Eye Movements Evoked by Cerebellar Stimulation in the Alert Monkey

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CEREBELLAR STIMULATION has long been known to evoke eye movements (11, 20). Such evoked movements have been reinvestigated by many others (e.g., 8, 19, 21, 28) and most recently by Cohen et al. (5). There is not much agreement among the many studies concerning which areas of the cerebellum produce eye movements when stimulated and the nature and direction of those movements. The only agreement is that stimulation of the vermis, lobes VI and VII, evoke ipsilateral, horizontal eye movements (5, 17, 18, 20, 21). The most controversial results relate to stimulation of the hemispheres. A variety of eye movements have been reported that included ipsilateral, horizontal movements (20), nystagmus, contralateral or up movements (8), and rotatory up movements (11). Controversial results were also obtained from cerebellar nuclei stimulation. Stimulation of some areas of the cerebellum were considered to evoke eye movements without any apparent correlation between the site stimulated and the direction of the evoked movement (5, 8, 9, 18, 19). Often, the results from only one or two sites in a given cerebellar subdivision were reported rather than a thorough local exploration. The fact that there is not a single cerebellar structure from which stimulation by one or another investigator did not evoke eye movements would imply that they are represented everywhere in the cerebellum.

Eye movements were not the primary interest of most investigators (11, 18, 19, 21, 25, 28); the eye movements were not studied in detail and descriptions of them were qualitative and subjective. Studies done on anesthetized animals are difficult to interpret because anesthesia is known to change the time course of the evoked movements, raise the stimulus threshold, or suppress the eye movement (34). Early studies seldom reported stimulus intensity or, if they did, reported electrode voltage rather than current intensity, again making comparisons difficult. Most important, the time course of the movements were not recorded (except in one report by Cohen et al. (5)). Since saccades, pursuit movements, and nystagmus are products of independent oculomotor control systems, it is quite important to note which type or types of eye movements are evoked by stimulation of particular cerebellar subdivisions. Consequently it was not clear from previous studies which parts of the cerebellum were involved in which types of oculomotor control.

This project was undertaken to study quantitatively the direction and type of eye movements evoked by stimulation of each subdivision of the entire cerebellum in the alert, intact monkey. Each subdivision was systematically explored. Eye movements and stimulus current were accurately measured and recorded. The results present a fairly coherent picture of the types of eye movements that are associated with the various cerebellar subdivisions. Hopefully, it will clear the way for more complex experiments that will provide an understanding of the role of the cerebellum in the control of eye movements.

METHODS

Three Macaca mulatta monkeys, each weighing 6-7 lb., were used as the experimental animals. Under general anesthesia and aseptic procedures, each monkey had chronically implanted in it a coil of wire on the eye to measure eye movements, a crown, and a chamber.
When the monkey was placed in two alternating magnetic fields (horizontal and vertical), 90° out of phase, a signal was induced in the implanted eye coil. Phase detection of this signal produced two voltages proportional to the horizontal and vertical positions of the eye. The instrument sensitivity was 15 min of arc, with a bandwidth of 1 kHz. Details of the eye coil and measuring technique have been described elsewhere (14, 30). A metal crown was bolted to the skull so that the animal's head could be immobilized during recording sessions. The chamber was implanted over a trephined hole on the skull. It held the electrode holder during the experiments and enabled the closing of the exposed dura the rest of the time by replacing the electrode holder with a plug.

The electrode was guided by two stainless steel guard tubes, one within the other; the electrode in the inner one. The outer tube was used to penetrate the dura and allow the inner tube and the electrode to penetrate the occipital cortex with minimal resistance until they reached the tentorium; a landmark used for depth reference. The inner guard tube eventually penetrated the tentorium. Both guard tubes were sharpened to allow easier penetration. The chamber was implanted above one-half of the occipital cortex, the outer circumference reaching the superior nuchal line posteriorly. The stereotaxic coordinates of this location were noted and subsequent chambers in the other monkeys were placed with the same coordinates.

For practical purposes, the inner diameter of the chamber was much smaller than one-half of the cross-sectional area of the cerebellum so that parallel electrode tracks were not sufficient for a full exploration. Therefore, the electrode holder had to be constructed with sufficient degrees of freedom so that any desired site within the cerebellum could be reached with the electrode tip in a reproducible manner and a method of reconstructing the stimulated sites in the cerebellum had to be developed. At the end of the experiments, with the animal under deep anesthesia, the inner guard tube and the electrode were replaced by a colored thread (No. 50) supported by a stiff, thin wire. This thread was passed through the outer guard tube, which served as a support and guide, and was pushed all the way through the cerebellum along a stimulation track. The wire was carefully pulled back after the guard tube was taken out, leaving the thread in the brain to mark the track. Colored threads were passed in all the tracks. The animal was then sacrificed and sliced in thicknesses of 0.8-1 mm in a horizontal plane; a total of 19-20 slices were typically obtained from one cerebellum. Since the threads tended to slip when the slices were cut, the section to be sliced was first frozen by a spray freezing material (Cyrkwik). A picture is thus obtained of a section of the cerebellum with different colored threads marking the location of the different tracks. In Fig. 1 a typical slice in seen with 55 tracks in six colors (not distinguishable in this black and white picture).

The following method was used to reconstruct the location along each track of each site stimulated. The distance from the tentorium to each stimulated site was recorded during the experiments. However, the tracks were, in general, not perpendicular to the brain slices and a correction was made from the slant distance along the track to the equivalent perpendicular distance so that the depth of each stimulated site could be properly assigned to a given brain slice. A more detailed description has been given elsewhere (35). In each of the three monkeys studied, 50-60 tracks were run. The stimulated sites along each track were between 0.5 and 1 mm apart.

After a postoperative recovery period of sev-
eral days, experimental sessions lasting about 6 hr were held daily for a period of about 2 months. Before the monkey was returned to his cage after each experiment, the electrode holder was replaced with a stainless steel screw plug. All objects that came in contact with brain tissue, such as the electrode holder and plug, were sterilized. The monkey was supported by 200 mg/day chloramphenicol for 2 weeks and 200,000 units of penicillin twice a week for the remainder of the experiments.

Monopolar electrodes of tungsten (0.125 mm diameter) coated with Teflon tubing (0.2 mm diameter) were used. The exposed metal tip (0.4 mm in length) was sharpened to a point. Bipolar tungsten electrodes were also used to compare the stimulus intensity required to evoke eye movements using monopolar and bipolar electrodes. As no difference in the stimulus intensity was found, the use of bipolar electrodes was discontinued. Trains of rectangular, cathodal pulses from a constant-current stimulator were used. Typical stimulus parameters were: pulse width, 0.5 msec; pulse rate, 500/sec; intensity and train length as needed. These stimulus parameters may be assumed unless otherwise noted. Stimulus current was never permitted to exceed 1.0 ma. It can be roughly estimated that 1.0 ma excites cells from 1 mm (39) up to 6 mm (29) away from the electrode tip and current spread in excess of this would seriously distort anatomical localization. We felt that if an eye movement did not occur at 1.0 ma, that region of the cerebellum was not related to the oculomotor system. Stimulus current and both components of eye position were recorded on analog tape and later reproduced for analysis with an overall bandwidth of 1 kHz.

RESULTS

Figure 2 summarizes the findings. Stimulation of much of the cerebellum, such as lobes I–IV, the paramedian lobes, and the paraflocculus, produced no eye movements. Only three regions did; saccades were evoked from the vermis, lobes V–VII; saccades and smooth movements from the hemispheres, crus I and II and lobulus simplex; and nystagmus from the flocculus, nodulus, and uvula. Before describing these regions in detail, many common properties of the eye movements themselves will be described. An example of each evoked eye movement type is shown in Fig. 3. They were all conjugate.

Two evoked saccades and one spontaneous one are shown in Fig. 3A. The durations of such evoked movements of many different amplitudes were measured for each...
monkey and compared to the amplitude-duration relationship of that monkey's spontaneous saccades. They were the same and the evoked quick eye movements were classified as saccades (12). Evoked saccades only occurred above a certain current intensity (typically 0.5 ma) called the threshold. At threshold, the saccade amplitude could be large (25°) or small (2°) depending on the site stimulated. The latency between the start of stimulation and the beginning of the saccade was typically 35 msec. Saccade amplitude and direction were independent of the width of the pulses in the pulse train (0.2–2 msec) and the rate (200–1,000 Hz). Saccade amplitude increased with current intensity at most sites. This is quite unusual because saccades evoked from stimulation of other brain structures such as the frontal eye fields (34) and superior colliculi (32) are all-or-nothing responses, their amplitudes being independent of stimulus intensity. To differentiate the two response patterns, the former are called graded saccades. A typical example of graded saccades is shown in Fig. 4. The amplitude of saccades in the text following refers to the amplitude at threshold. Figure 4 also shows that in a typical response the increase in amplitude was greater in the horizontal direction than in the vertical direction. In the example in Fig. 4B, when the stimulus was doubled, the amplitude more than doubled for the horizontal component but increased by only one-half for the vertical component. The rate of amplitude increase with current increase varied greatly from site to site.

Saccades were usually evoked with a pulse train length of 100 msec. Longer trains (e.g., 1 sec) evoked a sequence or staircase of saccades. For 50 sites where this was studied, the intersaccadic interval in these sequences ranged from 220 to 110 msec at threshold (depending on stimulus site) and decreased to 80–100 msec at a stimulus intensity of 3 times threshold. If the train length became too short (e.g., 40 msec) the amplitude of the saccade began to drop and for shorter trains (e.g., 20 msec), no saccades were evoked. With the exception of initial-position dependency (see below) the properties of evoked saccades did not depend on the animal's visual state; that is, a normal visual scene, a ganzfeld (a uniform untextured visual field), or darkness.

The velocity of the evoked smooth movements (Fig. 3B) was also graded; it increased with an increase in stimulus current, frequency, and pulse width, from zero up to as high as 150°/sec depending on stimulus site. Figure 5 illustrates the dependency of velocity on stimulus parameters at a typical site. Smooth movements had no threshold but for purposes of analysis, the current at which a 2°/sec movement was evoked was defined as threshold because it was the smallest velocity easily recognizable in a typical 400-msec intersaccadic interval. Typically, the velocity was about 12°/sec at twice the threshold current. The latency was about 15 msec but could decrease to 10 msec for strong stimuli. The smooth movement continued after the stimulus for about 20 msec (range 10–50 msec).

Visual texture had a marked influence on the evoked smooth movements. When stim-
examples of both saccades and pursuit movements whose amplitudes or velocities changed with initial eye position. At other sites, stimulation evoked eye movements which were initial-position dependent but in such a way that no goal was formed or movements which were independent of initial position. Eye movements depicted subsequently refer to the movement evoked from the primary position.

A typical example of nystagmus evoked from the vestibulocerebellum is shown in Fig. 3C. Slow-phase velocity increased with stimulus intensity (current, pulse width, or frequency) and an artificial threshold was again defined as the current intensity which produced an initial slow-phase velocity of 2°/sec. For long trains at moderate intensities, this nystagmus was clearly distinguishable from the smooth movements (Fig. 3B) by two features; an afternystagmus that usually persisted for many seconds (depending on stimulus intensity) but never less than 200 msec (a smooth movement persisted for only about 20 msec), and the fact that a smooth movement could be interrupted by saccades in either direction (but usually the same), whereas the smooth phase of nystagmus was interrupted by saccades (i.e., quick phases) in the opposite direction.

Optokinetic nystagmus was induced by rotating a large mirror in front of the animals. When stimulation was then simultaneously applied, the eye velocity was not a mixture of those induced by the two stimuli separately but the optokinetic velocity was suppressed and replaced by the electrically evoked velocity.

The saccade amplitude and direction and smooth movement velocity and direction usually depended on initial eye position prior to stimulation. Often the evoked eye movements tended toward a goal and could thus be called goal directed but the goal usually lay well outside the oculomotor range. For example, if the goal lay at 80° left, then saccades were horizontal and left in the primary position, became smaller from leftward positions, larger from rightward positions, had a down component when the eye was up, and an up component when the eye was down. Figure 6 shows
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In some vestibular sites, animal discomfort prevented the application of long stimulus trains so that only a single slow phase was evoked with no quick phase. This was still followed by a long aftermovement and, considering the area's anatomical connections with the vestibular system, these slow-phase fragments were also classified as nystagmus.

Many saccades were observed that were clearly associated with the end of the stimulus. The term "rebound" has been applied to such movements but three separate types, collectively called secondary saccades, and illustrated in Fig. 7, were found with cerebellar stimulation. A rebound occurred immediately after the cessation of stimulation (typically at 35 msec, always less than 50 msec, as short as 12 msec for strong stimuli). A delayed rebound was correlated in time with the end of the stimulus and occurred about 200-300 msec after the end of stimulation. An opposite saccade occurred after stimulation ceased but was linked to the start of stimulation. It occurred about 450 msec (300-600) after the start of stimulation. The last two types could easily be distinguished from each other by varying the pulse train length as shown in Fig. 7. If the train length was too long, opposite saccades were suppressed. All three types of secondary saccades were about the same amplitude and in the opposite direction as the primary evoked saccade, although this relationship was altered greatly when the secondary saccades and/or the primary saccades were initial-position dependent. Secondary saccades were also graded and had a threshold, typically 1.5 times the threshold of the primary saccades. In an alert monkey, an evoked saccade was often followed by a return saccade simply because it wished to refixate the object at which it was looking before the stimulus. This would appear as an opposite saccade but could easily be distinguished from it by placing a ganzfeld before the animal which eliminated voluntary return saccades but not stimulus-evoked secondary saccades.

The effects of anesthesia were similar to results obtained in the frontal eye fields (34). Six sites in one monkey were studied under 3, 6, and 9 mg/kg of pentobarbital sodium (intravenously). At 3 mg/kg, saccades were still graded but became slower and thresholds increased by 2–3 times; smooth movements became very slow and their thresholds increased by 4–5 times; the directions of either eye-movement type were unchanged and the ability to maintain eccentric fixation was lost. At 6 mg/kg, all spontaneous eye movements stopped, saccades could still be evoked but, when evoked repetitively by long stimulus trains, each saccade was followed by a smooth, passive return movement, giving the false appearance of nystagmus. At 9 mg/kg, no saccades were evoked but at 3–5 ma, disjunctive slow eye movements were elicited. In contrast to other studies (22, 34) in which anesthesia increased the incidence of centering movements when different brain areas were stimulated, no centering movements with or without anesthesia were seen in this study. Secondary saccades were affected by anesthesia in the same way as primary saccades.

Nonvestibular eye movements from vermis mapping. Lobes V–VII were the only structures in the vermis where stimulation evoked saccades. They were always conjugate with an ipsilateral horizontal component. Stimulation of the vermis, lobe V, evoked saccades that ranged from straight up to horizontal while stimulation of veri-
The cerebellar cortex is highly folded and the stimulating electrode could pass from gray matter to white matter many times when moving through these folia along a track. Since white matter is much easier to stimulate than gray, a significant variability in the threshold current occurs. However, two general trends in the threshold were seen for evoked saccades and smooth movements: 1) the deeper layers generally have lower thresholds, presumably because they contain relatively more white matter; and 2) paramedian sites have higher thresholds than sites closer to the midline. For the outer layer, L₁, the mean threshold to evoke saccades was 0.74 mA and for consecutively deeper layers was 0.38 mA for L₂ and 0.25 mA for L₃. The mean threshold to evoke smooth movements was 0.93 mA for the first layer, L₁, 0.58 and 0.41 mA for the deeper layers, L₂ and L₃, respectively. The saccadic threshold was usually less than or equal to the smooth movement threshold.

SACCADES. Of the sites where stimulation evoked saccades, graded responses were elicited from stimulation of 76% and non-graded responses from 14%. For the remaining 10% the threshold was 1 mA, which was the highest current used in this study (see METHODS). The typical latency in the outer layer, L₁, at threshold was 35 msec (range 30-50 msec). It could drop to only 25 msec at 3 times threshold. Stimulation of deeper layers produced a progressive decrease in the latencies with typical values of 25 msec (range 15-30 msec) at threshold in the third layer, L₃, which could decrease to as little as 15 msec when the stimulus intensity was 3 or 4 times threshold. Stimulation of about 25% of the sites in the vermis evoked secondary saccades which were about evenly distributed among the three types.

The amplitude and direction of the eye movements evoked from all the stimulated sites in this part of the vermis were position dependent. The evoked response could depend on either the horizontal or vertical component of initial eye position, or both.
The position dependency of the saccades formed a goal at 71% of all sites. At 93% of those sites the goal lay outside the oculomotor range. However, the remaining 7% of the goals lay at the edge of the oculomotor range (that is, about 50° from the primary position), or actually within it; typically 55° from the primary position. With the latter cases, however, the eye movements were still always ipsilateral; that is, if the eye were initially beyond the goal, stimulation evoked no response rather than a movement in the opposite direction. A change from normal vision to a ganzfeld or darkness decreased the initial-position dependency and, in a few cases, abolished it.

Smooth movements. Most of the sites where stimulation elicited smooth eye movements were near the lateral edge of the vermis. Since smooth movements were elicited from stimulation of the paravermis (see below) at lower threshold currents than in the vermis, it is very probable that the smooth movements obtained from vermal stimulation were due to current spread to the paravermis. A further indication of this is the fact that stimulation of the vermis, lobe V, evoked saccades with an up component and smooth movements with a down component, the latter being in the direction of the smooth movements evoked from the nearby paravermis. Interestingly, this movement could be taken for vertical nystagmus, but to interpret it as a true optokinetic or vestibular nystagmus rather than simply the simultaneous stimulation of two different brain regions would be, we feel, a serious misinterpretation.

Nonvestibular eye movements from hemispheres

Mapping. Stimulating lobulus simplex and crus I–II in the hemispheres evoked saccades and smooth movements that were always conjugate and the great majority of which had ipsilateral horizontal components. Movements with down components were evoked by paravermis stimulation and movements with up components were obtained from stimulation of the lateral hemisphere.

The structures under consideration are shown in a posterior view of the cerebellum at the top of Fig. 9. In order to present the data for this highly curved surface, the areas best seen in a dorsal view (A, Fig. 9) and those best seen in a caudal view (B, Fig. 9)
are pulled into a common plane. As in the vermis, the structures shown in both these views were divided into three, 2-mm-thick, consecutively deeper layers, \( L_1, L_2, \) and \( L_3. \) In all three layers 362 sites were stimulated. Eye movements were evoked from stimulation (with 1.0 ma or less) of only 32\% of the sites located in \( L_1 \) but from about 90\% of the sites in the deeper layers. The stimulated sites in \( L_2 \) are shown in Fig. 9. The mean threshold current for saccades and smooth movements was lower for the deeper layers. To evoke saccades, the mean threshold was 0.62 ma for \( L_2 \) and 0.32 ma for \( L_3, \) while for smooth movements, the mean threshold current was 0.75 ma for \( L_2 \) and 0.45 ma for \( L_3. \)

The data presented in Fig. 9 indicate that stimulation of the hemisphere, lobe V (up to a maximum current of 1 ma), either did not evoke eye movements or evoked limb movements at a lower threshold than that required for possible eye movements. Stimulation of several sites in the hemisphere on the posterior edge of lobe V and the anterior edge of lobe VI evoked blinking. The blinking was usually complete and bilateral and appeared to involve levator inhibition without obicularis oculi contraction. Although the eyes often wiggled slightly during a blink, no consistent eye movement resulted. When a photoelectric device was used to measure lid movement, the latency to the start of lid movement was found to be 120 msec. It is thus of passing interest to note that the fissure in the hemisphere between lobes V and VI is associated with blinking.

SACCADES. Of the sites where stimulation elicited saccades, graded responses were evoked from 89\% and nongraded responses from 6\% of the sites. The remaining 5\% had a threshold current of 1 ma. Saccades evoked by threshold stimulation of sites in layer \( L_2 \) had a typical latency of 30 msec (range 25–40 msec), those evoked by stimulating the deeper layer, \( L_3, \) had a latency of 28 msec (range 22–40 msec, analyzed for 22 sites). For strong stimuli the latency decreased to about 25 msec for \( L_2 \) and to 20 msec for \( L_3 \) sites. Secondary saccades were more common in the hemispheres. All three types occurred, equally distributed, at about 25\% of the sites in crus II. Rebounds or delayed rebounds occurred at about 50\% of the sites in crus I. Rebounds were very frequent (about 75\% of the sites) in a zone straddling the fissure between crus I and crus II just lateral to the paravermis.

Another rather strange type of saccade occurred here, especially in the deep layers, called an incomplete saccade (Fig. 10A). When the pulse train length was decreased (with the same stimulus intensity) to the point where it stopped before the normally evoked saccade was over, the movement also stopped prematurely. The result was a small saccade that looked like a truncated piece of a larger saccade. The remarkable consequence of this is that these saccades have durations much smaller and peak velocities much higher than normal saccades of the same size. Thus, saccades of

![Incomplete saccades](https://example.com/incomplete_saccades.png)

**FIG. 10.** Incomplete saccades. A: trajectories of a normal (complete) saccade and of an incomplete saccade with the same initial time course. B: amplitude-duration relationship of a set of 53 incomplete saccades (dots) evoked from the same site and its linear regression line (dashed line) compared with the amplitude-duration relationship (solid line) for normal voluntary saccades. Vertical bars indicate standard deviations from means calculated from 16 data points at each calculated amplitude.
amplitudes 25°, 10°, and 5° whose normal durations are 50, 32, and 27 msec, respectively, might have durations of only 40, 17, and 12 msec, respectively, when they occur as incomplete saccades (Fig. 10B). Since saccades are preprogrammed neural events with a rather fixed amplitude-duration relationship, these superfast incomplete saccades, not observed when other oculomotor brain areas are stimulated (32, 34), suggest that this cerebellar region could have rather intimate internal connections with the saccadic neural programmer itself.

Position-dependent saccades were evoked by stimulation at 90% of the saccadic sites, and non-position-dependent saccades at the remaining 10%. Of the position-dependent saccade sites, 82% formed a goal-directed pattern. For 90% of these the goal lay outside the oculomotor range in the ipsilateral direction. The remaining 10% had goals in the oculomotor range. These responses had a marked difference from the goal-directed saccades evoked from the vermis for which the goal was in the oculomotor range; the evoked saccades moved either left or right toward the goal, depending on the initial position. As in the vermis, when the visual conditions changed to darkness or a ganzfeld, the saccades became less position dependent. In a few extreme cases, saccades directed to a goal within the oculomotor range actually became non-position dependent.

**Smooth Movements.** Stimulation of 36% of the sites in each of layers L2 and L3 elicited smooth movements. In each layer, there appeared to be two areas where stimulation evoked smooth movements: the paravermis and the far lateral part of the hemisphere, as shown in Fig. 9. The general direction of the smooth movements evoked from 72% of the sites in layers L2 and L3 was the same as that of the evoked saccades (Fig. 9). For 20% of the sites, the direction of the smooth movements differed from that of the saccades in the vertical component. For example, if the direction of the saccade was up and ipsilateral from the primary position, the direction of the smooth movement could be down and ipsilateral. For 8% of the sites the evoked smooth movement had a contralateral horizontal component. This eye movement, a combination of oppositely directed saccades and smooth movements, might be interpreted as nystagmus. However, as discussed in connection with the vermis, these movements should not be considered true optokinetic or vestibular nystagmus. At these sites where stimulation evoked contralateral smooth movements, the threshold was higher than normal and the velocity at twice the threshold level was only about 6°/sec. Smooth-movement sites where saccades were not obtained were in the paravermis (movements down and ipsilateral) and the lateral hemisphere (up and ipsilateral smooth movements). For sites where both saccades and smooth movements were evoked, putting the monkey in a ganzfeld resulted in fewer saccades with the least number of saccades appearing in darkness. Most position-dependent smooth movements were interrupted by saccades at least every 300–500 msec. Consequently their change in velocity appeared to be abrupt as each saccade suddenly took the eye to a new position and so a new velocity. It was difficult, therefore, to see if the velocity was capable of changing smoothly or only changed with a saccade and was constant between saccades.

Vestibular eye movements from cerebellum flocculus. Stimulation of most sites (40 of a total of 42) evoked a contralateral nystagmus (quick-phase direction) which changed to ipsilateral nystagmus when the stimulus intensity was increased. Stimulation of the vestibular nerve or nuclei in this and other studies (40) evoked predominantly ipsilateral nystagmus. Therefore, stimulation of the flocculus, which inhibits the ipsilateral vestibular nuclei, would be expected to evoke predominantly contralateral nystagmus, as found in this study. The change in the direction of the nystagmus with increased stimulus intensity when the electrode was in the flocculus could thus be expected because of the spread of current to the nearby, more sensitive brain stem vestibular complex. The direction of the nystagmus and its reversal
with stimulus intensity confirms well-known anatomical connections and offers a convenient guide in the live animal (before histological verification) that the electrode is, in fact, in the flocculus.

The eye movements evoked were, at first, only slow phases with a typical threshold of 0.08 ma. With an increase in stimulus current the slow-phase velocity increased and quick phases were added, thereby forming a full nystagmus. With further increases in current the slow-phase velocity decreased and eventually reached zero (no eye movement). A further increase in stimulus intensity reversed the direction of the nystagmus in either both horizontal and vertical directions or in only one of them. At 28 sites the slow phases reversed in both directions, whereas at the rest of the sites the direction reversed in only one direction (usually horizontal). Stimulation of two sites 0.5 mm apart could evoke vertical components (at threshold stimulus intensity) in opposite directions. Because of this a meaningful map of slow-phase direction within the floccular lobe cannot be offered. This is probably because the flocculus is both small and highly folded. However, a general impression was gained that up slow phases were evoked rostrolaterally, horizontal centrally, and down slow phases caudomedially.

UVULA AND NODULUS. The eye movements evoked from stimulation of the uvula and nodulus (vermis, lobes IX and X) were similar to those evoked from the flocculus. The map in Fig. 11 indicates that the results for each of the two lobes can be roughly divided in two: stimulation of the dorsal part of the uvula and ventral nodulus evoked slow phases with up components, whereas stimulation of the ventral part of the uvula and dorsal nodulus evoked slow phases with down components. Of a total of 39 sites, no eye movements were evoked from 4. All the evoked movements were either nystagmus or only the slow phases of nystagmus since current intensity or pulse train length could not be increased without the monkey becoming too excited. At 26 sites the stimulus current could not be increased to a maximum of 1 ma as the monkey became very restless

FIG. 11. Map of vermis, lobes IX–X, where stimulation elicited slow phases of nystagmus. A, left: midsaggital section of the cerebellum; A, right: the rotated vermis, lobes IX–X. B: separation of vermis IX and X to bring their radial axes (dotted line) parallel. C: stimulated sites and directions of evoked slow phases as shown looking at the outer surface of the lobes (from the right), as oriented in B. V, vertical slow-phase component down; D, dorsal, V, ventral with respect to normal position (as shown in A); ©, body movement threshold lower than eye movement threshold.

and made vigorous body movements. The monkey vomited several times when stimulus current was about 3 times threshold (typically 0.2 ma) for either short or long stimulus trains, depending on the site. All the evoked eye movements were followed by afternystagmus which was usually only a slow phase but rarely included a quick phase (for a pulse train of 1 sec). This afternystagmus which lasted 200 msec or longer clearly differentiated the slow-phase movements from the smooth movements evoked from the hemispheres.

The direction of the horizontal component of the evoked slow phases could be either ipsilateral or contralateral but slightly favored the latter. However, since stimulation of two sites only 0.5 mm apart could evoke horizontal slow phases in op-
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posite directions, no consistent relationship was found between site location and the horizontal component of the slow phases. For this reason horizontal components are not included in Fig. 11. The velocities of the horizontal and vertical components of the slow phases also varied greatly from one site to another so that the movements could change from predominantly horizontal to predominantly vertical. At several sites the direction of the vertical component reversed when stimulus intensity was increased.

An attempt to add thresholds to the map was unsuccessful because of habituation and variability (not found in other regions). The threshold could increase by a factor of three with repeated stimuli. On repeated stimulation with the same parameters, different slow-phase velocities could be evoked (e.g., from 2 to 15°/sec). By increasing the stimulus parameters (current, pulse width, or frequency) the velocity of the slow phase and the probability of evoking a nystagmus (slow and quick phases) rather than only a slow phase were usually increased. However, it was impossible to measure such changes quantitatively, primarily because of the instability of the slow-phase velocity and the fast habituation that occasionally occurred.

Cerebellar nuclei

Mapping. Stimulation of all the cerebellar nuclei evoked eye movements with ipsilateral horizontal components. The results from stimulation of 71 sites in the cerebellar nuclei and the adjacent white matter are summarized in Fig. 12. Stimulation of the fastigial nuclei evoked saccades with up or down components in all but the most inferior part where slow phases of nystagmus were elicited. Stimulation of the interpositus nuclei principally evoked saccades and smooth movements with down components and stimulation of the dentate nuclei principally evoked saccades and smooth movements with up components. In addition to these movements, direct responses were also elicited and will be discussed subsequently. The shapes of the nuclei were reconstructed in four horizontal slices, each roughly 1 mm thick. The shaded areas are those which receive projection (24) from those regions of the cerebellar cortex shown in Fig. 2 which, in this study, did not appear to be associated with eye movements. Allowing for some current spread, the responses in Fig. 12 came mainly from the nonshaded areas.

Saccades and Direct Responses. The latencies of the evoked saccades varied greatly between the sites and depended on stimulus intensity. A typical latency for the fastigial nuclei was 20 msec (range 15–28 msec) and for the interpositus nuclei was 24 msec (range 18–30 msec). Saccades evoked from the dentate nucleus and adjacent white matter had latencies of 15 msec

FIG. 12. Mapping of the cerebellar nuclei and adjacent white matter. Panels from top to bottom represent those horizontal 1-mm sections of the cerebellum, cut successively from superior to inferior, which contain nuclei. Symbols are the same as in Figs. 2, 5, and 6 with this addition; M represents direct responses. Experiments were done in a ganzfeld.
(range 12–26 msec) except for some sites with remarkably short latencies; 5–6 msec for the vertical component, 8–9 msec for the horizontal component. In view of the fact that the latency from motoneuron activity to the beginning of an eye movement is 8 msec (range 4–12 msec) (31), these sites must be intimately connected with both the motoneurons and the neural circuitry which creates saccades.

A subgroup of six of these short-latency saccade sites, marked M in Fig. 12, produced evidence for direct dentatooculomotor fibers. When they were stimulated just below their saccadic threshold, eye movements were evoked similar to those elicited when the motor nerves are stimulated; that is, similar to an isotonic muscle twitch or tetanus response. These movements had a latency of 9 msec and thus appeared to be the result of stimulating fibers making monosynaptic connections with the oculomotor neurons. They were called direct responses. Direct responses appeared only in the vertical components of the movements. This response confirms the anatomical findings (2) that the influence on eye movements of the direct fiber projection of the dentate nuclei on the oculomotor nuclei may be confined to motoneuron groups involved in vertical eye movements.

**SMOOTH MOVEMENTS.** Smooth movements with a typical latency of 15 msec (range 10–40 msec) were evoked by stimulation of the dentate and interpositus nuclei and the adjacent white matter. The direction of all the evoked smooth movements was the same as that of the evoked saccades. The only difference between stimulation of the cerebellar cortex and of the nuclei was that the threshold to evoke smooth movements in the latter was about the same as that required to evoke saccades.

**NYSTAGMUS.** Stimulation of the caudal part of the fastigial nuclei and the adjacent white matter evoked nystagmus or only its slow phase (if the stimulus current could not be increased) similar to those obtained from stimulation in the vermis, lobes IX and X. Slow phases were also evoked by stimulating three sites in the caudal part of the dentate nucleus and its adjacent white matter (Fig. 12). The monkey was restless and stimulus intensity could not be increased, but the appearance of slow phases and of occasional nystagmus was clear.

*Structures where eye movements were not evoked*

The shaded areas in the unfolded cerebellar map in Fig. 2 illustrate the areas where stimulation did not elicit eye movements. These may be divided in two groups. The first are structures where the threshold to evoke limb or body movements or general excitation in the monkey was lower than the stimulus intensity for which eye movements might possibly have been evoked. Such sites were not explored further for humane reasons and were not considered to be related to eye movements. These structures include the vermis lobes I–IV, hemisphere lobes III–V, and the anterior part of lobe VI. In these structures stimulation of individual sites elicited limb, tail, or finger movements, in general agreement with results obtained by others (15, 16, 28). A total of 94 sites were stimulated in these structures. Stimulation was applied to a total of 38 sites in the pyramidal lobe (lobe VIII) and 72 sites in the paraflocculus (both dorsal and ventral). In all these structures the stimulus current to overexcite the monkey was lower than the current to elicit possible eye movements. On stimulating the dorsal paraflocculus strong eyelid closure occurred, which was always associated with some highly variable and complicated eye movement.

In the second type of structure, stimulation did not evoke eye movements or any other type of response when a maximum stimulus current of 1.0 ma was applied. This only occurred in the paramedian lobe. When stimulus intensity was occasionally increased to 2 ma at a few sites close to the vermis, some eye movements which could be interpreted as nystagmus were elicited. It may be assumed that at such a high current the nodulus and uvula were excited, which might explain previous results (8, 19) when the paramedian lobe was stimulated and stimulus intensity was not reported. Also, stimulation of several lateral sites in
the paramedian lobe near crus II with 2 ma evoked some up and contralateral smooth movements. Clearly, if one increases stimulus intensity without limit until some type of eye movement occurs, then many regions of the cerebellum will appear to be associated with eye movements. We feel that this procedure is misleading and that if a stimulus intensity of 1.0 ma did not produce an eye movement, that region of the cerebellum was unrelated to the oculomotor system.

**DISCUSSION**

It is difficult to compare these results with the wide variety of results previously reported due, in part, to technical reasons. In this study, the masking effects of anesthesia were avoided; an intact animal was used to insure alertness and reveal the spinal results of stimulation when they occurred at a lower threshold than eye movements; stimulus intensity was controlled and limited to avoid undue spread; many points within each structure were stimulated and reconstructed to avoid assigning a single movement direction to an entire structure based on a few samples; and, most important, eye movements were recorded and classified into types. However, the major difference in interpreting our results is conceptual. Since there are four major semi independent eye movement control systems; saccadic, pursuit, vergence, and vestibular; the question is, in which of these subsystems do various cerebellar subdivisions play a role? For this purpose eye movement type is far more important than eye movement direction. Classification by type permits a clear separation of the oculomotor cerebellum into three, distinct, nonoverlapping regions with quite clear boundaries, each of which appears involved in a separate task in oculomotor control and within which all directions of eye movements are represented. This reinforces the idea that one should not look for regions of constant direction for all types of eye movement control but rather regions of a constant type of control for all directions.

As a result, if one considers any previous report of an eye movement direction evoked from some structure, one can often find a point nearby in the present results where that direction did occur. For example, our results agree with the horizontal, ipsilateral movements often reported for the vermis (5, 18, 19, 21), the up movements reported for the vermis, lobes II–V (5, 11, 28), if one assumes current spread to the rostral edge of lobe V and the up and/or ipsilateral movements for the ansiform lobes (5, 11, 21). It is, perhaps, more important to point out major differences. Down components were clearly obtained from the vermis, lobe VII, yet of all previous studies, only Cohen et al. (5) found down movements there. The present results seem incompatible with the down and contralateral movements obtained in the vermis, lobes II–V (19, 21, 25). Stimulation of the ansiform lobes did not evoke nystagmus as reported by Hare et al. (19) although, as reported above, there are several situations in which saccades and smooth movements, either with or without anesthesia, can give the illusion of nystagmus. Current spread is another obvious explanation. In this study, for example, caudolateral stimulation of crus I, about 3 mm from the flocculus, produced saccades and smooth movements at 0.8 ma but nystagmus occurred at 1.5 ma.

An important result is the delineation of those structures not related to eye movements since this will permit future studies to concentrate on those that are. Here, of course, there is the most disagreement with previous results, which is probably due to the excessive current spread that can occur if current is unknown and no upper limit is placed on it.

The flocculus undoubtedly participates in the vestibuloocular reflex. Its importance and possible functional role in this reflex has recently been emphasized by Ito (23). An important element in this reflex is a neural integrator (33). In the frequency range between about 0.03 (10) and 1.0 Hz, the discharge rate of vestibular neurons is proportional to desired eye velocity while oculomotoneuron discharge rate is proportional to eye position. A neural integrator must exist to convert velocity to position information. Carpenter (3) has shown that in the decerebrate cat, the vestibuloocular reflex is affected by cerebellectomy in a way
which is just compatible with removal of this integrating process. If the integrator is in the cerebellum, it would seem most likely to be in the flocculus which receives primary vestibular afferents. Yet if that were true, stimulation within the flocculus would simulate a signal at the integrator output to be passed directly to oculomotor neurons. This would lead to a steady eye deviation, not nystagmus. If, however, the integrator were central to the flocculus, stimulation would, as it did, produce nystagmus. This suggests that the integrator is not in the flocculus. Llinás et al. (27) found no Purkinje cells in the frog auricular lobe whose dynamic responses to rotation indicated that this lobe was integrating semicircular canal signals. Clearly the specific data processing of the flocculi remains unknown.

What role does the vermis, lobes V–VII, play in the control of saccades? It is interesting to compare this area to one more closely connected to the visual system such as the superior colliculus. There, saccades were spatially coded (32); that is, different saccade sizes and directions were represented by neural activity in different anatomical locations. Thus, evoked saccade size and direction depended on where the superior colliculus was stimulated and not on stimulus intensity (or number of excited efferent fibers) or other stimulus parameters. In the vermis, the motor map of Fig. 8 indicates that saccade direction was also spatially coded but the fact that evoked saccades were graded means that saccade size was not spatially coded. Size was not temporally coded either since, just as in the colliculus, saccade duration was not equal to stimulus duration. This behavior is compatible with the idea that saccades are produced by neural pulse generators (32–34) whose outputs are clearly seen in the motoneurons (31) as a burst of high-frequency discharges (e.g., 400 spikes/sec) whose duration is just equal to the saccade duration. Once a pulse generator is triggered it runs a preprogrammed course followed by a refractory period during which stimulation has no effect. This explains why continued stimulation produced a staircase of saccades, one after the other, separated by about 100 msec.

Since saccade size is primarily controlled by pulse duration, the question then arises of how the spatially coded signals from a visual structure like the superior colliculus are transformed into a signal which can control pulse duration. The question is made more interesting by the phylogenetic consideration that the first quick eye movements came about in vestibular nystagmus. There is good evidence (36) that saccades and vestibular quick phases are identical and the product of the same neural pulse generators. If that is true, then the neural pulse generators were initially designed to operate from signals of vestibular origin which are analog signals of head motion coded in discharge rate (10). If the visual system later utilized the pulse generators for saccades, an interface circuit became necessary to translate spatially coded signals into ones suitable to the pulse generators.

Could the interface be in the vermis? This area receives both visual and auditory signals (37) which may contain information about the location of a stimulus with respect to the observer. This suggests that the interface may be more concerned with localization per se rather than a specific modality. Since the appropriate oculomotor command would depend on initial eye position in the head, it is not unreasonable that this area also receives extraocular muscle proprioception (13). Thus, these ideas are compatible with the theory that the vermis receives teleceptive information about stimulus location with respect to an observer's head, corrects this information for initial eye position, and sends out a signal, spatially coded in direction and "population" coded in amplitude, to saccadic pulse generators which move the eyes to acquire the stimulus.

Recently Aschoff and Cohen (1) investigated this sort of theory. They showed that destruction of this area did not abolish spontaneous saccades in monkeys so that other pathways are available, perhaps from higher cortical areas. However, asymmetrical lesions resulted in unequal spontaneous saccade sizes in opposite directions, suggesting an ocular dysmetria. However, since the animals were not trained to look at targets, it is not clear whether the animals did not, or could not, make saccades of appro-
appropriate sizes. Consequently, it is still not clear whether the vermis, lobes V-VII, is a primary pathway in translating location-specific teleceptive information into pre-motor commands of the correct amplitude or whether it plays a more subtle role in adapting sensorimotor quantitative relationships when some failure in the normal machinery has taken place, a capacity which requires plasticity and learning (23).

The saccades evoked from the hemispheres had the same properties as those from the vermis; their directions were spatially coded; their amplitudes were neither spatially nor temporally coded, but population-size coded. That the cerebellum is rather intimately connected with the pulse generator networks is indicated by two other types of saccades seen in this study, short-latency saccades whose stimulated fibers could lie only one or two synapses away from the motoneurons and incomplete saccades in which the seemingly inviolate relationship between saccade amplitude and duration was broken. This intimacy with and control over the pulse generators could explain the severe disturbances in optokinet- netic nystagmus quick phases in the rabbit found by Collewijn (6) after cerebellectomy.

The smooth movements evoked in the ansiform lobes were a novel finding since they have not been reported on stimulation of other brain regions such as the frontal eye fields (34) or superior colliculi (32), with the exception of the pontine reticular formation (4). As was true for nystagmus, smooth movements indicate that the evoked discharges were being integrated by a neural integrator central to the cerebellar cortex. Since smooth movements were also evoked from the cerebellar nuclei and even the brachium conjunctivum, this integrator also does not appear to be in the cerebellum. As was the case for vestibular nystagmus, eye velocity increased with increases in stimulus current, pulse width, and frequency, all of which would have increased both the number of fibers firing and their firing rate. This behavior is compatible with that expected of a neural integrator and means that the integrator was accepting part of the cerebellar population discharge rate as a signal proportional to desired eye velocity. Consequently, velocity is not spatially coded in the cerebellum; that is, different eye velocities are not represented by electrical activity in different parts of the cerebellum. Just as muscle tension is coded both by firing rate and the number of active motoneurons, velocity seems coded in the cerebellum in the same way.

The smooth pursuit system appears to be designed to match eye velocity to target velocity, thus stabilizing images on the retina (7). In the dark, when the system has no visual feedback, the eyes drift about due to internal disturbance of neural unbalances and noise. In the light, when the visual scene is stationary, this system prevents the eyes from drifting about and holds them stationary. Cerebellar stimulation is also a disturbance and when the eyes moved in an evoked smooth movement, this reflex counteracted that movement in an attempt to reduce retinal image motion. This reduced the eye velocity for a given stimulus intensity. When the monkey was deprived of visual texture this reflex could no longer act. Yet during optokinetic nystagmus, the pursuit system, now actively tracking rather than holding, did not seem able to alter the velocity of the evoked movement. Why a stationary visual field can influence evoked eye velocity while a moving one cannot is not clear. Perhaps the stimulus intensity used during optokinetic nystagmus was too strong. Collewijn (6) found in the rabbit that cerebellectomy did not abolish the slow tracking phase of optokinetic movements. It thus appears likely that the cerebellum is not in the direct pathway of the smooth pursuit system but that the ansiform lobes introduce only a modifying contribution for certain purposes.

This purpose can only be guessed, but, since the cerebellar hemispheres are thought to be associated with the control of distal musculature and are especially enlarged in manipulative animals such as primates, both the saccades and smooth movements evoked here may be associated with hand-eye coordination. In the simple act of picking up and examining an object, the need arises first to place one's hand where one is looking and then, the reverse process, to look at the held object and track it, as it is manipulated, with both saccades and pursuit eye
movements. It has been shown (38) that ocular tracking of a target improves, over the case where the subject is a passive observer, if the object is carried in the subject’s passively moved hand (somatosensory information only) and improves again if the subject actively moves the target (efference copy information). The benefit of this improvement is clear for animals that manipulate objects.

The cerebellum would require such information as limb position and velocity as sensed by joint, skin, and muscle afferents (17, 37) as well as seen by the retina (26), all of which it apparently has. From this, visual information would be used to prepare quantitatively appropriate premotor signals for limb positioning on the one hand, and limb position information would be used to augment visual signals in guiding eye position (saccades) and velocity (smooth movements) on the other hand. It is the latter path that is revealed in this study by stimulation. In the hemispheres, the diffuseness with which eye movement information is spread over so much neural tissue makes it unlikely that single-unit recording techniques will be of much help. However, behavioral testing, after lesions, although necessarily subtle and complex, may be able to test this hypothesis.

Stimulation of the cerebellar nuclei essentially confirmed the orderly projection of the cerebellar cortex on them, both medial to lateral and rostral to caudal. The nuclear responses generally reflected the responses of the overlying cortex which project to a given part of a particular nucleus. The responses do, however, raise the following question: if cortically evoked movements were all ipsilateral and the cortex inhibits the nuclei, why were the nuclear responses not contralateral rather than ipsilateral, as they were when first the flocculus and the vestibular nerve were stimulated? There are two possibilities: either antidromic impulses in mossy and climbing fibers excited the nuclear cells by collaterals, overpowering the Purkinje fiber inhibition, or the antidromic impulses passed completely back to the brain stem and, through collaterals there, excited oculomotor neural networks directly. If the latter were true, the eye movement maps shown better reflect the oculomotor input to the cerebellum rather than its output. However, the former hypothesis is supported by the occurrence of secondary saccades. The rebounds could be explained by the fact that when nuclear excitation through antidromically driven collaterals was suddenly withdrawn at the end of stimulation, the longer lasting discharge of Purkinje fibers inhibited the nuclear cells and caused a reversed eye movement. This, of course, does not explain delayed rebounds, or opposite saccades, or why rebound smooth movements were never seen, but the great frequency of rebound saccades lends support to the former hypothesis. If that is true, then the eye movements reported here, and eye and limb movements reported by others, do not so much reflect the excitation of Purkinje cells but the excitation of the nuclear cells which are their targets. This would not affect the applicability of any of the above results or discussion except to imply that if it were possible to stimulate only Purkinje cells and no other fibers, the movements would all have been in the opposite direction.

Clearly the next step is to test these hypotheses and replace them with better hypotheses that are much more specific about the nature of the data processing involved. There is one advantage in studying the oculomotor cerebellum; the oculomotor system is one of the simplest of all the motor systems. It deals with a constant mechanical load that is free of external mechanical disturbances; it has no stretch reflex: and it is composed of four semi-independent systems, each of which has but one, simple, clearly understood function which it performs in a machinelike, stereotyped fashion (33). It thus may be possible to work out its circuitry and see what role the cerebellum plays. This, in turn, could suggest hypotheses for the far more complex role of the cerebellum in the control of the skeletal musculature.

**SUMMARY**

1. Eye movements evoked by cerebellar stimulation were recorded in the alert, intact monkey. The cerebellum was systematically and thoroughly explored. The dependence of the eye movements on stimulus
parameters, electrode position, initial eye position, and visual texture were explored.

2. Three regions of the cerebellum participated in oculomotor control. Within each region the type of eye movement was the same but the direction varied with stimulus location so that all eye movement directions were represented in each region.

3. One region was the vermis, lobes V-VII, from which saccades were evoked. The directions of the saccades varied with electrode location from straight up in the midline of V, around the clock, through horizontal (ipsilateral) on lobe VI, to down on the midline of lobe VII. Saccade latency was 15-35 msec. Saccade amplitude was independent of pulse train frequency, pulse width, or pulse train length but, above threshold, increased with increasing stimulus current.

4. Another region was the hemisphere, crus I and II and lobulus simplex, from which saccades, similar to those in the vermis, were evoked in addition to smooth movements whose velocity increased with an increase in all stimulus parameters. Smooth movements and saccades usually occurred together and usually had the same direction, down and ipsilateral in the para-vermis, changing gradually through horizontal to up and ipsilateral in the lateral part of the hemisphere. Visual texture decreased the velocity of smooth movements. Smooth movements began about 10-15 msec after the start of stimulation and lasted about 20 msec after it stopped.

5. The third region was the vestibulocerebellum; the flocculus, nodulus, and uvula. Nystagmus was evoked from this region, but it was too small and convoluted to obtain a map of direction within it except that the slow phases were generally up in the dorsal uvula and ventral nodulus and down in the ventral uvula and dorsal nodulus. Slow-phase velocity increased with an increase in all stimulus parameters. Nystagmus was always followed by afternystagmus.

6. All other structures were considered unrelated to the oculomotor system because no eye movements could be evoked by a stimulus current of 1 ma or the threshold for limb movement was below that of any possible eye movements.

7. Rebound saccades and two other types of secondary saccades occurred frequently at the end of stimulation.

8. Stimulation of the dentate nucleus confirmed the anatomical findings of direct dentatooculomotor fibers.

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