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FUNCTIONAL MAPPING OF THE MOTOR CORTEX OF THE WHITE MOUSE BY A MICROSTIMULATION METHOD

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Studies on 33 anesthetized white mice were used to determine the motor representation of facial muscles and limb muscles by an intracortical microstimulation method. Microstimulation produced predominantly ipsilateral movement responses of facial muscles and contralateral responses in fore- and hindlimb muscles. Low-threshold stimulation in the left and right hemispheres showed a clear asymmetry of the motor representation of the facial muscles. Movement responses of the hindlimbs were obtained on microstimulation of the frontal regions of the neocortex, demonstrating the existence of multiple motor representations of muscles in the neocortex.

Key words: *Mouse motor cortex, intracortical microstimulation, motor representation, corticomotor asymmetry.*

Electrical microstimulation methods have in recent years been used for detailed studies of the cortical motor representations of the limbs and facial muscles in primates [16, 17], cats [11, 18], rabbits [1], guinea pigs [6, 14], and, in most detail, white rats [8, 9, 12, 19]. In our previous studies on white mice, the focus has been placed on mapping of the representations of the vibrissae and facial muscles [2, 3, 4], and these studies identified important features of the organization of the corticofacial system in mice: pronounced lateral asymmetry in the representation of the vibrissae and jaw, and a predominance of ipsilateral control over contralateral. The motor representations of the limbs have remained unstudied. Since studies thus far reported in mammals have shown that corticomotor control of the facial and limb muscles followed the general rule of contralateral (crossed-over) dominance [2], more detailed comparisons of the corticofacial and cortico-limb motor responses in mice are needed. With this aim, we elected to carry out systematic bilateral mapping of the anterior parietal and frontal regions of the neocortex in white mice, cytoarchitectonic maps of which have been published previously [7], using a microstimulation method with recording of local, slightly suprathreshold motor responses.

METHODS

Acute experiments were performed using 33 mongrel white mice of both sexes, weighing 20-37 g, under thiopental (70-80 mg/kg, i.p.) anesthesia. Animals were given preliminary s.c. doses of 0.33 ml of 0.1% atropine sulfate. Scalping and craniotomy over the motor cortex region were carried out using s.c. analgesia with 0.5% novocaine. A fast-setting resin was used to attach the holders of a stereotaxic apparatus tightly to the skull, and the abdomen was supported in an elastic sling. The exposed surface of the cerebral hemispheres was covered with warmed Vaseline.

Microstimulation was carried out using glass electrodes filled with 1.5-2.0 M sodium citrate; the tip diameter was 4-8 μm and the input resistance was 0.7-1.5 MΩ. Electrodes were inserted transdurally using a mechanical micromanipulator, perpendicularly to the surface of the cortex, with 0.5-mm spaces between tracks, in the mediolateral and caudorostral directions. Stimulation was with short series of rectangular impulses of duration 0.4 msec, frequency 333 Hz, generally with 3-7 impulses

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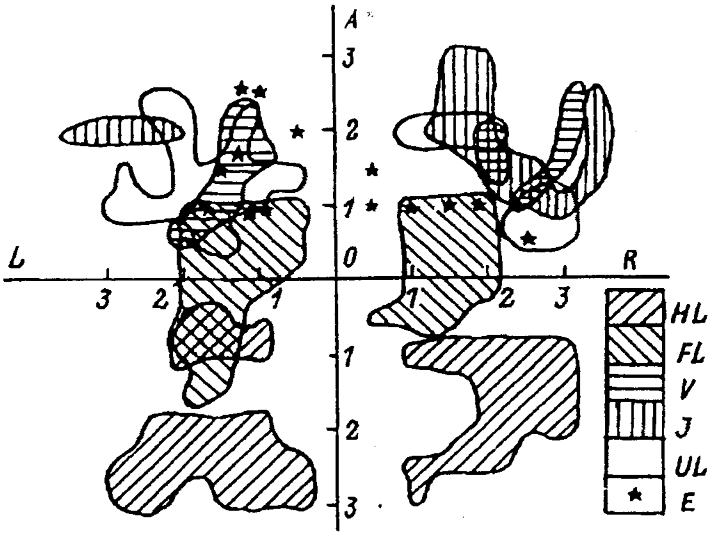

Fig. 1. General map of motor representations of the facial and limb musculature in the neocortex of the white mouse ($n = 33$). The vertical line indicates the sagittal suture, and the horizontal line shows the coronal suture. *O* is the bregma, *A* is the frontal band, *P* is the caudal band, *L* is the left hemisphere, *R* is the right hemisphere. Continuous lines show the margins of representations; *HL* and *FL* are the representations of the hindlimb and forelimb respectively; *V*, *J*, *UL* and *E* are the representations of the vibrissae, jaw, upper lip, and eyelids + eyeball respectively.

per series, and an intensity of no more than 40 μA [2-4]. Currents were measured for each stimulation in terms of the voltage drop over a calibration resistance of 10 kΩ. Responses were recorded from the facial and limb muscles using a photodiode [1]. Recorded responses were photographed from an oscilloscope screen using an FOP-2 camera.

RESULTS

General Motor Map. Figure 1 shows an overall map of the motor representations of the facial and limb musculature in the neocortex of the white mouse (data from 33 animals). Low-threshold stimulation in both hemispheres produced predominantly ipsilateral responses in the facial muscles (in 40 of 57 tracks). Contralateral facial responses were obtained in only seven tracks, while bilateral responses were seen in 10 tracks. At the same time, responses at the distal joints of the fore- and hindlimbs (fingers, hands, forearms, feet) were strictly contralateral. Only occasional tracks in some of the animals produced ipsilateral responses of the proximal parts of the limbs (shoulders, thighs), as has previously been observed by a number of investigators in studies on cats [11], rabbits [1], and monkeys [17].

Facial motor representations occupied very large territories in both hemispheres: the caudal margin bordered the motor representation of the forelimbs, without any overlap, some 0.5 mm anterior to the bregma, and spread rostrally at least 3 mm; the lateral margin was up to 3.5 mm from the sagittal suture in both hemispheres. The zone from which forelimbs responses were obtained occupied a band of cortex 1 mm wide and running from 1 mm from the bregma in the rostral and caudal directions. The parietal cortex contained the representation of the hindlimbs, which bordered the caudal margin of the representation of the forelimbs.

The overall map of the motor representation of the snout and limbs in the mouse creates the impression that although the sizes and configurations of particular representations in each hemisphere were significantly different, there are fairly large regions of mutual penetration (Fig. 1). However, during experiments on individual animals, zone margins were clearer and showed less overlap, more precisely reflecting the topographic plan of the representations of particularly muscle and joint groups, as has previously been noted in primates [17].

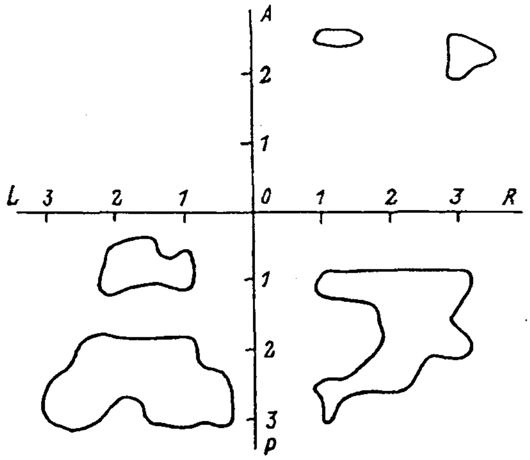

Fig. 2. Map of the motor representation of the hindlimbs in the neocortex of the white mouse. For further details see caption to Fig. 1.

Limb Representations. The motor representation of the forelimbs in the mouse neocortex occupied an intermediate position, extending to equal extents on both sides of the bregma (Fig. 2). The region of overlap with other representations was very insignificant, as shown in the overall map (Fig. 1). In most tracks, stimulation of this zone produced contralateral responses of the wrist or individual fingers (extension), indicating that the neocortex representations of the forelimb muscles of the mouse show fine spatial differentiation. The response thresholds of forelimb muscles varied from 10 to 35 μA. Despite the evident separation of zones responsible for controlling the muscles of distal joints, we were unable to detect any indication of geometrical ordering in the distribution of points eliciting movements of the muscles. It would appear that the zone controlling the wrist and fingers is compact, occupying most of the representation, while the zone controlling the forearm and shoulder muscles is diffuse.

The zone eliciting hindlimb responses was usually located about 1 mm posterior to the bregma, spreading up to 3 mm caudally (Fig. 2). The forelimb representation was located rostral to this zone, as described above. Microstimulation laterally, medially, and caudally to the hindlimb response zone produced no motor responses. The thresholds for eliciting movements of the feet and knees ranged from 0.5 to 30.0 μA, while those for movements of the thigh muscles were 15-35 μA. Stimulation of the rostral part of the hindlimb representation generally produced responses from the foot and knee muscles, very rarely with movements of the toes. Stimulation of other parts of this representation led to motor responses from thigh muscles.

Small regions of the frontal cortex of the right hemisphere were also found, in which stimulation led to hindlimb (foot, thigh) responses; these were located 2.0-2.5 mm rostral to the bregma, which corresponded predominantly to the representation of the facial musculature. Admittedly, the thresholds for producing these responses were rather higher – of the order of 40 μA – though these observations demonstrate the possibility of double (multiple) hindlimb representations in the mouse motor cortex.

Vibrissa Representation. Figure 3 shows an overall map of the motor representation of the vibrissae in the frontal cortex of the mouse. All experiments showed clear dominance of ipsilateral vibrissa responses at threshold or slightly suprathreshold stimulation intensities (from 10 to 35 μA). Significantly more rarely, bi- and contralateral vibrissa responses were seen, i.e., in 10 and 7 of 57 tracks respectively. Ipsilateral vibrissa responses were easily produced by short series of rhythmic current impulses. In most cases, 4-5 impulses were sufficient, while in the remaining cases 2-3 impulses produced responses; however, the most effective low-threshold stimulation consisted of trains of seven impulses.

Significant differences were seen in the locations of the vibrissal representations in the left and right hemispheres of the brain. In the left hemisphere, the vibrissa motor zone occupied a large territory with coordinates from 0.5 to 2.5 mm anterior of the bregma to 0.5 to 3.0 mm from the sagittal suture. Ipsilateral responses were initiated by stimulation in the middle part of the vibrissa representation, while the marginal zones produced contra- and bilateral responses. In the right hemisphere, the vibrissa representation was located more laterally than in the left, and was separated into two small subzones (Fig. 3, *A*). Stimulation in both hemispheres mostly produced responses of small groups of vibrissae, with simultaneous move-

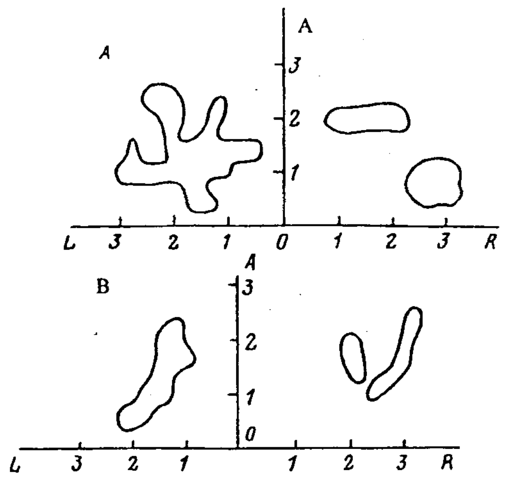

Fig. 3. Map of the motor representations of the facial vibrissae (*A*) and upper lip (*B*) in the neocortex of the white mouse. For further details see caption to Fig. 1.

ments of 4-5 vibrissae, along with other random vibrissae or horizontally neighboring vibrissae; responses from single vibrissae were seen more rarely.

Representation of the Upper Lip. The location of the representation of the upper lip also showed significant interhemisphere differences (Fig. 3, *B*). The map showing all "lip" tracks shows that two separate zones producing upper lip responses were seen in the right hemisphere, located between the "vibrissa" zones. In the left hemisphere, the upper lip zone showed a large extent of overlap with the "vibrissa" zone. In most cases, microstimulation of both hemispheres produced ipsilateral responses of the rostral parts of the upper lip, close to the nose itself, and was arbitrarily termed the "muzzle." Lip response thresholds varied from 4 to 30 μA. Some tracks showed mixed movements of the lip and vibrissae when stimulation intensity was close to threshold, which could be associated with entry of the electrode into the marginal areas of these representations.

Representations of the Jaw Muscles, Eyelids, and Tongue. Figure 4 shows a map of the motor representations of the lower jaw. In the left hemisphere, this occupied a small band of cortex, located 2 mm anterior to the bregma and 2-3.5 mm from the sagittal suture. Conversely, in the right hemisphere, the jaw representation occupied a large area, characterized by a variety of response types; this was the dominant of the facial representations. Responses of the jaw muscles due to stimulation in the left hemisphere generally consisted of protraction or opening of the mouth, while stimulation in the right hemisphere produced a variety of jaw movements: protraction, retraction, deviation, opening, and closing of the mouth. Response thresholds for the jaw were higher than those for other facial muscles: the smallest threshold current was 15 μA.

Tracks initiating eyelid movements were located in a narrow band of cortex located along the sagittal suture, corresponding essentially to cytoarchitectonic field 8 [7], as shown in Fig. 3, *B*. Eyelid responses had the lowest stimulation thresholds, starting from 1 μA. Both ipsi- and bilateral movements were seen. Apart from these response variants to stimulation in the left and right hemispheres, some tracks also provoked responses from the tongue, corner of the mouth, and throat (with accompanying vocalization), though these responses were most commonly produced in combination with jaw movements, with the result that individual zones responsible for these motor responses could not be delineated.

DISCUSSION

The present experiments on white mice supported previous observations of the stable predominance of ipsilateral responses of the vibrissae and parts of the upper lip to microstimulation in regions of the "precentral" cortex [3, 4], which correspond to cytoarchitectonic field 6 [7]. The low stimulation thresholds exclude the direct uptake of current by ipsilateral stem nuclei or descending tracts, and the presence of short-latency responses to short series of impulses makes it unlikely that cortex-stem-face responses predominate, given the difference in latent periods between vibrissal and upper lip responses elicited from the motor cortex and the motor nucleus of the facial nerve, which were less than 10 and 4.9 msec respectively [4]. Addi-

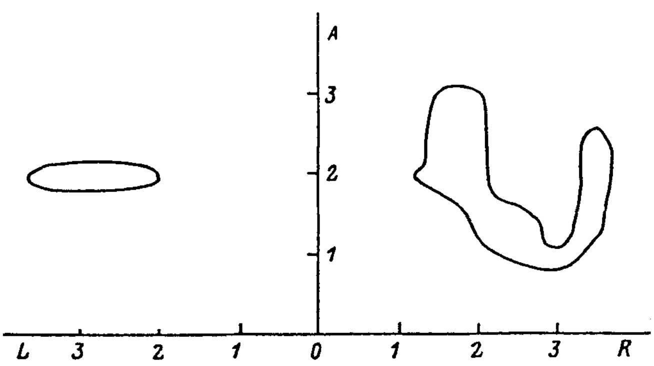

Fig. 4. Map of the motor representations of the lower jaw in the neocortex of the white mouse. For further details see caption to Fig. 1.

tionally, the clear predominance of contralateral responses in the distal parts of the fore- and hindlimbs, differing from the predominantly ipsilateral facial responses in the same experiments and in exactly identical stimulation conditions, can be regarded as an additional functional control, excluding artefactual results. There is reason to suppose a predominantly ipsilateral trajectory for corticofacial projections in mice. The existence of ipsilateral corticobulbar connections has been demonstrated in studies on rats [10] and cats [13]. Studies of the cytomorphological features of the vibrissal zone in field 6 of the mouse neocortex [19] demonstrated ipsilateral transport of horseradish peroxidase into the sensory vibrissal subfield in area C1, as well as into field 29C, the ventral nuclei of the thalamus, and some other areas of the brain, though unfortunately there are no data on the corticobulbar tracts.

The predominantly contralateral nature of cortical influences on the distal limb muscles is a rule applicable to all mammals studied. However, with regard to the means of cortical control of the facial musculature, a number of observations suggest a more complicated picture. Thus, studies of the effects of electrical stimulation of the motor representation of the facial musculature in the neocortex of conscious rabbits showed, along with contralateral movements of the vibrissae, lips, and chewing muscles, there were quite frequent ipsi- and bilateral responses of parts of the upper lip to stimuli close to threshold [1]. Studies on white rats have demonstrated the predominantly contralateral nature of corticofacial responses [8, 12], though some reports describe the finding of ipsi- and bilateral effects [18]. One possible reason for the appearance of these effects could be a superficial level of anesthesia, which is in agreement with earlier observations of the properties of corticofacial responses in primates and humans, in which ipsi- and contralateral responses of the facial muscles were elicited during superficial anesthesia [15].

The dominant position of the jaw and vibrissa-lip zones in the representation of the facial musculature in the mouse neocrotex would appear to be associated with the important roles of these muscle groups in the motor repertoire of this species of rodent. The clear asymmetry in the sizes of these zones in the hemispheres could result from different rates of maturation of the motor representations of the vibrissae and jaw muscles, such that one of these zones comes to occupy "vacant" territory in the corresponding hemisphere. This hypothesis requires further verification.

The interhemisphere asymmetry described here in the organization of the motor representations of the facial musculature thus far lacks analogies in studies of other mammals [8, 9, 11, 12, 14, 16]. This may partially result from the fact that studies mapping the neocortical motor representations in the rat and other mammals have not paid special attention to the effects of stimulation in different hemispheres. However, our data on mice, considering a multitude of observations on interhemisphere asymmetry in the cortical organization of a variety of functions in animals and humans [5], indicate that there is a need for a purposeful comparison to be made between the neocortical motor representations of different parts of the musculature in other mammals, with the aim of obtaining a better understanding of the origin, developmental history, and functional roles of different types of interhemisphere asymmetry.

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