

Japan-US Brain Research Cooperative Program  
The Group Joint Study Report

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1. The Representative of Group Joint Study:

Affiliation/ Title/ Name

National Institute for Physiological Sciences, National Institutes of Natural Sciences/ Professor/ Atsushi Nambu

2. The Project Title:

Pathophysiology of dystonia studied with transgenic mouse model

3. Japanese Investigator's Name, Title, Affiliation and Phone Number:

Chief:

Atsushi Nambu, Professor, National Institute for Physiological Sciences, National Institutes of Natural Sciences, +81-564-55-7771

Collaborator:

Satomi Chiken, Assistant Professor, National Institutes for Physiological Sciences  
Yoshihisa Tachibana, Assistant Professor, National Institutes for Physiological Sciences

4. U.S. Investigator's Name, Title, and Affiliation:

Chief:

Pullanipally Shashidharan, Associate Professor, Mount Sinai School of Medicine

Collaborator:

Thomas Wichmann, Associate Professor, Emory University School of Medicine  
Peter L Strick, Professor, University of Pittsburgh School of Medicine  
Okihide Hikosaka, Section Chief, National Eye Institute

5. The Term of Research: From 2006. 4. 1. To 2009. 3. 31. ( 3 Years)

6. The Abstract, the Result and the Significance of Research (300 Words):

Dystonia is a neurological disorder characterized by sustained or repetitive involuntary muscle contractions and abnormal postures. To understand the pathophysiology of dystonia, neurophysiological analyses were performed on hyperkinetic transgenic mice generated as a model of DYT1 dystonia. Abnormal muscle activity, such as coactivation of agonist and antagonist muscles and sustained muscle activation, was frequently observed in these mice. Recording of neuronal activity in the awake state revealed reduced spontaneous activity with bursts and pauses in both the external and internal segments of the globus pallidus. Motor cortical stimulation evoked responses composed of excitation and subsequent long-lasting inhibition in both pallidal segments, which were never observed in the normal mice. In addition, the somatotopic arrangements in both pallidal segments were disorganized. Long-lasting inhibition induced by cortical inputs in the internal pallidal segment may disinhibit thalamic and cortical activity, resulting in the motor hyperactivity observed in the transgenic mice.

7. The Others (Other Comments):