

COMMENTARY

Orderly Somatotopy in Primary Motor Cortex: Does It Exist?

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INTRODUCTION

In the current issue of *NeuroImage* and an upcoming issue of *Cerebral Cortex* appear data relevant to a fundamental question about the functional organization of the primary motor cortex (M1) of primates (Beisteiner *et al.*, 2001; Hlustik *et al.*, 2001; Indovina and Sanes, 2001), that is, does there exist an orderly somatotopy in M1 and, by extension, in other major motor areas of the brain. A fundamental finding of these papers provides support for separation between representations for finger and hand movement that adheres to a somatotopic organization. The new findings extend previous reports of somatotopically ordered representations for voluntary movements of various joints of the human upper extremity, fingers, wrist, elbow, and shoulder (Grafton *et al.*, 1993; Kleinschmidt *et al.*, 1997; Lotze *et al.*, 2000), but conflict with others (Rao *et al.*, 1995; Sanes *et al.*, 1995). However, as others and we have noted, the degree of somatotopic representation within the upper extremity representation appears rather limited (Schieber, 1999; Sanes and Donoghue, 2000).

Clearly the major body parts—lower limb (hindlimb), upper limb (forelimb), and head—have functional and largely independent subdivisions to represent the muscles and movements controlled by the respective parts of M1. These functional subdivisions of M1 are commonly laid out along the cortical surface of primates with the lower (hind) limb most medial, the head most lateral, and the upper (fore) limb in between; they have acquired the designation of “areas,” such as the “M1 arm area,” though the term “representation” might provide a more suitable functional name. No serious challenge has emerged for this basic large-scale organization pattern in M1, but

debate has grown in recent years about whether organized somatotopy exists within an M1 region representing a major body part. In the following commentary, we mostly restrict our discussion to work that investigated organization of the upper extremity representation of humans and nonhuman primates, assuming that the principles identified here will also apply to the face and lower extremity representations and to other mammalian species.

Because a good scientific theory should account for all data sets, we rhetorically ask how two seemingly mutually exclusive points of view—orderly somatotopy versus a lack thereof—can be true at the same time. Briefly, our answer is that the cortical territory activated during movement of any single finger or other joint of the upper extremity constitutes a large fraction of the total upper extremity representation, such that the representations of different parts of the upper extremity must overlap considerably. Indeed, there appears fundamental agreement that finger and hand movement representations in human M1 exhibit extensive overlap (Rao *et al.*, 1995; Sanes *et al.*, 1995; Hlustik *et al.*, 2001; Indovina and Sanes, 2001). Nevertheless, movements of progressively more ulnar fingers or more proximal joints may indeed involve activation of cortical territories whose representation centroids have a progressively more posteromedial location along the central sulcus. (We use “centroids” to refer conveniently to both center of mass and center of gravity though the two quantities could have different locations.) However, as reviewed below and documented in Indovina and Sanes (2001), the territories activated by each movement are relatively large and overlap extensively, so that shifts in a representation centroid for different arm movements must necessarily be small compared to the spatial extent of the activation.

LESSONS FROM HISTORICAL ACCOUNTS

While we do not intend, nor pretend, to provide a full accounting of the history of the guiding principles of

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motor cortical organization, it is useful to recall certain pertinent aspects of the historical record on the issue of M1 somatotopy, which we arbitrarily begin with observations of the neurologist John Hughlings Jackson and end with those of the neurophysiologist Clinton Woolsey and his collaborators.

The concept of a somatotopic motor representation in the brain originated from clinical observations of epileptic patients. In the later half of the 19th century, when brain functions generally were thought to be very diffusely organized, Jackson observed that epileptic patients with "convulsions beginning unilaterally" demonstrated systematic spread of seizure activity (Jackson, 1863, 1931). If the seizure began in the face, for example, the repetitive jerking might spread to the arm and then to the leg, but never to the leg and then to the arm. On the basis of such observations, Jackson speculated that somewhere in the brain there exists an orderly representation of bodily movement. While providing the first hypothesis of somatotopic organization, Jackson did not envision a separate representation of each body part. Rather, he reasoned:

"Since the movements of the thumb and fingers could scarcely be developed for any useful purpose without fixation of the wrist (and of parts further and further in automaticity according to the force required), we should *a priori* be sure that the centre 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" (J. H. Jackson, *Selected Writings*, Vol. 1., 1931, p. 69, as quoted by Walshe (1948)).

The seminal observations of Jackson stimulated a lengthy debate now enduring some 130 years about whether *within-area* somatotopy exists in M1. Indeed, some other "early" neurological observations would seem to support the tenet of discrete M1 organization, particularly those of Foerster, who described "focal" finger paralysis among many individual cases from his extensive clinical observations on patients with presumed small lesions within the Rolandic region, many identified at surgery (Foerster, 1936). Foerster also reviewed work of others on the issue of M1 somatotopy, some of which supported, and some of which did not, his own views on functional separation of muscle control in M1. Clinical observations without objective means of data collection and analysis can provide important insights into function, but clearly require scientific verification.

In the mid-20th century, methods to more directly assess the functional connectivity of the cerebral cortex to motor neuron pools became available. Electrical stimulation applied to the cortical surface of humans and non-human primates yielded data summarized as a somatotopically ordered representational map for movements (or muscles) that resembled a distorted cartoon of the body (Penfield and Rasmussen, 1950; Woolsey *et al.*, 1952). Functional maps resulting from these methods

commonly depicted body parts, joints, or movements in a continuous representation laid out upon the M1 surface. Following Jacksonian principles, a general medial to lateral topography of the leg (hindlimb in quadripedal mammals), arm (forelimb, including digits), and head and face functional map emerged. However, no unequivocal evidence emerged to suggest more discrete somatotopic organization within a major representation, and one doubts that the structured somatotopy suggested by the summary homunculus (or simiusculus) cartoons was ever intended (Schott, 1993). Indeed, both Penfield and Woolsey cautioned against such an interpretation. Penfield and Rasmussen (p. 56, 1950) in referring to the homunculus cartoon noted:

"Reconsideration of our findings in regard to somatic motor representation in the precentral and postcentral gyri may be assisted by reference to Fig. 22. 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 scientific accuracy is impossible."

Similarly, in commenting upon the classical cartoon simiusculus figure, Woolsey *et al.* (1952) noted on pp. 251–252 (italics in the original)

"It must be emphasized, however, 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, not only in the motor but also in the sensory areas. If this warning is heeded, Figure 131 may serve to outline in general the localization pattern of the precentral motor field, and to show its relation to the supplementary motor area."

Despite these cautions, the scheme of discretely organized somatotopy became widely adopted and has profoundly influenced concepts of motor cortex organization. Most notably, a homunculus plan clearly suggests that representations for each body part have specific and orderly spatial relationships, with each part occupying nonoverlapping cortical space. By extension, a highly ordered somatotopy likely implies that specific neural elements, such as a cortical column or an aggregate of voxels, become dedicated to controlling a single body part (Asanuma and Ward, 1971), perhaps even an individual phalanx of one digit.

CLINICAL LESIONS IN HUMAN PATIENTS

The large-scale face/arm/leg somatotopy of motor representation is evident in daily clinical practice. Lateral cortical lesions produced by stroke in the middle cerebral artery (MCA) territory affect the face and arm more than the leg; medial lesions in the anterior cerebral artery (ACA) territory affect the leg more than the arm and face. Though less common, cortical lesions

producing paresis limited to the face, to the arm, or to the leg also are well known.

Within each of these major representations, however, overlap always has been evident in clinical lesions. Thus, lesions encroaching upon human M1 that produce profound weakness of one joint without accompanying weakness of adjacent joints in the same extremity do not occur in clinical practice. As might be expected from a system that is distributed but not entirely homogeneous, some lesions that affect a small portion of human M1 produce greater impairment of some joints than others within a limb. For example, whereas lesions of the entire corticospinal output impair distal movements more than proximal movements (reflecting the greater control normally exerted by the corticospinal system over distal compared to proximal musculature), this pattern is reversed in the "man-in-a-barrel" syndrome associated with infarction in the MCA/ACA watershed. This may reflect greater representation of proximal than of distal musculature of both the upper and the lower extremities at this location, consistent with Penfield's homunculus. The hand and foot are not unaffected in the man-in-a-barrel, however; rather, the hand and foot are not as profoundly weak as are the shoulder and hip.

Similarly, small lesions within the hand representation indicate considerable overlap of the representations of different fingers, as well as overlap of finger representations with those of more proximal joints. Although Foerster (1936) clearly thought that cortical lesions could weaken single digits (or even single muscles) selectively, modern examiners fail to find such cases. One of us, in the course of general neurological practice, has sought such cases for the past 10 years. Of nine patients identified with small Rolandic strokes, five cases had all five digits affected uniformly; three had greater weakness in the thumb, index, and middle fingers than in the more ulnar digits; and one had greater weakness in the little and ring fingers than in the more radial digits (Schieber, 1999). In all patients with more than trace finger weakness, proximal joints showed lesser degrees of weakness as well. Other case reports of weakness predominantly in the thumb have also described weakness in the index finger (Terao *et al.*, 1993; Lee *et al.*, 1998). While these observations have consistency with greater representation of distal than of proximal musculature in the lateral aspect of the upper extremity representation, and with greater representation of movements of the radial digits laterally and the ulnar digits medially, they simultaneously indicate considerable representational overlap across all parts of the upper extremity.

In human patients, evidence of representational overlap often has been discounted by two arguments. First, it often has been argued that lesions produced by disease simply do not respect physiological boundaries. This argument assumes that the underlying M1 soma-

topic representation consists of discrete zones for each body part, but that any lesion large enough to produce clinical symptoms inevitably crosses many of these discrete zones. If such were the case, however, then some rare patient should have a lesion that produces profound weakness of the proximal upper extremity plus the little finger, while producing no weakness of the remaining digits, or a lesion that produces weakness of the face and the thumb without affecting the fingers. (Again, we suspect that rare cases of single finger paralysis described in the early 20th century and summarized by Foerster (1936) would not withstand reexamination with contemporary methods.) It is then secondarily argued that lesions produced by disease are not sharply demarcated, so that they never affect the representation of one joint without a penumbra affecting the representation of adjacent joints. These arguments date from a time, however, when the spatial distribution of M1 activation during movement in human patients could not be compared with the spatial location of the lesion resolved with the precision of modern neuroimaging. We argue that lesions cannot reveal sharply demarcated representations of different fingers because physiological boundaries between finger representations simply are not present. Future studies of such patients should combine quantitative evaluation of the distribution of weakness with both precise anatomical MRI localization of the lesion relative to anatomic landmarks, such as the M1 "knob" (Yousry *et al.*, 1997, but see comment below about this landmark), and functional imaging of activation during remaining finger movements.

EXPERIMENTAL LESIONS IN NONHUMAN PRIMATES

Experimental studies traditionally have provided the opportunity to observe the consequences of discrete lesions placed under precise, physiological guidance. Though classic studies typically aimed at determining the motor behaviors affected by lesions of M1 rather than probing the details of somatotopic organization, functional overlap was evident nonetheless. Denny-Brown and Botterell (1948), for example, observed from their experience with excisional lesions that "Loss of power of movement in the hand... was by no means limited to lesions of the hand area, or of the foot to the foot area, so that this relationship of paralysis to cortical area of representation [defined by threshold electrical stimulation] must be regarded as only relative" (pp. 311–312). Similarly, after carefully controlled microinfarction limited to zones defined by intracortical stimulation as having hand function, squirrel monkeys demonstrated not only decreased use of the hand but also tonic flexion at the elbow and adduction of the extremity close to the torso (Friel and Nudo, 1998). Reversible inactivation of small regions of M1 similarly affected the whole hand when only the

zones related to thumb and the index finger movements were injected (Brochier *et al.*, 1999) and failed to affect the digits in somatotopic order when different locations along the central sulcus within the physiologically defined hand representation were inactivated (Schieber and Poliakov, 1998). Hence more carefully controlled lesion studies in nonhuman primates also indicate considerable representational overlap of different parts of a given limb.

ORGANIZATION OF M1: EXPERIMENTAL ANALYSIS OF NONHUMAN PRIMATE MOVEMENT REPRESENTATION

Experimental studies in nonhuman primates at the "microscopic" level also have revealed overlap and a general distributed organization of M1 functional representations. These data have accrued from anatomic, neuronal recording, and electrical stimulation methods. In their aggregate these findings, especially when carefully evaluated, uphold separation of M1 leg, arm, and head representations, but cast serious doubt upon a strict interpretation of fully organized somatotopy. Before reviewing them, and later analogous data obtained from humans, we briefly note the criteria that would seem appropriate to satisfy for concluding that organized somatotopy exists as seemingly conceptualized by outgrowths from the homunculus cartoon. First, functional representations should be clearly separable as revealed by electrical recordings or output maps generated by intracortical or surface stimulation. Second, there should exist a single, contiguous representation of each function. Third, functional and perhaps also structural overlap between adjacent (or non-adjacent) representations should be minimal. On all three counts, the available data obtained from experimental animals (and from humans as reviewed in the next section) provide little support for such organized somatotopy in M1, except in a very general sense.

The projection patterns of corticospinal neurons and intrinsic connectivity of M1 belie organized somatotopy for movement control. Axon-filling studies have indicated a widespread projection of single descending M1 neurons to multiple segments in the spinal cord that can span motor neuron pools across joints of the forelimb and even across the upper and lower limb (Shinoda *et al.*, 1979, 1986). Further, intrinsic connectivity within the upper limb representation in macaque monkeys appears to distribute widely, interconnecting sites "best" related (as determined from intracortical stimulation) to different segments of the forelimb, while largely avoiding crossovers into other major representations (Huntley and Jones, 1991). The corticospinal and intrinsic connectivity patterns of M1 would seem to indicate that functional divergence and convergence are basic features of M1 organization rather than a separation and specialization of functionality at the cortical level.

The intermixing of cortical output and intrinsic connectivity is supported by results from electroanatomical studies dating to the 1960s that used stimulation methods more refined than those available to Penfield and Woolsey and their colleagues that activated small clusters of M1 neurons. Phillips and co-workers and others (reviewed in Phillips and Porter, 1977) found evidence for widespread convergence onto a hand muscle's spinal motor neuron pool from large territories of nonhuman primate M1 and that the cortical territories representing different muscles overlap extensively. Echoing the anatomical divergence of corticospinal neurons observed by Shinoda *et al.* (1979), several groups have found that corticospinal neurons have relatively direct connection to the motor neuron pools of multiple muscles as demonstrated by intracortical stimulation or with the physiologic method of spike-triggered averaging (Sesse and Wiesendanger, 1982; Buys *et al.*, 1986; Gould *et al.*, 1986; Fetz *et al.*, 1989; Nudo *et al.*, 1992). The divergence of M1 control of the upper limb has repeatedly been shown to include combinations of proximal with distal muscles (Gould *et al.*, 1986; Donoghue *et al.*, 1992; McKiernan *et al.*, 1998). A review of other data sets claiming to have found organized somatotopy in M1, such as that of "horseshoe shaped rings" (Kwan *et al.*, 1978) or duplicate hand representations (Strick and Preston, 1982), reveals that many such claims were likely not fully supported by the existing data (Porter and Lemon, 1993). Last, recordings of single M1 neurons show that they rarely modulate with the action of a single joint or hand part: each neuron appears to participate in multiple hand motor actions, and neurons influencing different digits or the wrist appear to have a seemingly random topographic distribution (Schieber and Hibbard, 1993; Poliakov and Schieber, 1999). This pattern does not easily find reconciliation with a discrete, topographically segregated organization for M1. The existing facts of "microscopic" anatomy and physiology would seem to suggest that a considerable degree of representational overlap is inevitable, thereby likely precluding organized somatotopy.

ORGANIZATION OF M1: EXPERIMENTAL ANALYSIS OF HUMAN MOVEMENT REPRESENTATIONS

Contemporary neuroimaging methods that detect local changes in blood flow and transcranial activation methods have also allowed exploration of the organization of human motor cortex; these methods too have mostly provided data that tend to argue against organized somatotopy in the M1 arm representation. In functional neuroimaging, low-resolution studies with positron emission tomography found overlapping activation patterns for distal and proximal arm movements within the M1 arm area (Colebatch *et al.*, 1991; Grafton *et al.*, 1991). The similarly low-resolution transcranial stimulation method also yields evidence

for overlapping representations of arm muscle representations and convergence and divergence of corticospinal outputs (Wassermann *et al.*, 1992), though this work did provide some evidence for an orderly distal-to-proximal progression of evoked movements along the cortical surface. The higher resolution available with functional MRI has also revealed overlapping, distributed activation in M1 for distinctive movements of the fingers, wrist, and elbow (Rao *et al.*, 1995; Sanes *et al.*, 1995), thus showing consistency with a distributed organization within the M1 arm subregion. Some contemporary experiments with higher resolution functional MRI methods than those applied previously have found evidence of organized somatotopy in M1, as reviewed and claimed by Beisteiner *et al.* (2001) and Hlustik *et al.* (2001). We note, however, that within-limb somatotopic order is identified only by examining the locations of different representation *centroids* or by subtracting the activation during movement of one limb part from the activation found during movement of another part (Kleinschmidt *et al.*, 1997). When the extent of territory activated (relative to rest) with movements of two different limb parts is compared, considerable spatial overlap is found (Sanes *et al.*, 1995; Hlustik *et al.*, 2001; Indovina and Sanes, 2001). Consequently, the somatotopic shift of centroids is small compared to the total extent of the activated regions (Indovina and Sanes, 2001). For example, the three-dimensional distance between the centroids for index and little finger movements reported by Beisteiner *et al.* (2001) averages 2.46 mm (less than the thickness of M1 cortex), whereas Penfield and Boldrey (1937) reported eliciting finger movements with electrical stimulation for an average of 55 mm along the Rolandic fissure. Functional representations of different parts of the upper extremity in human M1 thus are not separate, contiguous, nor free of overlap, though the subtle shift in centroid locations indicates a gradual somatotopic gradient of representation from anterolateral to posteromedial along the Rolandic fissure.

WHY SHOULD M1 SOMATOTOPY BE SO DISTRIBUTED?

A germane issue when considering the functional organization of M1, and other motor structures, concerns the job of the motor system, and for the purposes of this commentary how it might intersect with organized somatotopy. Clearly, and most simply, M1 contributes to movement control. Exactly what M1 contributes constitutes yet another debate that would require another commentary. Nevertheless, consider that the motor system often must convert instructions derived from sensory signals into neural commands to control movements of multiple limb parts in three-dimensional space. Each body part has several components that require simultaneous control. Since we have mostly restricted the commentary

to brain representations for arm movement control, consider that the arm has four principal rotation points (shoulder, elbow, wrist, and fingers) with 27 degrees of freedom and more than 50 muscles to control reaching and grasping. Considerable effort has been expended to understand the psychophysics of reaching and grasping with the general consensus that the process involves high-level interactions among neural controllers. As indicated above, a discretely organized M1 somatotopy with separate territories for different joints would suggest that substrates for simultaneous control of multiple limb parts are not found at the level of the cerebral cortex, but at a subcortical level, perhaps in the cerebellum, brain stem, or spinal cord. However, for the past two decades studies have shown that single neurons and neuron populations of M1 encode the direction of whole arm reaching movements (Georgopoulos *et al.*, 1982, 1988). Of course, reaching in two- or three-dimensional space requires simultaneous control of the shoulder, elbow, and wrist. We suggest that the distributed organization of M1 cortex is well suited to provide such control and other motor actions requiring interplay among joints.

Biomechanical issues also may influence the nature of somatotopy in M1. Due to location of insertion points onto tendons, many muscles of the arm have multijoint actions, many muscles contribute to actions about various arm joints, and these muscles have complex arrangements. Further, individuated finger movements occur by coordinated action of multiple muscles, some controlling more than one finger, and not by independent sets of muscles each acting upon a single digit (Schieber, 1995). Lastly, a single joint movement of arm parts occurs in the context of stability of the remaining arm parts, and this stability commonly involves active postural maintenance, which also may be controlled simultaneously from M1 (Humphrey and Reed, 1983). Thus, it would appear that biomechanical and postural constraints might prevent the evolution of a discrete somatotopic organization in M1 or other CNS motor structures. This may be particularly the case for movements of the fingers, which have considerable biomechanical interdependence. In comparison, the fingers and shoulder are somewhat less interdependent, so although their cortical territories overlap extensively, the centroids of their representations might be somewhat separated. Even more biomechanically independent are movements of the fingers and the toes, so their representations can be entirely separated in M1.

SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

We have reviewed the historical and contemporary account of an important issue concerning M1 functional organization, namely the existence of well-ordered somatotopy. Even before 1960, the historical record provides a relatively clear guide of serious reservations that precisely ordered representations for

bodily movement or muscles exist in M1. More contemporary research using a panoply of direct and indirect methods to reveal M1 organization has fueled these doubts. Nevertheless, some researchers and many clinicians continue to claim existence of evidence having some consistency with somatotopic representations for the fingers, wrist, elbow, and shoulder. We concur, up to a point, that M1 may have specialization for some upper limb function; it may be the case that proximal arm movements have a greater representation more posterior and superior along the course of the precentral gyrus, and distal movements have a greater tendency for representation more anterior and inferior in M1. However, the extensive overlap, the "sharing" of representations within a functional element (neuron, voxel, or otherwise), and the widespread distribution of movement (and muscle) representations in the upper limb zone of M1 all indicate that precisely ordered, within-limb somatotopy does not exist.

There appears no ready answer for why notions of a detailed somatotopy in M1 have persisted despite repeated demonstrations, including those that purportedly led to the concept, to the contrary. The persistence has more perplexity when considering that one parsimonious implication of highly ordered somatotopy—that of labeled line output—would seem to preclude a role for M1 in high-level movement control, thereby leaving such control to subcortical structures. Perhaps, the perseverance of the hypothesis of M1 somatotopy has three motivations. First, it has consistency with the notion that M1 functions as an "upper motor neuron," insofar as segments of M1 would have direct-labeled lines to spinal motor neuron pools. This concept has been largely discarded from scientific discourse on the function of M1 (Porter and Lemon, 1993). Second, M1 somatotopy mirrors that of primary somatic sensory cortex (S1), but only to the extent of major body representations. If M1 somatotopy completely mirrored that of S1 then there might be a ready substrate for precise somatic sensory-motor integration within a body part. Necessarily, the possible existence of mirrored somatotopy in M1 and S1 ignores the fundamentally different functions of S1 (for somatic sensation) and M1 (for motor processing, including integration of multiple modal sensory stimuli). S1 somatotopy functions to provide a veridical representation of the body surface, much like primary visual cortex does for the visual scene, while M1 likely functions to bring together, not to separate, functionality across a limb's joints. Finally, a clear, organized somatotopic representation pattern in M1 may have provided a simplifying scheme on which to base subsequent inquiries into M1. Indeed, Penfield and Woolsey introduced (but with appropriate caveats) their cartoon figurines as summary diagrams. And their work surely has stimulated further inquiry.

While conclusions from scientific investigation must ebb and flow until a consensus is reached, we believe that sufficient evidence now exists to allow the field to advance beyond proof or disproof of M1 somatotopy. In attending to facts about overlap, distribution, and multiplicity of upper limb representations in primate M1, researchers will free themselves to discover the secrets of M1. As a start, we urge researchers to desist from using certain terminology. For example, since the hand appears to have a wide distribution throughout the upper extremity representation, the term "M1 hand area" should be supplanted with "M1 hand representation." Similar shifts in nomenclature should be instituted for component parts of the M1 representations of each major body part. Application of the term "hand area" to an anatomic feature observed consistently within the upper-limb representation of humans (the "knob"; Yousry *et al.*, 1997) does not seem consistent with data obtained with physiological methods. A final recommendation applies to motor control researchers and researchers in general: View data critically, and use all that become available.

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REFERENCES

- Asanuma, H., and Ward, J. E. 1971. Patterns of contraction of distal forelimb muscles produced by intracortical stimulation in cats. *Brain Res.* **27**:97-109.
- Beisteiner, R., Windischberger, C., Lanzenberger, R., Edward, V., Cunningham, R., Erdler, M., Gartus, A., Streibl, B., Moser, E., and Deecke, L. 2001. Finger somatotopy in human motor cortex. *NeuroImage*, 1014-1024.
- Brochier, T., Boudreau, M. J., Paré, M., and Smith, A. M. 1999. The effects of muscimol inactivation of small regions of motor and somatosensory cortex on independent finger movements and force control in the precision grip. *Exp. Brain Res.* **128**:31-40.
- Buyse, E. J., Lemon, R. N., Mantel, G. W., and Muir, R. B. 1986. Selective facilitation of different hand muscles by single corticospinal neurones in the conscious monkey. *J. Physiol. (London)* **381**: 529-549.
- Colebatch, J. G., Deiber, M. P., Passingham, R. E., Friston, K. J., and Frackowiak, R. S. 1991. Regional cerebral blood flow during voluntary arm and hand movements in human subjects. *J. Neurophysiol.* **65**:1392-1401.
- Denny-Brown, D., and Botterell, E. H. 1948. The motor functions of the agranular frontal cortex. *Res. Publ. Assoc. Nerv. Ment. Dis.* **27**: 235-345.
- Donoghue, J. P., Leibovic, S. J., and Sanes, J. N. 1992. Organization of the forelimb area in squirrel monkey primary motor cortex: Representation of individual digit, wrist, and elbow muscles. *Exp. Brain Res.* **89**:1-19.
- Fetz, E. E., Cheney, P. D., Mewes, K., and Palmer, S. 1989. Control of forelimb muscle activity by populations of corticomotoneuronal and rubromotoneuronal cells. *Prog. Brain Res.* **80**:437-449.

- Foerster, O. 1936. Motorische Felder und Bahnen. In *Handbuch der Neurologie* (O. Bumke and O. Foerster, Eds.). Springer-Verlag, Berlin.
- Friel, K. M., and Nudo, R. J. 1998. Recovery of motor function after focal cortical injury in primates: Compensatory movement patterns used during rehabilitative training. *Somatosens. Mot. Res.* **15**:173–189.
- Georgopoulos, A., Kalaska, J., Caminiti, R., and Massey, J. 1982. On the relations between the direction of two-directional arm movements and cell discharge in primate motor cortex. *J. Neurosci.* **2**:1527–1537.
- Georgopoulos, A. P., Kettner, R. E., and Schwartz, A. B. 1988. Primate motor cortex and free arm movements to visual targets in three-dimensional space. II. Coding of the direction of movement by a neuronal population. *J. Neurosci.* **8**:2928–2937.
- Gould, H. J., 3rd, Cusick, C. G., Pons, T. P., and Kaas, J. H. 1986. The relationship of corpus callosum connections to electrical stimulation maps of motor, supplementary motor, and the frontal eye fields in owl monkeys. *J. Comp. Neurol.* **247**:297–325.
- Grafton, S. T., Woods, R. P., and Mazziotta, J. C. 1993. Within-arm somatotopy in human motor areas determined by positron emission tomography imaging of cerebral blood flow. *Exp. Brain Res.* **95**:172–176.
- Grafton, S. T., Woods, R. P., Mazziotta, J. C., and Phelps, M. E. 1991. Somatotopic mapping of the primary motor cortex in humans: Activation studies with cerebral blood flow and positron emission tomography. *J. Neurophysiol.* **66**:735–743.
- Hlustik, P., Solodkin, A., Gullapalli, R. P., Noll, D. C., and Small, S. L. 2001. Somatotopy in human primary motor cortex and somatosensory hand representations revisited. *Cereb. Cortex*, **11**:312–321.
- Humphrey, D. R., and Reed, D. J. 1983. Separate cortical systems for control of joint movement and joint stiffness: Reciprocal activation and coactivation of antagonist muscles. In *Motor Control Mechanisms in Health and Disease* (J. E. Desmedt, Ed.), pp. 347–372. Raven Press, New York.
- Huntley, G. W., and Jones, E. G. 1991. Relationship of intrinsic connections to forelimb movement representations in monkey motor cortex: A correlative anatomical and physiological study. *J. Neurophysiol.* **66**:390–413.
- Indovina, I. A., and Sanes, J. N. 2001. On somatotopic representation centers for finger movements in human primary motor cortex and supplementary motor area. *NeuroImage*, **1025–1032**.
- Jackson, J. H. 1863. Convulsive spasms of the right hand and arm preceding epileptic seizures. *Med. Times Gaz.* **1**:589.
- Jackson, J. H. 1931. *Selected Writings of John Hughlings Jackson*. Hodder & Stoughton, London.
- Kleinschmidt, A., Nitschke, M. F., and Frahm, J. 1997. Somatotopy in the human motor cortex hand area. A high-resolution functional MRI study. *Eur. J. Neurosci.* **9**:2178–2186.
- Kwan, H. C., MacKay, W. A., Murphy, J. T., and Wong, Y. C. 1978. Spatial organization of precentral cortex in awake primates. II. Motor outputs. *J. Neurophysiol.* **41**:1120–1131.
- Lee, P. H., Han, S. W., and Heo, J. H. 1998. Isolated weakness of the fingers in cortical infarction. *Neurology* **50**:823–824.
- Lotze, M., Erb, M., Flor, H., Huelsmann, E., Godde, B., and Grodd, W. 2000. fMRI evaluation of somatotopic representation in human primary motor cortex. *NeuroImage* **11**:473–481.
- McKiernan, B. J., Marcario, J. K., Karrer, J. H., and Cheney, P. D. 1998. Corticomotoneuronal postspike effects in shoulder, elbow, wrist, digit, and intrinsic hand muscles during a reach and prehension task. *J. Neurophysiol.* **80**:1961–1980.
- Nudo, R. J., Jenkins, W. M., Merzenich, M. M., Prejean, T., and Grenda, R. 1992. Neurophysiological correlates of hand preference in primary motor cortex of adult squirrel monkeys. *J. Neurosci.* **12**:2918–2947.
- Penfield, W., and Boldrey, E. 1937. Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. *Brain* **60**:389–443.
- Penfield, W., and Rasmussen, T. 1950. *The Cerebral Cortex of Man: A Clinical Study of Localization of Function*. Macmillan, New York.
- Phillips, C. G., and Porter, R. 1977. *Corticospinal Neurones*. Academic Press, London.
- Poliakov, A. V., and Schieber, M. H. 1999. Limited functional grouping of neurons in the motor cortex hand area during individuated finger movements: A cluster analysis. *J. Neurophysiol.* **82**:3488–3505.
- Porter, R., and Lemon, R. 1993. *Corticospinal Function and Voluntary Movement*. Clarendon Press, Oxford.
- Rao, S. M., Binder, J. R., Hammeke, T. A., Bandettini, P. A., Bobholz, J. A., Frost, J. A., Myklebust, B. M., Jacobson, R. D., and Hyde, J. S. 1995. Somatotopic mapping of the human primary motor cortex with functional magnetic resonance imaging. *Neurology* **45**:919–924.
- Sanes, J. N., and Donoghue, J. P. 2000. Plasticity and primary motor cortex. *Annu. Rev. Neurosci.* **23**:393–415.
- Sanes, J. N., Donoghue, J. P., Thangaraj, V., Edelman, R. R., and Warach, S. 1995. Shared neural substrates controlling hand movements in human motor cortex. *Science* **268**:1775–1777.
- Schieber, M. H. 1995. Muscular production of individuated finger movements: The roles of extrinsic finger muscles. *J. Neurosci.* **15**:284–297.
- Schieber, M. H. 1999. Somatotopic gradients in the distributed organization of the human primary motor cortex hand area: Evidence from small infarcts. *Exp. Brain Res.* **128**:139–148.
- Schieber, M. H., and Hibbard, L. S. 1993. How somatotopic is the motor cortex hand area? *Science* **261**:489–492.
- Schieber, M. H., and Poliakov, A. V. 1998. Partial inactivation of the primary motor cortex hand area: Effects on individuated finger movements. *J. Neurosci.* **18**:9038–9054.
- Schott, G. D. 1993. Penfield's homunculus: A note on cerebral cartography. *J. Neurol. Neurosurg. Psychiatr.* **56**:329–333.
- Sesse, B. J., and Wiesendanger, M. 1982. Structural and functional definition of the motor cortex in the monkey (Macaca fascicularis). *J. Physiol. (London)* **323**:245–265.
- Shinoda, Y., Yamaguchi, T., and Futami, T. 1986. Multiple axon collaterals of single corticospinal axons in cat spinal cord. *J. Neurophysiol.* **55**:425–448.
- Shinoda, Y., Zarzeki, P., and Asanuma, H. 1979. Spinal branching of pyramidal tract neurons in the monkey. *Exp. Brain Res.* **34**:59–72.
- Strick, P. L., and Preston, J. B. 1982. Two representations of the hand in area 4 of a primate. I. Motor output organization. *J. Neurophysiol.* **48**:139–149.
- Terao, Y., Hayashi, H., Kanda, T., and Tanabe, H. 1993. Discrete cortical infarction with prominent impairment of thumb flexion. *Stroke* **24**:2118–2120.
- Walshe, F. M. R. 1948. *Critical Studies in Neurology*. Livingstone, London.
- Wassermann, E. M., McShane, L. M., Hallett, M., and Cohen, L. G. 1992. Noninvasive mapping of muscle representations in human motor cortex. *Electroencephalogr. Clin. Neurophysiol.* **85**:1–8.
- Woolsey, C. N., Settlage, P. H., Meyer, D. R., Sencer, W., Hamuy, T. P., and Travis, A. M. 1952. Patterns of localization in precentral and "supplementary" motor areas and their relation to the concept of a premotor area. *Res. Publ. Assoc. Res. Nerv. Ment. Dis.* **30**:238–264.
- Yousry, T. A., Schmid, U. D., Alkadhi, H., Schmidt, D., Peraud, A., Buettner, A., and Winkler, P. 1997. Localization of the motor hand area to a knob on the precentral gyrus. A new landmark. *Brain* **120**:141–157.