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Feed-Forward Control of Preshaping in the Rat Is Mediated by the Corticospinal Tract

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Abstract

Rats are used to model human corticospinal tract (CST) injury and repair. We asked whether rats possess the ability to orient their paw to the reaching target and whether the CST mediates this skill, as it does in primates. To test this ability, called preshaping, we trained rats to reach for pieces of pasta oriented either vertically or horizontally. We measured paw angle relative to the target and asked whether rats used target information attained before contact to preshape the paw, indicating feed-forward control. We also determined if preshaping improved with practice. We then selectively lesioned the CST in the medullary pyramid contralateral to the reaching forepaw to test whether preshaping relies on the CST. Rats significantly oriented their paw to the pasta orientation before contact, demonstrating feed-forward control. Both preshaping and reaching efficiency improved with practice, while selective CST lesion abrogated both. The loss of preshaping was greatest for pasta oriented vertically, suggesting loss of supination, as seen with human CST injury. The degree of preshaping loss strongly correlated with the amount of skill acquired at baseline, suggesting that the CST mediates the learned component of preshaping. Finally, the amount of preshaping lost after injury strongly correlated with reduced retrieval success, showing an important functional consequence for preshaping. Thus, we demonstrate, for the first time, preshaping in the rat, and dependence of this skill on the CST. Understanding the basis for this skill and measuring its recovery after injury will be important for studying higher-level motor control in rats.

Keywords

Motor learning; motor control; injury; repair; motor cortex; activity

INTRODUCTION

Shaping the hand to the reaching target is critical for effective grasp. Non-human primates and humans use visual information to match the conformation of the reaching hand to the

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visual attributes of the target, termed preshaping (Jeannerod et al., 1995; Rizzolatti and Luppino, 2001). This is an example of anticipatory, or feed-forward, control. Preshaping, or control of underlying finger joint forces, relies on the corticospinal system (Lemon and Griffiths, 2005; Pettersson et al., 2007). The loss of preshaping is associated with loss of hand function (Castiello and Begliomini, 2008). A major goal of motor rehabilitation is to restore preshaping and other aspects of feed-forward motor control (Jones et al., 2009).

Rats are commonly used to study both motor control of reaching and corticospinal injury and recovery. They are dexterous animals whose reach to grasp mimics that of humans (Sacrey et al., 2009). Much is known about how rats target and retrieve objects. Rats identify the location of a food object to grasp using olfaction (Whishaw and Tomie, 1989; Hermer-Vazquez et al., 2007). In addition, rats rely on sensory cues of the target object after contact to modify the grasp and initiate retrieval (Ballermann et al., 2000). However, between when the object is selected and when the paw contacts and manipulates the target, the movement is thought to be stereotyped and not modifiable by the characteristics of the target object (Ballermann et al., 2000).

Here we asked if rats can use target sensory information, as primates do, to preshape their paw during reaching. This hypothesis was based primarily on our studies in the cat, which demonstrated feed-forward kinematic planning during reaching and a loss during reversible motor cortex inactivation (Martin et al., 1993; Martin et al., 2000). It is likely that rats, which are more dexterous than cats (Iwaniuk et al., 1999), are also likely to demonstrate elements of feed-forward control and a loss with injury to the corticospinal tract (CST). We further hypothesized that preshaping would improve with training. This is based on the role of motor cortex and the CST in motor learning and motor control (Martin, 2005; Shadmehr and Krakauer, 2008). In support of this, rats can be operantly conditioned to slow the reaching movement, implicating motor learning in the extension phase of reaching (Zhuravin and Bures, 1986).

We trained rats to orient their paw to the orientation of a food reward to be grasped, which is an element of preshaping. We found that rats do orient their paws to the orientation of the target before contact, demonstrating feed-forward control. This skill improved with training and was abrogated by selective lesion of the CST. Finally, CST injury impaired reaching efficacy, and this loss of function strongly correlated with loss of preshaping, indicating functional impairment associated with loss of preshaping. We suggest that the corticospinal system in the rat shares important attributes with primates for the higher-level control of movement, making this behavior important in modeling the types of skill that people with CST injury need to recover.

METHODS

Overview

To test whether rats preshape, we measured the angle of the reaching paw in relationship to the angle of the target. To test whether preshaping is learned, we measured paw angles at the beginning of training and again at the end. We then subjected rats to a CST lesion in the medullary pyramid to test the reliance of preshaping on the CST. Rats were tested regularly after injury to determine if preshaping recovered. Finally, we measured efficiency of pasta retrieval to determine the functional effect of the loss of preshaping.

Subjects

All experiments were approved by the Institutional Animal Care and Use Committees of Columbia University College of Physicians and Surgeons, New York State Psychiatric Institute, and City College of City University of New York. Adult female Sprague-Dawley

rats, approximately 225g (Hilltop Lab Animals, Inc., Scottsdale, PA, USA), were housed in a pathogen-free facility with a 12 hour light-dark cycle. Prior to training, rats were food restricted to 20g daily until they reached 95% of their normal body weight. They were then fed sufficiently to gain weight along the normal weight curve, except for the week after surgery when they were fed ad libitum.

A total of 11 rats were used in these experiments. All of them had measurement of paw angles soon after learning the task. Six randomly chosen rats ("long-trained") had a prolonged training period (average 10 weeks) to determine if preshaping improved with training. Five rats ("short-trained") did not have prolonged training. A total of 8 rats (3 long-trained and all 5 of the short-trained) underwent CST lesion.

Reaching task

We used a custom-made reaching apparatus similar to that of Ballerman et al. (Ballermann et al., 2000). The reaching apparatus is made of clear plexiglass (presented schematically in Figure 1A), with an aperture on one of the narrow sides allows rats to extend their forepaw but not their nose and mouth through it. Outside of the aperture a small shelf and walls allow pieces of pasta (gray lines) to be presented to the rat either horizontally (H) or vertically (V). The vertical pieces were placed in a hole in the shelf located at one edge of the aperture and 1.5 cm distant to it. The height of the shelf was 5 cm above the floor of the box, and the pasta protruded 2.5 cm upward from the shelf. The horizontal pieces were also placed 1.5 cm distant from the aperture in holes on the walls. They were fixed 2 cm lateral to the edge of the aperture and extend 2.5 cm medially. These positions ensured that the rat reached to the same location in space for both horizontal and vertical pasta pieces and only allowed the rat to reach the pasta with one forepaw.

Approximately 1 week prior to training, rats were introduced to dry pasta so that they would recognize it as food. We used thin spaghetti (Barilla, width 1.35mm) as the target. In preliminary testing, this thickness pasta was found to offer the appropriate difficulty for breaking. Thinner pasta allowed rats to break the pasta without preshaping. Thicker pasta was too difficult for animals with CST lesions to break. Rats were allowed at least 2 minutes to habituate to the reaching apparatus before testing. Each pasta piece was manually loaded, and rats were prevented from reaching or seeing the pasta by blocking the aperture with an opaque barrier. After removing the barrier, rats were allowed to reach as many times as necessary to break the pasta piece. If the animal successfully reached for and broke the pasta piece but did not retrieve it, the pasta was removed from the shelf. Between reaches, rats were required to move to the back of the cage before the next piece of pasta was presented.

Training

Rats received training for approximately 1 hour a day, 3 days a week until they began to reach effectively for pasta. Once rats started reaching for pasta, the pieces were moved more distant to the aperture until rats began reaching to the final position. At this point, rats began to train on a protocol of 50 pasta pieces presented in a pseudorandomized pattern of horizontal and vertical orientations. Rats were given at least 2 sessions of training on this paradigm before filming the reaches and analyzing the results for the baseline paw angle measurements. This process took an average of 2 weeks to complete (range 8–22 days).

All rats (n=11) had paw angles measured at this time. Six rats received an average of 8 weeks of additional training ("long-trained") to test whether preshaping improved with training. The training paradigm during these 8 weeks was identical to the baseline training paradigm. Three of these rats were subjected to CST lesion. An additional five rats ("short-trained") were subjected to CST injury after baseline measurements, to test the effect of

injury on preshaping and the ability to acquire preshaping after injury. Thus, the rats used to test the effects of injury included 3 long-trained rats and 5 short-trained rats. Rats were randomly assigned to the short- or long-trained groups. After injury, rats ($n=8$) continued to be trained in the same paradigm, beginning one week after CST injury for an average duration of 50 days, which was similar for long- and short-trained rats.

Video Analysis

We used a Canon ZR60 digital video camera to record testing sessions (30 frames/sec; 60 video fields/sec, $1/2000^{\text{th}}$ sec shutter speed). For the long-trained rats, video was transferred to a VHS cassette tape and analyzed with a Panasonic S-VHS VCR that permitted stop action analysis of the each of the two video fields that comprise each video frame. Thus, reaches were analyzed at intervals of $1/60^{\text{th}}$ of a second. For the short-trained rats, videos were imported to MaxTraQ analysis software (Innovision Systems, Columbiaville, MI, USA) using a deinterlace function that also splits each 30 Hz frame into two 60 Hz fields (i.e., 16.66 ms field-to-field time interval). Paw angles measured using both systems yielded identical results (data not shown). Additionally, the paw angles for long-trained rats at week 2 (measured by transparency over a VCR screen image) were the same as for short-trained rats at week 2 (measured by motion analysis software, ANOVA, $F=0.24$, $p=0.63$). Testing sessions were performed at the end of the training period and at various times after CST lesion. Rats had 1 to 4 prelesion testing sessions (average 2.4) and 2 to 5 post-lesion sessions (average 3.3).

As shown in Figure 1B, we measured the angle between the pasta and a line drawn through the second and fifth metacarpal-phalangeal joints of the forepaw. Horizontal pasta pieces were oriented at 0° and the vertical pasta pieces oriented at 90° . The video field containing the point of contact was identified and used to define the video fields to be analyzed. Given the $1/60^{\text{th}}$ of a second recording rate, the field at contact was taken 0–16.7 msec after the paw contacts the pasta. In the long-trained rats, three video fields were analyzed: the point of contact, the field immediately before (0.1–16.7 msec before contact, time point “–1”), and the field subsequent to contact (16.7–33.4 msec after contact, time point “+1”). In the short-trained group the field two fields before contact (16.7–33.4 msec before contact, time point “–2”) was also included.

Measurements were performed on successful reaches only to prevent rats from using sensory cues to orient their paws. In addition to paw angle measurements, we also recorded the number of attempts to retrieve a pasta piece. An attempt is defined as movement of the forepaw through the aperture towards the pasta target. A successful reach is defined as grasping and breaking the pasta. Success rate equals the number of successful reaches divided by the total number of reaches $\times 100$. Thus, all reaches were measured to gauge the efficiency of reaching (success rate), but paw angle was measured only for reaches in which the first attempt was successful. This prevented any tactile information about the pasta orientation from being used to change the paw orientation.

Statistical analyses

As demonstrated in Figure 1C, we used two measures of preshaping. First, we compared paw angles between reaches for vertical and horizontal pasta, which we call “preshaping between” to signify a measure of preshaping between the vertical and horizontal conditions. Second, we compared paw angles within a reach at different time points, which we call “preshaping within” the same orientation condition. For comparisons across multiple time points, we used ANOVA with a Bonferroni post hoc test. Correlation between variables was made with linear regression. Statistical analyses were made with Prism 5 (Graph Pad), Kaleidagraph (Synergy Software), and Excel (Microsoft).

CST lesion

All rats had complete unilateral lesion of one CST. Similar to our previous study (Brus-Ramer et al., 2007), rats were anesthetized (ketamine 80mg/kg; xylazine 10mg/kg), placed supine in head fixation of a stereotaxic frame, and the pyramid contralateral to the reaching forepaw exposed by blunt dissection and a craniotomy. Under direct visualization, the pyramid was completely transected at the rostral medulla using iridectomy scissors and a second pass with a microknife. Lesions were confirmed to be histologically complete without extension into adjacent structures (Figure 1A) using Kluver-Barrera staining (Kluver and Barrera, 1953) of the lesion site. Postoperative analgesia was provided with buprenorphine (0.05mg/kg delivered by intraperitoneal injection every 12 hours for 2 days).

RESULTS

We adopted a reaching task in which pasta is presented in one of two orientations, vertical or horizontal, to test whether rats preshape their paws to fit the orientation of their target. We also tested whether the ability to preshape the paw improved with training by comparing animals at the beginning and end of a 10-week training period. Finally, we asked whether lesion of the CST at the medullary pyramid abrogates preshaping that had already been acquired, and we continued to train rats to test their ability to reacquire preshaping after injury.

Representative reaches to horizontal and vertical pasta are depicted in Figure 2. After removing the barrier in front of the target, rats position themselves with their nose at the aperture and quickly initiate a reach. Rats lift their nose and extend the reaching paw through the aperture. At the -2 time point, the rat has just extended the reaching paw through the aperture of the reaching box. The rat further extends the forelimb at the -1 time point and begins to rotate the paw to match the target orientation. Importantly, we saw no interaction of the long guard hairs of the paw or the hairs of the forelimb with the pasta before contact (Hermer-Vazquez et al., 2007). At the point of contact, which is any interaction of the paw and the pasta, the hairless portion of the paw touches the pasta first. While reaching for the vertical pasta the second digit makes initial contact, whereas the fifth digit initially contacts the horizontal pasta (arrows in Figure 2, Contact). By time point $+1$, most of the digits contact the target. Rats do not fully grasp the pasta until several frames after contact (usually $+3$ or more).

To determine the degree to which rats preshape their paws, we made two comparisons for each animal. First, we compared the paw angles between reaches to vertical pasta with those to horizontal pasta (e.g. Fig. 1C, “preshaping between”). Our prediction was that paw angles would diverge significantly while reaching to targets of different orientation. Second, we measured the change in paw angle within a reach, at each successive time point or over all time points (e.g. Fig. 1C, “preshaping within”). We predicted that the paw angle would change within the reach to approximate the angle of the target.

Figure 3 depicts the paw angles over time while reaching for vertically oriented pasta (black) or horizontally oriented (gray) pasta. Animals included in this analysis ($n=8$) were tested both before (A) and after (B; described below) CST injury. Before injury there was a highly significant difference in paw angles when reaching for pasta of different orientations (preshaping between, $F_{1,42}=182.0$, $p<0.0001$, repeated measures ANOVA). At the -2 time point, the average paw angle for vertical reaches was not significantly different than the angle for horizontal reaches ($p>0.05$). The angles did differ at the -1 time point ($p<0.01$, Bonferroni post hoc test). Thus, even before contact of the paw with the target, the paw angles were different when reaching for objects of different orientations, indicating feed-forward control. The paw angles diverged further at the point of contact ($p<.001$) and at the

+1 time point ($p < .001$). Importantly, paw angles did not differ whether the previous reach had been to the same orientation or not (data not shown). This demonstrates feed-forward control of paw angle based on sensory information about the target acquired before tactile feedback.

In addition to comparing paw angles when reaching for targets of different orientations, the amount of preshaping can also be measured by angle changes at successive time points within each reach (preshaping within). If rats display feed-forward control of their paw, then the paw angle should become progressively closer to the angle of the target with each successive measurement (i.e. vertical paw angles trend towards 90° and horizontal paw angles trend towards 0°). Indeed, paw angles changed significantly between time points for both horizontal (ANOVA, $F_{3,26}=7.13$, $p=0.001$) and vertical ($F_{3,26}=10.57$, $p=0.0001$) reaches. For horizontal reaches, there was a paw angle decrease of 5° (denoted by the negative sign, “ -5° ”) between time point -2 and -1 ($p > 0.05$). Vertical reaches increased by 1° between time point -2 and -1 ($p > 0.05$). However, from the -1 time point to the time of contact, there was a significant change in paw angle towards the angle of the target for both horizontal (-5° , $p=0.001$, Bonferroni post hoc test) and vertical reaches (7° , $p=0.009$). From the time of contact to time point $+1$ there was also a highly significant change in paw angle for horizontally and vertically oriented pasta pieces (-5° , $p=0.008$ and 13° , $p=0.0003$, respectively). Thus, rats demonstrate preshaping of their paws, both by comparing the paw angles between horizontal and vertical reaches (preshaping between), and by measuring paw angle change over time within each reach (preshaping within).

Preshaping increases with training

To test if preshaping improved with training, we trained a cohort of rats ($n=6$; “long-trained;” see Methods) to the point at which each was consistently reaching for pasta, an average of 2 weeks. We then continued to train the rats daily for an additional 8 weeks. We compared preshaping and reaching efficiency at the beginning of training with performance at the end of 10 weeks of training. Figure 4A plots the amount of preshaping according to the length of training. Preshaping is determined as the difference in paw angle between vertical and horizontal reaches (e.g. Fig. 1C, preshaping between) at the point of contact. The long-trained rats showed significant increases in preshaping with training (Fig. 4A week 2 (gray) versus week 10 (black); repeated measures ANOVA, $F_{1,33}=11.54$, $p=0.008$). In addition, we tested whether the efficiency of pasta retrieval increased during this period. As demonstrated in Figure 4B, the success rate for retrieval improved for all of the long-trained rats (t-test, $t_{11}=3.11$, $p=0.01$). These results indicate that both preshaping and reaching efficiency improved with training.

CST lesion abrogates preshaping

To test whether preshaping relies on the CST, we subjected rats to complete unilateral lesion of the medullary pyramid (Fig. 1A), which severs all of the CST axons emanating from one hemisphere and causes deficits in the reaching paw opposite to the lesion. We asked whether the loss of the CST would diminish the amount of forepaw preshaping during reaching. Figure 3B demonstrates the forepaw angle progression in rats ($n=8$; same rats as Fig. 3A) that underwent unilateral pyramidotomy. Two changes from baseline angle progression can be appreciated. First, and most obvious, CST lesion abolishes vertical preshaping (ANOVA of paw angles at each time point after injury, $F_{2,21}=0.09$, $p=0.91$). In addition to there being no significant difference in paw angles at each time point after CST injury, paw angles were significantly diminished by injury (black lines, Fig. A versus Fig. B; repeated measures ANOVA, $F_{1,42}=5.07$, $p=0.03$). Second, the change in horizontal angle begins later in the reach after injury (gray lines, Fig. 3A versus Fig. 3B; repeated measures ANOVA, $F_{1,42}=4.56$, $p=0.04$).

To further demonstrate the effect of injury on paw orientation change, we plotted the preshaping within vertical and horizontal reaches before and after CST injury in Figure 5. Preshaping within is the difference in paw angle from time point -2 to time point +1 (Fig. 1C). For vertical reaches, the effect of injury is a large and highly significant decrease in preshaping (t-test, $t_{15}=5.88$, $p<0.0001$). For horizontal reaches there was no significant difference in preshaping with injury ($t_{15}=0.90$, $p=0.38$). So, while there was a significant delay in horizontal angle change with injury, the predominant effect of CST injury on preshaping was the complete loss of vertical preshaping. Thus, CST lesion abrogates preshaping primarily through its effect on vertical reaches.

Effects of CST injury persist

We measured paw angle during reaching at several times after CST lesion to determine if preshaping recovered. Rats ($n=8$) were first tested an average of 14 days after pyramidotomy and at least weekly thereafter to an average of 50 days after injury. They continued to receive 2–3 reaching sessions a week during this period, similar to the initial training period. To determine if preshaping recovered over time, we compared the difference in paw angles when reaching for vertically or horizontally oriented pasta soon after injury and at the last testing time. For each time point, there were no significant differences (-1 time point: 5° at day 14 versus 4° at day 50; contact: 17° versus 11° ; +1 time point: 26° versus 20° ; repeated measures ANOVA, $F_{2,44}=1.93$, $p=0.17$). Neither horizontal nor vertical reaches demonstrated improvement (data not shown). Thus, preshaping does not recover after CST lesion.

Preshaping lost after injury correlates with the amount of baseline preshaping

From the data presented thus far, preshaping is a motor skill that depends, in part, on the CST. We reason that if learning to preshape depends on the CST, the more a rat preshapes its paw to fit its target, the more preshaping will be lost by severing the CST. Thus, we expected that there would be a strong relationship between amount of baseline preshaping and the amount of preshaping lost due to injury. This relationship is demonstrated in Figure 6 for values at the point of contact. The abscissa plots the angle difference between horizontal and vertical reaches before injury (preshaping between). The ordinate represents the effect of CST lesion on preshaping between, measured as the difference in preshaping before injury and preshaping after CST lesion. The graph demonstrates two important phenomena. First, the hypothesized relationship holds true: the amount of preshaping lost due to CST lesion is strongly and positively correlated with the amount of preshaping ($R_7=0.88$, $p=0.004$). There were also strong correlations at the -1 time point ($p=0.0005$) and +1 time point ($p=0.04$) as well (data not shown). Second, Figure 6 demonstrates a clustering of the long-trained rats (open squares) and the short-trained rats (closed squares). Long-trained rats demonstrated greater preshaping before injury. Thus, not only do the long-trained rats acquire more preshaping before injury, but they also lose more preshaping after CST injury.

Loss of preshaping after CST injury lowers reaching success

To determine whether loss of preshaping was associated with reduced capacity to retrieve the pasta, we measured retrieval rates before and after CST lesion. Figure 7A shows the success rate for pasta retrieval before and after injury. At baseline, rats ($n=8$) succeeded in retrieving a piece of pasta on 47% of attempts. After CST lesion, the success rate fell to 30%, a significant reduction (t-test, $t_{15}=2.60$, $p=0.02$). This loss of skill persisted. The success rate did not change between early times after CST lesion (average 12 days; 32%) and late times (average 26 days; 27%; t-test, $t_{15}=0.54$, $p=0.60$).

We asked whether the loss of reaching skill correlated with loss of preshaping (Figure 7B). If this were true, it would suggest that loss of preshaping has a functional consequence. To do this we created a ratio for each animal of performance before CST lesion and the performance after for both retrieval efficiency (abscissa; retrieval ratio) and preshaping between (ordinate; preshaping ratio). The relationship between these measures is very strong ($R^2=0.82$, $p<0.01$). Rats that had substantial loss of preshaping also had substantial loss of retrieval efficiency, whereas rats that had little change in preshaping also had no loss of retrieval efficiency. This indicates that loss of feed-forward planning of wrist orientation, one component of a complex reaching and grasping movement, has an important functional consequence.

DISCUSSION

We demonstrate, for the first time, that rats preshape their paws during reaching, a high-level form of adaptive motor control. Rats are capable of extracting sensory information about the target to plan a movement, in this case, optimized to grasp the pasta. As with adaptive, feed-forward, control in general, the ability to orient the paw to the orientation of the target is a learned response and improved with training. We further show an important role for the CST in this response. The amount of preshaping learned was highly correlated with the amount of preshaping lost after CST injury, demonstrating an important role for the corticospinal system in mediating this adaptive skill.

Feed-forward control of reaching in the rat

Rats preshaped their paws using only sensory information they acquired before contacting the target. The paw approached the target with the bare palm leading, preventing any interaction of the pasta and the hairs of the forelimb that might be used to provide feedback. We also measured only reaches in which the rat grasped and broke the pasta on the first attempt, eliminating the chance a previous attempt had given haptic cues about pasta orientation. In addition, paw angles did not differ whether the previous reach had been to a pasta piece in the same or a different orientation, indicating that rats did not change paw angle based on memory of the previous reach or learning the pattern of presentation. This indicates that sensory information about pasta orientation before contact drives preshaping.

We measured paw orientation during four sequential video images: two before contact, one image at contact, and the next one after contact. We submit that paw angles at each of these times were determined by feed forward control. There are two obvious alternative explanations for the change in paw angle: tactile feedback from the reaching paw and a physical interaction between the paw and the pasta.

Tactile feedback is unlikely to change paw orientation in such a short time period. Between contact and +1 time point a maximum of 33 ms elapsed. For tactile information to change paw angle, the motor program produced by supraspinal centers (presumably M1) must be modified. We estimate the latency for activation of forelimb somatic sensory cortex to be at least 15 ms (Foffani et al., 2008), transfer of information to the motor systems to be approximately 30 ms (Jensen et al., 2006), and the descending pathway conduction time 15 ms (Raineteau et al., 2001). Thus, we conservatively estimate 60 ms is needed to begin the process of tactile feedback. This does not account for the time needed to produce the necessary mechanical changes by muscle contraction. Even if subcortical tactile control is important, it is unlikely to be fully implemented within 33 ms. Thus, it seems implausible that these signals could be turned into changes in movement by the +1 image.

A physical interaction between the paw and pasta also seems unlikely to cause change in orientation for two reasons. First, there typically was no deflection of the pasta by the paw

within 33 ms of contact (e.g. Fig. 2), indicating that no force is being transmitted in either direction. Second, in rats with CST injury, there was little preshaping when reaching for vertical pasta. If physical interaction explained paw angle change at the point of contact or +1 time point, then this effect should remain after injury, even if preshaping is lost earlier in the reach. Finally, and most importantly, horizontal and vertical reaches differ significantly at the -1 time point, before any contact is made.

The determination that rats exhibit feed-forward control of reaching begs the question of what sensory information is used to plan and alter the reaching movement. In primate reaching, motor control is driven largely by visual information and, as discussed above, premotor cortical circuits play a role in the visuo-motor transfer. We suspect, but have not tested, that visual information also controls the paw angle adaptation to the target orientation. Although olfaction leads rats to their food target (Whishaw and Tomie, 1989), it is not well suited to discriminate between pasta pieces of different orientation. This is reinforced by our observation that rats initiate the reach quickly after the barrier between the rat and the target is raised, without pausing to sniff the target. However, the fact that rats use feed-forward sensory information to preshape the paw is key; it validates differential responding to target angle as a model of primate preshaping, regardless of the sensory modality used.

Preshaping in rats and primates

The characteristic feature of preshaping in primates, including humans, is the capacity to use information about the shape of an object to plan and execute a grasp. While it is recognized that rodents are capable of flexible paw and digit control in reaching for a variety of objects (Whishaw and Coles, 1996), our study is the first to quantify the relation between stimulus and response (i.e., pasta orientation and paw orientation). In humans, preshaping begins soon after the onset of movement and hand shape is progressively refined as the hand approaches the object, when a precise match is achieved (Jeannerod et al., 1985). By contrast, preshaping in the rat is a “just in time” phenomenon, occurring immediately prior to contact and grasp. Although wrist orientation is simpler kinematically than configuring the digits to match object shape, it is amenable to simple and accurate analysis and, as such, can be useful in assaying for damage and repair of a motor function that is highly relevant for human motor control.

In primates, we know that visual information is analyzed and transmitted from visual cortex to motor cortex via a complex and hierarchically-organized corticocortical network (Rizzolatti and Luppino, 2001). While corticocortical circuits are not well understood in the rat, they are apt to be less complex than in the primate because the sensory-motor cortical areas are not known to be fractionated into hierarchically-organized subregions (Neafsey et al., 1986) as in the primate. Moreover the higher speed of the reach and the late paw adjustments in the rat than primate suggest a different control pathway. Nevertheless, our findings point to a critical corticospinal system dependence on the output side.

Loss of vertical preshaping is greater than horizontal

Injury of the pyramid caused changes in both horizontal and vertical contralateral preshaping. Horizontal preshaping was significantly delayed in injured rats compared with baseline, suggesting deployment of neural circuits that are not optimized for rapid distal control. Vertical preshaping was abolished (Figure 3A versus 3B; Fig. 5). The greater loss of vertical preshaping likely reflects an imbalance in joint motion control. The key kinematic change to produce vertical paw orientation is wrist supination. Previous studies have reported that supination is more affected than pronation after corticospinal system

injury or inactivation in several species: rats(Whishaw et al., 1993), cats(Martin et al., 2000; Martin et al., 2004), primates(Pettersson et al., 2007), and humans(Taub et al., 2007). Importantly, in the rat single pellet reaching task, of the 10 component movements for reaching to grasp, the 2 supination movements were the most highly affected by pyramidotomy(Whishaw et al., 1993). We propose that corticospinal tract injury in the rat impairs the sensory-motor transformation for preshaping and, additionally, impairs supination more than pronation control. As such, restitution of supination in this preshaping task may be an important target for discriminating the restoration of corticospinal function versus adoption of compensatory movements.

CST role in motor learning

Selective CST injury caused loss of preshaping that was commensurate with the amount of preshaping acquired before injury (e.g. Figure 6). This implies that the component of preshaping that is learned is mediated by the CST and not via another pathway that remains intact. While motor learning has been ascribed to changes in motor cortex(Kleim et al., 2002;Monfils et al., 2005) and injury or inactivation of motor cortex prevents learning(Krakauer, 2006), the output of the learning has not been described. Our experiments suggest the learning that occurs in motor cortex is carried by the CST. In addition, because of the stability of both paw angle measurements and retrieval success rate after injury, no other neural circuits are used to mediate the transfer of learned preshaping from the motor cortex to the spinal cord.

In addition to the loss of the learned component of preshaping with injury, CST injury also appears to limit reacquisition of preshaping. Even with 7 weeks of continued practice after injury, injured rats did not recover any ability to orient their paw to the target. This suggests that learning to preshape itself relies on the CST, although a motor performance deficit could also explain this. Rats either lack compensatory mechanisms for the loss of preshaping and reaching efficiency or fail to use those mechanisms. The stable loss of preshaping performance after injury not only shows the importance of CST control in its execution but also that preshaping would be a sensitive metric for measuring recovery of function after therapeutic intervention.

Abbreviations

CST corticospinal tract

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Figure 1.

A. Reaching apparatus. Rats reach through the aperture of a clear plastic box to grasp a piece of pasta (gray lines) oriented either horizontally (H) or vertically (V). The aperture, platform, and pasta are drawn to scale; the box is not. Measurements are in centimeters. B. Paw angle measurement. Pictured is a reach for horizontal pasta (between black arrowheads) at the point of contact. The orientation of the horizontal pasta is defined as 0° and the vertical pasta, as 90°. C. An idealized schema of 2 measures of preshaping. The paw angle is expected to trend towards 0° for horizontal reaches and 90° for vertical reaches. The difference between the paw angles at any time is referred to as “preshaping between” (black). The difference in paw angle within a vertical or horizontal reach is referred to as

“preshaping within” (gray). D. Representative lesion of the medullary pyramid at the level of the inferior olive. This transverse section was processed using the Kluver-Barrera method, which stains myelin and cell bodies. The right pyramid is intact and the left pyramid is fully transected without intrusion into the underlying brain stem. The black line indicates the boundary of the pyramid and the underlying brain stem; there is some gliosis on the left (injured) side where the pyramid was transected. Olympus BX60 microscope, magnification 40×, scale bar 500 μ m.

Figure 2. Representative reaches for pasta oriented either vertically (VERT) or horizontally (HORIZ) shown in consecutive 16.7msec video frames. Contact is defined as the time when the paw first touches the pasta (white arrows).

Figure 3.

Preshaping in the rat is abrogated by CST injury. Paw angle is measured at successive 16.7msec time points while reaching for pasta oriented vertically (vert, 90°, black) or horizontally (horiz, 0°, gray). The schematic relation shown in Fig. 1B is similar to the actual data shown in Fig. 3A. A. Before injury, rats (n=8) significantly preshape their paws to the reaching target (see Results for full description). B. Injury significantly diminishes preshaping, especially when reaching for vertical pasta.

Figure 4.

Preshaping (A) and reaching efficiency (B) increased with training. Long-trained rats ($n=6$) had paw angles and retrieval rates measured at 2 weeks and at the end of training, 10 weeks. A. Pictured is the difference between paw angles for vertical reaches and horizontal reaches (preshaping between, Fig. 1B) at successive time points. Preshaping increased significantly from week 2 (gray) to week 10 (black; repeated measures ANOVA, $F_{1,33}=7.67$, $p=0.01$) of training. B. Reaching efficiency increases for all rats (t-test, $t_{11}=3.11$, $p=0.01$).

Figure 5.

CST injury diminishes vertical preshaping. We compared the amount of preshaping within a reach, which is the change in paw orientation between time points -2 and $+1$ (as indicated in Figure 1B), before and after selective CST injury. Vertical preshaping was strongly abrogated by CST injury (t -test, $t_{15}=5.88$, $p<0.0001$), while horizontal preshaping was unchanged ($t_{15}=0.90$, $p=0.38$).

Figure 6.

Amount of preshaping before injury predicts the effect of injury on preshaping. Preshaping improves with practice (e.g. Fig. 4) and worsens with CST injury (e.g. Fig 3A versus 3B). We reasoned that if preshaping depends on the CST for learning, then the amount of preshaping at baseline would predict the amount of preshaping lost after injury. Indeed, these measures are highly correlated ($R^2 = 0.88$; $p = 0.004$), and their relationship is described by $y = -0.90x + 11.5$.

Figure 7.

Injury reduces reaching efficiency, an effect that correlates with loss of preshaping. A. The success rate for pasta retrieval declined significantly after injury (pooled from all times tested, t-test, $t_{15}=2.60$, $p=0.02$). B. Decline in success rate correlated strongly with loss of preshaping. The preshaping angle ratio represents “preshaping between” after injury divided by “preshaping between” before injury. The retrieval ratio is success rate after injury divided by success rate before injury. This relationship is strong ($R^2=.82$, $p<0.01$) and is described by $y=0.99x+0.05$. This indicates an important functional role for preshaping.