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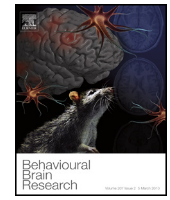

Research report

Forelimb training drives transient map reorganization in ipsilateral motor cortex

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HIGHLIGHTS

- Motor training results in trained forelimb map plasticity in ipsilateral cortex.
- Map expansion was observed after three months of training.
- Map normalization occurs within six months of continued training.
- Task performance is retained despite map normalization.

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ABSTRACT

Skilled motor training results in reorganization of contralateral motor cortex movement representations. The ipsilateral motor cortex is believed to play a role in skilled motor control, but little is known about how training influences reorganization of ipsilateral motor representations of the trained limb. To determine whether training results in reorganization of ipsilateral motor cortex maps, rats were trained to perform the isometric pull task, an automated motor task that requires skilled forelimb use. After either 3 or 6 months of training, intracortical microstimulation (ICMS) mapping was performed to document motor representations of the trained forelimb in the hemisphere ipsilateral to that limb. Motor training for 3 months resulted in a robust expansion of right forelimb representation in the right motor cortex, demonstrating that skilled motor training drives map plasticity ipsilateral to the trained limb. After 6 months of training, the right forelimb representation in the right motor cortex was significantly smaller than the representation observed in rats trained for 3 months and similar to untrained controls, consistent with a normalization of motor cortex maps. Forelimb map area was not correlated with performance on the trained task, suggesting that task performance is maintained despite normalization of cortical maps. This study provides new insights into how the ipsilateral cortex changes in response to skilled learning and may inform rehabilitative strategies to enhance cortical plasticity to support recovery after brain injury.

1. Introduction

Skilled motor training causes reorganization of movement representation maps in the motor cortex contralateral to the trained limb [1–4]. This reorganization is specific to the trained movement, and repetitive unskilled movements do not result in map reorganization [1,2].

Neural circuits in ipsilateral motor cortex also contribute to motor function in both healthy [5–8] and injured subjects [9,10]. Unilateral motor cortex injury has been shown to result in ipsilateral motor dysfunction [11,12]. Additionally, after unilateral brain injury, significant reorganization occurs in the undamaged hemisphere (the hemisphere ipsilateral to the affected limb) [13]. This ipsilateral reorganization is believed to contribute to recovery of motor function [14,15]. Despite the presence of ipsilateral motor

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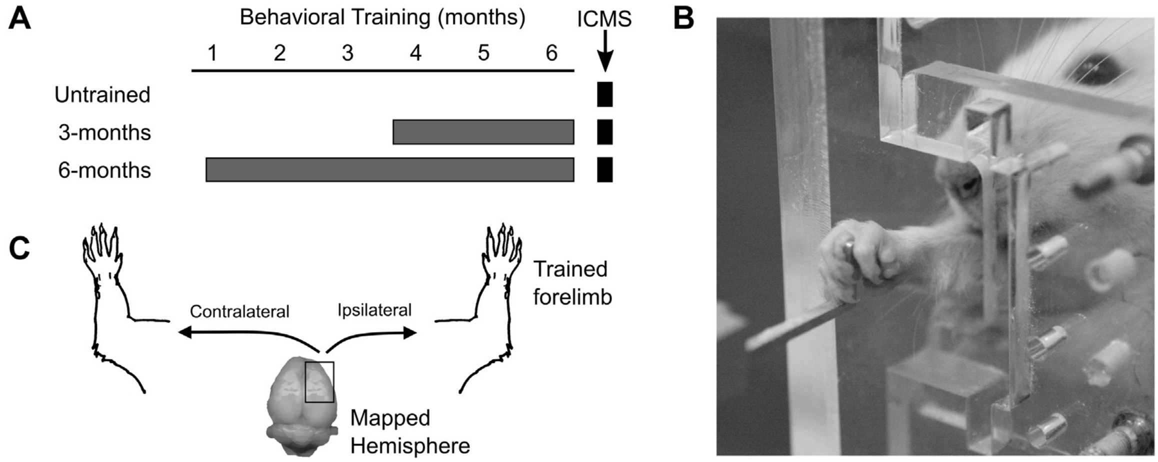

Fig. 1. Experimental Design. (A) Rats were trained on the isometric pull task for 3 or 6 months and then underwent ICMS mapping. An additional group of untrained controls rats was mapped. (B) Example of a rat performing the isometric pull task. (C) ICMS was performed in the right hemisphere in all rats. The primary outcome measure was the number of ipsilateral (right) forelimb responses observed during ICMS. Contralateral (left) movements evoked by ICMS in the right hemisphere were also recorded.

control in both healthy and injured conditions, little is known about how motor training affects plasticity in the ipsilateral hemisphere.

We hypothesized that unilateral skilled motor training would increase the representation of the trained forelimb in the ipsilateral motor cortex. To test this, we trained rats to perform the isometric pull task, which involves skilled usage of the right forelimb. After several weeks of training, standard ICMS was used to derive motor cortex organization in the right hemisphere (ipsilateral to the trained limb) in trained rats and untrained controls.

We found that training increases the area representing the trained forelimb in ipsilateral motor cortex. Additionally, we observed that these map changes are transient despite continued training, similar to reports examining the motor cortex contralateral to the trained limb [16]. This study documents novel cortical map plasticity of trained forelimb representations in ipsilateral motor cortex and may inform strategies to enhance ipsilateral reorganization to support recovery after unilateral brain injury.

2. Methods

2.1. Subjects

Seventeen adult female Sprague-Dawley rats were used. All rats were 4–5 months old and weighed at least 250 g at the beginning of the experiment. Rats were food deprived to no less than 85% of their normal body weight throughout the experiment. 85% of normal body weight was calculated using each rat's weight at the beginning of the experiment. The rats were housed in a reverse 12:12 h light cycle. All handling, housing, surgical procedures, and behavioral training of the rats were approved by the University of Texas Institutional Animal Care and Use Committee.

2.2. Experimental design

The rats were separated into three experimental groups: untrained controls (n = 6), 3-months training (n = 6), and 6-months training (n = 5). Each of the training groups performed the isometric pull task for two 30 min sessions each day, 5 days per week (Fig. 1A and B). Rats in the 3-month training group were trained for 11–13 weeks, and rats in the 6-month training group were trained for 22–24 weeks. Untrained rats underwent ICMS mapping to document baseline cortical representations. After completion of the prescribed duration of training, all rats underwent ICMS to investigate right-sided movement representations in the ipsilateral (right) hemisphere (Fig. 1C). Both untrained and trained rats were between 7 and 10 months of age at the time of ICMS.

2.3. Behavioral apparatus

The behavioral apparatus and software were used as described in previous studies [17–20]. The isometric pull task is designed to assess overall skilled forelimb function and volitional forelimb strength. The apparatus consisted of an acrylic box (25.4 × 30.5 × 12.1 cm) (MotoTrak Base Cage, Vulintus, Inc., Dallas, TX). The box contained a slot in the front right corner that the rat could reach through to access an aluminum pull handle. The slot was sized and positioned such that rats could only reach and pull using their right forelimb. For fully trained rats, the pull handle was centered in the slot at a height of 6.4 cm from the cage floor and 1.9 cm outside the cage relative to the inner cage wall. The aluminum handle was connected to a force transducer that could measure pull force with sub-gram accuracy (Pull Behavior Module, Vulintus, Inc., Dallas, TX). The force transducers were inspected daily and recalibrated when necessary. Matlab software was used to control the behavioral apparatus. A microprocessor controller (Controller, Vulintus, Inc., Dallas, TX) sampled the force transducer at 100 Hz and sent the information to the Matlab software which displayed the data on screen, controlled the behavior session, and saved the data to permanent files.

2.4. Behavioral training

Rats underwent training for two 30-min sessions per day, five days per week, with at least 2 h between daily sessions. In initial training sessions, shaping procedures were similar to those previously described [17–20]. Rats were trained to pull on the handle with at least 120 g of force, and single reward pellets were dispensed following successful trials (45 mg dustless precision pellet, BioServ, Frenchtown, NJ). If rats did not receive at least 50 pellets per day, they were given 10 g of additional pellets after daily training sessions were completed.

A trial was initiated when at least 10 g of force were applied to the pull handle. After initiation, the force on the pull handle was sampled for 4 s. If the 120 g force threshold was met within a 2 s window after force initiation, the trial was recorded as a success and a reward pellet was delivered. If the force threshold was not reached within 2 s, the trial was recorded as a failure and no reward was delivered.