Japan-U.S. Brain Research Cooperation Program Group Joint Study Project Program FY2019- FY2022: Report

Field: Behavioral Systems/ Cognitive

Principal Researcher
 Name: Kazuhiko SEKI
 Title: Director, Department of Neurophysiology,
 Affiliation: National Institute of Neuroscience, National Center of Neurology and Psychiatry

- 2. Research Title: Sensory gain modulation during movement: Cortical and subcortical neuronal mechanisms
- 3. Japanese Group Organization Names, Titles and Affiliations of the Principal Researcher and Collaborating Researchers

Principal Researcher Name: Kazuhiko SEKI Title and Affiliation: Director, Department of Neurophysiology, National Institute of Neuroscience, NCNP

Collaborating Researcher Name: Tatsuya Umeda Title and Affiliation: Associate Professor, Kyoto University Name: Shinji Kubota Title and Affiliation: Postdoctoral fellow, NCNP Name: Moeko Kudo Title and Affiliation: Technical staff, NCNP Name: Saeka Tomatsu Title and Affiliation: Project Associate Professor, National Institute for Physiological Sciences

4. U.S. Group Organization

Names, Titles and Affiliations of the Principal Researcher and Collaborating Researchers

Principal Researcher Name: Eiman Azim Title and Affiliation: Assistant Professor, Molecular Neurobiology Laboratory, The Salk Institute for Biological Studies Assistant Adjunct Professor, UCSD Division of Biological Sciences, Section of Neurobiology

Collaborating Researcher Name: James Conner Title and Affiliation: Staff Researcher, The Salk Institute for Biological Studies Name: Andrew Bohannon Title and Affiliation: Postdoctoral Fellow, The Salk Institute for Biological Studies

- 5. Research Period, from/to (yyyy/mm/dd) and total number of years. From 2019/0401 to 2022/0331 (3 years)
- 6. Abstract, Results, and Research Significance (300 words): Voluntary movements have long been shown to have a distinct influence on the sensory processing stream. The

sensory activity resulting from self-motion (reafference) has to be differentiated from that arising from external stimuli (exafference). One hallmark of sensory responses to self-motion is the attenuation of sensory signals during ego-motion, a phenomenon known as sensory gain modulation. Besides its well-established concepts, the detailed mechanisms of sensory gain modulation still need to be clarified and very few studies address the wide variety of gating mechanisms across modalities and species. Most importantly, a comprehensive analysis of their synaptic and network mechanism is lacking. In this proposal, we would like to address these vital issues through US-Japan collaborative research.

During the period of collaboration, we have been working on the neural mechanism of sensory gain modulation from the synaptic level (i.e., PSI) to the systems level. For the Japanese side, we first established a method for precise electrode insertion into the subarea of macaque Cuneate Nucleus (CN), where neurons receive somatosensory afferent input from the hand. We then recorded the activity of CN neurons and characterized their response probability to electrical stimuli applied to cutaneous and proprioceptive afferents in monkeys performing wrist movements. We found that both cutaneous and proprioceptive signals were suppressed in the CN during voluntary movements. Because this suppression was observed within a region of the CN where afferent signals are sent to cuneo-thalamic relay neurons, it is likely that S1 and higher cortical structures operate on somatosensory signals that have already been pre-processed by the CN, rather than on genuine afferent signals. For the US side, they developed viral and optogenetic approaches to map and manipulate the cortico-cuneate pathway in rodents. They found the unique projection pattern from the motor and sensory cortex. In general, the period of the Covid-19 pandemic have entirely overlapped with this proposed joint project, and exceptionally unfortunately, the planned joint experiment on both sides could not be accomplished. However, the online discussion of both teams and our short-term visit to San Diego during the Society for Neuroscience meeting greatly facilitate sharing achievements of both sides.

7. Other (Research-related concerns, particular points of note):

*Please attach any reference materials as necessary.