Advanced Engineering Forum *Online: 2013-06-27*
ISSN: 2234-991X, Vols. 8-9, pp 631-638
doi:10.4028/www.scientific.net/AEF.8-9.631

Prefrontal cortex magnetic stimulation, a simulation analysis

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Keywords: Transcranial magnetic stimulation (TMS), Brain stimulation, Computer simulation, Finite element methods.

Abstract. The presented work aims to elucidate where stimulation occurs in the brain during transcranial magnetic stimulation (TMS), taking into account cortical geometry. A realistic computer model of TMS was developed comprising a stimulation coil and the human cortex. The coil was positioned over the right dorsolateral prefrontal cortex (right DLPFC) and the distribution of the induced electric field was analyzed. A computer simulation was constructed, where the coil is positioned at an angle of 45^0 relative to the sagittal plane. The results highlight the influence of cortical geometry on the distribution of the electric field in the brain and show that the highest values are not obtained directly under the center of the stimulator.

Introduction

Transcranial Magnetic Stimulation (TMS) allows direct initiation of cortical activity, adding a new dimension to studies of the human brain. In TMS, the cortical cells are stimulated non-invasively by strong magnetic field pulses that induce a flow of current in the tissue leading to membrane depolarization and thereby to neural excitation.

TMS is used in neurology to determine different conditions by evaluating the cortical-motor threshold [1] or to assess the continuity of nervous pathways. TMS can be viewed as interacting with voluntary movement in two ways: it can be used to probe the excitability of central nervous system pathways before, during and after a movement; alternatively, it can be used to interfere with movement and give information about the role of different cortical areas in different aspects of a task [2].

Repetitive transcranial magnetic stimulation (rTMS) can induce "virtual lesions" in the brain by interfering with the normal activity of different cortex areas, thus being used as an investigation tool in neurosciences [3]-[5].

Investigators can also use rTMS to test the brain's response to rapid rate [6] or low rate repetitive magnetic stimulation [7]-[10], and there are also studies to test the plasticity of the brain [11]-[14].

In recent years rTMS has proven its capabilities in treating psychiatric conditions like depression or schizophrenia [15]-[17]. Most rTMS depression trials have given high-frequency rTMS to the left prefrontal cortex, encouraged by positive early results for this approach [18]. A few investigators have chosen to trial low-frequency (≤1 Hz) rTMS to the right prefrontal cortex [19]. One important use for rTMS is for the treatment of drug resistant depression [20]-[22].

There are also experiments that test treatments for panic disorder with the use of 1Hz rTMS applied to the right dorsolateral prefrontal cortex [23].

Because many psychiatric treatments imply stimulation (or inhibition) of the dorsolateral prefrontal cortex, we designed a simulation to see the effects of a 70 mm double coil on a realistic model of the cortex.

The highest value for the magnetic field produced by the coil is under the center of the stimulator [24]. Taking into account our previous work that showed deviations for the induced electric field from the center of the coil [25], the coil was positioned at different angles over the right DLPFC

and we examined the location and intensity of stimulation for each angle. We also compared the effects of each position on four sulci positioned under the coil.

TMS – basic principles

The neurons are stimulated by applying a rapidly changing magnetic field. In TMS the excitation is obtained through a pulse current that drives a coil situated in the vicinity of the head (Fig. 1). The source of the activation of neurons is the electric field E (Fig. 2) induced in the tissue by the varying magnetic field (Faraday's Law) [24]:

$$\nabla \times E = -\frac{\partial B}{\partial t} . \quad (1)$$

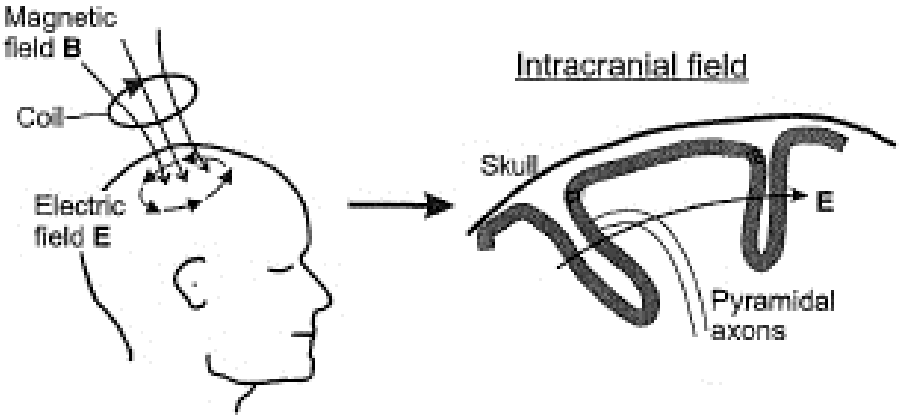


Figure 1. TMS mechanism – macroscopic view [24]

At cellular level the electric field E affects the transmembrane potential witch may lead to local membrane depolarization and firing of the neuron [26].

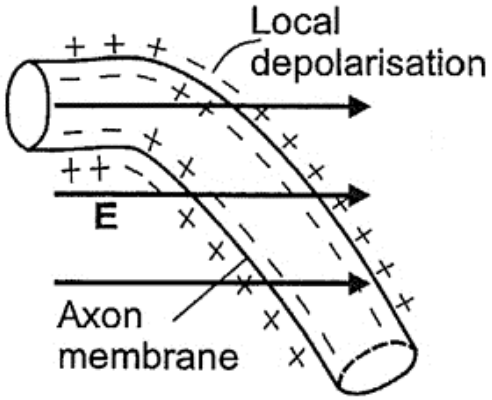


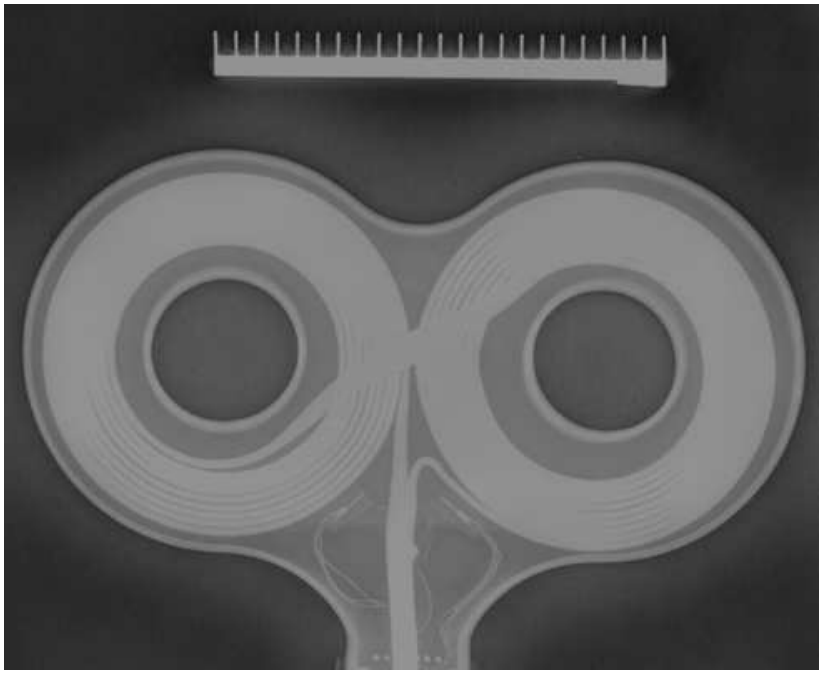
Figure 2. TMS mechanism – cellular level [24]

Because the surface of the cortex is highly irregular, we wanted to view the effects of stimulation on a realistic brain model. To reach our goal we designed a double 70 mm copper circular coil placed in the vicinity of the brain. The brain is represented by an anatomically correct right side hemisphere.

Simulation setup

The generally accepted time periods for TMS are 200-500 μs. The coil is excited by a 5 kA current with a frequency of 2.5 kHz, which corresponds to duration of 400 μs for each pulse. This time period is similar to the one used by Magstim Rapid^2 magnetic stimulator.

The coil was modeled based on calibrated X-ray images of a 70 mm double stimulator from Magstim (Fig. 3). Table I offers the measurements for the coil dimensions which were used in our setup.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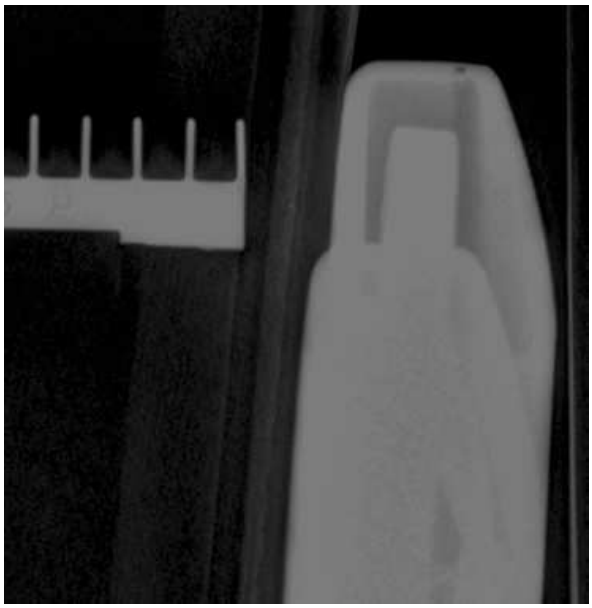

(b)

Figure 3. X-ray scans for 70 mm double coil from Magstim: (a) frontal view, (b) side view

TABLE I. 70mm double coil - relevant dimensions

Element	**Dimension**
Winding Exterior diameter	88 (mm)
Winding Interior diameter	53.8 (mm)
Distance between the two windings	1.4 (mm)
Conductor thickness	1.5 (mm)
Conductor height	4.5 (mm)
Plastic thickness	2 (mm)
Coil-exterior distance	3.5 (mm)
Number of turns per winding	9 (turns)

Because most experiments with TMS stimulating the DLPFC involve only one side of the brain, we decided to model only the right side, with the prefrontal cortex depicted in Fig. 4.

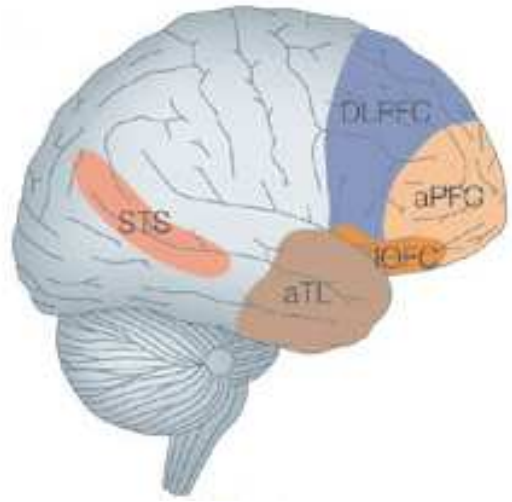


Figure 4. Location for the dorsolateral prefrontal cortex (DLPFC), depicted in dark blue [27]

The brain hemisphere was modeled as a 3D solid object composed of 261 faces, and was built using CT and MRI scans (Fig. 5). Conductivity of the brain was set according to recent research regarding brain conductivity. For body temperature and frequencies between 10 Hz…10 kHz, the conductivity was set to 1.79 S/m [28].

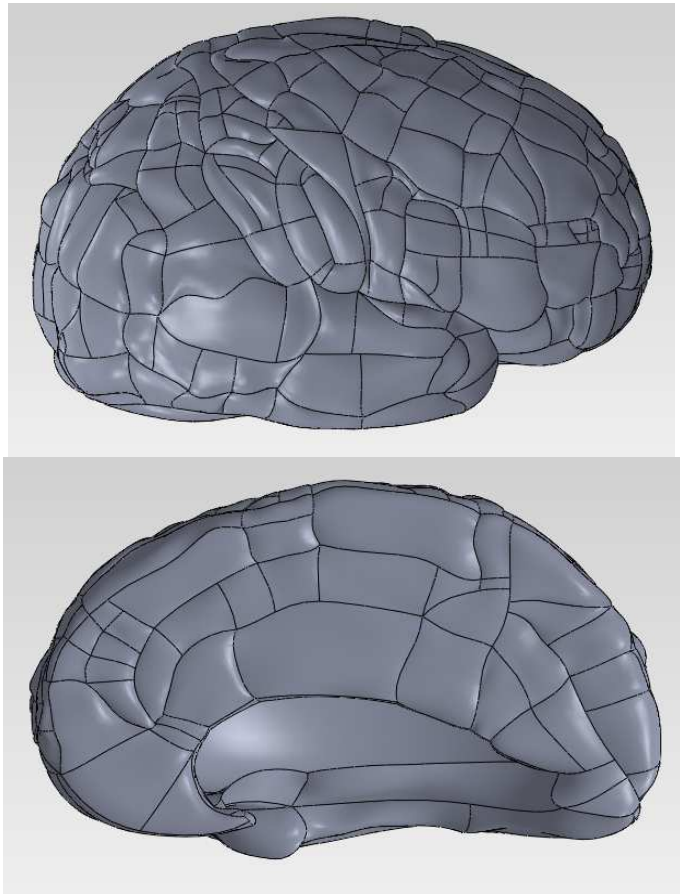


Figure 5. Cortex model overview

The medium diameter of the coil windings is 70 mm. The coil was positioned over the right DLPFC at an angle of 45^0, where the angle is measured between the handle of the stimulator and the sagittal plane. Fig. 6 depicts the position of the stimulator.

The coil was oriented parallel to the neuronal structures at a distance of 11.5 mm, corresponding to the cranium thickness plus the distance between the windings and the exterior of the stimulator.

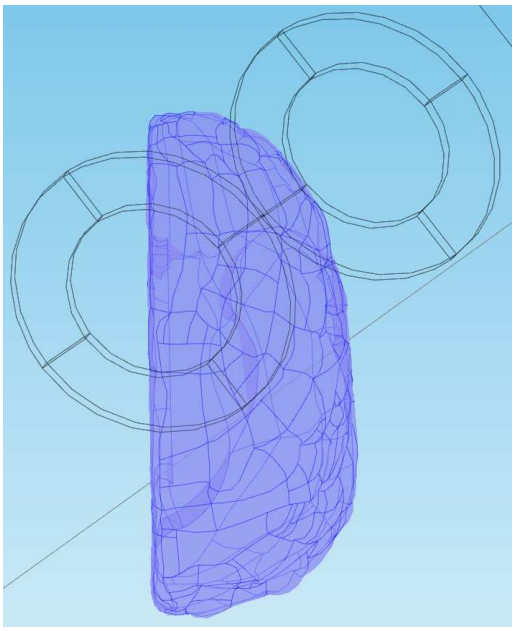


Figure 6. Position of the coil relative to the brain at an angle of 45^0

Results and discussions

The solutions were solved for more than 800000 degrees of freedom with finite element method (FEM) software Comsol.

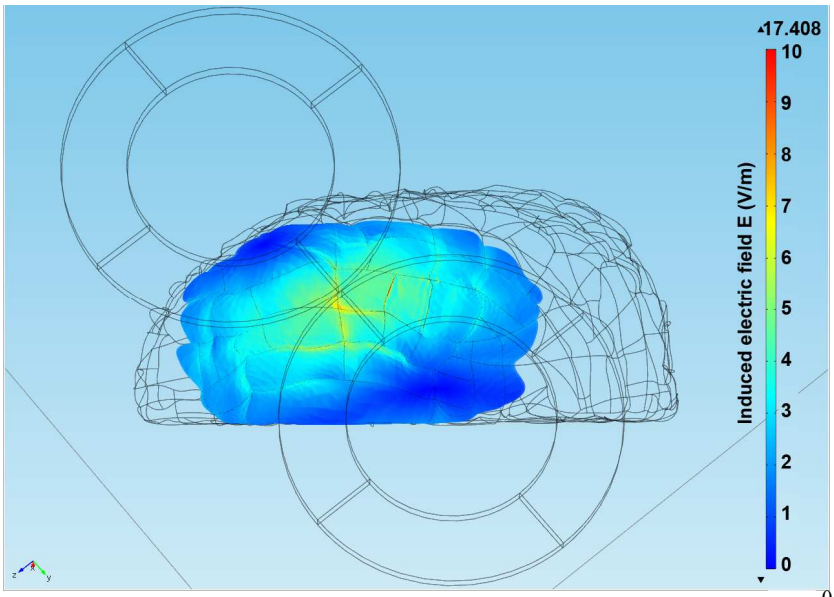
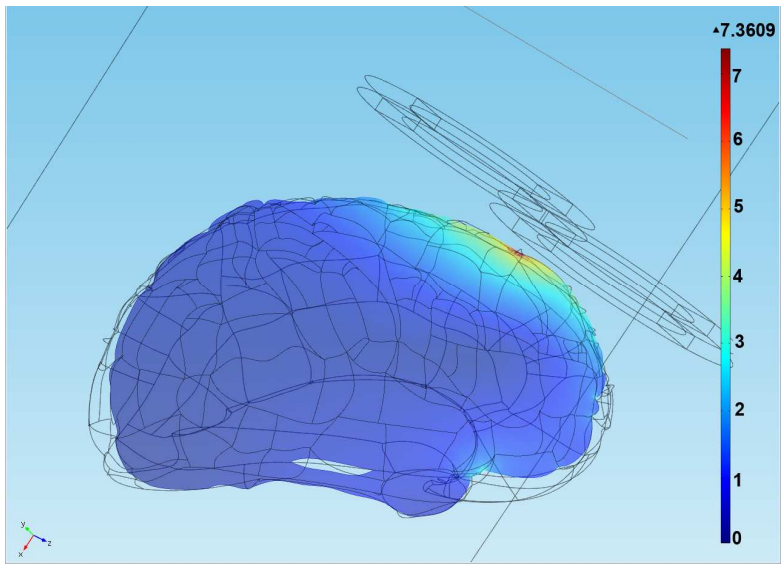


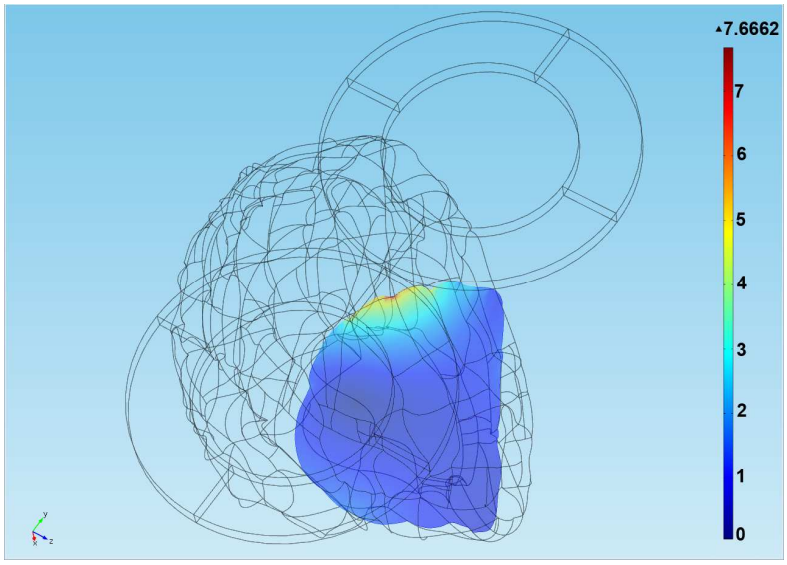
Figure 7. Overview of induced electric field E (V/m), coil oriented at 45^0 degrees

Although one could expect bigger values for the electric field in the gyri, since they are closer to the coil, we find higher intensities along the channels (called sulci) between them. Because the relative positions between the coil and the sulci are different, the distribution and the maximum values of the induced electric field (E) changes significantly for each sulci (Fig. 7).

If we look at different slices through the cortex, we realize that the biggest values for the electric field are not necessarily directly under the center of the stimulator, but rather in the tight sulci close to the center. The slices were selected to include the largest values close to the center of the stimulator (Fig. 8).



(a)



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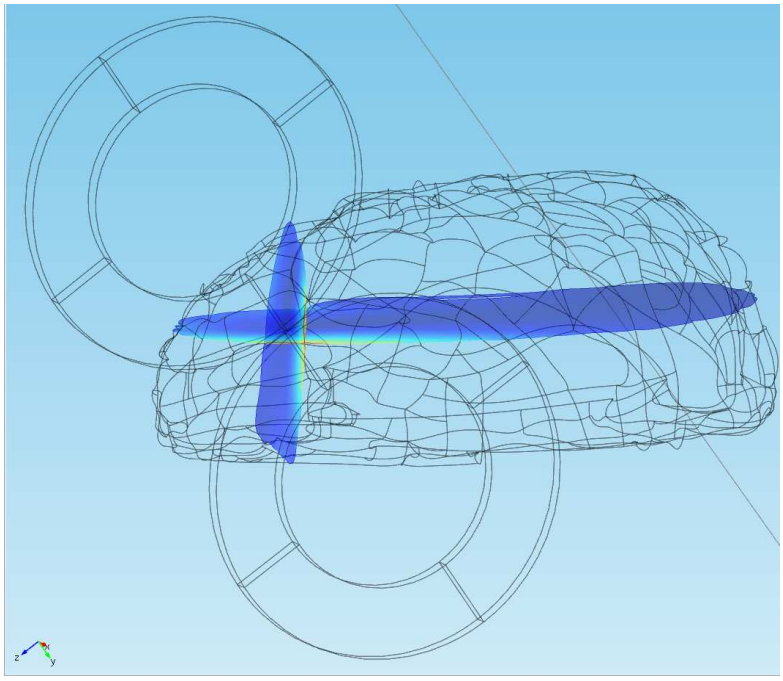

(c)

Figure 8. Slices for induced electric field E (V/m), coil oriented at 45^0: (a) sagittal plane, (b) coronal plane, (c) relative position of the two slices

Conclusions

The overview of our results shows that the biggest values for induces electric field are not located directly under the center of the stimulator, and sometimes the highest values are not even under the windings, even though they are close to the center of the stimulator.

The maximum values are contained in the sulci, and peak values migrate from one sulcus to another as we rotate the stimulator. For the same location of the coil we can stimulate different areas of the brain by rotating the coil.

Our results show that the shape of the targeted area of the cortex greatly influences the distribution of the induced electric field during TMS.

More studies are needed to confirm our findings, including more complex models that contain the skull, cerebrospinal fluid and the cortex.

ACKNOWLEDGMENT: This paper was supported by the project "Development and support of multidisciplinary postdoctoral programmes in major technical areas of national strategy of Research - Development - Innovation" 4D-POSTDOC, contract no. POSDRU/89/1.5/S/52603, project co-funded by the European Social Fund through Sectoral Operational Programme Human Resources Development 2007-2013.

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