Clinical Neurophysiology 118 (2007) 464–474

www.elsevier.com/locate/clinph

Anodal vs cathodal stimulation of motor cortex: A modeling study

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Accepted 11 September 2006
Available online 5 December 2006

Abstract

Objective: To explore the effects of electrical stimulation performed by an anode, a cathode or a bipole positioned over the motor cortex for chronic pain management.

Methods: A realistic 3D volume conductor model of the human precentral gyrus (motor cortex) was used to calculate the stimulus-induced electrical field. The subsequent response of neural elements in the precentral gyrus and in the anterior wall and lip of the central sulcus was simulated using compartmental neuron models including the axon, soma and dendritic trunk.

Results: While neural elements perpendicular to the electrode surface are preferentially excited by anodal stimulation, cathodal stimulation excites those with a direction component parallel to its surface. When stimulating bipolarly, the excitation of neural elements parallel to the bipole axis is additionally facilitated. The polarity of the contact over the precentral gyrus determines the predominant response. Inclusion of the soma-dendritic model generally reduces the excitation threshold as compared to simple axon model.

Conclusions: Electrode polarity and electrode position over the precentral gyrus and central sulcus have a large and distinct influence on the response of cortical neural elements to stimuli.

Significance: Modeling studies like this can help to identify the effects of electrical stimulation on cortical neural tissue, elucidate mechanisms of action and ultimately to optimize the therapy.

Keywords: Motor cortex stimulation; Chronic pain; Anode; Cathode; Neuron; Modeling; Precentral gyrus; Central sulcus

1. Introduction

Motor Cortex Stimulation (MCS) is a promising therapy in the treatment of chronic, otherwise intractable pain. Introduced by Tsubokawa and his colleagues (Tsubokawa et al., 1993), it was accepted and developed in several centers worldwide (Garcia-Larrea et al., 1999; Meyerson et al., 1993; Nguyen et al., 2003). Until now, about 350 cases have been reported (Meyerson, 2005) and so far central and facial pain are considered to be the main indications for MCS (Brown and Barbaro, 2003; Nguyen et al., 2003).

Because the electrode lead is implanted epidurally (i.e. between the dura mater overlying the sensorimotor cortex and the skull), the technique is generally safe and therefore attractive. Since the brain surface is not exposed, visual guidance cannot be used for target localization. Therefore, the central sulcus is identified using somatosensory evoked potentials and neuronavigation data. The somatotopy of the motor cortex is mapped for each patient individually as it is important that the electrodes used in chronic stimulation are positioned over the cortical representation of the painful body part (Nguyen et al., 1999; Nguyen et al., 2003). This is generally done peroperatively using bipolar stimulation. In chronic stimulation, the stimulus amplitude is typically set at 20–50% of the motor threshold, a value large enough to cause analgesia without any motor effects. The lead most commonly used for stimulation is the Resume™ (Medtronic Inc., Minneapolis, MN, USA). This lead has a paddle with four disc electrodes having a diameter of 4 mm and spaced by 10 mm (center–center). The insulating paddle has a thickness of ~2 mm. Until now, the electrode combination, polarity and stimulation param-

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doi:10.1016/j.clinph.2006.09.012

eters have been chosen in a purely empirical manner, often with little knowledge of their influence and role.

The mechanism by which MCS alleviates pain is not known. PET studies have shown an increase in cerebral blood flow during MCS in the VA-VL complex of the ipsilateral thalamus, the cingulate gyrus and the brainstem. However, it remains unknown which neural elements are the immediate targets of the stimulus-induced electrical field in the region of the motor cortex (Nguyen et al., 2003). Acquiring this knowledge is important because: (1) the neural elements in the cortex affected by the stimulus mediate the analgesic phenomena and (2) the clinical result may be improved when the stimulation technique (lead, its position and the stimulation parameters) can be optimized based on knowledge of the neural elements which should be targeted.

Computer modeling has proven helpful in answering similar questions. In the past, our spinal cord stimulation (SCS) model was validated and helped to identify important parameters influencing the results of SCS (Holsheimer, 2002). In a previous paper (Manola et al., 2005), our model of MCS was introduced and described. Model predictions regarding the stimulus-imposed electrical field and activating functions were presented. Simple nerve fiber models were used to simulate the response of neural elements to the applied electrical field. However, instead of just axons (as in SCS) the motor cortex also includes *cell bodies* and *dendrites* of several types of neurons. Among these neurons are pyramidal cells having an apical dendritic tree proximal to the electrode which may alter the axonal response to the applied field. In this modeling study, a pyramidal cell model including a cell body (soma) and a dendritic trunk representing the apical dendritic tree was introduced.

The aim of this study was to evaluate the effect of anodal and cathodal electrode positions on activation of the cortical neural elements during MCS.

2. Methods

2.1. Models

Similar to our SCS models, the MCS model comprises two parts.

2.1.1. 3D volume conductor model with stimulating electrode(s)

The 3D volume conductor had a size of 66 × 43 × 57 mm and was represented by 121 × 73 × 80 cubic elements. A 50% larger size of the model changed the results only by a few percent. The precentral gyrus (PCG) flanked by the precentral sulcus on the anterior and the central sulcus (CS) on the posterior side constitute the central part of the model (Fig. 1).

The PCG includes the premotor cortex (Brodmann area 6) anteriorly and the primary motor cortex (area 4) posteriorly and in the anterior wall of CS (Zilles, 1990). A layer of highly conductive cerebrospinal fluid (CSF) separates the dura mater from the cortical surface. The thickness of the CSF varies among patients and is likely reduced by the thickness of the lead placed between the dura mater and the skull compartment in the model. Models with a CSF thickness ranging from 0.5 to 2.0 mm were made in order to assess the influence of this parameter. Contrary to our previous MCS model, the model presented here had the lead paddle oriented *perpendicular* to CS as commonly used in clinical practice (Nguyen et al., 2003). *Monopolar* stimulation with a single *cathode* or *anode* positioned over the center of PCG and over CS was modeled. The electrode diameter was 4 mm (see Section 1). The potential at the boundary of the model was set at 0 V (Dirichlet boundary condition), thus providing the return path for the stimulation-induced current. In addition, *bipolar* stimulation with poles positioned over PCG and CS (electrode diameter 4 mm, center-to-center spacing 7 mm) was modeled. The *electrical potential field* induced by the stimulus pulse in the 3D space of the model was calculated at the vertices of the cubes forming the model by solving a discrete form of the Laplace equation using numerical techniques. A detailed description of the volume conductor model and the calculation methods are presented in our previous publication (Manola et al., 2005).

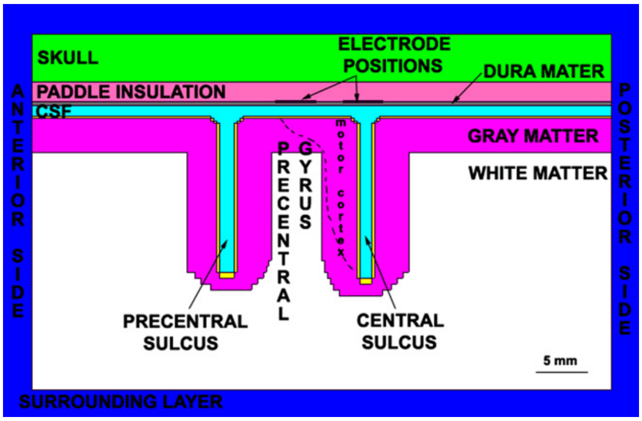

Fig. 1. Anterior–posterior cross-section of the model. Model compartments are labeled. Electrode positions and approximate position of the motor cortex are indicated.

2.1.2. Models of cortical neural elements

The same myelinated fiber types as in our previous model were considered. They include afferent ('A') fibers *parallel* and efferent ('E') fibers *perpendicular* to the cortical laminae. However, the 'E' fibers originating from *pyramidal cells* have an apical *dendritic tree* extending up to lamina I. Their position is between the axon and the stimulating electrode(s) and, therefore, their presence might affect the stimulation conditions and outcome. In order to account for these aspects, the 'E' *fiber* models were extended with a (simple) model of the *cell body (soma)* and *apical dendritic trunk*. Hence, such a complex structure is referred to as a *pyramidal neuron*. The modeled neural elements are shown in Fig. 2. The 'A' fiber is parallel to the cortical surface and was placed at 1.1 mm depth in the