

You might find this additional information useful...

This article cites 15 articles, 7 of which you can access free at:

<http://jn.physiology.org/cgi/content/full/81/4/1960#BIBL>

This article has been cited by 25 other HighWire hosted articles, the first 5 are:

Cerebellar Inputs to Intraparietal Cortex Areas LIP and MIP: Functional Frameworks for Adaptive Control of Eye Movements, Reaching, and Arm/Eye/Head Movement Coordination

V. Prevosto, W. Graf and G. Ugolini

Cereb Cortex, May 22, 2009; 0 (2009): bhp091v1-bhp091.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

Adaptation to Visuomotor Rotation and Force Field Perturbation Is Correlated to Different Brain Areas in Patients With Cerebellar Degeneration

K. Rabe, O. Livne, E. R. Gizewski, V. Aurich, A. Beck, D. Timmann and O. Donchin

J Neurophysiol, April 1, 2009; 101 (4): 1961-1971.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

Dynamic Changes in Brain Activity during Prism Adaptation

J. Luaute, S. Schwartz, Y. Rossetti, M. Spiridon, G. Rode, D. Boisson and P. Vuilleumier

J. Neurosci., January 7, 2009; 29 (1): 169-178.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

Acquisition of internal models of motor tasks in children with autism

J. C. Gidley Larson, A. J. Bastian, O. Donchin, R. Shadmehr and S. H. Mostofsky

Brain, November 1, 2008; 131 (11): 2894-2903.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

Effect of Simvastatin on Cognitive Functioning in Children With Neurofibromatosis Type 1: A Randomized Controlled Trial

L. C. Krab, A. de Goede-Bolder, F. K. Aarsen, S. M. F. Pluijm, M. J. Bouman, J. N. van der Geest, M. Lequin, C. E. Catsman, W. F. M. Arts, S. A. Kushner, A. J. Silva, C. I. de Zeeuw, H. A. Moll and Y. Elgersma

JAMA, July 16, 2008; 300 (3): 287-294.

[\[Abstract\]](#) [\[Full Text\]](#) [\[PDF\]](#)

Medline items on this article's topics can be found at <http://highwire.stanford.edu/lists/artbytopic.dtl> on the following topics:

Veterinary Science .. Cerebellum
Veterinary Science .. Cerebral Cortex
Medicine .. Uvula
Medicine .. Ataxia
Physiology .. Humans
Physiology .. Monkeys

Updated information and services including high-resolution figures, can be found at:

<http://jn.physiology.org/cgi/content/full/81/4/1960>

Additional material and information about *Journal of Neurophysiology* can be found at:

<http://www.the-aps.org/publications/jn>

This information is current as of November 11, 2009 .

Cerebellar Lesions and Prism Adaptation in Macaque Monkeys

JOAN S. BAIZER,¹ INES KRALJ-HANS,² AND MITCHELL GLICKSTEIN²

¹ *Department of Physiology, SUNY, Buffalo, New York 14214; and* ² *Department of Anatomy, University College London, London WC1E 6BT, United Kingdom*

Baizer, Joan S., Ines Kralj-Hans, and Mitchell Glickstein. Cerebellar lesions and prism adaptation in Macaque monkeys. *J. Neurophysiol.* 81: 1960–1965, 1999. If a laterally displacing prism is placed in front of one eye of a person or monkey with the other eye occluded, they initially will point to one side of a target that is located directly in front of them. Normally, people and monkeys adapt easily to the displaced vision and correct their aim after a few trials. If the prism then is removed, there is a postadaptation shift in which the subject misses the target and points in the opposite direction for a few trials. We tested five Macaque monkeys for their ability to adapt to a laterally displacing prism and to show the expected postadaptation shift. When tested as normals, all five animals showed the typical pattern of adaptation and postadaptation shift. Like human subjects, the monkeys also showed complete interocular transfer of the adaptation but no transfer of the adaptation between the two arms. When preoperative training and testing was complete, we made lesions of various target areas on the cerebellar cortex. A cerebellar lesion that included the dorsal paraflocculus and uvula abolished completely the normal prism adaptation for the arm ipsilateral to the lesion in one of the five monkeys. The other four animals retained the ability to prism-adapt normally and showed the expected postadaptation shift. In the one case in which the lesion abolished prism adaptation, the damage included Crus I and II, paramedian lobule and the dorsal paraflocculus of the cerebellar hemispheres as well as lobule IX, of the vermis. Thus in this case, the lesion included virtually all the cerebellar cortex that receives mossy-fiber visual information relayed via the pontine nuclei from the cerebral cortex. The other four animals had damage to lobule V, the classical anterior lobe arm area and/or vermian lobules VI/VII, the oculomotor region. When tested postoperatively, some of these animals showed a degree of ataxia equivalent to that of the case in which prism adaptation was affected, but prism adaptation and the postadaptation shift remained normal. We conclude that in addition to its role in long-term motor learning and reflex adaptation, the region of the cerebellum that was ablated also may be a critical site for a short-term motor memory. Prism adaptation seems to involve a region of the cerebellum that receives a mossy-fiber visual error signal and probably a corollary discharge of the movement.

INTRODUCTION

If a laterally displacing prism is placed in front of their eyes, people and monkeys misreach in a direction opposite to the base of the prism. After a few tries, the reach becomes accurate. When the prism is removed, subjects misreach to the other side of the target. Helmholtz (1962) interpreted the misreaching as caused by an error in the judgement of the direction of gaze. However, if this was the sole cause, the adaptation should transfer between the two arms. Under controlled conditions in

which movement of other muscles is restricted, there is no such transfer.

In addition, Bossom and Hamilton (1963) showed that monkeys in which the optic chiasm and corpus callosum had been sectioned in the midline still showed interocular transfer of prism adaptation when tested with the adapted arm. For these and other reasons, Harris (1965) suggested that the effect of the prism was to cause recalibration of the felt position of the limb.

Anatomic and physiological evidence suggests that the cerebellar cortex may be a critical site for prism adaptation (Stein and Glickstein 1992). The cerebellum receives proprioceptive and corollary discharge information from the limbs and a powerful visual input that could serve as an error signal. Some years ago we presented evidence (Baizer and Glickstein 1973) that cerebellar lesions abolished the capacity for prism adaptation on the side of the lesion in one case, whereas four other monkeys with moderate-to-large cerebellar lesions still could adapt to the prism. At the time that the experiments were done, these findings seemed hard to interpret because lesion of vermian lobules VI and VII, areas that then were known to receive a visual input, did not affect prism adaptation. Recent anatomic studies now can help to interpret these results. We now know that the major target of visual information from cerebral cortex is to more caudal areas of the cerebellum. Cerebral cortical visual areas project to the dorsolateral region of the pontine nuclei (Glickstein et al. 1980, 1985). Cells in the dorsolateral pontine nuclei in turn project heavily to the caudal posterior lobe, especially the dorsal paraflocculus, paramedian lobule, rostral uvula, and Crus II (Glickstein et al. 1994). Here we present evidence that in the monkey in which prism adaptation was abolished, the lesion included nearly all of the regions that receive cortical visual input via the pontine nuclei. Lesions elsewhere in the cerebellum produced an equivalent degree of ataxia, but they had little or no effect on prism adaptation. The results suggest that visual input to the cerebellum may be involved in rapid and flexible short-term adaptation of the limbs to altered sensory input.

METHODS

Five adolescent rhesus monkeys (*Macaca mulatta*) were housed in individual cages and maintained on a combination of standard primate laboratory chow and fruit-flavored reward pellets. Animals were kept at the highest weight at which they would run readily in the behavioral situation. For the daily experimental session, they were restrained in a Plexiglas primate chair. Head movement was restricted by a sliding neckpiece, which held the head up, and by panels that were adjusted to press lightly against the sides and back of the head. The monkeys viewed the chamber through two eyeholes in front of which could be placed an occluder or a wedge prism that produced a lateral deflection of $\sim 12^\circ$. Two arm holes in the front of the chair, which could be

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

covered by sliding panels, permitted selection of the arm that the animal was to use.

The chair faced a metal arc with the monkey's eyes at its center. A series of 11 radially arranged microswitches separated from one another by $\sim 6^\circ$ visual angle were placed at successive angular distances from the center. One switch was directly in front of the monkey. The switches were mounted so that an upward movement of the lever was required to close the switch. Three small white indicator lights were mounted in front of the chair, one central, the other two $\sim 18^\circ$ to the right or left of the central light and directly above one of the microswitches. Below the level of the lights and switches there was a wooden box that enclosed another microswitch. Pressing down on the top of the box closed this switch and initiated a trial. An opaque occluder was used on occasional trials to allow the monkey to see the lights but blocked its view of the switches and of its own arm.

The animals were trained to press the starting key to initiate a trial. The starting key turned on one of the three lights, which remained on for a brief period of time. The time during which the light was on was variable, but always ≤ 500 ms; short enough so that the monkeys aimed their arm rapidly at the target without correcting the direction in midtrajectory. All monkeys learned to reach out rapidly upward to close the switch directly below the light that was on. If the animals hit an incorrect switch, the light went off and the trial was terminated. Hitting a switch when no light was on had no effect. A correct response activated the feeder on a continuous or variable basis (variable ratio 2), which delivered a fruit reward pellet to a small trough directly in front of the animal's mouth.

On each day an animal viewed the lights and switches through one eye and was run for a maximum of 750–1,000 trials. Data were recorded under three conditions with one-third of the number of trials in each condition: responses before insertion of a prism (preadaptation), responses after the prism was in place (adaptation), and responses when the adapting prism was removed (postadaptation). Preoperatively all monkeys learned to adapt to the placement of the prism. They reached rapidly in the appropriate direction on virtually all trials, although there was considerable variability in the number of trials that were required to adapt. In one animal, adaptation was complete after 10 trials. On average the monkeys required 70 trials

TABLE 1. Summary of lesions

Cerebellar Lobules	Left Side				Right Side
	MA	HU	ST	MR	RA
Hemispheres					
HIII	+	++	+++	-	-
HIV	+++	+++	+++	+	-
HV	+++	++	+	+	-
Simple Lobule	+++	+++	+++	+	-
Crus I	+++	+	+++	-	+
Crus II	+++	+++	+++	++	+
Paramedian Lobule	+++	+	+	++	+
Dorsal Paraflocculus	++	-	-	-	-
Ventral Paraflocculus	+	-	-	-	-
Flocculus	+	-	-	-	-
Vermis					
I	-	-	-	-	-
II	-	-	-	-	-
III	-	+++	-	-	-
IV	-	+++	-	-	-
V	-	+++	-	-	-
VI	-	+++	-	-	-
VII	+	+++	+	-	-
VIII	+	+++	+	+++	-
IX	+++	++	-	+++	-
X	-	-	-	-	-

+++ , complete lesion; ++ , 50% of the lobule removed; + , 25% of the lobule removed; - , lobule intact.

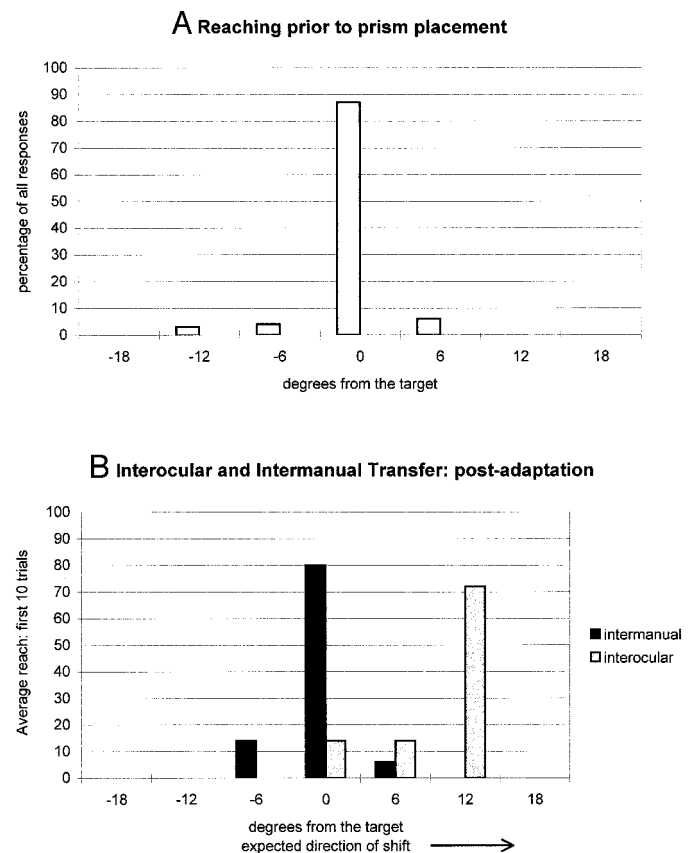


FIG. 1. Intermanual and interocular transfer of prism adaptation: average performance of all animals tested preoperatively. Animal's response on each trial was recorded. Numbers on the abscissa represent degrees to the left and to the right of the target light, placed at 0. Numbers on the ordinate reflect the percentage of the total responses (as in A) or percentage of the responses in the first 10 trials after the prism was removed (as in postadaptation, B). A: average performance of all trained animals at the beginning of the session, reaching without prism and using the preferred eye and preferred hand. Distribution of responses peaks at 0, indicating that nearly all of the animals' responses were directed accurately to the switch just below the illuminated light. B: average performance of all animals in the first 10 trials just after the prism was removed. Shift to the right reflects a postadaptation shift. When the majority of responses are at 0, there has been no effect of the prior experience with the prism. To test for the presence of intermanual transfer, the animals reached with the untrained arm after adaptation of the contralateral arm had been achieved. As the figure shows, prism adaptation did not transfer between the arms. For testing interocular transfer of adaptation, the animal viewed the panel with the eye that had been occluded during adaptation. Average performance in the first 10 trials after prism removal peaks at 12° to the right of the target, demonstrating the expected postadaptation shift.

when first tested. Adaptation typically took fewer trials with further training. When adaptation was complete, the animals then were run with the prism in place for ~ 300 trials before being tested for a postadaptation shift.

On most days only a single eye-hand pair was used. On successive days, the monkeys were tested for the presence of prism adaptation and postadaptation shift with all eye-hand pairs, both before and after cerebellar lesions were made. For testing intermanual transfer of adaptation, the same eye was used, with the arm switched half way through the session. For interocular transfer tests, the same arm was used throughout, but the eye that viewed the target light was switched.

Surgical procedures

All surgery was performed under aseptic conditions. The monkey was premedicated with phencyclidine (Sernylan), and anesthetized and

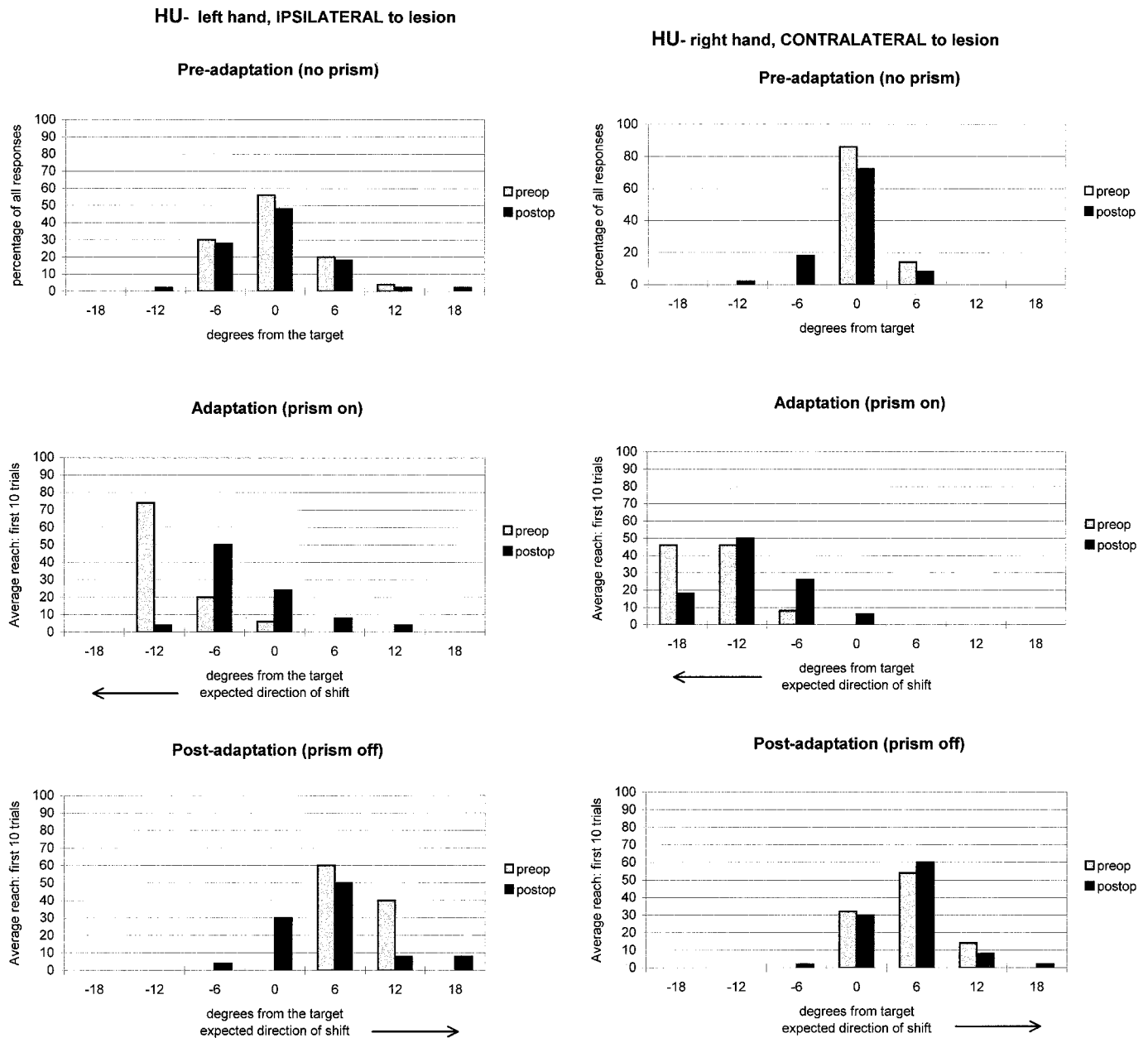


FIG. 3. *A*: pre- and postoperative performance in *monkey HU* with left hand. *B*: pre- and postoperative performance in *monkey HU* with right hand. This animal showed normal adaptation and postadaptation shifts despite a large unilateral cerebellar lesion, which included the arm area of lobule V (Adrian 1943) and the classical visual/oculomotor area of vermal lobules VI/VII (Noda and Fujikado 1987).

RESULTS

When initially tested as normals, all of the monkeys showed a similar pattern of adaptation to the prism. When the prism first was placed in front of its eye, the monkey misreached in the direction opposite to the base of the prism. Monkeys took a variable number of trials to correct the reach, but all of them soon adapted to the prism and now would reach accurately to the switch underneath the light that had been illuminated. When the prism was removed, they showed the typical post-adaptation shift. They now misreached in a direction opposite to that of the initial misreaching. Like the initial adaptation, the postadaptation shift was corrected in a few trials.

The pattern of interocular and intermanual transfer is similar to that described for human subjects (Harris 1965). Figure 1 shows the averaged data from all of the monkeys trained preoperatively.

If a monkey was trained to prism adapt using its right eye and right arm, there was complete interocular transfer of adaptation when viewing was shifted to the left eye. If the monkey was trained to prism adapt using the right eye and right arm, the adaptation failed to transfer to the left arm.

The fact that the pattern of intermanual and interocular transfer is similar to that reported for human subjects demonstrates that the monkey is a good model for human perfor-

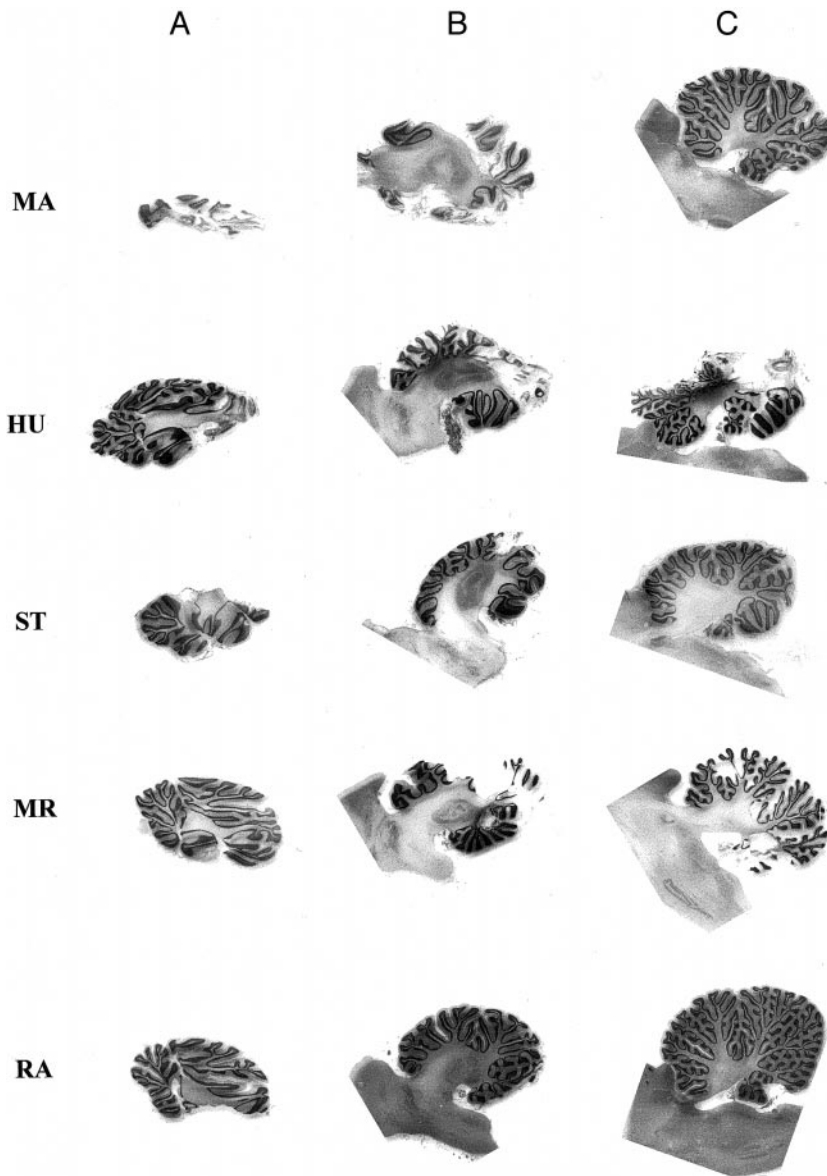


FIG. 4. Parasagittal sections through the cerebellum of all the cases. A–C: sections correspond to the plates numbered 35, 27, and 19 respectively, in the atlas of Madigan and Carpenter (1971).

mance. Postoperatively, all the animals showed some signs of unsteadiness in the limbs ipsilateral to the cerebellar lesion. Although they preferred to use the arm contralateral to the lesion site when retrieving pieces of food, all recovered use of the affected limbs. Testing resumed from 5 days to 4 wk after the surgery.

Prism adaptation and the postadaptation shift obviously were present both pre- and postoperatively in four of the five animals. Only one of the five animals, *monkey MA*, failed to adapt to the prism or show the typical postadaptation shift when using the limb ipsilateral to the lesion (Fig. 2A). Adaptation was unaffected on the side contralateral to the lesion (Fig. 2B).

Monkey MA at first was unwilling to use the arm ipsilateral to the cerebellar lesion. The coordination between her arm and hand was poor after the surgery, but her climbing was not affected. With training over several days, she started to reach with the affected arm but now failed to adapt to the prism or show the usual postadaptation shift. When the prism was put in

place the first time, she reached out directly in front of her. She was given a pellet from time to time to prevent extinction. The postadaptation trial showed clearly that there had been no effect of viewing the lights through the prism. Her responses were varied but remained centered on the central light. The lesion in *monkey MA* included the caudal regions of the posterior cerebellar hemispheres, including most of Crus II, paramedian lobule, and dorsal and ventral paraflocculus. Thus the lesion removed the great majority of the mossy fiber visual input to the cerebellar cortex (Glickstein et al. 1994) (see Table 1 and Fig. 4).

Animals with equally large cerebellar lesions that spared most or all of these regions of the cerebellum showed similar initial postoperative motor deficits, but when recovered, adapted normally to the prism and showed the expected postadaptation shift. Figure 3 shows the behavioral results for one such animal, *monkey HU*.

This animal was also initially reluctant to use the arm and

had a pronounced ataxia postoperatively. With training, he recovered the ability to reach accurately with the affected arm. Prism adaptation and postadaptation shift remained normal bilaterally. The cerebellar lesion in this case included most of the arm area of lobule V of the anterior lobe (Adrian 1943) as well as the visual/oculomotor area in vermal lobules VI and VII (Noda and Fujikado 1987).

Figure 4 shows photographs of the cerebellar sections, cut parasagittally, of all five monkeys. In all cases, only the cerebellar cortex was damaged, while the cerebellar nuclei were intact.

DISCUSSION

Prism adaptation was blocked in only one animal of the five that were studied. In this case, the lesion included those regions of the posterior lobe of the cerebellum that receive nearly all of the cortically originating visual mossy-fiber input.

Although this single case cannot firmly establish the role of these visual target regions in the posterior lobe of the cerebellum in adaptation, it was only in this one animal that the regions of the cerebellum that receive cortical visual input had been abolished almost completely. The failure of prism adaptation suggests that cortically originating visual input to this region may be necessary for normal adaptation to displaced vision. In all of the other four cases, all or most of these regions were spared, and prism adaptation remained unaffected.

A similar deficit in prism adaptation has been described in cerebellar patients. Weiner et al. (1983) described a failure of patients with lesions of the cerebellum to adapt normally to a laterally displacing prism. Although Weiner's seven cerebellar patients showed a clear deficit in prism adaptation, the locus of cerebellar lesions is not described. Five of the seven patients had a "degenerative process"; one had an infarct and the last one had "drug-induced cerebellar signs." Prism adaptation was independent of motor deficits because control subjects with Parkinson's disease or other neurological conditions showed essentially normal adaptation and postadaptation shift. Similarly, Martin et al. (1996) compared adaptation in normal human subjects and neurological patients throwing at a target that was viewed through a laterally displacing prism. Only those patients whose lesions involved the territory of the posterior inferior cerebellar artery showed impaired adaptation to the prism. The lateral branch of the posterior inferior cerebellar artery supplies the regions of the cerebellum in which the lesion produced a deficit in prism adaptation in the present study. It seems likely that the deficit in adaptation in our monkey and in these patients is caused by the absence of mossy-fiber visual input.

The cerebellum is necessary for other sorts of visuomotor modification. The vestibuloocular reflex (VOR) and saccadic eye movements for example can be modified by systematic alteration of the visual input (Optican and Robinson 1980; Robinson 1976). In the case of the VOR, the amount of training required is extensive, and the change in the gain or phase of the VOR persist during a long period of time. Miles and Eighmy (1980), for example, found that monkeys reach an asymptotic

level of increased VOR gain only after 4–5 days of continuously wearing magnifying spectacles. The present results suggest that in addition to such long-term modifications the cerebellum mediates rapid and transient visuomotor plasticity. Harris' (1965) interpretation of the mechanism of prism adaptation was that it involves a change in felt position of the limb but it seems likely that conscious awareness of limb position is not necessary. We propose that the cerebellum contains circuitry for very short term and highly labile "scratch pad" motor memories; the ability to recalibrate the position of a limb within a few trials and to quickly recalibrate the position again when a source of optical distortion is removed.

Present addresses: J. S. Baizer, Dept. of Physiology, SUNY, 329 Cary Hall, Buffalo, NY 14214; I. Kralj-Hans, Dept. of Anatomy and Developmental Biology, University College London, Gower Street, London WC1E 6BT, UK.

Present address and address for reprint requests: M. Glickstein, Dept. of Anatomy and Developmental Biology, University College London, Gower Street, London WC1E 6BT, UK.

Received 20 July 1998; accepted in final form 14 December 1998.

REFERENCES

- ADRIAN, E. Afferent areas in the cerebellum connected with the limbs. *Brain* 66: 289–315, 1943.
- BAIZER, J. AND GLICKSTEIN, M. Role of cerebellum in prism adaptation. *J. Physiol. (Lond.)* 236: 34–35, 1973.
- BAIZER, J. AND GLICKSTEIN, M. Cerebellar lesion effects on prism adaptation in a Macaque monkey (Abstract). *J. Physiol. (Lond.)* 476: 27, 1994.
- BOSSOM, J. AND HAMILTON, C. R. Interocular transfer of prism altered coordination in split-brain monkeys. *J. Comp. Physiol. Psychol.* 56: 769–774, 1963.
- GLICKSTEIN, M., COHEN, J., DIXON, B., HOLLINS, M., LA BOSSIERE, E., AND ROBINSON, F. Cortico-pontine visual projections in macaque monkeys. *J. Comp. Neurol.* 190: 209–229, 1980.
- GLICKSTEIN, M., GERRITS, N., KRALJ-HANS, I., MERCIER, B., STEIN, J., AND VOOGD, J. Visual ponto-cerebellar projections in the Macaque. *J. Comp. Neurol.* 349: 51–72, 1994.
- GLICKSTEIN, M., MAY, J., AND MERCIER, B. Corticopontine projections in the Macaque. The distribution of labelled cortical cells after large injections of horseradish peroxidase in the Pontine nuclei. *J. Comp. Neurol.* 235: 343–359, 1985.
- HARRIS, C. Perceptual adaptation to inverted, reversed, and displaced vision. *Psychol. Rev.* 72: 419–444, 1965.
- HELMHOLTZ, H. *Handbuch der Physiologischen Optik*. New York: Dover, 1962, vol. III, p. 246.
- MADIGAN, J. AND CARPENTER, M. *Cerebellum of the Rhesus Monkey*. Baltimore: University Park Press, 1971.
- MARTIN, T. A., KEATING, J. G., GOODKIN, H. P., BASTIAN, A. J., AND THACH, W. T. Throwing while looking through prisms. I. Focal olivo-cerebellar lesions impair adaptation. *Brain* 119: 1183–1198, 1996.
- MILES, F. A. AND EIGHMY, B. B. Long-term adaptive changes in primate vestibulo-ocular reflex. I. Behavioral observations. *J. Neurophysiol.* 43: 1406–1425, 1980.
- NODA, H. AND FUJIKADO, T. Topography of the oculomotor area of the cerebellar vermis in macaques as determined by microstimulation. *J. Neurophysiol.* 58: 359–378, 1987.
- OPTICAN, L. M. AND ROBINSON, D. A. Cerebellum-dependent adaptive control of the primate saccadic system. *J. Neurophysiol.* 44: 1056–1076, 1980.
- ROBINSON, D. A. Adaptive gain control of vestibulo-ocular reflex by the cerebellum. *J. Neurophysiol.* 39: 954–969, 1976.
- STEIN, J. S. AND GLICKSTEIN, M. The role of the cerebellum in the visual guidance of movement. *Psychol. Rev.* 72: 967–1017, 1992.
- WEINER, M., HALLETT, M., AND FUNKENSTEIN, H. H. Adaptation to lateral displacement of vision in patients with lesions of the central nervous system. *Neurology* 33: 766–772, 1983.