Constraints on Somatotopic Organization in the Primary Motor Cortex

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Schieber, Marc H. Constraints on somatotopic organization in the primary motor cortex. J Neurophysiol 86: 2125–2143, 2001. Since the 1870s, the primary motor cortex (M1) has been known to have a somatotopic organization, with different regions of cortex participating in control of face, arm, and leg movements. Through the middle of the 20th century, it seemed possible that the principle of somatotopic organization extended to the detailed representation of different body parts within each of the three major representations. The arm region of M1, for example, was thought to contain a well-ordered, point-to-point representation of the movements or muscles of the thumb, index, middle, ring, and little fingers, the wrist, elbow, and shoulder, as conveyed by the iconic homunculus and simiusculus. In the last quarter of the 20th century, however, experimental evidence has accumulated indicating that within-limb somatotopy in M1 is not spatially discrete nor sequentially ordered. Rather, beneath gradual somatotopic gradients of representation, the representations of different smaller body parts or muscles each are distributed widely within the face, arm, or leg representation, such that the representations of any two smaller parts overlap extensively. Appreciation of this underlying organization will be essential to further understanding of the contribution to control of movement made by M1. Because no single experiment disproves a well-ordered within-limb somatotopic organization in M1, here I review the accumulated evidence, using a framework of six major features that constrain the somatotopic organization of M1: convergence of output, divergence of output, horizontal interconnections, distributed activation, effects of lesions, and ability to reorganize. Review of the classic experiments that led to development of the homunculus and simiusculus shows that these data too were consistent with distributed within-limb somatotopy. I conclude with speculations on what the constrained somatotopy of M1 might tell us about its contribution to control of movement.

INTRODUCTION

Somatotopic organization long has been the hallmark of the primary motor cortex (M1). The concept of a cortical region systematically organized to control movements of different body parts was first hypothesized by Hughlings Jackson in the 1870s, based on his observations of certain epileptic patients in whom convulsive movements systematically marched from one part of the body to adjacent parts (Jackson 1958). The existence of such a cortical region was demonstrated contemporaneously by Fritsch and Hitzig using electrical stimulation of the canine cortex, one of the earliest demonstrations of a specific function of a particular cortical region (Walshe 1948). As techniques for electrical stimulation improved, increasingly detailed maps of body part representation in M1 became available, culminating in the well-known summary diagrams of Penfield’s homunculus (Penfield and Rasmussen 1950) and Woolsey’s simiusculus (Woolsey et al. 1952). These icons of neuroscience commonly are interpreted as showing a systematic, spatially organized, point-to-point mapping of control of different body parts by different pieces of M1 cortex (Schott 1993). Indeed, in its ultimate form, Penfield’s homunculus included a line representing the mediolateral ribbon of M1, broken into sequential line segments representing different body parts, down to different segments for the thumb, index, middle, ring, and little fingers.

In the last quarter of the 20th century, however, experimental evidence has accumulated indicating that the control of different body parts from M1 is not nearly so somatotopically organized as the homunculus and simiusculus seem to suggest. While it remains clear that the head, upper extremity, and lower extremity have sequential and largely separate representations, the representations of smaller body parts are widely distributed within these major regions. In retrospect, data obtained from the 1870s to the present can be seen to be consistent with this distributed organization as well. Consequently, the territory controlling one body part overlaps extensively with the territory controlling adjacent body parts. For example, the M1 territory controlling the thumb overlaps extensively with the territories controlling the fingers.

Here I review this evidence in a framework of six factors that constrain the somatotopic organization of M1. 1) Convergent output from a large M1 territory controls any particular body part, joint or muscle. 2) Divergent output of many single M1 neurons reaches multiple spinal motoneuron pools. 3) Horizontal connections interlink the cortex throughout a major body part region. 4) Widely distributed activity appears in a major body part region whenever any smaller body part is moved. 5) Partial inactivation of a major region affects multiple smaller body parts simultaneously. 6) Plasticity limits the degree to which control of a specific body part can be assigned to a particular piece of cortex. Although I will deal mainly with...
the upper extremity region (from which the most experimental evidence is available), these six factors appear to apply as well to the representations of the face and lower extremity. No one factor alone unequivocally disproves a detailed within-limb somatotopy, nor can any single experiment. Yet considered altogether, they compel us to conclude that control of each part of the upper limb, lower limb, or face is widely distributed within the overall representation. To progress in understanding M1’s contribution to motor control, we must consider the implications of these constraints on the somatotopic organization of M1.

CONVERGENCE

Outputs from large territories of M1 converge on the spinal motoneuron pool of any given muscle. The cortical territory for each muscle is so large as to preclude spatially separate territories for each muscle. Instead, the M1 territories from which outputs converge on two upper extremity muscles overlap extensively. This principle of convergence was articulated most precisely by the work of Charles Phillips and his collaborators (described in the following sub-sections), but all studies of movements evoked by stimulation of M1 have been consistent with such convergence and overlap, from the classical studies with cortical surface stimulation that led to the homunculus and simiusculus, to more recent studies using intracortical microstimulation (ICMS).

Classical studies employing stimulation of the cortical surface

Because the classical studies that employed stimulation of the cortical surface commonly are assumed to have demonstrated a detailed within-limb somatotopic organization, I begin by reviewing exactly what was demonstrated in these studies. By modern standards, the electrical stimuli employed in these studies were intense and prolonged, exciting relatively large regions of cortex, and evoked overt movements rather than the brief flicks and twitches evoked by ICMS. Penfield and Boldrey (1937) published a map of 77 precentral locations from which cortical surface stimulation elicited movements of the different digits of the hand in studies of 126 human subjects (Fig. 1A). The overall region from which stimulation produced finger movements extended 55 mm along the central sulcus. Inspection of their figure shows that thumb movements were elicited at both the lateral and medial limits of this region, as were movements of the little finger, and of the other digits as well. Furthermore, comparing the region from which finger movements were evoked with the region from which arm movements were evoked showed large, extensively overlapping territories representing different proximodistal parts of the upper extremity (Fig. 1B).

Because data from multiple subjects were compiled in these maps, inter-individual variation might have accounted for the large and overlapping territories of different digits and more
proximal parts of the upper extremity. In single subjects, an orderly, segregated somatotopic arrangement might have been apparent. Inspection of records from single patients reveals, however, that such was not the case. Figure 2 shows, for example, detailed results of intraoperative stimulation in one patient studied by Penfield and colleagues. Although an overall somatotopic trend was apparent in this single case, with movements of the digits being evoked more often laterally along the Rolandic fissure and movements of more proximal parts of the upper extremity being evoked more often medially, movements of different parts were not elicited from discrete locations arrayed in simple somatotopic order. The thumb, for example, was involved in the movements produced by stimulation at three points along the central sulcus, and at each of these points stimulation evoked movements of other digits as well (points marked by upside-down L, N, M). Finger movements were elicited from two more medial points as well (Z and O), with the most medial of these (O) surrounded by other points from which more proximal arm movements were evoked (7, R, X). Thus a well-ordered somatotopic representation of the upper extremity was not evident in the details of single cases such as this.

Penfield and Rasmussen (1950, p. 56), commenting on their homunculus, noted: “A figurine of this sort cannot give an accurate indication of the specific joints in which movement takes place, for in most cases movement appears at more than one joint simultaneously. . . . The motor homunculus may be used as an aid to memory in regard to movement sequence and the relative extent of cortex in which such movement finds representation. It is a cartoon of representation in which sci-

FIG. 2. Details of intraoperative stimulation in an individual human patient. The sketch reproduced here from case records shows the borders of the craniotomy (cross-hatching) and locations of paper markers placed at stimulated locations (upside-down letters and numbers), both drawn by Penfield and colleagues on their standard map of the hemispheric surface based on their intraoperative photograph. To this reproduced sketch, I have added selected details from the transcribed intraoperative notes recording the results of stimulation at each location, linked to each marker by a straight line. No response to stimulation was obtained at point B, 10, or 11; and no transcribed note was available for point H or 2. Note that, although movements of the digits were generally obtained laterally and more proximal movements medially, movements of different digits or more proximal parts of the extremity were not obtained from separate, somatotopically ordered points. This particular case was chosen here because of the relatively large number of points stimulated along the precentral gyrus (in many other cases, because of the possible risk of setting off seizures by stimulation of the motor cortex, many points along the postcentral gyrus were stimulated, and only a few along the precentral gyrus; personal communication, Dr. William Feindel), and because no cortical lesion was evident at surgery. The only lesion found was a meningeal cicatrix close to the midline (in the sketch reproduced here, the wandering dashed line close to the midline delimited a territory of “whitening of the arachnoid”). Although a detailed description of the patient’s typical seizures was not available, he had “Jacksonian epilepsy” with an epigastric aura. This patient (MO) was described by Penfield and Rasmussen (1950, their Fig. 32) in reference to eye turning. Transcribed operative notes, an intraoperative photograph of the brain with paper markers placed on the cortical surface, and the sketch reproduced here, all were provided courtesy of the Penfield Archive (Montreal Neurological Institute, Dr. William Feindel, Curator).
cient accuracy is impossible.” Although the overlapping representations of adjacent body parts observed by Penfield and colleagues might have resulted from current spread across an underlying discrete and orderly somatotopic representation, the overlap also could have been a genuine feature of the underlying representation in M1.

The detailed results of similar studies on a rhesus monkey and on a human from the work of Woolsey and colleagues are illustrated in Fig. 3. In both species, evoked movements typically involved more than one digit and/or more proximal joint. In both species, movements involving the thumb were elicited by stimuli delivered at different locations scattered over much of the upper extremity representation. Similarly, stimulation at many different locations elicited movements involving the little finger. Although the thumb appears more heavily represented in the lateral aspect of the upper extremity representation and the little finger appears more heavily represented medially, the territory in which evoked movements involved the thumb overlaps considerably with the territory in which evoked movements involved the little finger. As with Penfield’s studies, given the possible spread of stimulating current, Woolsey’s data would be consistent either with discrete somatotopically segregated representations of the thumb and little finger, or with overlapping representations in which outputs to the muscles serving each digit converge from large cortical territories. The same argument would apply to other pairings of digits, or pairings of digit and wrist, wrist and elbow, and elbow and shoulder. In the text bracketing the motor simiusculi (their Fig. 131), Woolsey and colleagues wrote, “It must be emphasized . . . that this diagram is an inadequate representation of the localization pattern, since in a line drawing one cannot indicate the successive overlap which is so characteristic a feature of cortical representation. . . .” (Woolsey et al. 1952, p. 252).

While the examples illustrated above come from the work of Penfield’s group and Woolsey’s group, similar evidence consistent with convergence and overlap was present in the detailed results of other investigators who employed cortical surface stimulation in systematic exploration of M1. The number of such studies is too large for each to be mentioned here, but some additional examples may illustrate two general features of this literature. First, the impression of discrete somatotopic order versus convergence and overlap varied with the number of points stimulated. Stimulating a limited number of widely spaced points along the central sulcus often demonstrated a progression from shoulder movements medially to finger and thumb movements laterally (Bucy 1949; Fulton and Keller 1932). Even in these studies, however, some points failed to follow a strict somatotopic order. In studies sampling a larger number of points, convergence and overlap became more apparent. In studies of anthropoid apes, for example, Leyton and Sherrington (1917) stimulated a relatively large number of points in each animal studied, and listed 135 different combinations of primary, secondary, tertiary, and quaternary evoked upper extremity movements; these studies show considerable overlap of the representation of different joints.

FIG. 3. Convergence and overlap in Woolsey’s data. Maps of evoked movements obtained by Woolsey and colleagues (A) in a monkey (Macaca irus) (Woolsey et al. 1952), and (B) in a human (Woolsey et al. 1979). Inset figures of an entire brain indicate the areas enlarged. In A, dashed lines indicate areas in the anterior bank of the central sulcus (right) and posterior bank of the arcuate sulcus (left) exposed for stimulation. In both A and B, figurines show which parts of the body moved on stimulation at each location, with black shading indicating the most vigorous, cross-hatching intermediate and stippling the least movement. In both species, the territories from which movements of the thumb and different fingers were evoked were large and extensively overlapping. (Modified from Schieber 1990)
and movements. Here, then, is a second general feature: focusing only on the initial or most prominent elicited movement was more revealing of somatotopic order, whereas attending to all the movements elicited by stimulation at each point suggested more extensive convergence and overlap (Beevor and Horsley 1887; Ferrier 1873; Hines 1940; Murphy and Gellhorn 1945). For example, by focusing only on the primary movement evoked by stimulation at each site, and comparing non-adjacent joints (e.g., shoulder vs. fingers), Leyton and Sherrington demonstrated a gradual somatotopic progression consistent with the homunculus and simiusculus (e.g., their Figs. 16 and 17), even though their data are consistent with extensive overlap when all movements of all joints were considered.

Studies in which muscle contraction was measured during cortical surface stimulation, instead of observing evoked movement, also were consistent with convergence and overlap. Recording the tension developed by a number of monkey hindlimb muscles, for example, revealed that cortical surface stimulation only occasionally evoked contraction of one of the recorded muscles alone; much more often, multiple muscles contracted simultaneously, although the cortical locations from which maximal contraction was evoked differed from muscle to muscle (Chang et al. 1947). Similar results in humans have been obtained in recent years by recording compound muscle actions potentials in response to transcranial magnetic stimulation (Krings et al. 1998; Wassermann et al. 1992).

Were convergence and overlap artifactual?

Until the 1970s, much if not all of this evidence of convergence from large and overlapping territories moving different body parts could have been attributed to the spread of stimulus effects, for two reasons. First, relatively large stimulating currents (on the order of 0.5–1.5 mA) had to be used at the cortical surface to evoke movements; in comparison, currents an order of magnitude smaller evoked movements when applied to a peripheral nerve. The large currents applied to a point at the cortical surface inevitably spread through a considerable volume of tissue. At threshold for evoking simple flick movements (e.g., 10-ms pulses of 0.5–1.5 mA), for example, surface stimulation evoked repetitive discharge in Betz cells up to 4 mm horizontally distant from the surface point stimulated (Phillips 1956; see also Asanuma et al. 1976; Jankowska et al. 1975a). Direct excitation of corticospinal neurons by surface stimulation thus occurred within a rather large area around the stimulated point, but even a 4-mm horizontal spread of direct Betz cell excitation could not account for the observed overlap of up to 55 mm.

Second, corticospinal neurons at an even greater horizontal distance in theory could be excited indirectly. Single electrical stimuli delivered at the cortical surface evoked multiple descending volley in the corticospinal tract. The earliest volley (D-wave) was produced by direct excitation of corticospinal neurons; later descending volleys (I-waves) resulted from excitation of intracortical neurons which indirectly (trans-synaptically) excited the corticospinal neurons (Patton and Amassian 1954). D-waves were evoked by current spread from the point of surface stimulation through the superficial cortical layers, exciting the corticospinal neuron soma in layer V (Patton and Amassian 1954), or their axons still deeper (Landau et al. 1965). At threshold for direct activation of corticospinal neurons, then, more superficial cortical interneurons were excited as well. These interneurons could excite corticospinal neurons not only directly beneath the stimulating electrode, but also lateral to the electrode (see Horizontal connections, below). Horizontal spread through transynaptic excitation of corticospinal neurons might artifactually enlarge the cortical territories from which a given movement was evoked, producing even more overlap. To limit such horizontal spread of excitation, vertical incisions in the cortex could be made to isolate small (3 × 5 mm) islands of cortex; however, this experimental manipulation failed to eliminate the extensively overlapping territories (Murphy and Gellhorn 1945).

Nevertheless, it remained possible that if only a few, closely packed corticospinal neurons could be excited directly, the map of evoked movements would resolve into discrete territories for different movements or muscles. This possibility diminished, however, when Phillips and co-workers found that brief (0.2-ms) low-amplitude, surface-anodal stimuli directly excited corticospinal neurons without indirect excitation (Hern et al. 1962). Recording intracellularly from baboon cervical motoneurons, and accounting for current spread in the cortex, they used such stimuli to demonstrate that the colony of corticospinal neurons projecting monosynaptically to a single cervical motoneuron must, in many instances, be spread over a cortical territory of at least several square millimeters (the largest minimal territory they measured covered 20 mm²) (Landgren et al. 1962). Moreover, the minimal territories containing corticospinal neurons projecting to radial, ulnar, or median nerve motoneurons (i.e., innervating different muscles) often overlapped. Thus even single motoneurons were shown to receive converging input from relatively large cortical territories, which overlap with the territories providing input to motoneurons of other muscles.

Studies employing ICMS

In the late 1960s and early 1970s, Asanuma and colleagues developed the technique of ICMS. Rather than stimulating with a large electrode touching the pial surface of the cortex, a microelectrode was advanced into the M1 cortex and positioned close to layer V. Here, 0.2-ms pulses of only a few microamperes, delivered in trains of 10–12 pulses at approximately 300 Hz, could evoke visible movement or recordable electromyographic (EMG) activity. Single 10-μA 0.2-ms cathodal current pulses delivered in layer V were estimated to directly excite neuronal somata within a radius of only 88 μm, which in cat anterior sigmoid gyrus would encompass only about 28 pyramidal neurons (Stoney et al. 1968). Initial studies with ICMS indicated that a particular movement of a part of the forelimb, or contraction of a particular muscle, was evoked by threshold ICMS applied within a small columnar zone of approximately 0.5–1 mm radius (Asanuma and Rosen 1972). Multiple small efferent zones scattered in the overall forelimb representation could be found for the same movement or muscle. Discrete efferent zones representing different movements or muscles appeared intermingled like the different colors of tiles in a mosaic.

The initial report of Asanuma and Rosen (1972) showed this mosaic arrangement by superimposing data from 10 Cebus monkeys (their Fig. 8). Subsequent studies from numerous
laboratories in many species, including detailed studies of single subjects, have continued to show that maps of threshold responses evoked by ICMS include the same features. Two examples are shown in Fig. 4. In anesthetized owl monkeys (Fig. 4A), although a general within-limb somatotopic gradient could be appreciated (distal representation stronger posterolaterally and proximal representation stronger anteromedially), movement of a given part (such as the digits) was evoked by ICMS at multiple foci scattered over a considerable portion of the upper extremity representation, and these foci were intermingled with points at which stimulation elicited movements of other parts of the limb (Gould et al. 1986). In awake stump-tailed monkeys (Macaca arctoides, Fig. 4B), although the thumb had more representation laterally, movement of any given digit was evoked by ICMS at foci scattered over a large portion of the upper extremity representation, and the territory from which ICMS evoked movement of a given digit overlapped with the territory from which ICMS evoked movement of any other digit (Kwan et al. 1978). A similar pattern of scattered threshold foci for individual muscles, intermingled with foci for other muscles, has been described by recording evoked EMG activity during ICMS in squirrel monkeys (Donoghue et al. 1992; Strick and Preston 1978, 1982), macaques (Humphrey 1986), and baboons (Waters et al. 1990). Thus even with threshold ICMS, a particular movement of a given body part, or a contraction of a specific muscle, is evoked by stimulation at several sites scattered in the forelimb representation, and these sites are intermingled with sites where stimulation evokes other movements of the same body part, or movements of adjacent body parts, or contractions of other nearby muscles. At the same time, gradual somatotopic gradients—indicating gradual shifts in the part(s) most heavily represented—can often be appreciated in ICMS maps of the forelimb representation. Similar features appear in ICMS maps of the face representation as well (Huang et al. 1988).

What is revealed with ICMS?

At this point, one might come away with the interpretation that M1’s somatotopic organization consists of a mosaic of small discrete zones, with each movement or muscle represented in multiple scattered zones. The large and overlapping cortical territories demonstrated by the older methods of cortical surface stimulation then could have resulted from stimulation of many of these tiny zones at the same time. The extent to which the efferent zones mapped by threshold ICMS are actually discrete, however, is called into question by two major considerations.

First, even with ICMS, stimulation does not occur entirely at a single point. Many of the corticospinal neurons that discharge in response to ICMS are excited directly at the soma or axon hillock, and these neurons do indeed lie within a small zone...
close to the electrode tip. As noted above, in cat M1, low-amplitude ICMS pulses have been estimated to directly excite on the order of 28 pyramidal neuron somata within a radius of 88 μm (Stoney et al. 1968). In the baboon, a 0.2-ms × 5-μA pulse delivered in layer V was estimated to directly excite 90–900 small and 1–5 large pyramidal neurons within a radius of 40–125 μm, whereas at 90 μA, a generous estimate of the effective spread of stimulating current was only 0.6 mm (Andersen et al. 1975). Direct excitation of neuronal somata or axon hillocks by ICMS thus is reasonably focal.

Shortly after ICMS came into use, however, investigators realized that the same pulses could excite additional corticospinal neurons at greater distances through two mechanisms. One mechanism is direct excitation of the intracortical collaterals of pyramidal tract axons, which may extend horizontally up to 1 mm away from the soma (Asanuma et al. 1976). A second mechanism is indirect, trans-synaptic excitation. Indeed, the greatest part of the descending volley produced by ICMS results from such trans-synaptic excitation of corticospinal neurons, even when the stimulating electrode is within layer V and currents are as low as 5 μA or less (Jankowska et al. 1975b). Moreover, repetitive ICMS of the same intracortical point at frequencies of 200–400 Hz, the type of stimulation needed to evoke detectable movement or EMG activity in the studies described above, produces powerful temporal summation of this trans-synaptic excitation (Asanuma et al. 1976; Jankowska et al. 1975b). Although most trans-synaptically excited corticospinal neurons probably lie relatively close to the ICMS microelectrode, some somata may be more distant. Horizontally extending axon collaterals can produce excitatory postsynaptic potentials (EPSPs) in M1 pyramidal tract neurons within a 1- to 2-mm radius (Asanuma and Rosen 1973; Matsunaga et al. 1996), and intracortical microstimulation can excite some pyramidal tract neurons within this radius (Baker et al. 1998). While most of the effects of ICMS result from excitation of pyramidal tract neurons quite close to the microelectrode, a penumbra of other pyramidal tract neurons may be excited as well. Quantitative estimates of what fraction of observed muscle contraction or movement results from direct excitation of local somata versus excitation of penumbral neurons are not available.

A modified ICMS technique recently has been developed that avoids the temporal summation of repetitive stimulation at high frequency (~300 Hz) used in conventional ICMS to produce detectable output effects in quiescent animals. In stimulus-triggered averaging (StTA), single ICMS pulses are delivered at much lower frequencies (10–20 Hz) while awake monkeys perform active movements, and triggered averaging then is used to extract the effects of these pulses from ongoing voluntary EMG activity (Cheney and Fetz 1985). Because the temporal summation of EPSPs is eliminated, StTA probably produces much less of its effect via indirect, trans-synaptic excitation. Yet maps made with StTA continue to show large cortical territories for individual muscles that overlap extensively with the cortical territories of other muscles (Park et al. 2001).

This brings us to the second consideration: exactly what is being mapped with threshold electrical stimulation? Threshold ICMS mapping in M1 entails placing the electrode tip at a certain point in or near layer V, and gradually adjusting stimulus strength until on half of stimulation trials the discharge of some motor units is just detected, either by recording EMG activity, or by having enough motor units discharge to produce an externally observable movement. With either assay, the experimental observation means that the evoked output from M1 to a particular muscle (or potentially a combination of muscles when observing movement) was greater than the output to other muscles, not that output occurred to that muscle alone. Output may well have occurred to motoneurons of other muscles; such output to other muscles simply was insufficient to cause them to discharge (or to discharge enough to produce observable movement). The apparently discrete zones of ICMS maps obtained with threshold stimuli thus represent the quantitatively greatest outputs, not qualitatively exclusive outputs.

What happens, then, if the stimulus strength is increased beyond threshold? Are outputs to additional muscles revealed? Phillips and colleagues recorded simultaneously from single motor units in the thenar eminence (thumb muscles), in the first dorsal interosseous muscle (FDI, an index finger muscle), and in extensor digitorum communis (EDC, which extends the 4 fingers) while using ICMS to map the forelimb region of baboon M1 (Andersen et al. 1975). Threshold stimulation at most points evoked discharge in only one of the three motor units. Using currents up to 80 μA, however, they found that the three motor units recorded from these three muscles each could be brought to discharge with ICMS at many points spread over a wide cortical territory, and that the total territories from which each motor unit could be discharged overlapped extensively (Fig. 5). Their calculations showed that spread of the higher currents did not account for the overlap. Even at 90 μA, a current larger than they routinely employed, a generous estimate of the spread of current effective for direct stimulation of somata and axons was only 0.6 mm, while the motor unit territories overlapped several millimeters. Hence the colony of Betz cells whose output excited each motor unit necessarily was spread over a considerable cortical territory, largely intermingled with the colonies of Betz cells exciting the motor units of the other muscles. Similar findings were obtained with intracellular recordings from hindlimb motoneurons (Jankowska et al. 1975a).

Subsequently, several investigators have confirmed that ICMS maps show multiple scattered loci from which threshold stimulation evokes movement about a particular joint, or EMG activity in a particular muscle. In between are scattered threshold loci for other movements or muscles, forming a “complex mosaic.” As stimulus intensity is increased systematically above threshold, however, movements are produced at additional joints (Sessle and Wiesendanger 1982), or contractions

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1 Indeed, recent studies of electrical excitation in slices of rat visual cortex indicate extracellular stimulation excites axonal branches more readily than axon initial segments or somata (Nowak and Bullier 1998a,b).

2 The large spatial extent of the “colony” of layer V neurons projecting to the EDC motoneuron pool of macaques recently has been demonstrated anatomically by retrograde transneuronal transport of rabies virus injected into the EDC muscle belly (Rathelot and Strick 2000).

3 These authors did not consider excitation of additional, penumbral neurons via horizontal axon collaterals or indirect trans-synaptic excitation. Even if one considers a 2-mm penumbra of lesser excitation, however, the overlap they demonstrated for cortical territories of different muscles is too extensive to attribute entirely to spread of excitation and therefore indicates intermingling of corticospinal neurons exciting different muscles.
are evoked in more and more muscles (Donoghue et al. 1992), so that the loci for any particular muscle tend to expand and coalesce, revealing the large total territory representing that muscle, which overlaps extensively with the territories representing other muscles (Humphrey 1986; Sato and Tanji 1989). This expansion and coalescence into large and overlapping territories cannot be attributed entirely to current spread and indirect, trans-synaptic excitation. Thus ICMS, like surface stimulation, indicates convergence of M1 outputs from large and overlapping M1 territories onto different muscles or movements.

Because even ICMS involves some spread of current to multiple neurons, and because such current can excite neurons both directly and indirectly, the question of whether stimulation at a single “point” in M1 actually produces output to more than one muscle cannot be resolved with extracellular electrical stimulation. The ideal experiment for resolving this question (recording intracellularly from the spinal motoneurons of several muscles while stimulating intracellularly in the somata of single corticospinal neurons in M1) remains technically inaccessible even now. In the 1980s, however, separate lines of evidence developed rendering much of the previous arguments moot.

DIVERSION

For many years neuroscientists generally believed that a given corticospinal neuron made monosynaptic connections to the motoneurons of only one muscle. These specific connections to particular muscles enabled the “upper motor neurons” in M1 to selectively activate the muscles needed to perform fine, relatively independent movements (Phillips and Landau 1990). Shortly after Phillips and colleagues had articulated the concept of convergence from wide M1 territories onto spinal motoneurons, evidence appeared demonstrating that the output projections from single M1 neurons often diverge to innervate the motoneuron pools of more than one muscle.

Anatomic evidence of such divergence was obtained by filling single corticospinal axons with horseradish peroxidase (HRP), revealing that collateral branches of a single corticospinal axon often ramified over several spinal segments providing terminal arbors in the motoneuron pools of up to four muscles (Shinoda et al. 1981). Physiologic evidence of divergence came from the use of spike-triggered averaging of rectified EMG activity to identify functional, short-latency connections from M1 neurons to spinal motoneuron pools (Fetz and Cheney 1978, 1980). Many single M1 neurons produced postspike effects, indicative of relatively direct corticomotoneuronal connections, in up to six different forearm muscles. Spike-triggered averaging also has shown divergent outputs from M1 neurons controlling the intrinsic muscles of the hand; those used in the finest of relatively independent movements (Buys et al. 1986; Lemon et al. 1986). Furthermore, a recent study indicates that the functional connections of single M1 neurons may diverge, not only to different muscles moving the fingers and wrist, but also to muscles moving the elbow and shoulder (McKiernan et al. 1998). These divergent projections from single M1 neurons obviously constrain the degree to which M1’s output can be organized in a strict within-limb somatotopy. The set of muscles receiving the output of a single M1 neuron may act on multiple fingers; on
the fingers and the wrist; or even on the fingers, wrist, elbow, and shoulder.

**Horizontal Interconnections**

The concept of a strict somatotopic organization implied that different sites within M1 acted on their output targets relatively independently. By providing site-specific outputs to selected elements, the somatotopic map in M1 was thought to act like a piano keyboard on which higher levels of the cortex could play out motor programs. This notion has been supported by anatomic studies demonstrating that the majority of intracortical connections within M1 are relatively local, spreading horizontally over a radius of only 1–2 mm. Lesions made by passing a microelectrode through monkey M1 cortex radially (normal to the pial surface) resulted in dense fiber degeneration spreading horizontally from the lesion over a radius of 200–300 μm, and less densely over a radius of 2–3 mm (Gatter and Powell 1978). Intracellular injections of HRP into cat pyramidal tract cells showed axon collaterals spreading horizontally in layers V and VI, densely over a radius of 0.5–0.8 mm, and less densely over 1.5–2.0 mm radius, with a few extending as far as 2–3 mm from the soma (Landry et al. 1980). Neurobiotin-filled cat pyramidal neurons in layers II and III extend horizontal axons collaterals within these layers for up to 1 mm (Keller and Asanuma 1993).

These anatomic findings are consistent with studies demonstrating that the strongest physiologic interactions are found between M1 neurons separated by 1–2 mm. Low-amplitude (4 μA) ICMS in cat M1 evokes monosynaptic postsynaptic potentials (PSPs) in neurons within only a 0.5-mm horizontal radius, and polysynaptic PSPs chiefly within 1-mm radius (Asanuma and Rosen 1973). Spike-triggered averaging of intracellular potentials in monkey M1 likewise has shown that EPSPs and inhibitory postsynaptic potentials (IPSPs) are strongest and most common within 1–2 mm (direct rather than horizontal distance) of the triggering neuron (Matsumura et al. 1996). The observations that two sequential 20-μA ICMS pulses delivered through the same electrode produce intracortical facilitation of evoked EMG, whereas sequential pulses delivered through electrodes separated horizontally by 1.5–2.0 mm do not also support the notion that the strongest physiologic interactions between M1 neurons occur within 1.0 mm, although the same ICMS pulses do affect the discharge of some pyramidal tract neurons 1.5–2.0 mm away (Baker et al. 1998). Similarly, synchronous discharges in the action potential trains of two neurons (indicating shared or serial inputs) are found more commonly when the two neurons are close enough to be recorded from the same microelectrode, and the likelihood of finding synchronous discharge decreases with horizontal separation until synchrony is rarely detected between neurons.

**FIG. 6.** Divergence in the projection of single corticospinal neurons. A: a horseradish peroxidase (HRP)-filled corticospinal axon has been reconstructed in the transverse plane of the ventral horn of the monkey spinal cord. The cord midline and central canal are to the left; the lateral column to the right. The filled corticospinal axon enters the spinal gray matter from the lateral column and branches repeatedly, ultimately giving off terminal ramifications in the outlined motoneuron pools of 4 different muscles (reproduced from Shinoda et al. 1981). B: averages of rectified electromyographic (EMG) activity are shown from 6 muscles [extensor digitorum secundi et terti (ED23), extensor carpi ulnaris (ECU), extensor digitorum quarti et quinti (ED45), extensor digitorum communis (EDC), extensor carpi radialis longus (ECRL), and extensor carpi radialis brevis (ECRB)] that act on the wrist and/or fingers in macaque monkeys. Each average of rectified EMG was triggered from several thousand spikes discharged by the simultaneously recorded M1 neuron whose averaged action potential is shown in the top trace. The brief (~10 ms) peaks that appear in each of the 1st 4 EMG traces shortly after the neuron spike indicate that motoneurons innervating these 4 muscles received synaptic excitation at a short and fixed latency following the discharge of action potentials by the M1 neuron (modified from Fetz and Cheney 1980).
separated by more than 2.0 mm (Grammont and Riehle 1999; Kwan et al. 1987; Riehle et al. 1997; Smith and Fetz 1989). Horizontal interconnections extending 1–2 mm may mediate interactions between M1 neurons contributing to the control of different muscles acting about the same joint (Capaday et al. 1998), or neighboring joints of the same extremity (Kwan et al. 1987).

Although the strongest intracortical interconnections thus occur within a 1-mm radius of a given pyramidal neuron, recent anatomical studies have shown that many M1 neurons extend axon collaterals even further horizontally, interconnecting much larger regions of M1 (Fig. 7). HRP injections in the ICMS-defined digit region of monkey M1 revealed that neurons near the injection site extended terminal arbors throughout the upper extremity region, including the territory where threshold ICMS had evoked movements of the shoulder, elbow, or wrist (Huntley and Jones 1991). Conversely, neuronal somata throughout the upper extremity representation were filled retrogradely by the HRP injection in the digit region, indicating that neurons throughout the upper extremity territory send axon collaterals into a single focus within the digit representation. When the injection was placed laterally, close to the face representation, labeled terminals and somata still were found in the ICMS-defined shoulder representation, 7–8 mm medial to the injection site. Similarly, when Fast Blue (FB) was injected in the digit representation, and Diamidino Yellow (DY) was injected 7–8 mm away in the shoulder region of monkey M1, retrogradely labeled FB and DY somata were found intermingled throughout the M1 cortex between the two injections, including some double-labeled neurons (Tokuno and Tanji 1993).

Horizontally projecting axon collaterals interconnecting the entire upper extremity representation have been demonstrated as well in the cat and the rat, where the collaterals have been shown to arise predominantly from pyramidal neurons in layers III and V, and to have predominantly excitatory, glutamatergic effects (Aroniadou and Keller 1993; Keller 1993; Weiss and Keller 1994). In monkey M1, inhibitory, GABAergic neurons have predominantly vertically oriented projections (DeFelipe and Jones 1985), although the axons of GABAergic basket cells may project horizontally for 1–3 mm. Furthermore, the effective range of intracortical inhibition may be much greater (Kujirai et al. 1993), in part because local inhibitory interneurons may receive excitatory inputs from long-range horizontal projections within M1 (Jacobs and Donoghue 1991). Long-range horizontal interconnections within M1 thus provide a substrate for information to be interchanged through a network distributed widely through the M1 upper extremity representation, again limiting the degree to which a particular M1 site can be associated with control of a particular body part.

Besides long-range intrinsic connections within M1, afferent inputs to M1 also show considerable horizontal distribution. Given that any particular locus within M1 tends to receive somatosensory input from the same body part moved by ICMS at the locus (Murphy et al. 1978; Rosen and Asanuma 1972), it is not surprising that somatosensory inputs to M1 also have a scattered and intermingled distribution (Lemon 1981; Wong et al. 1978). In large part, somatosensory inputs to M1 arrive

![Fig. 7](http://jn.physiology.org/)

**Fig. 7.** Horizontal interconnections in the M1 upper extremity representation. After using ICMS to map the M1 upper extremity representation in a macaque monkey’s left hemisphere, HRP was injected in the low-threshold digit representation at the site indicated by the large, filled black circle with surrounding coarse-stippled penumbra. This injection resulted in widespread terminal labeling (fine stippling in A) and retrograde filling of neuronal somata (small black dots in B). ICMS was delivered at sites indicated by the large black dots in both A and B. Regions where stimulation at many contiguous sites elicited movement of the same body part are delimited with dashed lines, exceptional sites being indicated individually. Stars indicate points where stimulation up to 40 μA failed to evoke observable movement. The solid line at the right indicates the central sulcus, and data from its anterior bank have been represented as if projected to the hemisphere’s surface. Scale bars at bottom represent 1 mm. Anterior is to the left; posterior, right; medial, up; lateral, down (modified from Huntley and Jones 1991).
via short U-fibers from the primary somatosensory cortex, fibers that arborize over a considerable rostrocaudal distance in M1. In macaques, these corticocortical axons may give off two to three terminal arborizations separated by up to 800 μm (DeFelipe et al. 1986). Similar arborization patterns have been found for corticocortical afferents to M1 from area 5 in the cat (Kakei et al. 1996). Thalamocortical afferents to M1 from the cat ventroanterior and ventrolateral (VA/VL) nuclear complex distribute their terminal fields even more extensively, some covering areas up to 5.0 × 4.8 mm (almost 25 mm²) in rostrocaudal and mediolateral dimensions (Shinoda et al. 1993). Both corticocortical and thalamocortical afferents thus distribute their information widely in the M1 forelimb representation.

The functional role played by long horizontal connections within M1 remains uncertain. Nevertheless, physiologic studies in awake behaving animals have demonstrated a number of types of correlations between the discharge of M1 neurons that may in part be mediated by these long horizontal interconnections. One form of correlation between relatively distant M1 neurons has been demonstrated by averaging the intracellular (IC) potential of one neuron triggered from the extracellular (EC) action potentials of a second neuron (Matsumura et al. 1996). These averages frequently reveal a broad depolarization of the IC neuron straddling the triggering spikes of the EC neuron. Such average synchronous excitation potentials (ASEPs) indicate that the IC and EC neurons both receive some sort of synchronous excitation. ASEPs, although most common and most intense in pairs of neurons separated by <2 mm, also have been found in pairs of neurons separated by up to 4.5 mm in monkey M1.

A second type of long-range correlation has been demonstrated by examining the trial-by-trial variation in the discharge of monkey M1 neurons averaged over 600 ms during a reaching task (Maynard et al. 1999). The trial-by-trial variation in average discharge rate of two neurons was more likely to be correlated if the two neurons had similar preferred directions, suggesting that functionally similar neurons receive shared inputs that fluctuated from trial to trial. The strength of such correlations did not depend on the horizontal distance between the two neurons, however. Although interneuronal separations of only up to 2 mm were examined, that the correlation strength was independent of separation distance suggests that this type of correlation extends beyond 2 mm.

The most extensive evidence of long-range interactions within M1, however, comes from studies of local field potential (LFP) oscillations, which occur synchronously over regions of the M1 upper extremity representation extending 14 mm mediolaterally along the central sulcus of monkeys (Donoghue et al. 1998; Murthy and Fetz 1992, 1996a). These LFP oscillations are coherent with simultaneous oscillations in EMG activity (Baker et al. 1997; Hari and Salenius 1999). Neurons at sites separated by up to 10 mm have been found to have oscillatory modulation of their discharge in phase with these LFP oscillations, and pairs of such neurons often show peaks in cross-correlograms of their spike discharges recorded during LFP oscillations (Baker et al. 1999; Murthy and Fetz 1996b). The fact that such correlations during LFP oscillations can be found between neurons in the left and right M1 indicates that intrinsic horizontal connections are unlikely to be the sole anatomic basis for such widespread synchronization. Nevertheless, horizontal connections intrinsic to the M1 upper extremity representation may contribute to synchronous LFP oscillations, associating the widespread neurons needed to perform a coordinated movement of the entire extremity.

**Distributed Activation**

For many years, authorities debated whether it was muscles per se, or the movements they produced, that were represented somatotopically in M1 (Phillips 1975). The convergence of M1 outputs to single motoneuron pools from wide and overlapping cortical territories, and the divergence of output from single M1 neurons to multiple motoneuron pools, both necessarily constrain any somatotopic representation of individual muscles in M1. The overlapping cortical territories of different muscles raise the possibility, however, that different combinations of activity in multiple muscles are represented at different cortical sites. Voluntary movements, even movements of a single joint or a single finger, typically involve simultaneous contractions of multiple muscles (Beevor 1903; Schieber 1995). The simultaneous contractions of a such a set of muscles producing movement of one body part might be represented at one location in M1, while the simultaneous contractions of a partially overlapping set of muscles producing movement of a different body part might be represented at a different location. Although electrical stimulation mapping had also suggested overlap of movement representations (above), electrical stimulation is unlikely to mimic accurately the natural cortical activation that occurs during voluntary movements.

Since the 1960s, a number of techniques (including single neuron recording, functional neuroimaging, and magnetoencephalography) have become available for probing cortical activity during voluntary movements performed by awake subjects. A well-ordered, discrete somatotopic organization of M1 would imply that movements of different body parts involve activation of spatially distinct regions of M1, with these regions arrayed in somatotopic order. Somatotopically ordered activation during voluntary movements should be demonstrable with these modern techniques.

Experimental studies examining M1 activity during movements of different parts of the upper extremity, however, have revealed relatively little evidence of activation in spatially distinct regions of M1. In monkeys performing individuated movements of each finger and of the wrist, single neurons were found to discharge in relation to movements of several different fingers, which obviously constrains the degree to which movements of different fingers could be represented in spatially distinct regions of M1 (Schieber and Hissbitt 1993). Moreover, the M1 territories containing neurons active during movements of different fingers were virtually coextensive, with little evidence of a somatotopic shift in the center of activity from lateral to medial for movements of the thumb through little finger and wrist (Fig. 8). Similarly, functional magnetic resonance imaging (fMRI) in humans has shown extensive overlap of the cortical territories activated during performance of thumb, index finger, ring finger or wrist movements (Sanes et al. 1995). Magnetoencephalography in humans likewise has shown that the dipole sources of the neuromagnetic fields generated during movements of different digits are not arrayed in somatotopic order, either in a single subject or averaged across multiple subjects (Cheyne et al. 1991; Salenius et al. 1994).
that the territory active during movements of multiple fingers should be larger than the territory activated during movement of a single digit. When this hypothesis has been tested experimentally, however, the extent and amplitude of activation in the primary sensorimotor cortex has been found to be significantly larger during movement of a single finger than during simultaneous movement of multiple fingers (Kitamura et al. 1993; Remy et al. 1994). Such results indicate that the process of moving multiple fingers is not simply the sum of activating multiple separate M1 territories, each controlling a different finger; rather, moving a single finger without the others requires more M1 activity than moving multiple fingers simultaneously. Presumably, such extra activation occurs because, besides controlling the motion of the one finger, M1 actively participates in stabilizing other parts of the upper extremity during the individuated movement of a particular finger (Humphrey and Reed 1983; Schieber 1990).

Could the distributed activation observed in awake behaving subjects reflect activation of somatotopically organized cortex, with one region producing the movement and other regions stabilizing other body parts? If one considers only studies of activation in awake behaving subjects, this interpretation certainly is possible. But ICMS should have demonstrated such an underlying somatotopic organization (see Figs. 4 and 5), and the divergence of output from single M1 neurons to muscles that move all four fingers and the wrist (Fig. 6), or to muscles acting on both the digits and the shoulder (McKiernan et al. 1998), would certainly limit the degree of somatotopic segregation of these representations. Distributed representation provides a more parsimonious interpretation of all these observations considered together.

Several studies have demonstrated comparatively small, somatotopically ordered shifts in the location of activation during movements of different parts of the upper extremity. It must be recognized, however, that these shifts are detected by using analytic approaches that minimize the contribution of activation common to different movements. For example, somatotopically ordered shifts may be detected in the centroids of activation calculated for movements of different fingers. These shifts are small, however, compared with the total spatial extent of the territory activated. In monkeys, the centroids of activation during different finger and wrist movements were found to be spread over 2 mm along the central sulcus, whereas the field containing active neurons extended 8–9 mm (Fig. 8) (Schieber and Hibbard 1993). In humans, centroids of fMRI activation for movements of different fingers may be spread over 2.46 mm (no greater than the thickness of the cortex itself!) (Beistener et al. 2001; Hlustik et al. 2001; Indovina and Sanes 2001), whereas the total extent of the hand representation along the central sulcus is roughly 50 mm (Hlustik et al. 2001; Penfield and Boldrey 1937). In both species, comparing the spatial separation of the centroids with the spatial extent of the hand representation indicates that the territories activated during movements of different fingers must overlap extensively.

Analytic techniques that make even less use of the activation common to different movements have demonstrated greater apparent separation. Although the territory of fMRI activation is mediated by the activity of neurons widely distributed in the M1 upper extremity representation.

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during thumb movements is lateral to that during little finger movements (Kleinschmidt et al. 1997). Similarly, when the activation peaks during thumb, index finger, wrist, elbow, and shoulder movements were compared using positron emission tomography (PET), a somatotopic progression from lateral to medial was demonstrated (Grafton et al. 1993). These observations become consistent with observations of distributed activation, as well as with observations of convergence, divergence, and horizontal interconnections, when the gradual shift in peak activation or centroid of activation is recognized to be present on a base of extensively overlapping representation.

**Partial Inactivation**

A strictly somatotopic organization of M1 also would predict that in some instances lesions should affect certain parts of the upper extremity without affecting others. In human patients, where lesions of M1 may be produced by a variety of disease processes, the resulting upper extremity weakness affects distal strength in the fingers and wrist more profoundly than proximal strength in the shoulder and elbow (Bucy 1949; Colebatch and Gandevia 1989). Uncommonly, more selective lesions weaken the fingers and wrist much more profoundly than the elbow and shoulder (Foerster 1936). Even in these cases, however, some weakness is evident at these proximal joints, unless the weakness of the hand itself is minimal. Even more uncommonly, human patients have been reported with weakness greater in some fingers than in others. Most often, the thumb is the weakest digit, with some weakness of the index as well (Lee et al. 1998; Terao et al. 1993). Greatest weakness of the thumb (and index) could result from a greater representation of the thumb and index throughout the M1 hand area, rather than selective involvement of a region controlling only the thumb. Other cases have been reported, however, in which the little and ring fingers were weakest (Foerster 1936; Kim 2001; Phan et al. 2000; Schieber 1999). Notably absent are cases in which the index, middle, or ring fingers were the weakest. Human cases thus suggest that, rather than discrete regions of M1 controlling different parts of the upper extremity, control of each part is mediated by an extensive territory that overlaps with the territories controlling other parts. Nevertheless, on top of this widely distributed control of each finger, two somatotopic gradients may be present, consistent with the general order suggested by the homunculus. First, the proximal upper extremity is represented more heavily mediially than laterally, while the reverse is true for the distal upper extremity. Second, within the distal representation, the thumb and index are represented more heavily laterally than medially, while the little and ring fingers are represented more heavily medially than laterally.

The exact location and extent of lesions in human cases, of course, cannot be controlled experimentally. Relatively few investigations in experimental animals have attempted to correlate the location of a lesions within the M1 upper extremity representation with the resulting motor deficits in the upper extremity. In monkeys performing individuated finger movements, however, partial inactivation of the M1 hand area produced by intracortical injection of the GABA<sub>A</sub> agonist, muscimol, impaired some finger movements more than others, but which finger movements were impaired was unrelated to the mediolateral location of the inactivation along the central sulcus (Schieber and Poliakov 1998). Similarly, when muscimol was injected at loci where ICMS evoked thumb and index finger movements, movements of the whole hand were impaired (Brochier et al. 1999). Microinfarction of ICMS defined hand representation in squirrel monkeys resulted not only in decreased use of the hand, but also in tonic flexion at the elbow and adduction of the extremity close to the torso, similar to the involuntary tonic posturing of the upper extremity seen in human patients after much more extensive lesions of M1 (Friel and Nudo 1998). The deficits produced by controlled lesions in animal studies, like those resulting from lesions produced by disease in humans, suggest that control of each finger, and of each more proximal joint, is widely distributed in the M1 upper extremity representation.

**Plasticity**

Observations indicative of what we now call plasticity are almost as old as stimulation mapping of M1. In their classic study of somatotopic organization of M1 in the great apes, for example, Leyton and Sherrington (1917) took pains to describe the “functional instability of cortical motor points.” They found that after the movement evoked by stimulation of a given point was first identified, intervening stimulation of the same point or other nearby points could result in facilitation, reversal, or deviation of the movement evoked when stimulation of the given point subsequently was repeated. These investigators inferred that “... the functional instability of cortical motor points are indicative of the enormous wealth of mutual associations existing between the separable motor cortical points, and those associations must be a characteristic part of the machinery by which the synthetic powers of that cortex are made possible.” When M1 was considered to contain a point-to-point somatotopic map of body parts, movements, or muscles, with each corticospinal neuron monosynaptically connected to one and only one spinal motoneuron pool, the possibility of plastic reorganization in M1 seemed remote. The convergence, divergence, horizontal interconnections, and distributed activation described above, however, provide a substrate that would appear capable of considerable plastic reorganization.

As reviewed in detail elsewhere (Nudo et al. 2001; Sanes and Donoghue 2000), in the past decade M1 has been shown to undergo plastic reorganization in response to a variety of changes, including peripheral lesions, central lesions, and motor skill acquisition. Here we focus only on the latter, which may be most relevant to the normal organization of somatotopic representation in M1. In a variety of motor skill acquisition paradigms, the M1 representation of the trained body parts has been shown to enlarge, typically at the expense of the representations of less trained body parts. In rats trained to reach and grab small food pellets, for example, the ICMS defined M1 representation of digit and wrist movements was expanded at the expense of elbow and shoulder movement representation (Kleim et al. 1998). In monkeys trained to retrieve small objects, ICMS mapping likewise revealed expansion of the digit representation, whereas in monkeys trained to perform forearm pronation/supination movements the representation of forearm movements expanded (Nudo et al. 1996). These changes are progressive as training continues, and reverse after training stops (Fig. 9).
Additional evidence obtained in human subjects indicates that M1 reorganization occurs both within a single session and over the longer term needed to acquire a complex skill. When normal human subjects, initially unaware of any sequence, practice a repeating sequence of finger movements instructed by visual cues, the amplitude and extent of finger muscle representation assessed by trans-cranial magnetic stimulation increases in M1 contralateral to the performing hand as the speed of performance increases over a single day of training (Pascual-Leone et al. 1994). Several days of such training produce progressive expansion of finger muscle representation, whether the training involves physical practice or only mental rehearsal (Pascual-Leone et al. 1995). Practicing a finger movement sequence over several weeks results in greater fMRI activation of the M1 hand representation during performance of the practiced sequence than during performance of a comparable, but unpracticed sequence (Karni et al. 1995). An example of very long-term changes related to motor skill is found in experienced Braille readers, whose M1 representation of the first dorsal interosseous muscle (used to sweep the tip of the index finger over Braille letters) is expanded in M1 contralateral to their reading finger (Pascual-Leone et al. 1993).

If reorganization of M1 in normal subjects can be driven by learning and practicing a particular skill, then reorganization is likely to be proceeding continuously as each individual performs the motor tasks used frequently in their daily life. The patterns of representation in M1 thus are likely to change as an individual performs more of one motor activity and less of another from day to day. Such a continual process of reorganization places yet another constraint on somatotopic organization in M1.

**WHY SHOULD THE PRIMARY MOTOR CORTEX HAVE SO DISTRIBUTED AN ORGANIZATION?**

The ease with which we can comprehend a well-ordered, discrete, somatotopic representation makes the concept of somatotopy an attractive organizing principle with which to understand the function of the primary motor cortex. Somatotopy seems so straightforward that it ought be so. The primary somatosensory cortex (S1) has a well-ordered somatotopic representation, and the primary visual cortex (V1) has a well-ordered retinotopic representation. The evidence reviewed above indicating that within-limb somatotopy in M1 is limited, and that a more complex, widely distributed organization exists instead, therefore is likely to reflect important features of...
One such feature may be the dimensionality of the information processed in M1. Well-ordered representations exist where a two-dimensional receptor sheet (the skin surface or retina, respectively) can be mapped isomorphically onto the two-dimensional cortex. Movements and the muscles that generate them are three-dimensional, however, and cannot be mapped simply into a two-dimensional cortex. The number of dimensions represented in M1 is arguably much more than three, if each muscle, each degree of freedom at each joint, and each kinematic or dynamic parameter of movement constitutes a possible dimension. Even in S1, the most discrete and well-ordered somatotopic representation of the different fingers is found in area 3b, where cutaneous inputs predominate (Iwamura et al. 1983a; Pons et al. 1987). In areas 1 and 2, where cutaneous inputs are combined with inputs from deep mechanoreceptors in joints and muscles, increasing numbers of receptive fields span multiple digits, and somatotopic organization becomes more complex, particularly in awake animals (Iwamura et al. 1980, 1983b, 1993; Pons et al. 1985). In contrast, V1 represents additional dimensions by nesting them within the two-dimensional retinotopic representation. Ocular dominance columns, orientation columns, and color blobs can be considered additional dimensions of visual stimuli, the representations of which are nested within the two-dimensional representation of each retinotopic location. Little evidence of such a fine-grained nesting has been found in M1, however, which presumably reflects some additional difference in cortical processing for control of movement versus perception of sensory stimuli.

A second feature of functional organization may have to do with what needs to be processed simultaneously by M1. The well-ordered representations in S1 (area 3b in particular) and V1 are thought to be computationally advantageous because two adjacent receptors are much more likely to receive similar input simultaneously than two distant receptors. If a mechanoreceptor on the thumb is responding to an indenting stimulus, for example, another mechanoreceptor on the thumb is much more likely to be responding simultaneously than a mechanoreceptor on the little finger. Some economy of neural processing presumably is achieved by representing thumb mechanoreceptors close to one another, with little finger mechanoreceptors represented at a distance. In the much less likely event that the thumb and little finger are indented simultaneously, however, the requisite neural processing is more costly than if the thumb and little finger mechanoreceptor representations were intermingled with one another.

Control of movement, particularly the control provided by M1, is fundamentally different. Innumerable combinations of muscle contractions and movements with relatively similar likelihood must be represented. In this way M1 provides the capacity to generate a huge repertoire of movements, as well as the potential to generate previously unperformed movements. To achieve these abilities, the organizational substrate of M1 must be able to access virtually any different combination of muscle contractions and body part movements with equal facility. A well-ordered, discrete, somatotopic representation would limit its ability to do so. Such a well-ordered somatotopic representation in M1 often has been likened to a piano keyboard, on which other cortical areas play out movements, as illustrated in Fig. 10A, where colors have been added to the white keys to identify individual notes. Although many different tunes can be played on such a keyboard, a 21st century composer might be disappointed that certain combinations of notes simply cannot be played. For example, a single pianist cannot play the five notes indicated by black dots in Fig. 10A. If, however, a modern two-dimensional keyboard is created in

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4 Indeed, the resolution of somatotopic organization in area 3b exceeds that which would be expected based on the divergence of thalamocortical afferents carrying somatosensory input from a given finger, and the overlap of thalamocortical afferents carrying input from different fingers (Garraghty et al. 1989; Rausell et al. 1998). The precise somatotopy in area 3b therefore indicates that active mechanisms normally increase the somatotopic resolution in S1, in contrast to the mechanisms organizing M1.
which each note (white keys only for simplicity) is re-represented at multiple locations (Fig. 10B), then at some location the desired combination of five notes can be accessed as easily as any other combination. Distributed organization thus can provide much more flexible access to a wide variety of combinations.

In theory, all possible combinations could be equally represented. In practice, equivalent representation of all possible combinations might come at the cost of an excessively large cortical area. More area is required to re-represent any element multiple times (compare the size of Fig. 10, A vs. B), and the right connections must be established and maintained throughout a relatively large area, with relatively long conduction delays. A compromise therefore might exist in which more frequently used combinations are represented at more locations than less frequently used combinations. Hence when activated by electrical stimulation, the extent of cortical territory representing these frequently used combinations, and the corresponding body parts, would appear magnified relative to other less frequently used combinations and body parts. As the individual learns new motor skills (or quits practicing old ones) such a distributed system (with the underlying structural substrates of convergence, divergence, and horizontal interconnection) could be reorganized to represent new combinations (at the expense of now less used combinations) more readily than a well-ordered somatotopic system.

Distributed organization also provides greater resistance to the disruptive effects of lesions. A tiny lesion the size of a single piano key, for example, could eliminate any ability to produce a given note (such as the pale yellow E) in the well-ordered keyboard of Fig. 10A. The same tiny lesion would go virtually unnoticed in the distributed keyboard of Fig. 10B. A considerably larger lesion covering many keys, would be needed to noticeably compromise use of any given element on the distributed keyboard. When such a lesion occurs, however, use of many notes all along the musical scale would be compromised, consistent with the observations reviewed above that inactivation in the M1 hand representation sufficient to produce detectable deficits affects movements of multiple fingers, not just one.

In a distributed system, networked by convergence, divergence, and horizontal interconnections, somatotopic organization is theoretically unnecessary. Even if one subset of locations representing a particular element (such as the pale yellow E, or thumb flexion) is active during one movement, and another subset is active during another movement, no a priori requirement forces the two different subsets to be spatially segregated. Movement control from the primary motor cortex is not distributed to the point of homogeneity, however. As noted above, the face, arm and leg representations are distinct from one another. Within the upper extremity representation, gradual somatotopic gradients also can be identified on top of an underlying distributed representation. At some point, the costs of distributed representation outweigh the benefits, which may have to do with a third feature of functional organization in M1, the biomechanical interactions of the body parts being controlled.

The degree of somatotopic segregation in M1 generally parallels the biomechanical independence of different body parts. Thumb movements are biomechanically independent of lip movements, and the representations of the thumb and lips therefore can be quite segregated in M1. Movements of the thumb and the wrist are not so independent. Extrinsic muscles acting on the thumb (flexor pollicis longus, extensor pollicis longus, and abductor pollicis longus) act across the wrist as well, and because the proximal segment of the thumb is connected to the wrist directly, motion of the thumb will exert interaction torques at the wrist. Precise control of thumb movement therefore will always require some control of the wrist, even when the wrist is being stabilized so as not to move when the thumb does. Because movement of the thumb always requires some degree of simultaneous control of the wrist, then, representation of the thumb and the wrist is intermingled to a considerable degree in M1. Even more intermingled in M1 are representations of thumb and fingers. Movements of the different digits are not entirely independent (Hager-Ross and Schieber 2000; Schieber 1991). In functional uses of the hand, even when performing sophisticated tasks such as typing or playing the piano, the thumb and fingers are in motion simultaneously (Engel et al. 1997; Fish and Soechting 1992; Santello and Soechting 1998).

The need to control a wide variety of movements in biomechanically coupled, simultaneously moving body parts may have constrained evolution of a well-ordered, spatially segregated, discrete somatotopic map in M1. Indeed, when Huglings Jackson initially proposed localization of control of movements in the brain, he recognized that, “... since the movements of the thumb and fingers could scarcely be developed for any useful purpose without fixation of the wrist... we should a priori be sure that the center discharged, although it might represent movements in which the thumb had the leading part, must represent also certain other movements of the forearm, upper arm, etc., which serve subordinately” (Jackson 1958, p. 69).

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