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Research report

Parallel stages of learning and recovery of skilled reaching after motor cortex stroke: "Oppositions" organize normal and compensatory movements

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Abstract

Forelimb/hand motor cortex injury in rodents and primates causes impairments in skilled paw/hand movements that includes a period of movement absence followed by functional recovery/compensation. Although the postsurgical period of movement absence has been attributed to "shock" or "diaschisis", the behavior of animals during this period has not been fully described. Here, rats were trained to reach for single food pellets from a shelf and then the vasculature of the forelimb region of the sensorimotor cortex contralateral to the reaching limb was removed. A control group received a posterior parietal cortex devasularization. Frame-by-frame video analysis of reaching behavior showed that the stages of the acquisition of skilled reaching and the stages of recovery after motor cortex stroke were similar. The animals sequentially learn three relationships or "oppositions" between a body part and the food target. The oppositions are invariant relationships but each can be achieved with movements that can vary from reach to reach and between rats. A snout-pellet opposition organizes the movements of orienting, a paw-pellet opposition organizes limb transport and grasping the pellet in the digits, and a mouth-pellet opposition organizes limb withdrawal and the release of the food into the mouth. The three oppositions and the movements that they recruit were disrupted after motor cortex damage, but not parietal cortex damage. The oppositions were reestablished after stroke in the order in which they were acquired prior to stroke. Enduring impairments were more noticeable in transport and withdrawal oppositions. That the stages of recovery from motor cortex stroke parallel those of initial acquisition are discussed in relation to contemporary explanations of diaschisis and the contribution of motor cortex to motor learning.

Keywords: Cortical stroke; Motor cortex; Motor engram; Motor learning; Motor skill; Oppositions; Skilled reaching; Skilled reach learning; Recovery from stroke; Sensorimotor cortex; Parietal cortex

1. Introduction

Rats like many other animals are adept at reaching for and grasping food using a single paw, a behavior termed skilled reaching [48]. Because the actions of the limb, forepaw, and the digits are in the main consistent between rats and primates [51], rats can serve as a model for exploring the neural basis of skilled movements, motor learning, and processes of disease [46,47]. Several lines of evidence suggest that motor cortex, especially the rostral forelimb area (RFA) and the caudal forelimb area (CFA), is central to skilled reaching [16,38]. Within these regions, forelimb muscle contractions can be obtained with microstimulation [15,31]. Also, morphological adaptations including increased complexity of dendritic arborization [14,56] and synaptogenesis [20,22], neurophysiological adaptations such as facilitation of synaptic efficacy for long-term potentiation (LTP) [29,39], and reorganization of motor movement representations [21,22] are localized in the forelimb regions of motor cortex in association with the acquisition and performance of skilled reaching. Finally, damage to motor cortex by trauma, disease, or stroke results in impairments of skilled reaching [2,9,27,45,52]. For an initial period of hours or days after injury, animals may make no attempts to use the contralateral-to-lesion limb and can be considered to be in a state of behavioral depression or shock. During the next 2 weeks postsurgery, reaching success again approximates presurgical levels [9,45,52], but

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now includes compensatory movements such as the substitution of body rotation for lost limb aim, advance, pronation, and supination [9,27,52]. Together these findings show that the motor cortex is involved in both the learning and the performance of skilled reaching.

There are two distinctive features of the behavioral effects of motor cortex damage/stroke relative to the effects of damage to other portions of the motor system. First, rats with motor cortex damage display a strong tendency to change limb preference [3,36,48]. Although damage to other motor system regions will eventually produce a switch in limb preference as a compensatory strategy [11,19,48], switch in limb preference is evident almost immediately after motor cortex injury. This change in limb preference allows animals with motor cortex injury to display more rapid acquisition with the non-preferred paw than occurs for control animals [1,36]. The change in preference also necessitates the use of bracelets or other restrictions on the ipsilateral-to-lesion paw if use or "recovery" in the contralateral-to-lesion paw is to be obtained [1,48]. Second, there is an initial period of depression of reaching behavior following which success only gradually improves [45]. The uniqueness of these symptoms to motor cortex damage is evident as rats with basal ganglia lesions [28,37,48], red nucleus lesions [54], or corticospinal tract cuts [50], although motorically impaired do not show similar behavior. Although there might be numerous neural mechanisms mediating the acute depression in reaching after motor cortex damage, neural depression or diaschisis [8] is a potential leading explanation. In diaschisis [44], behavioral depression is proposed to be due to transient shock in neural structures connected to, but distant from, the site of injury. Recovery is proposed to be due to the abatement of neural depression in these regions. Surprisingly, although patterns of recovery have been described as primitive to mature [4,41] and proximal to distal [25,43] there has been little study of the causes of behavioral depression of limb use in the immediate postoperative period. The objective of the present study was to examine skilled reaching in the acute period after motor cortex damage with the expectation that documentation of the first movements of recovery could provide insight into the organization of skilled reaching.

For the experiment, rats were trained on a single pellet reaching task and then received a stroke via blood vessel devascularization to the forelimb regions of motor cortex (experimental group) or to the parietal cortex (control group) in the hemisphere contralateral to the trained paw for reaching [9,11,45]. The area damaged in the experimental group was selected to ensure that the forelimb areas as defined by intracortical microstimulation [15,21,31], behavioral [3,36,45] and anatomical [5,55] studies, which could vary from rat to rat, were consistently damaged in all subjects. An area comparable in size but posterior in location was devascularized in the control group with the objective of damaging the same amount of neocortical tissue but at the same time sparing as much of the forelimb motor areas as possible. In order to directly compare initial learning with postsurgical recovery, all behavior was video recording for subsequent frame-by-frame study. Because the behavior of animals when first re-exposed to the task can consist of a variety of behaviors both related to and unrelated to the act of skilled reaching, an analysis based on movement notation [7] was used to identify invariances in behavior. This approach has been successful in decomposing complex behaviors such as play [33], courtship [57], and aggression [35] into simpler goals of maintaining oppositions between a body part of one animal and a target body part of a conspecific.

2. Materials and methods

2.1. Animals

Twelve female Long-Evans hooded rats, 120 days old, and weighing 290–320 g from the University of Lethbridge vivarium were used. The experiments were conducted in compliance with the guidelines of the University of Lethbridge animal care committee and the Canadian Council for Animal Care. Rats were housed in Plexiglas cages (36 cm long, 20 cm wide, and 21 cm deep) with sawdust bedding, in groups of three in a colony room maintained on a 12/12 h light/dark cycle (08:00–20:00 h).

2.2. Feeding

For initial and subsequent training, the rats were gradually food deprived to 90–95% of their body weight by once a day feeding of a measured quantity of Purina rat chow. For the week prior to reach training, each rat received twenty 45 mg dustless precision banana-flavoured pellets (product #F0021, Bioserve Inc., Frenchtown, NJ, USA) 1 h prior to the daily chow ration. The objective was to introduce rats to the pellets, which would later serve as reaching targets, in a familiar environment. Once reach training began and until the end of the study, only rat chow was served in the home cage once a day in sufficient amounts to maintain all rats at 90–95% of their original body weight. The number of banana-flavoured pellets a rat received on a given training day depended on the rat's reaching accuracy, but it did not exceed 25 pellets (1.125 g).

2.3. Surgery

2.3.1. Motor cortex devascularization

Lesions were made in motor cortex to ensure that forelimb areas as defined by previous behavioral [3,36,45], anatomical [5,55], and electrophysiological [5,15,21,31] studies were damaged. Animals received an injection of atropine nitrate (0.1 mg/kg i.p.; Sigma–Aldrich, St. Louis, MO) to facilitate respiration throughout surgery and were then anesthetized with sodium pentobarbital (65 mg/kg, i.p.; Sigma–Aldrich, St. Louis, MO). Four holes were drilled using a fine dental burr in the skull overlaying the motor cortex at stereotaxic coordinates measured from Bregma (anterior (A) and lateral (L)) were A = −1.0 mm, L = +1.0 mm; A = +4.0 mm, L = +1.0 mm; A = −1.0 mm, L = +4.0 mm; A = +4.0 mm, L = +4.0 mm. The rectangular area enclosed by the four points was then trephinated and the dura was removed. The underlying tissue was devascularized by gently wiping away the pia mater and blood vessels with a saline-soaked cotton swab [23,40]. The incision was closed and the animal's condition was monitored in a recovery room for 24 h, at which time it was returned to the colony room.

2.3.2. Parietal cortex devascularization

Procedures were identical to motor cortex surgery but the coordinates measured from Bregma were A = −3.5 mm, L = +1.0 mm; A = −3.5 mm, L = +4.0 mm; A = −8.5 mm, L = +1.0 mm; A = −8.5 mm, L = +4.0 mm.

2.4. Reaching boxes

Single pellet reaching boxes [49] were made of clear Plexiglas, with the dimensions 45 cm × 14 cm × 35 cm. In the center of each front wall was a vertical slit 1 cm-wide, which extended from 2 cm above the floor to a height of 15 cm. On the outside of the wall, in front of the slit, mounted 3 cm above the floor, was a 2 cm-deep shelf. Two indentations on the surface of the shelf were