Exp Brain Res (1987) 66: 638–652

Experimental Brain Research

The role of the monkey sensory cortex in the recovery from cerebellar injury

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Summary. The aim of the study was to investigate the contribution of the primary sensory cortex in the compensation of cerebellar deficits during self-paced movements. For this purpose, monkeys were trained on motor tasks which required goal-reaching and independent finger movements. The intermediate and lateral deep cerebellar nuclei and the sensory cortex were lesioned in isolation and in sequence and the course of motor recovery was studied on the test performances. The deep nuclei were lesioned by kainic acid injections, the sensory cortex was removed by ablation. Cerebellar lesions in isolation produced obvious deficits at proximal and distal joints, affecting both slow and fast motor adjustments. Only lesions of the anterior portions of the intermediate and lateral deep nuclear complexes produced deficiencies in voluntary movements. Lesions of the posterior portions produced postural disturbances. The process of recovery following cerebellar lesions was slow and, depending on the nature of the task, was found to be differentially disruptive for motor performances requiring fast and slow motor adjustments. The deficits at distal joints appeared to be more enduring than those at proximal joints. Sensory cortical lesions in isolation produced much less severe and more transient motor deficits. They consisted of hand clumsiness and their recovery was fast and reached higher levels of performance than following cerebellar lesions. When the sensory cortex was removed secondarily to a cerebellar lesion and after recovery from the cerebellar deficits, the initially recovered motor performance became much worse again (decompensation). Removal of the sensory cortex prior to a cerebellar lesion exaggerated the cerebellar deficits and severely limited their recovery. Slow and fast motor performances were completely abolished for three weeks following sequential lesions. Signs of recovery subsequently appeared and stabilized at low levels of performance by five to seven weeks. The effects of combined, sequential cerebellar and sensory cortical lesions were much worse than expected if the effects from the two lesions were merely additive. This indicates that there is some functional interrelationship between the sensory cortex and the cerebellum, which promotes compensation. The somatosensory cortex appears to play a crucial role in the process of recovery from cerebellar motor deficits and it is likely that sensation is an important component in the process of recovery. It is suggested that the sensory cortex exerts its compensatory actions via a structure or structures which receives convergent cerebellar and sensory cortical inputs.

Key words: Cerebellum – Sensory cortex – Compensation – Motor performance

Introduction

Damage to the primate cerebellum is typically associated with disturbances in voluntary movements. Lesions of the cerebellar cortex alone produce little motor deficit but lesions of the deep cerebellar nuclei, notably the intermediate and lateral nuclear complexes, produce severe deficiencies. These are characterized by ataxia, dysmetria and loss of independent finger movements (Keller et al. 1937; Botterell and Fulton 1938a, b; Carrea and Mettler 1947; Growdon et al. 1967; Horvath et al. 1970; Goldberger and Growdon 1973; Gilman et al. 1976; Trouche et al. 1979; see also Brooks and Thach 1981), a symptomatology which resembles closely the "decomposition of movements" described in human patients (Holmes 1922, 1939).

It is well known that there is recovery or compensation from cerebellar deficits following extensive

lesions and complete removal of the cerebellum (Aring and Fulton 1936; Carrea and Mettler 1947; Growdon et al. 1967; Goldberger and Growdon 1973). Patients suffering from severe cerebellar anomalies may be remarkably asymptomatic (Dow and Moruzzi 1958), indicating that extracerebellar structures compensate for the loss of cerebellar tissue. However, very little is known about which structures might mediate compensation. In attempts to identify such structures, secondary lesions of various sites have been made to see if these cause a return of cerebellar symptoms after recovery has occured (decompensation). Because of the association of cerebellar deficits with voluntary movements, motor cortex has long been considered a likely site (cf. Dow and Moruzzi 1958 and see discussion). However, lesions of the motor cortex itself (Aring and Fulton 1936; Carrea and Mettler 1947) or the corticospinal tract (Carpenter and Correll 1961) are inconclusive, as they lead to motor paralysis which would mask any cerebellar symptoms. On the other hand secondary lesions of premotor cortex (Aring and Fulton 1936; Carrea and Metteler 1947), or of the dorsal columns (Carpenter and Correll 1961) or dorsal roots (Liu and Chambers 1971) do lead to decompensation of cerebellar symptoms. These structures, like the cerebellum, provide inputs to motor cortex (Pandya and Vignolo 1971; Brinkman et al. 1978; Muakassa and Strick 1979; Asanuma et al. 1980). It is possible that their compensatory actions are exerted through their actions on the motor cortex, with inputs remaining intact substituting for loss of cerebellar input (see also discussion).

A major source of input to motor cortex, which has not been studied by the above paradigm, is the primary sensory cortex (Jones et al. 1978; Vogt and Pandya 1978). Recently, sensory cortex has been shown to be involved in neuronal rearrangements (a possible mechanism for compensation, see discussion) following removal of another input to motor cortex (in this case thalamic, Asanuma and Arissian 1984; Asanuma et al. 1985). It is very possible that the sensory cortex may similarly be involved in compensation following lesions of the cerebellum. Indeed, such a possibility is suggested by the development of a field potential over the sensory cortex in parallel with recovery on a motor task following cerebellar hemispherectomy (Sasaki and Gemba 1984).

It is therefore the aim of this work to investigate the possible role of sensory cortex in recovery from cerebellar deficits using the sequential lesion paradigm. For this purpose, the sensory cortex was removed following or prior to a cerebellar lesion. The effects of the isolated and combined, sequential lesions were examined by following performance on motor tasks requiring self-initiated movements. If a putative source of compensation is removed secondarily to the cerebellar lesion (which is the sequence used by previous investigators) then the cerebellar deficiencies are expected to be decompensated. If the sensory cortex is lesioned prior to the cerebellum, then the earlier removal of the potential source of compensation should prevent recovery from cerebellar deficits. These hyphotheses were tested in the present study.

Methods

The study was conducted on five monkeys (*macaca cynomolgus*) weighing between 3.5 and 4.5 kg. All monkeys (A–E) were preoperatively trained on behavioral tasks and subjected to sequential cerebellar and primary sensory cortical lesions. In three monkeys the cerebellar lesion was performed prior to the cortical lesion and the lesioning sequence was reversed on the contralateral side, after study of the effects following the first set of lesions. In two monkeys the sensory cortex was removed prior to a contralateral cerebellar lesion. Table 1 describes the lesioning sequences for all monkeys.

Preoperative training typically lasted about 10 days. The tests were performed daily and the monkeys were trained on both hands. Testing was resumed 2 days after operations. The observation period following a sensory cortical lesion in isolation typically lasted two weeks, that following a cerebellar lesion four weeks.

Table 1. Lesioning sequences in different monkeys

Monkey	Lesions I	II	III	IV
A	Cerebellum (right) Inc.[a]	Sensory ctx. (left)	Sensory ctx. (right)	Cerebellum (left) Inc.[a]
B	Sensory ctx. (right)	Cerebellum (left)		
C	Sensory ctx. (left)	Cerebellum (right) Post.[b]		
D	Cerebellum (right)	Sensory ctx. (left)	Sensory ctx. (right)	Cerebellum (left)
E	Hemicerebellectomy (right)	Sensory ctx. (left)	Sensory ctx. (right) +motor ctx.[c]	Hemicerebellectomy (left)

Unless otherwise stated, sensory cortex lesions were complete and cerebellar lesions were complete lesions of the anterior 2/3rds (at least) of the intermediate and lateral deep nuclei

[a] Incomplete lesion covering only the dorsal part of the deep nuclei

[b] Posterior lesion restricted to the posterior 1/3rd of the nuclei

[c] Lesion had encroached upon the motor cortex

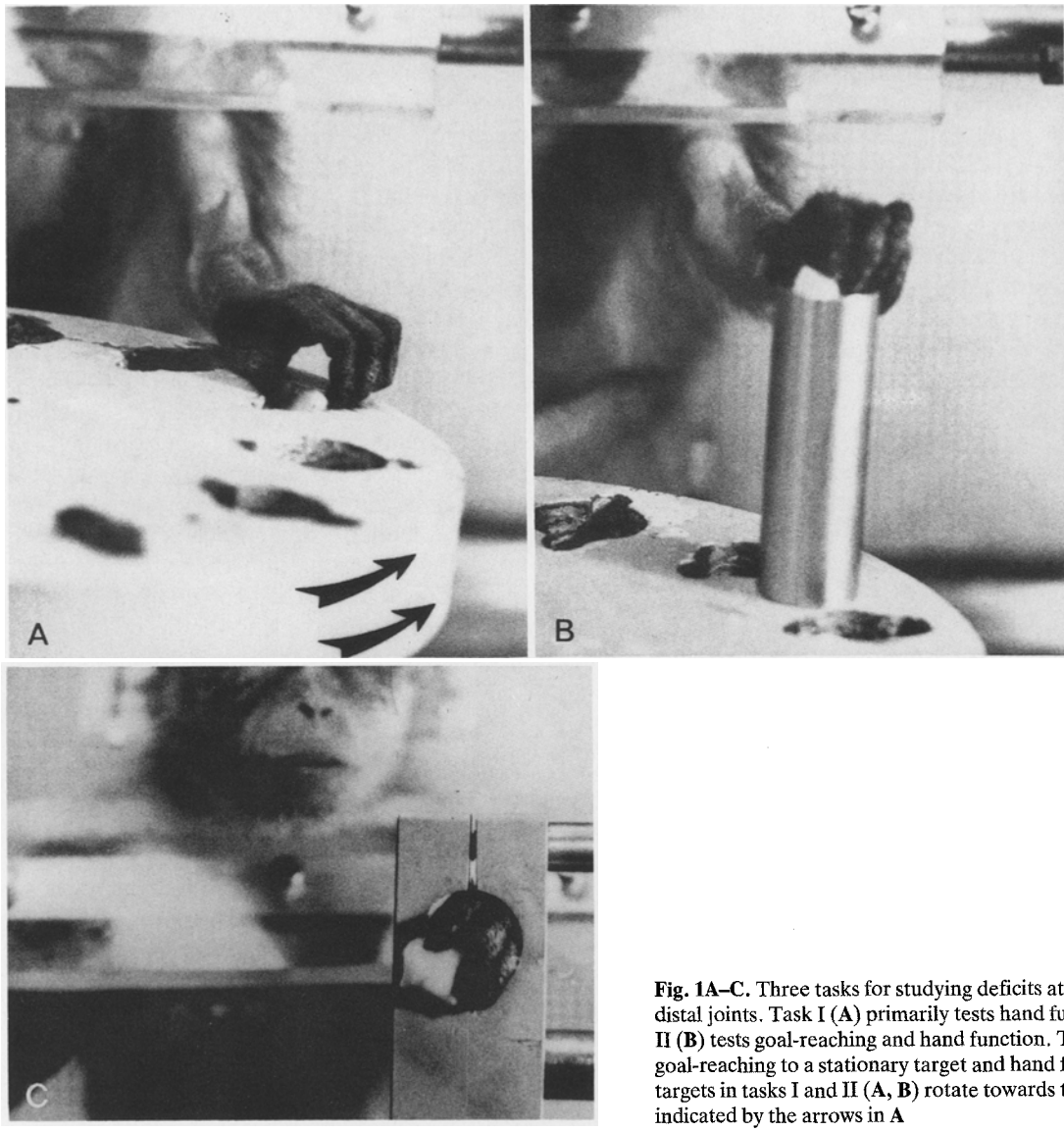

Fig. 1A–C. Three tasks for studying deficits at proximal and distal joints. Task I (**A**) primarily tests hand function. Task II (**B**) tests goal-reaching and hand function. Task III tests goal-reaching to a stationary target and hand function. The targets in tasks I and II (**A, B**) rotate towards the animal, as indicated by the arrows in **A**

This was usually sufficient for maximal recovery to occur. The observation period following the second lesion lasted at least three months. The recovery curves following secondary lesions usually stabilized by five to six weeks postoperatively. All behavioral performances were videotaped for later analysis.

Behavioral tasks

Three tasks (Fig. 1) were used to study motor performances which required control at both proximal (elbow, shoulder) and distal (hand) joints of the upper extremity. Such tasks were used since cerebellar lesions cause disturbances at both sites (Holmes 1922; Growdon et al. 1967)

Task I. The first testing paradigm was adopted from the work of Asanuma and Arissian (1982, 1984). The animals were seated in a primate chair and were required to pick up small morsels of food from holes drilled in a rotating platform (Fig. 1A). The food rewards were always placed in slits of identical size (2 cm in diameter and 3.5 cm in length). The food board rotated towards the animal, as indicated by the arrows in Fig. 1A. The animals had to adjust their performances to increasing speeds of rotation of the board. Performance at a particular speed of rotation was considered successful (reached control level) when the animal was able to pick up the food within one rotation cycle of the board in at least 80% of the trials (usually 10) at that speed. The fastest speed used was 0.6 rotations/second because all monkeys could perform preoperatively at 80-100% at this speed, whereas at higher speeds performance of different monkeys was variable.

While performance was routinely examined at different speeds of board rotation, for task I it became clear that deficits following lesions were most obvious on fast speeds. Therefore, task acquisition (Fig. 2) and deficits (Fig. 6) were summarized across monkeys by illustrating performance on a fast speed of rotation. This method differs from that of Asanuma and Arissian (1982, 1984), who measured the fastest speed of rotation at which a monkey was successful on 50% of the trials. While the two methods result in

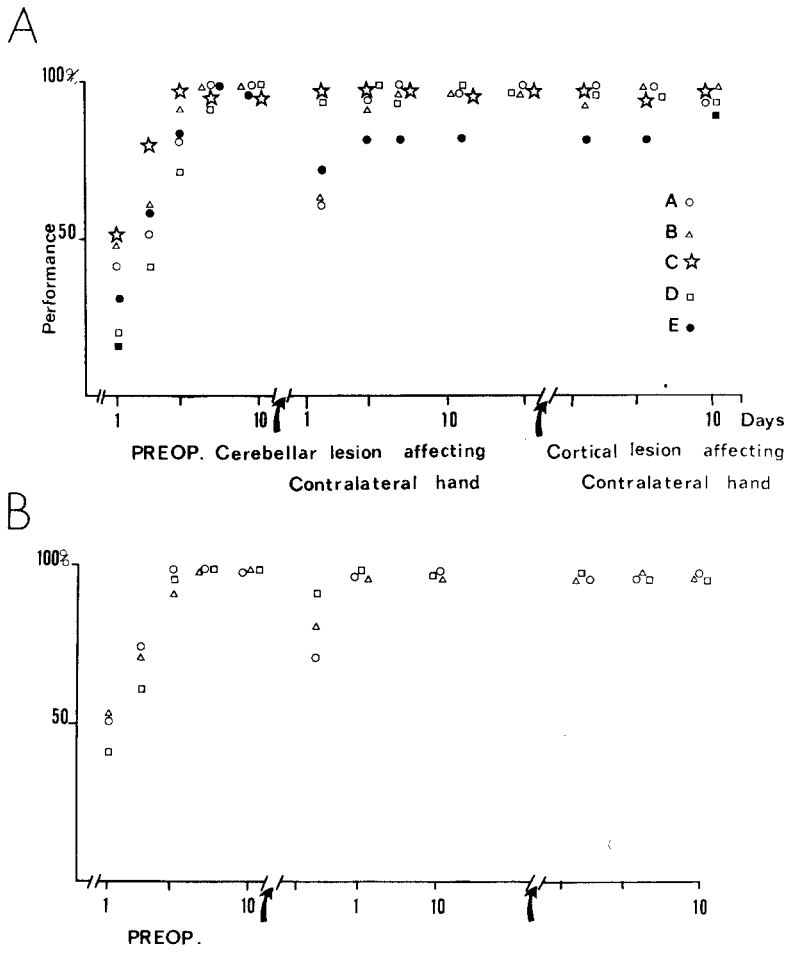

Fig. 2A, B. Performances of intact hands on tasks I (**A**) and II (**B**) on a fast speed of rotation (0.6 rotations/second), during task acquisition (Preop.) and after sequential lesions (arrows) affecting the contralateral hands. The arrows in **B** refer to the same lesioning sequence as in **A**. Pre- and post-operative training spans (days) are illustrated on the abscissae

rather similar time courses of recovery (from sensory cortical lesions), the present method avoids a priori assumptions about changes in performance with changes in rotation speed (for example, that performance at 0.6 rotations/s is twice as good as performance at 0.3 rotations/s) and is somewhat more sensitive (see below).

Acquisition of task I is summarized in Fig. 2A, which shows that the task was quickly learned: performance on the fastest speed of board rotation stabilized at high levels by 7 to 10 days of training. Control levels of performance on slower speeds of rotation (0.2–0.4 rot/s) were achieved within 1 to 3 days. (Note that using Asanuma and Arissian's (1982, 1984) method of assessment, most monkeys would have attained successful performance already on the first or second day of training rather than the fifth to seventh). Since the monkeys were preoperatively trained on both hands, performances using both hands were monitored in parallel. Figure 2 illustrates that lesions (in isolation or combination) affecting one hand had in general no effect on performance using the contralateral (unaffected) hand: the animals continued to perform at the 80–100% level. For some monkeys the performance was poorer immediately after the cerebellar operation, probably as a result of the toxic after-effects of the kainic acid. Although Fig. 2 shows data for intact hands, the preoperative curves for the hands affected by the lesions were similar.

The testing paradigm of task I is entirely based on self-paced movements and no conditioning stimuli were introduced to shape the performance. Regardless of whether the animals used a strategy for stabilizing their arm (for instance by adducting it against their body or by resting the lower arm on the rotating platform), accurate hand and distal finger movements were the key for a successful performance on this task. Preoperatively food retrieval was typically achieved by using a precision grip, i.e. index-thumb opposition (Asanuma and Arissian 1984).

Task II. The second paradigm (Fig. 1B) was a modification of the first task and was designed to emphasize deficits at the shoulder and elbow joints. Here, a post (1.5 cm in diameter and 10 cm in height) was attached to the foodboard. The top of the post was slightly concave, so that a morsel of food could be placed in it. The platform containing the food reward was mounted at shoulder height of the monkey. To retrieve the food, the monkey projected its arm towards the target, holding it up and away from the trunk, and usually used a quasi-precision grip for picking up the food. The monkeys typically held their arms out for one or two seconds (longer at slow speeds of rotation and shorter at faster speeds of rotation) at the level of the approaching rotating platform and lifted the reward out of the holder as it passed under their hands. The speeds of rotation of the food board and the means of scoring performance were the same as those described for the first paradigm. Task acquisition is illustrated in Fig. 2B. Preoperatively, performance curves for task II resemble those for task I. High levels of performance were attained by five days at the fastest speed of rotation, and earlier at slower speeds. As with task I, lesions affecting one hand had no effect on performance of the contralateral hand, aside from slightly poor performance on the first test following kainic acid injections.

Task III. The third paradigm tested goal-reaching movements towards a stationary target. Here, the animal had to reach out to retrieve food from a tube (diameter: 2.5 cm) placed in front of it, at the level of the shoulder joint (Fig. 1C). This task resembles the task used by Gorska and Sybirska (1980) to test target reaching and food retrieval in cats (also see Horvath et al. 1970; Gilman et al. 1976). Normally, the monkey needed no training for accurately and smoothly performing this task. Once aware of the food, the monkey projected his hand straight to the tube and inserted two or three fingers for retrieving the reward. The number of trials (out of ten) on which the monkey was able to project his hand into the tube was counted. Additionally, only for successful reaches, the number of times the monkey was able to retrieve the reward was also counted, and expressed as a percentage of successful reaches. In this way an estimate could be obtained as to the severity of both proximal deficits (failure to accurately project the hand into the tube) and distal deficits (failure to retrieve the reward once the target was reached).

Lesioning procedures

All lesioning procedures (see also Table 1) were performed under Nembutal anesthesia (30 mg/kg) and under strict aseptic conditions. After the operative procedures, the animals were given, i.m., a long lasting antibiotic (Bicillin L–A, Wyeth) and the suture lines were cleaned daily with an antiseptic solution (Providone/ Iodine, Triad medical products).

Cerebellar lesions. In four monkeys (A–D), the intermediate (interpositus) and lateral (dentate) parts of the deep cerebellar nuclei were lesioned by injecting 2 (A, C) or 3 (B, D) microliters of kainic acid (2.5 mg/cc), using stereotaxic coordinates (Kusuma and Mabuchi 1970; Szabo and Cowan 1984). These nuclei, and particularly the anterior portions, were chosen because they receive afferent information from the forelimbs via the cerebellar cortico-nuclear projections (Voogd 1967; Ekerot and Larson 1982), project to anterior brain structures (Ito 1985) and evoke forelimb movements upon electrical stimulation (Rispal-Padel et al. 1982).

The cerebellar lesions were achieved by two or three consecutive injections (1 µl in each trajectory) in the anterior-posterior stereotaxic planes (P2 to P5, lateral 5), using a Hamilton syringe mounted vertically on the drive of a micromanipulator. 0.3 µl of kainic acid were injected at three different depths (horizontal planes −4, −5 and −6) along the same trajectory, covering the dorso-ventral extent of the deep nuclei. This approach requires no traumatic surgery, only a small hole in the skull is necessary for inserting the needle of the Hamilton syringe. A guiding tube (made up of a hypodermic needle) was used to penetrate the dura overlying the cerebral cortex and the cerebellum, in order to avoid mechanical deviations of the fine tip of the injection needle.

For comparison with older studies (Aring and Fulton 1936; Botterell and Fulton 1938a, b; Carrea and Mettler 1947), the cerebellum was surgically removed in one monkey (E) by performing two (sequential) hemicerebellectomies. The unilaterality following the first hemicerebellectomy was reflected in the test performance of the contralateral intact extremity. The intact hand performed within control range (see Fig. 2), while the performance of the hand affected by the lesion was severely depressed. Briefly, a unilateral craniotomy was performed over the occipitoparietal lobe, the dura opened and the cortex carefully elevated with a Q-tip to expose the underlying cerebellum. The dura over the cerebellum was opened, the large sinuses tied off and the small veins coagulated. The cerebellar hemisphere was removed by suction in its anterior extension until the floor of the fourth ventricle could be visualized under the operating microscope. After the surgery the cortex was allowed to fall back over the posterior fossa, the dura closed, the bone flap replaced and the overlying muscles and skin sutured. Removing the cerebellum surgically is a traumatic procedure when compared to the injection of kainic acid and the deficits were accordingly severe and enduring, as described by the earlier investigators (see above). Kainic acid injections are more circumscribed, are restricted to the destruction of the nuclear complexes and, furthermore, do not cause possible retrograde changes in precerebellar relay nuclei (Ito et al. 1980). The latter point raises the possibility that cerebellectomy has side effects due to degeneration of precerebellar relay neurons, which could partly account for the massive and enduring deficits described in the older literature.

Cortical lesions. The arm-hand representation areas in the primary sensory cortex were removed contralateral to the side of prior or subsequent cerebellar lesions (see Table 1). A craniotomy was performed exposing the central sulcus and the caudal bank of the arcuate sulcus. The dura was opened and the cortical tissue removed by suction. The ablation typically extended 6 mm in the mediolateral plane, 2 mm in the anterior-posterior plane and 5 mm in depth, extensively covering the target area. The caudal bank of the arcuate sulcus is a good landmark for localizing the hand-arm area in the sensory cortex since the latter is typically located on the same medio-lateral level (Marshall et al. 1937; Pons et al. 1985). After the lesion, the dura was closed and the lesion site covered with a flap of sterile gelfoam. The overlying muscles and skin were sutured and the animals returned to their cages.

At the end of the observation period the animals were perfused under deep Nembutal anesthesia (50 mg/kg) and the lesioned brain areas removed for histological analysis, using the Kluver-Barrera method (1953).

Results

Extent of the lesions

The lesion sites are shown in Fig. 3 for monkeys A–C and in Fig. 4 for monkey D, and are summarized in Table 1. The areas of cerebellum lesioned by kainic acid injections were identified by the absence of cell bodies in the nuclear complexes (indicated by stippling in the figures). The lesions covered at least the anterior 2/3rds of the deep nuclei (target area) in 3 monkeys (A,B,D). In one monkey (C) the lesion was restricted to the posterior 1/3rd of the deep cerebellar nuclei. The intermediate and lateral nuclei were completely lesioned in three monkeys (B–D) but incompletely in one case (A). In this case, the ventralmost half (left side) or third (right side) of the nuclei were spared. However, performance (see below) was similar to that of other monkeys. In monkeys B and D the lesions encroached upon the most anterior part of the fastigial nuclei (P2–P3 in monkey B and P1 in monkey D in Figs. 3 and 4).

Representative examples of lesions of sensory cortex are shown in Fig. 4 for monkey D. It can be seen that the lesion was restricted to the postcentral gyrus and did not encroach upon the motor cortex, as indicated by the intact central sulcus and cortical

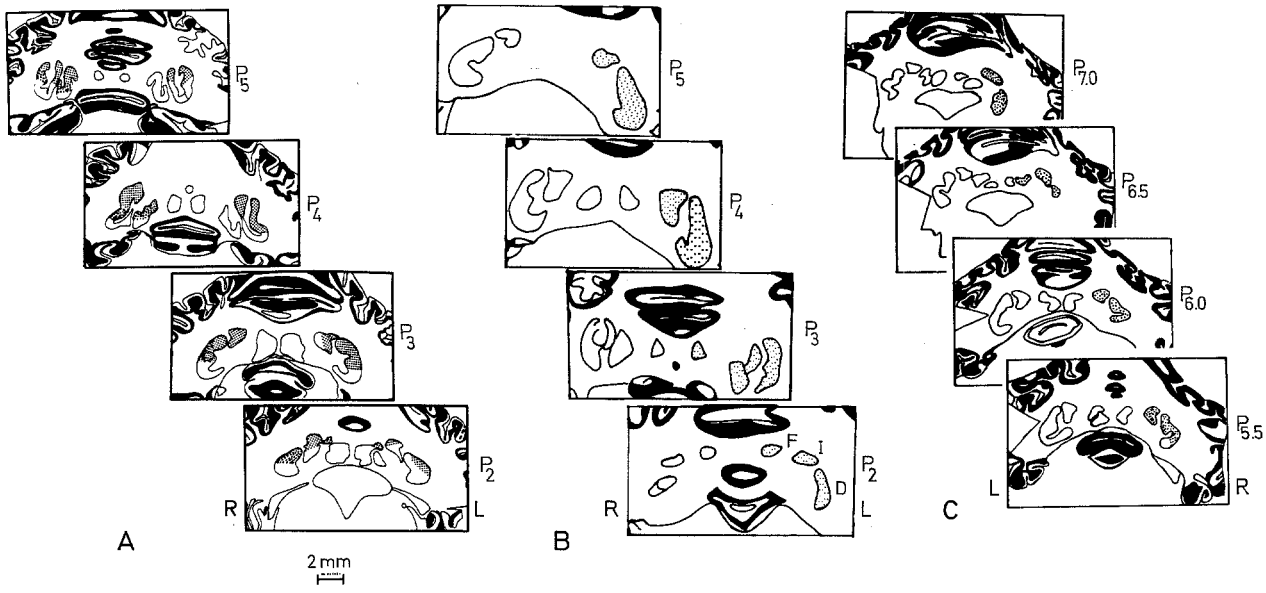

Fig. 3A–C. Kainic acid lesions of the deep cerebellar nuclei (stippled) in monkeys **A–C** on the right (R) and left (L) sides of the cerebellum. The anterior-posterior coordinates (P) are indicated along the coronal sections through the cerebellum. D (dentate nucleus), I (interpositus nucleus), F (fastigial nucleus)

tissue rostral to it. This was essential, since damage to the motor cortex would permanently abolish independent finger movements (see below) and make the testing paradigms futile.

The sensory cortical lesions were extensive in all animals (and comparable to the examples shown in Fig. 4). In one monkey (E) one cortical lesion (right side) was too close to the central sulcus and had encroached upon the motor cortex (see inset, Fig. 8B). As a consequence the monkey's test performances recovered proximally following this lesion, but not distally (task III, Fig. 8B). In two monkeys (C and D, right sides) the lesions impinged upon area 5 of the parietal lobe, as indicated by their encroachment upon the intraparietal sulcus. It is, however, unlikely that this had a significant effect on the test performance, since all monkeys recovered equally well from lesions in the postcentral gyrus. Lesions of area 5 are known to cause less severe somatic deficits than lesions of the primary sensory cortex (cf. Hyvarynen 1982). The lesions probably did not include areas 3a and 3b, which receive mainly proprioceptive input (Heath et al. 1976). Therefore, whether such input is involved in recovery was not tested.

General observations

Cerebellar lesions. Lesions of the intermediate and lateral deep nuclei consistently produced dysmetria, ataxia and loss of independent finger movements, ipsilateral to the lesion site. Dysmetria was characterized by over-shooting (hypermetria) of targets in reaching tasks, ataxia by swaying movements at the shoulder joint, and loss of skilled movements by the inability to use the fingers independently during manipulatory tasks. Index-thumb opposition was lost and the fingers were opened and closed together ("in concert") not unlike the deficits seen following pyramidal tract (Lawrence and Kuypers 1968) or motor cortical (Denny-Brown 1966; Passingham et al. 1983) lesions. The movements were occasionally slow and looked "weak". This condition was, however, not observed in all monkeys and for those in which it was (monkeys A and D) it was transient and never outlasted the first postoperative week. If the slowness and "weakness" of movements are the equivalent of hypotonia (Holmes 1922; Botterell and Fulton 1938a, b; Carrea and Mettler 1947), then this was the least disabling feature of the cerebellar symptoms.

Only lesions of the anterior parts of the deep nuclei (complete or incomplete, see above and Figs. 3 and 4) caused disturbances in voluntary movements. Lesions of the posterior deep nuclei (see monkey C, Fig. 3) led to postural disturbances (for instance, head deviation and falling to the side of the lesion or postural ataxia). Abnormal eye movements (smooth pursuit or nystagmus) were never observed upon clinical examination, regardless of whether the lesions were in the anterior or posterior nuclear

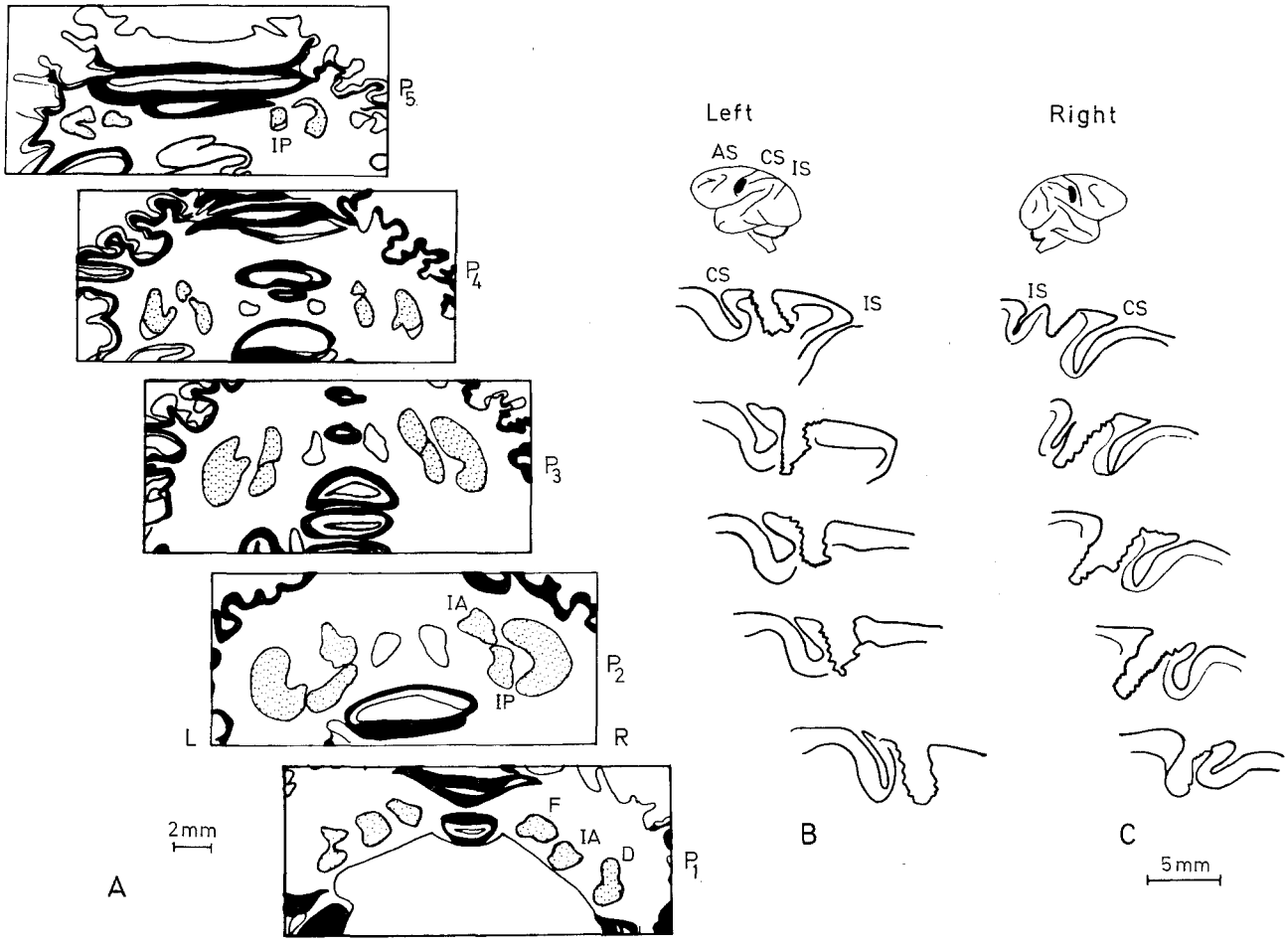

Fig. 4A–C. Lesions of the deep cerebellar nuclei (**A**) and the sensory cortices (**B, C**) of monkey D. The lesions are indicated by stippling in the coronal sections through the anterior-posterior plane (P1–P5) on the left (L) and right (R) sides. **B, C** illustrate the cortical lesions and representative sagittal sections are shown underneath. D (dentate nucleus), IA (interpositus anterior), IP (interpositus posterior), F (fastigial nucleus), CS (central sulcus), AS (arcuate sulcus), IS (intraparietal sulcus)

complexes or whether they had encroached upon the fastigial nuclei (monkeys B and D). The symptoms progressively lessened with time, with hand clumsiness (notably, impairment of independent finger movements and index-thumb opposition) being the most persistent. Noticeable improvement from ataxia and dysmetria occured around two weeks postoperatively. Precision grip and independent finger movements returned after three weeks.

Cortical lesions. Removing the arm-hand representation of the primary sensory cortex produced anesthesia in the contralateral extremity. This was clinically tested by the monkeys non-responsiveness to pinch and pin prick. There was occasionally anesthesia in the leg and the face, indicating that the lesions had encroached upon areas neighbouring that of the upper limb representation. There were no obvious motor disturbances aside from hand clumsiness which was evident for 4–5 days postoperatively, confirming previous observations (Travis and Woolsey 1956; Asanuma and Arissian 1982, 1984; Passingham et al. 1983). In contrast, following the one lesion involving motor cortex (monkey E), use of the hand was impaired throughout the observation period. No cerebellar like symptoms were observed following removal of the sensory cortex.

Secondary lesions. Removal of the sensory cortex secondary to the recovery from a cerebellar lesion led to a decompensation (reappearance) of the cerebellar symptoms. Decompensated ataxia and dysmetria showed signs of recovery by 6–8 weeks following a secondary lesion, while index-thumb opposition (precision grip) did not return throughout the observation period.

Lesions of the intermediate and lateral deep nuclei secondary to removal of the sensory cortex

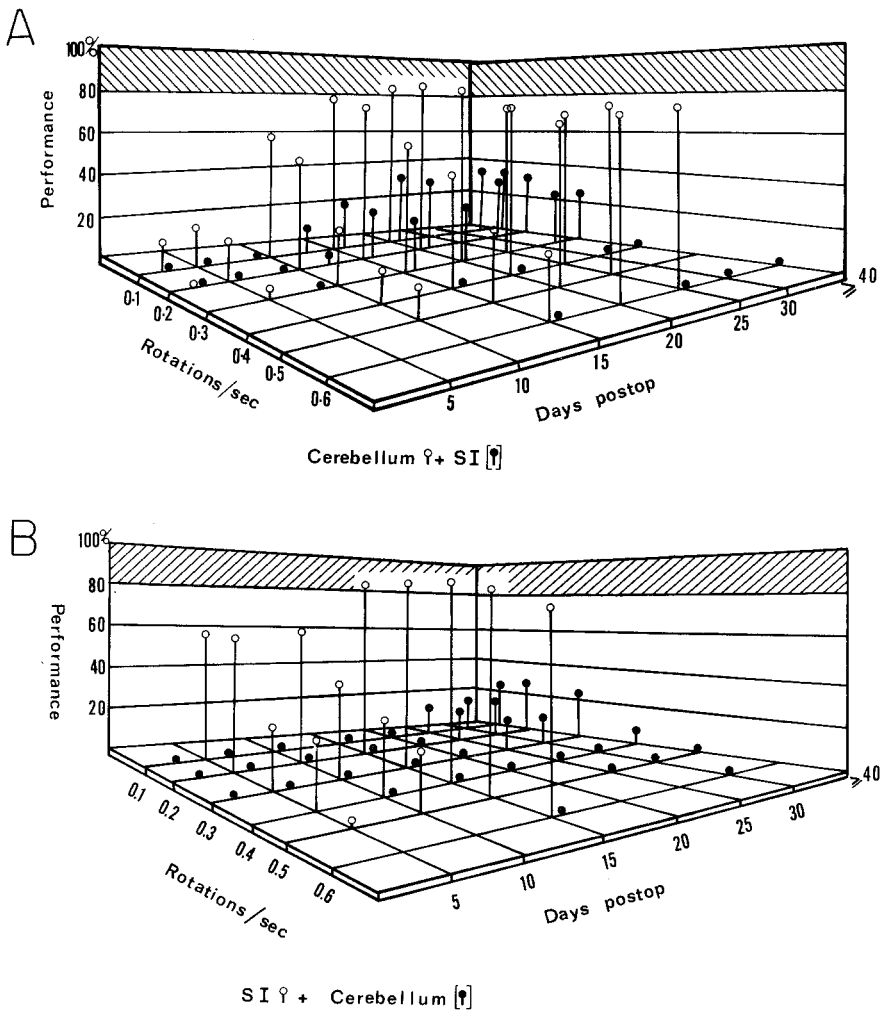

Fig. 5A, B. Postoperative performances (%) of monkey D on task I, during different speeds of board rotations (rotations/sec) and at selected postoperative times (typical 5-day intervals). **A** illustrates the performances following a cerebellar lesion (♀) followed by a secondary removal of the primary sensory cortex (♀). **B** illustrates the performances of the contralateral hand after a primary sensory cortical lesion (♀) and followed by a secondary cerebellar lesion (♀). Hatched area indicates the preoperative control range of performance. Notice that the recovery following cerebellar lesions is faster and to a higher level of performance on slow than on fast speeds of rotation, particularly in **A**

elicited the typical cerebellar symptomatology (see above). The symptoms were, however, severe and persisted much longer than after a cerebellar lesion in isolation. Ataxia and dysmetria showed little recovery and the precision grip was abolished for the duration of the observation period.

Test performances

All monkeys were tested on task I (Fig. 1A), monkeys A, B, D additionally on task II (Fig. 1B), and monkeys D and E on task III (Fig. 1C). Task II and III were introduced when it became apparent that, following cerebellar lesions, monkeys adopted the strategy on task I of adducting their upper extremity against their trunk and thereby minimizing interference from proximal ataxia. This strategy had, however, no effects on finger movements. Task I can therefore be considered primarily a test of hand function, while tasks II and III additionally reveal proximal deficiencies and thus take into account the full cerebellar symptomatology.

Task I. Figure 5 presents a representative example of performance on task I, illustrating data from one monkey (monkey D, lesions shown in Fig. 4). The three dimensional graph shows the monkey's performances for different speeds of board rotations, at various postoperative times. Figure 5A shows the performance following a primary cerebellar lesion, followed by a secondary removal of the contralateral sensory cortex. Figure 5B shows the performances on the same task after reversing the sequence of lesions to affect the contralateral hand. While effects following secondary lesions were studied for three to four months postoperatively, performances are illustrated up to forty days, since recovery had stabilized by this time and no further improvements were seen thereafter.

The figure shows that test performances returned toward control levels (80–100%) following either

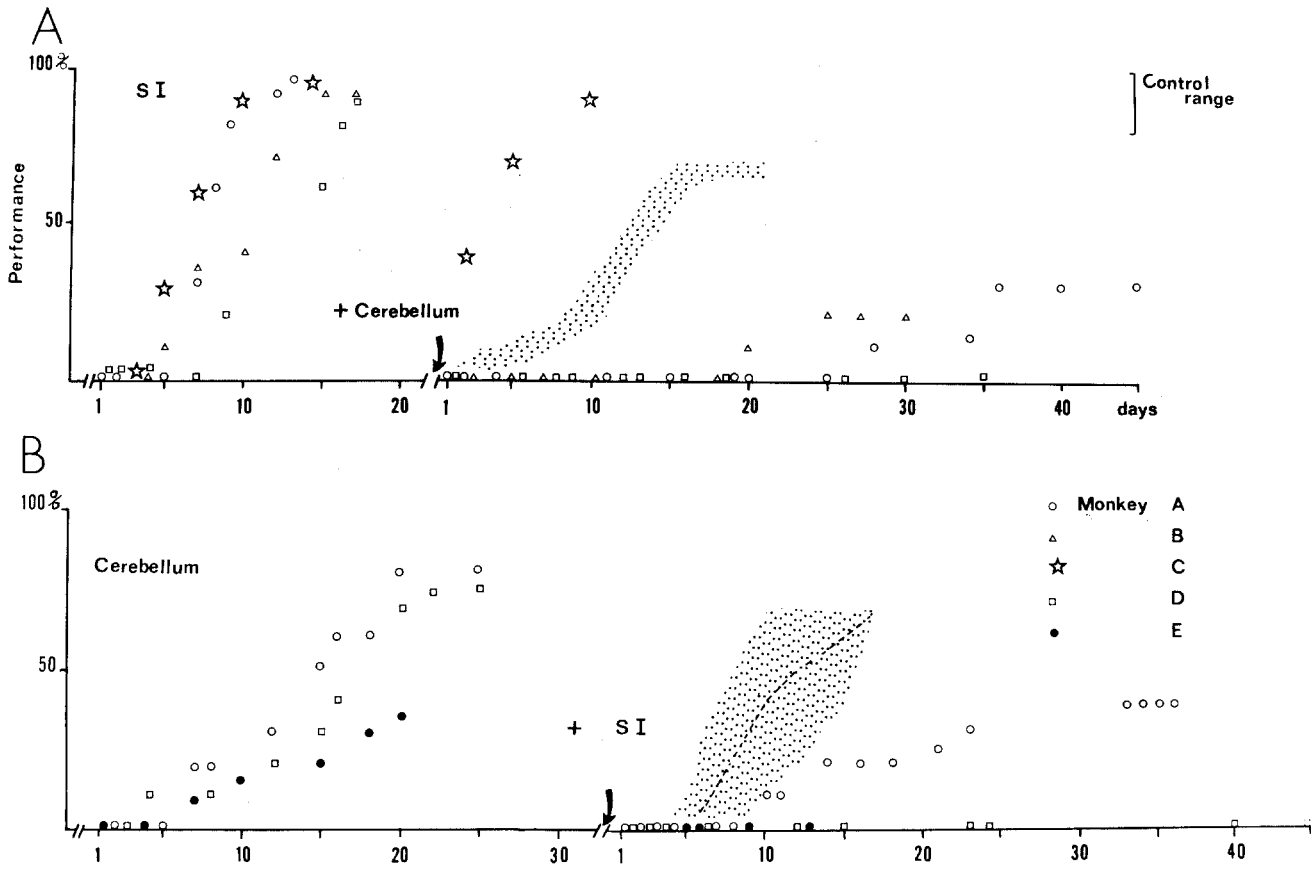

Fig. 6A, B. Recovery curves of the performances of all monkeys on task I at a fast speed of rotation (0.6 rotations/second). **A**, when the sensory cortical lesions preceded the cerebellar lesions and **B**, when the cerebellar lesions preceded the cortical lesions. The cerebellar lesion of monkey C was outside of the target area, and had little effect on performance. The stippled areas represent the calculated, expected performance range if the lesions were purely additive (see text. The expected range in **A** is derived from performances of monkeys after kainic acid lesions of the cerebellar nuclei, shown in **B**. The expected range in **B** is derived from the performances after sensory cortex lesions, shown in **A**; the interrupted line is the mean expected performance). Note that some coinciding data points at 0% performance are placed next to each other

cerebellar or sensory cortical lesions in isolation. Recovery was faster, and to a slightly higher final level, after sensory cortical than after cerebellar lesions. In contrast, performance remained severely impaired after secondary lesions in both lesioning sequences. At best, the monkey was able to retrieve the food morsel from the rotating board in only 20% or fewer of trials, depending upon the speed of rotation.

Generally, performances recovered better (faster, to a higher final level) when the board rotated at slow rather than fast speeds. Presumably, at higher speeds the manipulatory maneuvers necessary to remove the food from its slot must be made more rapidly, so that the task is more difficult, and the effects of hand clumsiness exacerbated. This is most apparent after secondary lesions, when the ability to use the fingers independently was lost: monkey D (Fig. 5) was never successful at the fastest speeds. The monkey did have some success at slow speeds (Fig. 5). The degree of success after secondary lesions shown by this and other monkeys very probably dependend upon adoption of a new strategy for food retrieval. It was observed that, instead of picking up the food out of its slot, monkeys inserted several fingers together into the slot and used a raking movement to obtain the food.

Figure 6 illustrates the recovery curves for all monkeys on a fast speed of rotation, where the deficits were most pronounced. In general, the performances of all monkeys (aside from the exceptions noted) conformed to the features described for monkey D (Fig. 5). The shapes of the recovery curves following cortical lesions in isolation (Fig. 6A) are quite different from those following cerebellar lesions (Fig. 6B). Recovery to control levels of performance following sensory cortical lesions occurred within 10–14 days: in fact, once the monkeys

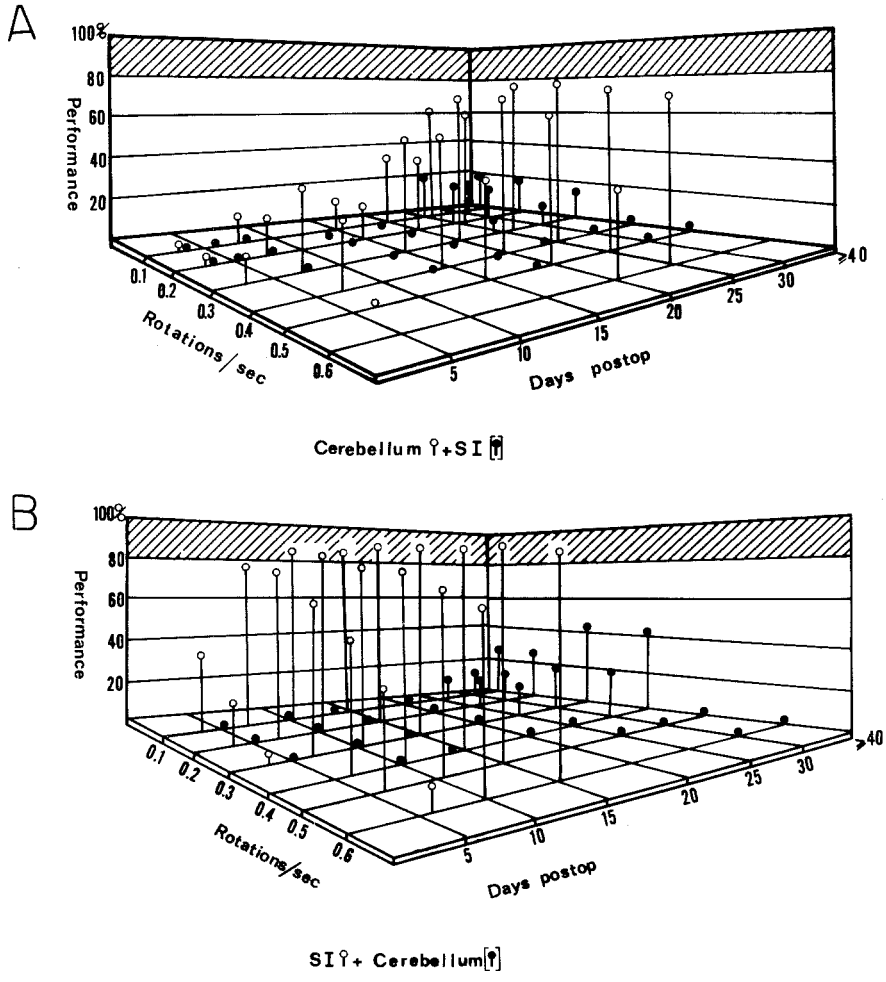

Fig. 7A, B. Postoperative performances of monkey D on task II, during different speeds of rotation and at different postoperative times. **A** illustrates the performance after a primary cerebellar lesion (♀) followed by a secondary sensory cortical lesion (♀) and **B** illustrates the performance following a cortical lesion followed by a cerebellar lesion (♀, ♀) on the contralateral side. Notice (when compared to figure 5) that the recovery following cerebellar lesions is poorer on slow than on fast speeds of rotation

showed some degree of success on the task (days 5–9 postoperatively), the progress of recovery was quite rapid (5–10 days). In contrast, recovery following cerebellar lesions took about three weeks, with the course of recovery, once some success was achieved, progressing relatively slowly. Performance of the hemicerebellectomized monkey (E) was generally poorer and recovery worse than in the monkeys where the deep nuclei were destroyed by the injection of kainic acid (see also methods).

Following secondary lesions, the ability to perform task I disappeared again, with at best a slow and modest degree of recovery. The most enduring effects were in cases where cerebellar lesions were complete lesions of the anterior deep nuclear complexes (B, D, E). A slightly better degree of recovery was shown by monkey A where there was some sparing of the ventral portions of the deep nuclei. When the cerebellar lesion was restricted to the posterior part of the deep nuclei (monkey C), there was little effect on the task performance, suggesting that the posterior portions play no significant role in the skilled movements tested.

For sequential lesions, deficits in performance following the second lesion were much greater than expected if the effects of the two lesions were simply additive. If effects were additive, the progress of recovery from the second lesion would be expected to mimic the time course seen following that lesion in isolation, adjusted to the final level of recovery from the first lesion. There are several ways of roughly estimating the adjusted performance, which give rather similar results for the present data. The simplest is to add the deficits in performance following cerebellar or sensory cortical lesions in isolation to the deficits remaining from the first lesion (as illustrated in Fig. 6). As just described there is fairly good recovery within two weeks following sensory cortical lesions and by three weeks following cerebellar lesions: similar progress of recovery would be expected for the secondary lesions if effects were independent. However, following secondary lesions,

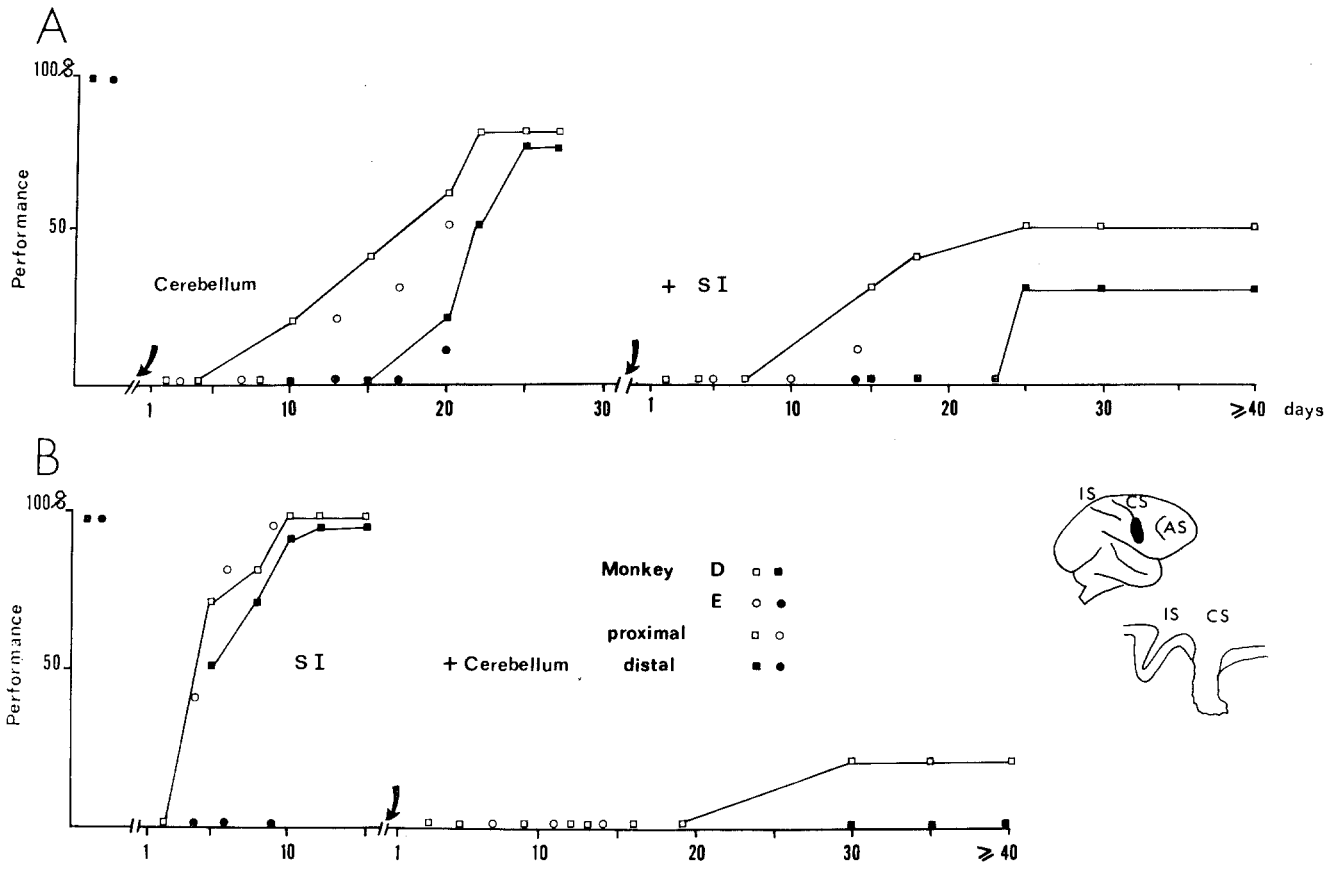

Fig. 8A, B. Performances of monkeys D and E on task III after a cerebellar lesion followed by a sensory cortical lesion (**A**), and after the reversed lesioning sequence to affect the contralateral side (**B**). Successful reaches (proximal component) are indicated by open symbols. Successful food retrieval by closed symbols (see methods for definition of successful reaches and retrieval). The arrows refer to the type and time (days) of occurence of the lesions. Lines are drawn through data points obtained on monkey D on the distal and proximal tests. In **B**, the sensory cortical lesion of monkey E encroached upon the motor cortex (see inset), resulting in proximal but not distal recovery of performance

there was either no recovery or recovery with a slow time course to a low level of performance. The deficits, much greater than expected if additive, are compatible with the interpretation that there is some functional interaction between sensory cortex and cerebellum which promotes compensation. Additionally, as described under general observations, the symptomatology following cerebellar or sensory cortical lesions in isolation was entirely different, which mitigates the possibility of entangling two types of symptoms. The cerebellar symptoms returned after secondary cortical lesions and were exaggerated when the cerebellar lesion was preceded by the cortical lesion. These sets of observations support the hypothesis that lesioning the sensory cortex removes a source for compensation.

It can also be seen from Fig. 6 that the recovery curves look similar whether monkeys were subjected to two (reversed) lesioning sequences (monkeys A, D, E) or only to one (B, C). Additionally, as illustrated in Fig. 2 and described in the methods, the first sequence of lesions did not affect performance of the intact hand which was monitored in parallel with performance of the affected hand. Finally, after recovery had occured following one lesioning sequence, reversing the lesions to affect the contralateral hand had no effect on the recovered performance of the first hand. These observations would indicate that the cerebellum or sensory cortex contralateral to those unter study were not involved in recovery.

Task II. Figure 7 illustrates the performance of monkey D on task II. The most striking difference to the results obtained for task I (Fig. 5) was noticed after cerebellar lesions. In contrast to performance on task I, for all monkeys tested on task II, performance was poorer (at least initially) at slow speeds of board rotation rather than at fast speeds.

The poorer performances on slow speeds of board rotation were most likely the result of the proximal deficits which became prominent on task II. During slow speeds of rotation, the monkeys typically stretched their arms towards the approaching target and ataxia developed during this reach. The monkeys overreached (hypermetria) or missed the target due

to swaying movements at the shoulder joint. Once this occured, the monkeys were unable to correct their error because ataxia and hypermetria worsened and the movements became erratic, although the rotating platform was still within reach. During fast rotations of the board, the monkeys typically swung their arms towards the target and were able, occasionally, to hit it. With recovery from ataxia and dysmetria after cerebellar lesions in isolation, the monkeys were able to project their hand to the target in a smoother trajectory. No trajectory disturbances were seen following sensory cortical lesions.

Task III. Task III was introduced during the course of the experiments in an attempt to assess proximal and distal deficits separately. Performance on task III is illustrated for monkeys D and E in Fig. 8. Monkey E (hemicerebellectomy) was less extensively tested because the development of an infection necessitated shortening of the observation period. The general course of the test performance is, however, comparable to that of monkey D.

Figure 8A shows that following cerebellar lesions, the monkeys recovered their ability to project their hands to the target (proximal component) before they succeeded in inserting their fingers into the tube and picking out the reward (distal component). For example, when monkey D was able to reach the target in 50% of the trials (day 15), he was still unable to retrieve the food following these successful reaches. 50% success on food retrieval occured by day 21, at which time the performance on goal-reaching had already stabilized. This difference in the progress of recovery was again apparent following a subsequent cortical lesion, where both performances (target reaching, food retrieval) were worse than following the lesion in isolation. Successful retrieval following the second lesion was not the result of a recovered precision grip: instead the monkey pushed several fingers into the tube, once on target, and used a raking movement. Figure 8B shows that removal of the sensory cortex alone had a much lesser effect on goal-reaching or hand movements. The distal performance of monkey E never recovered probably because in this case the cortical lesion had encroached upon the motor cortex (see inset, Fig. 8B). A secondary cerebellar lesion produced severe deficiencies and for three or four months abolished the ability to retrieve food from the tube.

Discussion

The results from all behavioral tasks showed that cerebellar deficiencies were invariably more severe than deficiencies resulting from sensory cortical lesions. The distal deficits appeared more disabling than the proximal deficits, since the distal recovery lagged the proximal recovery. This ist consistent with other observations (Growdon et al. 1967; Goldberger and Growdon 1973). Impaired motor performances were primarily the result of hypermetria, ataxia and loss of independent finger movements. These deficiencies were only observed after lesions of the anterior part of the deep nuclear complexes. (Lesions of the posterior part of the deep nuclei produced postural disturbances). Obvious hypotonia was never observed (Aring and Fulton 1936). Cerebellar lesions were found to be differentially disruptive for slow and for fast motor adjustments, depending on the nature of the task. This finding differs from what used to be believed (Kornhuber 1971), namely that the cerebellum is primarily involved in fast, ballistic ("open-loop") type movements (see, however, also Brooks and Thach 1981; Beppu et al. 1985).

Impairment of skilled finger movements following cerebellar lesions has received relatively little attention in clinical and experimental studies, despite their explicit descriptions by Holmes (1922) and Growdon et al. (1967), Holmes emphasized the inability of his patients to perform independent finger movements. Instead his patients could only flex and extend their fingers together, not unlike the deficiencies observed following motor cortical or pyramidal tract lesions (Denny-Brown 1966; Lawrence and Kuypers 1968; Passingham et al. 1983). This symptomatic similarity following cerebellar and motor cortical injury supports the much older assumption that the motor cortex mediates cerebellar deficits in voluntary movements via the cerebello-thalamo-cortical route and that withdrawal of a facilitatory drive causes the disturbances which are typically seen (cf. Dow and Moruzzi 1958). More recent electrophysiological findings indeed showed that the outflow from the deep cerebellar nuclei exerts an excitatory influence on the motor cortex (Sasaki et al. 1976; Shinoda et al. 1985), the thalamic relay nuclei (Uno et al. 1970; Massion and Sasaki 1979) and the red nucleus (Tsukahara et al. 1975). The thalamic relay nuclei and the red nucleus (and for that matter any or all structures to which he cerebellum projects) could be involved in compensation. It is, however, the motor cortex's intimate involvement in the control of independent finger movements (Denny-Brown 1966) which makes it a good candidate for mediating and possibly compensating skilled motor performance.

The possibility that the cerebellum itself may compensate for partial loss of its tissue was recently raised (Kawaguchi et al. 1986). It was shown in kittens that cerebellar projections to anterior brain

structures displayed substantial sprouting when their contralateral counterparts were interrupted. In the light of the present findings in the adult monkey it would, however, appear that recovery of motor function occurs in extracerebellar structures, since a cerebellar lesion did not affect recovered motor performances following an earlier lesion on the contralateral side.

The present study has shown that the sensory cortex may be added to the small number of other structures previously implicated in recovery of function following cerebellar lesions (see introduction). Lesioning the sensory cortex secondarily to a cerebellar lesion decompensated recovery from proximal and distal deficits. Similarly, removal of the sensory cortex prior to a cerebellar lesion severely affected recovery from cerebellar deficiencies. In contrast, secondary lesions of a number of other sites, such as various frontal and parietal cortical association areas (Aring and Fulton 1936; Carrea and Mettler 1947) or descending pathways (Carpenter and Correll 1961; Growdon et al. 1967), lead to no such decompensation. Thus, the actions of sensory cortex lesions are not non-specific, are not merely due to removal of additional amounts of tissue ("mass action", Lashley 1933).

That sensory cortex has the inherent capability for mediating compensatory actions has recently been shown by Asanuma and coworkers (1984, 1985). These authors showed that recovery from motor deficits following dorsal column lesions occurred as long as the sensory cortex was intact (and received spinothalamic input). When it was removed or when its projection to the motor cortex was severed, recovery from dorsal column lesions was abolished (Asanuma and Arissian 1984). In a parallel study, sensory cortical input to motor cortex was found to be enhanced 2–3 weeks after removal of another input to motor cortex (Asanuma et al. 1985). These findings were taken to indicate that the compensatory actions were mediated via the motor cortex, presumably involving strengthening and reorganizing the cortico-cortical projections from the sensory to the motor cortex. Involvement of sensory cortex in recovery would suggest that sensory feedback and active touch are essential components in the process of compensation from the motor deficits. Indeed, this suggestion receives support from the older studies on compensation following cerebellar lesions (see introduction). In these studies, the structures which, when lesioned, caused decompensation, were ones either carrying or processing sensory information.

Lesions of the structures which are known to decompensate recovery from cerebellar symptoms, notably the sensory cortex (present study), the dorsal column system (Carpenter and Correll 1961) and the premotor cortex (Aring and Fulton 1936), do not produce cerebellar symptoms or other severe and enduring motor disturbances (Travis and Woolsey 1956; Brinkman et al. 1978; Asanuma and Arissian 1984; Freund and Hummelsheim 1985; see, however, Alstermark et al. 1986 for the consequences of dorsal column lesions in the cat). Lesions of anterior brain structures which are major recipients of cerebellar input, notably the thalamic relay nuclei and the red nucleus, do produce cerebellar like symptoms (Ranish and Soechting 1976; Bornschlegl and Asanuma, unpublished). This raises the issue of whether the actual sites of compensation from cerebellar deficits are to be found in loci which are normally devoid of cerebellar input and destruction of which produces no cerebellar deficits, or in loci which have been deprived of their cerebellar inflow and lesions of which causes cerebellar disturbances. In the light of the work of Tsukahara and coworkers who deprived the red nucleus of its cerebellar input (Tsukahara et al. 1975) and of Asanuma and coworkers who deprived the motor cortex of its thalamocortical input (Asanuma et al. 1985), it would appear that the deprived structures might be the final loci of compensation, since synaptic rearrangements of remaining inputs were found to occur in the deprived structures regardless of whether the deprivation was induced directly (Tsukahara et al. 1975; Asanuma et al. 1985) or transneuronally (Tsukahara et al. 1982; Asanuma and Arissian 1984). Removal of an important input created synaptic vacancies in the deprived structures and it was found that these vacant sites became the targets of invasion by remaining inputs (Murakami et al. 1982; Ichikawa et al. unpublished). These findings suggest with respect to the present study that compensation of cerebellar deficits occurs in "deprived" structures, which receive normally also input from the sensory cortex. As has been discussed at length, a good candidate is the motor cortex. Another possibility is the set of thalamic relay nuclei which mediate cerebello-cortical influences and which may also receive input from the sensorimotor cortex (Frigyesi et al. 1972). Future experiments will clarify the relative roles of these candidate structures and thus provide a physiological basis for the recovery from cerebellar injury.

Acknowledgements. The author would like to thank Dr. Asanuma for continuous support of the study, Drs. Asanuma and Brink for reading and commenting on the manuscript, and Mrs. Arissian and Aubourg for excellent technical assistance. The study was supported by grant NS–10705.

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Received September 8, 1986 / Accepted November 26, 1986