5

The Motor Cortical Circuit

Apostolos P. Georgopoulos and Costas N. Stefanis

The core motor cortical circuit (cMCC) consists of a cell column ("minicolumn"), perpendicular to the cortical surface, ~30 μm in width (Georgopoulos et al., 2007). Each minicolumn contains pyramidal (~72%) and nonpyramidal (~28%) cells (Sloper et al., 1979). The greater MCC (gMCC) comprises minicolumns surrounding the core and receiving dense horizontal (i.e., tangential to the surface) projections from the core. These projections form a cylinder of ~500 μm diameter, centered on the core minicolumn (Gatter and Powell, 1978) (Figs. 5.1A and B). This cylinder contains ~278 minicolumns, given a minicolumn tangential area of $\pi R^2 = 3.141 \times {\sim}15^2 = {\sim}707\ \mu m^2$, and a cylinder tangential area of $3.141 \times 250^2 = 196{,}312\ \mu m^2$. Afferent fibers to, and efferent fibers from, the MCC are arranged in parallel to the minicolumns. Inputs external to the MCC (from the thalamus, contralateral hemisphere, and ipsilateral hemisphere) are excitatory and terminate mostly on dendritic spines of pyramidal cells and dendritic shafts and somata of nonpyramidal cells. Finally, the MCC also receives extensive monoaminergic innervation from all monoamine systems (dopamine, norepinephrine, serotonin, and acetylcholine) the functional role of which is not well understood.

Spatial Aspects

In the arm area of the motor cortex, MCC neurons are tuned to the same direction of movement (Georgopoulos et al., 2007). Preferred MCC directions are repeatedly mapped with a spatial repetition periodicity of ~240 μm (Georgopoulos et al., 2007). Remarkably, this periodicity closely corresponds to the radius of the gMCC (Fig. 5.1C), as defined above based on degeneration studies. This finding indicates that a given cMCC with preferred

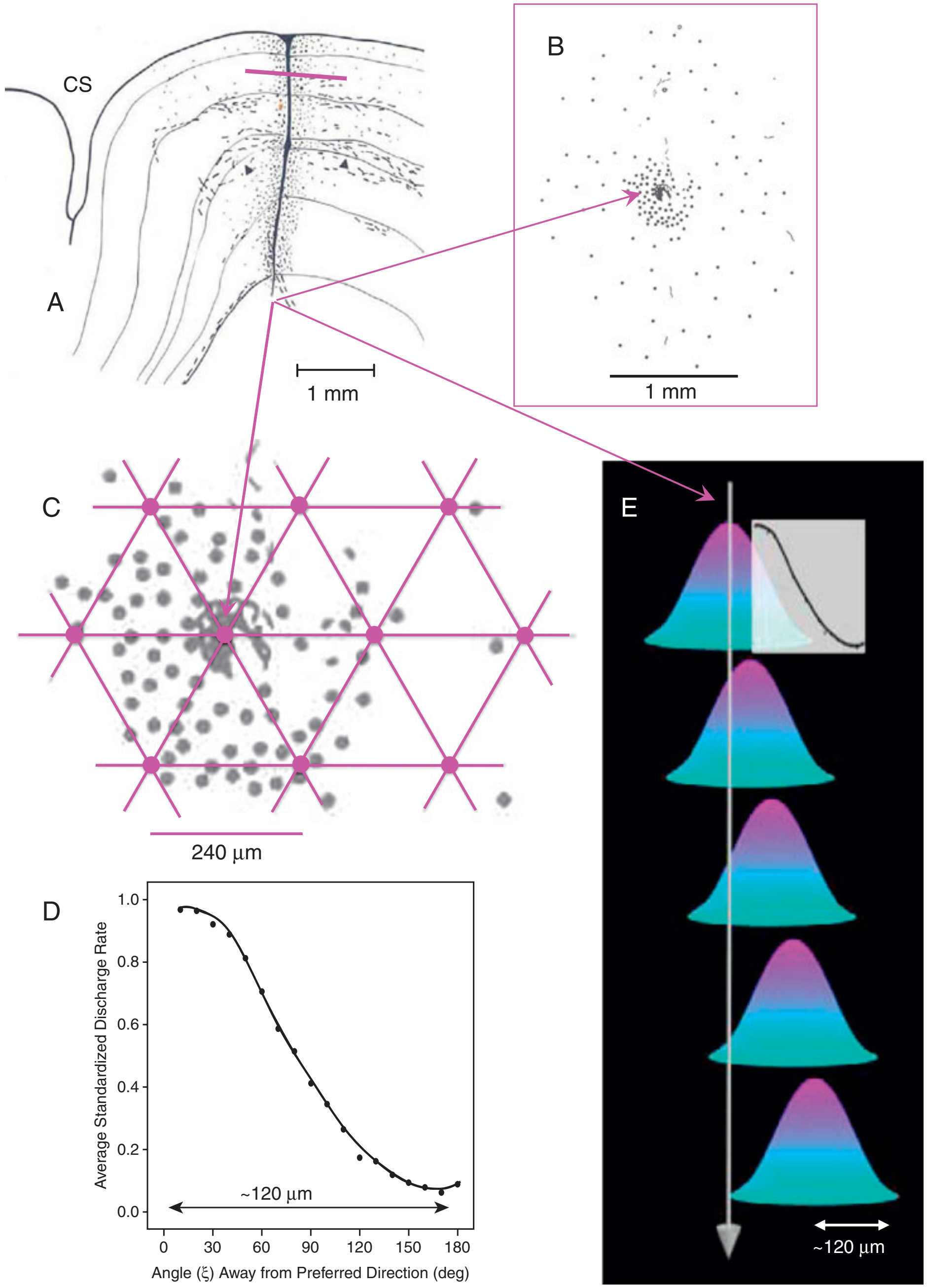

Figure 5–1. Spatial aspects of the motor cortical circuit. (*A*) Pattern of degeneration following insertion of a microelectrode in monkey motor cortex. Dots indicate degeneration of terminals (adapted from Fig. 1 of Gatter and Powell, 1978). (*B*) Distribution of terminal degeneration in a tangential section of the motor cortex (adapted from Fig. 9 of Gatter and Powell, 1978). (*C*) The greater motor cortical circuit (area of dense terminal degeneration from *B*, blown up to scale) is demarcated by minicolumns (cMCC) with the same preferred directions, placed at the corners

Figure 5–1. continued
of a regular hexagon (adapted from Georgopoulos et al., 2007). The remainder of the lattice is filled with minicolumns of spatially orderly varying preferred directions (see Figs. 6 and 7 of Georgopoulos et al., 2007). (*D*) Standardized, average directional tuning in the arm area of the motor cortex (adapted from Fig. 2 of Georgopoulos and Stefanis, 2007). (*E*) Observed average standardized directional tuning of *D* above partially superimposed on a model of spatial tuning field (adapted from Fig. 5 of Georgopoulos and Stefanis, 2007). The arrow indicates the fixed position of a hypothetical microelectrode recording from a cell for which the preferred direction coincides with the direction at the center of the field. The displaced directional tuning field indicates activation of other preferred directions farther and farther away from that of the top. It is hypothesized that the directional tuning curve of the recorded cell reflects the progressively decreasing influence of the spatially moving away directional tuning field, visualized, for example, as the length of the line crossing the directional tuning field at a particular location.

direction ***C*** interacts intensely with the other ~278 minicolumns within the gMCC demarcated by cMCCs of the same preferred direction ***C***, roughly placed at the corners of a regular hexagon (Fig. 5.1C).

The MCC directional tuning (Fig. 5.1D) arises from orderly interactions among neighboring cMCCs (Georgopoulos and Stefanis, 2007; Merchant et al., 2008). This is illustrated in Figure 5.1E, where the observed directional tuning curve (insert) has been placed next to a spatial tuning profile (Georgopoulos and Stefanis, 2007). A systematic increase in the angle between the preferred direction ***C*** of a *cMCC* and the preferred direction ***C′*** of cMCCs at distances farther and farther away from ***C*** (Georgopoulos et al., 2007). This local shaping of the gMCC arises from the orderly excitatory and inhibitory interactions among neighboring cMCCs within a given gMCC, as follows.

TEMPORAL ASPECTS

The driving force for the local shaping of the gMCC (Georgopoulos and Stefanis, 2007) comes from the recurrent collaterals of pyramidal cell axons and their spatially orderly excitatory and inhibitory effects mediated through MCC interneurons (Stefanis and Jasper 1964a, 1964b; Eccles 1966; Stefanis, 1969). Figure 5.2A illustrates these recurrent effects in a diagrammatic form (Eccles, 1966). Figure 5.2B illustrates antidromically elicited postsynaptic potentials recorded intracellularly from pyramidal tract cells in the motor cortex (*a*, excitatory postsynaptic potential; *b* and *c*, inhibitory postsynaptic potentials, IPSP). The key player here is the *recurrent inhibition* (Stefanis and Jasper 1964a, 1964b; see Eccles, 1966 for a review). Recurrent inhibition is most likely polysynaptic and can last for up to 200 ms (Eccles, 1966), as evidenced by (*1*) the duration of antidromically elicited IPSPs and (*2*) the duration of depression of cell response following conditioning antidromic stimuli (Stefanis and Jasper, 1964a, 1964b).

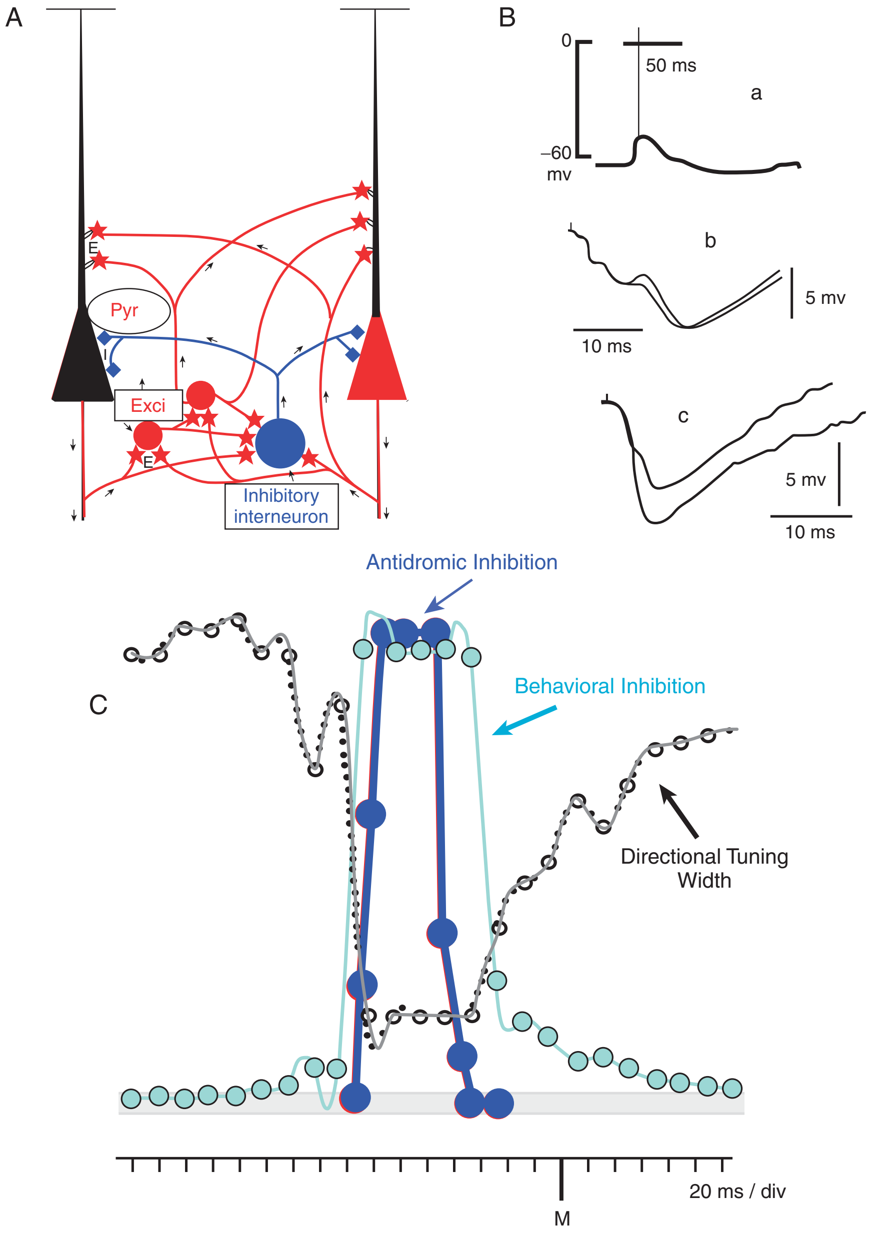

FIGURE 5–2. Recurrent and behavioral inhibition. (*A*) Schematic diagram of local motor cortical circuitry (adapted from Eccles, 1964). Synaptic actions are color coded; all pyramidal cell actions (in blue) are excitatory. (*B*) Examples of postsynaptic potentials recorded intracellularly from pyramidal tract neurons in cat motor cortex in response to antidromic stimulation (see Stefanis and Jasper, 1964a; Stefanis and Jasper, 1964b for experimental details). (*a*) Excitatory PSP followed by a shallow IPSP (adapted from Fig. 3 of Stefanis and Jasper, 1964a); (*b*) Graded, summed IPSPs (adapted from Fig. 5 of Stefanis and Jasper, 1964a); (*c*) Graded IPSPs in response to graded stimulus intensity (adapted from Fig. 5 of Stefanis and Jasper, 1964a). (*C*) Time course of recurrent and behavioral inhibition. Gray and turqoise lines denote time-varying change in tuning width and in behavioral inhibitory drive, respectively (adapted from Fig. 8 of Merchant et al., 2008, where experimental details can be found). Thick blue denotes the time course of an instance of recurrent inhibition (adapted from Fig. 3 of Stefanis and Jasper, 1964b; the solid line in that figure was inverted and rescaled in time to the behavioral inhibition curve). IPSP, inhibitory postsynaptic potential; M, movement onset.

BEHAVIORAL ASPECTS

Motor cortical cells in the arm area are directionally tuned (Georgopoulos et al., 1982), such that a cell discharges the highest for a movement of the arm in a particular direction, the cell's *preferred direction*, whereas the discharge rate decreases progressively with movements farther and farther away from this preferred direction. A recent study (Merchant et al., 2008) examined in detail the role of putative inhibitory mechanisms underlying the directional tuning, as follows. Cells were recorded during free, reaching movements of the arm toward eight targets in 3-D space, and their directional tuning calculated. Next, a combination of measurements was used to classify recorded cells into three categories: putative pyramidal cell 1 (PP1), putative pyramidal cell 2 (PP2), and putative interneurons (PI). Then, a detailed analysis was carried out, for every cell, on two concurrently estimated parameters, namely (*1*) the time-varying tuning width (i.e., sharpness of tuning), and (*2*) the time-varying putative inhibitory drive ("behavioral inhibition"). It was found that the two were significantly and positively correlated, such that the tuning width decreased as the inhibitory drive increased (see Fig. 7 in Merchant et al., 2008). An example is illustrated in Fig. 5.2C (gray and turqoise lines). Interestingly, this association was observed only for the PP1 cell. It was concluded that a timely inhibitory drive plays a major role in "sculpting" pyramidal cell discharge during the preparation and execution of movement. It was further hypothesized that this inhibitory drive may arise from recurrent pyramidal cell collaterals.

Indeed, a close examination of the time courses of the recurrent and behavioral inhibition supports this hypothesis. An example is shown in Figure 5.2C, where the time course of an instance of recurrent inhibition (Stefanis and Jasper, 1964b) is superimposed on an instance of behavioral inhibition (Merchant et al., 2008). Of course, more important than a single illustration is the quantitative picture. First, we deal with the duration of inhibition. With respect to recurrent inhibition, IPSPs typically lasted from 100–150 ms (Stefanis and Jasper, 1964a) and recurrent inhibition typically lasted from 25 to 120 ms (Stefanis and Jasper, 1964b). Behavioral inhibition lasted from 60 to 225 ms (Figs. 8 and 9 in Merchant et al., 2008). These values are very similar, in support of the hypothesis that recurrent inhibition underlies behavioral inhibition. In general, the latter tended to be a little longer than the former, and this can reasonably be accounted for by temporally staggered recurrent inhibitory effects arising from staggered pyramidal cell recruitment (Georgopoulos et al., 1982). The second quantitative aspect refers to the relative frequency of observed occurrence of recurrent and behavioral inhibition. Recurrent inhibitory effects were observed in 48 of 172 tested neurons (27.9%) (Stefanis and Jasper, 1964b). In the behavioral inhibition study (Merchant et al., 2008), 1206 cells were identified as pyramidal cells (928 as PP1 and 278 as PP2, see above). Behavioral inhibition was observed only in directionally tuned PP1 neurons (N = 366). This yields a prevalence of behavioral inhibition of 366/1206 = 30.3%. These two percentages are very close. Thus, both lines of evidence (i.e., duration and frequency of occurrence) speak for a key role of recurrent inhibition in shaping the directional tuning.

Spatial, Temporal, and Behavioral Integration

We reviewed earlier the basic layout of the motor cortical circuit as well as spatial, temporal, and behavioral aspects of it, with an emphasis on recurrent inhibition. The MCC operates as an integrated network at the gMCC level the output of which is an orderly tuning function. This tuning function can refer to the direction of arm movement in space in the arm area (Georgopoulos et al., 1982, 2007; Georgopoulos and Stefanis, 2007) or to a combination of finger movements in the hand area of the motor cortex (Georgopoulos et al., 1999). It is likely that a suitable tuning function pertains in different parts of the motor cortex, depending on the relevant parameters dictated by the somatotopic arrangement; for example, tuning of motor cortical cells with respect to the direction of tongue protrusion has been described in the orofacial area of the motor cortex (Murray and Sessle, 1992).

In real time, external, synchronous, excitatory, converging inputs to the relevant part of the motor cortex would initiate *gMCC* activation and pyramidal cell discharge; within a short time (a few tens of milliseconds), recurrent excitatory and inhibitory actions would ensure shaping the local motor cortical landscape, enhancing activity at its center (by boosting excitation) and gradually reducing activity at its periphery (by recurrent inhibition), that is, enhancing the *motor contrast* (Stefanis and Jasper, 1964b; Georgopoulos and Stefanis, 2007). External inputs might also preshape the field by suitable feedforward activation of inhibitory interneurons (Eccles, 1966). The graded output of the tuning field is then transmitted downstream to spinal and other subcortical areas as well as to other cortical areas. It is remarkable that directional tuning has been observed in practically all motor areas that have been investigated, including the premotor cortex, parietal cortex, and cerebellum. This indicates a formal correspondence in the coding of movement direction in space across motor areas.

Acknowledgments

This work was supported by the United States Department of Veterans Affairs and the American Legion Brain Sciences Chair.

REFERENCES

Eccles JC (1966) Cerebral synaptic mechanisms. In: Eccles JC, ed. *Brain and Conscious Experience*, pp. 24–58. New York: Springer.

Gatter KC, Powell TPS (1978) The intrinsic connections of the cortex of area 4 of the monkey. *Brain* 101:513–541.

Georgopoulos AP, Stefanis CN (2007) Local shaping of function in the motor cortex: Motor contrast, directional tuning. *Brain Res Rev* 55:383–389.

Georgopoulos AP, Kalaska JF, Caminiti R, Massey JT (1982) On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. *J Neurosci* 2:1527–1537.

Georgopoulos AP, Pellizzer G, Poliakov AV, Schieber MH (1999) Neural coding of finger and wrist movements. *J Comput Neurosci* 6:279–288.

Georgopoulos AP, Merchant H, Naselaris N, Amirikian B (2007) Mapping of the preferred direction in the motor cortex. *Proc Natl Acad Sci USA* 104:11068–11072.

Merchant H, Naselaris T, Georgopoulos AP (2008) Dynamic sculpting of directional tuning in the primate motor cortex during three-dimensional reaching. *J Neurosci* 28:9164–9172.

Murray GM, Sessle BJ (1992) Functional properties of single neurons in the face primary motor cortex of the primate. III. Relations with different directions of trained tongue protrusion. *J Neurophysiol* 67:775–785.

Sloper JJ, Hiorns RW, Powell TPS (1979) A qualitative and quantitative electron microscopic study of the neurons in primate motor and somatic sensory cortices. *Phil Trans Royal Soc London B* 285:141–171.

Stefanis C (1969) Interneuronal mechanisms in the cortex. In: Brazier MAB, ed. *The Interneuron*, pp. 497–526. Berkeley: University of California Press.

Stefanis C, Jasper H (1964a) Intracellular microelectrode studies of antidromic responses in cortical pyramidal tract neurons. *J Neurophysiol* 27:828–854.

Stefanis C, Jasper H (1964b) Recurrent collateral inhibition in pyramidal tract neurons. *J Neurophysiol* 27:855–877.