Role of the Cerebellar Posterior Interpositus Nucleus in Saccades
I. Effect of Temporary Lesions

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Robinson, Farrel R. Role of the cerebellar posterior interpositus nucleus in saccades. I. Effect of temporary lesions. J Neurophysiol 84: 1289–1302, 2000. The ventrolateral corner of the cerebellar posterior interpositus nucleus (VPIN) contains many neurons that respond during saccades. To characterize the VPIN contribution to saccades, I located this area in three monkeys with single-unit recording and injected the GABA<sub>A</sub> agonist muscimol among saccade-related neurons there to reduce or eliminate neural activity. I compared the size, direction, velocity, and duration of saccades recorded before and after a unilateral injection in all three monkeys. In two of three monkeys, I also examined saccades after bilateral injection. After unilateral VPIN inactivation, upward saccades were abnormally large (avg. across all 3 monkeys = 112% of normal) and downward saccades were abnormally small (avg. across all 3 monkeys = 94% of normal). In the two monkeys tested, bilateral inactivation increased these abnormalities. Upward saccades went from 111% of normal size in these two monkeys after unilateral inactivation to 120% after bilateral inactivation; downward saccades went from 97 to 86%. VPIN inactivation caused changes in saccade gain and did not add of a constant offset to saccades. (The 1 exception was upward saccades in 1 monkey in which both gain and offset changed.) Neither unilateral nor bilateral VPIN inactivation consistently affected the size of horizontal saccades (uni- avg. = 101% normal; bi- avg. = 97% normal). In two of the three monkeys, saccades to horizontal targets angled significantly upward after VPIN inactivation (uni- avg. = 3.6° above normal, bi- avg. = 10.3° above normal). The velocities of horizontal saccades were not strongly affected, but downward saccades exhibited abnormally low peak velocities and long durations. Upward velocities were inconsistently changed. I interpret these results to mean that the activity of some VPIN neurons helps drive the eyes downward and the activity of others helps drive the eyes upward. The downward drive outweighs the upward drive. The net effect of VPIN inactivation is to deprive all saccades of a downward component and to slow downward saccades.

INTRODUCTION

Cerebellar damage disrupts saccades in humans (e.g., Selhorst et al. 1976) and monkeys (e.g., Ritchie 1976). Anatomical and recording studies to date indicate that there are two parts of the cerebellar nuclei that participate in saccades: the caudal fastigial nucleus (CFN), also called the fastigial oculomotor region (e.g., Ohtsuka and Noda 1990), and the ventrolateral corner of the posterior interpositus nucleus (VPIN).

Both the CFN and VPIN are positioned to receive eye-movement-related input and to influence saccades. The CFN receives descending saccade-related input via relays in the pontine nuclei from the frontal eye field, the supplementary eye field, and the superior colliculus. The frontal eye field (Stanton et al. 1988) and the supplementary eye field (Shook et al. 1990) project to the nucleus reticularis tegmenti pontis (NRTP). The superior colliculus (Harting 1977) projects to the dorsolateral pontine nucleus (DLPN). The NRTP and DLTP both project to the CFN (Noda et al. 1990) and to lobules VI and VII of the cerebellar cortex in the posterior vermis (Yamada and Noda 1987). These lobules, sometimes called the oculomotor vermis, project to the CFN (Yamada and Noda 1987). Activity in CFN neurons can influence saccades via CFN efferent connections to regions of the brain stem associated with three elements of the burst generator for horizontal saccades: inhibitory burst neurons, excitatory burst neurons, and omnipause neurons (Noda et al. 1990; Scudder 1997).

Like the CFN, the VPIN receives saccade-related input from the pontine nuclei. The DLTP projects heavily to a large, laterally placed part of the cerebellar cortex, the dorsal paraflocculus (Glickstein et al. 1994). This part of the cortex, in turn, sends a large projection to the VPIN (Swales et al. 1997). VPIN efferents terminate in two regions through which they could influence saccades. One is the contralateral superior colliculus, in which VPIN axons terminate throughout much of the intermediate layers (May et al. 1990). The other is a projection to the contralateral interstitial nucleus of Cajal (INC), though this projection may be small (May et al. 1992). The INC projects to the oculomotor and trochlear nuclei (Kokkoroyannis et al. 1996; Steiger and Büttner-Ennever 1979), and INC activity is critical to vertical saccades (Fukushima and Fukushima 1992; Helmcen et al. 1996).

Consistent with their anatomical connections, the CFN and VPIN both contain neurons that modulate their activity during saccades. CFN neurons discharge a burst of action potentials for nearly every saccade, whatever its size or direction (Fuchs et al. 1993; Ohtsuka and Noda 1991). This activity is clearly important for the production of normal saccades; when it is reduced or eliminated by muscimol injections, saccades become dysmetric and abnormally slow and variable (Robinson et al. 1993). VPIN neurons also discharge a burst of action potentials for...
nearly every saccade. Saccade-related VPIN responses were first described in a study of limb movement-related responses in the interpositus nuclei of the monkey cerebellum (van Kan et al. 1993). This work used observations from video tapes to document the existence of a distinct region of eye-movement-related neurons in the VPIN. It did not, however, measure eye movements and so did not characterize the relation between eye movement metrics and neural responses.

Why are there two separate regions in the cerebellar nuclei (the CFN and VPIN) containing neurons that burst vigorously during nearly every saccade? To answer this question, we need to know what each region contributes to saccades. The role of the CFN has been studied and modeled (e.g., Dean 1995; Lefèvre 1998), but to date we know little about the role of the VPIN.

To investigate the role of the VPIN in saccades, I compared saccades made by monkeys before and after I injected muscimol among saccade-related neurons there. The results are presented in this article. A subsequent paper will describe the data obtained when VPIN neurons were recorded while the monkeys made a variety of saccades (F. R. Robinson, A. F. Fuchs, and A. Straube, unpublished data). Preliminary results from both the inactivation and recording studies of the VPIN have been reported in an abstract (Robinson et al. 1996).

**Methods**

**Animal preparation**

Subjects were three adolescent male rhesus macaques (Macaca mulatta), monkeys 1, 2, and 3. In sterile surgery under general anesthesia, each monkey was implanted with three turns of fine Teflon-coated wire around one eye and acrylic lugs used to stabilize the head during experiments (Fuchs and Robinson 1966). A recording chamber was implanted over a small hole cut through the skull. The chamber was centered with a stereotaxic apparatus on the midline 8 mm posterior to ear bar zero and pointed directly downward.

I recorded eye movements with the search coil technique (Robinson 1963) and trained the monkeys with applesauce reward to foreshadow a small (0.3°) spot of light and to track the spot’s movements with saccades. The target spot was projected onto a screen 57 cm in front of the monkey via two galvanometers that allowed a computer to control the spot’s horizontal and vertical positions.

All surgical and behavioral training procedures were approved by the Animal Care and Use Committee at the University of Washington. The animals were cared for by the veterinary staff of the Regional Primate Research Center. They were housed under conditions that comply with National Institutes of Health standards as stated in the Guide for the Care and Use of Laboratory Animals (DHEW Publication NIH85-23, 1985) and with recommendations from the Institute of Laboratory Animal Resources and the American Association for Accreditation of Laboratory Animal Care.

**Locating the VPIN**

To find the VPIN, I first located the CFN 1–2 mm lateral to the midline, near the anterior-posterior center of the chamber, and ~25 mm below the surface of the brain. It was identifiable by the characteristic bursting of many of its neurons during saccades. The VPIN was located ~4 mm lateral to the CFN and ~2 mm more ventral. It too was identifiable by the saccade-related bursts of its neurons. I made small electrolytic lesions at the sites of some eye-movement-related neurons in the VPIN by passing of 30 µA for 30 s (electrode positive) through the recording electrode.

**Injecting muscimol**

I mapped the position of saccade-related neurons in the VPIN with several electrode penetrations and injected muscimol into the center of this region. I recorded single-unit activity with epoxy-coated tungsten electrodes and standard amplification and filtering. Once single-unit activity confirmed the presence of saccade-related activity at the intended injection site, I withdrew the electrode and replaced it with an injection pipette. The pipette consisted of a length of 32-gauge hypodermic tubing with a pulled-glass micropipette tip (ID = 25 µm) glued over one end. Several feet of polyethylene tubing connected a solenoid valve to the other end of the hypodermic tubing. The pipette and several centimeters of the connected tube were filled with a solution consisting of 1 mg/ml (8.75 mM) muscimol in normal saline. The pipette was inserted in the same guide tube that was used for the recording, and its tip was advanced to the dorsal-ventral center of the region from which saccade-related activity had just been recorded. The muscimol solution was injected with the use of a solenoid valve system (WPI PV830), which delivered a number of brief (~15 ms) air pressure pulses to move the meniscus a calibrated distance down the tube. With the aid of a ×50 microscope to view the meniscus, injected volumes could be resolved to within ~10 nl. The injections took 5–20 min. The pipette was left in place for 5 min after each injection and then withdrawn.

*Monkey 1* received a 1-µl injection into its left VPIN. *Monkey 2* received a 1-µl injection into its right VPIN and then, ~30 min later, after I recorded a variety of saccades, I made a second 1-µl injection into its left VPIN, and then recorded more saccades. This procedure allowed me to evaluate the effects of both unilateral and bilateral VPIN inactivation. *Monkey 3* also received two injections but in reverse order, i.e., first into the left VPIN and then into the right.

**Data collection and analysis**

Before each injection in each monkey I recorded normal horizontal and vertical saccades while it tracked the target spot jumping from one position to another. In *monkey 1*, I recorded horizontal and vertical saccades to targets 10 and 20° from the center of gaze (centrifugal saccades) and back to the center of gaze (centripetal saccades). In *monkeys 2* and *3*, I recorded these saccades as well as horizontal and vertical saccades tracking target steps of other sizes ranging from 2 to 30°.

Within ~10 min of the end of an injection, its oculomotor effects were evident, most noticeably as an increase in the number and size of corrective saccades after vertical saccades. Starting then, I recorded saccades to the same type of preinjection target steps presented before the injection. The effects of the muscimol injection were still clear, with no apparent changes, when recording was stopped 1.5–2 h after the injection. There were no abnormalities in the monkeys’ eye movements during recording on the day after the injection. Analog voltages corresponding to the monkeys’ horizontal and vertical eye positions and horizontal and vertical target positions were recorded on videotape with a PCM recording adapter (Vetter 4000A). Eye and target records were digitized from the videotape at 1 kHz. A custom saccade analysis program measured saccade gain, velocities, latencies, and durations and displayed the trajectories of selected saccades. The program smoothed eye velocity with a moving 3-point average thus introducing a maximum delay in the constructed velocity record of 3 ms. For analysis, saccades began when eye velocity exceeded 20°/s and ended when it fell <20°/s. Eye acceleration was the average change in eye velocity between the saccade start and the point of peak velocity; deceleration was the average change in eye velocity between peak velocity and saccade end. Acceleration duration was the interval between saccade start and the point of peak velocity; deceleration duration was the interval between peak velocity and saccade end. Saccade latency was the difference between the time the target moved to a new location and saccade start.
I used a simple ANOVA with the Bonferroni correction for repeated tests to compare averages of measurements before and after injections. I used a t-test for the difference in slopes to compare data fit with lines. For both comparisons, I considered $P < 0.05$ to be significant.

RESULTS

Neurons with saccade-related bursts were located in a region extending ~1 mm medial-lateral, ~1 mm anterior posterior, and centered ~4 mm lateral to the eye-movement-related part of the CFN. Marking lesions confirmed that this small eye-movement-related region was in the VPIN (Fig. 1).

Saccade size and direction

In each monkey, VPIN inactivation caused vertical saccades to end above their targets. Upward saccades became too large and downward saccades became too small. In addition, in monkeys 1 and 2, leftward and rightward saccades angled upward from horizontal to end above their targets. About 200 ms after each saccade that ended above its target, the monkey made downward corrective saccades to foveate the target. Often several corrective saccades were necessary because the hypometria of downward saccades made the first, and sometimes the second, corrective saccade fall short.

Figure 2 shows the effect of VPIN inactivation in monkey 2 on the trajectories of saccades to 10° target displacements. Bilateral inactivation made saccades in all four directions end above their targets by changing the size of vertical saccades and the direction of horizontal saccades (Fig. 2C). Inactivating only the right VPIN caused smaller changes in the size of vertical saccades and the direction of horizontal saccades (Fig. 2B). I measured the changes caused in saccade size and saccade direction in all three monkeys.

SACCADe SIZE. I measured the size of a saccade as gain, i.e., the size of a saccade divided by the distance to the target. VPIN inactivation caused no consistent effect on the gain of horizontal saccades to 10° target displacements (Fig. 3, A and B). For example, inactivating the left VPIN slightly decreased the gain of right centrifugal saccades in monkey 1 but slightly increased the gain of these same saccades in monkey 3. All three monkeys exhibited a significant increase in the gain of upward saccades and a significant decrease in the gain of downward saccades after VPIN inactivation (Fig. 3, C and D), although the pattern of gain changes was slightly different in each monkey.

Inactivation of the left VPIN in monkey 1 caused a significant increase in upward saccade gain and a significant decrease in downward saccade gain. The initial unilateral inactivation of the right VPIN in monkey 2 caused a significant increase in the gain of upward saccades but did not change downward saccade gain. The subsequent inactivation of the left VPIN in this monkey caused a further significant increase in the gain of upward saccades and a significant decrease in the gain of downward saccades. The initial unilateral inactivation of the left VPIN in monkey 3 caused no significant change in the gain of either upward or downward saccades. Subsequent inactivation of the other VPIN made upward saccades significantly larger than normal and downward saccades significantly smaller than normal.

I examined centrifugal and centripetal saccades separately because previous results (e.g., Ritchie 1976) suggested that the cerebellum may be involved in compensating for the starting position of a saccade. If the VPIN had a role in compensating for the initial eye position, one might expect to see differences in the effect of VPIN inactivation on the gains of centrifugal and centripetal saccades. As Fig. 3 shows, VPIN inactivation had nearly identical effects on the gain of centrifugal and centripetal saccades. Therefore these data provide no support for the idea that VPIN activity compensates for initial eye position.

GAIN OR OFFSET? In the preceding text, I describe the overshoot in upward saccades and the undershoot of downward saccades after VPIN inactivation as a gain change. However, it is also possible that the dysmetria of vertical saccades reflects a constant upward offset added to the end position of each vertical saccade. This is plausible because data from cat gaze movements (Goffart and Pelisson 1994) and preliminary results from monkey saccades (Goffart and Sparks 1996) indicate that changes in the offset of saccade end position, not changes in saccade gain, account for the overshoot of ipsilateral saccades after unilateral inactivation of the CFN.

I measured the relative contributions of gain and offset by graphing the distance to targets against the size of the saccades elicited by those targets (Fig. 4). In these graphs, the slope of a line fit to the data represents the gain of the saccades and the intercept represents the offset. The numerical descriptions of these line fits are in Table 1. With one exception VPIN inactivation caused very little change in gain or offset of horizontal saccades (each slope comparison $P > 0.05$, offsets not tested statistically; Fig. 4, left; Table 1, left). The one exception was a significant reduction in the gain of leftward saccades in monkey 2 ($P < 0.001$). VPIN inactivation significantly in-
creased the gain of upward saccades and significantly decreased the gain of downward saccades in all three monkeys (each $P < 0.05$; Fig. 4, right; Table 1, right).

Saccade gains, measured as the slope of a line in Fig. 4, were slightly different from the gains illustrated in Fig. 3. For example, Fig. 4 and Table 1 show that VPIN inactivation caused no significant gain change rightward saccades in any monkey, but Fig. 3 shows significant changes in the some types of rightward saccades in monkeys 1 and 2. These differences occur because the two figures represent different data. Figure 3 shows separate centrifugal and centripetal saccades to only 10° target displacements and represents saccades after both unilateral and bilateral injections. Figure 4 combines centrifugal and centripetal saccades to a variety of target displacements and, for monkeys 2 and 3, shows only saccades after bilateral injection.

Inactivation changed the offset of the fit to vertical saccades <1° in monkeys 1 and 3. In monkey 2 bilateral VPIN inactivation shifted upward saccades 1.7° upward and downward saccades 2.6° downward. Therefore the overshoot of upward saccades in this monkey resulted in part from the addition of 1.7° to the end point of each upward saccade and in part from increasing the gain (slope) from 0.98 to 1.2. The offset of downward saccades by itself would make them overshoot their targets by making each downward saccade end 2.6° farther below its target than normal. Thus the undershoot of downward saccades to 10° target displacements (Fig. 3C, middle panels) resulted from the decrease in downward gain, not from the change in offset, which was in the wrong direction to contribute to the undershoot.

SACCADE DIRECTION. Figure 5 shows the average error in the direction of saccades to 10° horizontal and vertical target displacements before and after VPIN inactivation. Direction errors are expressed as the differences in degrees between saccade and target directions. For example, monkey 1’s centrifugal right-
ward saccades normally ended an average of \(\sim 1.4^\circ\) below the target but, after inactivation of the left VPIN, ended an average of \(\sim 4.7^\circ\) above the target (Fig. 5A, left). Unilateral VPIN inactivation in both monkeys 1 and 2 caused both leftward and rightward (i.e., both ipsiversive and contraversive) saccades to end significantly above their normal end positions. The subsequent bilateral VPIN inactivation in monkey 2 caused a further significant increase in the upward angle of its horizontal saccades (Fig. 5, A and B, middle). VPIN inactivation had no consistent effect on the direction error of monkey 3's horizontal saccades. Inactivation of monkey 3's left VPIN caused rightward (contraversive) saccades to end significantly lower than normal (Fig. 5, A and B, right). Subsequent inactivation of the other VPIN caused most leftward and rightward saccades to end near normal. An exception was leftward centrifugal saccades which ended significantly above their normal end position.

**FIG. 3.** Average gains of saccades to targets 10° from the fixation point before inactivation (NRM, ◆) and after injection into the left VPIN (LT, ○), right VPIN (RT, single-hatched bars), or both VPINs (BI, ●). Results obtained for each monkey are arranged by columns. Rows show gains for centrifugal saccades from the central position toward targets 10° eccentric or centripetal saccades from 10° eccentric toward the central position. Numbers at the bottom are the number of saccades contributing to the average. CONTRA and IPSI in the bars representing horizontal saccades after unilateral injections indicate, respectively, that the saccades were contraversive or ipsiversive to the side of the injection. Error bars are 1 SD. *, gains that are significantly different from normal (\(P < 0.05\)).
VPIN inactivation caused no consistent effect on the direction error of vertical saccades in any monkey. For example, unilateral VPIN inactivation caused centrifugal upward saccades to end significantly to the left of their normal direction in both monkey 1 and 2 (Fig. 5C, left 2 panels). However, because the left VPIN was inactivated in monkey 1 and the right VPIN in monkey 2, the effects in these monkeys were in opposite directions, i.e., toward the side of the inactivated VPIN in monkey 1 and away from it in monkey 2.

Saccade velocity

EYE VELOCITY PROFILES. Figure 6 shows average eye velocity profiles of saccades to 10° target displacements before and after VPIN inactivation. The numbers in Table 2 are the percent of normal values exhibited by saccades after VPIN inactivation, i.e., 100 represents a postinactivation value the same as normal, 200 is twice normal, and 50 is half normal.

VPIN inactivation had small variable effects on the eye velocity of horizontal saccades. When VPIN inactivation affected the velocity of horizontal saccades, it reduced peak velocity, reduced eye acceleration and/or deceleration, and prolonged eye acceleration and/or deceleration (Fig. 6, A and B). The largest changes occurred in monkey 3, in which bilateral VPIN inactivation significantly decreased the peak velocity of leftward saccades and prolonged them. Bilateral inactivation also caused these same changes in centripetal rightward saccades.

VPIN inactivation significantly changed the velocity profiles...
of vertical saccades. In all three monkeys, unilateral inactivation significantly decreased the peak eye velocity of downward saccades. Generally, deceleration duration was longer than normal for downward saccades after unilateral inactivation. (The exception was downward centrifugal saccades in monkey 3; Table 2.) Acceleration of downward saccades was lower than normal in monkeys 2 and 3 but normal in monkey 1. Acceleration duration was normal in all monkeys after unilateral inactivation.

Unilateral inactivation affected upward saccades inconsistently, significantly increasing peak velocity in monkey 1, decreasing it in monkey 3, and in monkey 2, increasing it for centrifugal but not centripetal saccades. Changes in acceleration and deceleration after unilateral inactivation were similarly mixed.

Bilateral VPIN inactivation caused abnormally low peak velocities for downward saccades in both monkeys tested (i.e., monkeys 2 and 3). In both monkeys, acceleration and deceleration were abnormally low for both upward and downward saccades (Fig. 6, C and D, right; Table 2). The effect of bilateral inactivation on the peak velocity of upward saccades was mixed: normal in monkey 2 but significantly lower in monkey 3. Acceleration duration was normal for both upward and downward saccades in both monkeys but deceleration duration was significantly prolonged (the exception was upward centrifugal saccades in monkey 3).

ARE SACCADES AFTER VPIN INACTIVATION ON THE MAIN SEQUENCE? All of the saccades in Fig. 6 and Table 2 were to 10° target displacements. As the data in Fig. 2 shows, vertical saccades to 10° target displacements were often larger or smaller than 10°. It is possible that the velocity profiles of saccades after VPIN inactivation are abnormal simply because the saccades were not their normal size. This seems unlikely from the information in Figs. 3 and 6. Upward saccades after VPIN inactivation were significantly larger than saccades to the same target before inactivation, increasing from ~10° to as large as ~17° (Fig. 3D, monkey 2, up). Normally 17° saccades exhibit a higher peak velocity than 10° saccades (Fuchs 1967). Yet after bilateral VPIN inactivation, hypermetric upward saccades reached peak velocities that were the same as or lower than those of normal saccades (Fig. 6). Thus it seems that saccades made after VPIN inactivation do not conform to the normal relation between saccade size and peak velocity, called the “main sequence” (Bahill et al. 1975).

Figure 7 illustrates how the peak velocity and the duration of vertical saccades varied with saccade amplitude before and after bilateral VPIN inactivation. In both monkeys after bilateral inactivation upward and downward saccades achieved abnormally low peak velocities and long durations. For example, in the right panel of Fig. 7A, normal saccades to 10° target displacements (C near 10° on the horizontal saccade amplitude scale) had an average peak velocity, ~500°/second. Post-inactivation saccades to the same target step were larger (~spread around 15° on the saccade amplitude scale) but exhibited peak velocities that were a bit lower than those for the normal saccades. This is consistent with the velocity profiles in Fig. 6, C and D, for monkey 2’s upward saccades. If VPIN inactivation did not change the main sequence relationship, then 15° saccades would have been faster than 10° saccades. Thus the data in Fig. 7 indicate that vertical saccades were abnormally slow for their size when both VPINs were inactivated.

Saccade latency

Neither uni- nor bilateral inactivation of the VPIN caused a consistent change in the latency of saccades to 10° target displacements. For example, unilateral VPIN inactivation increased the latency of most types of horizontal saccades in monkey 1 (not leftward centripetal) by 10–20 ms but either decreased or did not affect the latencies of horizontal saccades in monkeys 2 and 3. Unilateral inactivation decreased (monkey 1), increased (monkey 2), or did not affect (monkey 3) the latencies of upward centrifugal saccades and did not significantly change the latency of upward centripetal saccades in any monkey. Downward saccades showed similarly mixed effects after unilateral inactivation. Bilateral inactivation did not significantly change the latency of any type of saccade except for increasing the latency of downward saccades in monkey 2 by ~40 ms.

Postsaccadic drift

After bilateral VPIN inactivation in monkey 2, a slow upward drift often followed upward saccades. No drift followed downward saccades. In monkey 3, upward saccades before inactivation were often followed by a downward drift. After bilateral VPIN inactivation this drift was rarely evident. Again, no drift followed downward saccades.

To characterize this drift, I measured eye velocity in the first 50 ms following 14–77 vertical saccades in both monkeys.
**FIG. 5.** Errors in the direction of saccades to targets 10° from the fixation point before inactivation (NRM, □) and after injection into the left VPIN (LT, □), right VPIN (RT, □), or both VPINS (BI, □). Errors in directions are expressed as degrees of difference from target direction. Numbers of saccades contributing to each average are the same as for the same type of saccade in Fig. 3. Error bars are 1 SD. *, direction errors that were significantly different from normal (P < 0.05).
Fig. 6. Average eye velocity records during saccades before inactivation (thin solid trace), after unilateral VPIN inactivation (dashed line), and after bilateral VPIN inactivation (thick solid line). Velocity traces for each monkey appear in a vertical column. Rows show velocities for centrifugal saccades from the central position toward targets 10° eccentric (A and C) or centripetal saccades from 10° eccentric toward the central position (B and D). Numbers of saccades contributing to each average trace are the same as in Fig. 4.
Figure 8 shows average eye position records and the average velocity of the drift following vertical saccades in each monkey. In *monkey 2* bilateral VPIN inactivation caused a significant increase in the average velocity of upward drift after upward saccades, from 1.87 to 5.42°/s. It also caused a significant, but very small, change in the average velocity of drift after downward saccades, i.e., from downward 0.4 to upward 0.79°/s. In *monkey 3*, which normally had a large downward drift of 10.52°/s after upward saccades, bilateral VPIN inactivation significantly reduced drift velocity to 2.75°/s and caused no significant change in the drift following downward saccades, i.e., from downward 1.25 to 0.04°/s. Thus in both monkeys, bilateral VPIN inactivation added a significant upward velocity to the drift following upward but not downward saccades.

### Table 2. Velocity measurements of saccades after inactivation of VPIN

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Numbers are percentage of values in normal saccades. Boldface numbers are significantly different from normal.

Nonoculomotor deficits

None of the monkeys showed severe postural instability on return to their home cages after inactivation of one or both VPINs. However, they all seemed to have difficulty moving their arms accurately to retrieve food offered by hand or from the hopper attached to their cages. A typical example occurred when *monkey 2*, with both VPINs inactivated, tried to reach into a circular hole (~50 mm diam) in the food hopper in the front of its cage. The first reach missed to the left of the hole. The monkey withdrew its arm and tried again, this time missing to the right. The next reach again missed to the left. After five misses to alternating sides of the hole the monkey changed strategy and pushed its hand gently against the front surface of the hopper to one side of the hole. It then moved its hand along the surface of the hopper toward the hole until its hand went
through the hole and retrieved a biscuit. It had no trouble grasping the biscuit. Ordinarily this monkey never missed while reaching through the hole nor did it use the alternate strategy at any other time.

The monkeys showed no evidence of dizziness, disorientation, or nausea after any of the injections. During testing they tracked the spot for the same amount of time that they did when their VPINs were not inactivated and were calm and eager eat. In their home cages after injections they were calm and ate food offered to them.
DISCUSSION

The major finding of this study is that inactivating the VPIN with muscimol made upward saccades too large and downward saccades too small. Generally these dysmetrias reflected changes in saccade gain rather than offset. In two of the three monkeys, VPIN inactivation also caused horizontal saccades to angle upward so that they ended above their targets.

Our muscimol injections almost certainly affected saccades by inactivating saccade-related neurons in the VPIN. I recorded saccade-related activity at each injection site immediately before each injection. Marking lesions confirm that the activity recorded was in the VPIN. The reaching deficit evident after the VPIN inactivation probably resulted from spread of muscimol to adjacent limb-related areas of the posterior interpositus nucleus. This deficit is similar to that of monkeys receiving muscimol injections into the limb-related part of the posterior interpositus nucleus. Such injections cause deficits in directing the ipsilateral arm accurately but not in using the hands to grasp (Mason et al. 1998).

Role of the VPIN in saccades

VPIN inactivation caused saccades in all directions to end above their targets (with the exception of horizontal saccades in monkey 3). A simple explanation for this effect is that VPIN activity drives the eyes downward. This, however, does not explain why bilateral inactivation made downward saccades decelerate slower than normal and sometimes made upward saccades accelerate slower than normal and reach slower than normal peak velocities. If this proposal is correct, the downward drive must outweigh the upward drive to account for postinactivation saccades ending above their targets.

If downward and upward drives were nearly equal, bilateral VPIN inactivation would cause only small changes in saccade gain and direction but would still reduce saccade acceleration, deceleration, and peak velocity. This is the pattern monkey 3 exhibited. Bilateral VPIN inactivation may have affected monkeys 2 and 3 differently because upward and downward drives from monkey 3’s VPINs were more nearly balanced.

How does the VPIN influence saccades?

The VPIN projects to two structures that could influence the vertical component of saccades, the superior colliculus and the INC. Axons from the VPIN and the adjacent dentate nucleus terminate throughout a large part of the intermediate layers of the contralateral superior colliculus (May et al. 1990), an area representing saccades of many sizes and directions, including, presumably, vertical saccades. There is currently no information about the VPIN influence on the superior colliculus.

The VPIN also sends a projection to the contralateral INC, though this projection is described is “sparse” (May et al. 1992). The description of this projection comes from a large stereotaxically placed injection of tracer into the posterior interpositus nucleus. There is no indication that this injection included many saccade-related VPIN neurons, and so it may not accurately show how large the projection is from the VPIN to the INC.

The VPIN projection to the INC could influence the vertical component of saccades. The INC contains many saccade-related burst and burst-tonic neurons with vertical on directions.

FIG. 8. Average eye position records for normal saccades (—) and saccades after bilateral VPIN inactivation (---) aligned on the end of saccades (i.e., when eye velocity falls <20°/s) for upward and downward saccades. Numbers near the right end of each trace are the average eye velocity for the 50 ms after the end of the saccade and the number of saccades contributing to each average trace. *, postsaccadic eye velocities that are significantly different from normal (P < 0.05).
(Dalezios et al. 1998; Helmchen et al. 1996), and INC axons terminate in the trochlear nucleus and in the parts of the oculomotor nucleus related to vertical movements (Horn and Büttner-Ennever 1998; Kokkoroyannis et al. 1996; Steiger and Büttner-Ennever 1979). As its efferent connection lead us to expect, lesions of the INC in cat (Fukushima and Fukushima 1992) and monkey (Helmchen et al. 1998) severely impair vertical saccades.

**Postsaccadic drift**

Why does bilateral VPIN inactivation add upward velocity to the eye immediately after upward but not downward saccades? Many VPIN neurons exhibit a burst for upward saccades that continues as much as 50 ms beyond saccade end. Bursts for downward saccades often end before or near saccade end (F. R. Robinson, A. F. Fuchs, and A. Straube, unpublished observations). If the activity of these neurons drives the eyes downward, the extended burst for upward saccades would apply a downward drive to the eyes for ∼50 ms after saccade end. Removal of VPIN activity with muscimol would remove this postsaccadic downward drive, effectively adding an upward component to eye movement after the saccade. This explanation is consistent with VPIN activity but does not explain why it is necessary for the VPIN to normally provide a downward drive to the oculomotor system after upward, but not downward, saccades.

**Differences between the VPIN and CNF**

Some VPIN neurons increase their firing rate with decreasing vergence angle and accommodation and thus are called “far response neurons” (Zhang and Gamlin 1998). These cells are in the same area as neurons with saccade-related responses, but no neuron exhibits sensitivity to both the vergence and saccades. In contrast, CNF neurons increase their firing rate during increases in vergence angle and accommodation, i.e., the near response (Zhang and Gamlin 1996). CNF inactivation with muscimol reduces vergence speed and size (Gamlin and Zhang 1996). Sixty-three percent of CNF neurons that respond to convergence also modulate during saccades (Zhang and Gamlin 1996).

A role of the CNF in convergence may be consistent with the proposal that CNF activity on one side drives the eyes toward the contralateral side. CNF activity could aid convergence by driving the ipsilateral eye nasally. This could happen only if the activity of some CNF neurons influenced movements of the ipsilateral eye more than movements of the contralateral eye. CNF neurons have not been tested for unequal influence on the movements of the two eyes, but it is possible that they have such influence because other neurons show it. Unequal influence on the two eyes has been described in preoculomotor neurons in the brain stem (Zhou and King 1998) and in unidentified neurons in the cerebellar nuclei (Zhou and King 1996). If, as VPIN inactivation indicates, VPIN activity influences the vertical component of saccades, this activity is unlikely to affect the relative angle of the eyes. There may be no VPIN neurons sensitive to both vergence and saccades because there would be no functional advantage to saccade-related VPIN activity during vergence.

Although CNF clearly influences the vertical component of saccades, its strongest influence is on the horizontal component (Robinson et al. 1993). VPIN seems concerned almost entirely with the vertical component. This is the best answer we currently have to why neurons in both the CNF and VPIN burst during nearly every saccade, i.e., each area contributes distinct components of every saccade.

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