Journal of Vestibular Research, Vol. 2, pp. 235–245, 1992
Printed in the USA.

0957-4271/92 $5.00 + .00

CHARACTERISTICS OF NYSTAGMUS EVOKED BY ELECTRICAL STIMULATION OF THE UVULAR/NODULAR LOBULES OF THE CEREBELLUM IN MONKEY

S. J. Heinen,* D. K. Oh,*† and E. L. Keller*†

*Smith-Kettlewell Eye Research Institute, 2232 Webster, San Francisco, California;
†Department of Electrical Engineering and Computer Sciences, University of California, Berkeley, California
Reprint address: Dr. S.J. Heinen, Smith-Kettlewell Eye Research Institute, 2232 Webster Street, San Francisco, CA 94115

□ **Abstract—Electrical stimulation in the monkey vestibulocerebellum has previously been shown to produce ocular nystagmus, but large stimulating current values were used. Using long duration (≤10-second) stimulus pulse trains and low current values (<50 μA), we studied the nystagmus evoked by microstimulation in the uvular/nodular regions of the cerebellum. In doing this, we found quantitative differences in the nystagmus evoked from these two regions. Stimulation of the nodulus typically produced a vigorous nystagmus with a contralateral slow phase and a prolonged afternystagmus in the same direction. In contrast, stimulation of the uvula typically produced a regular ipsilateral nystagmus pattern with a very short, if any, afternystagmus in the same direction. In addition, at some stimulation sites in the uvula we observed an adaptation in the slow phase eye velocity during the time that the stimulation remained on. This effect could result in a secondary nystagmus, with a slow phase velocity direction opposite to that first evoked by the stimulation, followed by a prolonged afternystagmus in the direction of the secondary nystagmus at stimulus offset. The nystagmus evoked by these cerebellar stimulations differs from both natural nystagmus produced by large field visual motion and from the nystagmus produced by electrical stimulation of the nucleus of the optic tract. The nystagmus produced by uvular and nodular stimulation shows a shorter latency and a more rapid slow phase eye velocity buildup. The uvula stimulations also showed a much shorter afternystagmus. Also, the same nystagmus was evoked whether the animal was in a lighted or dark surround. These characteristics and recent single-unit recording studies in the uvula seem to suggest that the uvula acts not as a direct input to the velocity storage mechanism, but instead perhaps as part of an internal regulator for balance between the bilateral vestibular nuclei which are normally part of the nystagmus response. On the other hand, the nodulus, with its prolonged afternystagmus in the same direction as the evoked nystagmus, may be involved as a part of the velocity storage mechanism.**

□ **Keywords—cerebellum; uvula; nodulus; vestibular nuclei; optokinetic nystagmus.**

Introduction

The uvula/nodulus (lobules IX and X respectively of the cerebellar vermis) and the flocculus/ventral paraflocculus are all classically considered to be part of the vestibulo-cerebellum (1). Thus, these cerebellar regions have often been lumped together in terms of their functional role in the control of eye movements. In support of this idea, studies have shown that lesions of the flocculus/paraflocculus (2) and the uvula/nodulus (3) both affect the monkey's ability to use a stationary visual background to suppress nystagmus. It has also been demonstrated that Purkinje cells in both areas respond to angular acceleration of the head (4,5). Furthermore, it has been shown shown that single climbing fibers from the inferior olive can branch and project to both regions (6).

On the other hand, some significant differences in the functional role (with regard to eye movements) of these two regions, and even between the nodulus and the uvula, have been

RECEIVED 14 April 1992; REVISED MANUSCRIPT RECEIVED 22 June 1992; ACCEPTED 23 June 1992.

suggested by the results of other studies. Lesions in the flocculus/paraflocculus disrupt the rapid rise in optokinetic nystagmus (OKN); while lesions of the uvula/nodulus (3) or the uvula alone (7) have little effect on this component of OKN, although one study involving uvula/nodulus lesions in monkey did show such an effect using high speed optokinetic stimulation (8). The response of Purkinje cells to constant velocity optokinetic or vestibular stimuli appears to be quite different in the two regions. Cells in the flocculus/paraflocculus respond crisply with short latencies to stimuli of these types, even during smooth pursuit eye movements (5,9), while most cells in the uvula/nodulus respond sluggishly with long latencies following the onset of these same types of stimuli (4,7). The dorsal folia of the uvula receives a strong projection of visual mossy fiber input from the cerebro-pontocerebellar system (10,11) as does the flocculus/ventral paraflocculus (12–14). The nodulus seems to receive a visual input, but only via the visual climbing fiber system (15).

In the present study, we used electrical microstimulation in the uvula/nodulus to determine if we could gain further information about the functional role of this cerebellar region that might supplement our recently completed single-unit recording and lesion studies in the uvula (7,16).

Ron and Robinson (17) have previously reported that nystagmus is evoked by electrical stimulation of the uvular/nodular region of the cerebellum, but in their study very large currents were used ($\leq$1 mA) which very likely excited both structures as well as other adjacent regions by current spread. Thus, an additional goal was to determine, by the use of very small currents, if we could show any differences in the effect of stimulation between the uvula and the nodulus.

Materials and Methods

Preparation

Three monkeys (Macaca fascicularis) were prepared for these studies by the chronic implantation of three devices. Each animal was implanted with a coil of Teflon-coated stainless steel wire mounted under the conjunctiva of one eye (18) to record eye movements using the search coil method (19). A stainless steel chamber (17 mm diameter) was stereotaxically positioned (with a posterior angle of 10°) over the uvular/nodular lobules of the cerebellum to allow single-cell recording and electrical microstimulation in this cerebellar region. Finally, two transverse stainless steel rods were implanted to allow immobilization of the head with respect to the magnetic fields during subsequent experimental sessions. The chamber and the rods were fixed in place with dental acrylic cement. All surgeries were performed under sodium pentobarbital anesthesia and sterile conditions. Sutured incisions were treated with antibiotic ointments, and penicillin was administered during the postsurgical recovery period. Analgesics (torbutrol, 0.05 mg/kg, intramuscular) were given after recovery from the anesthesia to relieve any postsurgical pain. Following recovery from these surgical procedures, the monkeys were taken to the recording room on a daily basis for sessions lasting several hours to obtain the electrical stimulation results described here. The care and use of all animals used followed the guidelines of the National Research Council.

Recording and Stimulation

We recorded single cells in the uvula/nodulus lobules as previously described (7). During some microelectrode penetrations, after recording the activity of single units in these regions, we delivered electrical stimulation beginning at the depth on the penetration of the deepest isolated unit. The microelectrode was then withdrawn in 500 μm steps, and the effect of stimulation was tested at each location. High-frequency pulse trains (pulse width 0.25 ms, frequency 300 pulses/s) were used as the standard, while current strength and pulse train length were varied.

Before data were collected, the threshold

current for evoking an eye movement was determined. Threshold levels of stimulation were always determined with the animal in a totally dark surround. In between stimulations the animal fixated a moveable visual spot for liquid reward (a task on which it has been previously trained) in order to maintain alertness. Train length was set to 50 ms and current was fixed at 10 μA. If no eye movement was evoked, current was then increased in step amounts up to a maximum level of 100 μA. If no eye movement occurred using this current, the location of the site was marked on the log as non-responsive for eye movements. The electrode was then withdrawn to a new location. If an eye movement was evoked, the threshold current was noted and then doubled in strength, and all eye movement data which were analyzed were collected using this supra-threshold level. Stimulus train length was varied up to a maximum value of 10 seconds. Stimulation data were gathered with the animal in complete darkness except when explicit tests were done to assess the effects of visual surrounds on stimulation-evoked eye movements. Because the nystagmoid-like eye movements that were routinely evoked showed adaptive characteristics, we were not able to test longer train lengths and as a precaution we waited several minutes between the delivery of stimulations.

In order to compare the eye movements that we evoked with electrical stimulation with visually-evoked nystagmus, we rotated an optokinetic drum about a vertical axis passing through the animal's head at constant speeds of either 40° or 100°/s. The drum was lined with alternating light and dark stripes having random widths that averaged 8° in width. In a typical trial, the drum was accelerated with the drum lights off until it reached one of the constant speeds used in this study. OKN was evoked when the drum lights were turned on, presenting the animal with a step-like increase in visual surround velocity. Drum rotation continued at a constant velocity for a fixed period of time, after which the drum lights were again turned off allowing for assessment of the ensuing optokinetic afternystagmus (OKAN).

Data Analysis

During stimulation sessions, eye position signals were differentiated by analog hardware to produce analog voltages proportional to eye velocity (high-frequency cutoff at 150 Hz). Eye position, eye velocity, and a signal giving the time envelope of the stimulus train were digitized at 500 Hz for short stimulus trains (<4 seconds) or at 100 Hz for longer pulse trains. Data were stored on computer disk during stimulation sessions and later analyzed off-line using either a PDP 11/73 or a PC/AT compatible computer.

Location of Recording Sites and Histology

Microelectrode tracks were made in parasagittal planes. The placement of the end of the guide tube just below the tentorium minimized the length of microelectrode travel, consequently minimizing the possibility of deviations of the tip away from a selected position in the parasagittal plane.

Before the animals were sacrificed, several electrolytic marker lesions were made at known stereotaxic locations by passing DC current at 20 μA for 20 seconds through the tungsten microelectrodes. Histological material was obtained by deeply anesthetizing the animal with pentobarbital and perfusing with buffered 10% formalin. Frozen serial sections (60 microns thick) were cut in the parasagittal plane and every fifth section was subsequently stained with cresyl violet. Stimulation sites were then reconstructed from the locations of the recovered lesion marks. We are confident about the laterality of our stimulation sites both because of the marker lesions, and since tracks were never run closer than 1 mm from the midline (to avoid the parasagittal sinus). However, since these sites were reconstructed on the basis of a few lesions at the end of the experiment, some uncertainty remains about the exact location of some of the stimulation sites with respect to the border between the uvula and nodulus.

Results

Stimulation Sites

We stimulated at sites along 27 penetrations in three monkeys. The locations of a group of representative stimulation sites from all three animals are superimposed and illustrated on a schematic reconstruction of a parasagittal section of the cerebellum in Figure 1. This figure was traced from a section located 1 mm from the midline in one monkey. In two of the monkeys, most of the penetrations went into the nodulus and ventral folia of the uvula, and in the other animal most went into the region of the dorsal folia or the central connective stem of the uvula. Nystagmic eye movements were evoked from sites scattered throughout the whole area explored in the three animals, from both the white matter and from the cortex, without any apparent pattern in stimulus threshold. However, quantitative differences were noted in the type of nystagmus that was evoked at uvular sites and nodular sites as described below. The initial movement evoked by stimulation throughout this region was always a smooth movement, and as stimulation duration was increased, this smooth movement was followed by a saccade in the opposite direction and then a typical alternating pattern of slow and fast eye movements.

The onset of the first slow evoked movement varied in latency from 20 to 50 ms with a mean value of 28 ms when averaged across all stimulated sites. The direction of the evoked nystagmus (categorized on the basis of the direction of the initial slow phase eye movement) could be either ipsilateral or contralateral and usually also contained a vertical

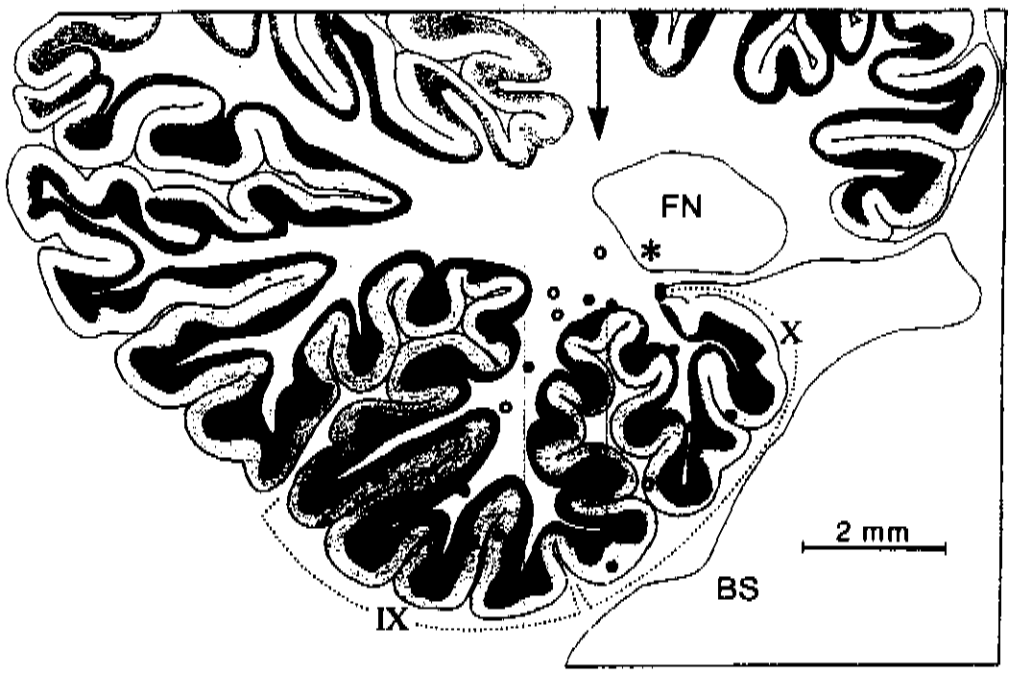

Figure 1. Stimulation sites in the uvula and nodulus. Locations where stimulation evoked nystagmus at current strengths less than 100 μA are shown as filled circles. Stimulated sites where no nystagmus was produced at this current strength are shown with open circles. Representative sites from all three monkeys are superimposed on one sagittal section (1 mm from the midline) of the cerebellum of one animal. The vertical arrow indicates the approximate direction of the vertical stereotaxic plane. FN = fastigial nucleus; BS = brain stem; IX = lobule 9 of the cerebellar vermis (the uvula); X = lobule 10 of the vermis (the nodulus). The * indicates a location just dorsal to the nodulus at which saccadic eye movements instead of nystagmus was evoked.

component. From 13 penetrations that were clearly off the midline and in the uvula, the direction of the slow phase of the evoked nystagmus was ipsilateral in 11. However in the nodulus, the opposite directional bias was found with seven out of nine penetrations yielding contralateral nystagmus. There was a sharp transition depth along nodular tracks (as the electrode was withdrawn) at which the evoked eye movement changed from nystagmus to a saccade, probably indicating entry of the stimulating electrode into the posterior fastigial nucleus, a region known to be involved in saccade generation (20).

Optokinetic Drum Stimulation

In order to better interpret the effect of uvular/nodular electrical stimulation, it is helpful to first illustrate the effect in the same animal of natural full-field moving visual stimulation having similar time durations to the pulse-train lengths used during electrical stimulation. Typical results are shown in Figure 2 for visual motion durations of about 4, 10, and 30 seconds. Drum speed was 40°/s in each of the tests, a speed similar to the eye movements evoked by electrical stimulation in the uvula/nodulus at many sites. When a drum motion duration of 4 sec was used, the nystagmus slow phase velocity built up very rapidly, was sustained for the duration of the drum rotation, but then declined rapidly after the drum lights were extinguished. However, even for these short periods of optokinetic (OK) stimulation there was a prolonged period of low velocity OKAN (most clearly seen on the eye position trace). Thus, even rela-

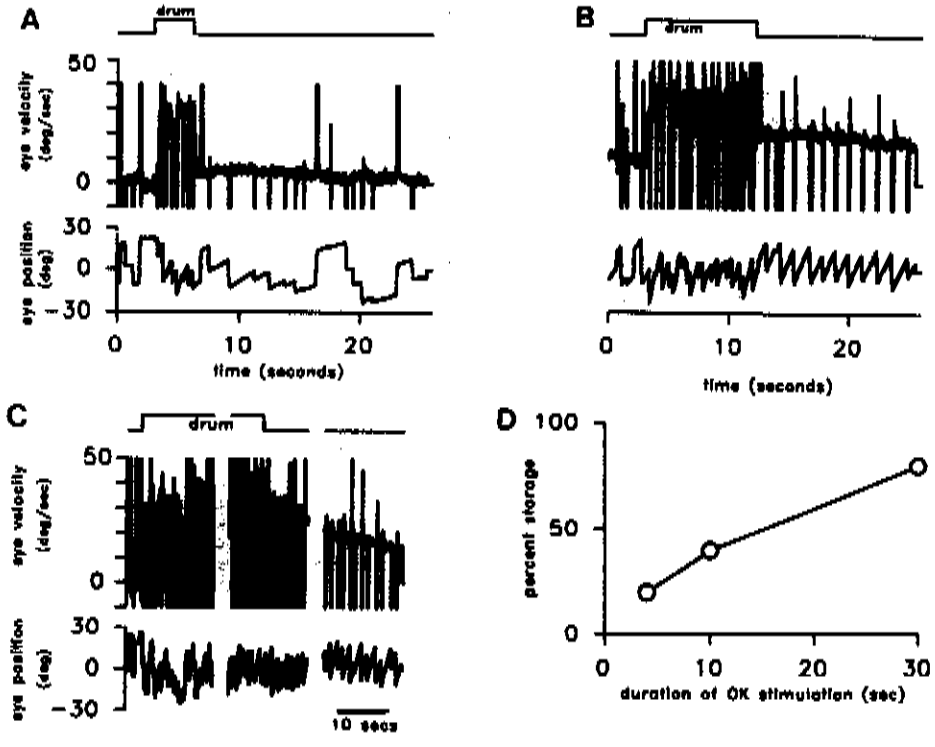

Figure 2. Nystagmus produced by striped drum rotation of about 4 (A), 10 (B), and 30 seconds duration (C). In A, B, and C the upper trace shows the time course of lighted drum rotation, the middle trace horizontal eye velocity, and the lower horizontal eye position. Quick phase eye velocities are clipped for clarity. All drum rotations shown are rightward. The breaks in C occur in a continuous trace at times when the stored data on the computer was written to disk. D: Graph shows an estimate of the percent of the maximum stored velocity for drum rotations of 4, 10, and 30 seconds (see text for details of the method). Each point represents the mean of 6 measurements in one animal.

tively short periods of electrical stimulation of 4 second duration would be expected to lead to clear after nystagmus, if the electrical stimulation engaged the normal optokinetic pathways in a manner similar to that produced by natural stimulation. Ten- and thirty-second periods of OK stimulation resulted in similar patterns of sustained nystagmus during drum rotation, but these longer periods of visual stimulation produced more velocity storage as seen in the higher values and longer durations of slow phase eye velocity during OKAN. For each speed, we defined the percent of velocity storage as the ratio of the peak value of observed OKAN slow phase velocity (normally found immediately after the drum light was turned off) to the OK slow phase velocity just before the drum light was turned off. Figure 2D shows the mean values of the results of these calculations for one animal. This figure shows that at 4 seconds of moving field stimulation only about 20% of the speed reached during OKN was stored. Maximum values of storage (about 80%) were reached with 30 seconds of drum rotation, and longer stimulation periods of up to 1 min in duration did not further increase the level of storage. In conclusion, natural OK stimulation given to our animals produced nystagmus similar to that previously reported for monkeys (21,22). Velocity storage is relatively low at drum rotation durations of 4 seconds (the most commonly used electrical stimulation duration), but the small amount of stored velocity decays slowly during OKAN and is still clearly seen for 10 seconds or more (Figure 2A) after the drum light is turned off. Ten-second drum rotations produced even more vigorous OKAN for times that exceeded the 15-second post-stimulus recording period (Figure 2B).

Thus, our typical electrical stimulations of either 4 or 10 second durations might be expected to evoke eye movements with afternystagmus having similar durations, if the nystagmus was evoked by stimulation of the same neural pathways that are normally used to generate OKAN. Stimulation in the uvula, although eliciting strong nystagmus during the stimulus train, produced only minimal afternystagmus when the stimulation was turned off. In contrast, some sites in the nodulus produced prolonged afternystagmus following the offset of electrical stimulation. We describe these results below.

Uvular Stimulation

Sites producing little afternystagmus. Figure 3 shows the type of eye movement typically

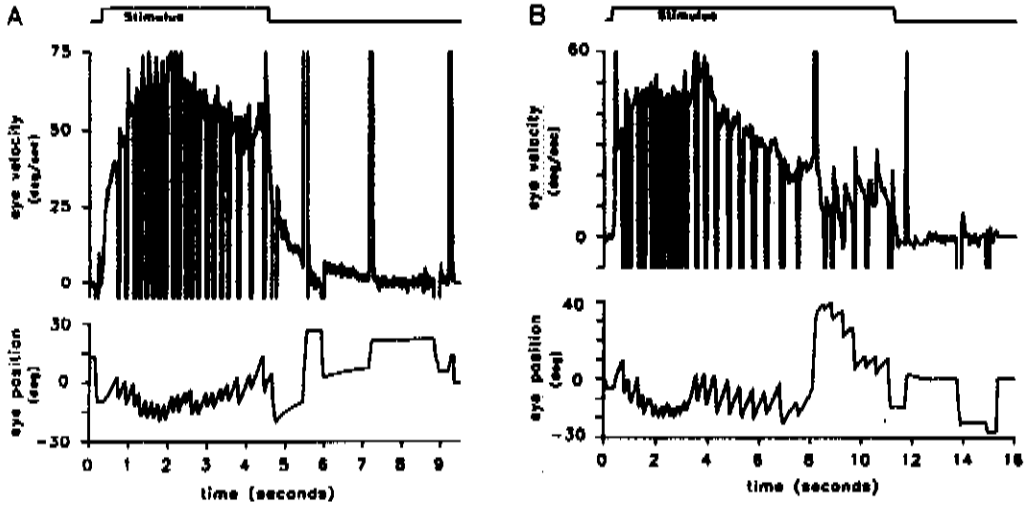

Figure 3. Eye movements produced by stimulation at a representative site in the right uvula. (A) A 4.2 second stimulation. (B) A 10.9 second stimulation at the same site. Traces from top to bottom: electrical stimulation envelope, horizontal eye velocity (rightward direction shown as positive), horizontal eye position (right shown as positive). Results from the same animal shown in Figure 2 for drum stimulation.

evoked by electrical stimulation (train duration was about 4 sec in this example) in the uvula. Stimulation at this uvular site produced a smooth acceleration of the eyes (after a latency of about 20 ms) in an oblique (right-down) direction. We found, in general, that the vertical component of the electrically evoked nystagmus was often much smaller in amplitude, and was often not sustained or waxed and waned in amplitude during the stimulation. Therefore, we have only shown the horizontal component of the nystagmus in this and the following figures. The evoked movement continued with a typical nystagmoid pattern of alternating slow- and fast-phase eye movements. The horizontal slow phase eye velocity reached a plateau in about 1 sec and then continued as a rather regular nystagmus of approximately constant velocity for the duration of the 4-second stimulation. When the stimulation was turned off, slow phase eye velocity decayed rapidly back to zero with a short period (about 2-second duration) of afternystagmus in the same direction as the peri-stimulation nystagmus. Longer duration stimulation (about 10 sec) at this site showed that the nystagmus tended to adapt as illustrated in Figure 3B. Slow phase eye velocity declined during the stimulus train for longer stimulations so that little (at this site) or no slow phase velocity (at other sites) remained by the end of the 10-second stimulation train. Even less afternystagmus was produced by the longer period of electrical stimulation as compared to that produced by the 4-second stimulus durations.

Stimulation during fixation of a visual target. Figure 4 shows the result obtained at this same uvular site when the stimulus train was applied while the monkey was fixating a small stationary spot projected onto the screen directly in front of it. A qualitatively similar nystagmus was evoked during the peri-stimulation interval, although the peak value of the evoked slow phase eye velocity was reduced from 67°/sec (in the case of no fixation point, see Figure 3A) to 57°/sec (when a fixation point was present, see Figure 4). A difference also existed at the time of stimulation offset. When the stimulus was turned off with no fixation point present, the ongoing slow phase eye velocity declined exponentially to produce a short afternystagmus in the same direction as that evoked during the peri-stimulus interval (Figure 3A). When the animal was attempting to fixate, although it was unable to suppress the effect of the stimulation, it showed a rapidly declining slow phase eye velocity that reversed direction at stimulus offset (Figure 4). The lower trace in this figure (eye position) illustrates that the animal was immediately able to regain fixation on the visual target when the stimulus was turned off, although its eyes were driven far off the target during the stimulation.

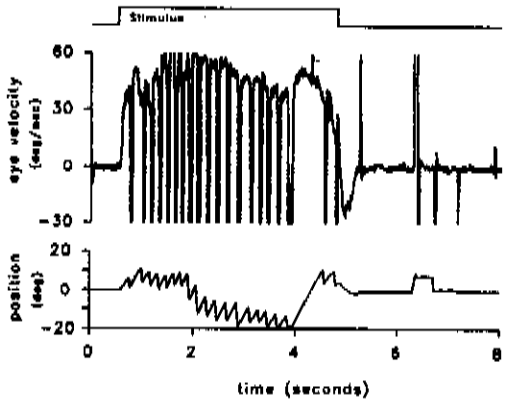

Figure 4. Stimulation in the presence of a stationary visual fixation point. Figure layout is the same as that in Figure 3A. Stimulation site is the same as that for Figure 3.

Nystagmus reversal during stimulation. At some sites in the uvula the adaptation that occurred during stimulation was very rapid, and in these cases the slow phase eye velocity often reversed direction during the time course of the electrical stimulation. This effect then resulted in a secondary nystagmus in the opposite direction which was larger than the spontaneous nystagmus seen in this animal in the dark. This effect is illustrated for one uvular site in Figure 5. This figure shows that a nystagmus in the left direction was evoked about 20 ms after stimulation onset, but that it reversed direction and went to the right after 2.5 seconds. When reversals of this type occurred during the stimulation, there was al-

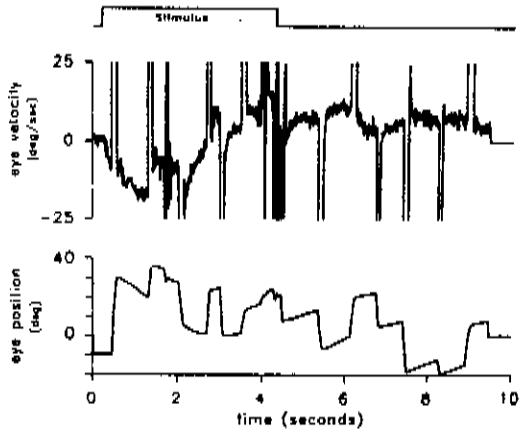

Figure 5. Four-second stimulation at a site in the uvula which produced a secondary nystagmus with reversed direction. Figure layout the same as in Figure 3.

ways a prolonged afternystagmus in the same direction as the secondary nystagmus as illustrated in Figure 5.

Nodular Stimulation

Long duration afternystagmus. In contrast to uvular stimulation, stimulation in the nodulus often produced a robust and prolonged afternystagmus in the same direction as that occurring during the stimulation. Figure 6A illustrates this type of result for a representative nodular site. Stimulation produced an initial rightward (contralateral slow phase) and upward eye acceleration with a latency of 20 ms. The vertical slow phase eye velocity (not shown) reached a small amplitude steady level after about one-half second, but the horizontal eye velocity continued to increase throughout the entire duration of the 4-second stimulation. At stimulus offset, in contrast to the rapid exponential drop in eye velocity seen following uvular stimulation, nodular stimulation produced a sustained afternystagmus that decayed only after 10 to 30 seconds (only the initial 5 seconds of this decline is shown in Figure 6A). At a few stimulation sites in the nodulus, the afternystagmus decayed more quickly, but even at these sites this afternystagmus decayed much more slowly (from 4 to 15 seconds) than that evoked by uvular stimulation. Sustained afternystagmus was found at sites along 10 of the 12 nodular penetrations made in two monkeys.

Adaptation to stimulation. Stimulation at some sites in the nodulus produced an initial nystagmus and adaptation similar to that found in the uvula (4 out of 12 penetrations

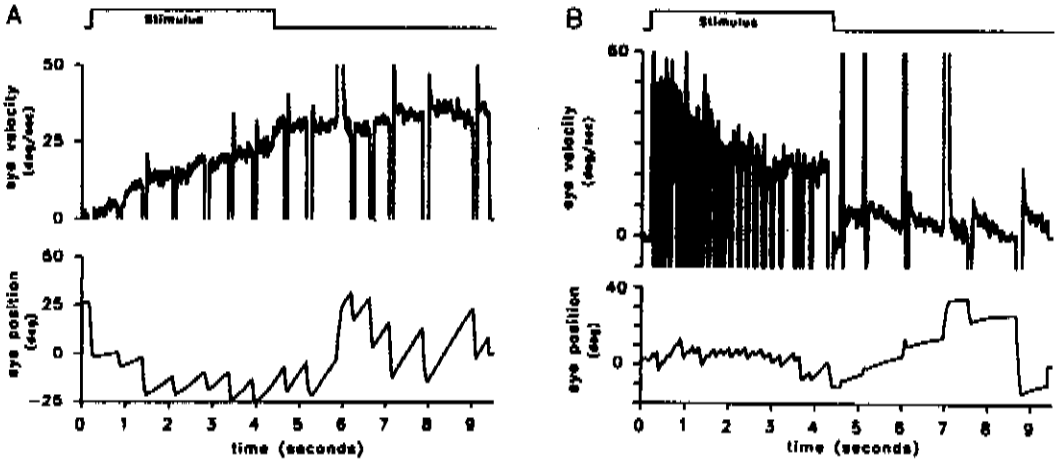

Figure 6. Four-second stimulations at representative sites in the left nodulus. Figure layout the same as in Figure 3. (A) Site where stimulation produced a prolonged afternystagmus. (B) Site where only modest afternystagmus was evoked. Note however, that afternystagmus is present here, unlike with uvular stimulation (Figure 3B).

in the nodulus). Figure 6B illustrates this effect for one site in the nodulus. Stimulation at this site produced an initial rightward nystagmus. This motion, however, was not sustained. The slow phase eye velocity begins to decline rather quickly (sometimes even reaching zero velocity before the stimulus offset). In some cases, as illustrated at this site, there is a small afternystagmus in the same direction as the peristimulus nystagmus unlike the case involving uvular stimulation. At others a modest amount of afternystagmus in the opposite direction occurred, but never to the extent that was seen with uvular stimulation.

Discussion

The common features of the responses produced by electrical stimulation at all sites in the uvula were the strong initial nystagmus and the almost total lack of afternystagmus (in the same direction as the peristimulus nystagmus) at the end of stimulation. With longer duration stimulations, a secondary nystagmus often appeared. It was always in a direction opposite to the original peristimulus nystagmus, and it could start even before the termination of electrical stimulation. When a strong secondary nystagmus was evoked, there was a prolonged afternystagmus, but always in the direction of this reversed secondary nystagmus.

Stimulation at most sites in the nodulus produced a prolonged afternystagmus in the same direction as the peristimulus nystagmus. In contrast to uvular stimulation, with nodular stimulation there were few cases of an actual reversal of the direction of the nystagmus during the stimulation, however, adaptation to the stimulus did occasionally occur. Any afternystagmus that was produced was still in the same direction as the initial nystagmus.

Thus stimulation in the nodulus differs from stimulation in the uvula in several ways. First, reversal of direction of nystagmus (secondary nystagmus) occurs much more commonly following uvular stimulation. In the uvula, this reversal may occur either during or after the stimulus. Second, adaptation in the nodulus leads only to an absence of afternystagmus or a small nystagmus nearly always in the same direction as the original nystagmus, while adaptation in the uvula leads to the reversal effect. Third, a sustained afternystagmus that resembles OKAN (slow phases in the same direction as those during OKN) occurs only with stimulation in the nodulus. Unless there is a secondary nystagmus (reversed direction afternystagmus), the initial nystagmus following uvular stimulation is small or abruptly disappears at the end of the stimulus, while the nystagmus following stimulation in the nodulus usually continues well after the current is turned off.

Ron and Robinson (17) have previously reported that electrical stimulation of the uvula or the nodulus led to the induction of nystagmus with similar properties from either structure. In their study, relatively large stimulating electrodes and currents (up to 1 mA) were used and no quantitative description of the nature of the evoked nystagmus was given. It is very likely that these levels of stimulating currents may have produced substantial current spread that prevented their observing any differences in the effect of stimulation in these two areas. In their study, a rapid adaptation in the nystagmus frequently occurred, but they did not report the reversal in direction that we frequently observed with uvular stimulation. They also reported afternystagmus which we observed only with nodular stimulation. They further noted that electrical stimulation of the flocculus produced a similar type of nystagmus.

Belknap and Noda (23) stimulated the flocculus with microelectrodes and used small currents (less than 22 μA) which were comparable to those we used. However, since they did not use train lengths longer than 500 ms, they only occasionally evoked nystagmus, and then, of only minimal duration. Thus it is difficult to compare our results to those obtained from floccular stimulation to determine if Ron and Robinson (17) are correct in their conclusion that similar types of results are obtained from electrical stimulation of all of these regions of the primate vestibulo-cerebellum. Belknap and Noda (23) argued that their floccular stimulation produced pursuit eye move-

ments. The consistent production of nystagmus from uvula/nodulus stimulation argues against this interpretation of our results.

Our experimental stimulations are more comparable to those of Schiff and colleagues (21) in which the nucleus of the optic tract (NOT) was stimulated with currents of 30 to 40 μA and train durations of 20 to 30 seconds. Stimulation of this structure produced (after latencies of 200 to 500 ms) horizontal, ipsilateral nystagmus and a prolonged afternystagmus in the same direction, but only when the animal was in the dark. The presence of a lighted stationary surround, however, inhibited the evoked eye movements. Because the characteristics of the evoked movements in darkness were so similar to natural OKN and OKAN, these authors argued that they were stimulating a structure which provided the input to the horizontal velocity storage integrator of the oculomotor system. The nystagmus we evoked from uvula/nodulus stimulation was quantitatively different from that evoked by stimulation of the NOT. Most significantly, our cerebellar stimulations produced virtually the same nystagmus whether the animal was in a lighted, stationary surround, or in darkness, although the speed of the slow phases were reduced in the presence of the stationary surround. The latency of the cerebellar evoked nystagmus was much shorter (typically 20 ms), and the build up of slow phase eye velocity took place over a very short time course (typically 1 second) which is much shorter than the build up of natural OKN and the nystagmus evoked by NOT stimulation (21). Uvular evoked afternystagmus was much shorter than that produced by NOT stimulation and not at all like the time course of OKAN. Finally, the nystagmus produced by uvular stimulation often showed adaptation to prolonged stimulation such that little movement remained after several seconds of stimulation, or the direction of the slow phase even reversed during or after the stimulation. Thus, it seems unlikely that we were stimulating an input to or within the velocity storage integrator.

Recent single-unit recording studies and chemical lesion studies in uvula have also produced somewhat paradoxical data concerning the role of this cerebellar lobule on oculomotor function (7,16). On the one hand, strong modulation of uvular neuronal response required prolonged periods of vestibular or large-field visual motion stimulation, but on the other, the time course of this change in neural activity did not mirror that of the build up of nystagmus or the decay of afternystagmus. Furthermore, the major effect of the chemical lesions in the uvula was on smooth-pursuit eye movements and not OKN or OKAN. These data and the uvular stimulations both support the notion that this lobule is not part of or a direct input to the velocity storage mechanism. The prolonged afternystagmus produced by stimulation at some nodular sites supports the idea that this structure, in contrast to the uvula, may be involved in this mechanism.

As a functional role for the uvula, we suggest that it helps to maintain long term balance between the bilateral vestibular nuclei through its direct input to vestibular neurons. Since one demonstrated role of the vestibular nuclei is velocity storage, stimulation of the uvula might be expected to lead to nystagmus through modulation of neurons in these nuclei. We hypothesize that the uvula's input to vestibular nuclei neurons does not constitute a normal velocity input pathway (for example, like that provided by input from the nucleus of the optic tract), but instead this structure functions more as part of an internal regulatory pathway. The long-term balance hypothesis would also explain the frequent production of a secondary nystagmus by uvular stimulation. Secondary nystagmus has been hypothesized to reflect the influence of such a mechanism (24).

REFERENCES

1. Ito M. The cerebellum and neural control. New York: Raven; 1984.
2. Zee DS, Yamazaki A, Butler PH, Gucer G. Effect of ablation of flocculus and paraflocculus on eye movement in primate. J. Neurophysiol. 1981;46:878–899.
3. Waespe W, Cohen B, Raphan T. Dynamic modifica-

tion of the vestibulo-ocular reflex by the nodulus and uvula. Science. 1985;228:199–202.
4. Precht W, Simpson JI, Llinas R. Responses of Purkinje cells in rabbit nodulus and uvula to natural vestibular and visual stimuli. Pflügers Arch. 1976;367: 1–6.
5. Lisberger SG, Fuchs AF. Role of primate flocculus during rapid behavioral modification of vestibulo-ocular reflex I. Purkinje cell activity during visually guided horizontal smooth pursuit eye movement and passive head rotation. J Neurophysiol. 1978;41: 733–763.
6. Takeda T, Maekawa K. Olivary branching projections to the flocculus, nodulus and uvula in the rabbit. Exp Brain Res. 1989;74:47–62.
7. Heinen S, Keller E. Cerebellar uvula involvement in visual motion processing and smooth pursuit control in monkeys. Ann N Y Acad Sci. [In press].
8. Igarashi M, Miyata H, Kato Y, Wright WK, Levy JK. Optokinetic nystagmus after cerebellar uvulonodulectomy in squirrel monkeys. Acta Otolaryngol. 1975;80:180–184.
9. Waespe W, Henn V. Visual-vestibular interaction in the flocculus of the alert monkey. II. Purkinje cell activity. Exp Brain Res. 1981;43:349–360.
10. Brodal P. Further observations on the cerebellar projections from the pontine nuclei and the nucleus reticularis tegmenti pontis in the rhesus monkey. J Comp Neurol. 1982;204:44–55.
11. Robinson FR, Cohen JL, May J, Sestokas AK, Glickstein M. Cerebellar targets of visual pontine cells in the cat. J Comp Neurol. 1984;223:471–482.
12. Glickstein M, Mercier B, Stein J, Legg C, Voogd J. Visual pontine projection to the cerebellar hemispheres of macaques. Soc Neurosci Abstr. 1990; 16:637.
13. Langer T, Fuchs AF, Scudder CA, Chubb MC. Afferents to the flocculus of the cerebellum in the Rhesus macaque as revealed by retrograde transport of horseradish peroxidase. J Comp Neurol. 1985;235: 1–25.
14. Gerrits NM, Voogd J. The topographical organization of climbing and mossy fiber afferents in the flocculus and the ventral paraflocculus in rabbit, cat and monkey. Exp Brain Res. 1989;17:26–29.
15. Maekawa K, Simpson JI. Climbing fiber responses evoked in vestibulocerebellum of rabbit from visual system. J Neurophysiol. 1973;36:649–666.
16. Heinen SJ, Keller EL. Cerebellar uvula correlates of moving visual stimuli. Soc Neurosci Abstr. 1990; 16:1083.
17. Ron S, Robinson DA. Eye movements evoked by cerebellar stimulation in the alert monkey. J Neurophysiol. 1973;36:1004–1022.
18. Judge SJ, Richmond BJ, Chu FC. Implantation of magnetic search coils for measurement of eye position: An improved method. Vision Res. 1980;20: 535–538.
19. Robinson DA. A method of measuring eye movement using a scleral search coil in a magnetic field. IEEE Trans Biomed Eng. 1963;10:137–145.
20. Noda H, Murakami S, Yamada J, Tamaki Y, Aso T. Saccadic eye movements evoked by microstimulation of the fastigial nucleus of macaque monkeys. J Neurophysiol. 1988;60:136–1052.
21. Schiff D, Cohen B, Raphan T. Nystagmus induced by stimulation of the nucleus of the optic tract in the monkey. Exp Brain Res. 1988;70:1–14.
22. Cohen B, Matsuo V, Raphan T. Quantitative analysis of the velocity characteristics of optokinetic nystagmus and optokinetic after nystagmus. J. Physiol Lond. 1977;270:321–344.
23. Belknap DB, Noda H. Eye movements evoked by microstimulation in the flocculus of the alert monkey. Exp Brain Res. 1987;67:352–362.
24. Maioli C. Optokinetic nystagmus: Modeling the velocity storage mechanism. J Neurosci. 1988;8: 821–832.