MOTOR CONTROL AND THE CEREBELLUM: ADAPTIVE CHANGES IN FASTIGIAL NEURONS TO SURGICALLY INDUCED EYE MOVEMENT DYSMETRIA

D. M. McGee1 and C. A. Scudder1,2
1Department of Neurobiology    2 Department of Otolaryngology
University of Pittsburgh, School of Medicine

INTRODUCTION: How does the nervous system modify itself to support motor learning and control? Few answers to this question have been found, partly because the basic circuit underlying a particular behavior must be understood before it is possible to identify the changes in the circuit accompanying learning. Lesions of the cerebellum produce muscular uncoordination by creating timing and force abnormalities devastatingly affecting movement. The question then is: How does the cerebellum maintain such control over the motor system? In this research the oculomotor system, specifically that of saccadic eye movements, is used as a model to study motor control and neural plasticity. Saccadic adaptation is proposed to be accomplished via the direct aid of the cerebellum. The cerebellum is considered to gather and integrate information about the saccadic command and the current situation (e.g., eye position) and compute an appropriate correction signal to ensure that the resultant saccade is accurate. The enduring saccadic dysmetrias produced from cerebellar lesions demonstrate that the cerebellum plays an important and possible essential role in the adaptation of saccadic accuracy. The long-term goal of this research is to determine how the brainstem and cerebellum collectively act to generate accurate saccadic eye movements. This particular experiment was designed to study how cerebellar neurons, specifically those from the fastigial nucleus, behave before, during and after an adaptive modification of saccade size.

METHODS/PROCEDURES: Adolescent Rhesus macaques were used to examine the neural mechanisms that underlie the regulation of saccade gain (saccade size/target amplitude) by the cerebellum. The primates were trained to make accurate saccades to a moveable target. Eye movements were measured in both eyes by a standard electromagnetic search coil technique. A recording chamber was installed and electrodes were passed into the fastigial nucleus in order to obtain extracellular recordings from single neurons. Characteristics of saccadic gain adaptation in these monkeys were monitored along with fastigial nucleus neuron activity by recording before as adaptation proceeded.

During the experiments the monkeys were seated in a primate chair with their heads immobilized. A “parietic paradigm” was established through an extraocular tenectomy of the lateral and medial recti muscles, i.e., the surgical shortening of these muscles in one eye. In this paradigm vision was restricted to monocular viewing. Initially saccades measured in the paretic, operated eye fall short of the target, but over time increase in size to become orthometric when allowed to be the viewing eye. Subsequent monocular vision using the unoperated eye restores saccades to the unadapted state.

RESULTS/DISCUSSION: Recordings have shown 2 different firing rates, 2 different number of spikes, and 2 different latencies for ipsiversive as opposed to contraversive saccades. During contraversive saccades, fastigial neurons
firing initiates prior to saccadic movement (figure 1) which is thought to cause an indirect excitatory stimulation to agonistic motoneurons and to promote agonistic muscle contraction throughout the course of the saccade. Fastigial neuron activity during an ipsiversive saccade demonstrated a later discharge correlated with saccade termination, producing an excitatory stimulation to antagonistic motor units. This verifies condition specific firing patterns for these neurons. Thus, contraversive saccades are under early control, which facilitate the agonist muscles, while ipsiversive saccades are under late control and mostly facilitate antagonists. The putative connection of cells would predict that changes in either ipsiversive or contraversive discharge parameters could bring about a change of gain in saccades.

Saccade size changed as a function of adaptation trial numbers (figure 2). To date, 25 fastigial saccadic related cells have been recorded during adaptation. Evaluation of recorded cells revealed an increase in fastigial latency for ipsiversive saccades amounting to 17 msec per 10-deg increase in saccade size. There was also a change in the number of spikes for contraversive saccades amounting to 5.5 spikes per 10-deg increase. The analysis of data has demonstrated fastigial neuron alteration from saccadic gain adaptation. These experiments do not show that the plastic neuronal changes were in the fastigial nucleus, but in conjunction with other experiments, we believe that the changes were within the cerebellum.

In summary, understanding the function of saccade related cells in the fastigial nuclei have given insight towards elucidating the overall role of the cerebellum in saccadic control and provide a model for somatic motor control in other areas.

Figure 1: Single unit extracellular recording of a fastigial neuron during saccadic movement. H.E. = horizontal eye movements; FR = neurons firing rate; upward direction is right; down is left.

Figure 2: Saccade side decreases (top) or increases (bottom) as a function of adaptation trial numbers. The rate depends on the pattern of available target positions; 2x1x20° = 2-horizontal by 1-vertical, 20° separation; 5x3x10° = 5-horizontal by 3-vertical, 10° separation. Significant changes can be achieved within one session. WEAK->NORMAL = viewing with the normal eye after long-term viewing with the weakened eye. NORMAL->WEAK = viewing with the surgically weakened eye after long-term viewing with the normal eye.