Lesions of the Cerebellar Nodulus and Uvula Impair Downward Pursuit

Mark F. Walker,1,2,6 Jing Tian,1 Xiaoyan Shan,1 Rafael J. Tamargo,3,4 Howard Ying,2 and David S. Zee1,2,4,5

Departments of 1Neurology, 2Ophthalmology, 3Neurosurgery, 4Otolaryngology-Head and Neck Surgery, and 5Neuroscience, The Johns Hopkins University School of Medicine, Baltimore, Maryland; and 6Department of Neurology, Case Western Reserve University School of Medicine and the Louis Stokes Cleveland Department of Veterans Affairs Medical Center, Cleveland, Ohio

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Walker MF, Tian J, Shan X, Tamargo RJ, Ying H, Zee DS. Lesions of the cerebellar nodulus and uvula impair downward pursuit. J Neurophysiol 100: 1813–1823, 2008. First published July 23, 2008; doi:10.1152/jn.01193.2007. We studied sinusoidal (SIN) and step-ramp (SR) pursuit in two rhesus monkeys, before and after surgical lesions of the cerebellar nodulus and uvula (Nod/Uv). Eye movements were recorded using the magnetic field scleral search coil method. Pursuit targets were generated by an LCD projector and back-projected onto a tangent screen in an otherwise dark room. After the lesion, pursuit was impaired. A recent clinical report suggested that the nodulus and uvula might play an important role in vertical pursuit. Here, we report for the first time the effect of experimental surgical lesions of the Nod/Uv on vertical pursuit in nonhuman primates.

INTRODUCTION

The function of the pursuit system is to maintain visual fixation of an object that is moving through the environment. To do this, the brain must extract the speed of the target from the motion of its image on the retina (retinal slip) and innervate the extraocular muscles to produce an eye velocity that matches target velocity and keeps the image of the target on the fovea. Studies of both humans and animals have shown that the cerebellum plays a critical role in the control and calibration of pursuit; in fact, complete cereblectomy abolishes pursuit (Burde et al. 1975; Westheimer and Blair 1973). In primates, the control of pursuit seems to be distributed among several cerebellar areas, including at least the flocculus and ventral paraflocculus (Rambold et al. 2002; Zee et al. 1981), the uvula (Heinen and Keller 1996), the dorsal vermis (Takagi et al. 2000), and the lateral cerebellar hemispheres (Straube et al. 1997). The exact anatomical and functional distinctions of these areas, however, remain uncertain (Büttner and Kremmyda 2007; Krauzlis 2004; Thier and Ilg 2005), and other than the study of Heinen and Keller (1996), relatively little attention has been given to the role of the nodulus and uvula (Nod/Uv) in pursuit.

Most prior studies focused on horizontal pursuit; less is known regarding the functions of specific cerebellar areas in vertical pursuit. In humans with cerebellar disease, however, vertical pursuit is frequently disturbed. In particular, a common finding is an asymmetry of pursuit in which downward pursuit is substantially reduced or even abolished while upward pursuit is relatively spared (Glasauer et al. 2005). It has been suggested that this asymmetry in vertical pursuit might be related to the spontaneous upward drift that characterizes downbeat nystagmus (Glasauer et al. 2005; Marti et al. 2005, 2008).

A few studies have examined vertical pursuit after cerebellar lesions. Bilateral ablation of the flocculus and paraflocculus impaired vertical pursuit, but this deficit appeared to be symmetric, rather than affecting downward pursuit selectively (Rambold et al. 2002; Zee et al. 1981). Lesions of the ocular motor vermis (lobules VI–VIII) produced hypometric horizontal pursuit but did not affect vertical pursuit (Takagi et al. 2000). Chemical lesions of the fastigial nuclei had variable effects on both horizontal and vertical pursuit (Robinson et al. 1997). In one monkey, gains of both upward and downward pursuit were reduced; in the second monkey, only downward pursuit was impaired. A recent clinical report suggested that the nodulus and uvula might play an important role in vertical pursuit (Helmchen et al. 2007). Here, we report for the first time the effect of experimental surgical lesions of the Nod/Uv on vertical pursuit in nonhuman primates.

METHODS

Two juvenile (1 female, 1 male) rhesus monkeys were the subjects of this study. All experimental procedures were approved by the Animal Care and Use Committee of the Johns Hopkins University. Approximately 10 mo before the experiments reported here were begun, one of the two animals (M1) underwent a right trochlear nerve section as part of a different study (Shan et al. 2007). This was followed by two corrective procedures: right inferior oblique denervation and exenteration (5 mo before the Nod/Uv lesion) and left inferior rectus recession (6 wk before the Nod/Uv lesion). Both pre- and postnodulectomy pursuit data were collected after the superior oblique palsy and corrective surgeries. At the time our study of pursuit was begun, there was little difference in pursuit from the original responses recorded before the animal had the trochlear nerve section. Here we show data from the right eye, but there was little difference in the responses of the two eyes.

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Surgical procedures

Surgical procedures were performed using aseptic technique under inhalation anesthesia and with approved postoperative analgesia. Each animal first underwent placement of an acrylic plate for immobilization of the head during experimental recordings. In one procedure for each eye, dual scleral coils made of stainless steel wire were implanted binocularly, as has been previously described (Tian et al. 2007).

Cerebellar lesions were performed under inhalation anesthesia by one of the authors (R.J.T.), using standard neurosurgical technique, including administration of intravenous mannitol, dexamethasone, fluids, and prophylactic antibiotics. A suboccipital craniotomy was

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**FIG. 1.** Sagittal histological sections through the vermis in each monkey along with corresponding sections from the atlas of Madigan and Carpenter (1971). The excised area on each section is shaded pink, and the relevant lobules are labeled. The alphanumeric labels indicate the location of the section (in mm) from the midline (e.g., “L3.5” is located 3.5 mm to the left of the midsagittal section). In both monkeys, part of the right dorsal uvula was spared, but the rest of the uvula and all of the nodulus were excised. The fastigial nucleus (FN) was intact in both animals, although the edge was reached by the lesion, and there were a few inflammatory cells in the FN in M2. (Nod, nodulus; Uv, uvula; PML, paramedian lobule; PAP, paramedian lobule, pars anterior).
performed, and the inferior vermis was visualized. The nodulus and uvula were exposed and aspirated. Following recovery from anesthesia, the animal was returned to its home cage, where it was closely monitored. Intramuscular buprenorphine was given for postoperative analgesia. The monkeys had mild titubation and postural instability immediately after the surgery, but they recovered quickly, and within several days they were moving normally around their cages and eating and drinking without difficulty.

Eye movement measurements

Eye movements were measured with the magnetic field scleral search coil method. Animals were trained to fixate and follow a small visual target for a liquid reward. During each experimental session, the animals were seated in a primate chair with head fixed. The primate chair was centered within a cubic frame consisting of three orthogonal magnetic fields (55.5, 83.3, and 42.6 kHz). Visual stimuli were generated by an LCD projector and were back-projected onto a tangent screen that was located 66 cm in front of the animal. Data from the right eye of each animal are shown and analyzed.

Experimental paradigms

Responses to both abrupt (step-ramp) and sinusoidal pursuit were tested. For step-ramp pursuit, each trial began with fixation of a central stationary target (subtending 0.6°) on a nontextured background in a room that was otherwise dimly illuminated (<1 lux). The target jumped to the right or left, for horizontal pursuit, or up or down, for vertical pursuit, by 4.4° (equivalent to 220 ms of the movement of the stimulus) and started to move in the opposite direction at a constant speed of 20°/s for a total displacement of ~20°. We also tested step-ramp tracking of larger stimuli with and without texture. Larger solid targets subtended 1.5 and 2.9°. The textured stimuli consisted of a central fixation spot (0.6°) surrounded by a square random-dot pattern whose size was 1.5, 2.9, 4.3, or 5.7°. A large-field target consisted of the same central target surrounded by a field of random dots that was 46° wide and 38° high.

Sinusoidal pursuit was tested with a continuously oscillating horizontal or vertical target (0.3 Hz, ±37.5°/s, ±20°). For each direction and monkey, 22–70 pursuit cycles were analyzed. The monkey was rewarded for maintaining fixation of the target within a window of ~4° for sinusoidal pursuit and 7° for step-ramp pursuit. When pursuit was very deficient (after the Nod/Uv lesion in M2), the animal was rewarded manually for attempting to follow the target.

For both types of pursuit, recordings were made with the target along the horizontal and vertical meridians and also offset by ±20° horizontally for vertical pursuit and ±20° vertically for horizontal pursuit. The intention of the offset target positions was to study the eye position dependence of pursuit kinematics. There was no effect of orbital position on pursuit gain; thus for the results presented here, all trials in a given direction are pooled, regardless of the absolute position.

Data analysis

Data were analyzed using custom programs written in MATLAB (The Mathworks, Natick, MA) and Python. As described elsewhere (Tian et al. 2007), rotation vectors representing instantaneous angular eye orientation were extracted from recorded coil signals (sampled at 1,000 Hz) and were used to calculate angular eye velocity vectors in space-fixed coordinates. For both step-ramp and sinusoidal pursuit, quick phases were excluded automatically using an algorithm based on the magnitudes of eye velocity, acceleration, and the derivative of acceleration, jerk (Wyatt 1998). For these data, thresholds of 25°/s (slow-phase eye velocity did not exceed target velocity during pursuit), 1,100°/s², and 70,000°/s³ were used for velocity, acceleration, and jerk, respectively. Somewhat higher thresholds were required for full-field following, as responses were brisker and had higher accelerations.

Step-ramp pursuit trials were included in the analysis only if the eyes remained within a specified position window relative to the target (±10° along the pursuit direction and ±5° in the orthogonal direction). This served to exclude occasional trials when the animal

FIG. 2. Single cycle of sinusoidal pursuit before and after Nod/Uv lesions (U, up; D, down; R, right; L, left). The dashed line depicts the position or velocity of the foveal target, i.e., the ideal eye movement to maintain fixation. Before the lesion, vertical pursuit was fairly symmetric, although the smooth eye velocity was slightly higher for downward pursuit. After lesioning, both animals showed a reduction in smooth eye velocity during downward tracking with little change for upward pursuit. In M2, downward slow phases were nearly abolished. Horizontal pursuit in M1 was unaffected by the Nod/Uv lesion. In M2, rightward pursuit was reduced, particularly toward the end of the half cycle.
was not attending to or attempting to follow the target. Individual trials in a group were aligned on the onset of target motion rather than on the onset of the eye movement, because in some cases (e.g., downward target motion in M2 after the lesion), there was little or no pursuit.

For the step-ramp stimulus, we calculated for each trial the median open-loop eye acceleration and the median velocity gain of sustained closed-loop pursuit. We considered the open-loop period to extend from 120 to 240 ms from the onset of target motion, because the pursuit latency was \(\approx 120\) ms. Defining the open-loop period based on the target made it possible to analyze data even when there was no smooth tracking (e.g., downward pursuit in M2). The closed-loop velocity gain was calculated as the ratio of the median eye velocity during the analyzed interval to target velocity. We averaged the gains from all trials of the same pursuit direction. The gain of sinusoidal pursuit was determined by robust least-squares linear regression of instantaneous vertical slow-phase eye velocity to target velocity (function rlm in R, invoked in Python using rpy). This calculation was performed separately for each direction of target motion, i.e., for each half-cycle of target velocity. The contribution of saccades to sinusoidal pursuit, also examined separately for upward and downward tracking, was calculated as the ratio of the summed saccade amplitude to the total amplitude of tracking (pursuit + saccades) in the same direction.

**Statistical measures**

For step-ramp pursuit, we performed \(t\)-tests on groups of similar trials (same direction) in each monkey, before and after the Nod/Uv lesions, applying the Bonferroni correction for multiple comparisons. For sinusoidal pursuit, we added an indicator variable to the linear model \(v_{\text{eye}} = \alpha \times v_{\text{target}} + \beta \times x\), where \(v_{\text{eye}}\) and \(v_{\text{target}}\) are the instantaneous eye and target velocities, respectively; \(x = 0\) for prelesion data, and \(x = 1\) for postlesion data, computing the \(P\) value corresponding to the \(t\)-statistic for the parameter \(\beta\), with the Bonferroni correction.

**Perfusion and histological techniques**

At the completion of experiments, each monkey was killed with sodium pentobarbital. A tracheal cannula was inserted, and the chest cavity was opened. The animal was artificially resired (Harvard Apparatus 613) via the cannula and perfused through the heart with 50 ml of phosphate-buffered isotonic saline with 0.5% \(\text{NaNO}_2\) (pH 7.4) followed immediately by a phosphate-buffered solution of 2% paraformaldehyde and 2% glutaraldehyde (pH 7.4). Following perfusion, the head was removed and immersed in the same fixative (5°C) after occipital craniotomy to expose the posterior fossa. Following fixation, the brain was removed, and the cerebellum was separated and prepared for histological section. Sagittal sections of 50 \(\mu\)m thickness were stained for Nissl substance.

**RESULTS**

**Cerebellar lesions**

The extent of the cerebellar lesions is shown in parasagittal histological sections in Fig. 1. In both monkeys, all of
the nodulus (to its lateral margins) and most of the uvula were excised. In both animals, a portion of the right lateral uvula was spared. M2 had a larger lesion that included portions of vermis lobule VIII and some of lobule VII. We examined the fastigial nuclei, which lie adjacent to the nodulus, for signs of damage. Overall, they appeared to be intact structurally, although they did contain a few chronic inflammatory cells at their edge.

**Sinusoidal pursuit**

Lesioning the Nod/Uv impaired downward but not upward sinusoidal pursuit. Representative eye position traces are shown in Fig. 2 for a single cycle of pursuit. Before the lesion, both animals tracked the target well, although downward pursuit was slightly better than upward pursuit. After the lesion, downward smooth eye velocity decreased, and larger compensatory saccades were required to keep the eyes on the target. The effect was most pronounced in M2, whose downward pursuit was essentially abolished. Figure 3 shows smooth eye velocity for all cycles combined. Again, the lesions disproportionately impaired downward pursuit, particularly in M2, but also in M1.

Pursuit gains were defined as the slope of the robust least-squares linear regression of instantaneous eye velocity to target velocity. Results are shown in Fig. 4. The largest and most consistent change was the reduction in downward pursuit. Compared with the prelesion values, downward pursuit gain decreased by 42% in M1 and 91% in M2, and upward pursuit gain increased by 9% in M1 and 11% in M2. There were decreases in horizontal pursuit (12% for rightward and 3% for leftward in M1; 63% for rightward and 24% for leftward in M2).

As expected, reductions in pursuit gain were accompanied by an increase in saccades. For downward pursuit, the saccadic component of tracking increased by 33% in M1 and 49% in M2. In contrast, the saccadic component of upward pursuit decreased by 23% in M1 and by 45% in M2, corresponding to the increase in pursuit slow-phase gain.

**Step-ramp pursuit**

The effect of the lesion on step-ramp pursuit was similar to that seen with sinusoidal pursuit. There was a reduction in smooth eye velocity during downward tracking and a smaller effect on upward pursuit (Figs. 5–7). We found this change only for closed-loop pursuit; eye acceleration in the open-loop period was not affected by the Nod/Uv lesions (Fig. 7;  P > 0.05 for all comparisons). The closed-loop gain decreased by 37% (M1) and 85% (M2) for downward pursuit and by 27% (M1) and 18% (M2) for upward pursuit.

The pursuit deficit following the Nod/Uv lesion was specific to foveal tracking. When the large-field random-dot stimulus was used for step-ramp tracking, vertical eye velocity was symmetric (Fig. 8). In fact, a random-dot stimulus as small as 1.5 (M1) or 2.9° (M2) was sufficient to improve downward tracking (Fig. 9).

**Spontaneous nystagmus**

We also examined the effect of the Nod/Uv lesions on spontaneous nystagmus. Neither monkey showed horizontal periodic alternating nystagmus (PAN) in light or darkness. Rhesus monkeys commonly have a spontaneous upward drift in the dark that is suppressed by fixation (unpublished observations). This was true of the two monkeys in this study [Fig. 10; mean upward slow-phase velocity (SPV), 1.43°/s]. After the lesion, upward drift in darkness increased in both monkeys (mean, 5.92°/s), and the greater increase was in M2. In both monkeys, however, when the lights were on, the downbeat nystagmus (DBN) was still suppressed. Similarly, there was no horizontal gaze-evoked nystagmus in the light.

**Saccades**

Saccades were not examined in detail in this study. After the Nod/Uv lesion in M2, however, we observed a new dysmetria of saccades that paralleled the pursuit deficits: downward and rightward saccades were hypometric and fractionated.

**Discussion**

Here we showed that lesions of the inferior vermis that include the nodulus and uvula impair foveal pursuit with a particular pattern: downward pursuit is impaired more than upward or horizontal pursuit. The vertical pursuit asymmetry is similar to that reported in patients with cerebellar lesions and downbeat nystagmus (Glasauer et al. 2005), including one human patient who had a focal lesion involving the nodulus (Helmchen et al. 2007). Moreover, as has been shown in humans with cerebellar disease, this asymmetry was present even when target motion was potentially predictable, i.e., for sinusoidal pursuit.

Facilitation of downward foveal pursuit can thus be added to other important functions of the Nod/Uv in the control of eye movements and vestibular reflexes. These include the control
of the time constant (Waespe et al. 1985) and orientation (Angelaki and Hess 1995; Wearne et al. 1998) of angular velocity storage, control of the torsional rotational vestibulo-ocular reflex (RVOR) (Angelaki and Hess 1994), and tilt suppression of postrotatory nystagmus (Wiest et al. 1999). A unifying purpose of these individual functions may be to facilitate the integration and transformation of sensory information into an inertial frame for the control, not only of eye movements, but also of balance and locomotion (Yakushcheva et al. 2007).

Implications for the cerebellar control of pursuit

Our study and the report of Helmchen et al. (2007) indicate that the cerebellar nodulus and uvula play an important role in the control of vertical pursuit. In fact, the findings in M2 show that a lesion of the inferior vermis can essentially eliminate downward pursuit. This does not mean that lesions elsewhere in the cerebellum do not affect vertical pursuit; for example, after flocculectomy, maximal upward and downward pursuit velocities were reduced, when tested with a manually moved target (Zee et al. 1981). In addition, a recent functional MRI (fMRI) study showed that the cerebellar paraflocculus was activated during downward pursuit in normal subjects but not in patients with downbeat nystagmus, suggesting that damage to the paraflocculus might contribute to impaired downward pursuit (Hüfner et al. 2007). Nonetheless, our results here show that an intact Nod/Uv is critical to normal vertical pursuit and that vertical pursuit asymmetry can be produced by lesions of the cerebellum that do not include the flocculus or paraflocculus.

How might the nodulus and uvula fit into the vertical pursuit pathways? A recent review by Voogd and Barmack (2005) summarized the afferent and efferent connections of the Nod/Uv, which include several areas that are important for pursuit. First, there are reciprocal connections with the vestibular nuclei. These include the superior vestibular nucleus (Carpenter and Cowie 1985; Walberg and Dietrichs 1988) and possibly the y-group (Xiong and Matsushita 2000), which have activity related to vertical pursuit (Chubb and Fuchs 1982; Chubb et al. 1984). Second, the uvula projects to the caudal fastigial nucleus (CFN) (Fuchs et al. 1994), but it is difficult to determine from available data whether they are limited strictly to the FOR or whether some might be located in adjacent areas of CFN that are targets of the uvula.
Also of interest are the pontocerebellar projections to the Nod/Uv, in particular from the nucleus reticularis tegmenti pontis (NRTP) and the dorsolateral pontine nuclei (DLPN). Both of these areas are important for vertical pursuit (May et al. 1988; Mustari et al. 1988; Suzuki et al. 1999, 2003), and both have been shown to project to the uvula (Brodal 1982; Glickstein et al. 1994). The heavier projection is from the DLPN, whereas the NRTP projects more strongly to the floccular complex (Brodal 1982). It has been proposed that the NRTP may play a greater role in the initiation of pursuit, whereas the DLPN may be more important for sustained pursuit (Ono et al. 2005). Taken together, these data suggest that impairment of sustained vertical pursuit in our monkeys after Nod/Uv lesions may be mediated by the disruption of the DLPN–uvula pathway.

This conclusion is notably different from that of Heinen and Keller (1996), who proposed that the uvula is not a part of the direct pursuit pathway. In their study, reversible lesions within the uvula did not impair pursuit, but rather led to an increase in the initial acceleration of horizontal step-ramp pursuit. It has been proposed that the NRTP may play a greater role in the initiation of pursuit, whereas the DLPN may be more important for sustained pursuit (Ono et al. 2005). Taken together, these data suggest that impairment of sustained vertical pursuit in our monkeys after Nod/Uv lesions may be mediated by the disruption of the DLPN–uvula pathway.

FIG. 6. Eye velocity during vertical and horizontal step ramp pursuit of a target moving at the constant speed of 20°/s. Solid traces show the median eye velocity for the series of similar trials, after exclusion of quick phase segments. The shaded areas include the 25th–75th percentiles, calculated from all the slow-phase data corresponding to a given time point. Trials are aligned on the onset of target motion (t = 0).

Could the impairment of downward pursuit have been caused by damage to structures or fiber tracts adjacent to the Nod/Uv? The margin of our lesions approached the caudal FN; FOR lesions have been shown to have variable effects on both horizontal and vertical pursuit (Robinson et al. 1997). In our histological sections, however, the FOR appeared to be intact. Moreover, our monkeys did not show the typical saccade deficits (ipsiversive hypermetria) of FOR lesions. M1 had normal saccades, and M2 had hypometria of downward and rightward saccades and normal leftward and upward saccades. In the vermis, the lesion extended somewhat beyond the uvula to involve portions of lobule VIII (more extensive in M2). It is unlikely that damage to lobule VIII contributed to the pursuit deficits in our monkeys, because Takagi et al. (2000) found no deficits of vertical pursuit with lesions of this area. It is unlikely, based on the
anatomical findings of Noda et al. (1990), that FOR axons were disrupted by the lesions.

Finally, could the lesions have affected the function of the floccular complex indirectly, by disrupting important afferent or efferent projections? Langer et al. (1985a) found that floccular axons lie more laterally than the reach of our lesions, so damage to floccular efferents is unlikely to explain our findings. In a companion paper (Langer et al. 1985b), neurons projecting to the flocculus were identified, but the paths of their axons were not. One of these areas, the basal interstitial nucleus (BIN), lies adjacent to the nodulus (Langer 1985) and could have been affected by our lesions. The physiology of these neurons has received only limited study; a relationship to saccade timing has been reported (Takikawa et al. 1998). Whether BIN neurons have responses related to pursuit is not known.

Effect of visual stimulus and motion type

In our monkeys, lesions of the Nod/Uv impaired downward tracking not only of step-ramp stimuli but also of sinusoidal target motion, even though before the lesion downward sinusoidal pursuit was better, as has been previously reported (Akao et al. 2007). The fact that the deficit was similar for the two very different stimuli and could not be overcome by the predictability of the sinusoidal target suggests that the Nod/Uv play a critical role in premotor processing for downward pursuit.

![Graph showing the effect of Nod/Uv lesions on step-ramp pursuit](image)

**FIG. 7.** Effect of Nod/Uv lesions on step-ramp pursuit. Left: the median eye acceleration during the open-loop period (120–240 ms from the onset of target motion), averaged for a set of similar trials. Right: the velocity gain (ratio of median eye velocity to target velocity) during closed-loop pursuit (240–840 ms from the onset of target motion). For both panels, the bar indicates the mean value for all similar trials in a single monkey, and the error bars shows the 95% CIs on those means. Individual t-tests were used to determine statistical significance, applying the Bonferroni correction for multiple comparisons (α = 0.006). None of the changes was significant for the open-loop period. All but 1 (M2 leftward) were significant (*P < 0.006) for the closed-loop period. Again, note the asymmetry in the effect on vertical pursuit: gains decreased more for downward than for upward pursuit.

![Graph showing eye velocity during step-ramp tracking](image)

**FIG. 8.** Eye velocity during step-ramp tracking of a large-field (55 × 42°) random-dot stimulus with a central fixation target after the Nod/Uv lesions. For comparison, the responses during foveal pursuit are also plotted (same as “post” data in Fig. 7). As in prior figures, the solid lines indicate the median of all trials and the shaded area encompasses the 25–75 percentiles of eye velocity. With the large-field stimulus, accelerations were much larger, and the deficit of downward tracking was partially overcome.
Downbeat nystagmus

Spontaneous DBN that cannot be suppressed by visual fixation is a characteristic feature of vestibulocerebellar lesions in humans (Cogan 1968) and animals (Zee et al. 1981). The mechanism of DBN, however, remains uncertain. A number of possibilities have been considered, including asymmetries in the vestibular system (Böhmer and Straumann 1998; Halmagyi et al. 1983), vertical pursuit (Zee et al. 1974), and the vertical neural integrator (Glasauer et al. 2003). That the position of the head relative to gravity can greatly influence downbeat nystagmus (Marti et al. 2002) indicates that the otolith system contributes to DBN. In fact, two or more mechanisms may combine to generate DBN, and these may not be the same in all patients.

Recent studies have suggested that RVOR asymmetries are unlikely to be the cause of DBN. DBN can be seen in patients with a symmetric vertical RVOR (Glasauer et al. 2004), and when the asymmetry is present it does not correlate with the magnitude of DBN (Walker and Zee 2005). On the other hand, several recent studies have focused again on the relationship of DBN to the pursuit system. Glasauer et al. (2005) confirmed that patients with DBN have impaired downward pursuit. Marti et al. (2005) showed that DBN can be induced in normal subjects following prolonged upward pursuit. Hüfner et al. (2007) related DBN to impaired activation of the cerebellar paraflocculus during downward pursuit. Finally, a model based on asymmetries in the responses and projections of floccular neurons was able to reproduce both DBN and a downward pursuit deficit (Marti et al. 2008).

In our monkeys, lesioning the Nod/Uv increased spontaneous upward drift in darkness, more so in the animal with the greater impairment of downward pursuit (M2). The difference, however, is that, unlike humans with cerebellar disease, DBN in our monkeys could be suppressed by vision. Thus, although vertical pursuit asymmetry may be related to DBN, it does not seem to be sufficient to generate nystagmus that persists in the light. It may be that the ability of our monkeys to suppress DBN is related to their preserved full-field tracking, which is likely mediated by a different part of the cerebellum or even extracerebellar structures.

In conclusion, we showed that experimental lesions of the cerebellar nodulus and uvula impair downward pursuit with little effect on upward pursuit, even when target motion is predictable. This finding reproduces a pattern that is commonly seen in humans with cerebellar disease. Responses to larger, random-dot stimuli remained relatively intact. These responses could be mediated through independent pathways that are responsible for short-latency ocular following responses (Miles et al. 1986).

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