42 A simulation study of the mechanisms that govern direct activation of neurons in the motor cortex by transcranial magnetic stimulation

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Objective: The present work aims to investigate the mechanisms of stimulation of various nerve cells by the electric field induced by Transcranial Magnetic Stimulation (TMS).

Method: The electric field induced by a figure-of-eight coil in a realistic model of the primary motor cortex (M1) was calculated using the Finite Element Method. A discretized version of the cable equation was then solved to model the response of idealized nerve cells to the induced electric field. Stimulation thresholds were calculated for a monophasic pulse waveform and for two orientations of the current induced in the tissue: posterior-anterior (PA) and anterior-posterior (AP). The model of the cortex and cells is shown in Fig. 1. The neuron labelled 'P' represents a pyramidal cell of layer V. The neurons labelled 'h' and 'v' represent cortical interneurons. The former (h 1-3) are tangentially aligned with the cortical surface, whereas the latter (v 1-3) are aligned perpendicular to the cortical surface.

Results: Stimulation of cortical interneurons is greatly influenced by the magnitude and orientation of the main component of the electric field with respect to the neuron. For the cells' orientations depicted in Fig. 1, the lowest stimulation thresholds were always attained with PA stimulation. In the wall of the sulcus, vertical ('v') interneurons have lower thresholds than horizontal ('h') ones. In the gyrus, the opposite happens – the lowest thresholds occur in horizontal cells, whereas stimulation of vertically oriented cells occurs only for very high stimulation intensities. In the lip of the gyrus, as neither type of cell is completely aligned with the field, the thresholds are similar for both 'h' and 'v' interneurons. Overall, as the electric field's magnitude is maximal at the gyrus, the lowest thresholds occur there, for the horizontal interneurons ('h1'). Regarding stimulation of 'P' cells, it always occurs at the bend of the axon, after it enters the white matter, where the field along the axon changes very rapidly. The lowest stimulation thresholds for interneurons are smaller than the thresholds for the pyramidal cells.

Conclusion: The results agree with experimental evidence supporting the D and I wave hypothesis concerning TMS monophasic PA stimulation of M1. Stimulation with the lowest thresholds (giving rise to the I-wave) occurs for cortical interneurons in the gyrus. Excitation of pyramidal cells (which generates the D-wave) occurs at higher thresholds.