Computerized Stimulation Parameter Adjustment of Deep Brain Stimulation Minimizing Side Effects and Power Consumption for Parkinson’s Disease

Wei-Yi Chuang  Paul Chang-Po Chao *  Ku-Y Young Young

Department of Electrical Engineering, National Chiao-Tung University, Hsinchu 300, Taiwan, ROC

Received 1 Oct 2012; Accepted 21 Jan 2013; doi: 10.5405/jmbe.1328

Abstract

Deep brain stimulation (DBS) is broadly applied for neuropsychiatric diseases and thus determining its mechanism is of interest, especially in terms of the neural structure surrounding the DBS probe and the volume of tissue activated (VTA) during DBS. For re-operations for battery replacement, a major issue is reducing treatment power consumption without compromising clinical benefits. To avoid side effects and to minimize power consumption, optimized adjustment of the stimulation parameters is required. This study thus proposes a scheme for determining the optimal stimulation parameters. An electromagnetic finite element model for a patient-specific physiological brain model is first established using magnetic resonance imaging (MRI) data. Using finite element analysis (FEA), varied stimulation parameters are applied to the electromagnetic model for VTA estimation. Optimal electrode contact(s) are selected based on the estimated VTA to avoid side effects. Moreover, a nonlinear programming method for optimizing the stimulation voltage and the pulse width is applied to minimize power consumption in DBS. The effectiveness of the model parameters was verified using five Parkinson’s disease patients. The results demonstrate that the estimates of the VTA are consistent with the observations within the desired region of the brain while avoiding side effects and reducing power consumption by 13% on average. The proposed method allows clinicians and researchers to efficiently select the optimal stimulation parameters. Moreover, it provides valuable information for closed-loop stimulation protocols in DBS.

Keywords: Deep brain stimulation (DBS), Volume of tissue activated (VTA), Side effects, Power consumption, Magnetic resonance imaging (MRI), Finite element analysis (FEA)

1. Introduction

Over the last decade, deep brain stimulation (DBS) has been adopted to treat various neuropsychiatric disorders, such as essential tremors, epilepsy, drug-resistant depression, and obsessive compulsive disorder [1]. In this approach, electrodes are implanted chronically into a selected brain target, such as the subthalamic nucleus (STN), to treat Parkinson’s disease (PD). A brain-electrode interface (BEI), which consists of the implanted electrode, a layer of peri-electrode space surrounding the electrode, and the surrounding brain tissue, is then formed [2-6]. Because the brain tissue content in the peri-electrode space varies with time, stimulation parameters should be adjusted during DBS to maintain the efficacy of therapy. To quantify the efficacy of DBS, the Unified Parkinson’s Disease Rating Scale (UPDRS) [7], based on a clinical evaluation of symptoms, has been established to assess the severity of PD symptoms. Among the problems that may be confronted during the adjustment of stimulation parameters in clinical practice, side effects and power consumption are considered to be the most serious [8-14]. Side effects could be induced when the stimulation region covers undesired parts of the brain, which commonly occurs in clinical practice. In addition, the stimulator’s battery might require frequent replacement because stimulation at constant amplitude consumes considerable power. On average, the mean lifetime of a stimulator’s battery in PD was found to be 47-83 months [15]. A battery replacement costs as much as twenty-five thousand US dollars [16].

The focus of the present study is preventing the neuropsychiatric side effects that can be induced when the DBS-stimulated region covers the limbic circuit on the antero-ventral part of the STN, which is related to emotion control [9,10]. Several methods have been proposed for reducing power consumption during DBS [11-13]; they can be classified into two main categories: (i) the development of new devices for DBS [11,12] and (ii) adjustment of DBS parameters [13]. In

* Corresponding author: Paul Chang-Po Chao
Tel: +886-3-5131377; Fax: +886-3-5752469
E-mail: pchao@mail.nctu.edu.tw
[11], a DBS device was developed with an improved stimulation circuit to reduce power loss during stimulation. In [12], the stimulation waveform was adjusted based on optimization and linear dynamic system theories to reduce the stimulation voltage. These approaches utilized animal experiments to verify the simulation results, even though there are functional differences between an animal model and a human head. DBS parameters include the parameters of the activated electrode contact(s), stimulation voltage, pulse width, and frequency. In [13], simulations were conducted for applying DBS within discrete time frames with the aim of reducing power consumption during stimulation. This method can predict the onset of PD tremors in human subjects, but PD is a progressive disease that demands treatment at more than a single time point. In summary, the avoidance of side effects and the reduction of power consumption have been investigated, but these goals have not been simultaneously considered. Since both these goals can be achieved via stimulation parameter adjustment, this study proposes a systematic method for optimizing stimulation electrode contacts and parameters (stimulation voltage and pulse width).

Performance evaluation requires a quantitative description of the effects of various stimulation parameters on the neural response. Many investigations developed computational models for predicting the electric field and for providing the stimulation generated by DBS [17-21], yielding the quantified representation of neuronal responses during stimulation as the volume of tissue activated (VTA), which is used as a performance index here. To provide an accurate prediction of VTA, a brain computing model with a non-homogeneous and anisotropic brain tissue medium has been established [19]. Additionally, to model the characteristics of the brain medium, diffusion tensor imaging (DTI) data have been utilized to represent a population of axons using a fiber tractography algorithm [17]. Instead of using these complicated, computationally intensive models [14,21-25], in this work, VTA determination is based on a computational model with a homogeneous and isotropic tissue medium to reduce model complexity because previous studies [23,24] have shown that the use of simplified models yields similar results.

2. Materials and methods

Figure 1 shows a block diagram of the proposed stimulation parameter adjustment scheme. The electrical potential distribution is simulated based on a BEI model via finite element analysis (FEA) to determine the VTA during stimulation. Patient-specific pre- and post-operation MRI data are used to construct a physiological model that includes the STN and electrode lead anatomies. Subsequently, the estimated VTA is used as the input to the patient-specific physiological model to localize the stimulation region in the STN for addressing any neuropsychological side effects. Additionally, a regression model is used to quantify the relationship between the stimulation parameters and corresponding VTA. To reduce power consumption, an optimization method implemented with nonlinear programming is used to determine the optimal stimulation voltage and pulse width. Details of these operations are described below along with an in vivo experiment.

![Diagram](image_url)

**Figure 1.** Proposed stimulation parameter adjustment scheme.

### 2.1 Finite element analysis

#### 2.1.1 Model geometry

A BEI finite element model was constructed for estimating the VTA. The model consists of three components/regions [2]: the implanted electrode, the surrounding brain tissue, and a peri-electrode space layer. The Medtronic DBS 3389 lead (Medtronic, Minneapolis, MN, USA), which is frequently used in STN stimulation for PD, was selected for the BEI model simulation. It contains four 1.5-mm-long electrodes, marked as contacts 0, 1, 2, and 3, respectively, with a radius of 0.635 mm. The distance between electrodes is 0.5 mm, as shown in Fig. 2 [26]. The brain tissue surrounding the lead is assumed to consist of homogeneous and isotropic volume conductors [23,24]. Brain tissue conductivity is actually heterogeneous and anisotropic, which impacts the VTA [17-20]. Because the current preferentially flows along the lower impedance regions, VTAs with a heterogeneous brain tissue medium are expected to be smaller than those with a homogeneous medium. Recent studies have shown that gray matter regions in the brain have relatively uniform electrical properties [23] and that anisotropy and heterogeneity do not have a substantial effect on the VTA from DBS [24]. The volume conductor is modeled as a cylinder surrounding the electrode lead with a radius of 5 cm and a height of 14 cm [27]. Doubling the density of the mesh or doubling the distance of the boundary from the electrode generates a potential distribution that differs by < 2% when compared to the default model. The encapsulation layer between the lead and surrounding brain tissue, known as the peri-electrode space, has a thickness of 0.25 mm [3,4]. The resulting mesh of the BEI model contains 41,615 nodes for FEA. Smaller elements of the resulting mesh are near the lead and larger elements are at the boundaries of the brain tissue.

#### 2.1.2 Governing equations

The BEI model is governed by Gauss’s law in Maxwell’s equations to describe the electric field. Here, it is assumed that
the fields in DBS and their sources vary slowly because the frequency range is within 1 kHz [28-30]. In clinical practice, the stimulation frequency range is about 90-170 Hz for optimal motor control with Parkinson’s disease patients [28,29]. The medium is thus simulated using a quasi-static model. The equations can accordingly be reduced to Laplace’s equation. The potential distribution induced by stimulation is calculated by solving Laplace’s equation:

\[ \nabla \cdot \sigma \nabla V = 0 \]  

(1)

where \( V \) is the potential (V) and \( \sigma \) is the conductivity (S/m), which is a constant for a given type of tissue. As in [17-19], the second derivative of the electrical potential distribution in the direction perpendicular to the electrode contact is used to define the activation threshold of the tissue around the electrode, which is needed for determining the VTA. In addition, the interpolation function used in FEA can be computed as [18]:

\[ E' = 22.7e^{-Xa}y + 4.3 \]  

(2)

where \( X \) is the product of the stimulation voltage potential (V) and the pulse width (\( \mu s \)). According to [18], the region of the VTA that is presented in the 2D spatial contours is similar to an ellipse, which is formulated as:

\[ \frac{(x - x_0)^2}{a^2} + \frac{(y - y_0)^2}{b^2} = 1 \]  

(3)

where \((x_0, y_0)\) is the center of the ellipse, and \(a\) and \(b\) are the semi-major and -minor axes, respectively.

**2.1.3 Simulation parameters for estimating VTA**

Electricity-related parameters based on [2,3,31] were adopted for VTA estimation, as listed in Table 1. Prior to obtaining the region of the VTA, Laplace’s equation, which follows the full set of Maxwell’s equations for electromagnetics under the condition that all of the time derivatives are zero, was used to compute the electrical potential distribution [2]. The Dirichlet boundary condition (\( V = 0 \)) was set on the sides of the brain tissue. The non-active electrode contact was set as continuity, namely \( \nabla \cdot V = 0 \), and the insulating surfaces were treated as electrically insulated. In addition, the second derivative of the electrical potential distribution in the direction perpendicular to the electrode contact was simulated with COMSOL Multiphysics 3.5 (Comsol Inc., Stockholm, Sweden) [17-19].

**Table 1. Tissue properties.**

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Definition</th>
<th>Value (Ref.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \sigma_t )</td>
<td>Electrical conductivity of brain tissue</td>
<td>0.2 S/m ([2,3])</td>
</tr>
<tr>
<td>( \sigma_i )</td>
<td>Conductivity of insulation portion of lead</td>
<td>( 10^{-9} ) S/m ([27])</td>
</tr>
<tr>
<td>( \sigma_e )</td>
<td>Conductivity of electrode portion of lead</td>
<td>( 4 \times 10^{-5} ) S/m ([27])</td>
</tr>
<tr>
<td>( \sigma_p )</td>
<td>Conductivity of peri-electrode space</td>
<td>0.125 S/m ([2,3])</td>
</tr>
</tbody>
</table>

**2.2 3D image construction**

To estimate the VTA within the STN, a 3D individualized patient physiological model, shown in Fig. 3, was first established. This model was constructed from post-operative magnetic resonance imaging (MRI) data and prior known physiological knowledge, including the location and boundary of the STN. In addition, the prior- and post-operation MRI data were compared to remove image artifacts due to the presence of the lead in the post-operation MRI. The subjective and manual illustration of the STN inherently has a bias. To ensure adequate accuracy of the lead position, the doctors utilized microelectrode recording for confirmation. The medical software package Mimics (Materialise NV, Leuven, Belgium) was used to construct the segmentation of the MRI data based on the projection theorem, during which a set of MRI slides were imported, and their geometry was displayed on three planes: short axis, sagittal, and coronal.

**Figure 3. Patient-specific brain model construction.**

(a) Segmentation of MRI data, (b) probe with electrodes (model 3389) with STN marked, and (c) patient-specific brain model reconstructed as a three-dimensional model.

The images for targeting were obtained from a 1.5-T MRI unit (General Electric). The standard settings included T1-weighted axial images (TR: 26 ms, TE: 6.9 ms, matrix size: 256 × 192, thickness: 0.7 mm) and T2-weighted axial images (TR: 4800 ms, TE: 95 ms, matrix size: 256 × 192, thickness: 2.0 mm). Each of these sequences was performed on contiguous slices. The estimated VTA was superimposed upon the patient physiological model to identify the stimulation region during DBS. To avoid neuropsychiatric side effects, the doctor can modify the stimulation region within the STN and minimize the perturbation of the limbic circuit by selecting optimal electrode contact(s) during clinical practice.

**2.3 Curve fitting**

To reduce power consumption, the relationship between the stimulation parameters and VTA was formulated based on
clinical trials and the BEI model. Variation in the stimulation parameters leads to a change in the size of the VTA, which is represented by an ellipse, with a and b representing the lengths of the semi-major and -minor axes, respectively. Because the brain medium is viewed as homogeneous and isotropic, i.e., the region of the VTA is axisymmetric, half of the region of the VTA was considered, with a and 2b as the variables (given below). By applying curve fitting to derive a linear regression model with the stimulation parameters (voltage and pulse width) as independent variables and a and 2b as response variables, the response variables were formulated as follows:

\[ a = f_1(x_v, x_{PW}) \]  
\[ 2b = f_2(x_v, x_{PW}) \]  

where \( x_v \) and \( x_{PW} \) are the stimulation voltage and the pulse width, respectively.

2.4 Nonlinear programming for optimization

With the regression model, the VTA can be predicted using the stimulation voltage and pulse width, which can be tuned by doctors during clinical trials. In a clinical setting, physicians tune the stimulation parameters depending on the subjective response and the objective examination of patients during DBS therapy [7]. During the adjustment process, selecting the most suitable stimulation parameters for the maximum symptom amelioration of PD is the ultimate goal [32]. To maintain a given level of improvement, the VTA size should not be altered. To find the optimal stimulation voltage and pulse width that minimize power consumption during DBS under the constraint of maintaining a given VTA size, the problem is formulated as a nonlinear programming problem. Let \( P \) be the power consumption of the stimulators during DBS [32,33]:

\[ P = \frac{V^2 \times F \times PW}{Z}. \]  

where \( Z \) is the impedance to be measured by a commercially available DBS programming device (N’Vision Clinician Programmer, Medtronic Inc.), \( V \) is the stimulation voltage level, \( F \) is the frequency of the stimulation waveform, and \( PW \) is the pulse width. Several studies reported that the effect of the stimulation frequency on the VTA size is insignificant [2,18]. Thus, the frequency is set to a constant value of 130 Hz, which is often used in clinical trials [33]. With a fixed frequency, the capacitance and consequently the impedance of the BEI are influenced by the pulse width and can be modeled as a function of pulse width [34]. Because the value of the impedance varied within 50 \( \Omega \) as the pulse width ranged from 60 to 90 (\( \mu s \)) during the experiments, the variation of the pulse width affected the calculation of power consumption only slightly.

To minimize \( P \) subject to the region of the VTA, the problem is formulated as:

\[ J = \min P = \min \left( \frac{V^2 \times F \times PW}{Z} \right). \]  

which is subject to Eqs. (4) and (5). This nonlinear programming problem was subsequently solved using the built-in function fmincon in MATLAB (The MathWorks Inc., Natick, MA, USA).

2.5 Clinical evaluation and model parameter verification

Five PD patients undergoing DBS surgery (1 female and 4 males, ages 67 \( \pm \) 8) were recruited. All patients signed informed consent forms for STN-DBS surgery, the procedures involved in the study, and scientific publication of contents and results. The evaluation procedures in the study were carried out with the ethical approval of the institutional review board (Tzu Chi General Hospital, Hualien, Taiwan) and in compliance with the Helsinki Declaration. The inclusion criteria were as follows: (1) good levodopa response on the UPDRS part III (\( > \) 30\%), (2) drug-related complications (e.g., dyskinesia and “on-off phenomenon”), even under optimal anti-parkinsonian medication adjustment, (3) no structural lesions in the brain MRI, and (4) absence of dementia. The severities of the motor symptoms of PD (UPDRS part III) were evaluated 1 month prior to surgery and also 3 months after surgery. An acute stimulation test was performed 1 week after operation to identify the optimal contact (among four electrodes) with good motor benefit and avoid neuropsychological effects (such as facial twitching or depression) for chronic stimulation. The test items included speech, facial expression, tremor at rest, action tremor, rigidity, finger taps, hand movements, hand pronation, supination, leg agility, arising from a chair, posture stability, and body bradykinesia [7,35]. Each measurement was scored on a 5-point scale (range of 0-4) with higher scores indicating more severe symptoms. The total UPDRS motor scores were 19 \( \pm \) 9 with DBS ON. In addition, neuropsychiatric side effects were monitored with clinical recording of a patient’s instant neuropsychological feedback. Scales were not used to quantify the non-motor outcomes [10].

Patients whose post-operative status remained stable for at least 6 months underwent the experiment with the proposed DBS parameter adjustment again. Note that the UPDRS ratings were single-blinded. The UPDRS motor scores were retested after DBS device with the new parameters had worked more than one hour to eliminate the delayed effect of stimulation.

3. Results

The stimulation parameters were optimized to allow the VTA to be within the targeted regions to avoid neuropsychiatric side effects and to minimize power consumption. First, to avoid side effects, the estimated VTA was incorporated into a patient physiological brain model. Then, to quantify the relationship between the stimulation parameters (stimulation voltage and pulse width) and the size of the VTA, a regression model was constructed. The optimization method was used to find suitable stimulation voltage and pulse width, which would maintain a proper VTA and lead to lower power consumption.
3.1 Estimated VTA

In simulations of the VTA, the DBS parameters were chosen to be voltage (-1.5 V), pulse width (90 μs), and frequency (130 Hz) at electrode contact 1. The electrical potential distribution was simulated based on Eq. (1). The second derivative of the electrical potential distribution in the direction perpendicular to the electrode contact was utilized to define the VTA. Via Eq. (2), the activation threshold value (Vth = 5.9) was obtained with a stimulation voltage of -1.5 V and a pulse width of 90 μs. When the ellipse was fitted to the VTA in Fig. 4(a), which is described in Eq. (3), a was determined as the distance from the electrode contact to the VTA boundary in the direction perpendicular to the electrode contact, and 2b was determined as the distance within the VTA boundary in the direction parallel to the electrode contact. For this case (voltage: -1.5 V, pulse width: 90 μs, and frequency: 130 Hz), a and 2b were found to be 2.315 and 1.770 mm, respectively.

![Figure 4](image)

Figure 4. (a) VTA region estimated via BEI model for 3389 DBS lead. (b) STN (brown) with electrodes implanted and VTA (red).

The estimated VTA was subsequently incorporated into the MRI patient-specific physiological model. Note that the patients had two-sided-STN DBS in clinical trials, i.e., they had one DBS lead in each side of the STN. The right-sided-STN DBS is considered here because the stimulation parameters of each DBS lead implanted into the STN can be adjusted independently. The simulated VTA via FEA and the surrounding STN are shown in Fig. 4(b). Figure 4(b) shows that the simulated VTA overlapped with the limbic sub-territory in the STN, explaining why the patient experienced a psychiatric problem after DBS. This finding demonstrates that the BEI and patient-specific physiological models are effective for evaluating whether side effects occurred during stimulation, thereby providing valuable information for the selection of optimal electrode contacts.

3.2 Relationship between VTA and stimulation parameters

To investigate how the stimulation voltage affects the size of the VTA, the stimulation voltage was set in the range of -1 to -5 V with a step size of -0.25 V, and the pulse width was set in the range of 60 to 210 μs with a step size of 30 μs. Figures 5(a) and 5(b) show the resultant size of the VTA represented by a and b (for the semi-major and -minor axes of the ellipse, respectively) versus the stimulation voltage. It was found that higher stimulation voltages and wider pulse widths resulted in larger VTAs. Additionally, a was more sensitive to variations in the stimulation voltage than was b.

![Figure 5](image)

Figure 5. Relationship between the stimulation voltage and the size of VTA for (a) semi-major and (b) semi-minor axes of ellipse.

To quantify the relationship between the stimulation parameters (stimulation voltage and pulse width) and the size of the VTA, curve fitting that minimizes the squared error was used to obtain the following linear regression model:

\[
a = -0.397 + 1.372x_v + 0.013x_{vw} - 0.129x_v^2 - 3.032 \times 10^3 x_{vw}^2
\]  
\[
b = 0.936 + 0.496x_v + 0.0001x_{vw} - 0.006x_v^2 - 1.736 \times 10^6 x_{vw}^2
\]

where \(x_v\) and \(x_{vw}\) are the stimulation voltage and the pulse width, respectively. The \(R^2\) values for the model fit were 0.97 and 0.98 for Eqs. (8) and (9), respectively.

3.3 Optimal stimulation voltage and pulse width

To extend the life of the stimulator battery, the relationship between the stimulation voltage, pulse width, and battery power loss was explored. Equation (6) was used to compute battery power consumption, and Eqs. (7)-(9) were used for its minimization. When a and 2b were 2.315 and 1.77 mm, respectively, the minimum power (34.65 μW) was obtained with a stimulation voltage of 1.1 V and a pulse width of 152 μs. Compared with the original DBS (-1.5 V, 90 μs, and 130 Hz), which consumes 38.15 μW, a 9% reduction in power consumption was achieved for this case, which was estimated to prolong the lifetime of the stimulator by approximately 4-7 (47×9% - 83×9%) months.
Table 2. Power consumption of stimulator battery obtained from trials.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Clinical settings</th>
<th>Model-derived settings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Voltage (V)</td>
<td>Pulse width (μs)</td>
</tr>
<tr>
<td>1</td>
<td>-4.4</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>-3.7</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>-3.8</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>-4.2</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>-4.0</td>
<td>60</td>
</tr>
</tbody>
</table>

To estimate the average reduction in power consumption, various stimulation voltages and pulse widths were used. Figure 6 shows the power consumption for various combinations of stimulation voltage and pulse width, and Fig. 7 shows that obtained with the stimulation voltage and pulse width altered from the initial values via the optimization procedure. Note that power consumption is formulated as a nonlinear function of stimulation voltage due to the voltage-doublers in the implantable pulse generator (IPG). The estimates of power savings for various combinations of stimulation voltage and pulse width are shown in Fig. 8. In Figs. 6 and 7, power reduction increases for larger voltages and wider pulse widths. It has been reported that PD symptoms are well suppressed when the stimulation pulse width is between 60 and 90 μs [28,29]. Figure 8 shows an average reduction in power consumption of 15% when the stimulation pulse width is between 60 and 90 μs. These results indicate that the proposed method efficiently suppresses PD symptoms while prolonging the lifetime of the stimulator by approximately 7-12 (47 × 15% - 83 × 15%) months.

3.4 In Vivo test results

Table 2 lists UPDRS motor scores (part III) for each patient during clinical and modeled DBS. For all of the patients, there was no significant UPDRS difference between the clinical and model-derived stimulation voltages and pulse widths (Wilcoxon rank-sum test, \( P = 0.89 \) with 0.05 considered statistically significant). The power consumption reduction of each patient after stimulation parameter adjustment was 13, 26, 26, 0, 0%, respectively. This observation of UPDRS (III) implies that the estimated region of the VTA was maintained, and power consumption at the optimal stimulation voltage and pulse width compared to that at the clinical settings was decreased by approximately 13% on average. The electrode configurations of each patient were mono-polar, with the cathodes on electrode contacts 2, 1, 3, 1, and 3, respectively, and the anodes on the IPG. For all patients, the electrode configurations were the same before and after stimulation parameter adjustment. Note that none of the patients suffered from neuropsychiatric side effects after stimulation parameter adjustment.

Figure 6. Power distribution with stimulation voltage set in the range of -1 to -5 V with step size of -0.25 V, pulse with set in the range of 60 to 210 μs with step size of 30 μs, and a fixed frequency of 130 Hz.

Figure 7. Power distribution with the stimulation voltage and the pulse width as altered from initial values by the optimization procedure based on the proposed scheme.

Figure 8. Estimates of power savings with stimulation voltage set in the range of -1 to -5 V with step size of -0.25 V, pulse with set in the range of 60 to 210 μs with step size of 30 μs, and a fixed frequency of 130 Hz.
4. Discussion

A patient-specific DBS model was established here to simulate current STN-DBS in PD and to attempt to elucidate the underpinning of the DBS mechanism by quantifying the stimulation effect. Since the calculation of the estimated VTA is independent of lead geometries and IPGs for voltage-controlled stimulation, the proposed approach would work with other lead geometries (such as Medtronic 3387) and other IPGs, but only for voltage-controlled stimulation. The biophysical characteristics of the brain are anticipated to be heterogeneous and anisotropic due to its complexity. Nonetheless, our assumption that the consistency is homogeneous at the location at which the brain surrounds a stimulating electrode was shown to provide correct predictions of the patient’s clinical response to different electrical parameters. Furthermore, the proposed scheme for stimulation parameter adjustment allows us to adjust different combinations of stimulations that are tailored to individual patients with DBS. Although the simulation results demonstrate the effectiveness of the proposed scheme, several issues deserve further discussion.

4.1 Side effects and reduction in power consumption

This study provides an alternative and scientific way to maximize DBS benefits and to prolong battery life. Ever since STN-DBS started to relieve PD patients’ symptoms, three parameters, specifically, the voltage, the pulse width, and the frequency, have been additional types of combinations in addition to the dopaminergic medications. Most clinicians rely on their intuition and experience to adjust these parameters. In clinical practice, neuropsychiatric side effects are monitored with clinical recording of a patient’s instant neuropsychological feedback, with no scales used to quantify non-motor outcomes. Our DBS model settings, which are selected according to the VTA within the STN, can limit current spread and minimize the perturbation of the limbic circuit [10]. Guidelines and reviews have suggested a range of settings for mitigating motor symptoms. Details of the neuropsychiatric side effects including the limbic circuit can also be found in the previous study [10]. The responses from individual patients vary, and unintentional psychological results still occur, even if the DBS electrode appears to be within target as obtained from imaging, such as with MRI [9].

Medtronic’s Soleta Model 7426 and Itrel II Model 7424, two commercially available stimulation devices, have 25480 stimulation parameter combinations each [26]. In clinical practice, the stimulation voltage, pulse width, and frequency have ranges of 1-4.0 V, 60-90 µs, and 90-170 Hz, respectively, for optimal motor control for PD [28,29]. DBS settings can have hundreds of combinations, making it impractical to perform trial-and-error adjustments for each patient. Given the limited sample sizes of this result for the current study, optimal stimulation parameters can be distilled by preliminaries. More patients will be considered in the next stage which can provide more information to reinforce the proposed methodology and further to achieve the required clinical efficacy and energy efficiency. Our preliminary findings show that the proposed simulation scheme can maintain DBS clinical benefits and prolong battery life while avoiding neuropsychological side effects by limiting the VTA within the motor STN.

For a heterogeneous real-life situation of brain tissue, a patient-specific accurate prediction of VTA would require the use of a more refined model that incorporates a realistic tissue conductivity distribution. Through this systematic approach to setting or adjusting the stimulation parameters, we can accurately simulate STN-DBS in PD with lower power consumption and provide DBS clinical benefits. DBS treatment has been used to treat movement disorders and psychiatric diseases (e.g., depression and obsessive compulsive disorders), and thus the application of patient-specific modeling treatments could also be extended to other pathological diseases.

4.2 Model limitations

Our study provides preliminary and encouraging results, but there are several limitations. First, the model parameters were tested on only five patients. In clinical practice, few patients were willing to participate in the trial because they had to spend more time to adapt to these new stimulation parameters and be tested using UPDRS motor scores (part III). Therefore, the diversity of the patients with respect to the disease severity, for example, was limited. A larger group of patients need to be included to verify and refine the modeling methods. Second, the MRI advancement has improved the resolution of brain structures. However, subjective and manual illustration of the STN was still required in our 1.5-T MRI, which inherently has a bias. A higher Tesla MRI might mitigate this user-dependent definition of the STN border. Third, the stimulation waveform affects the neural response to DBS [36]. In addition, the active electrode pulse magnitudes are substantially smaller than the programmed stimulation values. Moreover, the stimulation waveform also affects the amount of power. This study focused on stimulation parameter adjustment for power saving for a given IPG (Soleta). In future studies, the effects of a realistic stimulation waveform will be taken into consideration. Finally, most of the underlying DBS mechanisms remain elusive. Even if our proposed model paradigm takes both the STN topography and VTA of the DBS into consideration, its application in clinical practices could become more reliable with reproducible results when the therapeutic mechanism of DBS is clearly demonstrated.

5. Conclusion

A computational optimization scheme was proposed for adjusting the stimulation parameters in DBS for avoiding neuropsychiatric side effects and minimizing power consumption. A patient-specific physiological brain model was constructed from MRI data and the VTA was estimated based on the BEI model. Based on the estimated VTA, optimal electrode contact(s) were selected to avoid side effects. Furthermore, nonlinear programming was used for optimizing the stimulation voltage and pulse width to minimize power consumption in DBS. In vivo experimental results show that the levels of
symptom suppression were maintained for patients with a power consumption reduction of approximately 13% on average. This reduction is evident for long-term stimulation as a treatment of PD. Moreover, the proposed methodology also provides valuable information for closed-loop stimulation protocols in DBS. In future studies, the proposed scheme will be extensively applied in clinical trials to further improve the BEM and patient-specific physiological models.

Acknowledgments

The authors would like to thank Dr. Shin-Yuan Chen and Dr. Sheng-Tzung Tsai in the Department of Neurosurgery, Division of Functional Neuroscience, at Tzu-Chi General Hospital for helpful discussions and providing clinical data and Prof. Ta-Wei Ting of Yuan-Pei University for providing assistance with the medical software package Mimics.

References


[16] Direct correspondence with Dr. Sheng-Tzung Tsai, Department of Neurosurgery, Division of Functional Neuroscience, Tzu-Chi General Hospital, Hualien 970, Taiwan, August 13, 2012.


