Functional Reorganization of the Rat Motor Cortex Following Motor Skill Learning

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Kleim, Jeffrey A., Scott Barbay, and Randolph J. Nudo. Functional reorganization of the rat motor cortex following motor skill learning. J. Neurophysiol. 80: 3321–3325, 1998. Adult rats were allocated to either a skilled or unskilled reaching condition (SRC and URC, respectively). SRC animals were trained for 10 days on a skilled reaching task while URC animals were trained on a simple bar pressing task. After training, microelectrode stimulation was used to derive high resolution maps of the forelimb and hindlimb representations within the motor cortex. In comparison with URC animals, SRC animals exhibited a significant increase in mean area of the wrist and digit representations but a decrease in elbow/shoulder representation within the caudal forelimb area. No between-group differences in areal representation were found in either the hindlimb or rostral forelimb areas. These results demonstrate that motor skill learning is associated with a reorganization of movement representations within the rodent motor cortex.

METHODS

INTRODUCTION

Behavioral training

Eight male, Long-Evans hooded rats, ~5 months of age (450–550 g), were randomly assigned to either a skilled reaching condition (SRC; n = 4) or an unskilled reaching condition (URC; n = 4) in a manner that equally distributed littermates across condition. Animals were placed on a restricted diet (50 mg food/1 g body weight/d) for 3 days before training and housed in a large Plexiglas cage (40 × 40 × 35 cm) for the entire experiment. The cage was divided into two equal compartments by a clear Plexiglas barrier, and each compartment had a slotted opening (1 × 3 cm) at the front of the cage. The URC compartment also had a small lever (2 × 2 cm) located within the cage beneath the opening. Pressing the lever dispensed a food pellet (45 mg, Bioserv) into a nearby receptacle, and the animals retrieved the pellet by using the tongue and mouth. SRC animals were given a brief shaping procedure, 1 day before training, that encouraged them to reach through the slot to obtain food pellets (45 mg, Bioserv) from a circular, stationary table (16-cm diam) outside the cage. For the first 5 days of training, the table was moved 1 cm away from the opening, forcing the animals to grasp the pellets rather than simply scrape them into the cage. On training days 6 through 10, pellets were placed onto 16 equally spaced positions around the perimeter of the table, which was then slowly rotated (6 rpm). During each training session, SRC animals were allowed to retrieve pellets until a total of 400 reaches was made (~30 min). The number of reaches per successful retrieval was then calculated for each session. URC animals were given 400 pellets per day (for 10 days) that could be individually obtained ad libitum by pressing the lever. The paw used preferentially for lever pressing (URC) and skilled reaching (SRC) was noted. In addition to the food pellets obtained during training, animals in both conditions received a 20-g supplement of standard laboratory chow after each daily training session.

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maps of the motor cortex contralateral to the trained paw (see Nudo et al. 1990 for further details). Briefly, animals were initially anesthetized with ketamine hydrochloride (70 mg/kg ip)/xylazine (5 mg/kg ip) and received supplementary doses of ketamine (20 mg/kg ip) and acepromazine (0.02 mg/kg ip) as needed. Microelec-
trode (600–800 kΩ) penetrations were made at 250-μm inter-
vals at a depth of ~1,800 μm (corresponding to cortical layer V) with a hydraulic microdrive. Stimulation consisted of a 40-ms train of 13, 200-μs monophasic cathodal pulses delivered at 350 Hz from an electrically isolated, constant current stimulator. Pulse trains were delivered at a rate of 1 Hz. Evoked movements were examined while the animals were maintained in a prone position and the limb supported in a consistent position. At each site, stimulating current was gradually increased (~60 μA) until a movement could be detected (threshold current). If no movement could be detected at ~60 μA, the site was defined as nonresponsive.

A computer algorithm was used to define movement regions from the pattern of electrode penetrations made on the cortical surface (Nudo et al. 1990). An image analysis program (IMAGE v1.61) was then used to calculate the areal extents of each move-
ment category within the rostral forelimb area (RFA), the caudal forelimb area (CFA), and the hindlimb area (HLA) (Neafsey and Sievert 1982; Neafsey et al. 1986). Thresholds were also tallied to obtain a mean threshold for each movement category.

**RESULTS**

**Behavioral results**

An analysis of variance with DAY as a within-subject fac-
tor showed a significant effect of DAY on number of reaches

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**FIG. 1.** Performance on the skilled reaching task (n = 4). Mean number of reaches/retrieval (±SE) progressively decreased during both the station-
ary and rotating table phases.

**Electrophysiological mapping**

Within 2 days of the final training session, standard microelec-
trode stimulation techniques were used to derive high resolution
FIG. 3. Mean (±SE) total area of movement representations in the RFA (A) and CFA (B) for all SRC (n = 4) and URC (n = 4) animals. SRC animals had significantly increased areal representations of digit (F) and wrist (G) movements but decreased elbow/shoulder representations (H) in the CFA in comparison with the URC animals (*P < 0.05; **P < 0.01; ***P < 0.001). No significant differences were found in the RFA (C–E).

Electrophysiological results

Each evoked movement map was derived from ~198 (±8) microelectrode penetration sites (Fig. 2). Student’s t-tests (two-tailed, independent; P < 0.05) revealed no significant between-group differences in total areal representation of either the RFA [t(6) = 0.16; P = 0.88] or CFA [t(6) = 1.84; P = 0.12; Fig. 3, A and B]. Within the RFA, there were also no significant differences in areal representations of the digits [t(6) = 0.255; P = 0.83], wrist [t(6) = 0.05; P = 0.96], or elbow/shoulder [t(6) = 1.16; P = 0.30; Fig. 3, C–E]. Within the CFA, the SRC animals did show a significantly greater mean area of wrist [t(6) = 5.30; P = 0.006] and digit [t(6) = 2.87; P = 0.03] representations in comparison with the URC animals (Fig. 3, F and G). Conversely, the URC animals had significantly greater elbow/shoulder representations than the SRC animals [t(6) = 6.85; P = .0006; Fig. 3H] in the CFA. The mean representational area of the hindlimb did not differ significantly between the URC (1.17 ± 0.18 mm²) and SRC (1.13 ± 0.23
mm²) animals \( t(6) = 0.02; P = 0.98 \). No significant between-group differences in evoked movement thresholds were found for any movement category in either forelimb region (Table 1). Similarly, no significant differences in evoked movement thresholds were found between the URC \((45.5 \pm 3.32 \mu A)\) and SRC \((45.6 \pm 2.98 \mu A)\) animals within the HLA \( t(6) = 0.01; P = 0.97 \).

### DISCUSSION

Rodent models of skilled reaching have been used extensively to study the neural bases of movement (Whishaw et al. 1993), recovery from brain damage (Price and Fowler 1981), and motor skill learning (Greenough et al. 1985). These experiments have shown that the motor cortex is involved in executing reaching movements (Castro 1972) and exhibits structural/physiological changes in response to skillfully adapting these movements (Friedman et al. 1997; Greenough et al. 1985; Withers and Greenough 1989). This experiment extends these results to show that the functional organization of the rodent motor cortex is also systematically altered by motor skill learning. Rats trained to produce skilled forelimb reaching movements exhibited a greater area of wrist and digit representations with the CFA than the unskilled reaching animals. In these same rats, no changes were found in the hindlimb representation, presumably because it is not integrally involved in skilled forelimb placement (Barth et al. 1990). Whishaw and Pellis (1990) have shown that skilled reaching in the rat involves first targeting the paw with the shoulder and forelimb. This is followed by coordinated wrist and digit movements to grasp/retrieve the pellet. The increased cortical representation of the wrist and digits found in this experiment may reflect the acquisition of the skilled wrist and digit movements associated with successfully performing the task.

The changes in wrist/digit representations appear to occur at the expense of elbow/shoulder movement representations as URC animals had a significantly greater area of elbow/shoulder representations than SRC animals. It is possible that the larger elbow/shoulder representations seen in the URC animals resulted from pressing the lever. However, the URC maps in this experiment were similar to previously reported maps from untrained animals where the CFA was dominated by elbow/shoulder representations with some wrist and little or no digit representations (Neafsey and Sievert 1982; Neafsey et al. 1986; Nudo et al. 1990). It is also unlikely that the increased elbow/shoulder representations in the URC animals resulted simply from increased use as the reaching movements performed by the SRC animals also required use of the elbow and shoulder (Whishaw and Pellis 1990). Furthermore, increased use in the absence of skill acquisition has been shown to result in no net change in movement topography within the primate motor cortex (Nudo et al. 1997) or synapse number within the rat motor cortex (Kleim et al. 1996).

Given the robust changes in movement representations observed in the CFA, the failure to find any significant changes in movement topography within the URA was somewhat surprising. It is possible that, because of the small size of this area, subtle changes in movement topography might go undetected with the spatial resolution of the motor maps obtained here. The URA was suggested to be functionally distinct from the CFA based on differences in connectivity (Rouiller et al. 1993), its apparent lack of sensory input (Sievert and Neafsey 1986), and the presence of movement-related activity that precedes that of the CFA (Donoghue 1985). An intriguing possibility is that these two motor areas participate in different aspects of movement control (Barth et al. 1990) and thus exhibit different patterns of plasticity in response to motor skill acquisition.

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