Modeling of Spreading Cortical Depression Using a Realistic Head Model

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Introduction

Spreading Cortical Depression (SCD) has been an interesting yet physiologically complex question among researchers during the past half century. SCD is a slowly moving hyper-excitation followed by suppression of spontaneous cortical electrical activity in the cortex. Leao and Morrison [1] suggested that SCD might be related to migraine and epilepsy. Later SCD was studied extensively [2, 3, 4] both with EEG and MEG using animal models. SCD in humans has also been observed using cortical electrodes during neurosurgery [5] and in a single event, signals suggesting SCD were observed in positron emission tomography (PET) [6]. Magnetic signals consistent with what would be expected from SCD in humans have been observed by Barkley and colleagues [7] in migraine patients. We have previously shown that SCD can be modeled by using dipoles [13].

Methods

In this calculation, we have used a realistically shaped head model to investigate SCD. This model includes three different compartments for the scalp, skull, and brain. We have represented the sources, which are in the excited area of the cortex due to the propagating SCD, by dipoles which are located perpendicular to the surface of the cortex. During this investigation, we assumed that the shape of the sulcus is parabolic. At the macrocolumn scale, the dipole moment per unit volume and the current density are roughly equal. If $\vec{p}\,(p_x, p_y, p_z)$ represents the dipole moment of a unit volume of the cortex, then the magnetic field produced by current dipoles in a volume dV of the sulcus can be evaluated using the following equations;

$$B(\vec{r}) = B_0(\vec{r}) + \frac{\mu_o}{4\pi}\sum_{j=1}^{3}(\sigma_j^- - \sigma_j^+) \bullet \int_S V_j(\vec{r}\,')\frac{\vec{r}-\vec{r}\,'}{|\vec{r}-\vec{r}\,'|^3} \times d\vec{S}_j \qquad (1)$$

where μ_o is the permeability, J^s is the current dipole moment per unit volume of the sources, σ_j^- and σ_j^+ are the conductivities on the inside and outside of surface ds_j, V_j is the potential on that surface.

To evaluate the magnetic field given by Eq. (1), we divided the scalp, skull, and brain surfaces into triangles [9] as shown in Fig. 1. The magnetic field corresponding to the dipole $\vec{p}\,(p_x, p_y, p_z)$ in an unbounded volume conductor is given by the first term;

$$B_0(\vec{r}) = \frac{\mu_o}{4\pi}\frac{\vec{p}\times(\vec{r}-\vec{r}\,')}{|\vec{r}-\vec{r}\,'|^3} \qquad (2)$$

The second term represents the contribution of the volume current on the scalp, skull, and brain surfaces, where the integral is over the j[th] surface, $\vec{S}_j$, and $V_j(\vec{r}\,')$ is the potential on the j[th] surface. In the second term, if the potential is taken as constant over each triangle on the surface, the integral becomes [9]

$$\int_{S_j} V_j(\bar{r}')\frac{\bar{r}-\bar{r}'}{|\bar{r}-\bar{r}'|^3}\times dS_j = \sum_{k=1}^{N} V_{jk}\int_{\Delta jk}\frac{\bar{r}-\bar{r}'}{|\bar{r}-\bar{r}'|^3}\times d\bar{S}_{jk} \tag{3}$$

where the integrals are over the kth triangle, Δ_{jk}, on the jth surface. These integrals depend only on the head and coil geometries, and not on the dipole position.

The potential of a dipole in a homogeneous, unbounded volume conductor, V_o, is calculated at the center of each triangle using the equation

$$V_0(\bar{r}) = \frac{1}{4\pi\sigma}\frac{\bar{p}\bullet(\bar{r}-\bar{r}')}{|\bar{r}-\bar{r}'|^3} \tag{4}$$

where $\bar{r}$ is the position where the potential is calculated, $\bar{r}'$ is the position of the dipole, $\bar{p}$ represents the dipole moment of a unit volume of the cortex, and σ is the conductivity. The electrical potential is calculated using the algorithm developed by Hammalainen and Sarvas (1989). The integral equation for the potential is approximated as a set of linear equations [9];

$$V_{ik} = \sum_{j=1}^{3}\sum_{l=1}^{L(j)} B_{ijkl}V_{jl} + g_{ik} \tag{5}$$

where

$$V_{ik} = \frac{1}{\mu_{ik}}\int V(\bar{r})dS_{ik}, \quad g_{ik} = \frac{1}{\mu_{ik}}\frac{2}{\sigma_i^- + \sigma_i^+}\int V_o(\bar{r})dS_{ik}$$

$$B_{ijkl} = \Gamma_{ij}\frac{1}{\mu_{ik}}\frac{1}{2\pi}\int\Omega_{il}(\bar{r})dS_{ik}, \text{ and } \Gamma_{ij} = \frac{\sigma_j^- - \sigma_j^+}{\sigma_i^- - \sigma_i^+}. \tag{6}$$

Here μ_{ik} is the area of the kth triangle (k=1,...,L(i)) on the ith surface (i = 1,2,3), V_{ik} is the potential averaged over that triangle, $\Omega_{jl}(r)$ is the solid angle subtended from $\bar{r}$ by the lth triangle (l = 1,...L(j)) on the jth surface (j = 1,2,3) σ_i^- and σ_i^+ are the conductivities inside and outside of the ith surface, L(i) is the number of triangles in the ith surface, and $V_0(\bar{r})$ is the potential produced at $\bar{r}$ by a dipole in an unbounded conductor with a conductivity 1 S/m. We modified Hamalainen and Sarvas's algorithm slightly by using a low-order integration formula to solve the integrals in Eq. 6 instead of evaluating the integrals at the center of each triangle . Solid angles are calculated using the analytical expressions presented by van Oosterom and Strackee [10].

Equation (5) has no unique solution because the potential is defined only up to an arbitrary constant. Therefore, there is a resulting ambiguity in the solution [11]. By means of deflation we can remove the ambiguity with the following alteration

$$C_{ijkl} = B_{ijkl} - 1/N \tag{7}$$

where N is the total number of triangles. Our deflated potential obeys the equation

$$V_{ik} = \sum_{j=1}^{3}\sum_{l=1}^{L(j)} C_{ijkl}V_{jl} + g_{ik} \tag{8}$$

This equation can be rearranged to give

$$\sum_{j=1}^{3}\sum_{l=1}^{L(j)}(I_{ijkl}-C_{ijkl})V_{jl}=g_{ik} \tag{9}$$

where

I_{ijkl} = {1 if i=j and k=l) or (0 otherwise)}

is the identity matrix. We use a direct solution of matrix equation using Gaussian elimination [12]. An accurate calculation of the potential using Eqs. (5) and (6) is difficult if the skull conductivity is much less than the conductivity of the scalp and brain [11]. Therefore, we have implemented the scheme presented by Hamalainen and Sarvas [11] to first determine the potential on the brain in air, and then use this result to get the potential on all three surfaces.

When SCD propagates over the cortex, both the directions and positions of dipole moments change. Hence, it is difficult to formulate a general mathematical formula for the magnetic field created by a dipole moment located at any arbitrary location in a volume conductor. Therefore, we divide dipole moments into their x, y, and z components (p_x, p_y, p_z). Then we consider these components individually and calculate the corresponding magnetic fields. By summing these magnetic field components over the active region of the cortex, we can obtain the total magnetic signal arising from the SCD which is detected by the SQUID coil.

For calculating the magnetic field arising from SCD as it propagates across a sulcus, it is necessary to represent the curvature of the sulcus by a mathematical expression. Without knowing the shape of sulcus, the path of the traveling disturbance associated with SCD can not be determined. For this investigation, the used cross-sectional shape of the sulcus is given by Eq. (10);

$$x^2=\frac{z-d_s}{(a-z)}\ , \quad \text{for} \quad a > z \geq d_s \tag{10}$$

where d_s is the depth of sulcus measured from the origin of the spherical coordinate system and a is the distance to the skull-brain boundary from the origin of the coordinate system.

Evaluating the first derivative of z with respect to x, we obtain an expression for the gradient of this curve at any point on it. Using the value of the gradient, we can determine the orientation of the dipole at the same point where the gradient was obtained. Since, in our model, we assume that the sources associated with SCD are oriented perpendicular to the surface of the sulcus, we can obtain the orientations of these sources using these gradients. Thus we can evaluate the magnetic field created by this dipole at the point where the magnetometer pickup coil is located. As described earlier, in order to deal with the rapidly changing orientations of dipoles encountered by SCD as it travels across a sulcus, we have divided the sulcus region into very small surface elements and represented them by tiny individual dipoles.

Results and Discussion

Figure 2a shows the recorded LAW signals from a patient during migraine aura. We simulated the signals shown in Fig. 2b for comparison with the signals shown in Fig. 2a. These two figures are sufficiently similar to suggest that reasonable selection of model parameters can lead to the modeling of real data.

Additional simulations, not shown for brevity, suggest that amplitudes and durations of the simulated signals increase with the increase of active sulcus area. This is because when active sulcus area increases, the total number of dipoles involved in the simulation increases. Similarly when the active region is wider, the time required for the SCD region to propagate across the sulcus increases leading to the longer duration signal.

Thus, we show that the large amplitude waves (LAWs), reported by Barkley and coworkers [7] in time series magnetoencephalography (MEG) recordings from migraine patients but not controls, may arise from propagation of Spreading Cortical Depression (SCD) across a sulcus. SCD propagates very slowly across the cortex in all species in which it has been observed. In our model, current dipoles represent the excitable neurons in the cortex. Using this model, we are able to simulate signals very similar to the LAWs. The simulated waveforms suggest that shapes, amplitudes, and durations of the SCD signals depend on the size of the active area of cortex involved in SCD, as

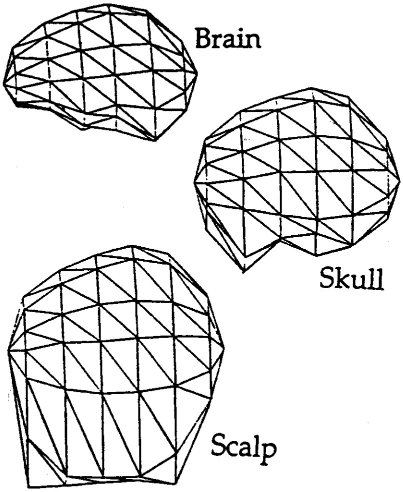

Fig. 1 Digitized scalp, skull, and brain surfaces.

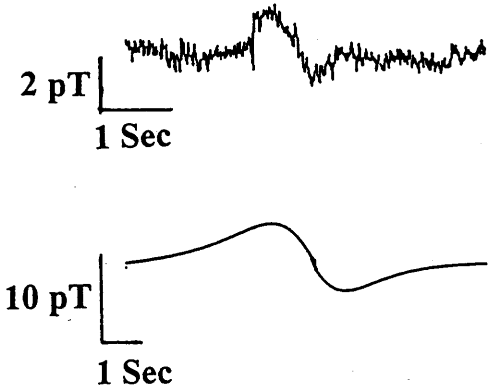

Fig. 2. a) MEG signal from reference 7 detected from migraine patient. b) Simulated signal for SCD using our model.

well as the relative orientation of the pickup coils. The shape of the simulated LAW waveform is strongly influenced by the relationships between the detector location and orientation, the propagation direction of the SCD wave, and the orientation of the sulcus.

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Acknowledgment

This research supported by NIH/NINDS grant Nos. R01 NS30914 and P01 NS32399.