Dissociation of Sensorimotor Deficits After Rostral Versus Caudal Lesions in the Primary Motor Cortex Hand Representation


Department of Molecular and Integrative Physiology, Landon Center on Aging, and Smith Mental Retardation Research Center, University of Kansas Medical Center, Kansas City, Kansas

Submitted 7 December 2004; accepted in final form 25 April 2005

INTRODUCTION

Primary motor cortex (M1) has traditionally been considered a motor structure because low-level electrical stimulation of M1 results in contraction of skeletal muscles. Corticospinal neurons reside in layer V of M1 and project to the spinal cord, where they synapse mono- and disynaptically onto motoneurons. M1 also has well-known connections with other motor areas such as premotor and supplementary motor cortex (Goschalk et al. 1984; Stepniewska et al. 1993). It has been known since at least the early 1950s (Malis et al. 1953) that M1 also receives somatosensory input, predominantly from the ventrolateral and ventral posterolateral nuclei of the thalamus (Ansumana and Mackel 1989; Holsapple et al. 1991; Horne and Tracey 1979; Lemon and Van Der Burg 1979; Shindo et al. 1995) and somatosensory cortex (Caria et al. 1997; Jones and Powell 1968; Porter and Sakamoto 1988; Stepniewska et al. 1993; Tokuno and Tanji 1993; Yumii and Ghez 1984). The structure, organization, and function of sensory inputs to motor cortex have been studied extensively, especially in cats. The cat motor cortex receives its primary thalamic somatosensory inputs from the ventrolateral (VL) nucleus (Ansumana and Mackel 1989). Additionally, somatosensory area 2 of the cat projects to motor cortex and appears to be important in motor skill learning (Jones and Powell 1968; Porter and Sakamoto 1988).

Based on neuroanatomic connections and neurophysiologic response properties, the M1 hand area appears to be segregated into caudal (M1c) and rostral (M1r) subregions. In nonhuman primates, M1c has been shown to be connected primarily with areas 3a, 1, the second somatosensory cortex (S2), and the parietal ventral area (PV), and to a lesser extent areas 2 and 3b and the ventral premotor cortex (PMV), whereas M1r is connected primarily with areas 2, S2, dorsal premotor cortex (PMD), PMV, and to a lesser extent areas 1, 3a, and posterior parietal cortex areas 5 and 7b (Stepniewska et al. 1993). Intracortical microstimulation studies in the squirrel monkey have shown that the M1c hand area contains predominantly digit and wrist representations. However, the M1r hand area also contains proximal representations (elbow, shoulder) that are interspersed with distal representations (Donoghue et al. 1992; Nudo et al. 1997). Neurons responding to cutaneous stimulation are segregated to the M1c forelimb representation, whereas neurons responding to proprioceptive stimulation are largely segregated to M1r, although some proprioceptive responses can be recorded throughout the hand representation (Boudreau and Smith 2001; Nudo et al. 1997; Picard and Smith 1992a, b; Rizzolatti et al. 1981; Strick and Preston 1982; Tanji and Wise 1981). Cutaneous receptive fields in M1 are considerably larger than analogous receptive fields in somatosensory area 3b (Humphrey et al. 1994; Strick and Preston 1982; Tanji and Wise 1981). Cutaneous and proprioceptive inputs have also been identified in M1 of humans using functional magnetic resonance imaging (fMRI) (Moore et al. 2000), although...
submodality segregation within M1 may be beyond the spatial resolution of current fMRI techniques. Additional functional, anatomical, and neurochemical differences between the M1r and M1c subregions have been described in humans (Geyer et al. 1996).

Somatosensory intracortical projections to motor cortex have been shown to be important in motor skill learning (Jones and Powell 1968; Pavlides et al. 1993). After motor cortex lesions, animals exhibit decreased motor skill on manual tasks (Castro-Alamancos and Borrell 1993, 1995; Denny-Brown 1950; Friell and Nudo 1998; Hoffman and Strick 1995; Kendall 1936; Nudo et al. 1996a; Ogden and Franz 1917; Rouiller et al. 1998; Travis 1955). However, relatively little attention has been given to changes in sensory aspects of motor control after lesions confined to M1. To examine the effects of focal inactivation of cat motor cortex on reaching and grasping movements, Martin and Ghez (1993) injected muscimol, a \( \gamma \)-aminobutyric acid-A (GABA\(_A\)) agonist, into either rostral or caudal subdivisions. Both injections resulted in slowed movements, but rostrolateral M1 inactivation uniquely caused integrative deficits in aiming of the paw (hypermetria) and impaired use of somatosensory cues and deficits in adaptive control (Martin and Ghez 1991; Martin and Ghez 1993). Caudal M1 inactivation did not impair performance until much later, when the muscimol may have spread to the rostral portion of M1. Thus because of the differential connections of rostral and caudal M1 (Yumiyama and Ghez 1984), lesions to different parts of motor cortex may result in specific deficits in sensorimotor integration and, possibly, the integration of proprioceptive cues and visual information regarding the location of the target (Martin and Ghez 1993). These results suggest that rostral and caudal M1 may play different roles in sensorimotor integration required for skilled movements. Sensorymotor impairments may correspond with the segregation of sensory input to M1.

Because motor outputs (Donoghue et al. 1992; Nudo et al. 1997) and proprioceptive and cutaneous inputs (Strick and Preston 1982; Tanji and Wise 1981) are, to some extent, segregated in the primate M1, similar dissociation of deficits should be produced by focal lesions in monkeys. Thus the present study was conducted to assess sensory, or sensory-dependent, motor deficits in reaching and grasping behavior after lesions confined to either the rostral or caudal portion of the M1 hand representation in squirrel monkeys. The results demonstrate that aiming errors, similar to hypermetria in cats, result from lesions in primate rostral M1, i.e., the region receiving primarily proprioceptive input. Another type of sensory-dependent deficit, similar to a sensory agnosia seen after somatosensory cortex lesions (Randolph and Semmes 1974), results from lesions in primate caudal M1, i.e., the region receiving predominantly cutaneous input. These findings are likely a result of the differential distribution of motor outputs and somatosensory inputs in M1.

**METHODS**

**Subjects**

Eight adult squirrel monkeys, six males and two females (Saimiri spp.; 600 to 1,200 g), were used in the present study. All procedures were approved by the University of Kansas Medical Center’s Institutional Animal Care and Use Committee. Each of the eight monkeys underwent the identical behavioral and neurophysiological procedures except for the exact site of the ischemic injury (see following text). The monkeys are identified as subjects 1 through 4 in the caudal lesion group and 5 through 8 in the rostral lesion group.

The general procedures were conducted in the following order: 1) hand-preference testing; 2) prelesion motor training and behavioral assessment; 3) neurophysiologic mapping and cortical lesion; 4) postinfarct behavioral training and assessment. These procedures are described in detail below.

**Hand-preference testing**

The hand preference of each animal was determined by testing on a modified Klüver board, a 24 × 7.6 × 1.8-cm rectangular Plexiglas apparatus containing five cylindrical wells evenly spaced on the top surface of the board. The diameters of the wells were 25, 19.5, 13, 11.5, and 9.5 mm. Each well was 5 mm deep and had a conical bottom. The Klüver board was attached to the front of the monkey’s cage, and the monkey reached between the cage bars to retrieve pellets from the food wells. Wells were in full view at all times. Monkeys were able to look between the cage bars and see each well clearly. This apparatus is identical to that used in previous studies in this laboratory for examining hand use in squirrel monkeys (Friell and Nudo 1998). Hand-preference testing consisted of 50 trials per day for 2 consecutive days. Each trial began when a 45-mg food pellet (Bio-Serv, Frenchtown, NJ) was placed randomly into one of the five wells. Each trial ended when the monkey retrieved the pellet and brought it inside the cage. During each trial, all food wells were visible to the monkey, as is the animal’s hand. All trials were recorded using a video camera (Sony Hi-8).

To determine hand preference, videotapes of trials were reviewed using a Hi-8 videocassette editing deck. The hand used in each reach was tallied and the hand used in over 50% of successful retrievals was considered the dominant hand (Nudo et al. 1992).

**Prelesion training and baseline assessment procedures**

After hand preference was determined, each animal was fitted with a mesh jacket that had a mesh sleeve enclosing the nondominant arm. The sleeve was closed at the distal end, constraining the animal from using its nondominant hand to retrieve pellets from the Klüver board. The animal was able to use this arm for climbing and balance. The sleeve was used to encourage the animals to use the dominant hand exclusively during prelesion and postlesion training.

One to 2 days after the monkey was fitted with the jacket, prelesion training began. Two training sessions were conducted daily, one in the morning, one in the afternoon. The evening before each session, food was removed from the cage. Each session consisted of 25 probe trials followed by 30 min of training. In each probe trial, a food pellet was placed into one well and the monkey retrieved the pellet. The order of wells used was randomly assigned for each probe trial. Five trials were conducted in each of the five wells (randomized block design).

After the probe trials were completed, pellets were placed into a training well. Pellets were presented as rapidly as they were retrieved. The training session ended after 30 min or after the monkey failed to retrieve a pellet after 5 min. On the 1st day of training, the largest well was the training well. On the following days, the training well (or wells) was (were) determined using the monkey’s performance on the previous day. If the monkey retrieved a predetermined high criterion (HC) number of pellets from the training well, the next smallest well was used as the training well on the following day. If the monkey did not retrieve the HC number of pellets, but retrieved more pellets than a predetermined low criterion (LC), the training well did not change on the following day. If the monkey retrieved a number of pellets lower than the LC, on the following day, 75% of trials would be introduced into the same well used on the previous day and 25% of trials would be introduced into the next largest well. The training...
series was complete when the monkey had retrieved the HC number of pellets out of the smallest well for 2 consecutive days. Monkeys required an average of 23.6 ± 8.9 days to complete prelesion training.

For most monkeys, the HC number of pellets was 600 and LC was 500. However, if the monkey weighed <700 g, the HC and LC were reduced to 500 and 400, respectively. Smaller animals were rarely able to eat 600 pellets per day, even when pellets were introduced into the largest well. After the monkey reached HC on 2 consecutive days on the smallest well, random probe trials were conducted over the next 2 days. Each day, two sessions of 50 trials were conducted.

All probe trial and training sessions were videotaped. Random probe trials on the final 2 days were used to define baseline performance (see following text).

**Intracortical microstimulation methods**

Within 3 days after prelesion training was complete, animals were sedated with ketamine (Fort Dodge Animal Health, Fort Dodge, IA), 20 mg/kg, administered intramuscularly. The trachea was intubated and the saphenous vein was catheterized. During the entire procedure, body temperature was maintained using a homeothermic blanket system; respiration rate, CO2 output, heart rate, and blood oxygen saturation were continuously monitored. Monkeys were placed into a stereotaxic frame and were given a mixture of nitrous oxide (750 ml/h), oxygen (250 ml/h), and halothane (1.5–3%) anesthetic. Under sterile conditions, a 1.5-cm² portion of skull over the precentral gyrus containing the hand representation of primary motor cortex (M1) was removed. The exposed dura was removed, and a plastic chamber was secured to the skull surrounding the opening. The chamber was filled with silicone oil (Applied Silicone, Ventura, CA) warmed to 38°C.

After the surgical opening was complete, nitrous oxide/halothane anesthesia was withdrawn, and ketamine (20 mg · kg⁻¹ · h⁻¹) combined with acepromazine (0.01 mg · kg⁻¹ · h⁻¹; Fort Dodge Animal Health) or diazepam (0.01 mg · kg⁻¹ · h⁻¹; Roche Laboratories, Nutley, NJ) was used for anesthesia during the neurophysiologic mapping procedure. The alkyphenol anesthetic propofol (15 mg · kg⁻¹ · h⁻¹) was administered intravenously; Abbott Laboratories, Chicago, IL) was used in one case (9652) during mapping because a stable anesthetic state could not be maintained with ketamine/acepromazine or ketamine/diazepam in that animal.

A photograph of the exposed cortex (and calibration bar) was taken with a digital camera and imported into a graphics program (Canvas v3.5 for Mac, Deneba, Miami, FL). A 250-µm² grid was superimposed onto the photograph of cortex. At each grid crosspoint, a 3.5 M NaCl-filled glass electrode, with a tip diameter of 10–25 µm, was inserted perpendicular to the cortex to a depth of 1,700–1,800 µm. Cathodal pulses (300 Hz) were then delivered at a rate of 1/s by a monophasic current source (Digitimer, Hertfordshire, UK). Each grid crosspoint was tested by passing a small current level, which was determined as the threshold current, and the evoked movement was documented. Movements of the digits, wrist, forearm, elbow, shoulder, and face were documented. Cortical microstimulation continued until a border of elbow, shoulder, and face representations or nonresponsive sites surrounded all movement representations of the digits and wrist. Prelesion maps contained about 300–350 sites and took 10–15 h to derive. Because the cerebral cortex of squirrel monkeys is relatively unconvoluted, the entire M1 hand area is exposed on an un fissured sector, allowing accurate derivation of two-dimensional topographic maps.

**Cortical lesion procedure**

After the motor map was completed, ketamine–acepromazine or ketamine–diazepam anesthesia was withdrawn, and halothane–nitrous oxide anesthesia was given. Based on the neurophysiologic mapping data, the distal forelimb (or hand) representation (the area consisting of digit, wrist, and forearm representations) was arbitrarily divided into rostral and caudal halves for the purpose of lesion creation. Although neurophysiologic procedures to more precisely define zones receiving primarily cutaneous (caudal) versus proprioceptive (rostral) afferents have previously been used in this laboratory, we used a more arbitrary method to define the rostral–caudal border for the following reasons: 1) Microstimulation mapping procedures are more reliable in defining the full extent of the M1 hand area, and thus are necessary for these studies. 2) Sensory mapping during the same surgical procedure would require a considerably longer period under anesthesia, potentially compromising the animal’s recovery. 3) Previous studies of submodality segregation in M1 suggested that the cutaneous–proprioceptive border is roughly located at 1/3 to 1/2 of the distance from the caudal limit to the rostral limit of the M1 hand area as defined by microstimulation mapping (Nudo et al. 1997; Tanji and Wise 1981). A cortical lesion involving 30–45% of the total M1 hand representation was produced within the rostral or caudal half of the hand representation (Fig. 1). The lesion was targeted to the largest contiguous region of hand representations within the rostral caudal half of the map. However, because digit, wrist, and forearm representations within M1 are interspersed (Donoghue et al. 1992; Nudo et al. 1997), it was not possible to restrict the lesion exclusively to digit representations.

Surface blood vessels supplying the targeted area of cortex were permanently occluded using microforceps connected to a bipolar coagulator. This method has been found to produce restricted ischemia and subsequent necrosis through all layers of cortex, avoiding white matter. The size of the lesions and the survivability of adjacent tissue are precise and reproducible (Nudo and Milikien 1996; Nudo et al. 1996a). After the ischemic lesion was made, the exposed cortex was observed for 30–60 min to monitor potential reperfusion of any blood vessels that had been occluded. If any reperfusion was observed, the blood vessel was recuterized. Once it was decided that significant reperfusion was not likely to occur, the brain was covered with gelfilm (Upjohn, Kalamazoo, MI), the bone flap was cemented in place with dental acrylic (Lang, Wheeling, IL), and the skin sutured. Local anesthetic (lidocaine; Abbott Laboratories) was applied to the incised skin. The animal was then removed from the halothane–nitrous oxide anesthesia, and then from the stereotaxic frame, and placed in a temperature-controlled recovery chamber. When the monkey was fully alert and active (12 to 24 h), it was returned to its home cage.

**Postlesion testing procedure**

After the infarct, 2 days of probe trials (50 trials/day) were conducted over the first 2 days that the animal was able to perform pellet retrievals (typically days 3–6 postinfarct) to assess the impact of the lesion.

After the postlesion hand preference had been documented, monkeys were fitted with a jacket that restrained the arm ipsilateral to the lesion (same arm that was restricted prelesion). Thus the monkeys were required to use their impaired hand to retrieve pellets. The postlesion testing procedure was identical to the prelesion training procedure (probe trials on all wells, followed by testing on one well for 30 min; see above). Monkeys required an average of 26.3 ± 6.3 days to complete postlesion testing.

**Histological procedure**

After the postlesion training procedure was complete, animals were deeply anesthetized with a lethal dose of Euthasol (Delmarva Labs,
Doppler measurements have been shown to accurately identify the postlesion verified the location and permanence of the lesions. Laser infarcted tissue immediately after the lesion, 1 h post lesion, and 1 mo al. 2003; Nudo and Milliken 1996; Nudo et al. 1996a; Plautz et al. verified in subsequent mapping studies (Friel and Nudo 1998; Frost et al. 2000). Photographs of M1 before and 1 mo destroyed by the lesion (in square millimeters) was estimated (Friel these estimation methods, the areal extent of the cortical surface determination of the cortical territory spared by the lesion. Using microstimulation penetration. Stimulation was conducted at about 1,750 μm below the surface (layer V), using currents ±30 μA. Colors indicate movement evoked using threshold current levels. Red = digit; green = wrist or forearm; red + green = digit + wrist/forearm; blue = elbow or shoulder; black = no response at 30 μA. Yellow outline indicates boundary of hand representation (i.e., digit, wrist, and forearm). Black outline indicates proximal representations excluded within hand representation. Red outline indicates location of ischemic lesion. After occlusion of surface vasculature, the tissue within the targeted area became blanched, and eventually was reduced in size as a result of necrosis. Nonresponsive sites along the caudal boundary of the M1 hand representation typically correspond to area 3a (Nudo and Milliken 1996). M, medial; C, caudal. Midlothian, VA) and perfused with 0.9% phosphate-buffered saline followed by 4% phosphate-buffered paraformaldehyde fixative. In some cases, the brain was removed and motor cortex was cut into 50-μm parasagittal sections. The area 3a–area 4 border was defined cytoarchitectonically and the location of the lesion was verified. In previous studies in this laboratory, this cytoarchitectonically defined border has been shown to be well correlated with the neurophysiologically defined border of M1 based on intracortical microstimulation at a maximum current of 30 μA (Nudo and Milliken 1996). Thus these histological results are not repeated here.

This histological procedure was useful in verifying that the lesion extended through all layers of cortex, but cannot be used to accurately define the extent of the lesion. After several weeks’ survival after the lesion, substantial necrosis and scavenging of the tissue within the lesion occur. Therefore less-direct methods were used to estimate lesion size. Prelesion and postlesion digital photographs were used to estimate lesion area. Immediately after the lesion was made, the damaged cortex became blanched in color. The lesion could be easily seen in 1-mo postlesion photographs. Postlesion photographs of intact vasculature were superimposed onto prelesion photographs, enabling the determination of the cortical territory spared by the lesion. Using these estimation methods, the areal extent of the cortical surface destroyed by the lesion (in square millimeters) was estimated (Friel and Nudo 1998; Friel et al. 2000). Photographs of M1 before and 1 mo after a lesion are shown in Friel et al. (2000). The size and extent of lesions are highly reproducible, verified neurophysiologically, and re-verified in subsequent mapping studies (Friel and Nudo 1998; Frost et al. 2003; Nudo and Milliken 1996; Nudo et al. 1996a; Plautz et al. 2003). Additionally, in some cases laser Doppler measurements of infarcted tissue immediately after the lesion, 1 h post lesion, and 1 mo postlesion verified the location and permanence of the lesions. Laser Doppler measurements have been shown to accurately identify the lesion (Frost et al. 2003).

Analysis of motor performance

Videotapes of probe trial sessions during the prelesion and postlesion periods were examined in slow motion on a Hi–8 videocassette editing deck (Sony). Probe trials, rather than training trials, were used in the analysis because probe trials were conducted on every well, each day, whereas training trials were conducted on only one to two wells per day. Several measures of motor performance were tallied:

FINGER FLEXIONS PER RETRIEVAL. This parameter was defined as the total number of times the monkey flexed its fingers while the fingers were in the testing well, divided by the total number of successful retrievals. Finger flexions per pellet retrieval were averaged for each day of testing. Although data were collected from all five testing wells, results from the smallest well are presented (10 trials/day) because retrieval from the smallest well required the greatest skill, and resulted in the greatest postlesion deficits. Motor deficits were not evident on the largest well after the lesion.

MOTOR PERFORMANCE INDEX. Finger flexions per retrieval over the 2 days of testing before the lesion were averaged to yield a baseline measure of prelesion motor performance for each animal. Daily postlesion finger flexions per retrieval for each animal were divided by that animal’s baseline finger flexions per retrieval to generate a normalized motor performance index (MPI).

DURATION OF RETRIEVAL. This parameter was defined as the time beginning when the distal tip of the monkey’s hand crossed through the plane parallel to the cage bars toward the Kluver board until the time the distal tip of the monkey’s hand crossed the plane parallel to the cage bars when the hand was retracted into the cage after a successful retrieval. Duration of retrieval was measured in milliseconds every other day for ten probe trials on the smallest well. Duration of retrieval data were collected from a sample of trials during the periods from 2 to 5 days before the lesion and from 1 to 30 days after the lesion.

Assessment of somatosensory-related deficits

CUTANEOUS SENSORY ERROR. Videotapes of probe trials from all wells were reviewed in slow motion. A cutaneous sensory error was defined as an event in which the animal failed to grasp the pellet, but removed its hand from the testing well, brought the hand to or near the mouth, and then visually inspected the empty palm. An example of a cutaneous sensory error is shown in the supplementary video file frielcutaneous.mov. An example of a normal retrieval is shown in the supplementary video file frielnormal.mov. These errors are tentatively called cutaneous sensory errors here because they are similar to errors made after somatosensory cortex lesions in monkeys, and possibly clinically related to a type of sensory agnosia (Pavlides et al. 1993; Xerri et al. 1998). Subsequent to such an error, the monkey typically reached back into the well and made additional attempts to retrieve the pellet. It was possible for the monkey to make more than one
cutaneous sensory error per trial. A trial was defined as one successful pellet retrieval. Errors per trial were computed for each day of testing.

**AIMING ERROR FREQUENCY.** Videotapes of probe trials from all wells were reviewed in slow motion. An aiming error was defined as an event in which the animal reached toward the well and touched the top surface of the Klüver board with its fingers before inserting them into the well. A trial was defined as one successful pellet retrieval. An example of an aiming error is shown in the supplementary video file frielaiming.mov. Errors per trial were computed for each day of testing.

### Determination of relative lesion location

Maps of the M1 hand representation have irregular shapes (Fig. 1). Also, the shape and size of the M1 hand representation is highly variable between individual animals (Nudo et al. 1992, 1996b; Plautz et al. 2000). Thus to quantify the location of the lesion in the M1 hand representation in a standard way, a measure of relative lesion location was defined for the present study.

First, the rostral–caudal length of the hand representation was measured and the midpoint identified. Then the distance from the rostral border of the hand representation to the lesion midpoint was measured. The relative lesion location was determined using the following equation

\[
\text{Relative lesion location} = \frac{\text{Distance from rostral border of map to lesion midpoint}}{\text{Rostral–caudal length of map}}
\]

The computed value was a number between zero and one, with values near zero being located more rostrally and values near one being located more caudally.

### Statistical analyses

Because behavioral performance in an individual animal was often quite variable from day to day, daily behavioral measures were averaged to yield the weekly motor performance index, duration of retrieval, cutaneous sensory error rate, and aiming error rate. ANOVA was used to compare all weeks and Fisher’s least-significant difference (LSD) post hoc statistical measures were computed to determine group differences in behavioral results by week.

Nonparametric correlation analyses (Spearman coefficient) were performed to test the correlation of each behavioral measure on wk 1 postlesion with the relative location of the lesion. Analyses were restricted to wk 1 postlesion because the most marked behavioral deficits were seen in wk 1. Parametric analyses (Z-test) were performed to test the correlation of each behavioral measure on wk 1 postlesion with the size of the lesion and size of the representational areas destroyed by the lesion. These two different tests were used to test the correlation of behavioral measures to a relative measure (relative location of the lesion; Spearman coefficient) and to absolute measures (flexions per retrieval, cutaneous sensory error, aiming error; Z-test).

### RESULTS

#### Motor performance before and after lesion

Changes in the motor performance index (MPI) on the smallest well after an M1c lesion are shown in Fig. 2, A and B. Daily MPI results were pooled into 5 wks. Figure 2A summarizes average data by week. ANOVA indicated a significant effect of week \((F=4.29, P=0.018)\). During wk 1 after the lesion, the MPI increased significantly beyond prelesion performance \((P=0.003; \text{Fisher’s protected least-significant difference (PLSD)}, \text{indicating a decline in skill. During wk 2 after the lesion, the MPI returned to the normal range (P=0.290). During wk 3 after the lesion, the MPI again increased significantly beyond the prelesion measure, indicating a decline in skill (P=0.037). During wk 4 after the lesion, the MPI again returned to the normal range (P=0.737). Figure 2B depicts daily data for an individual animal. Three of the four animals in the M1c lesion group showed a two- to threefold increase in MPI in wk 1 after the lesion; for the fourth animal, MPI increased by 56%. Two of the four animals displayed a significant relapse in motor skill during postlesion wk 3. By postlesion wk 4, all MPI measures had returned to near-prelesion levels. Changes in the MPI after an M1r lesion are shown in Fig. 2, C and D. Figure 2C summarizes average data by week. ANOVA indicated that there was no significant effect
of week on the MPI ($F = 2.58, P = 0.091$). During the 4 wks after the lesion, the MPI remained within the normal range for each animal. Figure 2D depicts daily data for an individual animal.

Figure 3a summarizes average duration of retrieval by week, measured in milliseconds, after a caudal lesion. ANOVA indicated a significant effect of week ($F = 5.50, P = 0.010$), roughly paralleling the pattern seen for the MPI. During wk 1 after the lesion, the retrieval duration increased significantly beyond prelesion performance time ($P = 0.004$; Fisher’s PLSD). During wk 2 after the lesion, the retrieval duration returned to the normal range ($P = 0.468$) and remained within the normal range during wk 3 and wk 4 postlesion. Figure 3B depicts data for an individual animal. Changes in the duration of retrieval after a rostral M1 lesion are shown in Fig. 3, C and D. Figure 3C summarizes average data by week. ANOVA indicated that there was no effect of week on the duration of retrieval ($F = 0.28, P = 0.885$). During the 4 wks after the lesion, the duration of reach remained within the normal range for each animal. Figure 3D depicts data for an individual animal.

Somatosensory-related deficits before and after lesion

**CUTANEOUS SENSORY ERRORS.** Daily measures of cutaneous sensory errors per trial on all wells were grouped by week. Because most of the prelesion values were near zero, the distribution of data was not normal. Thus nonparametric analyses were performed on the data.

Changes in the cutaneous sensory error rate after an M1c lesion are shown in Fig. 4, A and B. There was a statistically significant effect of week on cutaneous sensory error rate ($H = 13.5, P = 0.009$; Kruskal–Wallis). Before a caudal lesion, monkeys rarely made cutaneous sensory errors. During wk 1 after the caudal lesion, all monkeys made many cutaneous sensory errors, an average of 1.53 errors per pellet retrieval. This was significantly greater than the prelesion error rate ($q = 3.5, P < 0.005$; Tukey post hoc analysis). The cutaneous sensory error rate was no longer statistically significant during wk 2 postlesion and remained statistically indistinguishable from the prelesion error rate through wk 4 postlesion.

Changes in the cutaneous sensory error rate after an M1r lesion are shown in Fig. 4, C and D. There was no statistically significant effect of week on cutaneous sensory error rate ($H = 2.6, P = 0.635$; Kruskal–Wallis). Before the lesion, monkeys rarely made cutaneous sensory errors. After the rostral lesion, the cutaneous sensory error rate remained within prelesion levels. For one animal in the M1r group, the cutaneous error rate increased from 0.05 to 0.17 error/trial after the lesion (monkey 4). Incidentally, the lesion in this animal was located more caudally (yet still confined to the rostral half of M1) than that of the other animals in this group. The cutaneous sensory error rate for the other three animals in this group did not change after the rostral lesion.

**AIMING DEFICITS.** Changes in the aiming error rate on all wells after an M1c lesion are shown in Fig. 5, A and B. There was no statistically significant effect of week on aiming error rate ($H = 3.24, P = 0.198$). Before a caudal lesion, monkeys rarely made aiming errors. During wk 1 after the M1c lesion, aiming error rate increased to 0.24 error/trial, although this increase was not statistically significant because of high individual variability. Of the four animals in this group, one showed a large increase in aiming errors (rate of 0.67 error/trial, monkey 5), whereas two made aiming errors at a rate of about 0.1 error/trial (monkeys 6 and 7). The fourth animal made no aiming errors after the lesion (monkey 8). During wk 2 through wk 4 after the M1c lesion, the aiming error rate remained within prelesion levels.

Changes in the aiming error rate after an M1r lesion are shown in Fig. 5, C and D. There was a statistically significant effect of week on aiming error rate ($H = 13.5, P = 0.009$). Before an M1r lesion, monkeys rarely made aiming errors. During wk 1 after the M1r lesion, monkeys made an average of 0.27 error/trial. This was significantly greater than the prelesion error rate ($q = 2.8, P < 0.05$). Each of the animals in the
M1r lesion group showed a ten- to thirtyfold increase in the number of aiming errors after the lesion. During wk 2 after the M1r lesion, monkeys made an average of 0.20 error/trial. This rate approached statistical significance (q = 2.7, P < 0.051). The aiming error rate returned to prelesion levels during wk 3 postlesion and remained within normal range through wk 4 postlesion.

**Group comparison of lesion size**

The relative lesion size was calculated by dividing the absolute lesion size (in square millimeters) by the absolute size of the hand representation (in square millimeters). There were no statistical differences between the groups with respect to either the absolute (t = 1.53, P = 0.177) or relative (t = 1.78, P = 0.125) lesion size.

**Group comparison of quantitative measures of lesion location**

By definition, lesions in the M1r versus M1c lesion groups were made in different physical locations within the M1 hand representation. Because, in many animals, M1r and M1c contained different proportions of digit, wrist/forearm, and proximal representational area, comparisons of the areas of specific movement representations contained within the lesion were made between the M1r and M1c lesion groups. Table 1 summarizes the areal contents of the lesion in each group of

**FIG. 4.** Cutaneous sensory errors per trial before and after an M1 lesion. A: cutaneous sensory error rate in weekly epochs before and after a lesion in M1c. Error rate was near zero before the lesion, but increased significantly during wk 1 postlesion, then returned to baseline levels during wk 2 through wk 4 postlesion (**P < 0.01). B: daily error rate for one representative animal before and after a lesion in M1c. C: cutaneous sensory error rate in weekly epochs before and after a lesion in M1r. Error rate was near zero before lesion and did not significantly increase during the postlesion period. D: daily error rate for one representative animal before and after a lesion in M1r.

**FIG. 5.** Aiming errors per trial before and after an M1 lesion. A: aiming error rate in weekly epochs before and after a lesion in M1c. Error rate was near zero before the lesion and did not increase during the postlesion period. B: daily error rate for one representative animal before and after a lesion in M1c. C: aiming error rate in weekly epochs. Error rate was near zero before a lesion in M1r. During wk 1 postlesion, aiming error rate was statistically higher than the prelesion error rate. During wk 2 postlesion, aiming error rate was nearly significantly different from the prelesion error rate. Aiming error rate returned to baseline levels during wk 3 and wk 4 postlesion (*P < 0.05; †P < 0.051). D: daily error rate for one representative animal before and after a lesion in M1r.
TABLE 1. Lesion locations

<table>
<thead>
<tr>
<th></th>
<th>Caudal Lesion Group</th>
<th>Rostral Lesion Group</th>
<th>Statistical Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average</td>
<td>Range</td>
<td>SD</td>
</tr>
<tr>
<td>Amount of representational area in lesion (mm²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit</td>
<td>2.32</td>
<td>2.00–2.82</td>
<td>0.36</td>
</tr>
<tr>
<td>Wrist/forearm</td>
<td>0.26</td>
<td>0.06–0.47</td>
<td>0.17</td>
</tr>
<tr>
<td>Proximal</td>
<td>0.18</td>
<td>0.06–0.26</td>
<td>0.09</td>
</tr>
<tr>
<td>Proportion of lesion containing representational area*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit</td>
<td>0.72</td>
<td>0.65–0.81</td>
<td>0.08</td>
</tr>
<tr>
<td>Wrist/forearm</td>
<td>0.08</td>
<td>0.02–0.12</td>
<td>0.05</td>
</tr>
<tr>
<td>Proximal</td>
<td>0.05</td>
<td>0.02–0.08</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*Because some lesions contained nonresponsive area, the proportion of lesion containing digit, wrist/forearm, and proximal area does not add to 1.

animals. The proportion of the lesion containing digit, wrist/forearm, and proximal representational areas is summarized for each case in Table 2. Lesion location was measured by the area of representation within the lesion (in square millimeters) and by the proportion of the lesion containing a representation. Representational areas within the lesion were defined as the prelesion motor mapping responses derived within the area that was later destroyed by the lesion.

Statistically significant differences were found between the two groups with respect to the absolute and proportional amount of digit ($P < 0.0001$) and wrist/forearm ($P < 0.02$) representational area in the lesion. There was a statistically significant difference in the proportional amount of proximal area in the lesion between the two groups ($P = 0.034$), and the difference between the two groups with respect to the absolute amount of proximal representational area destroyed by the lesion approached statistical significance ($P = 0.051$). Thus M1c lesions involved relatively more digit, but fewer wrist/forearm and fewer proximal, representations compared with M1r lesions. This variable stemming from the normal distribution of movement representations within the M1 hand area is considered in detail in the Discussion section.

Relationship between behavioral deficits and lesion size

The technique used to make lesions in the present study allows for lesions to be targeted to a very specific location within the M1 hand representation. Although this technique is very precise, there was small, although not statistically significant variability in the sizes of the lesions in different groups of animals, resulting from individual variability in vascular patterns in M1 (M1c: 45.5 ± 15.5%; M1r: 30.2 ± 5.3% relative lesion size; $t = 1.79, P > 0.16$).

TABLE 2. Proportion of lesion containing representational areas

<table>
<thead>
<tr>
<th>Case</th>
<th>Digit</th>
<th>Wrist/Forearm</th>
<th>Proximal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.12</td>
<td>0.61</td>
<td>0.13</td>
</tr>
<tr>
<td>2</td>
<td>0.03</td>
<td>0.10</td>
<td>0.68</td>
</tr>
<tr>
<td>3</td>
<td>0.13</td>
<td>0.39</td>
<td>0.41</td>
</tr>
<tr>
<td>4</td>
<td>0.14</td>
<td>0.58</td>
<td>0.27</td>
</tr>
<tr>
<td>5</td>
<td>0.81</td>
<td>0.07</td>
<td>0.02</td>
</tr>
<tr>
<td>6</td>
<td>0.67</td>
<td>0.02</td>
<td>0.05</td>
</tr>
<tr>
<td>7</td>
<td>0.65</td>
<td>0.10</td>
<td>0.08</td>
</tr>
<tr>
<td>8</td>
<td>0.72</td>
<td>0.11</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Relationship between behavioral deficits and quantitative measures of lesion location

Because these experiments demonstrate different behavioral deficits in groups of animals that received an M1r versus an M1c lesion, correlation analyses were performed to determine the relationship between the location of the lesion and postlesion behavioral measures. Lesion location was measured in two different ways: 1) the relative position of the lesion on the rostral-caudal axis (see METHODS), i.e., the physical location of the lesion; and 2) the areas of specific movement representations contained within the lesion, i.e., the functional location of the lesion.

Correlations between relative lesion location and behavioral measures are shown in Fig. 6. The wk 1 postlesion average of three different behavioral measures—motor performance index, cutaneous sensory errors per trial, and aiming errors per trial—are plotted against the relative lesion location measurement. The Spearman correlation between each behavioral result and the relative lesion location was calculated.

There was a statistically significant correlation between the relative lesion location and the wk 1 postlesion motor performance index ($Z = 2.14, P = 0.032, R = 0.81$). More rostral lesions resulted in a smaller motor deficit after the lesion, whereas more caudal lesions resulted in a larger motor deficit after the lesion.

There was also a statistically significant correlation between the relative lesion location and the average wk 1 postlesion cutaneous sensory error rate ($Z = 2.14, P = 0.032, R = 0.81$). More rostral lesions resulted in fewer cutaneous sensory errors per trial, whereas more caudal lesions resulted in a greater number of cutaneous sensory errors per trial.

The correlation between the relative lesion location and the average wk 1 postlesion aiming error rate was not statistically significant ($Z = -1.26, P = 0.208 R = -0.48$).

A second analysis of lesion location (i.e., the functional location of the lesion) was performed to determine a possible relationship between the amount of representational area of specific joints destroyed by the lesion and behavioral deficits. Table 3 shows the correlations between behavioral deficits and the amount of digit, wrist/forearm, proximal, and wrist/forearm+proximal (nondigit) representational area destroyed by the lesion. Significant correlations were found between wk 1 motor performance index and the absolute amounts of digit ($P = 0.037$) and nondigit ($P = 0.005$) representational area in the lesion. Significant correlations were also found between wk...
1 motor performance and the proportion of the lesion containing digit ($P = 0.005$) and nondigit ($P = 0.002$) areas. That is, performance was worse in monkeys with more digit and less nondigit area in the lesion. Significant correlations were also found between cutaneous sensory error rate and the proportion of the lesion containing digit ($P = 0.037$) and nondigit ($P = 0.023$). That is, the cutaneous sensory error rate was greater in monkeys with more digit and less nondigit area in the lesion. No significant correlations were found between wk 1 aiming error rate and wrist/forearm, proximal, or combined wrist/forearm + proximal representational areas. Proportions of lesions containing digit, wrist/forearm, and proximal areas for each monkey are summarized in Table 2.

Because lesions in the two groups of animals contained different amounts of digit and wrist/forearm representational area (Table 1), correlations were performed between functional lesion location and behavioral outcomes within groups to assess the correlation between the two measures independent of group differences, although the $n$ per group is low ($n = 4$). Z-scores and significance values are summarized in Table 4. Within the M1c lesion group, there were no statistically significant correlations between the proportions of any movement representation contained in the lesion with behavioral deficits. Within the M1r lesion group, there were no statistically significant correlations between the proportions of digit representations contained in the lesion with wk 1 postlesion motor performance. There were significant correlations between the proportion of wrist/forearm and proximal representations contained in the lesion with wk 1 postlesion motor performance. There were no statistically significant correlations between the proportions of any movement representation contained in the lesion with aiming or cutaneous sensory deficits.

**DISCUSSION**

The present study in nonhuman primates provides evidence that the M1 hand representation can be divided into rostral (M1r) and caudal (M1c) subregions based on differential behavioral effects of focal lesions. The behavioral dissociation appears to be correlated with at least two properties of M1 organization: 1) the segregation of cutaneous and proprioceptive inputs to M1c and M1r, respectively, as reported in other studies (see following text); and 2) the prevalence of sites in M1c at which electrical stimulation evokes movement of digits, as opposed to movements of wrist, forearm, and shoulder.

Structural and functional segregation within primary motor cortex (M1) has long suggested that the M1r and M1c subregions may serve somewhat different functions. Because in most primate species, M1c is buried in the anterior bank of the central sulcus, selective injury or inactivation has rarely been attempted. However, observations of M1 stroke patients (Kim 2001; Schieber 1999) and M1 inactivation in monkeys (Brochier et al. 1999; Fogassi et al. 2001; Kubota 1996; Schieber and Poliakov 1998) have demonstrated that caudal inactivation results in selective deficits in individuation of finger movements and relative preservation of reaching.

In certain South American primates, such as the squirrel monkey (and owl monkey), the frontoparietal cortex is relatively smooth and unfissured. The central sulcus is quite shallow (1–2 mm), and typically lies immediately caudal to the M1 hand representation. This species provides an excellent model to dissociate the effects of M1r and M1c lesions in detail.
Aiming error rate. The negligible change in the MPI or the error rate. However, monkeys displayed a significant increase also no statistically significant change in cutaneous sensory nor the duration of retrieval changed significantly. There was occurs and resolves are not understood.

et al. 2001). The mechanisms by which the motor skill relapse in the rat and expand again after the relapse (Goertzen 1993) identified differences in cat reaching behavior after M1r or M1c lesions in squirrel monkeys.

In the present study, M1c lesions resulted in an increase in the MPI, indicating a decrease in manual motor skill. M1c lesions also resulted in an increased duration of retrieval. Monkeys displayed a behavior suggestive of a cutaneous sensory deficit. That is, monkeys visually inspected the palm during a pellet retrieval, strikingly similar to observations in monkeys after somatosensory cortex lesions (Pavlides et al. 1993; Randolph and Semmes 1974; Xerri et al. 1998). M1c lesions did not result in any statistically significant increase in aiming error rate during the entire month of postlesion rehabilitative training.

After M1c lesions, the MPI increased beyond prelesion levels in wk 1, then returned to prelesion levels in wk 2. In wk 3, the MPI relapsed to beyond prelesion levels before returning to prelesion levels in wk 4. This motor skill relapse was seen in two of the four animals and has been discussed in a previous study (Nudo et al. 1996a). A similar relapse has been seen after M1 lesions in the rat. Motor maps shrink during the time of the relapse in the rat and expand again after the relapse (Goertzen et al. 2001). The mechanisms by which the motor skill relapse occurs and resolves are not understood.

In contrast to M1c lesions, after M1r lesions, neither the MPI nor the duration of retrieval changed significantly. There was also no statistically significant change in cutaneous sensory error rate. However, monkeys displayed a significant increase in aiming error rate. The negligible change in the MPI or the duration of retrieval in monkeys with M1r lesions appears counterintuitive because the size of the lesions in the two groups was similar (and was in fact larger in the M1r group). However, the monkeys typically made aiming errors by over-reaching. The fingers were then pulled back over the surface of the board to be inserted into the well. The time to accomplish a retrieval using this strategy only minimally affected reach retrieval times.

Aiming and cutaneous sensory error rates returned to normal levels a few weeks after an M1r or M1c lesion, respectively. It is possible that monkeys quickly adopt compensatory strategies that enable them to retrieve pellets efficiently, despite a sensory-related motor deficit (Friel and Nudo 1998). One plausible mechanism of compensation could be the use of visual feedback. Based on anecdotal observations, we suspect that monkeys gradually come to rely more heavily on visual guidance in the pellet retrieval task during the course of recovery. As recovery progressed, monkeys tended to look at the training well and their hand during pellet retrieval. Monkeys may rely heavily on visual information to assist in the accurate placement of the hand in the well and/or in verification that the pellet has been retrieved.

Previous studies demonstrating differential behavioral effects of lesions in motor cortex

Deficits in reaching and grasping after motor cortex lesions have also been demonstrated in the cat. Martin and Ghez (1993) identified differences in cat reaching behavior after

<table>
<thead>
<tr>
<th>Proportion of lesion containing representational area</th>
<th>Motor Performance Index</th>
<th></th>
<th></th>
<th>Cutaneous Sensory Error Rate</th>
<th></th>
<th>Aiming Error Rate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudal lesion group: wk 1 postlesion average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit</td>
<td>Z = 0.14; P = 0.888</td>
<td>Z = -0.26; P = 0.794</td>
<td>Z = -0.53; P = 0.600</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist/forearm</td>
<td>Z = -0.12; P = 0.907</td>
<td>Z = 1.77; P = 0.076</td>
<td>Z = 0.77; P = 0.442</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>Z = -0.06; P = 0.956</td>
<td>Z = -0.19; P = 0.852</td>
<td>Z = 1.02; P = 0.311</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rostral lesion group: wk 1 postlesion average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit</td>
<td>Z = 0.99; P = 0.323</td>
<td>Z = 0.30; P = 0.767</td>
<td>Z = 0.35; P = 0.729</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist/forearm</td>
<td>Z = 2.17; P = 0.030</td>
<td>Z = 0.22; P = 0.830</td>
<td>Z = 0.57; P = 0.567</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>Z = -2.35; P = 0.019</td>
<td>Z = -0.32; P = 0.752</td>
<td>Z = -0.73; P = 0.467</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cell values indicate results of Z-test on measures in corresponding row versus column.
rostral versus caudal M1 inactivations. All inactivations increased movement time and produced postural changes. Rostrolateral inactivation produced hypermetric aiming errors, grasping deficits, and an inability to correctly reach trajectories to avoid an obstacle. Rostromedial inactivation produced hypometric aiming errors, likely a consequence of muscle weakness, but not grasping impairments or deficits in trajectory adaptation. Caudal inactivation did not discernibly impair aiming, grasping, or trajectory adaptation immediately after the inactivation. The authors attribute these differences to vari- ances in the distribution of representational territory of different muscle groups (i.e., more proximal representations in the rostral areas) and suggest that rostrolateral motor cortex may be an important site for processing and integrating sensorimotor information. The present study supports this hypothesis.

The present study demonstrates a characteristic behavioral deficit after lesions to caudal M1. Such a deficit was not found in the cat (Martin and Ghez 1993), possibly explained by anatomical differences between cats and monkeys. Both cat and monkey paws possess glabrous pads, but the cat paw possesses much more hair than the squirrel monkey hand. It is possible that cats did not demonstrate cutaneous sensory errors after caudal M1 inactivations because hair receptors may have provided additional sensory cues during retrieval. Additionally, the target food reward in the cat studies was much larger, relative to the size of the cat paw, than the target pellets used in the present study, relative to the size of the monkey hand. Larger food rewards would provide a greater area of sensory activation on the paw, including hairy skin, potentially providing sufficient sensory feedback for the cat to detect the presence of the food in the paw. Thus the results from caudal M1 inactivations (Martin and Ghez 1993) and the present results are not incongruous, but may rather reflect differences in the animal models used.

Relationship between differential behavioral effects of lesions and motor output organization

The present results indicate that in prelesion motor maps in this study, M1c contained proportionately more area devoted to digit movements compared with M1r; M1r contained more area devoted to wrist/forearm and proximal representations. Thus the proportion of digit area contained in the lesion was positively correlated with the motor performance index and cutaneous sensory error rate between lesion groups. The proportion of wrist/forearm area contained in the lesion was negatively correlated with the cutaneous sensory error rate.

It is possible that the different behavioral effects of rostral versus caudal lesions are, at least in part, explained by the differences in amount of digit, wrist/forearm, and proximal representational area destroyed by the lesion. Perhaps caudal lesions result in manual motor deficits because cortical lesions destroy a greater proportion of digit area than rostral lesions. Conversely, rostral lesions produce aiming deficits because rostral lesions destroy a greater proportion of wrist, forearm, elbow, and shoulder area, a hypothesis that was suggested in a previous cat study (Martin and Ghez 1993). Additionally, motor cortical activity associated with finger movements appears to be greatest in caudal M1 (Lemon et al. 1986, 1990). Long-duration microstimulation of M1c in macaques produces complex grasping movements suggestive of feeding movements (Graziano et al. 2002).

Relationship between the differential behavioral effects of lesions and segregation of somatosensory afferents in M1

The effects of small lesions in M1 appear to be correlated with the distribution of motor outputs. However, one additional attribute of M1 organization—the distribution of cutaneous and proprioceptive inputs—potentially contributes to this relationship. Cutaneous sensory information appears to be very important for efficient pellet retrieval on the task used in the present study. Lesions to the cutaneous hand representation in somatosensory area 3b in owl and squirrel monkeys have been shown to result in a manual performance deficit on the pellet retrieval task identical to that used in the present study (Xerri et al. 1998). Because cutaneous sensory information is conveyed to the M1c, it is not unexpected that destruction of M1c would result in deficits in tasks requiring digital contact and skilled manipulation of objects.

In addition, M1c also receives some proprioceptive input. It is noteworthy that the mean aiming error rate for the M1c lesion group was nearly as high as that of the M1r lesion group during wk 1 postlesion. However, the error rate was not statistically different from prelesion levels because of high individual variability in the M1c group. Thus it is possible that a larger group of animals would demonstrate aiming errors after M1c lesions. Also, in the present study, rostral–caudal boundaries were arbitrarily assigned based on previous sensory mapping experiments in M1 in this species indicating that cutaneous responses were restricted to the caudal 1/3 to 1/2 of the M1 hand area (Humphrey et al. 1994). Individual variability in somatosensory submodality distributions within M1 may account for some of the variability in postlesion error rates. Notably, the animal in the M1c group that had the most rostral lesion of the group (monkey 5) also had the highest aiming error rate.

Likewise, M1r lesions destroy cortical tissue that receives predominantly proprioceptive, but little cutaneous, input. Thus after an M1r lesion, the aiming error rate increased significantly, whereas the cutaneous sensory error rate did not change. The M1r lesions in this study presumably did not destroy cutaneous sensory receptive fields in M1. This may account for the failure of M1r lesions to cause a motor performance deficit in the present study. It is likely that M1r lesions would cause a larger performance deficit on a task that required more accurate skilled aiming.

Two additional observations suggest that the different behavioral deficits of rostral versus caudal lesions are, at least in part, a result of the different sensory properties of M1r and M1c. First, the cutaneous sensory errors observed in this study are very similar to those seen after lesions confined to the area 3b hand area. Such deficits have been likened to sensory agnosias that occur in humans (Randolph and Semmes 1974; Xerri et al. 1998). Second, within the M1r or M1c lesion groups, there was no correlation between the amount of digit or proximal representational area with the number of cutaneous sensory or aiming errors.

In conclusion, the present study provides evidence that M1 plays an important role in sensorimotor integration. Pure M1 lesions resulted in behavioral deficits that are indicative of

J Neurophysiol • VOL 94 • AUGUST 2005 • www.jn.org
sensorimotor deficits and that generally correlate with both the segregation of motor outputs and somatosensory submodality inputs of the M1 hand representation. These two properties of M1 organization are difficult to disentangle. It is possible that other squirrel monkeys might have a more balanced digit distribution in M1r and could be used to examine this issue further in future studies. Further, if in future studies both somatosensory and motor data in M1 are derived in detail, it may be possible to use statistical methods to parse the relative contributions of these two factors.

ACKNOWLEDGMENTS

We thank Dr. Steve Delia, C. Knox-DuBois, D. Larson, M. Marucci, and Drs. Gary Milliken, Frank SiFuentes, Haiying Wang, and Brinie Wise for assistance with data collection.

GRANTS

This work was supported by National Institutes of Health Grants NS-11003 to K. M. Friel and NS-30853 to R. J. Nudo, a center grant from the National Institute on Aging (Kansas Claude D. Pepper Center for Independence in Older Americans, AG-14635), grants HD-02528 and HD-07523, and a Philanthropic Education Organization Scholar Award to K. M. Friel.

REFERENCES


