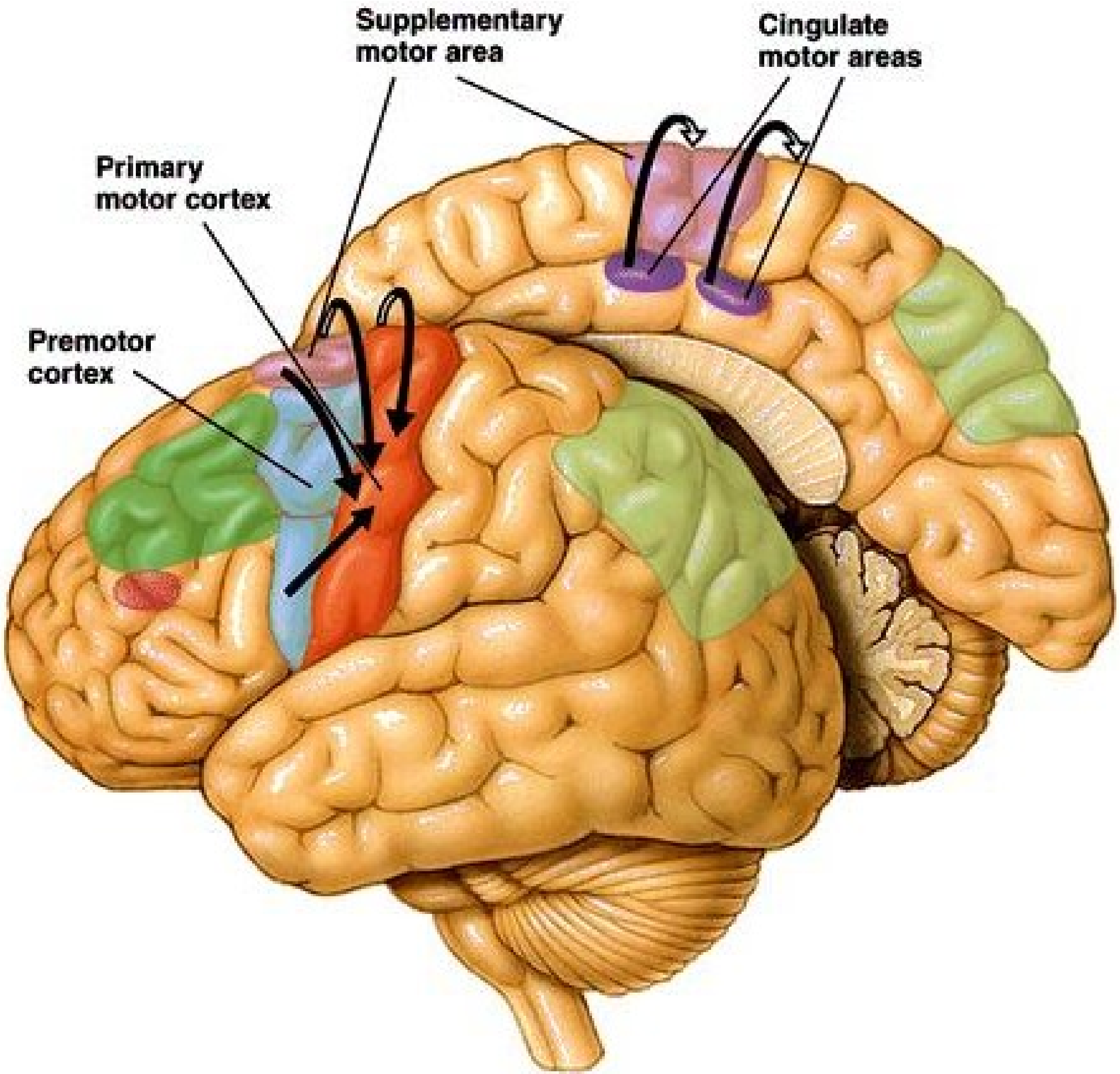
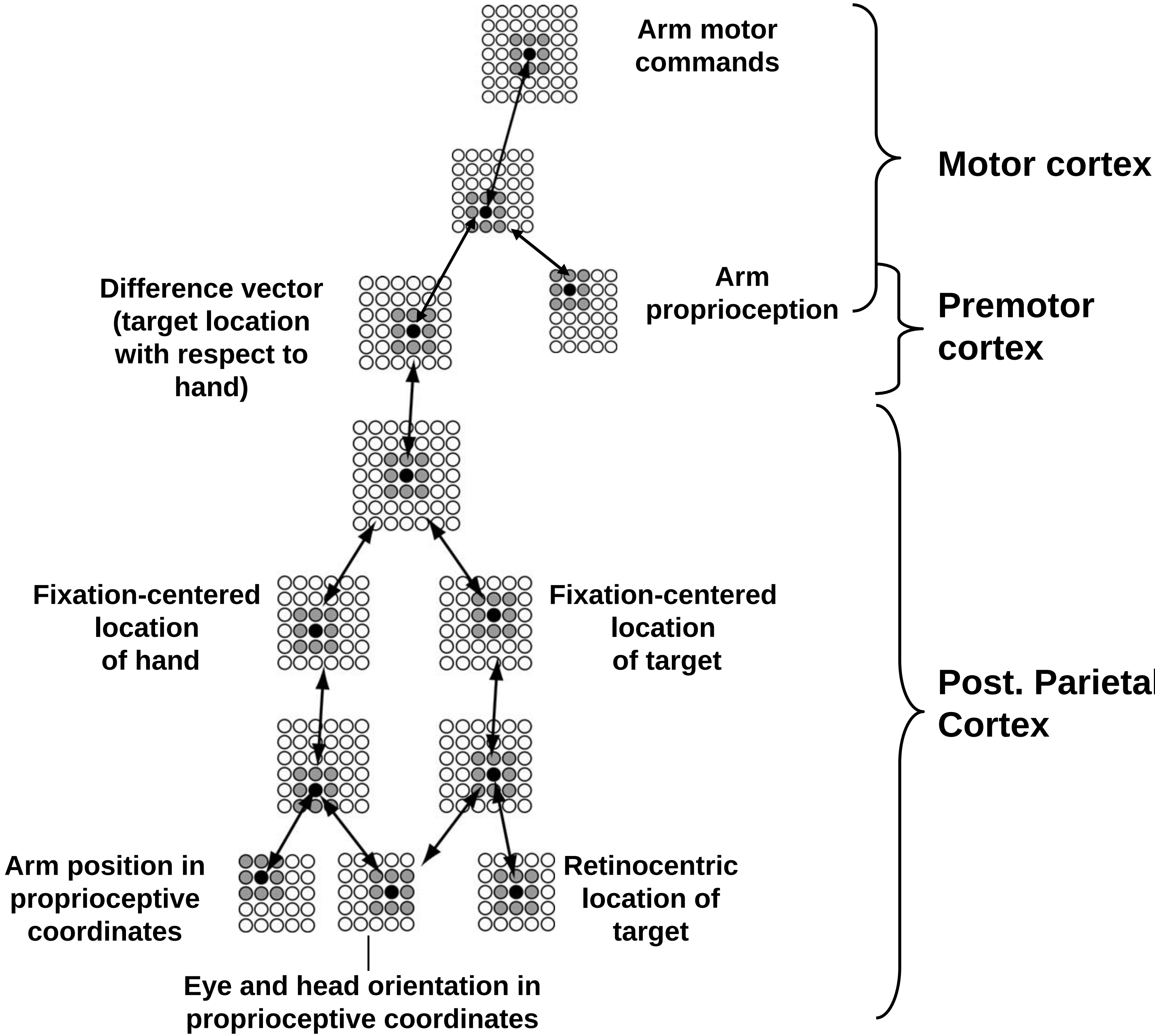
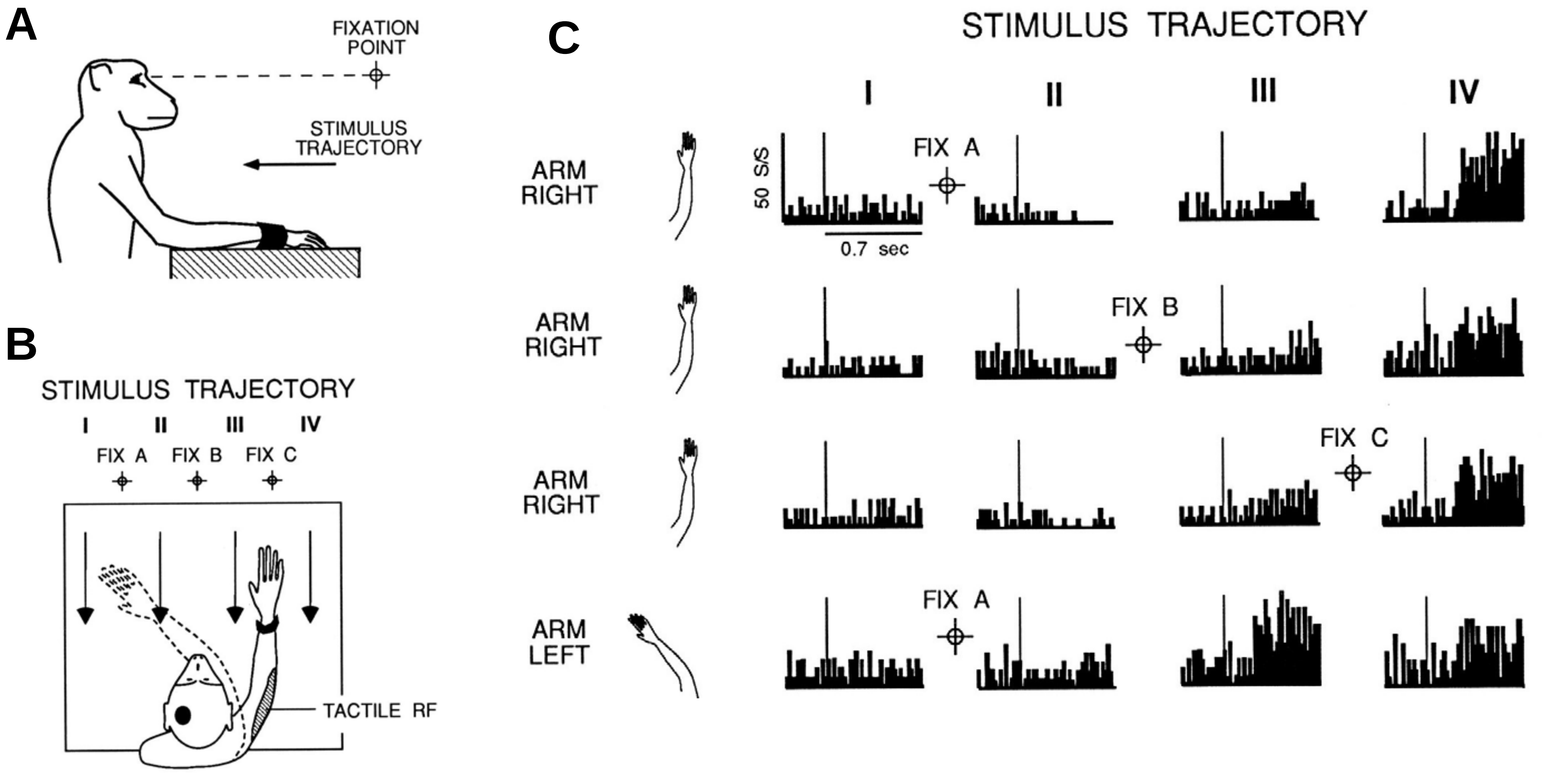
"Neuroscientists are like cryptographers trying to crack an alien code, in this case the code used by the nervous system to represent the external world."

V.S. Ramachandran, A brief tour of human consciousness, p. 25



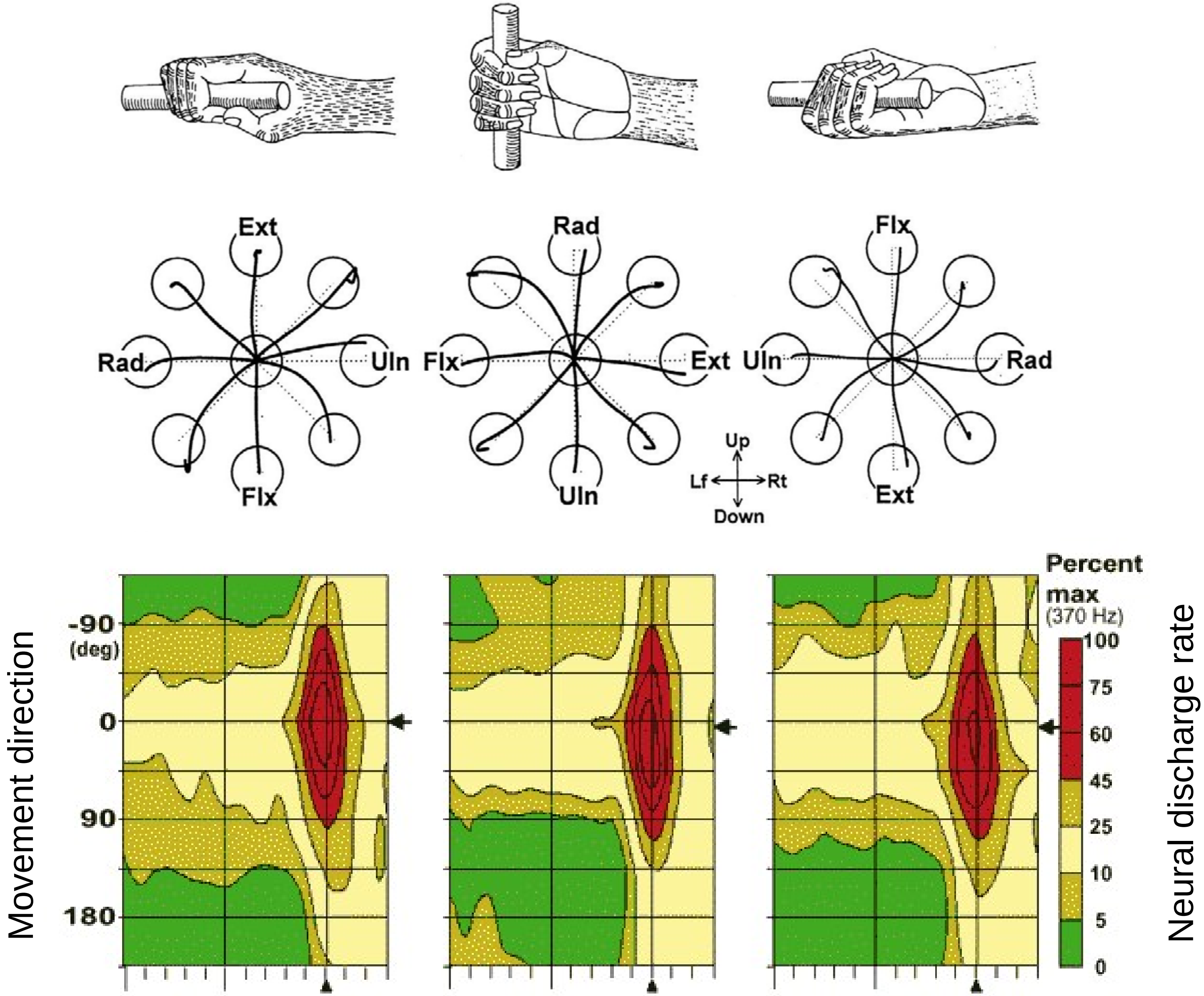

Arm motor commands
Motor cortex
Arm proprioception
Premotor cortex
Difference vector (target location with respect to hand)
Fixation-centered location of hand
Fixation-centered location of target
Post. Parietal Cortex
Arm position in proprioceptive coordinates
Retinocentric location of target
Eye and head orientation in proprioceptive coordinates

Coding object position with respect to the arm takes place in the premotor cortex



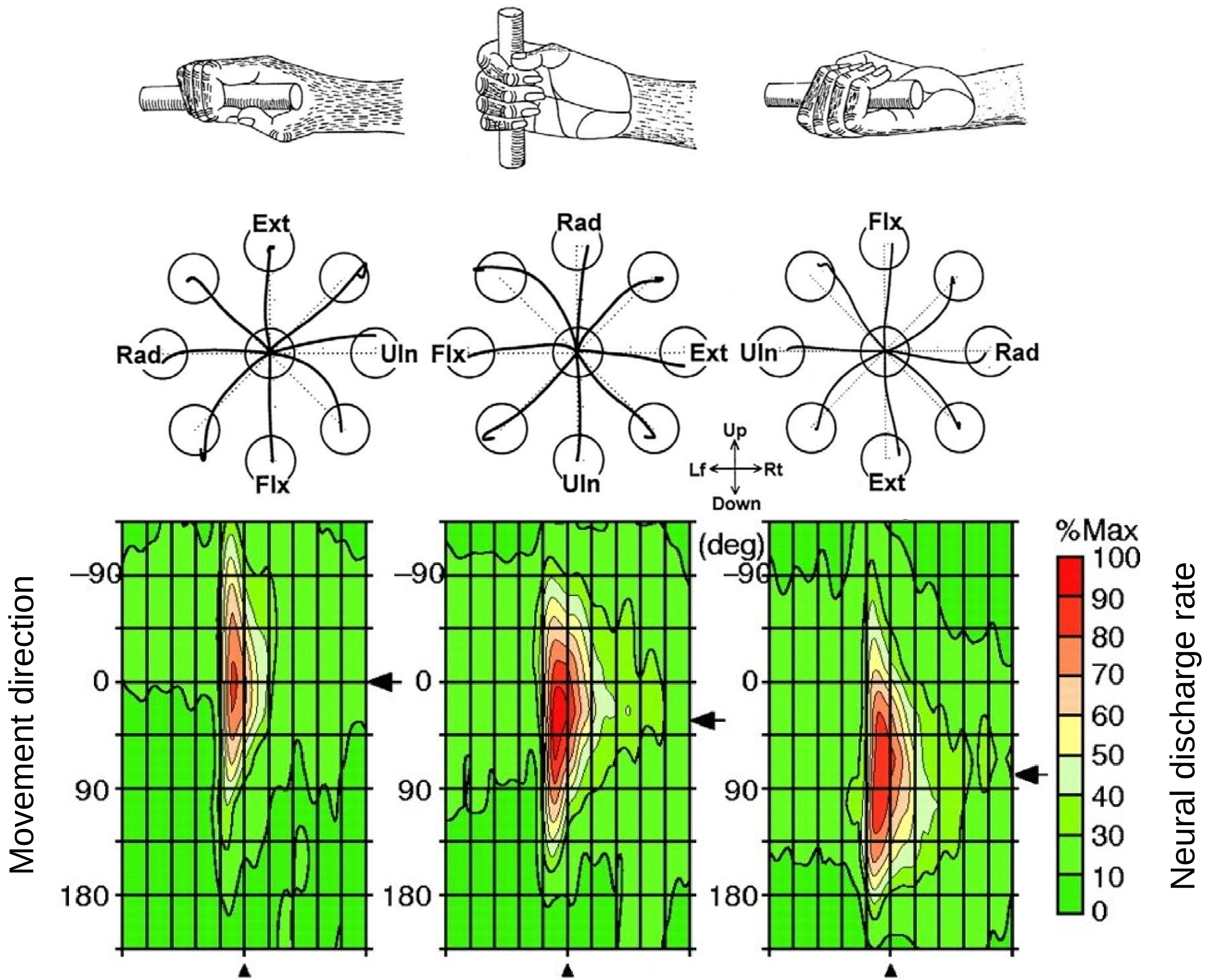
Graziano MSA et al. (1997) J Neurophysiol

Target of a reaching movement is coded with respect to the hand in the premotor cortex



Kakei, Hoffman & Strick Science 1999 and Nature Neurosci 2001

Neurons in the primary motor cortex are sensitive to forces that are necessary to perform a reaching movement



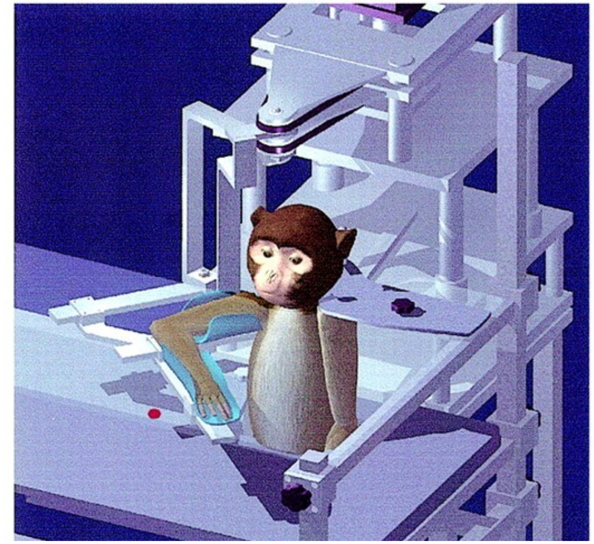
Kakei, Hoffman & Strick Science 1999 and Nature Neurosci 2001

Neuronal activity among some cells in the primary motor cortex relates to muscle forces

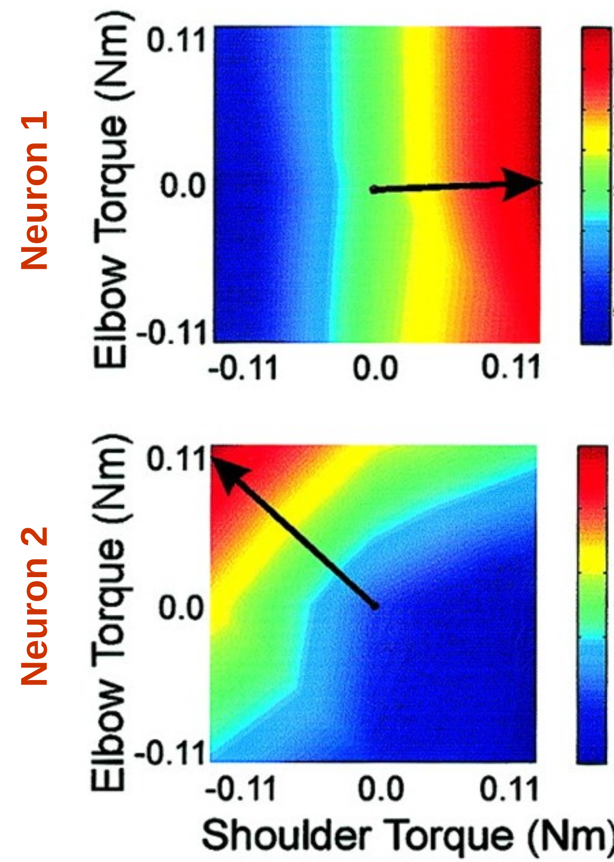
Experiment: A constant torque was applied to elbow and shoulder joints of the monkey's arm. The animal is trained to maintain constant arm position. Therefore, muscles produce activity to counter the imposed torque.

Neural activity is averaged over 2 seconds.

Neural activity for many cells varies with direction of torque. Different cells have different preferred directions of torque.



Cabel, Cisek & Scott J Neurophysiol 2001



Summary of functions

Posterior parietal cortex:

- aligns proprioception of arm with vision of hand and compute hand position in fixation-centered coordinates.
- computes target position in fixation-centered coordinates.

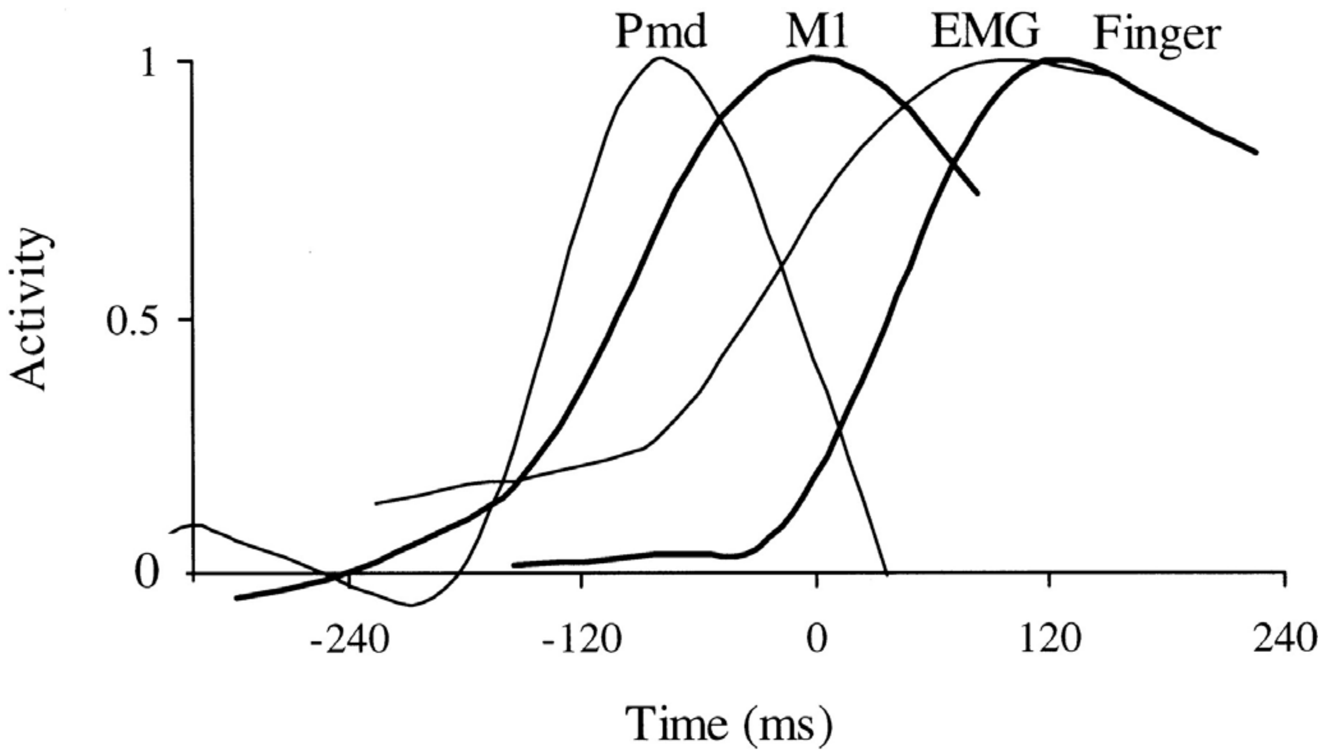
Premotor cortex:

- Subtracts target position with respect to hand position and codes the desired movement in terms of displacement of the hand.

Primary motor cortex:

- Transforms the desired movement to muscle activity patterns and sends this command to the spinal cord.

During a reaching movement, activity in premotor cortex cells precedes the activity in M1



Moran & Schwartz, J Neurophys 1999

Differing roles for the SMA, premotor cortex, and the primary motor cortex

Task: push lighted keys.

Visually guided and not a memorized sequence:

- A low tone comes on, then first key lights up, instructing animal to touch it.
- Second key lights up and after touching it, third key lights up.
- A random sequence of keys appears in each trial.

Memory guided sequence:

- A high tone comes on, then first key lights up and animal touches it, followed by 2nd and then 3rd key.
- The same sequence of keys (and lights) repeats for 6 trials.
- On the 7th trial and beyond, no lights appear, and the animal performs the key presses from memory.

Typical neuronal activity in M1, PM, and SMA during button press task

Visually guided

Memory guided

Primary motor cortex

Visually guided

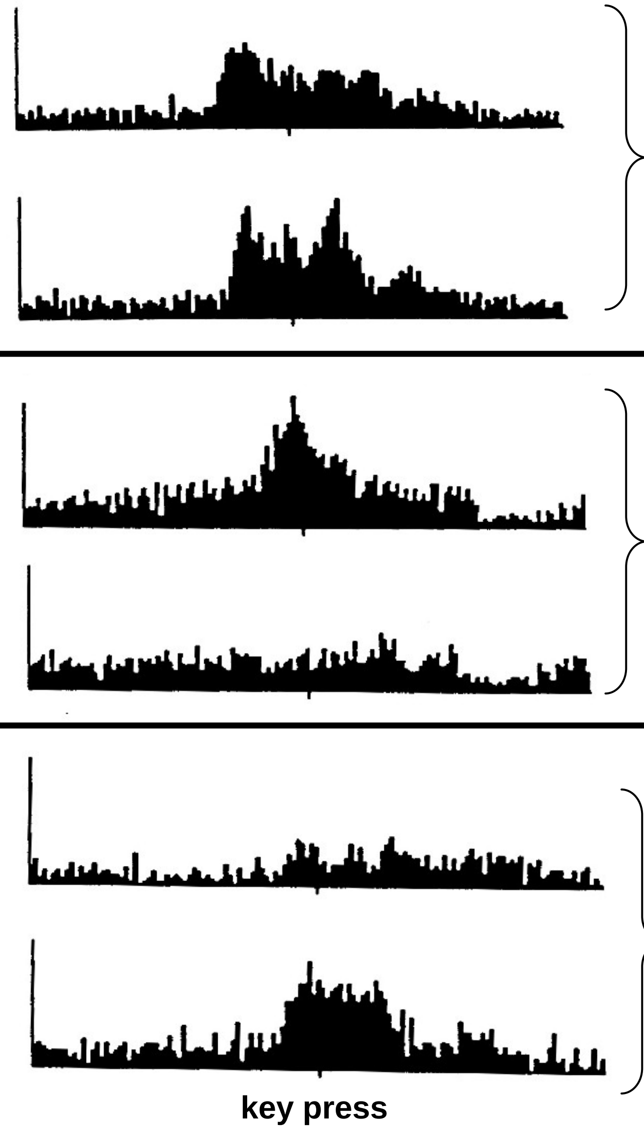
Memory guided

Premotor cortex

Visually guided

Memory guided

Supplementary motor area



Mushiake et al. (1991) J Neurophysiol

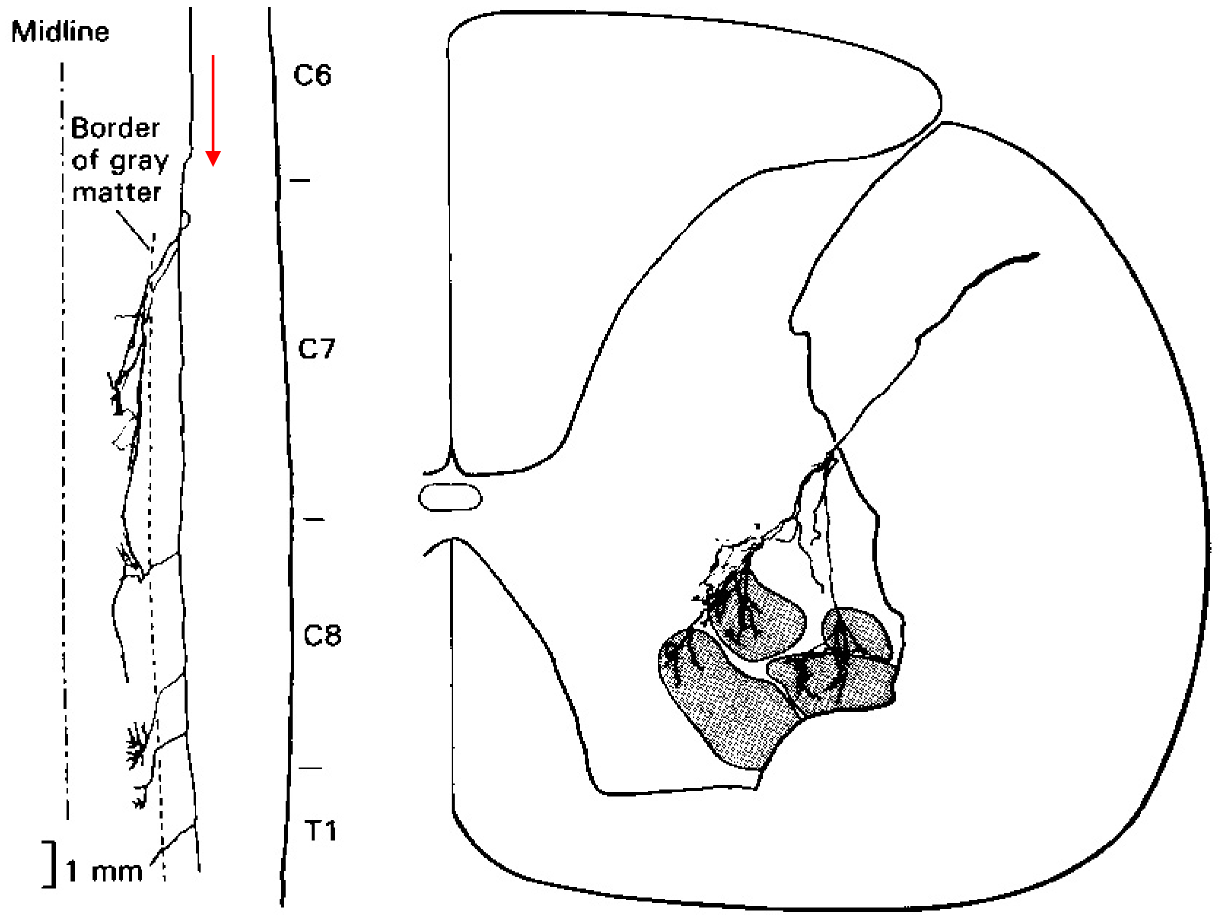
Summary of SMA and Premotor Cortex function

1. In premotor cortex, cell discharge encodes a movement plan in terms of the location of the stimulus with respect to the hand.
2. In M1, cell discharge encodes the forces that are necessary to perform that movement.
3. SMA cells are more active when the task requires the arrangement of multiple movements in the correct sequence and temporal order.
4. In contrast, premotor cortex cells are more active when the task is visually guided.

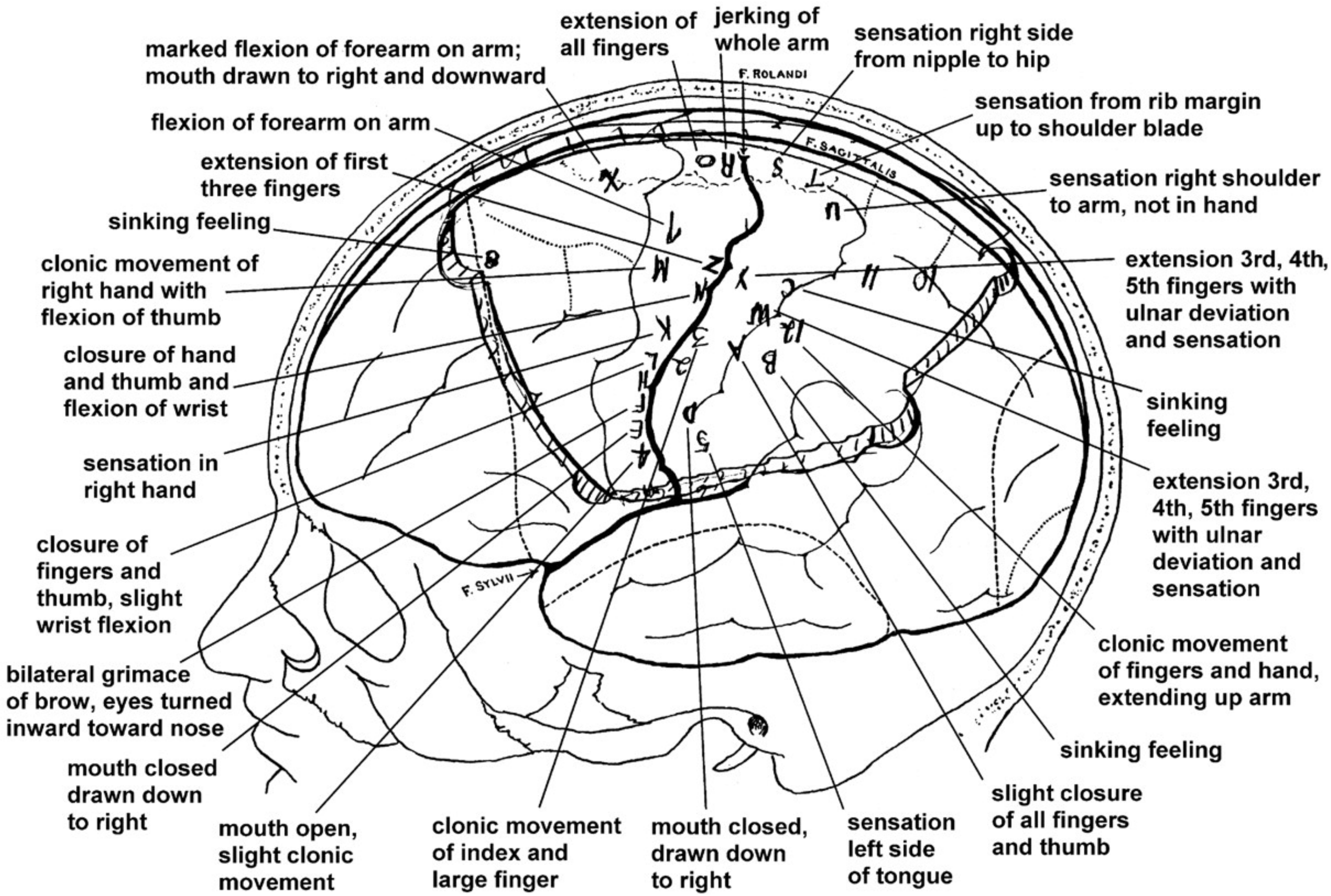
Corticospinal neurons project to multiple levels of the spinal cord, and contact multiple motor pools

A single motor cortical cell is likely to project to about 3 muscles on the arm/hand, but the projections are likely to be concentrated on the finger muscles.

Projection of a corticospinal axon to C7: hand motorneurons.



Stimulation of cortical surface in an individual



Penfield & Rasmussen *The Cerebral Cortex of Man* (1950), Redrawn by M.H. Schieber *J Neurophysiol* 2001

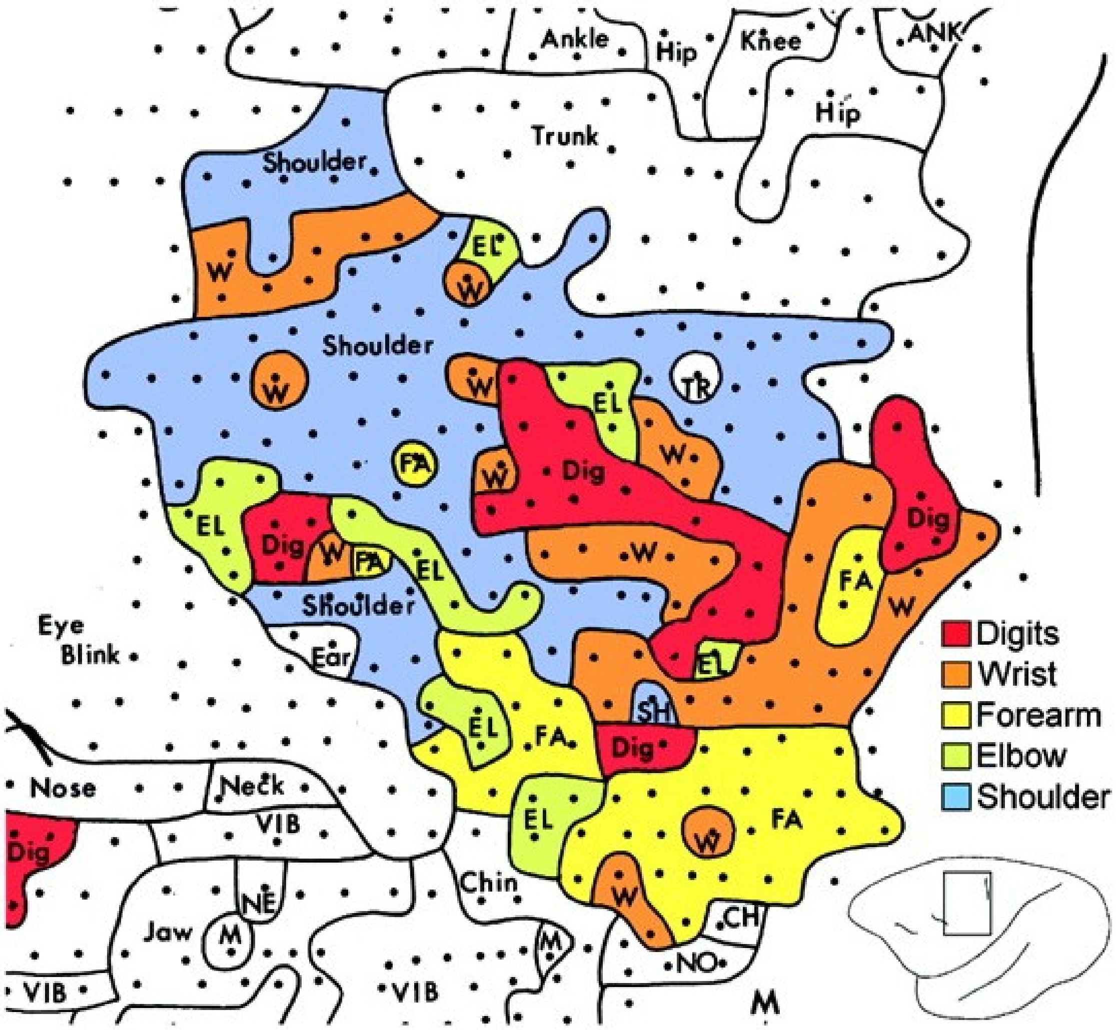
Intracortical microstimulation maps of monkey motor cortex

In anesthetized monkey, a microelectrode is positioned closed to layer V. Low current stimulation is delivered to excite ~30 pyramidal neurons.

Flick-like twitches of discrete parts of the contralateral side of the body are observed.

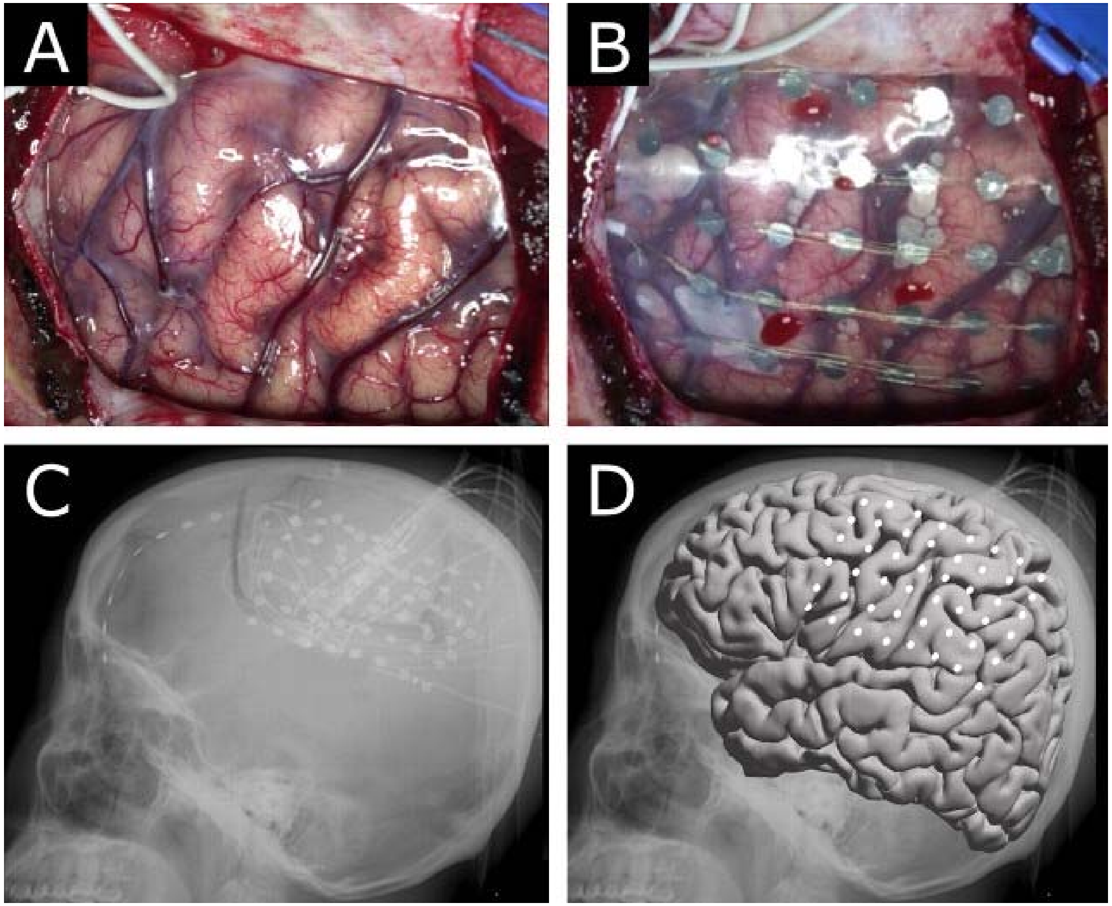
There is a general trend for somatotopy: trunk more medial, jaw more lateral.

However, movement of a given body part (e.g., digits) is evoked from multiple foci.

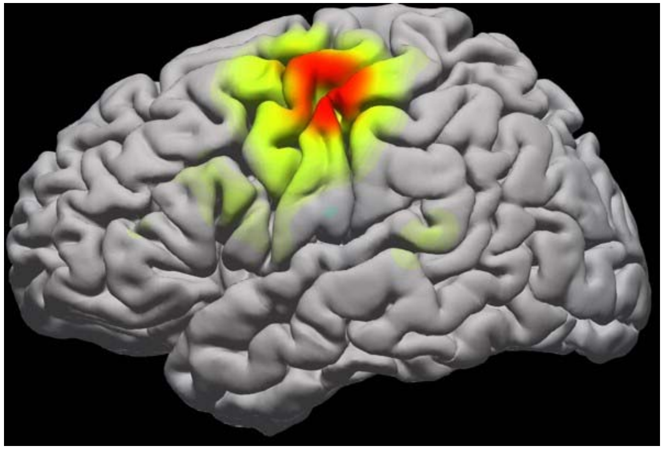


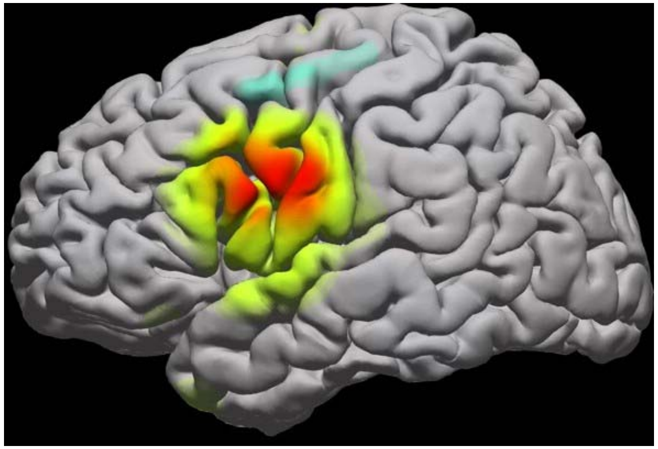
HC Kwan et al. *J Neurophysiol* 41:1120 1978, redrawn by Shieber *J Neurophysiol* 2001.

The motor map in the human brain as measured via grid electrodes



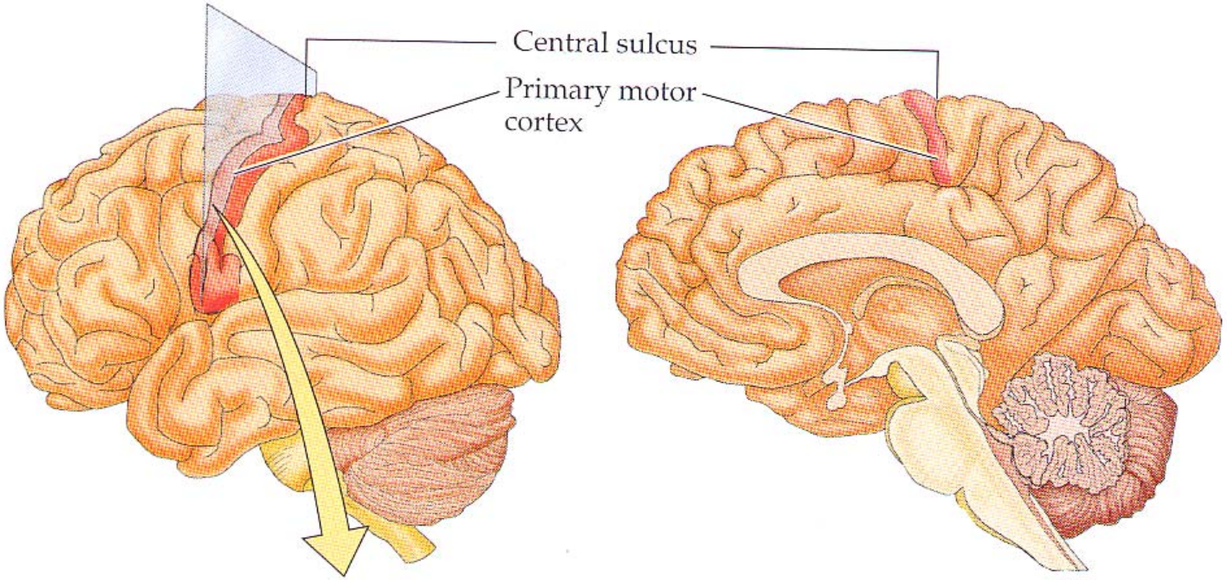
Hand movements



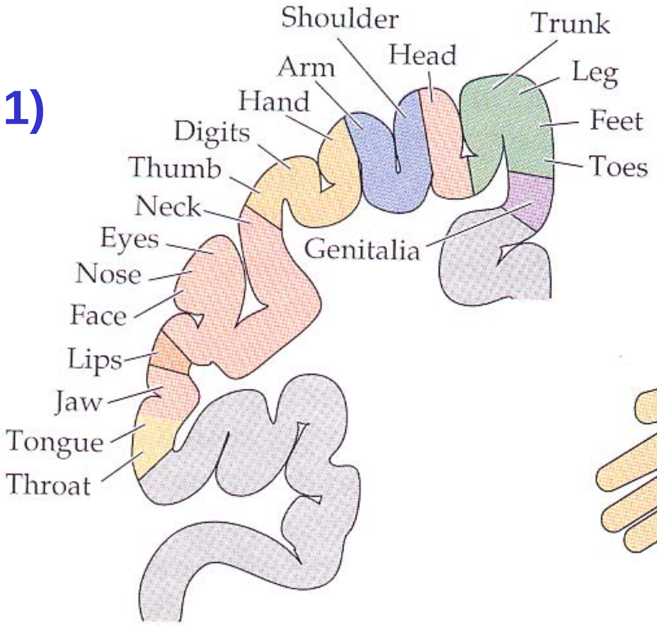


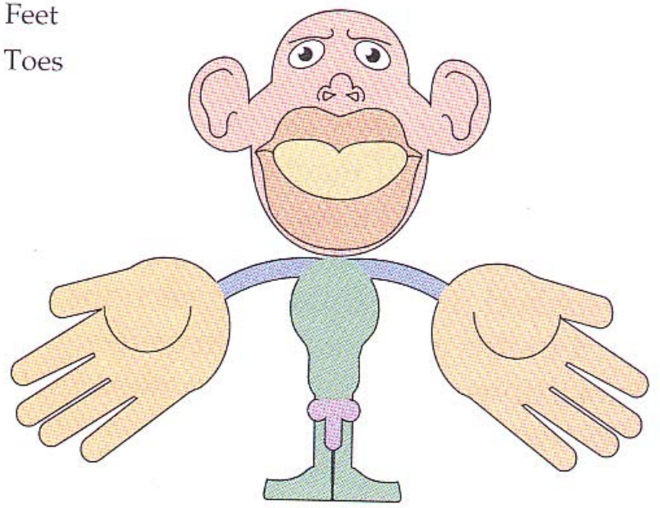
Tongue movements

Miller et al., Journal of Neuroscience, 27:2424, 2007.



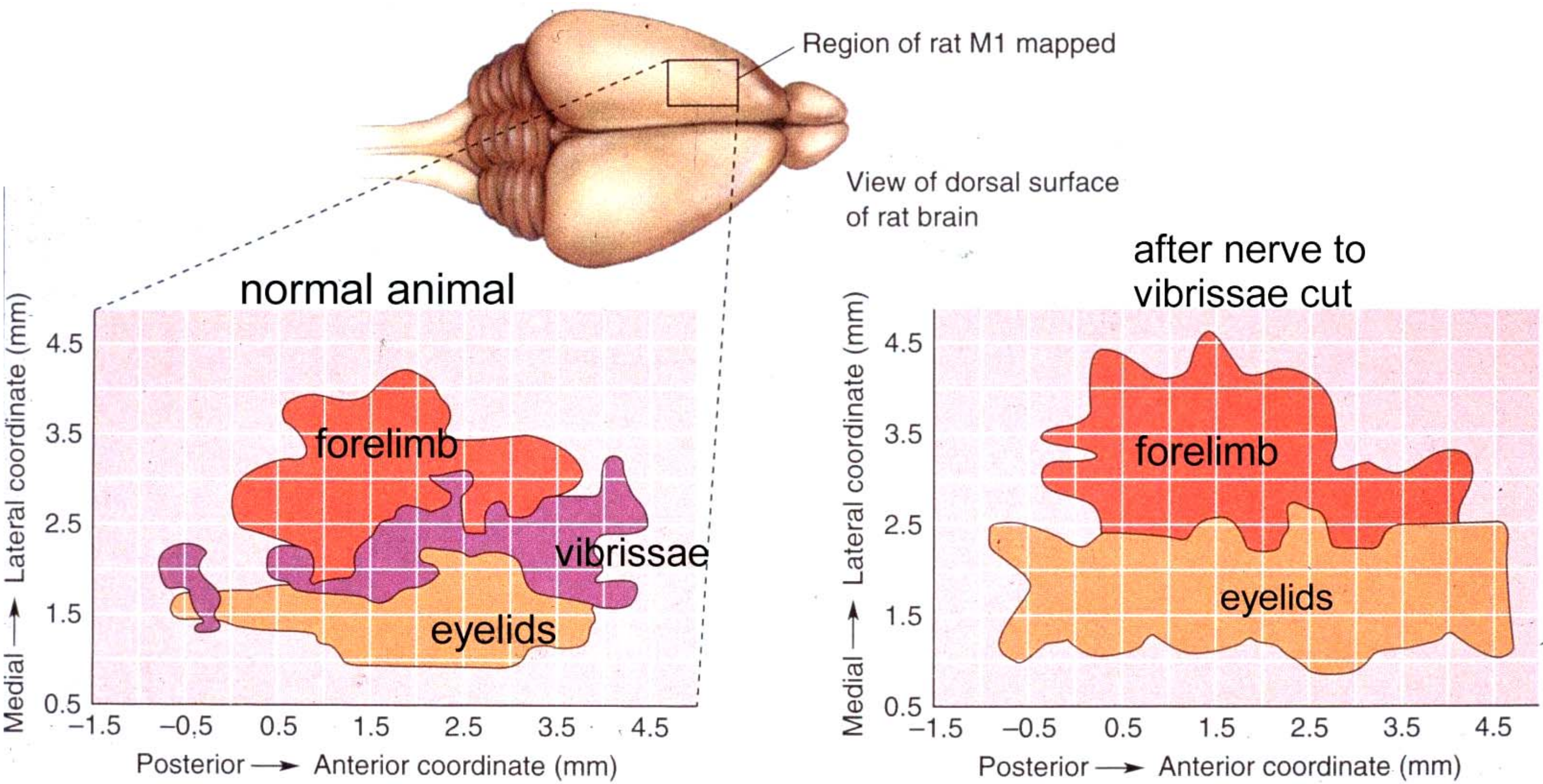
Primary motor cortex (M1)





Damage to peripheral nerves causes change in the motor map

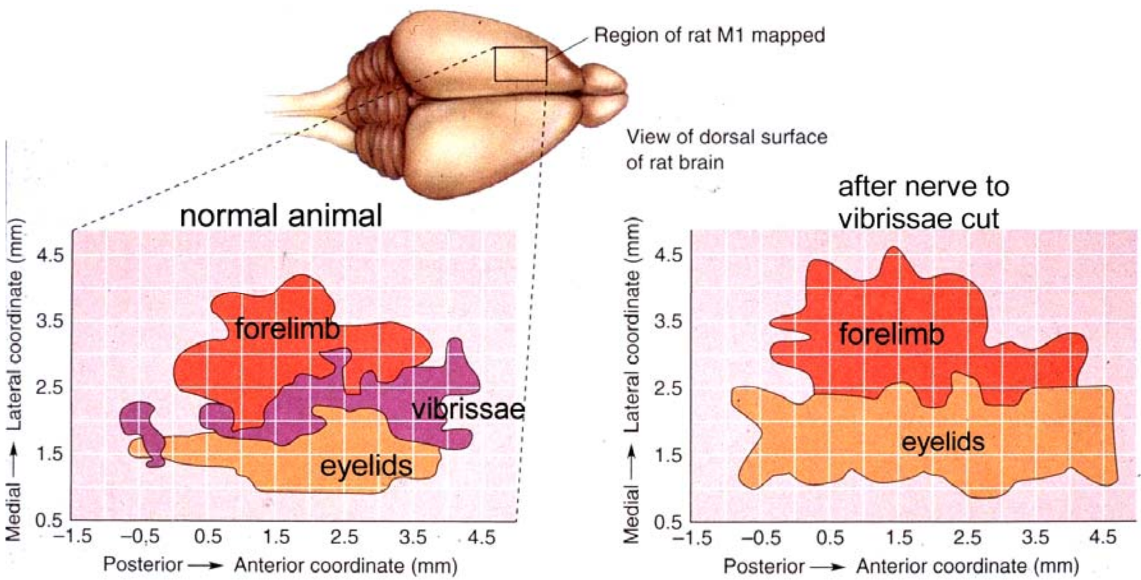
In adult rat, motor map can change a few hours after a branch of the nerve supplying motor axons to the muscle attached to whiskers (vibrissae) is cut. No sensory fibers are damaged.

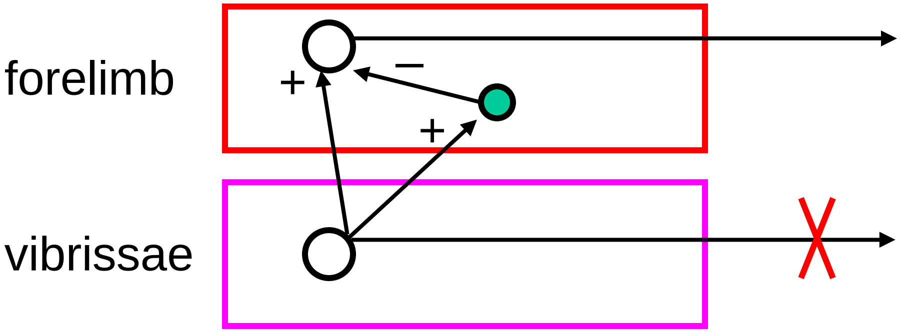


Neighboring regions of the motor cortex are connected via inhibitory interneurons.

Damage to the peripheral nerve, reduces the synaptic efficacy of the inhibitory pathway from vibrissae to the forelimb.

Stimulation in vibrissae area now causes motion of the forelimb.





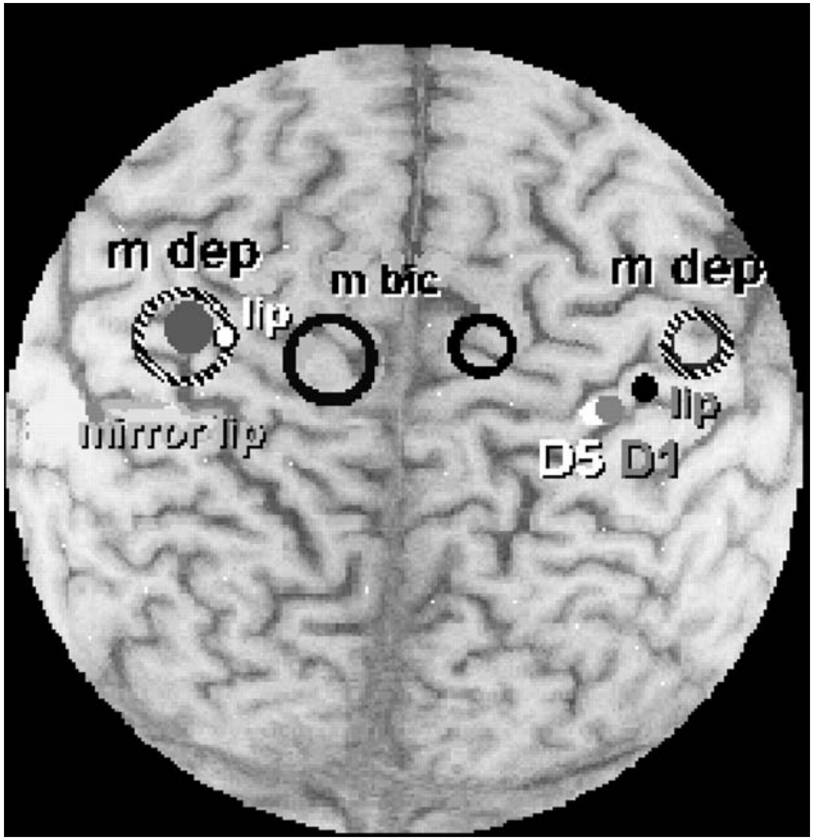
Amputation changes the motor map

This individual's **right arm** above the wrist has been amputated. The motor cortex is stimulated (via TMS) and muscle activity is recorded in biceps and depressor labii inferioris. The lip, and first and fifth digits are touched and evoked potentials are recorded from the brain.

Motor representation of biceps contralateral to the stump is larger than on the side of the intact arm.

Contralateral to the stump

Contralateral to the intact arm



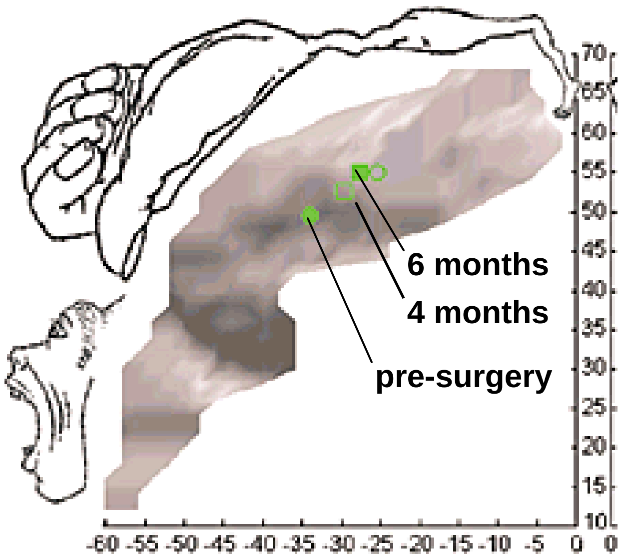
Karl A. et al. (2001) J Neurosci 21:3609

Motor cortex reorganizes after graft of hand

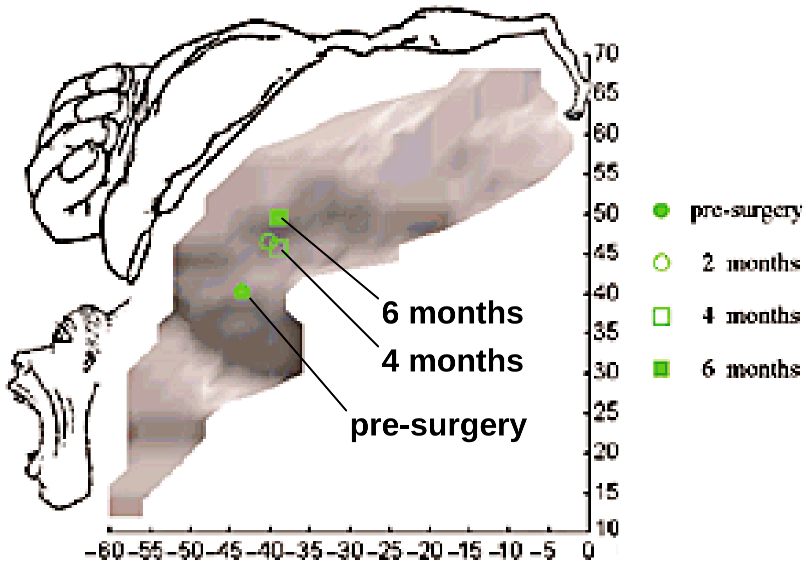
The patient CD suffered amputation of both hands during an accident. Four years later, CD underwent bilateral hand transplantation (from a brain-dead individual). Transplantation involved bone fixation, arterial and venous re-connection, nerve sutures, and joining of muscles and tendons. FMRI was used to describe regions of motor cortex that were active during flexion of fingers and elbow of right hand. Before the graft, the flexion of the missing fingers was monitored by the palpating the corresponding extrinsic muscle contractions at the forearm.

Before the graft, the elbow area had enlarged to take over the hand area. After the graft, both the elbow and hand areas move toward their normal locations.

Right elbow center of activation



Right hand center of activation



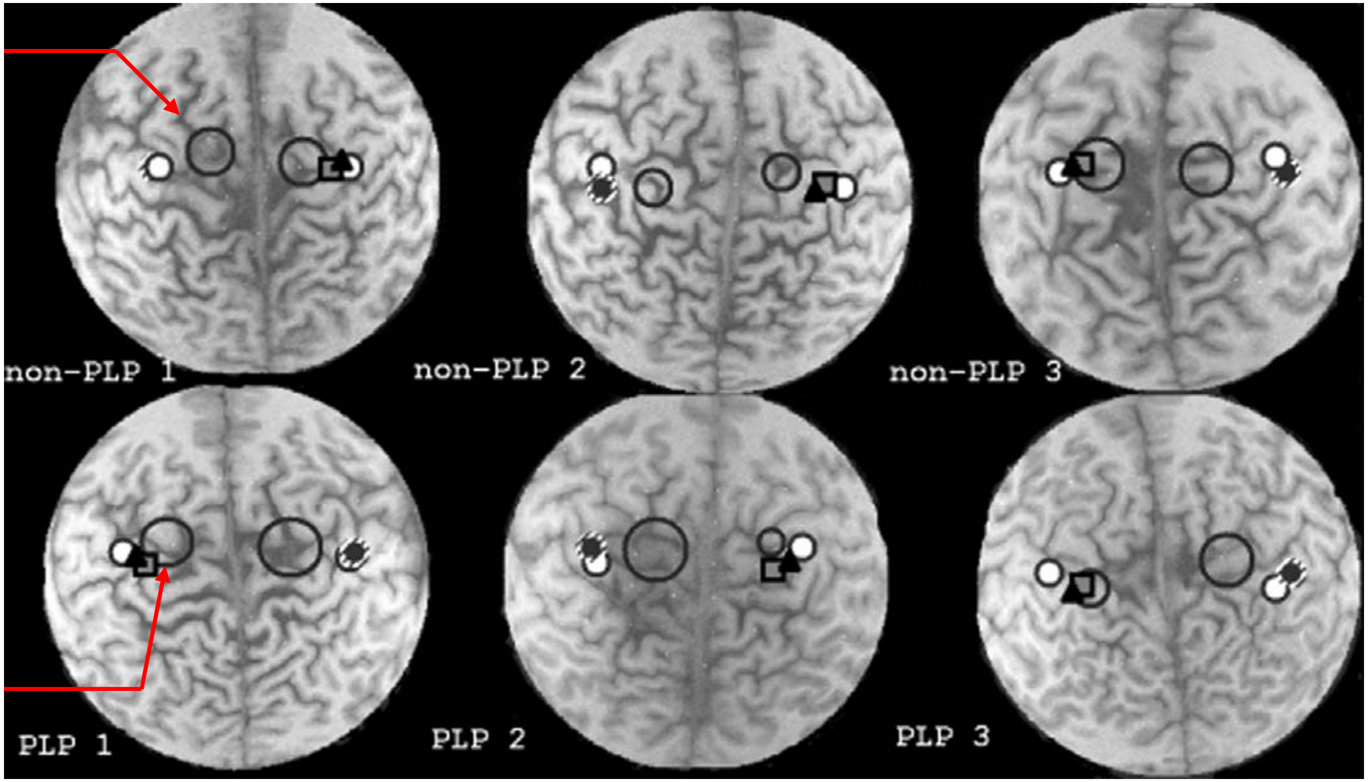
Giraux et al. (2001) Nature Neuroscience 4:691-692

Phantom Limb Pain (PLP)

After amputation, the individual is likely to experience chronic pain in the missing limb. The pain is more common in the initial years after amputation, but may remain for many years. The patient feels the amputated arm is in a clinched fist, unable to move. Patients with PLP tend to have an imbalance in the size of the motor map between the hemispheres.

Amputated hand **Right** **Right** **Left**

Biceps region



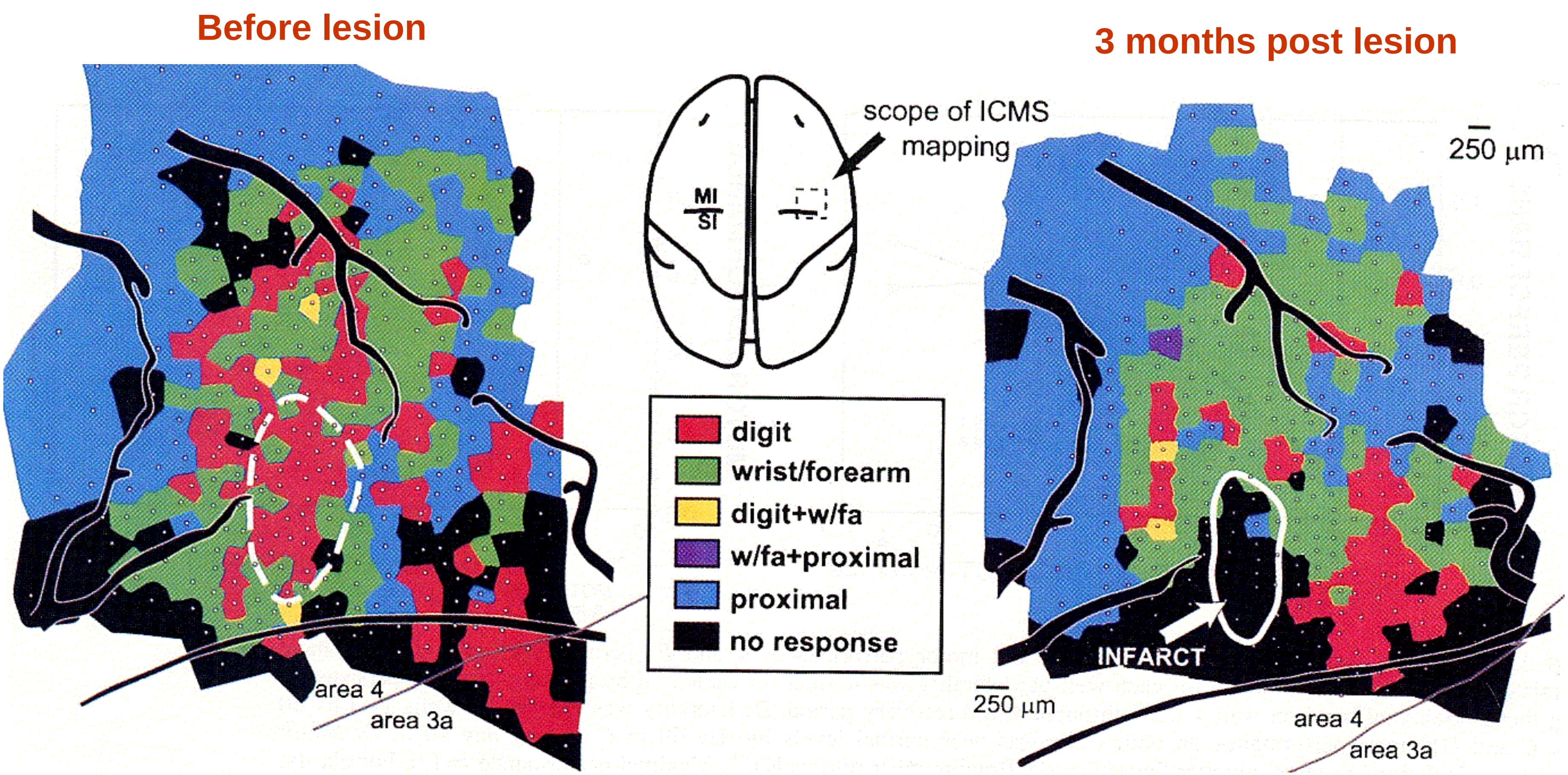
Biceps region

Amputated hand **Left** **Right** **Left**

Karl A. et al. (2001) J Neurosci 21:3609

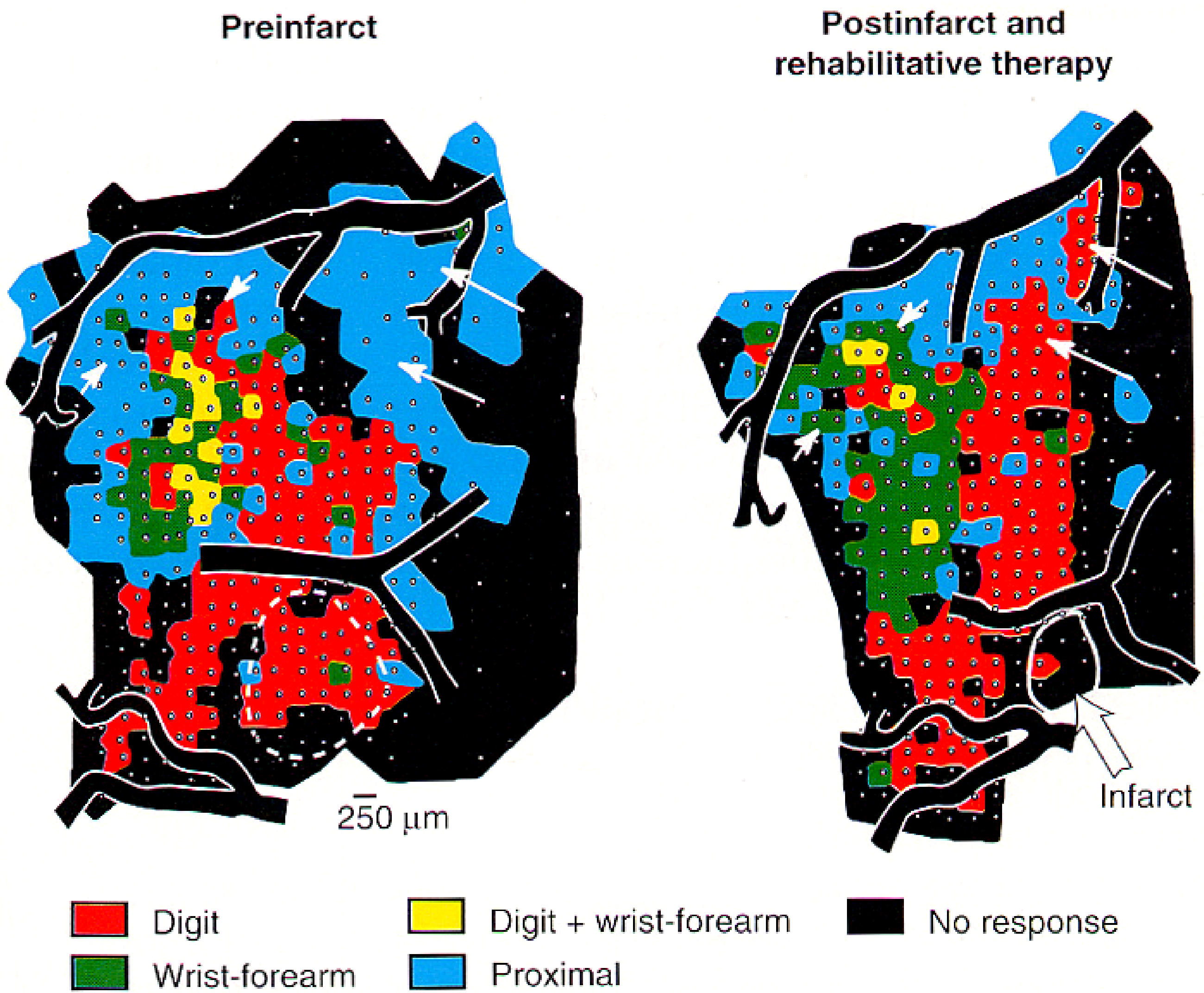
Effect of an infarct

A lesion in the monkey motor cortex destroys 21% of digit and 7% of wrist. After 3 months, the area for digits has been reduced in neighboring regions as well.



Nudo & Milliken, J Neurophys 1996

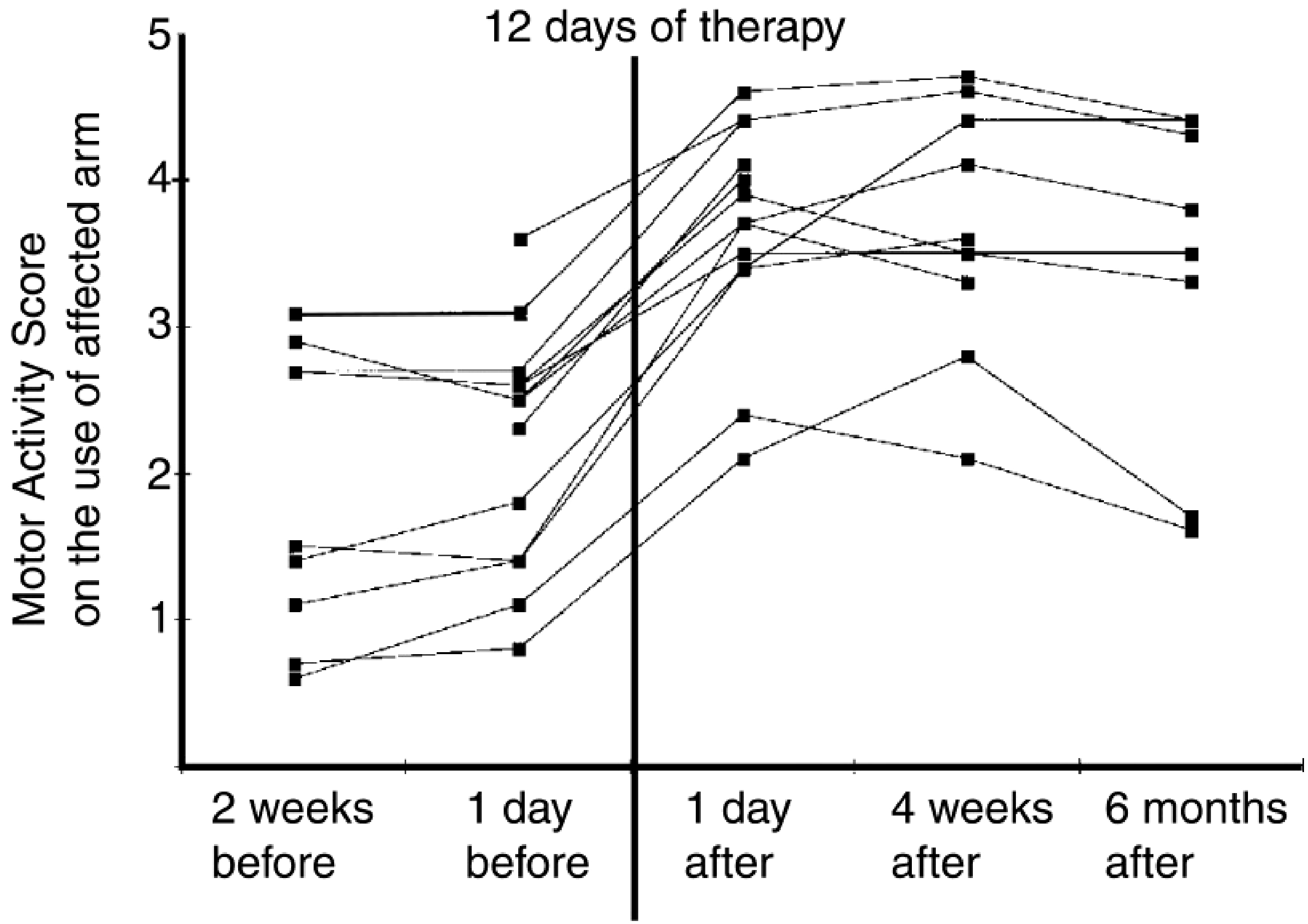
Lesion destroyed 22% of digit region. After rehabilitation, the spared digit area increased by 15%.



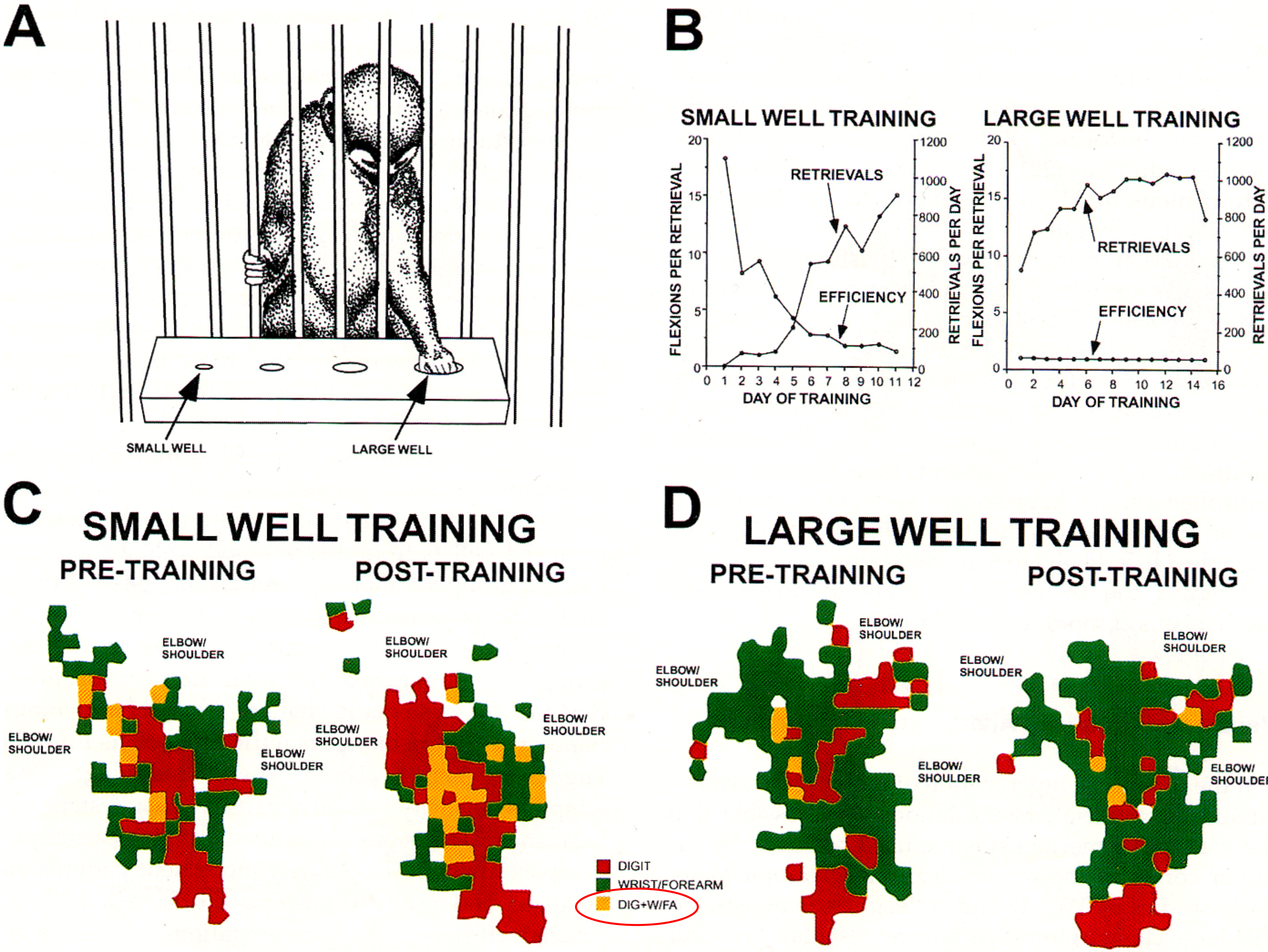
Nudo et al. *Science* 1996

Constrained motion rehabilitation

The unaffected arm is restrained for 8 hours a day, 12 days. During this period, the affected arm is trained.



Liepert, J. et al. *Stroke* 2000



Digit,wrist, and forearm

Nudo et al. *Sem Neurosci* 1997