DYSTONIA MEDICAL RESEARCH FOUNDATION

CIHR IRSC

Follow Up Report for CIHR Fellowship Award in the Area of Dystonia

Title: The Neuronal Origin of Voluntary Drive and its Expression in Human Motor Cortex

Source: Canadian Institute of Health Research (CIHR) and Dystonia Medical Research Foundation of Canada

Recipient: Zhen Ni

Supervisor: Robert Chen

Amount: Two years fellowship with stipend of CAD 40,000 and allowance of CAD 5,000 per year

Duration: July 2008 - June 2010

Scientific Achievements:
The recipient performed three research projects under the supervision of Dr. Robert Chen.

Project 1: Interaction between motor related cortical areas and primary motor cortex
Voluntary drive is expressed in primary motor cortex (M1) during voluntary muscle contraction. The excitability of M1 is modulated by the inputs from other motor related cortical areas. We performed three experiments both in healthy controls and in patients with movement disorders in this project to investigate the connectivity between these cortical areas and M1.

The first experiment tested the transcallosal interactions in healthy controls. We found that there was a widely distributed interhemispheric inhibitory system from motor related cortical areas to the contralateral M1. Detailed results can be found in a published paper (Ni *et al. Cerebral Cortex*, 2009, 19: 1654-1665).

The second experiment tested the interaction between cerebellum and M1 in the patients with Parkinson's disease. We found that the output from cerebellum inhibited M1 in age-matched controls but this inhibition decreased in the patients group. Moreover, the abnormality in this cerebellar inhibition correlates with tremor, a cardinal symptom of Parkinson's disease. The results were recently published (Ni *et al. Annals of Neurology*, 2010, 68: 816-824).

The purpose of the third experiment was to examine whether the cortical inhibitory and facilitatory systems interact with each other. The experiment was performed in patients with implanted spinal electrodes. With the recordings through the implanted electrode, we found that two inhibitory systems within the M1 inhibited with each other, by which one system did not show its usual inhibitory function in the presence of the other. We are preparing the manuscript for submission.

Project 2: Neural plasticity in primary motor cortex
The expression of voluntary drive is affected by the organization of neural elements in the M1. Reorganization caused by plasticity occurs in M1 in response to a variety of experience. In this project we tested the plastic changes of M1 in the patients who underwent the surgery of toe-to-thumb transfer after thumb amputation. It was found that there were plastic changes in these patients after amputation.

This was manifested as increased cortical excitability and reduced activity of cortical inhibitory systems in M1. These indicated that cortical reorganization occurred in M1. After the surgery of toe-to-thumb transfer the increased cortical excitability and reduced cortical inhibition returned back to the normal range, suggesting that the reorganization caused by amputation was reversed by the surgery of toe-to-thumb transfer. Detailed results can be found in a published paper (Ni *et al. Journal of Neurophysiology*, 2010, 103: 65-73).

Project 3: Interaction between internal globus pallidus and primary motor cortex in dystonia patients
The M1 excitability is also modulated by the basal ganglia. The input from internal globus pallidus to the M1 also affects the expression of voluntary drive in M1. This project was performed in the dystonia patients with implanted electrodes of deep brain stimulation on the internal globus pallidus. It was found that M1 excitability was inhibited by the activation of the neurons in the internal globus pallidus. The latency of this inhibition coincided with the conduction time between these two brain areas through synaptic connections. We are analyzing the data for this project and are preparing the manuscript for submission.

Significance
With the two years fellowship we performed the studies in healthy controls and in the patients with movement disorders. The results obtained from these studies are both scientifically and clinically significant. These studies confirm that there are complex neural networks connecting motor cortical areas. In particular, these neural networks are functionally relevant. Abnormality in the excitability of the neural networks may be further developed as a tool for diagnosis of movement disorders such as dystonia. Neural plasticity occurring in certain clinical settings may manifest as the changes in the excitability of these neural networks. The studies also improve our knowledge of the mechanism of action of internal globus pallidus stimulation for dystonia.

Signature: Zhen Ni Date: February 08, 2011