Cerebellar-Dependent Adaptive Control of Primate Saccadic System

LANCE M. OPTICAN AND DAVID A. ROBINSON

Department of Biomedical Engineering and Department of Ophthalmology,
The Johns Hopkins University, Baltimore, Maryland 21205

SUMMARY AND CONCLUSIONS

1. The ability of the central nervous system to compensate for saccadic dysmetria was demonstrated in rhesus monkeys. The behavior of this adaptive mechanism after cerebellar ablations was examined.

2. Monkeys were trained to fixate small target lights. Eye movements were monitored while the animals were seated, with their heads fixed, in a rotating magnetic field. The horizontal recti muscles of one eye were weakened by tenectomy. Saccades made by this weakened eye were hypometric and followed by postsaccadic drift.

3. When the patch was switched so that the weak eye was viewing, the hypometric saccades made by the weak eye gradually became larger, until after 3 days they were essentially orthometric. This indicated that the central nervous system could compensate for a peripheral weakness.

4. The tenectomy operation reduced the strength of the muscles, creating hypometria, and upset the ratio of viscosity to elasticity in the orbit, creating postsaccadic drift in the weak eye. The innervation required to make a saccade has both phasic and tonic components, the so-called pulse and step. The saccadic repair mechanism increased both the pulse and the step to compensate for the hypometria and also adjusted the ratio of the pulse to the step to eliminate postsaccadic drift.

5. Total cerebellarctomies were performed on two monkeys, each of which had one tenectomized eye. These ablations created an enduring saccadic hypermetria and postsaccadic drift in the unoperated eye of both animals. The total cerebellarctomy abolished all adaptive repair of the saccadic system.

6. Partial cerebellarctomies were performed on two monkeys, each of which had one tenectomized eye. Lesions of the vermis and paravermis (lobes IV–IX) and the fastigial nuclei created an enduring saccadic hypermetria without postsaccadic drift in the unoperated eye of both animals. These lesions abolished adaptive control of the pulse of innervation. Adaptive changes in the step of innervation still occurred, so that postsaccadic drift was always eliminated in the experienced, viewing eye. Thus the midline cerebellum (vermis, paravermis, and fastigial nuclei) appears to be important for repair of saccadic dysmetria, but not for repair of postsaccadic drift. Additional evidence that postsaccadic retinal slip cannot be compensated for in flocculonodularis monkeys suggests that the adaptive control of the step may depend on the flocculus.

7. After cerebellar lesions the monkeys were able to make saccades of all amplitudes and directions. The principal deficit in these animals seemed to be that the pulse and step of innervation were no longer appropriate to the target displacement. We conclude that the cerebellum’s principal contribution to saccadic eye movements is the adjustment of the gains of the pulse- and step-generating mechanisms. Hence this study supports the hypothesis that repair of dysmetria is a general function of the cerebellum.

INTRODUCTION

These experiments were designed to examine the ability of the central nervous system to repair dysmetria of saccadic eye movements. Saccades are the rapid eye movements used to change visual fixation. The consistently high accuracy of saccades, despite cranial nerve growth, a mechanism that is acquired after birth a function through diseases/lesions.

An example of compensatory adaptation was reported when Kornmiller patients with a monocular deficiency, where the partially visual field was used. The partially visual field was used to the experienced, viewing eye. Thus the midline cerebellum (vermis, paravermis, and fastigial nuclei) appears to be important for repair of saccadic dysmetria, but not for repair of postsaccadic drift. Additional evidence that postsaccadic retinal slip cannot be compensated for in flocculonodularis monkeys suggests that the adaptive control of the step may depend on the flocculus.
CEREBELLAR-DEPENDENT SACCADIC ADAPTATION

Control of eye movements may be affected by cerebellar lesions because the cerebellum modulates the activity of the vestibulocerebellum, which is involved in the control of smooth pursuit eye movements. This modulation is thought to be necessary for the accurate and stable control of eye movements during visual search, reading, and other tasks requiring sustained visual attention.

Despite changes in the eye muscles and central nervous system brought about by growth, aging, and disease, requires a mechanism that calibrates the system shortly after birth and then maintains that calibration throughout life. Evidence for such a mechanism has been found in patients with diseases affecting the saccadic system.

An example of saccadic plasticity was reported when this study was just beginning. Kommerell et al. (22) studied the effects of monocular visual experience on three patients with a unilateral abducens nerve palsy who, by chance, had greater visual acuity in the partially paretic eye and so normally viewed the world with that eye. Saccades made by the paretic eye acquired the fixation targets as accurately and rapidly as possible, given the eye’s mechanical limitations, while saccades made by the normal, vision-suppressed eye were too large. Three days after the paretic eye had been occluded, saccades made by the normal eye acquired the targets, while saccades made by the paretic eye were too small. In addition to correcting the amplitude of the saccades in the experienced eye, these patients also minimized the slow monotonic drifts that followed the saccades when the eye was inexperienced. Kommerell et al. concluded that the saccadic system of these patients was adaptively changing the phasic and tonic levels of innervation sent to the extracocular muscles, and their ratio, to reduce foveation time in the experienced eye.

A role for the cerebellum in the repair of saccadic dysmetria is suggested by the observation that patients with certain types of cerebellar degeneration have an enduring saccadic dysmetria (7, 45). The cerebellum is also known to be involved in the adaptive plasticity of the vestibular system. The vestibuloocular reflex, which stabilizes retinal images during head rotation, has an adaptive gain control mechanism, which can compensate for the effects of reversing prisms or telescope lenses (13, 26). It is (16) proposed that this adaptation was controlled by the vestibulocerebellum, and it was shown that the adaptive gain control of the vestibuloocular reflex could be abolished by ablating the vestibulocerebellum in rabbits (17) and cats (36).

The present experiments were designed to demonstrate an adaptive plasticity of the saccadic system and to quantify its properties in the monkey. Once the adaptive mechanism was quantified in the monkey, cerebellar ablations were performed to determine whether the cerebellum was essential for the adaptation. Another description of the results presented here, along with a discussion of possible mathematical models of an adaptive mechanism for saccadic eye movements, is available elsewhere (28).

METHODS

Six young, 3-kg rhesus monkeys (Macaca mulatta) were used in this study. Each animal received three chronic implants under pentobarbital sodium anesthesia and aseptic surgery: 1) a metal device was affixed to the skull by stainless steel screws and dental cement so that the head could be held still during the experiments; 2) a plastic plate was attached to the skull platform, like the visor of a cap, to which rigid, plastic, black patches could be attached to occlude either eye; 3) each eye had a coil of fine wire wound around the globe, under the insertions of the four recti muscles. When the monkey was placed in two magnetic fields held in spatial and temporal quadrature, phase detection of the voltages induced in the eye coils produced signals proportional to horizontal and vertical eye position with a sensitivity of 15° of arc and a bandwidth of 0–1 KHz (10).

In the experimental sessions each monkey was seated in a primate chair in the center of a wooden frame, which held the magnetic-field coils. The monkeys had been trained prior to surgery to fixate a target light. By switching between lights placed at 0, ±10, and ±20° in the horizontal plane and at 20° up in the vertical plane, the eye movement monitor could be calibrated. During the experiments the horizontal position of both eyes, the vertical position of one eye, and the target position were recorded on analog magnetic tape. After the experiments the signals were played back (filtered with a bandwidth of 0–300 Hz to reduce tape noise) and recorded on photosensitive paper using a mirror galvanometer system (Honeywell Visicorder). Using paper speeds up to 500 mm/s allowed the saccades to be examined with a very high temporal resolution.

Three experimental paradigms were used in this study. In each the monkeys had a tenectomy performed on one eye while under anesthesia: the tendon and about 5 mm of muscle were cut from both the medial and lateral recti muscles of one eye. The rest of the muscle was allowed to retract into the rear of the orbit. The eye coil,
previously implanted, was by this time attached to the globe by scar tissue and was unaffected by this procedure. Immediately following this operation movement of the eye in the horizontal plane was severely restricted. Over a period of days the muscles reattached to the globe and became strong enough to move the eye approximately ±10° away from the midline. A measure of the effective muscle strength was obtained by comparing the movements of the operated and unoperated eyes (see below). The experiments began after this strength stabilized, usually after 3 days. The effects of a typical tenectomy can be seen in Fig. 1A. The two major effects were an effective weakening of the muscles in the horizontal field, resulting in hypometria, and the alteration of the ratio of the elasticity to the viscosity of the orbital tissues, resulting in post-saccadic drift.

The mechanical gain, Gm, of the weak eye was quantified by plotting the horizontal position of the weak eye (ordinate) against the horizontal position of the normal eye (abscissa). Although such a plot was usually nonlinear for large deviations, it was fairly linear over the range ±25° and the slope of the regression line for the data in this region was taken as the mechanical gain, Gm. In most monkeys the mechanical gain remained low over many months, while in some monkeys Gm rose gradually over several weeks. If Gm rose above 0.6, the tenectomy operation was repeated.

Immediately after the tenectomy the weak eye was covered with a rigid plastic patch, which prevented vision but did not touch the animal’s face. In three monkeys the patch was switched to cover the normal eye after the mechanical gain of the weak eye had stabilized, and the changes in the size and waveform of the saccades were observed over time. After about 1 wk the patch was switched to cover the weak eye once more, and the changes in the size and waveform of the saccades were observed again. Every effort was made to minimize the visual experience of the animal when data were collected from the inexperienced eye. Data were always collected from the experienced eye first. Immediately after the patch was switched, data were collected as fast as possible over a period of less than 15 min duration, after which the patch was switched back. There appeared to be no change in the adaptive state of the animal after such brief exposures to viewing with the inexperienced eye.

In the other two paradigms the tenectomy-patch procedure was combined with cerebellar ablations. The ablations were made under pentobarbital sodium anesthesia using aspectic techniques. The cerebellum was exposed through the posterior fossa. Two monkeys had their entire cerebellum removed by aspiration. Two monkeys (including one from the first paradigm) had their posterior vermis and paravermis removed by aspiration. Following surgery the monkeys were monitored 24 h/day for 10 days. Steroids, anti-pyretics, and antibiotics were administered according to a strict schedule.

One monkey was used in both the normal and the partially ablated cerebellum experiments. In the other monkeys, the eye coil implant and tenectomy operations followed recovery from the ablations. The animal was considered to be recovered when it could move freely in the cage and feed itself. This took only a few days in the partially cerebellarcomized animals and about 3 wk in the totally cerebellarcomized animals. While it would have been desirable, as a control, to establish the existence of adaptation using the tenectomy-patch paradigm for each monkey before cerebellar surgery, this was impractical. So much time was required first to establish adaptation, perform the cerebellar ablations, and then wait for recovery from cerebellar lesions, that there was a high risk of an infection loosening the skull implant. Also, the close proximity of the skull implant to the cerebellar trephine hole greatly increased the risk of intracranial infection and death when the skull implant was attached before the ablations were performed. The lack of a control test for adaptation in each monkey before the cerebellar ablations was not considered critical. Since each of the first three monkeys showed the same characteristics of adaptation, we felt safe in assuming that all monkeys shared them.

The cerebellar-lesioned animals all had saccadic hypermetria. This made it difficult to calibrate the eye monitor since the monkeys could not maintain fixation, but rather exhibited a pattern of saccadic (square wave) oscillations. Interspersed with this pattern of rapid oscillations there would be periods with larger intersaccadic intervals wherein a series of small saccades would often be made toward the target. On rare occasions the animal would actually acquire the target in this way, evidenced by an abrupt increase in the number of times the animal successfully completed the behavioral task. The eye monitor was calibrated so that the mean eye position during the successful completion of the behavioral task matched the target position for 0°, ±10°, and ±20° in the horizontal plane, and up to 20° in the vertical plane. The overall system gain remained remarkably constant for a given monkey from day to day, giving us confidence in this calibration technique. While a normal monkey can be calibrated with this paradigm in just a few minutes, it often took up to half an hour to calibrate a monkey with a lesioned cerebellum.

The optokinetic and smooth-pursuit response of the cerebellar-lesioned animals was also meas-
CEREBELLAR-DEPENDENT SACCADIC ADAPTATION

FIG. 1. Saccadic adaptation in the monkey GS. The effect of tenectomy is shown in A. The normal eye makes a 10° saccade to the target (dashed lines). The weak eye makes a hypometric saccade with post-saccadic drift. Immediately after the patch is switched to cover the normal eye in B, saccades in the weak eye are still hypometric with drift and the monkey must make a staircase of saccades to get on target. C: effects of 5 days of visual experience with the weak eye. The saccade in the weak eye now is essentially orthometric and without drift, hence the saccadic system has adapted to the peripheral weakness.

since it is important in what follows, one must understand its cause.

The extraocular muscles, eyeball, and orbital tissues constitute a viscoelastic system (33). A saccade is made by a brief pulse of innervation, which drives the eye rapidly against the viscous drag of the orbital tissues, and a step of innervation, which holds the eye in its new position against the elastic restoring forces in the orbit. This pulse-step of innervation can be observed when recording from muscles during electromyography (5) or when recording from motoneurons in the brain stem motor nuclei (37). The effect of a mismatch between the size of the pulse and the step is shown in Fig. 2. When the pulse is too small for the step, the eye is driven rapidly to a point short of the final position and then drifts onward to the position determined by the step (dotted curves). When the pulse is too large for the step, the eye is driven rapidly to a point beyond the final position and then drifts back to the position determined by the step (dashed curves). These post-saccadic drifts have an exponential time course.

To quantify the effects of the tenectomy and adaptation, three measures were obtained from each saccade: 1) The pulse gain (Gp) was defined as the ratio of the amplitude of the rapid part of the saccade to the initial retinal error that elicited that
saccade. 2) The step gain ( \( G_s \)) was defined as the ratio of the amplitude of the complete movement (after drift velocity had become negligible) to the initial retinal error. (If a corrective saccade occurred before the drift had become negligible, the final eye position that would have been reached was estimated by extrapolation.) 3) The pulse-step mismatch (psm) was defined as the amount by which the pulse gain exceeded the step gain, expressed as a percentage of the pulse gain

\[
\text{psm} = \frac{G_p - G_s}{G_p} \times 100\%
\]

The values of psm given below are averages of the psm of individual saccades and, therefore, differ slightly from the psm that would be calculated using averages of \( G_p \) and \( G_s \) over many saccades.

Using these definitions, we defined a saccade to be orthometric if the pulse gain was one, hypometric if the pulse gain was less than one, and hypermetric if the pulse gain was greater than one. Post-saccadic drift occurred whenever the pulse gain and the step gain were not equal. If the pulse gain was greater than the step gain, the pulse-step mismatch was positive and the eye drifted back to its final position. If the pulse gain was smaller than the step gain, the pulse-step mismatch was negative and the eye drifted onward to its final position.

Tenectomy was designed simply to weaken the force produced by any innervation and was not expected to cause post-saccadic drift. However, the operation evidently also changed the ratio between viscosity and elasticity, which does cause post-saccadic drift. In all six monkeys the tenectomy caused a drift back (positive psm). Our guess is that scar tissue may have increased the elastic stiffness relative to the viscosity so that a given step of innervation resulted in a smaller final displacement of the eye and, thus, a post-saccadic drift back. Such a mechanical mismatch in the orbit can only be compensated for by a change in the pulse-step ratio of innervation. It should be noted that since the psm is defined with respect to the eye movement, it describes mismatches whether they are of neural or mechanical origin. The time constant of the postsaccadic drift in all monkeys was about 40 ms in the normal eye and 30 ms in the weak eye.  

Adaptive plasticity

The initial response of the saccadic system just after the patch was switched to cover the normal eye is shown in Fig. 1B. The weak eye had to make a staircase of saccades to acquire the target. However, the amplitude of the initial saccade made by the weak eye gradually increased until, after a few days, it appeared normal (Fig. 1C) and hence no staircase of saccades was needed. Simultaneously, the postsaccadic drift back in the weak eye decreased and was completely suppressed within 5 days (Fig. 1C). This demonstrates the two components of the adaptive plasticity of the saccadic system: 1) the correction of dysmetria, and 2) the suppression of drift.

The saccades in the unoperated eye showed corresponding changes with time. In Fig. 1C, it can be seen that after adaptation this eye made saccades that were hypermetric with a drift forward. The gain changes in the normal eye were roughly proportional to those in the weak eye. The differences between the gain changes in the
greater than the step gain, the mismatch was positive and the eye 
threw to its final position. If the pulse is smaller than the step gain, the 
mismatch was negative and the eye drifted toward its final position.

The current was designed simply to 
produce an artificial torque on the eye and not to expect a cause post-
drift. However, the operation also changed the ratio between 
the nystagmus, which does cause drift. In all six monkeys the 
test caused a drift back (positive) and back (negative). 

This is an elastic stiffness relative 
so that a given step of 
resulted in a smaller final 
position of the eye and, thus, a post-
drift back. Such a mechanical 
constraint in the orbit can only be 
completely lost by a change in the pulse-step 
observation. It should be noted that 
the term is defined with respect to the 
measurement, it describes mismatches 
that are of neural or mechanical 
time constant of the post-saccadic 
in all monkeys was about 40 ms 
in the normal eye and 30 ms in the weak eye.

Elasticity

The initial response of the saccadic 
step after the patch was switched 
off the normal eye is shown in Fig. 
2. The weak eye had to make a staircase 
response to acquire the target. However, 
the response of the initial mode made by 
the weak eye gradually increased until, after 
about 4 days, it appeared normal (Fig. 1C). 
There was no staircase of saccades was 
seen and the post-saccadic 
the weak eye decreased and was 
completely suppressed within 5 days.

This demonstrates the two 
results of the adaptive plasticity of the system: 1) the correction of dys-
fusions and 2) the suppression of drift.

Saccades in the unoperated eye 
were often seen to show corresponding changes with time. 
This suggests that after adaptation 
the eye made saccades that were 
roughly normal to those in the weak eye. The 
differences between the gain changes in the 
two eyes may be due to the fact that the 
the normal eye makes saccades about twice as 
large as the weak eye and may be working over a different range of the nonlinear 
orbital stiffness. However, the similarity of the gain changes in eye suggests 
that adaptation seems to follow a rule 
similar to Hering's law: any change in the 
inervation to one eye is accompanied 
by a similar change in the innervation to 
the other. The pulse-step mismatch also 
roughly reflects such a rule. The step in 
both eyes increased relative to the pulse 
during adaptation, lowering the psm. For 
example, for a 10°, rightward, centripetal 
saccade by monkey GS, the psm (in the 
weak eye) was lowered from +18% to 
eto 18% essentially zero, while in the normal eye 
the psm changed from essentially zero to 
about -27%.

Theoretically, the changes in each eye 
should only be approximately equal. Again, 
discrepancies in this are probably due to 
orbits for nonlinearities (see below). Measurements 
of gains before and after adaptation 
of the weak eye, for all three monkeys, are 
given in Table 1. The increase in step gain, 
Gs, for either eye should, almost by definition, 
equal the reciprocal of the mechanical 
gain Gm for each monkey. Table 1 shows 
that this is approximately the case. The increase in pulse gain, Gp, in either eye should 
be a little less than the step gain, 
because tenectomy always attenuated Gp 
less than Gs. The calculated value of the 
change in Gp should be the change in Gs 
times (1 - (psm/100)), where the psm 
refers to the value in the weak eye before 
adaptation. This prediction is also well 
borne out in Table 1. The values of psm in 
the weak eye after adaptation (and the 
values in the normal eye before adaptation) 
are small. All but one are less than 2.7%, 
which is considered negligible for all 
practical purposes.

Figure 3 shows how the step gain, 
for 10° centrifugal saccades by monkey GS, 
changed with time. The graph also shows 
some slow recovery of the mechanical gain 
of the plant in this monkey (crosses in Fig. 3). 
Note that more than half of the gain 
change occurred within the first 6 h. The 
time courses of the change of the pulse 
and step gains were nearly identical in all three 
monkeys. The time constant of the increase 
gain during adaptation over three 
monkeys is less than 1 day, and the time constant of the decrease in gain during recovery is

<table>
<thead>
<tr>
<th>TABLE 1. Changes in saccade metrics for three monkeys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weak Eye</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td><strong>Before</strong></td>
</tr>
<tr>
<td><strong>GS</strong>: 1/Gm = 2.19; 10° rightward, centrifugal saccades; 5 days experience</td>
</tr>
<tr>
<td>Gp</td>
</tr>
<tr>
<td>Gm</td>
</tr>
<tr>
<td>psm</td>
</tr>
<tr>
<td>n</td>
</tr>
<tr>
<td><strong>BR</strong>: 1/Gm = 2.44; 10° leftward; centrifugal saccades; 7 days experience</td>
</tr>
<tr>
<td>Gp</td>
</tr>
<tr>
<td>Gm</td>
</tr>
<tr>
<td>psm</td>
</tr>
<tr>
<td>n</td>
</tr>
<tr>
<td><strong>LZ</strong>: 1/Gm = 1.88; 20° rightward, centrifugal saccades; 10 days experience</td>
</tr>
<tr>
<td>Gp</td>
</tr>
<tr>
<td>Gm</td>
</tr>
<tr>
<td>psm</td>
</tr>
<tr>
<td>n</td>
</tr>
</tbody>
</table>

Values are means ± SD. After each animal's identification there appears the reciprocal of the mechanical 
gain (1/Gm) of the weak eye on the day the after data was taken, the type of saccades selected for these data, 
and the period of time for which the weak eye was experienced. After (after adaptation) indicates that the weak eye was 
experienced. n, number of saccades analyzed. The changes in step gain (Gp) and pulse gain (Gm) refer to the 
ratios of the after and before values. The changes in psm are the differences between the after and before values.
The nature of the saccadic adaptation was consistent in all three monkeys, both qualitatively and quantitatively. Each monkey clearly showed that both the gains of the pulse and the step could be adjusted independently. The consistent effect of the adaptation in all three monkeys was to make the pulse and step gains of the viewing, experienced eye close to one, and its pulse-step mismatch close to zero. This made saccades in the experienced eye orthometric and free from postsaccadic drift.

The question arises whether only a single gain adjustment can be made (which must apply to all saccades) or whether gains may be adjusted differently, if required by non-linearities in the mechanics of the orbit, for saccades going in different directions or starting from different positions. Our experiments were not designed to answer this question directly because we deliberately tenectomized both horizontal recti to obtain a simple decrease in mechanical gain without causing any marked asymmetry. Nevertheless, the mechanical gain (elasticity) was not constant for all eye positions, so that the step gain required for accurate saccades did depend somewhat on position. For example, after the monkey BR had adapted his saccadic system for viewing with the weak eye, saccades in that eye were orthometric and without post-saccadic drift in all directions and for all initial positions (see Table 2). When the corresponding gains in the normal eye are compared, however, it can be seen that they are not always the same. For example, the pulse-step mismatch of the innervation sent to the normal eye was ~25% for 10° leftward, centrifugal saccades, while it was almost zero for 10°, rightward, centrifugal saccades, and it was ~16% for 10°, leftward, centripetal saccades. Thus the adaptive mechanism had to create different corrections for 10° saccades, depending on their direction and position.

The tenectomy created non-linearities that caused the amount of the dysmetria (of both the pulse and step gains) to depend on eye position and saccade direction. These data indicate that the adaptive mechanism corrected the dysmetria by different amounts depending on position and direction, so that the saccades made by the experienced eye were accurate everywhere in the available oculomotor range. Adaptation also occurred for saccades of all amplitudes. There was a slight tendency for centripetal saccades to be slightly hypermetric, while centrifugal saccades were hypometric.

FIG. 3. Time course of saccadic adaptation in the monkey G5. The change of the step gain for a 10° centrifugal saccade is shown. The tenectomy (first arrow) lowers the mechanical gain of the weak eye to about 0.35. When the patch was switched to cover the normal eye (second arrow), the step gain increased with a time constant of about 1 day. When the patch was switched back after 5 days to cover the weak eye (third arrow), the step gain returned to its normal value with a time constant of about 0.5 day. (Circles are mean gains of normal eye. Squares are mean gains of weak eye. Crosses are mean mechanical gains. The number of points for the average normal gain was 6. Averages for the other points were computed with at least 33 points. Vertical bars are ±1 SD.)

**TABLE 2.**

<table>
<thead>
<tr>
<th></th>
<th>Weak G, G</th>
<th>G, (psm)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal G, G</td>
<td>(psm)</td>
<td>n</td>
<td></td>
</tr>
</tbody>
</table>

Values at (psm) in both essentially of starting position asymmetry and different movements. A range from right 10°...
centrifugal saccades were either slightly hypometric or orthometric. This tendency was exaggerated when the weak eye was experienced.

Saccadic waveform

Saccadic waveforms are usually characterized by two curves: the relationship between amplitude and peak velocity and that between amplitude and duration (2, 8, 33). Since the peak velocity and duration are functions of the shape of the pulse of innervation, these relationships are important in determining the way the neural control signal changes during adaptation. In this study, amplitude and duration of a saccade were defined as the amplitude and duration of the pulse-driven part of the eye movement. This was best determined by visual examination of high temporal resolution records. The end of the pulse-driven part of the saccade was marked by a sudden change in velocity. This criterion sufficed for hypometric and hypermetric saccades as well as orthometric saccades. The amplitude-duration relationship was fitted by linear least-squares regression. The amplitude-peak velocity relationship was fitted by a nonlinear least-squares method with a single exponential curve

\[ V_p = V_m(1 - e^{-t/a}) \]

This equation relates the peak velocity \( V_p \) to the amplitude of the saccade \( A \) with three parameters: an asymptotic maximum velocity \( V_m \), an angle constant \( k \), and an offset \( A_o \).

When the normal eye of monkey GS was experienced, the amplitude-duration line for saccades made by the normal eye had a slope of 0.8 ms/deg and an intercept of 17.6 ms \((n = 72, r = 0.88)\). Saccades made by the weak eye took longer, as reflected by a slope of 1.6 ms/deg and an intercept of 15.2 ms \((n = 66, r = 0.84)\). The corresponding amplitude-peak velocity relationship for the normal eye had an asymptote of 1.210/s, an angle constant of 15.5°, and an offset of −0.4°, while that of the weak eye had an amplitude-peak velocity relationship of only 601/s, with an angle constant of 7° and an offset of 0. Hence the saccades made by the weak eye fell off the main sequence, being too slow. The difference in the regression curves for the normal and weak eye can be explained quantitatively by the assumption that both eyes receive the same innervation, but that the weak eye’s response is simply scaled down by the muscles’ weakness. The ratio of the asymptotes is 0.50 and that of the angle constants is 0.45, which compare favorably with the static mechanical gain for these data, which was 0.4.

After the weak eye had been experienced, the main sequence of the saccades made by the normal eye was essentially unchanged. The amplitude-duration line had a slope of

<table>
<thead>
<tr>
<th>TABLE 2. Data from monkey BR</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th></th>
<th>0 → +10°</th>
<th>0 → -10°</th>
<th>+10 → 0°</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weak eye</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( G_p )</td>
<td>0.89 ± 0.03</td>
<td>0.88 ± 0.03</td>
<td>0.96 ± 0.06</td>
</tr>
<tr>
<td>( G_s )</td>
<td>0.88 ± 0.05</td>
<td>0.87 ± 0.04</td>
<td>0.97 ± 0.06</td>
</tr>
<tr>
<td>( psm )</td>
<td>2.1% ± 4.3</td>
<td>0.6% ± 2.0</td>
<td>-1.0% ± 1.3</td>
</tr>
<tr>
<td>( n )</td>
<td>10</td>
<td>23</td>
<td>10</td>
</tr>
<tr>
<td><strong>Normal eye</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( G_p )</td>
<td>1.73 ± 0.05</td>
<td>1.85 ± 0.15</td>
<td>1.66 ± 0.12</td>
</tr>
<tr>
<td>( G_s )</td>
<td>1.73 ± 0.09</td>
<td>2.47 ± 0.12</td>
<td>1.98 ± 0.13</td>
</tr>
<tr>
<td>( psm )</td>
<td>-0.1% ± 3.0</td>
<td>-24.9% ± 4.7</td>
<td>-16.3% ± 3.9</td>
</tr>
<tr>
<td>( n )</td>
<td>10</td>
<td>23</td>
<td>10</td>
</tr>
</tbody>
</table>

Values are means ± SD. Data show the pulse gains \((G_p)\), step gains \((G_s)\), and the pulse-step mismatches \((psm)\) in both eyes after the weak eye had been experienced for 7 days. Saccades made by the weak eye are essentially orthometric and without postsaccadic drift for 10° saccades in both directions and with different starting positions. Corresponding saccades made by the normal eye are marked by different degrees of hypermetric and different amounts of postsaccadic drift, depending on the direction and starting position of the eye movements. The columns present averaged data for saccades from 0° to right 10°, from 0° to left 10°, and from right 10° to 0°. \( n \), number of points in the sample.
of 0.65 ms/deg and an intercept of 19.7 ms ($n = 67$, $r = 0.74$). The amplitude-peak velocity curve had an asymptote of 1,400°/s, an angle constant of 18.4°, and an offset of −0.6° ($n = 67$). The corresponding relationships for saccades made by the weak eye changed a little. The amplitude-duration line had slope 1.2 ms/deg and intercept 15.1 ms ($r = 0.77$). The amplitude-peak velocity curve had an asymptote of 1,080°/s, an angle constant of 13.6°, and an offset of −0.1°. This increase in the speed of the saccades made by the weak eye corresponds with an increase in the mechanical gain (to 0.5). The scatter in these data was quite large. Even smaller changes were seen between the normal and adapted states of the monkey LZ. Hence we must conclude that the waveform of the saccade (as indicated by saccades made by the unoperated eye) did not change significantly with adaptation.

**Total cerebellectomy**

Two monkeys (BE and CJ) were used in this phase of the experiment. Postmortem gross examination of their brains after the experiment revealed an almost complete loss of cerebellar tissue. In monkey BE, a small piece of the anterior vermis (lobes I, IIa,b, and IIIa) was spared, along with a small piece of the flocculus on the right side, probably part of folia 7 and 8. In monkey CJ, only a small piece of the flocculus on the left side, probably part of folia 7 and 8, remained. Neither the functional integrity of these remaining pieces of tissue nor what disruptive influences they might have had on the rest of the brain was known. Microscopic examination revealed no sign of any damage to the brain stem of either monkey. In addition to the usual gross disorders of bodily movements, these animals exhibited the classical oculomotor signs of cerebellar dysfunction (3, 6, 43, 45). They had gaze-paretic nystagmus directed toward a null point, loss of smooth-pursuit eye movements, loss of optokinetic nystagmus, and saccadic dysmetria. Binocular drifts to the right, in the dark and in the light, with velocities of about 10°/s (in the normal eye) were also observed shortly after the cerebellar ablation in both monkeys. These drifts gradually decreased in velocity over the next few weeks.

The optokinetic response was tested with a full-field drum rotating at 60°/s. The peak eye velocity was measured after a 1-min exposure to the rotation. Monkey BE (which had a spontaneous drift to the right of 30°) had a slow-phase eye velocity of +42°/s when the drum went to the right and +25°/s when the drum went to the left. In monkey CJ (which had a spontaneous drift to the left of 9°/s), the corresponding values were +4° and −24°/s. Therefore, the net modulation of slow-phase eye velocity for monkey BE was 17°/s and for CJ, 28°/s. Hence the gains (eye velocity divided by drum velocity) were 0.14 and 0.23, respectively.

The smooth-pursuit response was tested with target velocities of 10, 20, and 40°/s. Monkey BE showed essentially no modulation of his spontaneous nystagmus in this task (correlation coefficient, 0.14). Linear regression of eye velocity on target velocity revealed a high correlation for monkey CJ. The slope of the regression line (a measure of the gain, eye velocity divided by target velocity) was 0.3, with a correlation coefficient of 0.91.

The effect of a total cerebellectomy on the saccades of the unoperated eye, when it was experienced and viewing, was to make the saccades extremely hypermetric, with marked postsaccadic drift. The gains for the pulse and step of innervation were greater than one for saccades of all directions, amplitudes, and initial positions. Figure 4A shows the effects of the total cerebellectomy on a 10° centrifugal saccade made by monkey CJ when the unoperated eye was experienced. For this monkey, centripetal saccades from right 10° to 0° had a pulse gain of $2.39 \pm 0.58$ ($n = 17$; since the pulse and step gains and the psm are all computed from the same data set, the value of $n$ is the same for all three). The step gain was $2.72 \pm 0.59$ and the pulse-step mismatch was $-14.6\% \pm 5.2$. For centrifugal saccades from 0° to right 10°, the pulse gain was $2.12 \pm 0.68$ ($n = 15$). The step gain was $2.99 \pm 0.68$ and the pulse-step mismatch was $-46.8\% \pm 20.1$. After cerebellectomy, the normal eye of monkey BE, when it was experienced and viewing, had a similar hypermetria (see Table 3). Thus cerebellectomy in the monkey creates saccades that are hypermetric by a factor of 2 to 3. The gains of the totally cerebel-
The saccadic response was tested with a rotating at 60°/s. The peak was measured after a 1-min adaptation. Monkey BE (which initially drift to the right of 30°/s) lose eye velocity of +42°/s went to the right and +25°/s went to the left. In monkey, a spontaneous drift to the corresponding values were 0.5. Hence, the net modulations eye velocity for monkey were 10% for C1, 28°/s. Therefore, the eye velocity divided by drum velocity and 0.23, respectively.

Pursuit response was tested for velocities of 10, 20, and 40°/s. Monkeys essentially no modulation of nystagmus in this range (coefficient, 0.14). Linear regression analysis revealed a target velocity correlation for monkey C1. This regression line (a measure of velocity divided by target velocity) is shown in Figure 3, with a correlation coefficient of R^2 = 0.79.

A total cerebellarectomy on both sides of the unoperated eye, when the patch was removed and viewing, was to induce extremely hypermetric, postaccadic drift. The gains in speed and step of innervation were the same for saccades of all directions, and initial positions, across the different conditions. The effects of the total cerebellarectomy on the unoperated eye were monitored. For this monkey, saccades from right 10° to 0° had a mean of 2.3 ± 0.58 (n = 17; since the gain and psm are all from the same data set, the value is the same for all three). The step gain was 3.5° and the pulse-step mismatch was 3.5% ± 5.2. For centrifugal 0° to right 10°, the pulse gain was 2.5° (n = 15). The step gain was 3.5° and the pulse-step mismatch was 3.5% ± 20.1. After cerebellar ablation of monkey BE, the eye velocity and viewing, had a hypermetric (see Table 3). Thus, the cerebellum in the monkey creates hypermetric by a factor of 2.5. Saccades of the totally cerebellar-
from 2.78 ± 0.41 to 2.72 ± 0.59, and the psm changed from −13.9% ± 4.8 to −14.6% ± 5.2. These changes are negligible compared to those seen in monkeys with an intact cerebellum. Nor were these small changes in the gains always in the direction appropriate for adaptation. In monkey BE, for example, centripetal saccades from right 20 to 0° had a pulse-step mismatch of 4.1% ± 6.4 (n = 14) in the normal eye after the weak eye had been experienced for 6 days, and a pulse-step mismatch of 8.7% ± 3.4 (n = 8) in the normal eye after the normal eye had been experienced for 7 days. This change was not adaptive because the post sacadic drift in the viewing eye increased with visual experience. Such small changes could have represented fluctuations in system parameters that had nothing to do with switching the patch. In summary, data from these monkeys imply that total cerebellar destruction destroys both pulse and step gain plasticity and the adaptive control of the saccadic system.

Partial cerebellectomy

Two monkeys (LZ and ML) were used to study the effects of a partial ablation of the cerebellar vermis on the adaptive control of saccadic eye movements. (Saccadic plasticity had already been established in monkey LZ in the first set of experiments with his brain intact.) The ablation in monkey ML included almost all of the cortex of the vermis and paravermis, extending as far anteriorly as Larsell’s lobe IV and as far posteriorly as lobe IX. The lesion was roughly symmetrical about the midline, extending as far laterally as crus Ia (Fig. 5A). The dentate and interposed nuclei appeared intact in the histological sections. The ablation was so deep in the midline, however, that the fastigial nuclei were completely removed bilaterally.

In monkey LZ, extensive portions of the posterior vermis and paravermis were also removed. The ablation extended anteriorly as far as lobe IV, posteriorly as far as lobe IXa, and laterally as far as crus Ia (Fig. 5B). The most posterior portions of the lesion were not symmetrical, with some of the uvula and nodulus being spared on the left side while there was almost nothing left of these lobes on the right side. Microscopic examination of the serial sections revealed that the dentate nuclei were spared bilaterally and the interposed nuclei suffered almost no damage. The fastigial nuclei, however, were almost completely ablated. The lesion was symmetric, sparing about 15 or 20% of the fastigial cells near the posterolateral pole of both fastigial nuclei.

These partially cerebellectomized monkeys had no gaze nystagmus, and their smooth-pursuit eye movements appeared normal. Their saccades, however, were extremely hypermetric. These findings are relevant to the clinical localization of cerebellar disease processes. While much clinical (3, 6, 45) and experimental (24, 32, 38) evidence has suggested that the region of the posterior vermis is involved in the control of saccadic eye movements, this is a clear experimental exhibition that gaze-holding and smooth pursuit are preserved after partial vermection, while saccades become abnormal.

Saccades made by the unoperated eye when that eye was viewing and experienced were hypermetric in both directions (leftward and rightward) and for all initial positions and all amplitudes of target displacement. Representative examples from monkeys LZ and ML show that the hypermetria was more pronounced for centripetal than for centrifugal saccades. In monkey LZ, the pulse gain of the centrifugal saccades made by the normal eye from 0 to 20° right was 1.06 ± 0.11, the step gain was 1.07 ± 0.11, and the pulse-step mismatch was −0.4% ± 1.2 (n = 41). For centripetal saccades from right 20 to 0°, the pulse gain was 1.59 ± 0.13, the step gain was also 1.59 ± 0.13, and the pulse-step mismatch was 0.0% ± 0.8 (n = 31). In monkey ML, the pulse gain of the centrifugal saccades made by the normal eye from 0° to 10° right was 1.57 ± 0.28, the step gain was 1.56 ± 0.27, and the pulse-step mismatch was 0.4% ± 0.4 (n = 14). For centripetal saccades from left 10 to 0°, the pulse gain of the normal eye was 2.05 ± 0.72, the step gain was 2.05 ± 0.72, and the pulse-step mismatch was −0.1% ± 0.8 (n = 17). The direct effect of the partial vermection on saccades was thus to make them hypermetric, but without introducing post sacadic drift.

To test the effect of the partial cerebellectomy on the adaptive control of the saccadic system, the monkeys were tested using the technique described in Fig. 6 shows that the eye movements of monkey LZ (dotted area) were hypermetric when the normal eye was driven for 13 days after the unoperated eye was driven for 19 days. The same adaptive effect was seen in monkey ML (dotted area) when the normal eye was driven for 19 days. The same adaptive effect was seen in monkey ML (dotted area) when the normal eye was driven for 19 days. The same adaptive effect was seen in monkey ML (dotted area) when the normal eye was driven for 19 days.
CEREBELLAR-DEPENDENT SACCADIC ADAPTATION

The fastigial nuclei were spared bilaterally and the interposed nuclei suffered damage. The fastigial nuclei were almost completely ablated. The lesion was symmetric, sparing about 20% of the fastigial cells near the ventral pole of both fastigial nuclei. In partially cerebellectomized monkeys, gaze nystagmus, and their associated eye movements appeared. Their saccades, however, were hypermetric. These findings are consistent with the clinical localization of disease processes. While much of the literature (3, 45) and experimental (24, 32, 33) research has suggested that the region of the inferior vermis is involved in the control of saccadic eye movements, this is a direct experimental indication that gaze-nystagmus and smooth pursuit are preserved after vermectomy, while saccades are hypermetric.

A: a dorsal view of the ablation in monkey ML (dotted area). Included were almost all of the vermis and paravernis cortex extending as far anteriorly as lobe IV and as far posteriorly as lobe IX. The lesion extended laterally to crus Ia. The fastigial nuclei were completely removed bilaterally, while the interposed and dentate nuclei were preserved. B: a dorsal view of the ablation in monkey LZ (dotted area). The lesion of the vermis and paravernis extended anteriorly as far as lobe IV and posteriorly as far as lobe Ixa. The lesion extended laterally to crus Ia. About 15 or 20% of the fastigial nuclei were spared bilaterally. The dentate and interpositus nuclei were also spared.

FIG. 5. Extent of cerebellar lesions in the monkeys LZ and ML. A: a dorsal view of the ablation in monkey ML (dotted area). Included were almost all of the vermis and paravernis cortex extending as far anteriorly as lobe IV and as far posteriorly as lobe IX. The lesion extended laterally to crus Ia. The fastigial nuclei were completely removed bilaterally, while the interposed and dentate nuclei were preserved. B: a dorsal view of the ablation in monkey LZ (dotted area). The lesion of the vermis and paravernis extended anteriorly as far as lobe IV and posteriorly as far as lobe Ixa. The lesion extended laterally to crus Ia. About 15 or 20% of the fastigial nuclei were spared bilaterally. The dentate and interpositus nuclei were also spared.

using the tenectomy-patch paradigm. Figure 6 shows the changes in the saccades made by monkey ML. Figure 6A shows the hypermetric without drift in the normal eye when the normal eye had been experienced for 13 days. Figure 6B shows the changes after the weak eye had been experienced for 19 days. Note that the rapid, pulse-driven, part of the saccade in either eye is the same amplitude both before and after adaptation, while the final, step-determined position is different. The pulse gain in monkey ML for centrifugal saccades from 0 to 10° right made by the normal eye when that eye had been experienced was 1.92 ± 0.27, the step gain was 1.92 ± 0.28, and the pulse-step mismatch was 0.0% ± 0.9 (n = 16). After the weak eye had been experienced for 19 days, the pulse gain in the normal eye for the same centrifugal movements was the same (2.03 ± 0.46), the step gain increased to 2.50 ± 0.58, and the pulse-step mismatch increased to -18.4% ± 5.4 (n = 16). The corresponding pulse-step mismatch in the weak eye decreased from 15.1% ± 8.4 (n = 16) to 6.0% ± 8.3 (n = 16) when the normal eye was viewing, and to 0.2% ± 2.6 (n = 16) when the weak eye was viewing.

The results with monkey LZ were similar.
causes a small mechanical time constant is not known. An explanation of these different time constants would require an understanding of the nonlinear properties of the orbital tissues.

Cerebellar lesions

The cerebellar lesions made in these studies created enduring saccadic dysmetrias and disrupted the adaptive compensation for peripheral weakness. That suggests that the adaptive mechanism depends on the cerebellum. An alternative hypothesis is that the adaptive mechanism depends entirely on the brain stem and that the cerebellectomy merely upset tonic levels of activity in the brain stem so that a saturation-like phenomenon blocked certain pathways mediating the adaptation. This must remain a possibility until the connections between the cerebellum and the saccadic system are better understood. However, we consider it unlikely, since cerebellectomies did not destroy the ability of the saccadic system to make saccades of any size in any direction. Furthermore, cerebellectomies created changes in pulse and step gains of about 2.5, and such changes (when created by tenectomy) were readily repaired by monkeys with an intact cerebellum. We cannot state that this (so called) motor learning takes place in the cerebellum itself, since these experiments did not address that issue directly. A similar uncertainty about the site of learning still exists concerning adaptive plasticity in the vestibuloocular reflex (14, 23, 36).

These conclusions relate previous clinical and experimental studies to each other. It is only recently that there has been general agreement that saccadic dysmetrias is a clinical sign of cerebellar disease (6, 7, 45). Cogan (3) pointed out that this dysmetria is usually a hypermetria. It can also be a hypometria, and may even be directionally dependent. The results of our experiments and those of Ritchie (32) imply strongly that this dysmetria is due to the degeneration in the posterior vermis, paravermis, and the fastigial nuclei, and not in other parts of the cerebellum. A relationship between lobes V through VIII of the vermis and paravermis and the saccadic system has also been shown in other experiments. Ron and Robinson (38) found that stimulation of the monkey posterior vermis elicited saccades with ipsilateral horizontal components at thresholds lower than in other parts of cerebellar cortex. Llinás and Wolfe (24) recorded single-unit activity that preceded saccadic eye movements from Purkinje cells in lobe VI and VII in the monkey. Kase and Noda (18) also found saccade-related single-unit activity in this region in the monkey, as did Waterhouse et al. (42) in cats. All these results imply that the region of the posterior vermis is that area of the cerebellum most concerned with saccadic eye movements. The only negative report is by Westheimer and Blair (43), who reported that saccades appeared normal in the cerebellomotorized monkey. However, their animals were not trained and hypermetria and oscillations could have been mistaken for saccadic hyperactivity. We conclude that our results are consistent with previous studies and support the hypothesis that the region of the posterior vermis is involved in control of the saccadic pulse gain.

Ritchie (32) studied the effects on saccades of ablating the posterior cerebellar vermis and paravermis in three trained rhesus monkeys. Our results are in basic agreement. He found that centripetal saccades were hypermetric, while centrifugal saccades were slightly hypometric. Our monkeys made hypermetric centripetal and centrifugal saccades, although the latter were less so than the former. Thus, one could view the difference in the findings as more quantitative than qualitative. This discrepancy between our data and Ritchie's is probably due to the larger extent of our vermian ablations. Ritchie proposed that this difference in dysmetria between centripetal and centrifugal saccades was caused by the failure of the saccadic system to take into account the nonlinearity of the elastic restoring forces of the orbital tissues. Since the innervation and eye position are in 1:1 correspondence with each other, this argument is incorrect. No matter how nonlinear the elasticity, if a given increase in innervation moves the eye centrifugally to a given point, the same decrease in innervation will return the eye centripetally exactly to its starting point. Consequently, the
CEREBELLAR-DEPENDENT SACCADIC ADAPTATION

The same change in innervation cannot produce a saccade of one size in one direction and another size in the opposite direction. (This discussion assumes that the effects of hysteresis are negligible. While a large hysteresis has been found between position and innervation in the human oculomotor system (5), single-unit studies have failed to reveal a marked hysteresis between innervation and position in monkeys (21, 35).) This means that the centrifugal-disparity in dysmetria is of central origin. Different innervation changes for the same retinal target error are sent to the eye, depending on where it is in the orbit and which way it is going. Why this occurs is unknown. The fact that these position and direction errors in innervation are revealed after cerebellar lesions suggests that the cerebellum acts as some sort of interface between visual commands and motor performance, which normally makes saccades accurate regardless of position and direction. The absence of this interface creates the observed dysmetrias, which do depend on position and direction.

Drift suppression

The totally cerebellar-resected monkeys lost control of both pulse and step gains, while the partially verriectomized monkeys lost their pulse-gain control but could eliminate post-saccadic drift, implying retention of their step-gain control. Hence the step-gain control must depend on some part of the cerebellum outside of the region of the posterior vermis. Since post-saccadic drift is a type of failure to hold gaze position, it is possible that step-gain control depends on the same part of the cerebellum as other gaze-holding mechanisms. There is evidence that suggests that gaze is dependent on the flocculus (14, 40, 44). Since this study was completed, we have been able to show that optically induced post-saccadic retinal slip causes an adaptive post-saccadic ocular drift to develop in monkeys with normal oculomotor systems (29). Preliminary results in two monkeys with bilateral flocculocystosities indicate that their adaptive response to post-saccadic retinal slip is severely deficient (L. M. Optican, D. S. Zee, and F. A. Miles, unpublished observations). The best working hypothesis at the moment seems to be that the flocculus is involved in the control of the step gain. However, we infer that its mode of operation is not to match the step gain to the target displacement, but rather to the pulse gain (dysmetria notwithstanding) to eliminate post-saccadic slip. This would suggest that vision is better served by eliminating retinal image slip, whether or not the eye gets on target. It is interesting that the most representative psm in the two totally cerebellar-resected monkeys in this study, averaged over saccades in various positions and directions, was about –15%, which is comparable to the value (–10%) seen in flocculocystostomized monkeys (L. M. Optican and D. S. Zee, unpublished observations). It suggests that the brain stem circuits that generate the step are intrinsically slightly hypermetric, and in the normal situation the step is made correct by the presence of the flocculus. When the latter is removed by partial or total cerebellectomy, the step gain becomes abnormally large.

Cerebellar interaction with brain stem motor systems

A great deal of evidence has accumulated that implies that brain stem circuits are involved in generating the innervation needed to make a saccade (4, 12, 19, 25) and can do so without the cerebellum (this report). One simple interpretation of the data from the totally cerebellar-resected animals is that the brain stem saccadic system of the monkey has a gain of 2–3 and the overall gain of the saccadic system is adjusted down to the desired value, normally 1, by a variable gain path, which depends on an intact cerebellum. This modifiable path would then regulate the gain by subtracting an adjustable signal from the fixed-gain, brain stem pathway. How this modification might be carried out on a neuronal level is not known. This model of parallel paths through the cerebellum and brain stem would explain why cerebellar tumour or cerebellar disease results in enduring hypermetrias.

It is impossible to say anything about the neural mechanism behind these cerebellar-dependent, adaptive processes until a theory describing the cerebellar contribution to saccades is developed. Single-unit
studies of cerebellar cortex in the vermis have demonstrated Purkinje cell activity, which is modulated in relation to saccadic eye movements (18, 24, 42). However it is premature to attempt to make anatomical or signal flow diagrams from the data currently available. For example, one investigation (11) failed to find any saccade-related activity in the fastigial nucleus, leaving open the question of how saccadic signals get from the vermis to the pontine reticular formation.

Another major problem that remains unresolved concerns the nature of the error signal used by the adaptive mechanisms. In the case of the step-control mechanism, a measure of retinal slip following a saccade might suffice. Single-unit studies have revealed mossy fibers in the flocculus that are modulated by retinal slip (27), so this information is probably available to a cerebellar adaptive-control mechanism. In contrast to this simple measure, it would seem that the gain of the pulse should be regulated by the retinal error following the first saccade to the chosen target, but where such a complex, cognitive signal might come from is not yet known.

Adaptive control as a cerebellar function

Our experiments support the hypothesis that the cerebellum is involved in the adaptive control of motor systems (16). This theory has been supported by research on the cerebellar dependence of the gain of the vestibulocular reflex. It has been shown that the adaptive control of this reflex depends on the vestibulocerebellum (17, 36). Our data have shown a similar dependence of another motor system—the saccadic eye movement system—on another part of the cerebellum: the posterior vermis, paravermis, and fastigial nuclei. The present experiments do not address the issue of the location of the modifiable gain element, but merely state that this pathway depends on an intact cerebellum. Nevertheless, our results suggest that the cerebellum might have, as a general function, the elimination of dysmetria in many types of motor control systems.

Clinical implications

These experiments have shown that marked changes in the gain of the saccadic system occur in order to compensate for peripheral muscle weaknesses. In particular, patching a normal eye can cause the saccades made by the other eye, with weakened muscles, to become normal. This work has already stimulated interest amongst clinicians. Because of our report (30), one subject with a medial rectus paresis was studied by Abel et al. (1). When the normal eye was patched, the gains of the patient’s saccadic system changed in an adaptive way. The time constant of a single exponential fit to their patient’s gain change was 0.85 days. When the patch was switched to cover the paretic eye, the gain returned to normal with a time constant of about 1.54 days. The patient also suppressed post-saccadic drift in the paretic eye, with a time constant of 3.85 days. The adaptation in this patient occurred without a change in the amplitude-peak velocity relationship of the saccades. One minor difference between Abel’s results and ours is that it took longer to adapt the gains of the monkeys to visual experience with the weak eye than it did to return the gains to their normal values when the weak eye was patched.

A more significant difference concerns the fact that the time course of post-saccadic drift adaptation measured by Abel et al. (1) is more than 4 times that of the adaptation of saccadic size in their patient. The gain measured by Abel’s group was presumably the pulse gain. They measured suppression of post-saccadic drift by determining the decline over time of the initial drift velocity. In our study, the pulse and step gains were measured independently and used to calculate the psm as a measure of drift. Since the time course of changes in the pulse gain and the step gain were the same in our monkeys, the time course of the psm also had to be the same. Abel’s results indicate that, in their patient, either the gain of the step changed much more slowly than the gain of the pulse or the time constant of the plant also changed. Whether this difference reflects a difference between man and monkeys or is caused by differences in the experimental procedures is not known.

The patch-switching paradigm used by Kommerell et al. (22) and Abel et al. (1) is a useful technique for studying adaptive control in patients with various clinical disorders. A fertile ground for studying various choices control mechanisms found in the parietal paresis complex.

Acknowledgments

We are very grateful to Dr. H. L. Lasker for his advice and Dr. D. H. Lasker for his care for the patients. We gratefully acknowledge the provision of photographs by Dr. E. B. B. Smith.

REFERENCES

Various characteristics of the adaptive-control mechanism for saccades might be found in those patients with a monocular paresis coupled with cerebellar degeneration.

Acknowledgments

We are very grateful to Guenther Giger, M.D., Ph.D. for invaluable assistance with the cerebellar ablations. We also give special thanks to David S. Zee, M.D. for his many contributions. Dr. R. J. Adams and Dr. D. H. Hopp provided advice on and excellent care for the monkeys. A. R. Friedrich and A. G. Lasker provided technical assistance, and C. Bridges provided surgical assistance.

This work was supported by National Eye Institute Research Grant EY-00598. Computer facilities were made available through National Eye Institute Grant EY-01765.

L. M. Optican was supported in part by National Institutes of Health Grants GM-00576, GM-07057, and EY-07047, and by grants from the Foundation for Research to Prevent Blindness, Inc.

Present address of L. M. Optican: Bldg. 36, Room 1D-18, Laboratory of Sensorimotor Research, National Eye Institute, National Institute of Health, Bethesda, MD 20205.

Received 20 November 1979; accepted in final form 10 June 1980.

References


26. Miles, F. A. and Fuller, J. H. Adaptive


