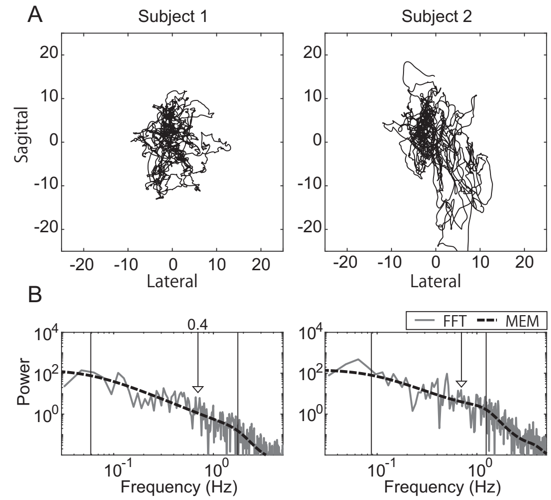


Fig. 1. Body sway of CIPA during standing

TABLE I
PEAK FREQUENCY OF BODY SWAY

	All condition	Eye Open	Eye Closed
Peak Frequency (Hz)	0.10 (0.04)	0.10 (0.06)	0.10 (0.04)
Peak Frequency (Hz)	1.51 (0.41)	1.33 (0.38)	1.67 (0.39)

Figs. 1B show the power spectrum density (PSD) analyzed using FFT and MEM. In order to estimate the characteristic of these PSDs, peak frequencies of PSD, defined as the inflection points of MEM, were searched. Then, peak frequencies were found at 1.51($\pm$ 0.41) Hz and 0.10($\pm$0.04) Hz as shown in Table I. Body sway of healthy subjects was reported to show peak frequencies at approx. 0.4 Hz and 1.3 Hz [2], [3], and thus the frequency component of 0.4 Hz was absent in CIPA patients. When we focused around 0.4 Hz in Fig. 1B based on the above notion, we can see some characteristic around 0.4 Hz, but this is too smooth to be peaks. Motion component with 0.4 Hz was reported to be generated by the no-control state or feedforward control [3]. Therefore, the present result is considered to reflect the decreasing motion of feedforward control in CIPA patients.

B. Synergy analysis of stroke patients for rehabilitation

In order to investigate a possible use of muscle synergy for quantitative evaluation of recovery after stroke, our group, in collaboration with A, B, C groups, analyzed muscle synergy of stroke patients. 11 stroke patients (2 trials for each person, 22 trials in total) and 7 healthy subjects (4 trials for one person and 3 trials for the other persons, 22 trials in total) participated in the experiment. In the experiment, each subject performed a movement of Fugl-Meyer Assessment (FMA) with 37 motion tasks. 41 muscle activities around upper body and trunk were measured, and muscle synergies were extracted using non-negative matrix factorization (NMF). As a result, 22-26 synergies were extracted from the motion of healthy subjects and 21-27 synergies were extracted from those of stroke patients. In order to investigate the effect of stroke in muscle synergy, we investigated (1) common muscle synergies of healthy subjects, and (2) change in muscle synergies after stroke.

1) Common muscle synergy of healthy subjects: In order to analyze the effect of stroke, unaffected state of synergies is necessary. Here, we investigate synergies commonly observed in healthy subjects and use them as standard synergies of unaffected state. The common synergies were defined as synergies those found in over a half of healthy subjects, and 29 muscle synergies were extracted. Then, in order to find the role of each common synergy, FMA tasks that used each common synergy was searched. In Fig. 2, 29 vertical numbers are synergies and 37 horizontal numbers are tasks. Colors in the tables show number of trials (among 22 trials) that have correlation between synergies and tasks.

2) Change in muscle synergies after stroke: In order to show the effect of stroke on synergies, relationship between muscle synergies of stroke patients and common synergies among healthy subjects were investigated. The relationship was evaluated using correlation coefficient. Fig. 3A shows the obtained relationship. There were three types of relationship (1) one to one correlation between stroke and common healthy synergies, (2) one stroke synergies related to multiple healthy synergies (one to multiple correlation), and (3) no correlation between stroke and healthy synergies. In one to multiple correlation, one synergy of stroke patients was constructed by unifying multiple synergies of healthy subjects as in Fig. 3B. Unification of synergies by stroke was reported in previous paper that compared the motion of affected and unaffected limb of stroke patients [1], and our result showed the existence of such a unification between healthy and stroke subjects.

We further investigated the degree of unification among patients, then the unification of synergies was found more in severe patients than in light patients. Therefore, such a degree of unification is considered to reflect the degree of recovery after stroke. This expects us a possible use of this characteristic as an indicator for rehabilitation. However, we also found some partly severe patients who does not show many unifications. Elucidation of this contradiction and further improvement of current method is our next target.

IV. Conclusion

- By the analysis of posture control in CIPA patients, movement by feedforward control was found to be decreased.
- By the analyssi of muscle synergies of FMA tasks, unification of synergies due to stroke was quantitatively evaluated.

Fig. 2. Relationship between common synergies and FMA tasks

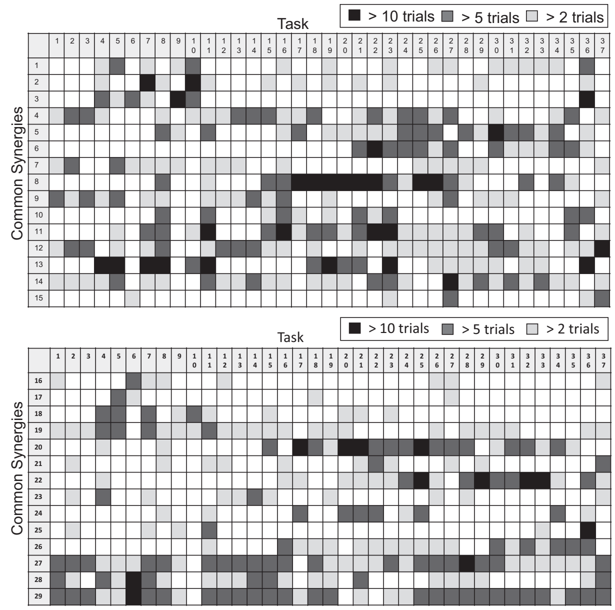
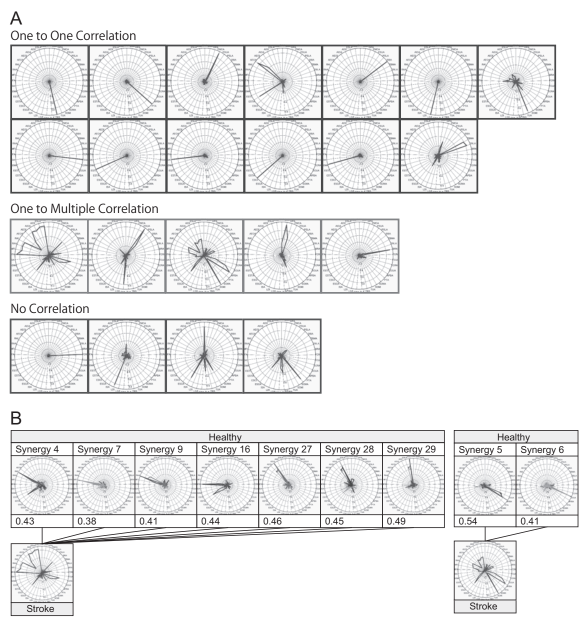


Fig. 3. Synergies of stroke patients (FMA Score: 9)



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Annual report of research project B03-2

Yasuhisa Hasegawa
Dept. of Micro-Nano Mechanical Science and Engineering, Nagoya University

***Abstract*—The purpose of our study is to clarify important factors and feedback information to facilitate body representation update for intuitive robot operation and to develop a man-machine interface to control a wearable robot as if it is a part of operator's body. In this year, we focus on an update of a body representation including an internal model of a new wearable robotic thumb in order to intuitively control it. As a result, we verified that a tactile feedback from fingers facilitates body representation update the most effectively in three kinds of feedbacks. Besides, we made a challenge to get an internal model about the wearable robotic thumb associating a vestigial muscle.**

I. Introduction

Wearable robotic limbs that aim to support the user as extra arms or fingers attract active attention from robotic researchers since they could enhance the users abilities by supplying additional supporting points for stable handling, expanding their reachable area, discharging role of their limbs, and so on [1]. Embodiment of the wearable robotic system is a key to upgrade its operability because their robotic system should be controlled in a coordinated manner with user's body motion. A new body representation of the robotic system as well as human body representation is therefore necessary for the cooperative motion planning. The rubber hand illusion and the tool embodiment imply that a body representation can be modified such as transferred and extended [2]. In our study, we aim to clarify important factors and feedback information to facilitate body representation update for intuitive operation of a robot which has multiple active joints controlled by a user.

II. Research topics

In this year, we focus on an update of a body representation including an internal model of a new wearable robotic thumb in order to intuitively control it. We study and conduct experiments

1) To find effective sensory feedback which improves Sense of Self-Location about a wearable robotic thumb,
2) To develop a vibration stimulation device for position perception of the wearable robotic thumb, and
3) To get a new internal model about the wearable robotic thumb associating posterior auricular muscle.

III. Achievements

A. Sensory feedback for update of Sense of Self-Location

The sense of self-location is one of the main embodiment aspects. We hypothesize that somatosensory feedback from fingers accelerates Sense of Self-Location update, because fingers are also used as the most common tactile sensor to know a position of own body part in infants [5]. We conduct experiments of a reaching task with a wearable robotic thumb (ERT) receiving one of three kinds of position feedback information in order to empirically verify that the somatosensory feedback from fingers accelerates sense of self-location update. As a somatosensory feedback information, we prepare tactile feedback from own fingers, tactile feedback from own face, and auditory feedback from an electric device (ADF) with three buttons on a plate. The fingers or the electric device are located around the face to simulate the same experimental condition as the second case. Six healthy men are participated

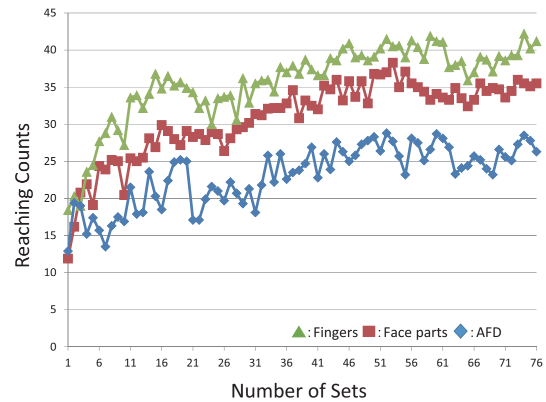

Fig. 1. Reaching counts of the target positions. Green line shows reaching counts of three fingertips indicated. Red line shows reaching counts of three positions on subject's face. Blue line shows reaching counts of three switches on the auditory feedback device.

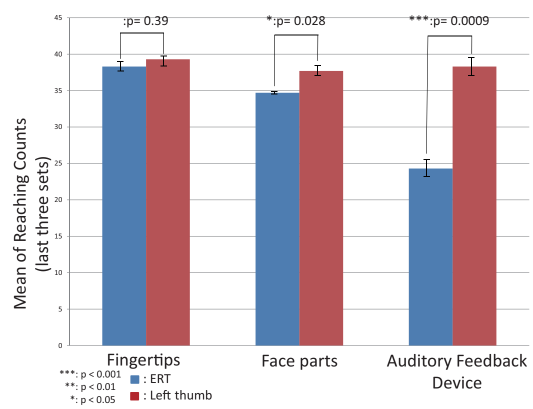

Fig. 2. Comparison of reaching counts between ERT and left thumb. Blue bar is mean of reaching counts of ERT controlled by right hand thumb in final three sets. Red bar is mean of reaching counts of his left thumb.

in the experiment. Time of one trial is 30 seconds, and one set is composed of ten trials. Fig.1 shows reaching counts by one participant. The reaching counts to three fingertips become the highest in three experimental cases, and the counts reaching the buttons on the AFD are the less in three experimental cases. The experimental results of other five participants are similar to the first case. Consequently, the tactile feedback from the fingertips could induce higher performance than other feedbacks. Fig.2 shows average of reaching counts executed by one participant in last three sets. We found that average of reaching counts of the ERT controlled by the right thumb was close to average of reaching counts of his own left thumb after the ERT operation was trained with tactile feedback from his fingertips. This result implies that the somatosensory feedback from own fingers accelerates body representation update and embodiment of the ERT.

B. Vibration stimulation for position perception of the ERT

When the ERT is controlled by right thumb, a wearer can perceive a position of the ERT tip through deep sensation from the right thumb even if the ERT is not visible. Because a muscle spindle informs muscle length and its contraction force all time. In order to control quality and quantity of the feedback information about the ERT position, we use posterior auricular muscle, which does not have a muscle spindle, in order to control the ERT. In addition, vibration stimulation is used as a controllable feedback information about CM joint angle of the ERT. A device for the vibration stimulation is developed based on vibrotactile phantom sensation (VPS). Two vibrators are put on the base of his index finger and little finger one-by-one and then the amplitude of the vibrators are adjusted independently. Fig. 3 shows mean of correct answer rates of stimulation positions among five subjects, where they are informed the number of the target positions in advance. In 3 and 4 points, subjects can distinguish the stimulus pattern higher accuracy than 70 percent. The subjects reported that they could perceive the position of the ERT tip based on the vibration stimulation.

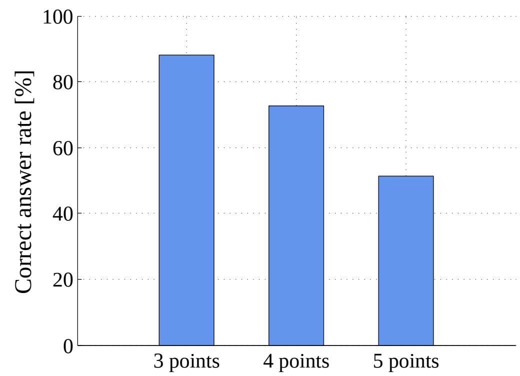

Fig. 3. Correct answer rates of stimulus patterns. Subjects can distinguish three or four stimulus patterns with high accuracy. The correct answer rate declined for five patterns.

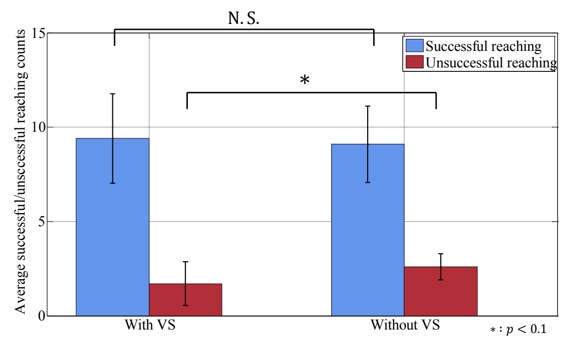

Fig. 4. The number of successful/unsuccessful reaching counts. Vibration stimulation (VS) helps the subject controlling the robotic finger more precisely, because the number of unsuccessful reaching counts is decreased by VS.

C. ERT controlled by posterior auricular muscle

We conducted reaching experiment using the ERT and the vibration stimulation device to verify the effectiveness of the feedback information as a preliminary experiment. Fig. 4 shows mean of successful/unsuccessful reaching with/without the vibration stimulation, which corresponds position of the ERT tip. As a result, feedback about the ERT tip decreased the number of unsuccessful reaching, while the success ratings are the same in two cases. When the ERT reaches one of the left hand fingers, a subject can know the ERT position based on tactile feedback from the touched finger. Therefore we could not control the position information about the ERT.

IV. Summary

In this year, we focused on a body representation update including an internal model of the ERT for its intuitive control. As a result, we verified that a tactile feedback from fingers facilitated body representation update the most effectively in three kinds of feedbacks. Besides, we developed the vibration stimulation device which displays the ERT position to an operator to learn an internal model of the ERT. Finally, we tried to generate a new internal model of the ERT through its operation using the posterior auricular muscle.

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Annual report of research project B03-3

Koh Hosoda and Shuhei Ikemoto
Graduate School of Engineering Science, Osaka University

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

I. Introduction

There are two major ways to acquire the body image in the viewpoint of system theory. One is utilizing physical consistency of the body, and the other is utilizing operability: deriving the body image from invariance through learning of a number of tasks. The latter is not really investigated thoroughly in engineering. It is important to study about it since it has a strong relation with the expression of the body image in the cognitive mechanism (Academic year 2017-2018).

Aim of the Group

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.

II. Research Topics

A. Development and Improvement 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 structure of the artificial pneumatic muscles and bones is already completed, but it only had pressure sensors to sense the states of the artificial muscles. To implement reflex such as stretch reflex, the robot should observe the length of the muscles. It needs additional sensors to observe/sense the length. This year, the project adopt a tension sensor and a new sensor that observe expansion of the muscle, which can estimate the length, and test them on the real robot.

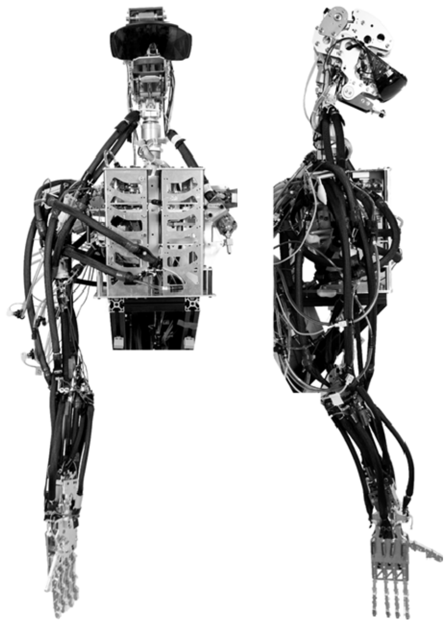

Fig. 1. Muscular-skeletal humanoid upper-body. *(The robot is equipped with 28 artificial pneumatic muscles and 1 spring. It has shoulder, elbow, an wrist joints, and a 1 DOF hand. The muscular structure is similar to that of a human.)*

B. Learning of Motion Control based on ReLU

To obtain the body image through invariance of the operation, it is necessary for the robot to learn the operation. A human is also learns its feedforward model though learning of the task, and obtains the body image.

A muscular-skeletal robot has strong non-linearity and highly complicated structure. It is very difficult for the robot designer to build its formal mechanical model. Therefore, the designer adopted a trial-and-error manner to develop the pattern of the control input. In this year, the project develops a control method to solve such a trial-and-error problem by designing learning method of the forward dynamics.

In what follows, we introduce briefly about the motion learning method. We adopt a 3-layer forward neural network for modeling the dynamics of the robot. The input of the network is the current state of the robot and the control input; the output is the state in the next step (Fig. 2). The middle layer unit is a restricted linear unit (ReLU) as an activation function. The ReLU enables to select activated unit at a time, and derive piecewise linear state equations.

The robot can utilize the equations to derive optimal control gain. Therefore, we can control the complicated robot by switching the optimal gain base on selected linear model depending on the situations. We conducted some simulations of a 2-DOF robot and a 7 DOF robot (Baxter) to demonstrate the effectiveness of the method.

III. Future Perspective

In the next year, we plan to conduct experiments to develop the relationship between the antagonistic drive and the body image.

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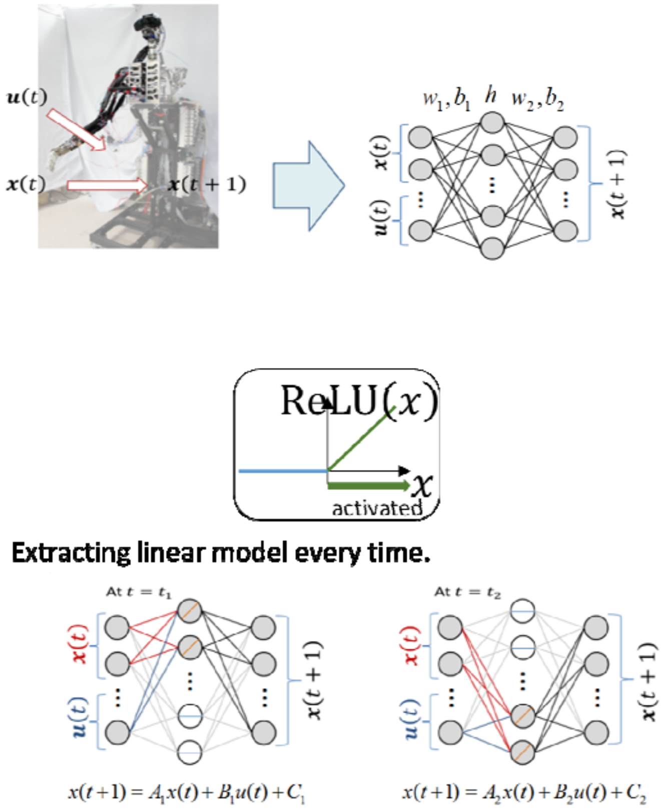

Fig. 2. A neural network for learning the forward dynamics of the muscular-skeletal humanoid upper-body. It has a restricted linear unit (ReLU) as activation function of the middle layers. The ReLU enable to pick the activated unit at the time, and derive linear state equation.

Annual report of research project B03-4

Natsuki Miyata
National Institute of Advanced Industrial Science and Technology

***Abstract*— This paper proposes a measurement of grasping strategy by healthy volunteers with artificially-disabled hand to substitute measurement of patients with disabilities in hand function to model such patients grasps for product design. As a first step of this research, we focused on limitation of the thumb and observed grasping strategy change when fixing the thumb joints range of motion using a taping technique. Different grasping styles and some typical contact regions were observed for the artificially-disabled hand.**

I. Introduction

To arrange rehabilitation plan for patients with the functionally-limited upper extremity and to design human-friendly products for such patients, we need to understand the relationship between the degree of disability and the executable function by such disabled hand. It is, however, difficult to collect such reference data by observing actual patients. Therefore, we aim to clarify adaptation process of the human upper extremity due to functional limitation by observing artificially-disabled healthy hand and to estimate and evaluate behavior of the disabled hand.

II. Aim of the Group

We concentrate on human hand grasp as a task to be executed and joints' range of motion as a target of functional limitation of the upper extremity. The aim of this group is to clarify change of grasping style according to the joint range of motion.

III. Research Topics

This year, we tested a method to realize artificial limitation of the thumb joints' range of motion. Then we studied change of two representative grasping styles according to the limitation of the thumb joints' range of motion.

A. Realization of Artificially-Disabled Thumb Joints in terms of their Range of Motion

As the thumb plays an important part in grasps [1], the carpometacarpal joint and the metacarpal joint were the target of limitation. The carpometacarpal joint was selected to resemble the disability of a patient who suffered carpal tunnel syndrome and strongly limited in its palmar abduction. The metacarpal joint was selected because this joint was indicated to work to adapt to the object size change in [2]. Their coupled range of motion were derived as in Fig.1 using the method proposed in [2] from variety of captured coordinated motions. The limitation target, CM joint, is a saddle joint that has two degrees of freedom but moves three-dimensionally. It is difficult to accurately estimate anatomic joint axes in vivo. Even though anatomic joint axes are estimated precisely, their directions are largely different from person to person and it is hard to compare among subjects. Therefore the method was extended to describe posture of the carpometacarpal joint of the thumb was using spherical coordinates as defined in the middle left side in Fig.2. The taping worked well and the joint range of motion of the fixed hand (drawn as boundaries in green) were smaller than those without any limitation (drawn as boundaries in red).

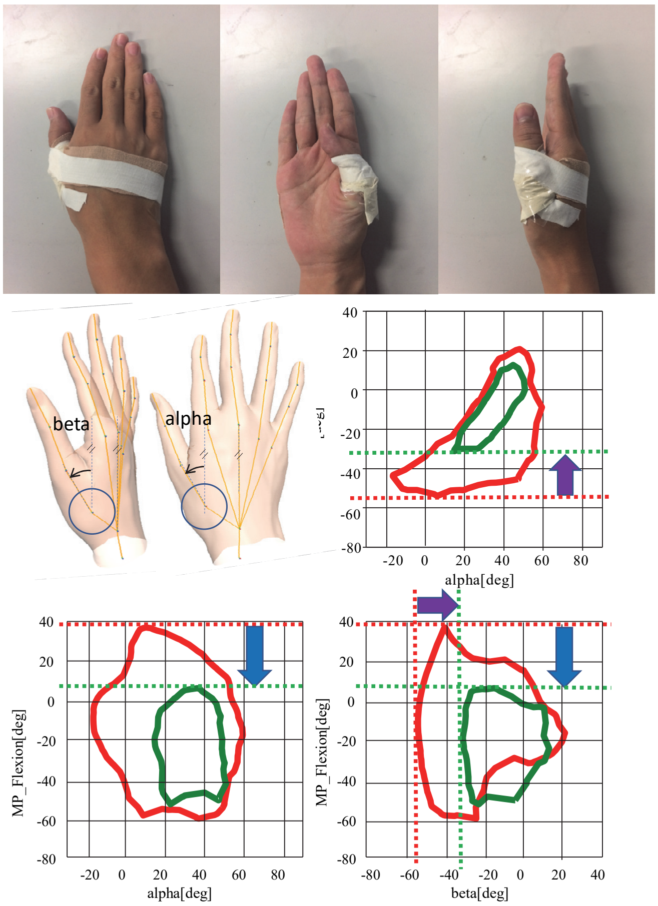

Fig. 1. Range of motion of the thumb joints with (in green) and without (in red) artificial-limitation

B. Adaptation of grasping style under the thumb range of motion

We observed grasping of two differently-sized cuboids by a volunteer with artificially-disabled healthy hand by the method shown in A. Generally, human grasping style changes according to the task to be executed. According to our preliminary experiment, several grasping styles were observed for the same condition (target object and task). Therefore, we asked the subject to repeat given tasks 10 times and observed contact region pattern and task execution time. Two tasks, “to lower a hammer” and “to transfer changing its posture”, expecting to observe two representative grasping styles: “a power grasp” and “a precision grasp”. To observe contact region as several discrete patterns, we divided hand surface into 34 regions[3]. Wooden objects were refrigerated beforehand and soon after each task execution, the regions in contact with the hand was identified manually by checking images of an infrared thermography camera and an RGB camera. To compare grasp by the artificially-disabled hand with that by the healthy hand, we also observed grasps by the left hand.

The experimental results showed that, at the beginning of repetitions, several different grasps in terms of contact regions were tested and it took longer time to execute a given task compared with that by the healthy hand. Contact region pattern converged at 10th repetition and task execution time became shorter as the same as that by the healthy hand (Fig.2). In addition, usage of the radial side of the thumb was often observed to be used, which had been rarely observed in the healthy hand grasps.

IV. Future Perspective

This year, the preliminary experiment was conducted for one healthy volunteer and the results showed that taping technique effectively worked to limit the thumb joint range of motion and radial side of the thumb was typically observed to contact the object to realize grasp when disabled. Observed grasps will be analyzed in terms of geometric and dynamics characteristics toward estimating grasps according to given limitation in our next step.

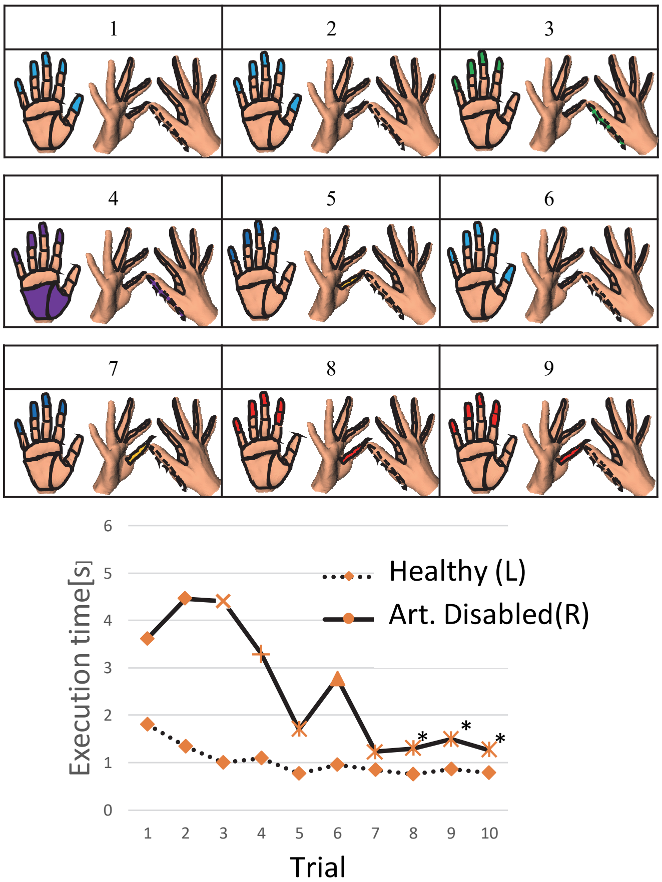

Fig. 2 Contact region pattern and task execution time transition in accordance with repeated grasp to move a small cuboid

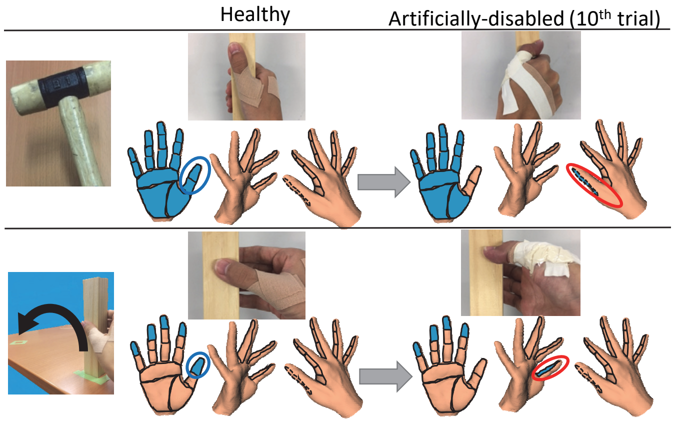

Fig. 3 Preferred contact regions under the limited range of motion of the thumb joints

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Activities of Group C (Rehabilitation medicine)

Shinichi Izumi
Graduate School of Biomedical Engineering, Tohoku University

I. PURPOSE OF THE RESEARCH

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

C01：Neurorehabilitation based upon brain plasticity on body representations

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.

C02：Rehabilitation for postural/movement impairments using sensory intervention

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

II. MEMBERS

Research Project C01

Shin-ichi Izumi (Tohoku University)
Tetsunari Inamura (National Institute of Informatics)
Naofumi Tanaka (Teikyo University)
Yutaka Oouchida (Tohoku University)
Kazumichi Matumiya (Tohoku University)
Hiroaki Abe (Konan Hospital)
Yusuke Sekiguchi (Tohoku University Hospital)
Masahiko Ayaki (Keio University)
Mitsuhiro Hayashibe (Tohoku University)

Research Project C02

Nobuhiko Haga (The University of Tokyo)
Takashi Hanakawa (NCNP)
Hiroshi Yokoi (The University of Electro-Communications)
Dai Owaki (Tohoku University)
Akio Ishiguro (Tohoku University)
Arito Yozu (Ibaraki Prefectural University of Health Sciences)
Masao Sugi (The University of Electro-Communications)
Kahori Kita (Chiba University)
Shin-ichi Furuya (Sofia University)
Kazumasa Uehara (NCNP)

Research Project C03 (2nd period)

C03-1 The relationship between body consciousness and motor control aspects of body representation in the brain
Arito Yozu (Ibaraki Prefectural University of Health Sciences)
C03-2 Motor Skill Training/Analysis of brain plasticity Through Muscle Contraction Pattern-Based Direct Rehabilitation
Keisuke Shima (Yokohama National University)
C03-3 Study on kinesthetic illusion induced by visual stimulation under the mixed reality and brain functional connectivity
Fuminari Kaneko (Keio University)
C03-4 Development of comprehensive measurement system of balance function to monitor the effect of rehabilitative interventions
Masahiko Mukaino (Fujita Health University)
C03-5 Effect of “Hybrid-Neurorehabilitation to improve Sense of Agency” for patients with stroke hemiplegia
Shu Morioka (Kio University)

III. ACTIVITIES

C01, 02, 03 group meeting

Date: Aug. 30. 2017
Place：Tohoku university
Contents: Discussion on collaborative research

A and C group meeting

Date: Jan. 22. 2018
Place：CiNet
Contents: Research reports and general discussion on the topic of "parietal network and apraxia".

Annual report of research project C01-1

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

I. Introduction

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

II. Aim of the Group

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

For this purpose, we hypothesized that there would be the cognitive mapper of body, which is a neural mechanism for estimating the body state and the environment neighboring to body utilizing the information from sensory and motor information. The states in body parts including paretic limb of the patients with hemiparesis would be coded in this mapper in the brain and this mapper could bring the body consciousness, such as body ownership and self-agency, to us when we move a body part. According to previous studies, because this mapper seems to be very flexible to the change in the body and environments, the body consciousness generated by the mapper also change when this mapper change. Thus, although it is natural that we could access the cognitive mapper of body in the brain through the body consciousness, we have no way to know and measure the change of the mapper by an intervention to body consciousness. 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. 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 paretic limb function and the body-specific attention

We showed the decline of body-specific attention to the paretic hand and the recovery of the decline as the function of a paretic hand was improved by rehabilitation. In this year, we conducted the same experimental protocol to the lower-limb amputees in order to examine the relationship between the proficiency of using a prosthesis and the body-specific attention to prosthesis. In this experiment, we measure the body-specific attention toward the prosthesis of the amputees at the two time points, immediately after starting to use a prosthesis and just before discharge of hospital in the same experimental procedure as the studies for stroke patients with hemiparesis. Comparing the two time points of the body-specific attention to a prosthesis, the higher maximum gait speed with highly skilled in using prostheses, the more body-specific attention paid to a prosthesis, suggesting that a prosthesis become a body part in the brain. Thus, the amount of the body-specific attention to prostheses reflects the proficiency of using the prosthesis objectively, and is possibly one of the scales for the embodiment of artificial body like a prosthesis and tool.

2) The rehabilitation utilizing the body ownership of paretic limb.

According to the evidences about body ownership by A01 group, the body ownership has potential influence on motor control in normal healthy volunteers. Thus, we examined the relationship between body ownership and motor control of paretic limb in stroke patients by using the rubber hand illusion technique during imitation training. Thirteen stroke patients with hemiparesis were required to wear a head mounted display (HMD) and watch the movie of a hand stroked with a brush repeatedly at the same time as their real hand stroked with a brush synchronously or asynchronously. After this modified rubber hand illusion procedure, they were asked to imitate the cyclic finger open-close movement, displayed through a HMD. We measured the range of motion of fingers during the imitation movement. After imitation movement, we interviewed the strength of illusory body ownership to the observing hand in a HMD. They answered the stronger illusory ownership in the synchronous condition than that in the asynchronous condition. Also, in synchronous condition they made statistically significant larger range of motion of paretic fingers than that in asynchronous condition, suggesting the close relationship between body ownership and motor control of paretic hand during imitation movement.

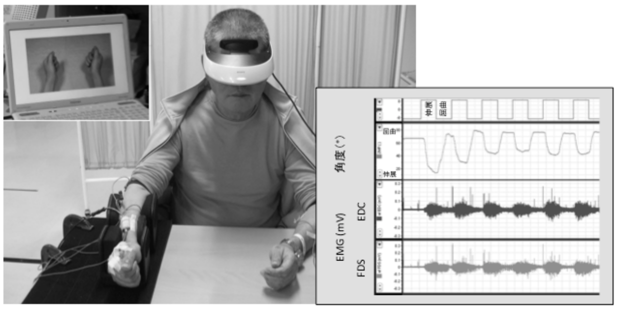

Fig. 1. Imitation training using the head-mounted display

B. Development of rehabilitation support system based on VR

Inamura Group (NII) continued to build and improve the cloud-based neuro rehabilitation system based on SIGVerse to promote collaborative research in the whole project. This year, we have improved the system configuration to use SIGVerse ver.3 which uses the integrated environment Unity for VR application development. The new platform enables the researcher to develop various experimental systems and accept a variety of requests from the clinical field.

1) Motion Augmentation for hemiplegia

We started to investigate whether it is possible to influence the behavior of the patient with hemiplegia by exaggerating the motion using VR. In this experiment, the system measured finger motions by a sensor glove device (VR Senso manufactured by Senso Devices Inc.), and exaggerates the bending angle of the finger in VR. Subjects observe the augmented finger motion through a HMD in real-time. Since a software module to use the VR Senso is provided by Senso Devices Inc., the labor for developing a rehabilitation application has been greatly reduced. Verification of the effect in actual patients is scheduled for in the next fiscal year.

2) Alien Hand Motion Experiment System

In collaboration with Prof. Shimada (C03-5 group), we developed an alien hand motion experiment system. We measured the finger open-close movements using VR Senso, reproduced the movement of the finger in VR in real time, and presented it visually in HMD. After opening/closing motion, visual stimulus of unexpected virtual finger movement was inserted when instructions were given from the experimenter to keep hands open. An experimental system was constructed to investigate the relationship between the motion induction at this time and the degree of effect/stimulus conditions. Experiments with 16 subjects revealed that motion induction occurred on the average of 2.34 degrees (S.D.=2.45 degrees) of the finger angle. The collected data was stored in a NII's cloud-based database, and it was confirmed that the same laboratory environment can be used simultaneously at multiple institutions.

3) An occupational therapy system using myoelectric sensor

In collaboration with Prof. Kondo (B01group), we connected the armband-type myoelectric sensor named Myo (manufactured by Thalmic Labs Inc.) to the platform and developed the basis for measuring various kinds of motion with myoelectric signals in VR. Since a software module for Unity is distributed by the manufacturer, the development efficiency has dramatically improved compared to the conventional system. Fig.2 shows a VR experiment environment of the OT based on the SIGVerse, which requires both of arm/hand motion and control of grasping force through the myoelectric signal.

Fig. 2. An occupational therapy system using myoelectric sensor

IV. Future Perspective

These results revealed that changing the stimulus presentation in the VR space was able to induce the same alteration in the actual body perception. Furthermore, the basis of developmental platform utilizing SIGVerse ver.3 based on Unity has been arranged. In the future, we will conduct experiments with clinical populations based on this platform, confirm the usefulness of the platform and verify long-term effects for rehabilitation.

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Annual report of research project C02-1

Nobuhiko Haga
The Tokyo University Hospital

I. INTRODUCTION

To perform motion properly, various types of sensory input must be reflected in posture/motor control prior to or concomitantly with the motion. Thus, the motor impairment is not just a musculoskeletal problem and related to sensory problems, 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.

Until last year researchers in project C02-1, in collaboration with other researchers in project in C02, A, and B, have started measuring muscle synergy and its related parameters in various disorders affecting motor system. They also tried to evaluate changes of the parameters after interventions like prosthetics transforming sensory modalities.

II. AIM OF THE GROUP

The aims of Haga/Yozu group (The University of Tokyo) 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 (National Center of Neurology and Psychaitry) is to discover imaging biomarkers of neural representation of body reflecting pathophysiology of movement disorders. To accomplish this aim, they conduct multi-modal imaging studies in patients with Parkinson's disease as a model of gait disturbance and those with focal dystonia as a model of impaired dexterity.

The aims of Yokoi/Sugi group (The University of Electro-communications) 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 measurement is proposed for detecting neuroplasticity produced in motion of limbs induced by muscle synergy control as FD.

Owaki/Ishiguro group (Tohoku University) proposed a novel biofeedback prosthesis that transforms weak or deficient kinesthetic feedback into an alternative sensory modality, for rehabilitation of sensory impairments. The goal of this group is to verify the long-term effect of this prosthesis in patients with sensory impairments.

III. RESEARCH TOPICS

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

Haga/Yozu group made the up-to-date summary of CIP. 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 and Funato groups. The immediate effect of intervention that compensates sensory disturbance was evaluated. Improvements were observed in kinematics, muscle synergy, and plantar pressure. The investigators also developed a system to measure brain activity. They also proposed new methodologies to express various types of gait [1-2]. Furthermore, Yozu has measured the gait of the CIP patients and is analyzing data in collaboration with Owaki and Funato groups.

B. *Changes of body representations in movement disorders*

Hanakawa group has found that distortion correction of resting-state functional connectivity fMRI (rsfcMRI) at a preprocessing stage improves detectability of the "default mode network", using both real and synthetic datasets [3]. By combining rsfcMRI and machine learning technique, they also identified that interhemispheric connectivity predicted severity of parkinsonian gait disturbance in patients with idiopathic normal pressure hydrocephalus (iNPH) [4]. They also found that patients with Parkinson's disease are slow not only in both execution and imagery of movement but also in mental calculation. This slowing was ascribed to functional disturbance in the cortico-thalamo-basal ganglia circuits that run parallel with each other [5]. Also, in patients with Parkinson's disease, abnormal connectivity in the basal ganglia, amygdala, and premotor cortex was found to be associated with gait disturbance (Togo et al. in preparation). In patients with embouchure dystonia, mouth representation of cerebellar activity was correlated with severity of dystonic symptoms (Uehara et al. in preparation).

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 realize intervention in muscle synergy control FD by functional electrical stimulation (FES), they have also developed an FES system with 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), and stimulation wave profiles, which are adjusted according to individual patient. In this context, they are now studying and doing experiments the following topics; (1) quick search of appropriate stimulation pattern for desired hand and finger postures, (2) stimulation wave profiles suitable for elbow-joint flexion, i.e., oscillation frequency and duty ratio of carrier-wave in burst-modulated rectangular stimulation wave.

D. Efficacy of prosthetics transforming sensory modalities

Owaki/Ishiguro group examined a one-month long-term walking rehabilitation (30min/day walking training on treadmill) for 2 stroke patients with severe sensory impairments. We conducted 7 times interventions with auditory biofeedback prosthesis during the first 2 weeks. We investigated the kinematic and kinetic effects of intervention at the pre-condition (before the intervention), 2w-condition (after 2 weeks), and 4w-condition (after 4 weeks) by using 3D motion capture system and force plate. To analyze rehabilitation effects and underlying mechanism, with the C01 group (Prof. S. Izumi's group), we measured an indirect biomarker (here, we employed "body specific attention") to capture the slow dynamics in the brain plasticity.

We confirmed the following results: (1) stride length during stance phase increased through the first 2 weeks but decreased through the second 2 weeks; and (2) body specific attention also increased through the first 2 weeks but decreased through the second 2 weeks. This fact suggests that increasing body specific attention enables stroke patients to load on paretic side, resulting in the increasing walking performance.

IV. Future Perspective

Until last year, groups in C02 project had started measuring muscle synergy and related parameters in motor impairments, collaborating with groups A and B. Interventions such as prostheses transforming sensory modalities had also started. This year they continued measurements, and clarified some changes in FD and SD by interventions. In the following year, our project will propose new theories for rehabilitation that aims to improve motor disorders using intervention to sensory system.

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Study on visually-induced kinesthetic illusion in mixed-reality environment and brain functional connectivity

Fuminari Kaneko
Department of Rehabilitation Medicine, Keio University School of Medicine

Abstract—**Temporal and spatial summation of multimodal inputs enhances neural plasticity. We have developed a mixed reality rehabilitation system, which can induce kinesthetic sensation using visual stimulation (KiNvis). The purpose of the present study was to clarify the influence on sensory-motor function by repetitively inducing KiNvis from the aspect of brain functional connectivity. Healthy subjects participated in the 1st study. KiNvis was administered five times in total to the participants, and functional magnetic resonance imaging (fMRI) experiments were performed in a stationary state. For the subjects who completed a series of experiments at the present time, fMRI data was analyzed to show functional brain connectivity. Matrix of the cross-correlation between ROIs (table) was represented for one subject (figure 1). The second study reports the consequences of the convergent approach (figure 2), including cognitive and physiological stimuli, on brain functional connectivity aspects. We analyzed fMRI data recorded before and after the intervention of our convergence approach to a patient with chronic stroke. We further accumulate this kind of analysis to clarify the effect of repeated administration of KiNvis on brain functional connectivity.**

I. Introduction

Conventionally, afferent input from the muscle spindle caused by vibration stimulation to the tendon part of skeletal muscle of a subject who is stationary is well known to induce perception of motion. It is called kinesthetic illusion [1]。 We called KiNvis (kinesthetic illusion induced by visual stimulation) the illusion of movement caused by visually inputting movements of limbs [2]. By placing artificial limbs (computer graphics, animations of the limbs of self and other people, mannequins, robots, etc.) at appropriate positions in front of the subject, it causes to feel body-ownership. KiNvis can be induced by visually inputting the state that artificial body is moving. KiNvis sustains changes in the corticospinal excitability by convergent with other stimulations. Furthermore, if the subject is experiencing KiNvis for a long time, a spontaneous movement occures that does not give rise to a sense of agency [3]. Thus, it is clear that the induction of KiNvis has a strong influence on the motor output system. Therefore, we began to examine the effectiveness of KiNvis on motor impairment caused by central nervous system including sensory motor paralysis after stroke [4]. Under the circumstances where KiNvis can be induced, by detecting the timing of intention for a limb movement from the biological signal, and synchronously controlling the artificial movement image appropriately, can induce obvious self-movement agency. So far, we have developed such a system by supporting of the Japan Agency for Medical Research and Development (Research and Development of Advanced Medical Devices and Systems to Achieve the Future of Medicine,) and it has already commercialized. We are aiming to use the achievement of the present study as the fundamental materials of neuroscience-based rehabilitation for patients with neurological impairment using KiNvis.

II. Aim of the Group

The purpose of this study is to clarify the mechanism of clinical significance of repeated induction of KiNvis from aspect of brain functional connectivity.

III. Research Topics

At the present moment, this experiment with 7 healthy participants was completed and data analysis is in progress. In addition, we have already begun clinical studies initially planed for next year, that is an analysis of brain connectivity change for a patient with stroke.

A. Investigation 1：Study on brain activity caused by repeating KiNvis

-Analysis on brain functional connectivity using fMRI-

The present investigation was designed as a prospective longitudinal intervention study using fMRI. fMRI measurement during resting-state is underwent for each subject, total 4 times measurements. The first measurement is a normal resting state, the second measurement is immediately after the first intervention of KiNvis, the third measurement is immediately after the fifth time KiNvis intervention was performed, the fourth measurement was, within 2 to 4 weeks from the end of KiNvis intervention, immediately after KiNvis.

In the MRI experiment, a T1-weighted image of the whole brain was taken with a 1.5T MRI scanner. During the resting state, subjects were instructed to keep their eyes opened and to remain motionless in the MRI gantry. At each session, whole-brain images was collected using a T2*-weighted gradient-echo echoplanar imaging sequence. fMRI data were preprocessed using AFNI (Scientific and Statistical Computing Core, National Institute of Mental Health, USA) software. Preprocessing steps included spatial realignment to the mean volume of a series of images, normalization into the same coordinate frame as the MNI template brain, band-pass table

ROI No.	Anatomic Location	x	y	z
1	Left Motor Cortex	-39	-26	51
2	Right Motor Cortex	38	-26	48
3	Supplementary Motor Area	0	-21	48
4	Left Precentral Gyrus	-33	-3	60
5	Left Superior Parietal Lobule	-36	-54	60
6	Left Inferior Parietal Lobule 1	-51	-42	45
7	Left Inferior Parietal Lobule 2	-33	-45	51
8	Left Insula Lobe 1	-30	18	6
9	Left Insula Lobe 2	-39	21	3
10	Left Fusiform Gyrus	-30	-81	-9
11	Right Precentral Gyrus	33	-3	60
12	Right Superior Parietal Lobule	36	-54	60
13	Right Inferior Parietal Lobule 1	51	-42	45
14	Right Inferior Parietal Lobule 2	33	-45	51
15	Right Insula Lobe 1	30	18	6
16	Right Insula Lobe 2	39	21	3
17	Right Fusiform Gyrus	30	-81	-9

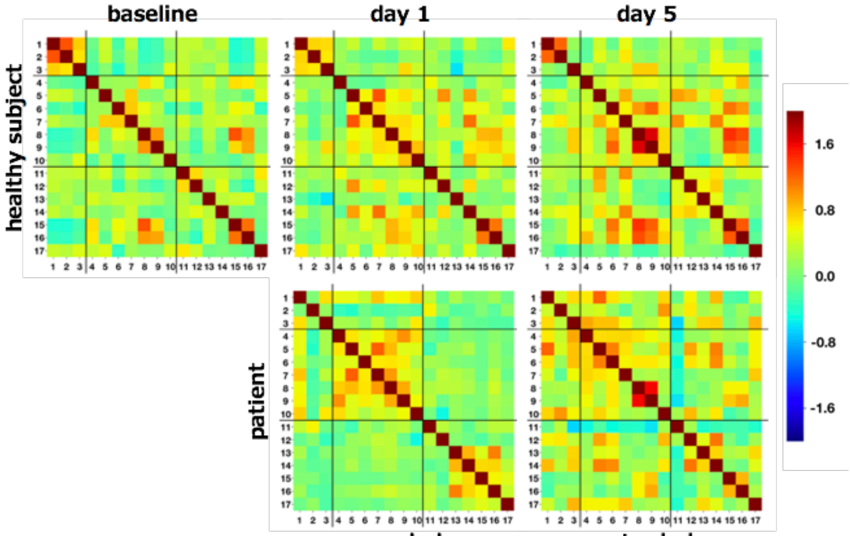

figure 1

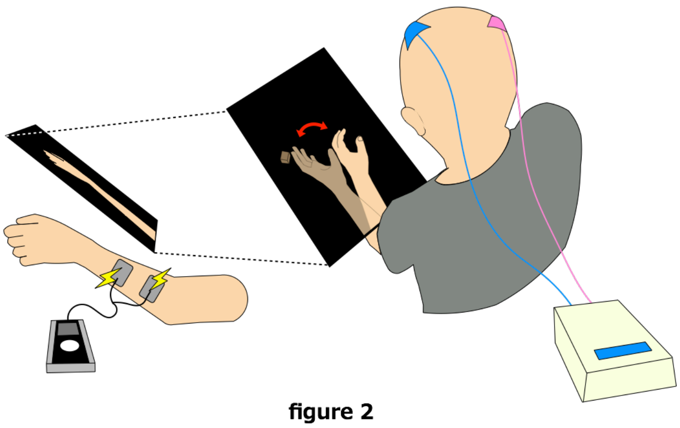

figure 2

filterin, and smoothing using a Gaussian filter of 8mm full width at half maximum.

As an analysis of fMRI data, a 6 mm spherical seed was placed in each region of interest (ROI) (table) referring to the previous studies. Correlation analysis was performed from the average BOLD signal extracted from each ROI and the correlation coefficient was converted to the value of Gaussian distributed values through Fisher z-transformation. Here, the correlation coefficient between each ROI obtained in one subject is shown as a matrix (figure 1).

B. Investigation 2 : The effect of convergent approach including KiNvis on sensory-motor impairment in a patient with stroke. –Analysis of brain functional connectivity-

The patient, a right-handed man in his 50s, presented with right putamen hemorrhage in the chronic stage, without cognitive impairment. The hemorrhage occurred 2 years before presentation; conventional post-stroke rehabilitation was performed. Before participating the present clinical study, he was at home. Activity of daily living was functionally independent with using t-cane. The approach we applied to this patient was a package of a course for 2 weeks. This convergent approach included transcranial direct current stimulation (tDCS), neuromuscular electrical stimulation (NMES) to the targeted muscle, furthermore the patient recalled a movement imagery following the movie projected on the display during KiNvis (figure 2). Namely, we carried out an approach assuming that the brain activity induced by KiNvis, the anode current of tDCS, the afferent input by NMES, and the brain activity due to recall of movement image influence convergently on damaged hemisphere. There was a functional change in the shoulder joint and the elbow joint in the behavioral indicators before and after this approach. The result of analysis on brain functional connectivity was shown in the lower part of figure 1.

IV. Future Perspective

We are expected to finish research 1 of healthy subject in the current fiscal year. In addition, data evaluated in patients was begun to accumulate and this clinical research can be said to be in progress favorably. Further analysis will be carried out.

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Annual Report for Research Project C03-4

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

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. In this study, we have developed 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. 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). In this year, based on the interrelationship between COG and COP obtained so far, we have tried (1) simulation of control of COG by COP based on the relationship between COP-COG distance and COG acceleration, (2) investigation of the COG movement during gait, (3) A preliminary study on the COG movement in response to perturbation. Previous study have shown that there is a correlation between the acceleration of COG and the difference in positional relationship between COG and COP. In this study, we further assumed that there would be the change of the moment of inertia due to the change in posture, that possibly influence the relationship between COG and COP movement. In fact, if we allow the different coefficient between the single stance phase and double stance phase, we could find the value for possible moment of inertia with which the COG movement could be accurately (±5%) estimated from COP movement. The COG-COP relationship during hemiparetic gait was also investigated. The relationship between indices based on COP-COG distance and COG speed during step could also be applied during gait. These results may 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.

In the rehabilitation clinics, stabilometer is common for objective measurement of the balance function, however, this could be used as . The stabilometer is to see the fluctuation of the COP during standing, and the total trajectory length, the outer circumference area, etc. are used as indices for evaluating balance function. Meanwhile, there is only a few reliable objective measurement method for balance ability during movement, and that require expensive devices. Accordingly, clinical scales are solely used for evaluation of balance ability during movements.

Previous studies have shown the positional relationship between the COG and the COP closely correlates with the acceleration of the COG. So far, we have shown that the indices based on COG-COP relationship during stepping correlates with the balance ability measured by the clinical scales.

In this year, we have tried to model the relationship between COP and COG on the basis of COP-COG relationships that we have clarified so far, and also compare the relationship between indices during stepping and walking. The development of experimental devices for evaluation of the COP - COG relationship in response to perturbation was also performed.

III. GROUP AIM

The purpose of this study is to model the balance control based on the correlation between indices of the balance function that have been developed so far and examine the application to the relationship of COP and COG during walking and in response to perturbation.

IV. RESEARCH TOPICS

Methods

A. Development of simulation model of COP-COG relationship

From the measured values obtained by simultaneous measurement of COP and COG by force plate and three dimensional motion analysis system, the relationships between the COP-COG lateral distance and the acceleration of COG was evaluated. As shown in the previous studies, the COP-COG lateral distance and the acceleration of COG was closely correlated (3). If the moment of inertia of the body could be assumed to be constant, the lateral component of the angular acceleration of the COG could be expressed as follows.

$$COG\alpha = Dx * (Dz / D) * mg / I$$

COGα : the angular velocity of COG, Dh: the difference in x (horizontal) coordinate of COG - COP, Dz : the height of COG, D : the distance on the frontal plane of COG - COP, m : body weight, g : gravitational acceleration, I: moment of inertia

In this case, since Dz and D are very large with respect to Dx, the acceleration could be assumed almost proportional to Dx, which is the horizontal component of the distance of COP-COG.

Assuming that this relationship is basically constant, the speed of COG in the X direction at a certain time point is considered to be expressed by the following equation.

$$COGV = COGv\ 0 + \int k\ (COGX - COPX)\ dt$$

COGX: X coordinate of COG, COPX: X coordinate of COP, COGV: COG speed, COGV 0: initial velocity of COG, k: constant

Using the data for five healthy subjects, we calculated the position of COG from the initial position of COG and COP and the speed of COP and examined whether there is a constant k that enables converging to the final COG position. As a result, constant k could be determined for each subject. The calculated COG movement was correlated with the actual movement of COG, with the correlation coefficient of 0.98 ± 0.01, and the difference average was 0.11 ± 0.02 cm. However, the amplitude of the COG movement was not comparable to the actual value, where the estimated value was 74.3 ± 20.4% of the actual value. The averaged absolute value of the difference was 0.52 ± 0.27 cm, and the proportional error was detected on Bland-Altman plot (Fig.1 left : Correlation coefficient 0.74 ± 0.36).

Considering that k is a constant that is influenced by the moment of inertia, values may differ between the single-stance phase and double stance phase. Therefore, we tried to set constant separately for the single stance phase and the double stance phase.

Then, in all cases, the best solution of the coefficient which is better than the case of assuming single coefficient was obtained (Fig.2). The correlation coefficients between the measured value and the estimated value were 0.99 ± 0.01, the average of the difference was 0.09 ± 0.03 cm, the average absolute value of the difference was 0.23 ± 0.03 cm, and the amplitude was 103.8 ± 6.5% of the actual value. Proportional error was slightly observed, though the correlation coefficient did not show a constant trend (Fig.1 right: Correlation coefficient -0.13 ± 0.37).

B. Examination of COG-COP relationship during gait

Subjects) 17 patients with stroke hemiplegia and 5 young healthy subjects were included.

Method) To evaluate the ability of balance control based on the COP-COG relationship, simultaneous measurement using three-dimensional motion analysis system and force plate was performed. COG was calculated from ten markers of the trunk and limbs. The subjects was asked to walk on the treadmill and measurement was performed for 20 seconds.

The indices calculated were; the average of difference between COP and COG position (Averaged (| COP | - | COG |) subtraction value: ASV) from the heel contact to the single leg support period, COG and COP speed and COP-COG agreement in direction during double stance was calculated. We also examined the relationship between COG acceleration and the COP - COG distance.

Result) In each case, ASV showed a high correlation with the center of gravity velocity at walking (r = 0.77 to 0.83), similar to the data of stepping. However, the ASV value was poorly correlated with the Berg Balance Scale (r = 0.45), compared with the data from stepping. COG speed varies with several factors such as gait speed and gait asymmetry, and supposed to be determined by various factors, not only balance ability. Additional experiments to clarify the determinants of COG movement is now planned.

C. Examination of COG-COP relationship at disturbance

In order to examine the COG-COP relationship in response to perturbation, we performed preliminary study with healthy subjects. Measurement was performed under predictive and reactive conditions in reaction to perturbation in two different speed.

There was a tendency that the correlation between COP and COG was lower (r = 0.03 to 0.49) in both perturbation conditions than in step conditions. In the perturbation condition, the change in constant corresponding to the moment of inertia, such as the change of the muscle tension, could be large. Assuming several different constants for three or four conditions during the response to perturbation, the estimated trajectory could be highly correlated (r=0.95~0.99) with the movement of the actual center of gravity. However, fixed bias of about -1.0 on average was observed. Further investigation in applying the model would be needed.

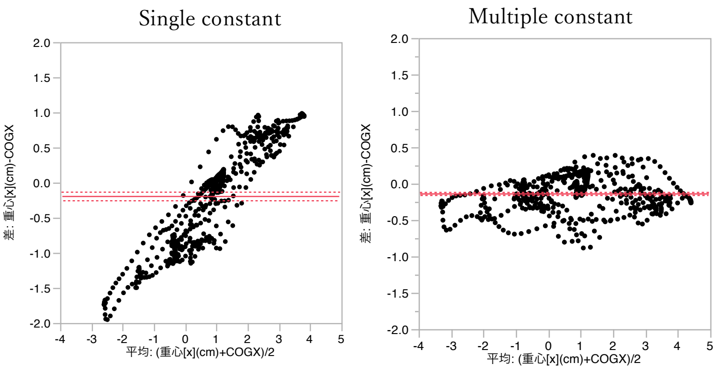

Fig. 1. Representative result of Bland-Altman plot of simulation results and actual COG

V. Future Perspective

In this study, we focused on a mechanism by which the COG acceleration is controlled by the COG - COP relationships.

Further, the relationship between the COG movement during gait, the study of the COG - COP relationship by perturbation (prediction condition, reaction condition), muscle activity pattern and lesion pattern would be considered.

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Annual report on research project C03-5

Shu Morioka
Kio University, Faculty of Health Science

***Abstract*—In the current research project, distorted embodiment in apraxia after stroke was evaluated using three delayed visual feedback detection tasks: visuo-tactile, visuo-proprioceptive, and visuo-motor temporal integration. We also conducted lesion analyses to investigate the relationship between lesions and apraxia with distorted embodiment. Temporal integration between sensory feedback was preserved in apraxic patients, but there was specific distortion of visuo-motor temporal integration. Lesion analyses revealed that the left inferior frontal gyrus and the left inferior parietal lobule were common lesions to both apraxia and distorted visuo-motor temporal integration. We also investigated the multisensory temporal integration function in hemiplegia after stroke. The results revealed that paralyzed limbs are associated with impaired visuo-proprioceptive and visuo-motor temporal integration. Furthermore, in healthy subjects, although sensorimotor temporal integration and sense of agency had a common foundation, sense of agency was influenced by personality.**

I. Introduction

It has been suggested that limb apraxia and hemiplegia after stroke represent a form of distorted embodiment (impaired sense of body ownership/agency, induction of abnormal sensation) due to the malfunctioning of multisensory integration (including motor signals). However, no studies have attempted to objectively and quantitatively understand the distorted embodiment associated with these symptoms, or investigated the relationship with lesions. It has also been suggested that there is an association between multisensory integration and the sense of embodiment, but the relationship is still unclear.

II. Aim of the Group

The specific purpose of this research project is to quantitatively measure distorted embodiment in apraxia after stroke and to clarify the relationship with lesion location. We also aim to clarify the relationship between sensorimotor integration and sense of agency in healthy subjects.

In Study A, we aimed to quantitatively understand distorted embodiment (multisensory integration, including of motion signals) in apraxic patients, using three types of delayed visual feedback detection tasks. In addition, we aimed to investigate the relationship between apraxia and distorted embodiment and lesion location by performing lesion analyses, such as subtraction and voxel-based lesion-symptom mapping.

In Study B, we aimed to quantitatively measure the multisensory integration function of post-stroke limb paralysis using three types of delayed visual feedback detection tasks.

In Study C, we aimed to clarify the relationship between sensorimotor temporal integration, sense of agency, and personality.

III. Research Topics

The three results that were obtained during this fiscal year are described below.

A. Deficits in visuo-motor temporal integration in limb-apraxia after stroke: Evidence from delayed visual feedback detection tasks and voxel-based lesion-symptom mapping

Three types of delayed visual feedback detection tasks were performed on apraxic and non-apraxic patients and multi-sensory temporal integration, including integration of motor signals, was evaluated. We also performed subtraction and voxel-based lesion-symptom mapping to investigate the relationship between apraxia and visuo-motor and multi-sensory integration and lesions.

The results showed that apraxic patients had normal temporal integration of visuo-tactile and visuo-proprioceptive integration, but a distorted time window for visuo-motor integration. There was a significant correlation between the severity of apraxia and the degree of distortion in visuo-motor temporal integration. Lesion analyses revealed that lesions in the left inferior frontal gyrus and left inferior parietal lobule, part of the left fronto-parietal motor network, were significantly associated with both apraxia and the distortion of visuo-motor temporal integration.

The present study showed that lesions in the left inferior frontal gyrus and the left inferior parietal lobule on the left ventro-dorsal stream are responsible not only for the apraxia but also for the deficits in visuo-motor temporal integration.

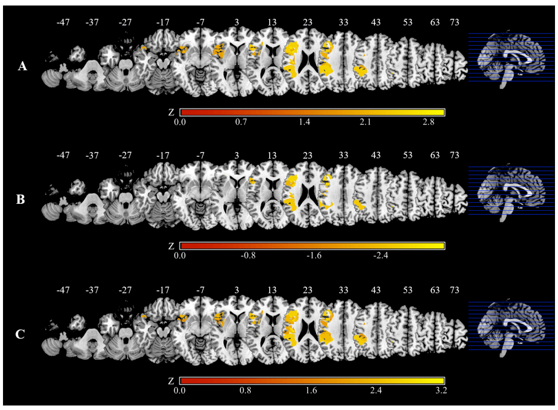

Fig. 1: Results of voxel-based lesion-symptom mapping (VLSM)

(A) VLSM for the severity of apraxia. (B) VLSM for the delayed detection threshold for detecting delayed visual feedback during active movement. (C) VLSM for the steepness of the probability curve for detecting delayed visual feedback during active movement.

B. Distorted multisensory integration in stroke patients

In this study, we investigated multisensory integration function in stroke patients (n = 27) without higher brain dysfunction using a feedback delay system. The patients were asked to detect the time delay between visual and tactile movement and passive and active movement under seven delay conditions (33, 99, 198, 297, 396, 495, 594 msec). To examine the differences in the shape of the judgment curve between tactile, passive, and active movement, logistic curves were fitted to the subjects' responses in the delayed detection task, and then we calculated the point of subjective equality (PSE).

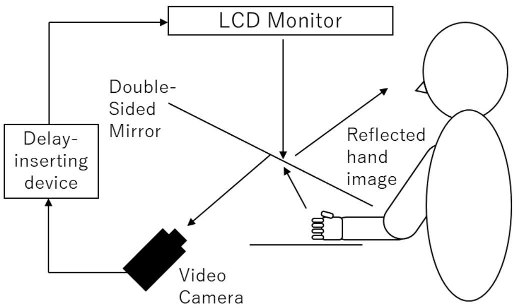

Fig. 2: Setup of the feedback delay system

The results showed that the detection threshold of the affected hand between visual and passive/active movement was significantly higher than that of them.

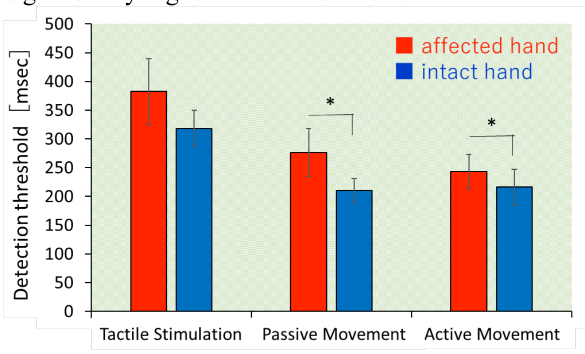

Fig. 3: Multisensory integration function in stroke patients

The delay detection threshold in the passive movement condition indicated the integration function between visual information and proprioception, and the threshold in the active movement condition indicated the integration function between visual and motor commands. Both sensory integration and motor structure processes are thus considered to be distorted in stroke patients. Our results demonstrated such a disturbance in multisensory integration in patients after stroke.

C. Sense of agency and multisensory integration

The mechanism of the sense of agency (SoA) is based on multisensory integration. However, personality (e.g., context, belief) is thought to influence SoA. We investigated the relationship between multisensory integration and SoA, and whether personality influenced SoA. We quantitatively measured the multisensory integration function and SoA using the feedback delay system and agency judgment task (Maeda et al. 2012).

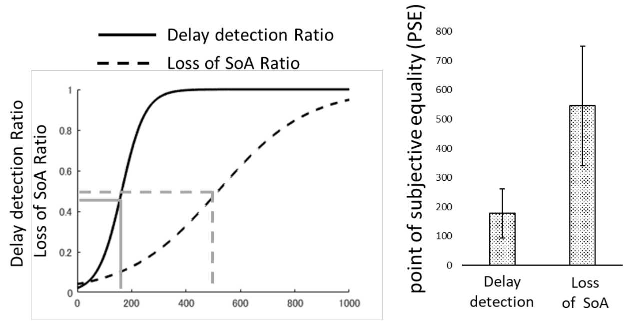

Fig. 4: Difference in the time window between multisensory function and sense of agency

There was an allowable time of about 300 sec between delay detection and loss of SoA. The relationship tended to be influenced by personality. These results indicated common and different mechanisms for multisensory integration and sense of agency.

IV. Future Perspective

Our studies revealed that specific impairment of sensorimotor integration occurs in apraxia after stroke, and impaired multisensory and/or sensorimotor integration occurs in hemiplegia after stroke. Our findings showed an association between sensorimotor integration, sense of agency, and personality. In our future research we will investigate whether an intervention to improve motor function can improve sensorimotor integration and sense of agency.

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52. F. Kaneko
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IEEE International Symposium Micromechatronics and Human Science (MHS2017) Nagoya, Japan 2017

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)
Funded Co-investigator	Eiichi Naito (Research Manager, NICT)
Funded Co-investigator	Shin-ichi Izumi (Professor, Tohoku University)
Funded Co-investigator	Toshiyuki Kondo (Professor, Tokyo University of Agriculture and Technology)
Co-investigator	Hiroshi Imamizu (Professor, The University of Tokyo)
Co-investigator	Kazuhiko Seki (Director, NCNP)
Co-investigator	Kaoru Takakusaki (Professor, Asahikawa Medical University)
Co-investigator	Hajime Asama (Professor, The University of Tokyo)
Co-investigator	Nobuhiko Haga (Professor, The University of Tokyo)
Co-investigator	Akira Murata (Associate Professor, Kinki University)
Co-investigator	Tetsunari Inamura (Associate Professor, NII)
Co-investigator	Takashi Hanakawa (Director, NCNP)
Research Collaborator	Yoshiaki Iwamura (Emeritus Professor, Toho University / Part-time Professor, Ueno Gakuen University)
Advisory Board Member	Yoshikazu Shinoda (Emeritus Professor, Tokyo Medical and Dental University)
Advisory Board Member	Eiichi Saito (Professor, Fujita Health University)
Advisory Board Member	Koji Ito (Emeritus Professor, Tokyo Institute of Technology / Guest Researcher, Tokyo Metropolitan Institute of Medical Science)
Advisory Board Member	Paolo Dario (Professor, Scuola Superiore Sant'Anna)

<u>Research Project A01-1: Neural mechanisms inducing plasticity on body representations</u>

Principal Investigator	Hiroshi Imamizu (Professor, The University of Tokyo)
Funded Co-investigator	Akira Murata (Associate Professor, Kinki University)
Funded Co-investigator	Yukari Ohki (Professor, Kyorin University)
Funded Co-investigator	Takaki Maeda (Assistant Professor, Keio University)
Co-investigator	Satoshi Shibuya (Assistant Professor, Kyorin University)
Co-investigator	Kenji Ogawa (Associate Professor, Hokkaido University)
Co-investigator	Tomohisa Asai (Researcher, NTT Communication Science Laboratories)
Co-investigator	Tsukasa Okimura (Assistant Professor, Keio University)
Co-investigator	Yuichi Yamashita (Section Chief, NCNP)
Co-investigator	Hiriaki Shigemasu (Associate Professor, Kochi University of Technology)
Co-investigator	Hiroshi Kadota (Associate Professor, Kochi University of Technology)
Co-investigator	Masahiro Yamashita (Researcher, ATR)
Co-investigator	Kei Mochizuki (Researcher, Kinki University)
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>

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

Co-investigator	Tatsuya Umeda (Section Chief, NCNP)
Co-investigator	Tomomichi Oya (Section Chief, NCNP)
Co-investigator	Masaya Hirashima (Senior Researcher, NICT)
Co-investigator	Tsuyoshi Ikegami (Researcher, NICT)
Co-investigator	Satoshi Hirose (Researcher, NICT)
Co-investigator	Naohiro Takemura (Researcher, NICT)
Co-investigator	Shintaro Uehara (Assistant Researcher, NICT)
Co-investigator	Kaoru Amemiya (Researcher, NICT)
Co-investigator	Ganesh Gowrishanker (Researcher, CNRS)
Co-investigator	Min Kyonbo (Senior Researcher, Tokyo Metropolitan Institute of Medical Science)
Co-investigator	Lee Zonho (Senior Researcher, Tokyo Metropolitan Institute of Medical Science)
Co-investigator	Takahiro Ishikawa (Researcher, Tokyo Metropolitan Institute of Medical Science)
Co-investigator	Takeru Honda (Researcher, Tokyo Metropolitan Institute of Medical Science)

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

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