Review of Krieg and Mogul's TMS Chapter in "Neural Engineering" (ed. Ben He)

Connection Between E Field and Neuronal Excitation

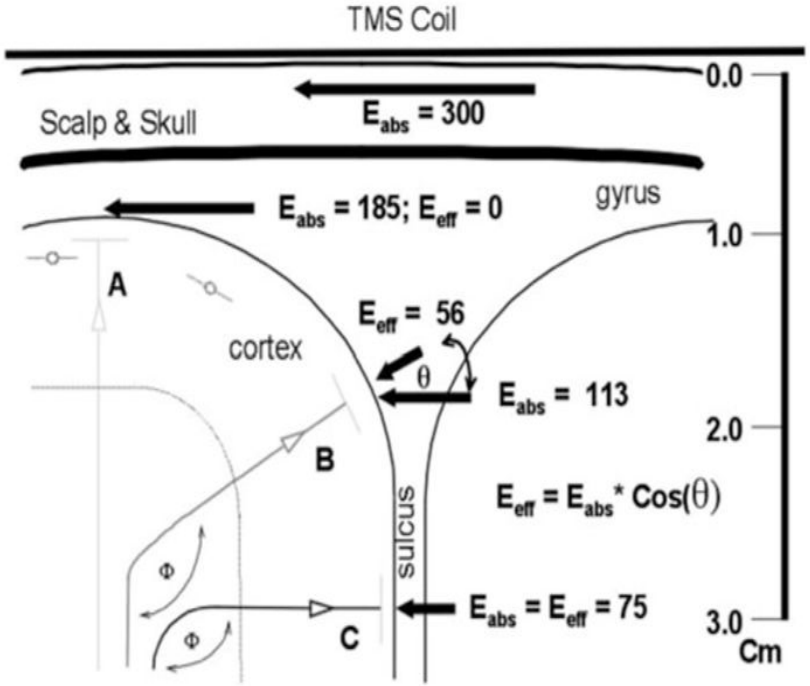
- Using PET Fox [1] imaged the brain during voluntary finger-tap exercise and again using TMS to elicit involuntary finger-tap.

- PET images of voluntary and involuntary cases were closely correlated. Activation in the sulcal bank of the motor region. Despite the greater induced E-field at the gyral crowns the region of activation was located farther away from the coil in the sulcal bank.

- Proposed C3 model: The activation of a pyramidal neuron is related to its major fiber direction by the cosine of the angle between it and the direction of induced current.

Connection Between E Field and Neuronal Excitation

- The C3 model provides an explanation of coil orientation studies [5–7] that found optimal stimulus with induced current perpendicular to the central sulcus.



Electric and Magnetic Stimulation of Corticospinal Neurons

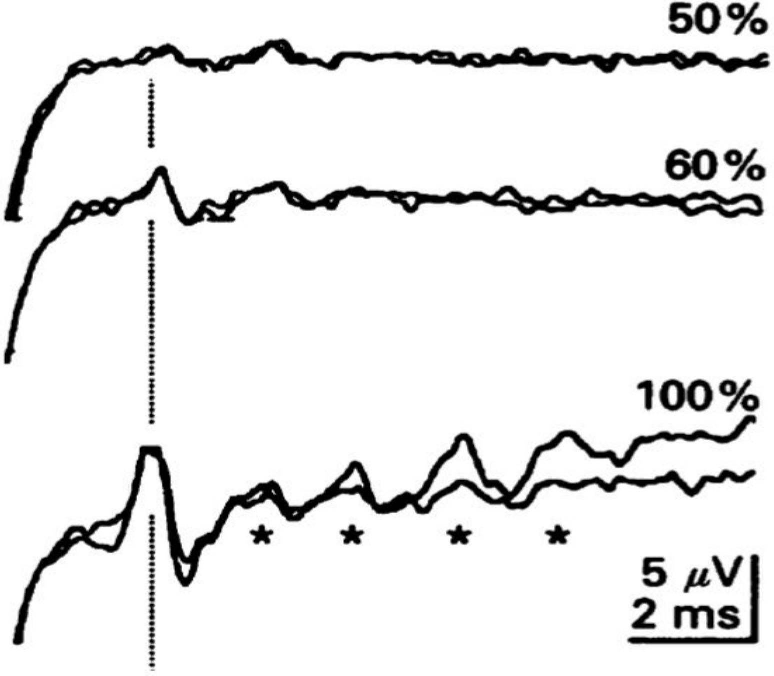
- Epidural recordings of CSNs during electrical stimulation of the motor cortex have shown that there are two distinct wavetypes generated [2].

- D-wave: Initial, high-amplitude wave that is thought to occur from direct activation of the CSN in the cortex because of its fast appearance and large amplitude.

- I-wave: Train of smaller amplitude waves following D-wave. Because of the longer latency and smaller amplitude, these action potentials are thought to come from other cortical circuits activating the CSN with associated synaptic delays.

Electric and Magnetic Stimulation of Corticospinal Neurons

- A typical recording of D- and I-waves elicited by TMS.
- Note that high-frequency D- and I-waves have never been recorded during natural, voluntary movement.
- Suggests that the encoding of the neural control signals for voluntary movement is more complex than that elicited by TMS or other stimulation.



Comparison of Direct Electrical Stimulation and TMS [3,4] : Primates and Humans.

- Single-pulse TMS does elicit both D- and I-waves responses from CSNs. The resulting wave consists of a D-wave followed by three to four I-waves at an interval of 1.6 ms.

- A wide range of CSNs with varying conduction velocities seem to be activated by TMS.

- Correlation between TMS threshold and the conduction velocity of the neuron. Faster CSNs have a lower TMS threshold while many CSNs with slow conduction times either have a threshold too high for current stimulator intensities or cannot be activated at all.

Comparison of Direct Electrical Stimulation and TMS [3,4] : Primates and Humans.

- As TMS intensity increases, slower CSNs initially only evoke I-wave response; D-waves appear once a higher threshold is reached. However, faster CSN are the opposite; D-waves appear initially at low intensities followed by I-waves at higher intensities.

- Baker [8] demonstrated in awake monkeys that voluntary tasks increase the amplitude of the induced action potentials by TMS.

More In Vivo Results

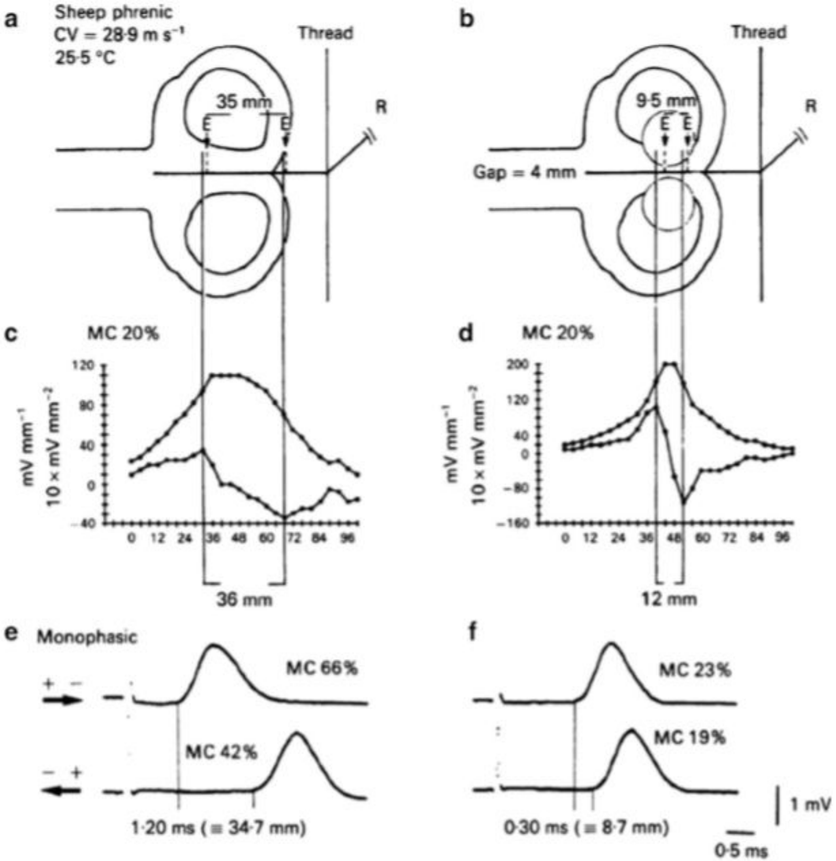
The E-field threshold of activation is a function of frequency

$$|E|_{thr} = \beta \, (1 + 2 \gamma f)$$

where constants β and γ are referred to as the rheobase and chronaxie values.

In Vitro Studies

- Sheep phrenic nerve in volume conductor excited by a TMS coil (Maccabee[9]).
- |E| field and spatial derivative were measu directly with E-field probe.
- Site of nerve excitation, denoted by E, determined by latency between stimulus pulse and recorded action potential.
- Shown are the two sites of activation corresponding to the current direction flowing in one direction and the other.



In Vitro Studies

- Excitation site located at regions of large and negative dE_T/ds where E_T is the component of the E field tangential to the nerve fiber and s is arc length along the tangential path.

- If the sign of E_T is changed then the sign of dE_T/ds is changed. Therefore changes in the polarity of the E field can produce changes in the site of activation.

- Monophasic pulses may have one site of activation whereas in the same experiment a biphasic pulse may have two sites of activation.

- For biphasic pulse the two depolarization sites will be at the same location as those for the monophasic pulses of different polarities.

In Vitro Studies Continued

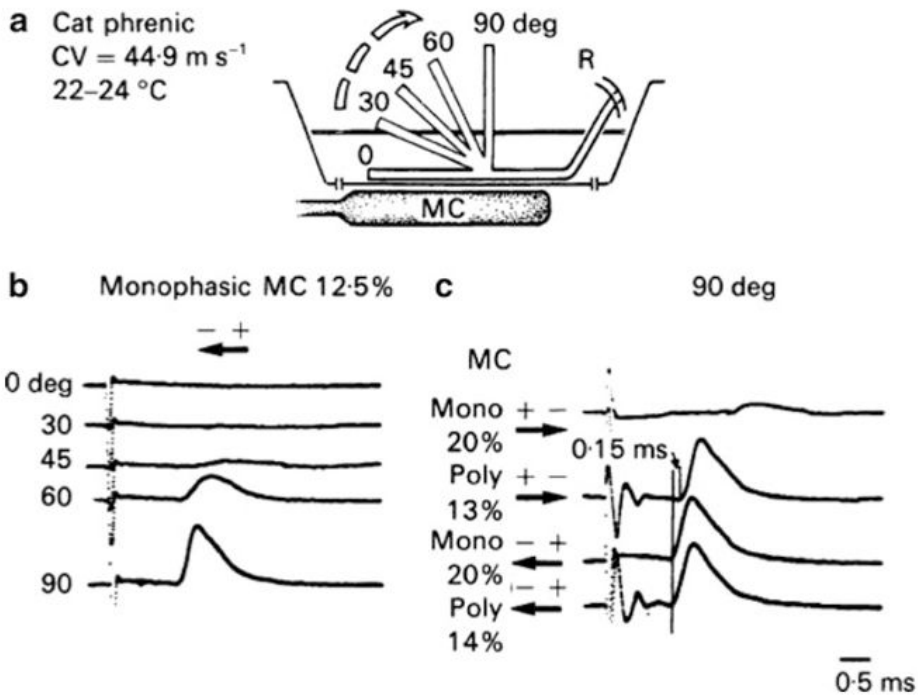
- This means that polyphasic (and by inference biphasic) pulses are not as sensitive to coil current direction as monophasic pulses are.

- Furthermore, polyphasic pulses tend to produce larger amplitude responses than similar monophasic pulses [10,11] leading one to conclude that the hyperpolarizing and then depolarizing (or vice versa) phases of the pulse provide a more efficient method of generating neuronal response.

- Conductivity inhomogeneities in the volumes can also create areas of increased spatial variation of the E field and thereby change the stimulation site. The previous figure illustrates this with the axon passing through two insulating cylinders meant to mimic the nerve exiting the neuroforamen.

In Vitro Studies Continued

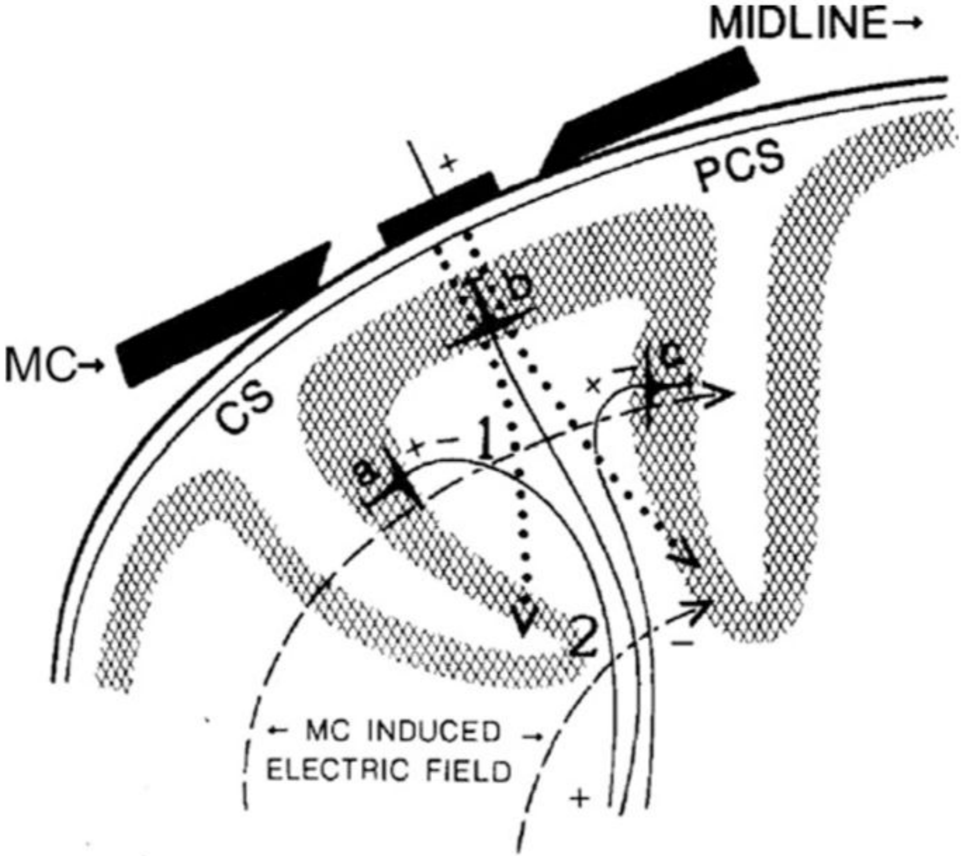
- $dE_T/ds = 0$ for a fiber in a uniform E field therefore no site of activation except possibly at fiber ends.
- Amassian[12] and Macabee[9] demonstrated that the area of lowest excitation threshold occurs where a nerve bends.
- More acute paths taken by the nerve decreased the threshold and increased the amplitude of activation.



In Vitro Studies Continued

- Regions of large axonal curvature seen near vertebral foramen and the infoldings of the neocortex making them regions of low threshold activation.

- The figure compares the possible sites of activation of three CSNs being stimulated by electrical stimulation (dotted lines) and TMS (dashed lines).



Take Home Message (Not in reviewed paper)

Continuity equation of electromagnetism:

$$\text{Div } J = d\rho/dt$$ (ρ is charge density, J is current density)

But $J = \sigma E$ so when conductivity σ transverse to the nerve fiber can be neglected then

$$\sigma dE_T/ds = d\rho/dt$$

Therefore dE/ds can lead to a local increase or decrease in charge density within a nerve fiber and therefore either a depolarization or hyperpolarization of the transmembrane potential.

References

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