Published in final edited form as:

Exp Brain Res. 2014 December ; 232(12): 3929–3938. doi:10.1007/s00221-014-4068-9.

Recovery of Precision Grasping after Motor Cortex Lesion does not require Forced use of the Impaired Hand in *Macaca mulatta*

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Abstract

We investigated whether precision grasping of small objects between the index and thumb of the impaired hand recovers without forced use after surgically placed lesions to the hand/arm areas of M1 and M1 + lateral premotor cortex (LPMC) in two monkeys. The unilateral lesions were contralateral to the monkey's preferred hand, which was established in pre-lesion testing as the hand used most often to acquire raisins in a foraging board task in which the monkey was free to use either hand to acquire the treats. The lesions initially produced a clear paresis of the contralesional hand and use of only the ipsilesional hand to acquire raisins in the foraging board task. However, beginning about 3 weeks after the lesion the monkey spontaneously began using the impaired contralesional hand in the foraging board task and increased use of that hand over the next few tests. Moreover, the monkeys clearly used precision grasp to acquire the raisins in a similar manner to pre-lesion performances, although grasp durations were longer. Although the monkeys used the contralesional hand more often than the ipsilesional hand in some post-lesion testing sessions they did not recover to use the hand as often as in pre-lesion testing when the preferred hand was used almost exclusively. These findings suggest that recovery of fine hand/digit motor function after localized damage to the lateral frontal motor areas in rhesus monkeys does not require forced use of the impaired hand.

Keywords

finger; grip; dexterity

Introduction

We have previously shown that recovery of grasping small food objects by the digits contralateral to lesions of the hand/arm areas of primary motor cortex (M1) and lateral

premotor cortex (LPMC) occurs within a few weeks after the lesion in rhesus macaques (Darling et al. 2009). However, this recovery occurred following occasional forced use of the contralesional hand/digits to perform a task requiring precision grasp of very small (0.5 mm diameter) food pellet targets located in small diameter wells of a dexterity board. Other work has shown that use of a jacket that restrained the ipsilesional upper limb and intensive daily training of the contralesional limb using small food pellets placed into progressively smaller wells of a dexterity board is required for recovery of precision grasping after M1 lesions of digit areas in rhesus macaques (Murata et al. 2008; Higo 2014). Similarly, Passingham and colleagues reported that forced use of the contralesional hand by restraining the ipsilesional hand or using a primate chair was necessary to induce recovery of fine hand/digit function in rhesus macaques after large M1 lesions (Passingham et al. 1983). An important question is whether such recovery of precise grasping of small objects can occur without any forced use of the impaired contralesional hand. Classical work from the early 1900s suggests that such recovery of fine hand/digit motor function can occur following lesions of the elbow/hand/arm areas of M1 in macaque monkeys and apes, although it is not clear how much encouragement the animals received to use the impaired hand in those studies (Graham Brown and Sherrington 1913; Leyton and Sherrington 1917; Darling et al. 2011b). Similarly, more recent work has shown good recovery of fine hand/digit movements without forced use after small M1 lesions in squirrel monkeys despite reduced digit representations in the area adjacent to the lesion (Nudo and Milliken 1996). Whether similarly good spontaneous recovery can occur in primates that use precision grasp such as rhesus macaques after larger lesions of M1 is an important question. Notably, some work has shown that rhesus monkeys can even learn a difficult novel fine motor task after a lesion of the arm areas of right and left M1, although learning appeared to be slower after the lesion compared to intact monkeys learning the task (Glees and Cole 1950). Thus, it seems likely that useful and effective levels of recovery are possible without forced use.

We tested the hypothesis that precision grasping of small objects recovers without forced use after a lesion to hand/arm area of M1 in one monkey, and a lesion to the arm/hand areas of M1 plus lateral premotor cortex (LPMC) in a second monkey. These animals were only tested for hand motor function before and after the lesion using a foraging board task in which either hand could be used to acquire small food targets. We were initially unsure whether these monkeys would even use the more impaired hand after the lesion without forced use as it was possible that learned nonuse (Morris and Taub 2001; Taub et al. 2006) would set in, but found that both animals spontaneously began to use the contralesional hand within 23 days after the lesion.

Methods

Subjects

Two adult rhesus monkeys (*Macaca mulatta*) were the subjects for these experiments (Table 1). The monkeys were housed and maintained in United States Department of Agriculture (USDA) and AAALLAC approved and inspected facility at the University of Kansas Medical Center. The surgical and behavioral protocols were approved by the University of Kansas Medical Center Institutional Animal Care and Use Committees and performed

according to USDA, National Institutes of Health and Society for Neuroscience guidelines for the ethical treatment of animals. Prior to testing, each monkey was evaluated by a primate veterinarian and judged to be healthy and free of any neurological deficits.

Behavioral Procedures

A foraging board (FB) consisting of a flat surface covered with artificial turf in which raisin targets were placed was used to test two monkeys (cases R and H). The monkeys reached out of their cage with either hand to acquire the raisins located in the artificial turf of the FB which was oriented horizontally in front of the cage. Raisins were placed either one at a time or several in different locations on the FB. Durations of testing sessions and number of trials with the foraging board varied with motivational level of the monkey, ranging from 14 - 47 trials within 1.5 - 7 minutes. In addition, some testing sessions began with the experimenter offering the monkey raisins to be retrieved from his hand, but these trials were not analyzed or included in the testing session duration. Spontaneous recovery was studied in these monkeys as there was no mechanism to force use of the contralesional hand. We simply assessed frequency of use and type of grasp used by each hand to grasp raisins on the foraging board from video records of task performance. During testing with the foraging board the raisins were placed in various locations, including close to and far from the contralesional hand. However, during the post-lesion phase when use of the contralesional hand began, the raisin was more often placed in locations where the monkey seemed to prefer to use the contralesional hand, but the raisin was always accessible to both hands. Both monkeys were always free to use either hand as the less impaired ipsilesional limb was never restrained when in the cage.

Surgical Procedures

Surgical lesions were made to rostral and caudal arm/hand areas of M1 or M1 + lateral premotor cortex (LPMC) in the hemisphere contralateral to the preferred hand, which was almost exclusively used by these monkeys during pre-lesion testing using the foraging board (Table 1). To accomplish this, each monkey was injected with atropine sulfate (0.05mg/kg), then immobilized with ketamine (10mg/kg) and placed in a Kopf stereotaxic head holder (Pizzimenti et al. 2007; McNeal et al. 2010). The monkey was intubated and anesthetized with isoflurane inhalation (1.2-1.5%) using a surgical grade oxygen mixture. Mannitol was administered (1.5g/kg) intravenously and a skin incision, bone flap and dural flap were made over the lateral frontal convexity. After cortical exposure, the animal was transferred to intravenous ketamine anesthesia to restore motor output for electrophysiological mapping. Monopolar surface stimulation with a 2 mm. diameter gold-plated silver ball electrode was then used to localize the dorsal, ventral and rostral boundaries of the arm representation of M1. Movements evoked during 0.5 - 1 s of surface stimulation (2 mm diameter ball electrode using threshold voltages at 50-100 Hz with 0.2 ms duration pulses) of M1 were confirmed by two observers and were used to identify the dorsal, ventral and rostral areas of the arm area on the lateral surface of M1, which were marked with cottonoid strips. After localization, the animal was transferred back to isoflurane anesthesia and the lesion was created using subpial aspiration of the lateral premotor cortex in one animal, and rostral M1 arm area and the adjacent caudal M1 arm area within the central sulcus of both animals. Extreme care was taken during the aspiration process to avoid extensive, unintended

postoperative subcortical white and gray matter damage. Following resection, the dural incision was sutured closed, the bone flap replaced and anchored and the temporalis muscle and skin closed using standard neurosurgical technique. Each monkey was administered prophylactic antibiotics 24 hours prior to surgery followed by a post-surgery drug regimen of analgesics to reduce pain and discomfort. This included Buprenorphine twice a day for three days, Tylenol every six hours for one week and Carprofen once per day if needed.

Behavioral Data Collection and Analysis

Video recordings of performances were made using a single camera (Panasonic DVX100 3CCD) with a frontal view at 30 frames/s. The video recordings were analyzed by an experienced research assistant to identify the type of grasp (Fig. 1 - precision, key, other; unknown – if unable to observe type of grasp due to position of thumb on video) and whether manipulation of the food pellet to change its position relative to the finger and thumb tips occurred. Precision grip was defined as grasp between the tips of the index and thumb (Fig. 1, top panels) whereas key grip was defined as grasp between the tip of the thumb and lateral (radial) surface of the finger (Fig. 1, middle panels). We also occasionally observed grasps between the 2nd and 3rd digits (Fig. 1C), and between a digit and the palm. Manipulation was defined as motion of the pellet by independent movement of the index or thumb tip to better secure it in grasp. Manipulation duration was also measured and defined as the time from first contact of the pellet until it was secured in grasp. Frequency of use of each hand and of precision, key and other grasps by the contralesional hand was evaluated as a percentage of all trials using either hand. Post-lesion we also qualitatively assessed whether mirror movements of the ipsilesional hand occurred during grasping with the contralesional hand, but these were never observed. However, the possibility of mirror movements cannot be completely ruled out, since monkeys often held the cage bars with the ipsilesional hand and sometimes the ipsilesional hand was not within the camera view.

Tissue Preparation and Lesion Site Analysis

Nissl stained tissue sections through the lesion site were prepared using standard histochemical methods as formerly described (Morecraft et al. 1992; Morecraft et al. 2004; Morecraft et al. 2012). Briefly, each monkey was perfused transcardially with 0.9% saline followed by 4% paraformaldehyde in 0.1M phosphate buffer at a pH of 7.4 (PB). The fixative was followed by infusion of a 10% solution of sucrose in 0.1M PB then a 30% solution of sucrose in PB. The central nervous system was removed and stored for several days at 4°C in 30% sucrose in 0.1M PB. Following an adequate time for cryoprotection, the cortex was photographed for data reconstruction purposes and frozen sectioned at 50µm in cycles of 10. One series of tissue sections was mounted on subbed slides, dried overnight and eventually stained for Nissl substance using thionin to evaluate cytoarchitectonic organization.

For lesion site analysis, Nissl stained tissue sections spaced 500µm apart through the lesion site were evaluated using an Olympus BX51 microscope (Leeds Precision, Minneapolis, MN) for gray matter removal and underlying white matter fiber bundle involvement. The subcortical bundles were defined according to the atlas of Schmammann and Pandya (Schmammann and Pandya 2006) and gray matter regions (cytoarchitectonic areas 6, 4, 3, 2

and 1) were defined according to the criteria of Morecraft and colleagues (Morecraft et al. 2004; Morecraft et al. 2012). After detailed microscopic analysis, the cortical and subcortical limits of each lesion site were plotted onto anatomically homologous Nissl stained tissue sections from the non-lesioned hemisphere (see Figs. 1 and 3 of Darling et al. 2011) using the microscope and an attached MAC 5000 motorized stage (Ludl Electronic Products, Hawthore, NY) which was connected to Neurolucida data collection software system (MBF Bioscience, Williston, Vermont, USA). Gray matter and white matter lesion site volumes were then calculated using Neurolucida software as previously described (Pizzimenti et al., 2007; Darling et al., 2009).

Results

Monkey R Lesion Analysis—Gray matter removal was restricted to the arm regions of M1 and LPMC (Fig. 2). In the central sulcus, the lesion involved the upper portion of area 4, which lined the anterior bank of the central sulcus (M1c or “new” M1 of (Rathelot and Strick 2009)) but spared the remainder of area 4 in the lower portion of the sulcus (see pullout in Fig. 2 of the anterior bank of the central sulcus). Specifically, our volumetric analysis estimate demonstrated that all (100%) of M1r was removed and approximately 26.7% of the M1c arm/hand region was extirpated with 73.3% being spared (Table 1). On the lateral surface, gray matter removal involved the entire portion of area 4 on the gyral surface (M1r or “old” M1 according to Rathelot and Strick, 2009) including the inferior half of areas 6DC and 6DR. The gray matter forming the banks of the arcuate sulcus and arcuate spur were spared. Subcortical white matter damage was limited to the general region located directly below the gray matter resection. All major subcortical white matter bundles were spared [e.g., superior longitudinal fasciculus (SLF) subcomponents I, II, II and fronto-occipital fasciculus (FOF)] as were all subcortical gray matter structures (e.g., basal ganglia and thalamus).

Monkey H Lesion Analysis—On the lateral surface of the hemisphere the lesion site involved area 4, effectively removing all cortical gray matter from the central sulcus extending anteriorly to the posterior tip of the spur of the arcuate sulcus (Fig. 2). At the level of the central sulcus, the ablation effectively extricated all cortical layers of area 4 on the dorsal-anterior operculum as the lesion extended inferiorly to involve approximately one-third to one-half of the gray matter that preoperatively, once formed this part of the anterior bank of the central sulcus (see pullout in Fig. 2 of the anterior bank of the central sulcus). Our volumetric analysis estimate demonstrated that all (100%) of M1r was removed and approximately 37.9% of the M1c arm/hand region was effectively extirpated with 62.1% being spared in the inferior region of the central sulcus (Table 1). This case sustained little subcortical white matter damage that was limited to the region directly below the gray matter resection, including the area corresponding to the location of the dorsal-most part of SLF II. All subcortical gray matter structures were intact.

Behavioral Data

Before the lesions both monkeys primarily used precision grasps of the raisin with the preferred (right) hand in the FB task with manipulation durations usually less than 0.5 s (Fig.

3), showing they were quite adept at this relatively simple task. Immediately after the lesion both monkeys showed clear impairment with flaccid paresis of the contralesional hand (i.e., opposite the lesion a pendulous hand hung limply at the side and was not used for postural support or grasping of objects). This paresis lasted up to a week after the lesion but then hand function began to recover for use to assist the unimpaired hand during feeding and in typical cage behavior such as grasping of the cage bars and climbing.

Both monkeys exhibited the first successful precision grasp with the contralesional hand (e.g., Fig. 4) at about 3 weeks post-lesion (Fig. 3). Monkey H used the contralesional hand on 30% of trials, with precision grasp on 24.9% of trials, in the testing session at 23 days post-lesion (Fig. 3A,B). Use of the contralesional hand increased to 63% of trials, with precision grip on 58% of trials (Fig. 3A,B), suggesting a return to pre-lesion right hand preference although at a lower rate than during pre-lesion tests (86.4%). However, this was the highest post-lesion use of the contralesional hand by monkey H as this animal used the ipsilesional hand more often on subsequent post-lesion tests (Fig. 3A,B). In contrast, monkey R used the contralesional hand on 21.4% of trials, with precision grasp on 14.3% of trials, at 21 days post-lesion. This increased to 87.5% use of the contralesional hand, with precision grasp used on 83.1% of trials, at 24 days post-lesion and then 100% of trials using the contralesional hand, with 85% using precision grasp, at 32 days post-lesion. However, in the last two test sessions this monkey decreased use of the contralesional hand to 47% and 68% of trials (all using precision grasp) (Fig. 3A,B). Thus, monkey R apparently returned to the pre-lesion right hand preference although percentage use was usually less than in pre-lesion tests in which the right hand was used on 99.4% of trials. Pre and post-lesion precision grasps by both monkeys were qualitatively similar (Fig. 4), suggesting that movement control over the digits was similar to pre-lesion. Manipulation durations by monkey R and monkey H were somewhat slower after the lesion (Fig. 3) but were mostly less than 0.5 s with occasional long durations (1 – 2 s for monkey H; 1 – 15 s for monkey R) causing higher mean manipulation duration and higher variability compared to pre-lesion (Fig. 4).

There was no clear influence of white or gray matter lesion volume or percent damage to M1c on recovery of contralesional hand fine motor function. Monkey R had much larger total (M1+LPMC) gray matter lesion volume and a larger white matter lesion volume than monkey H, but monkey H had a larger percentage of M1c arm/hand area damage. Recovery of manipulation duration appeared to be better in monkey H than in monkey R in that mean manipulation durations after recovery were closer to pre-lesion values and less variable in monkey H than in monkey R (Fig. 3). In contrast, recovery in terms of percentage use of the contralesional hand in the FB task was better in monkey R than in monkey H as the contralesional hand was used more often by monkey R after recovery (Fig. 3).

Discussion

These experiments clearly show that precision grasp and independent manipulation of small food objects between the index and thumb distal pads recover after lesions of arm/hand areas of M1 and M1 + LPMC without forced use of the contralesional hand. Both monkeys exhibited good recovery in terms of ability to grasp small objects with the contralesional

hand starting about 3 weeks after the lesion without any forced use. This recovery occurred even when the lesion involved over 1/3 of M1c arm/hand area (Rathelot and Strick 2009) which is thought to be most important for precision grasping and individuated digit motions due to the large number of corticomotoneuronal neurons (with monosynaptic connections onto motor neurons) contained in this area (Lemon et al. 1998; Cheney et al. 2000; Lemon 2008).

The recovery of contralesional hand fine motor function without forced use is striking in that the digit movements were qualitatively similar to pre-lesion in terms of the appearance of the movements of the index and thumb when viewed frame by frame in video records (Fig. 4, supplemental videos). Although there were obvious impairments in use of the contralesional hand observed during the first week or longer after the lesions, and no use of that hand in FB testing until 3 weeks after the lesion, once the monkey began to use that hand its digit movements were similar to pre-lesion, although slower and more variable in duration (e.g., Fig. 3). The monkeys also seemed to look at their hand to confirm the raisin was within grasp during the early grasps made at 3 weeks post-lesion, but this behavior was not observed in the later post-lesion period or in the pre-lesion period. Thus, the lesion may have also influenced processing of tactile sensations in the early post-lesion period. It seems likely that the animals choose not to use that hand until sufficient recovery had occurred so that it could be used in a fairly skillful manner. In contrast, we have shown previously that forced use of the contralesional hand in motor testing during the first few weeks after M1 and M1+LPMC lesions was associated with some clumsiness in digit movements and clearly longer manipulation durations than prior to the lesions in most monkeys (Darling et al. 2009). However, even under the “forced use” conditions of our previous work it was clear that monkeys generally did not make attempts to acquire the food pellet with the contralesional hand until some digit dexterity had returned (Darling et al. 2009). It should also be noted that we rarely saw “compensatory scooping” movements of the pellet toward the palm or “mass action” in which multiple or all fingers moved the pellet toward the palm of the hand as described following ischemic lesions of M1 (Moore et al. 2012), presumably because these monkeys did not attempt the task with the contralesional hand until they could move the hand/digits in a dexterous manner.

An important issue to consider is that in the present work the monkeys were reaching to acquire a raisin which, due its inherent compressibility, texture and stickiness, is easier to grasp than the smoother, more rigid and smaller food pellets used in our previous work (Darling et al. 2009). Also making the task easier in the present work was that there were no wells restricting motions of the finger and thumb tips. Thus, the relatively rapid recovery despite rather large white matter lesions in both monkeys and the large gray matter lesion in monkey R, may be partially due to the easier task used in this work. That is, it is possible that spontaneous recovery without forced use might not be observed if a more difficult fine motor task was used because the monkeys may not attempt the more difficult task without forced use. However, the similarity of thumb and index finger motions pre- and post-lesion suggest that these monkeys were likely able to at least dislodge pellets from the well of a dexterity board and, most likely, acquire them as they were clearly able to independently move the index and thumb in a highly coordinated manner to move the raisin toward the thumb for grasp (Fig. 4).

Further evidence for excellent recovery was that both monkeys used the more impaired contralesional hand more often than the ipsilesional hand in at least one post-lesion testing session. Indeed, monkey R, with the larger lesion, used the contralesional hand more often in most post-lesion testing sessions after recovery had occurred (Fig. 3A). Thus, it appeared that monkey R had returned to its pre-lesion hand preference, although not as strong as in pre-lesion testing when the preferred hand was almost exclusively used in the FB task. These findings are also similar to our previous work in which some monkeys used the contralesional hand more often than the ipsilesional hand in at least some post-lesion testing sessions in a learned nonuse task which is similar to the foraging board task in that the monkeys could choose which hand to use to pick up small food targets (Darling et al. 2010).

We were surprised that the much larger lesion in monkey R did not produce a clearly poorer recovery than in monkey H. In previous work we observed that recovery was partially dependent on lesion volume, but over a much larger range of lesion volumes than in the present work (Darling et al. 2009). White matter lesion volumes of monkey R and monkey H were similar and therefore cannot account for the differences in recovery seen here. Gray matter lesion volume was much larger in monkey R than in monkey H, which may explain the better recovery of manipulation duration in monkey H. However, despite the large gray matter lesion in monkey R, recovery of digit movements and manipulation duration appeared to be quite good (Figs. 3, 4). Notably, monkey H had a larger percentage of the caudal M1 arm/hand area damaged than monkey R, and after recovery used the contralesional hand less often than monkey R, but with shorter manipulation durations. Thus, it is possible that less damage to caudal M1 permits better recovery of manipulation duration in terms of learned nonuse in that the animal may choose to use the contralesional hand more often to pick up small objects. It is possible that damaging more/all of M1c hand/arm area, which contains most of the neurons with monosynaptic connections onto spinal motor neurons, would lead to greater learned nonuse for picking up small objects but confirming this would require larger lesions of M1c that include cortex in the lower part of the anterior bank of the central sulcus. Overall, there is no clear conclusion that can be drawn concerning lesion volume effects in these two monkeys.

The observed reduction in use of the contralesional hand after good recovery had apparently occurred by about 24-36 days post-lesion in both monkeys (Fig. 3) may be due to development of learned nonuse and/or some recurrence of paresis of the digits. The reduction in use of the contralesional hand occurred after an approximately 3- 4 week delay between testing sessions with the foraging board. It is possible that during this time the animals primarily used the ipsilesional hand for performing fine motor tasks outside of testing sessions, thereby causing development of learned nonuse (Taub et al. 1994). However, only case H showed a progressive reduction in use of the contralesional limb to almost exclusive use of the ipsilesional limb consistent with learned nonuse. Recurrence of paresis may also have occurred, but examination of video records of performance in the last 3 testing sessions for both monkeys did not show clear evidence of spasticity or problems coordinating the contralesional index and thumb compared to earlier post-lesion tests. It is also possible that the longer manipulation durations and greater use of the contralesional hand by case R indicate greater motivation to recover use of the impaired hand and may also

explain why this monkey maintained a higher use of that hand in the foraging board task after recovery occurred.

There are many potential mechanisms underlying recovery of fine hand/digit motor function after lesions to M1 and M1 + LPMC. In the case of lesions limited to M1, spared regions of M1 may contribute to recovery (Nudo et al. 1996). Since all of rostral M1 arm/hand area identified with cortical stimulation was damaged in these lesions but only about 30-40% of caudal M1 arm/hand area was damaged, it is possible that spared neurons in caudal M1 arm/hand areas reinnervated motor neurons and interneurons in C5-T1 levels of the spinal cord that were denervated by the lesion to re-establish control over movements of the hand and digits. Expansion of the hand region of ventral premotor cortex may also contribute as shown previously in squirrel monkeys (Frost et al. 2003). Similarly, we have previously shown that recovery after lesions of arm/hand areas of M1 + LPMC (similar to the lesion of monkey R) is associated with a substantial increase in the corticospinal projection from the spared ipsilesional supplementary motor cortex (SMC or M2) onto intermediate and ventral horn neurons at C5-T1 levels of the spinal cord (McNeal et al. 2010). Moreover, we demonstrated that subsequent damage to M2 arm/hand area after recovery from an M1 + LPMC lesion partially reinstates the fine movement control deficit (McNeal et al. 2010). It is also possible that there is an increase in the corticospinal projection from spared ipsilesional M1, LPMC and M2, as well as an increase in the corticospinal projection from the undamaged contralesional M1 onto propriospinal neurons located at C3-C4 levels of the spinal cord. It has recently been shown in the monkey that propriospinal neurons at these cervical levels project to ventral horn motoneurons of C5-T1 and aid in recovery of dexterous motor function (Sasaki et al. 2004; Alstermark et al. 2011; Kinoshita et al. 2012). Contralesional M1 projections to reticular nuclei which also project to C3-C4 propriospinal neurons provide another potential mechanism for recovery (Bradnam et al. 2013), among others. Thus, the recovery of precision grasping observed in this study is probably due to sparing of part of M1c and reorganization of peri-infarct cortex, including corticospinal neuron termination patterns from spared lateral and medial regions of motor cortex and indirect descending pathways, such as corticorubral, corticopontine and corticoreticular projections.

It is abundantly clear from the present findings, including our previous work and classical work that the non-human primate brain is capable of considerable recovery of function after lesions that damage a substantial portion of the arm/hand areas of M1, LPMC and other frontal lobe areas (Darling et al. 2009; Darling et al. 2011a). This has important implications for rehabilitation therapies as nearly exclusive forced-use of the impaired hand for an extended period of time, as in constraint induced movement therapy (Taub et al. 1993; Wolf et al. 2006), may not be required to enhance recovery of hand function after lesions limited to lateral frontal lobe motor areas that spare a portion of M1c. Indeed, recent research has suggested that modified forms of constraint induced movement therapy that are much less intensive than was studied in a large clinical trial (Wolf et al. 2006) are effective in producing improved hand function after stroke-induced hemiplegia (Smania et al. 2012; Treger et al. 2012).

Acknowledgments

Supported by U.S. National Institutes of Health grants NS064054, NS046367 and NS30853.

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Figure 1.

Video sequences of types of grasp observed in monkeys grasping raisins (marked with a red dot) from the foraging board. Precision grasp (top panel) was by far the most common, Key (middle) and other (e.g., between index and long fingers – bottom panel) types of grasps were rarely observed.

Figure 2.

Line drawings of the lateral surface of the cerebral cortex in monkeys KM2 and KM3 showing the extent of the lesion site (blackened area). The pull-out located below the prefrontal region in both drawings shows a flattened map of the cortex lining the anterior bank of the central sulcus. The lesion site is also denoted by the black region. The horizontal dotted line marks the boundary between the arm and shoulder region of M1c dorsally, and the arm and face region ventrally. Abbreviations: cs, central sulcus; ilas, inferior limb of the arcuate sulcus; ios, inferior occipital sulcus; ips, intraparietal sulcus; lf, lateral fissure; LPMcd, dorsolateral premotor cortex; ls, lunate sulcus; M1c, caudal (new) part of the primary motor cortex; M1r, rostral (old) part of the primary motor cortex; ps, principle sulcus; slas, superior limb of the arcuate sulcus; sts, superior temporal sulcus.

Figure 3.

Pre and Post-lesion percentages of all attempts in a single testing session that used the contralateral hand (A), contralateral hand precision grasps (B) and average manipulation durations (C) of precision grasps for cases R and H. Each plotted symbol is from a single testing session. The horizontal lines (solid for case H, dashed for case R) show average percentage use in prelesion tests of the contralateral hand (A), precision grasps by the contralateral hand (B) and average manipulation duration (C). Note that there were no precision grasps until 3 weeks after the lesion. Errors bars are 1 S.D. of manipulation durations.

Monkey R

Monkey H

Figure 4.

Video frame sequences of precision grasps. In the top two panels are shown pre-lesion (top) and at 58 days post-lesion (bottom) precision grasps of a raisin (indicated with a white dot) in the foraging board by monkey R. In the bottom two panels are shown pre-lesion (top) and at 24 days post-lesion (bottom) precision grasps of a raisin in the foraging board by monkey H. In each panel is shown the time relative to the first frame in the sequence.

Table 1

Subject Characteristics

Monkey	Age (yrs)	Wt (Kg)	Sex	M1 GMLV ^a		WMLV ^b (mm ³)
				M1r(%)	M1c(%)	
R	11	13	M	124.45 [*] (100)	16.31(26.7)	68.80
H	7	8.3	M	110.7(100)	22.7(37.9)	59.98

^a gray matter lesion volume (% of total volume of rostral primary motor cortex (M1r) and caudal primary motor cortex (M1c) arm/hand areas)

^b white matter lesion volume

^{*} This monkey's lesion also included part of dorsolateral premotor cortex for an additional GMLV of 134.8 mm² for a total GMLV of 275.5 mm³ (see Fig. 2)