MINIREVIEW

Cerebellar Control of Saccadic Eye Movements: 
Its Neural Mechanisms and Pathways

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CEREBELLAR REGION RELATED TO THE CONTROL OF SACCADIES

Involvement of the cerebellum in the control of eye movements has been known for more than a century from observations that cerebellar stimulation evokes eye movements [6, 11]. According to earlier literature, however, there is not much agreement concerning which areas of the cerebellum produce eye movements when stimulated and the nature and direction of those movements (for review, [5]). The only agreement is that stimulation of the posterior vermis evokes eye movements with an ipsilateral horizontal component. It must be assumed that differences in stimulating electrodes, intensities of stimulation, levels of anesthesia, and recording procedures were responsible for the confusing picture in the old literature.

In recent years, well-controlled stimulation experiments employing precise recording of eye movements have been performed in alert monkeys. RON and ROBINSON [30] recorded eye movements with a search coil technique after stimulation of lobules V–VII of the vermis in alert monkeys. They found that the eye movements evoked by the vermal stimulation were not different from spontaneous saccades. Saccades required a threshold current of about 500 μA and occurred with latencies of 15–35 ms. The eyes moved to the stimulated side in a manner that suggested a topographical organization in the vermal cortex with respect to the direction of evoked eye movements. The distribution of direction was that, if the intercept of the primary fissure and the midline was thought of as the center of a circle, then the evoked responses diverged radially away from this center [30]. McCelligott and Keller [16] also provoked saccades in monkeys by stimulating the vermis within 3 mm of the primary fissure. This area corresponds to lobules V and VI. Keller et al. [15] tested oculomotor responses in the same vermal area. It was commonly observed that currents necessary to evoke saccades from lobules V and VI always exceeded 100 μA, unless they were applied during the saccades [15] or applied to the deep white matter near the fastigial nucleus (FN) [16].

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Fig. 1. Topography of the oculomotor vermis in the cerebella of 9 monkeys. The oculomotor vermis was determined in each monkey by recording and stimulating systematically at 100 \( \mu \text{m} \) interval as an electrode penetrated through the posterior vermis. Mappings of saccade-related neural activity and low-threshold sites were conducted for 100–130 tracks. During the mappings, Purkinje-cell discharges with characteristic complex spikes intermingled with tonic simple spikes were examined as to whether or not their discharges were modulated with eye movements. The oculomotor vermis met the following criteria: i) saccades could be evoked with small currents; ii) saccade-related swish was obvious; and iii) Purkinje cell discharges were related to saccades (from Fig. 10 in [19], with permission).
More recently, Noda and Fujikado [19] discovered that saccades could be evoked with much smaller currents from a circumscribed region located more posteriorly than the cortical area previously described [15, 16, 30]. Neurophysiological experiments conducted on twelve macaque monkeys showed that the vermal region, which was characterized by a low threshold for evoking saccades (typically < 10 µA) and by the presence of saccade-related background activity, was confined to lobule VII in seven monkeys. This region, designated as the oculomotor vermis, extended into lobule VIc in the remaining five monkeys. The anterior border of the oculomotor vermis varied from monkey to monkey. However, it always ended in the folia (lobule VIc) that constitute the anterior wall of the posterior superior fissure and never included the folia (lobules VIa, b) that make up the posterior wall of the primary fissure [7, 19]. The low-threshold region coincided with the portion of the posterior vermis from which saccade-related Purkinje-cell activity was recorded in monkeys [13]. Figure 1 shows the locations of oculomotor vermes of nine monkeys. The area in each monkey is shown by the darkened granular layer on the parasagittal section (right 1.0 mm) of the cerebellum.

NEURAL MECHANISM FOR EVOKING SACCADES BY OCULOMOTOR-VERMIS STIMULATION

Thresholds for evoking saccades have been mapped along penetrations as a stimulating electrode advanced through the vermal tissue. Reconstructions of the stimulating-electrode tracks made on the appropriate histologic cerebellar sections demonstrated that the low-threshold region was located in the white matter and not in the Purkinje-cell or molecular layer [7, 19]. The cerebellar white matter contains not only Purkinje-cell axons but also receives mossy and climbing fibers. A question then arose as to whether the saccades were evoked by activation of the Purkinje cells or by antidromic activation of mossy fibers. The possibility of climbing-fiber excitation is unlikely because they do not discharge with saccades, and stimulation of the climbing fibers at the site of their decussation does not give rise to saccades [4]. Ron and Robinson [30] observed that stimulation of both the vermal cortex and the cerebellar nuclei produced only ipsilateral saccades. If cortically-evoked movements were all ipsilateral and the cortex inhibits the nuclei, stimulation of nuclear neurons may cause contralateral rather than ipsilateral saccades. The finding that both cortical and nuclear stimulation produced ipsilateral saccades led the same [30] and other authors [16] to hypothesize that the effect was due to antidromic activation of mossy fibers. Although both authors are of the opinion that mossy fibers were stimulated, two possibilities have been suggested: i) the antidromic impulses in mossy fibers excited the fastigial neurons via axon collaterals, overpowering the Purkinje-fiber inhibition [30]; ii) the antidromic impulses passed completely back to the brainstem and, through axon collaterals there, excited oculomotor neural networks directly [16]. If these hypotheses were true,
however, the eye movement maps observed better reflect the oculomotor input to the cerebellum rather than its output.

Recently, the antidromic excitation hypotheses have been denied by NODA and his associates [18, 22, 25]. Based on a series of neurophysiological experiments conducted on alert monkeys, they concluded that the saccades were evoked by orthodromic impulses conveyed through the Purkinje-cell axons, instead of antidromic activation of the afferent fibers. Their findings were: i) when the Purkinje cells were deleted from the cortical area, the cortical stimulation no longer evoked saccades despite the fact that afferent fibers were intact [18]; ii) the stimulation of the oculomotor vermis caused an inhibition of the fastigial neurons [26] and when this inhibitory synaptic action was blocked by bicuculline, the saccades evoked by the vermal stimulation were suppressed [22]; iii) the stimulation of fastigial neurons elicited saccades to the contralateral side [22], as has been speculated but not previously demonstrated; and iv) fastigial neurons show presaccadic burst prior to the onset of contralateral saccade [26].

SIGNIFICANCE OF PURKINJE CELLS IN EVOKING SACCADIES

The oculomotor vermis is characterized by i) low thresholds for evoking saccades, ii) vigorous saccade-related background activity which reflects discharges of mossy fibers, and iii) discharges of Purkinje cells associated with saccades. NODA and FUJIKADO [18] have tested the oculomotor responses in monkey preparations in which the cortex of a portion of the oculomotor vermis was chemically destroyed by kainic acid. Kainic acid is known to induce characteristic lesions in neurons receiving presumed glutamate-mediated neurotransmitter [3, 10, 28]. The characteristic of this neurotoxin is that it destroys neuronal cell bodies in the area of injection, while leaving terminals and axons of extrinsic neurons undamaged [3, 17]. The oculomotor responses to vermal stimulation were compared in the monkey preparations before and after injection of kainic acid [18]. In order to compare the oculomotor responses, maps of the threshold for evoking saccades were constructed by stimulating the oculomotor vermis systematically at 100 μm intervals. The levels of saccade-related neural activity were also mapped by recording at each cerebellar site with the same microelectrode, by switching between the stimulator and recording channels of the preamplifier. The maps of the threshold and the mossy-fiber activity constructed preoperatively showed that the cerebellar sites with thresholds < 10 μA and with vigorous saccade-related mossy-fiber activity were confined to the oculomotor vermis. After completion of these maps, 0.5 μl kainic acid (2 mg/ml in saline) was injected in the oculomotor vermis. Later histological examination proved that the injection resulted in severe losses of Purkinje cells within a radius of 1–2 mm of the injection site. After the kainic acid administration, the distribution of saccade-related mossy-fiber activity did not differ significantly from that of the preoperative mapping, despite severe losses of cortical neurons. Burst discharges of mossy fibers were found in the white matter near the
injection site, indicating that afferent fibers were relatively unaffected by kainic acid. However, the saccades could no longer be evoked by stimulation of the lesioned cortex. The stimulus sites from which saccades could be evoked after kainic-acid administration were always associated with the presence of intact Purkinje cells. In such cases, the threshold depended on the percentages of intact Purkinje cells spared. In the folia with normal Purkinje-cell layers, the amplitude and direction of evoked saccades and the thresholds for evoking such eye movements were almost comparable to the preoperative data. From these observations, Noda and Fujikado [18] have concluded that saccades in response to stimulation of the oculomotor vermis were caused by orthodromic impulses conveyed through the axons of the Purkinje cells.

**SACCades Evoked by Stimulation of Fastigial Neurons**

By injecting WGA-HRP in the oculomotor vermes of macaques, Yamada and Noda [43] have shown that axons of the Purkinje cells in the oculomotor vermis terminate ipsilaterally, in an ellipsoidal region in the mediocaudal part of the FN. Neurons in this region, designated as the fastigial oculomotor region (FOR), were inhibited by oculomotor-vermis stimulation [25]. On the other hand, when the deep cerebellar nuclei and white matter were systematically explored with microstimulation by applying currents <10 μA, the region from which saccades were evoked was confined to the FN and adjacent white matter [22]. As described by Ron and Robinson [30], when the stimulating electrode reached the low-threshold region, saccades were evoked in the direction of the stimulated side (ipsilateral saccades). However, when the electrode was advanced in the medial portion of the FN, the direction of the evoked saccades changed from the ipsilateral to the contralateral, as seen in Fig. 2.

The mappings with microstimulation disclosed that the ipsilateral saccades were elicited from a relatively wide region that included almost full extent of the FN. The low-threshold region yielding ipsilateral saccades continued in the white matter, caudally into the oculomotor vermis and rostrally into the uncinate fasciculus. On the other hand, the contralateral saccades were evoked from a relatively circumscribed region in the ventromedial portion of the FN [22]. The reversal in the direction of the horizontal component occurred always in a narrow zone in the core of the FN (Fig. 2). The caudal part of this zone coincided with the FOR where anterogradely-labeled axons of the Purkinje cells terminated when WGA-HRP was injected into the oculomotor vermis [43]. Noda et al. [22] demonstrated that the ipsilateral saccades evoked from the restral 2/3 of the FN were produced by stimulating different elements from those evoked from the caudal 1/3 of the nucleus. Based on the observations described below, they concluded that the neural element stimulated in the rostral 2/3 of the FN were fastigial fibers, while those in the caudal 1/3 were Purkinje-cell axons.

When bicuculline (0.2–1.0 μg) was injected into the FOR, the ipsilateral
Fig. 2. Distribution of low-threshold sites (<10 µA) which yielded saccades with ipsilateral horizontal components (○) and those with contralateral horizontal components (●) in the left fastigial nucleus and the adjacent white matter. A–E: parasagittal sections of the cerebellum, cut successively from medial to lateral at a 0.5 mm interval. In all sections the left side represents anterior portion of the cerebellum. F: dorsal view of the same cerebellum before cutting; the locations of the deep cerebellar nuclei, reconstructed from serial parasagittal sections of 60 µm thick, are superimposed on the drawing of the cerebellum. Approximate planes of the sections used in panels A–E are also indicated in F with letters corresponding to the panels. Each circle on stimulus tracks represents a location in which both thresholds of two consecutive stimulus sites, tested systematically at 100 µm intervals, were ≤10 µA. The portions of tracks without circles were locations which did not yield saccades with 10 µA and their thresholds were not determined. Lt, left; AI, the anterior interposed nucleus; PI, the posterior interposed nucleus; Fa, the fastigial nucleus; De, the dentate nucleus (from Fig. 1 in [22], with permission).
saccades evoked from the caudal 1/3 of the FN were suppressed for several hours [22]. On the other hand, the contralateral saccades evoked from the ventromedial portion of the FN were either unchanged or enhanced. Since the ipsilateral saccades were suppressed by bicuculline, Noda et al. [22] concluded that the saccades were evoked by stimulation of the presynaptic component of GABA-mediated synapses, namely the axons of Purkinje cells. Stimulation of the presynaptic component (Purkinje cells) of the inhibitory synapses evoked ipsilateral saccades. It is natural to assume, therefore, that the activation of the postsynaptic component (fastigial cells) would evoke contralateral saccades. In fact, the distribution of the fastigial sites yielding contralateral saccades coincided with the course of fastigial axons arising in the FOR [38]. Therefore, the contralateral saccades were evoked by stimulation of the axons of fastigial neurons [22].

The reversal in the horizontal direction of saccade occurred also in tracks through the rostral 2/3 of the FN [22]. This region is not related to the oculomotor function. In this region, there were no fastigial neurons that changed activity during saccades [25] and no labeled axons of Purkinje cells were found after WGA-HRP injection into the oculomotor vermis [43]. Furthermore, the ipsilateral saccades evoked from this region were not suppressed by bicuculline. Noda et al. [22] speculated that the ipsilateral saccades evoked from the rostral 2/3 of the FN were most probably evoked by stimulation of the decussated axons arising in the contralateral FN. The intracerebellar pathways of axons from the FOR have been clearly demonstrated in macaque monkeys by Sugita and Noda [39]. They showed that axons of the FOR neurons decussated at all rostrocaudal extent of the FN and that a significant portion of the fibers advanced rostrally within the ipsilateral FN before crossing the midline. The fibers traveled either through the ventromedial portion or around the dorsal border of the ipsilateral FN and, after decussation, advanced rostrally either penetrating through the dorsal part of the contralateral FN or in white matter along the dorsal border of the nucleus [39]. If the axons of the fastigial neurons are stimulated within the FN of the opposite side, the eyes would move toward the stimulated side because microstimulation of the axons of fastigial neurons produced contralateral saccades [22]. The ipsilateral saccades evoked by microstimulation of the dorsal portion of the rostral 2/3 of the FN were, therefore, the results of stimulation of the decussated fastigial fibers.

**SACCADE-RELATED DISCHARGES OF FASTIGIAL NEURONS**

Microstimulation of the oculomotor vermis and the ventromedial portion of the FN evokes saccades which differ in their directions, with vermal stimulation resulting in ipsilateral and FN stimulation resulting in contralateral saccades [22]. These data are consistent with the inference that signals from the oculomotor vermis are transmitted by the inhibition of the fastigial neurons. Ohtsuka and Noda [25] have shown that saccade-related neurons aggregate in the FOR and that they exhibit a presaccadic burst during visually-guided saccades to target
presented in the contralateral hemifield. The FOR neurons were spontaneously active but the overall firing rate differed considerably among units, ranging from 10 to 50 impulses/s. Each unit had a preferred direction for the presaccadic burst but exhibited a fairly wide range of directional selectivity. The optimal direction of the population of neurons covered the entire contralateral hemifield [25].

Discharges of a fastigial neuron during targeting saccades from the central target to each of eight peripheral targets and during microstimulation of the oculomotor vermis are shown with dot rasters in Fig. 3. The neuron showed a burst preceding contralateral saccades (presaccadic burst) and a pause followed by a burst (late saccadic burst) associated with ipsilateral saccades. The presaccadic burst led the onset of saccades approximately 20 ms [26]. The lead time of the presaccadic burst is shorter than that of burst neurons in the superior colliculus but longer than the medium-lead burst of neurons in the paramedian reticular formation (PPRF) and almost comparable to the long-lead burst of PPRF neurons [9]. It is most likely, therefore, that the cerebellar oculomotor impulses will reach the brainstem in time for modifying impending saccades. The duration of the pre-

![Fig. 3. Discharges of a direction-selective saccadic-burst neuron in the fastigial oculomotor region of a macaque monkey during visually-guided saccades. Saccades were elicited by turning on one of eight peripheral LEDs in a random sequence. While the monkey fixated the central LED. Data from 16 trials were selected for each direction based on the quality of oculomotor responses. A) Top: horizontal (upper) and vertical (lower) components of eye position. Middle: raster. Bottom: peri-saccadic time histogram. B–H) Discharges during visually-guided saccades in the direction indicated. I) Discharges during microstimulation of vermal lobule VII. The stimulus duration: 50 ms (from Fig. 1 in [25], with permission).](image-url)
saccadic burst was highly correlated with that of the accompanying saccades. Furthermore, the end of the presaccadic burst was sharply curtailed by the subsequent depression in activity [25]. These response features of saccadic-burst units suggest that the cerebellar-output signals are well defined as to the duration of saccade and thus suitable for regulating amplitudes of visually-guided saccades.

**DURATION OF PRESACCADIC BURST OF "FOR" NEURONS AND AMPLITUDE OF SACCADe**

The cerebellar output signals may regulate the amplitude of saccade. This inference can be substantiated if the duration of presaccadic burst can be experimentally changed and if the amplitude of the associated targeting saccade is modified. **OHTSUKA and NODA** [27] applied subthreshold stimulation to the oculomotor vermis and inhibited FOR neurons without causing any eye movements. The subthreshold stimulation (3 μA, 50 ms pulse train) applied to the oculomotor vermis gave an inhibitory effect on FOR neurons for about 75 ms after the cessation of the stimulation. They found that when the duration of the presaccadic burst of FOR neurons was reduced by stimulating the oculomotor vermis approximately 100 ms after the visual-target presentation, the duration of the resulting targeting saccades also became shorter and the eye movement was hypometric. As the targeting saccades occurred naturally with various latencies after target presentation (ranging from 200 to 330 ms), the effect of the vermal stimulation differed considerably depending on the latency of saccade. When a saccade started within 75 ms of the end of stimulation, the presaccadic burst was shortened and the resulting saccade was hypometric. When it started more than 100 ms after the end of stimulation, the duration was not affected and resulted in an orthometric saccade. Finally, when the latencies of saccades were between these cases, various degrees of hypometric saccades occurred [27].

**PROJECTIONS OF FASTIGIAL NEURONS IN THE OCULOMOTOR REGION**

The preceding physiological observations are consistent with the concept that signals from the oculomotor vermis are transmitted to the saccade-related nuclei in the brainstem via the FOR. The control of saccades by the cerebellum, therefore, depends on the signals conveyed by the fastigial neurons in the region. In order to study the anatomical connections of the FOR with the brainstem, **NODA et al.** [24] traced anterogradely-labeled axons after injecting WGA-HRP into the deep cerebellar nuclei of macaques. In order to locate the center of injection and to assess the size of effective injection site, the distribution of retrogradely-labeled Purkinje cells in the overlying vermal cortex was mapped. In addition to the well-known corticonuclear projections, a precise topographical organization has been demonstrated also from the caudal third of the medial accessory olive to various parts of the caudal FN in the macaques [12]. They assessed the extent of
the effective site from the distribution of retrogradely-labeled Purkinje cells and that of retrogradely-labeled neurons in the inferior olive [24].

The anterograde transport of HRP revealed that neurons in the FOR send their axons to specific regions in the brainstem that are related to the oculomotor function. The characteristics of the projection described by NODA et al. [24] can be summarized as follows: i) The FOR fibers terminate primarily in the regions of the medial brainstem reticular formation that have direct projections to the extraocular motor nuclei. Three regions of the medial brainstem reticular formation are known to have direct projections to the extraocular motor nuclei: these regions are the PPRF (location of horizontal preculomotor neurons), the dorsomedial medullary reticular formation (DMRF) (location of inhibitory burst neurons) and the rostral interstitial nucleus of medial longitudinal fasciculus (riMLF) (location of vertical preculomotor neurons). ii) The FOR project to the regions containing neurons which play a well-defined role in the generation of saccades, as demonstrated either by the presence of saccade-related neuronal activity or by virtue of yielding saccades when electrically stimulated. These regions include the ventral periaqueductal gray, the central MRF, the nucleus of posterior commissure, the superior colliculus, and the ventrocaudal part of the pontine raphe (location of omnipause neurons). iii) The FOR project back to the brainstem regions which are known to provide the cerebellum with afferent fibers. These regions are found among the precerebellar nuclei which include the nucleus reticularis tegmenti pontis, the dorsomedial pontine nucleus, the vestibular complex, and the inferior olivary complex. iv) On the other hand, FOR neurons send virtually no terminals to the brainstem regions known to be involved in the maintenance of eye position. These regions include the interstitial nucleus of Cajal and perihippglossal nuclei.

Summarizing the projections from the FOR, it is apparent that the primary target lies in the saccade-related structures of the brainstem. On the other hand, projections to the structures related to the maintenance of eye position, to vestibular functions, or to smooth-pursuit eye movements were either few or practically nonexistent. These regions included the interstitial nucleus of Cajal, the superior vestibular nucleus, the medial vestibular nucleus, the dorsolateral pontine nucleus, and the perihippglossal nuclei. However, labeled terminals appeared in these nuclei when the HRP injection involved more rostral portions of the FN [24]. It is possible, therefore, that the primary function of the FOR is related to the control of saccades, while regions related to vestibular and smooth-pursuit functions may lie in a more rostral portion of the FN. This inference is supported by OHTSUKA and NODA's physiological findings [25] that saccade-related units aggregated in the FOR and that these units were inhibited by stimulation of the oculomotor vermis. Units showing the Type-I or Type-II responses to head rotation were distributed in more rostral parts of the FN and they were not inhibited by the vermal stimulation [26].
DIVERGENT AXON COLLATERALS OF FASTIGIAL NEURONS

Saccadic eye movements, evoked by microstimulation of the cerebellum of macaque monkeys, are usually oblique. The duration and peak velocity of these oblique saccades, observed at many sites in the oculomotor vermis, increased monotonically with eye movement amplitude [19]. In contrast, the horizontal and vertical components of saccades evoked from other vermal sites did not show linear amplitude-duration and amplitude-velocity relations [7]. The time courses of the horizontal and vertical components were not identical in these saccades; they exhibited asynchronous onset and offset times, as well as difference in the time to peak velocity. The trajectory of such an oblique saccade was curved or had a hooked shape when plotted in two-dimensional space [19]. When these vermal sites were stimulated with different intensities, the trajectories of the evoked saccades were modified [7]. For example, a hooked saccade evoked with a threshold stimulation became near straight and more inclined when a stimulus 10× the threshold was applied. The increase in stimulus current caused an extension of the duration of the horizontal component without giving much effect on the vertical component. These findings indicate that the cerebellar output influences the horizontal and vertical components of saccades independently [7].

The PPRF is regarded as the supranuclear structure responsible for conjugate horizontal eye movements [2, 8, 9, 14]. Recordings of unit activity related to vertical eye movements have identified a site at the transition between the mesencephalon and diencephalon (mesodiencephalic junction) as the supranuclear structure concerned with vertical eye movements [1]. Cells concerned with vertical eye movements lie in the riMLF [1]. The anterograde transport of HRP indicated that neurons in the FOR terminate in both the PPRF and riMLF [24]. Stimulation of fastigial sites produce contralateral saccades in different oblique directions [22], suggesting that each fastigial site contains a mixture of neurons projecting either to the PPRF or to the riMLF. The proportion of these neurons may be different from site to site because oblique saccades were evoked in different directions [22]. These hypotheses have been supported by a fluorescent double-labeling study of SATO and NODA [31].

When fluorescent substances were injected into the riMLF and PPRF, neurons in the contralateral FOR were retrogradely labeled. Some neurons were labeled only from the riMLF, while some other neurons were labeled from the PPRF. As expected from the physiological observation, these single-labeled neurons intermingled within the FOR and the proportion of the neurons labeled by different fluorescent substances varied from site to site in the FOR. Interestingly, there were neurons which were double-labeled from both the riMLF and PPRF [31], demonstrating that some FOR neurons have divergent axon collaterals and may influence both the vertical and horizontal preoculomotor nuclei.

Some neurons in the FOR project to both the riMLF and PPRF [31].
Neurons in these regions will receive identical impulses from the same FOR neurons almost simultaneously, or with a short time lag which corresponds to the difference in conduction times from the FOR to these regions. On the other hand, there were neurons which projected only to the riMLF or to the PPRF. These two groups of neurons intermingled within the FOR [31]. These anatomical findings are in good agreement with the results from physiological recording of unit activity from the FOR of macaque monkeys [25]. The optimal direction of a large number of saccadic-burst neurons was horizontal, but some neurons showed either diagonal or vertical preferred directions [26]. It is known from an anterograde HRP transport in macaque monkeys that the majority of FOR fibers decussate within the cerebellum and terminate in the brainstem regions which are involved with the control of saccades [38]. Noda and Ikeda [20] have shown that saccade-related signals of the cerebellum are transmitted to the horizontal and vertical pre-oculomotor nuclei almost exclusively through the uncinate fasciculus (UF) of the contralateral side. Microstimulation of the juxtaarestiform body can not evoke saccades, indicating that FOR fibers projecting to the ipsilateral brainstem do not carry oculomotor signals [20]. On the other hand, microstimulation within the UF can produce saccades and the direction of the evoked movement is pure horizontal when the descending limb of the UF is stimulated [20]; whereas, when the ascending limb of the UF is stimulated near the brachium conjunctivum, the direction of evoked saccades was predominantly vertical [19]. These physiological observations indicate that the information about the saccade direction has already been separated into the horizontal and vertical components in the fastigiofugal fibers [21].

WHERE CAN WE PLACE THE CEREBELLUM IN THE CURRENT MODEL OF SACCADIC CIRCUITRY?

Despite ample evidence from physiological experiments implicating the cerebellum in oculomotor control, current models of the saccadic system [9, 29, 40-42] do not directly ascribe a role for cerebellar contribution to saccadic generation or modification. To study how cerebellar output impulses modify the processing of visuomotor signals, Noda et al. [23] studied the effect of cerebellar stimulation, applied during the period of saccadic latency, upon visually-guided saccades. It has been generally agreed that when the eyes were displaced by stimulating the superior colliculus [32, 35, 36, 38], thalamic medullary lamina complex [34], frontal eye fields [32-34], and supplementary eye fields [34], the monkeys compensated for the stimulation-induced perturbation by looking to the position of the target in space. However, Noda et al. [23] observed that when the eyes were displaced by stimulating the FN prior to intended eye movements, the monkeys did not acquire the target correctly. The line of sight missed the target location by a distance and direction almost equal to the vector of the stimulation-induced movements. Similar effects were observed when the eyes were displaced by stimulation of the abducens
Fig. 4. Oculomotor responses showing the interaction between the cerebellar output impulses injected by microstimulation and the signals from the natural processing of retinal error. Each circular X–Y plot (A–H) shows eye movement tracings for saccades evoked (direction is indicated with an open arrow) and visually-guided saccades (target location is indicated with an open circle). Three responses, collected from randomly executed saccades, are superimposed for each direction. Calibration scale at lower right corner of E applies also to the responses A–D, E–H and represents that for the vertical direction as well. To the right of each X–Y plot is an eye position versus time tracing for the horizontal (H) and vertical (V) components of the same saccades. T, target mark, showing the period of target presentation; S, fastigial stimulation. The fastigial stimulation was applied 125 ms after the target onset. Note that the eye position versus time records were triggered by the target onset (T) (from Fig. 3 in [23], with permission).
nucleus [32], trochlear nerve [37] or some pontine sites [38].

When the cerebellar stimulation was applied 75–130 ms after the onset of the visual target, the counterfeit impulses sometimes triggered impending visually-guided saccades prematurely. The premature triggering of visually-guided saccades was associated with intriguing phenomena resulting from the interaction between the cerebellar output impulses and the signals from the natural processing of retinal error. The oculomotor responses shown in Fig. 4 were recorded by stimulating the FN 125 ms after flashing the peripheral target (for 25 ms). The visually-guided saccades were executed based on stored information about the location of the retinal image. Stimulated 125 ms after the target onset, targeting saccades were either simultaneously triggered by the impulses \((B, E, F)\) or followed the evoked saccades with a very short latency \((< 50 \text{ ms})\) \((C, D, G, H)\). The direction and amplitude of the initial part of the responses in \(A, G, H\) were almost the same as those of the evoked saccade. In contrast, the initial direction of the responses in \(B–F\) were strongly influenced by the simultaneously occurring visually-guided saccades. For example, the initial part of the responses \(E\) and \(F\) was the vector sum of the evoked and visually-guided saccades and was followed by the outlasting portion of visually-guided saccades.

The initial direction of oculomotor responses depended on whether the signal processing had been completed or was still in progress. When the interval between the target and stimulus onsets was short \((75–100 \text{ ms})\), the initial direction of the majority of responses reflected that of the evoked saccade. The longer the stimulus latencies \((100–130 \text{ ms})\), the more the incidence of responses starting in the direction of the vector sum of the evoked and visually-guided saccades. Intriguing was the observation that the cerebellar output impulses could modify eye movements without disturbing the motor command for impending saccades. Suppose the cerebellum were the primary domain for the processing of visuomotor information, the impulses injected directly into the FN would jeopardize the signals which are being processed to execute a saccade. The oculomotor responses were observed to follow trajectories as if the cerebellar oculomotor impulses were added to the impulse train which was programmed to guide the impending visually-guided saccades. When the responses were preceded by evoked saccades, visually-guided saccades followed without any intervening period, based entirely on the information about the retinal error sampled before the electrical stimulation. This suggests that the retinal error was not erased by the cerebellar stimulation. On the other hand, if the fastigial stimulation was applied after the targeting saccades had already started, the eye movement strayed from the original course and terminated in a deviated location. These findings indicate that the cerebellum is not the primary domain of the signal processing and that the cerebellar impulses are projected downstream to saccade-programming circuits where visual information has already been converted into motor-commanding signals.
SUMMARY

Microstimulation studies on monkeys have shown that the cerebellar cortex which is related to saccadic function is located in lobules VIc and VII of the vermis. This vermal area is designated as the oculomotor vermis and characterized by low thresholds (<10 μA) and by saccade-related neuronal activity. The saccade evoked by the vermal stimulation has been shown to be the result of activation of Purkinje-cell axons. On the other hand, an anterograde WGA-HRP transport study has indicated that the Purkinje-cell axons of the oculomotor vermis terminate almost exclusively in a fatigial region which is designated as the fastigial oculomotor region (FOR). Microstimulation of the oculomotor vermis and the ventromedial aspect of the FOR results in saccades which differ in their horizontal directions, with vermal stimulation resulting in ipsilateral and fastigial stimulation resulting in contralateral saccades. Since the ipsilateral saccades evoked from the caudal part of the FN were suppressed by bicuculline, they were the results of stimulation of the Purkinje axons. It has been also shown that stimulation of the oculomotor vermis causes inhibition of FOR neurons. Furthermore, fastigial neurons bursting with saccades can be recorded only within the anatomical confines of the FOR. These data are consistent with the concept that signals from the vermis are transmitted to the saccadic nuclei of the brainstem via the FOR. Neurons in the FOR have been shown to project to various saccade-related nuclei, including the riMLF and PPRF. Some neurons in the FOR have divergent axon collaterals which terminate in both the vertical and horizontal preoculomotor nuclei. When the initial eye position is changed by stimulating the FN prior to visually-guided saccades, monkeys cannot compensate for the stimulation-induced movement. When the stimulation is delayed 75–130 ms after the target presentation, saccades are triggered prematurely. The visuomotor processing for saccades seems to be completed during this period, which is approximately half the latency of normal saccades. When saccades were triggered prematurely at an early stage of information processing, the eyes moved first in the direction of evoked saccade and then changed the direction toward the location of the target without any intervening period. The retinal error information sampled before the stimulation was not disturbed by the cerebellar stimulation. These observations suggest that cerebellar output impulses are projected downstream to saccade-programming circuits where visual information has already been converted into motor-command signals. The cerebellum is a domain for parallel processing of visuomotor information.

Key words: oculomotor vermis, fastigial oculomotor region, microstimulation, Purkinje-cell inhibition, visually-guided saccades.

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