Optical Stimulation of Primary Motor Cortex with 980nm Infrared Neural Stimulation

Man Q. Wang, Qing L. Xia, Xiao Y. Wu, Xing Wang, Xiao L. Zheng, Wen S. Hou

***Abstract*- To explore the penetration depth with short-wavelength infrared light, 980nm pulse infrared light was used to stimulate the primary motor cortex of rat. The heating model was created to simulate the temperature distribution for 1875nm and 980nm infrared neural stimulation. Post-stimulus time histogram was used to observe the neural response induced by Infrared neural stimulation on primary motor cortex. The model predicted the penetration depth of 980nm was deep into 1.2mm. Cortical neural located between 500μm to 1000μm were successfully activated by 980nm INS. The preliminary results suggested that, 980nm pulse INS could serve as a candidate for deep tissue stimulation.**

I. Introduction

Infrared neural stimulation (INS) has been proposed as a novel way to modulate the neural activities based on the photothermal effect of infrared energy in neural tissue, in which the pulsed infrared light was absorbed to build a temperature gradient [1]. In the latest studies, INS was widely used to stimulate the sciatic nerve [2]-[5], facial nerve [6], auditory nerves [7]-[8], somatosensory cortex [9], and even primary visual cortex [11] without contact. Currently, the infrared with wavelengths ranged from 1.8 μm to 2.2 μm was selected due to the high absorption coefficient of water. However, the absorption coefficient is inversely proportional to the penetration depth, and the latest experiment showed that pulsed infrared of 1875nm was limited to stimulate the cortex of 300-600 μ m depth [9][10]. By contrast, the short-wavelength infrared light is a candidate as greater penetrability because of the lower absorption coefficient, and has been affirmed in functional near-infrared neuroimaging [11], however, there is very few studies on the INS with short-wavelength infrared. So, in this study, we investigated whether neurons located from 200 μ m to 1200 μ m (layer Ⅰ to layer Ⅵ) can be stimulated with the 980-nm infrared.

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II. Materials and Methods

A. The Heating Model

To model how the temperature distributed in neural tissue during INS, a brain model was created by using COMSOL multiphysics software (COMSOL Multiphysics, 2013, version 4.3a, Stockholm, Sweden). First we built a 2D model in cylindrical coordinates (Fig.1), and rotated the model along z-axis to obtain a 3D model then. Referred to the literature [12], the model has a two-layered slab which consists of the cerebrospinal fluid layer (CSF) and Gray matter layer (GM) (see Fig.1). Using this model, the temperature distribution induced by 1875nm and 980nm INS was calculated respectively, and the infrared induced temperature profiles were evaluated in GM layer. Some important parameters used in this model were summarized in table 1.

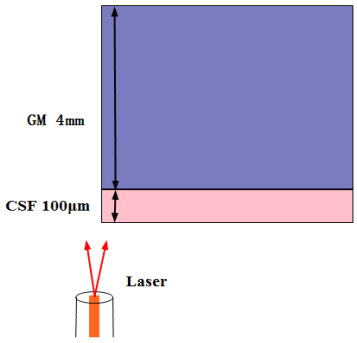

Fig.1 The 2D simulation model of cortex for INS

Table 1 Thermal parameters of the material in the model [13] - [15].

	CSF	GM
δ (W/(m.K))	0.64	0.5
ρ (Kg/m3)	1000	1080
C (J/(g.degC))	3.85	3.85
ω_b(1/s)	0	3.6e-3
Q_{met} (W/m3)	0	368.1
$\mu_{a1875nm}$ (1/m)	2650	3000
$\mu_{a980\text{-}nm}$(1/m)	46	60
μ_s(1/m)	240	1000

δ: thermal conductivity, ρ: density, C: specific heat, ω_b: the blood perfusion, Q_{met}: metabolic heat, μ_a: absorption coefficient, μ_s: scattering coefficients.

B. Surgical Procedure

The procedures performed in our study were conducted in accordance with the "Laboratory Animal Management

Regulations" instituted by the State Science and Technology Commission. Spraque- Dawley rats (180g-200g) used in the study were initially anesthetized with intraperitoneal injection of urethane solution (1.2 g/kg). The animal was fixed in a stereotactic frame and a craniotomy and durotomy were conducted to expose primary motor cortex (1-3mm anterior to the bregma and 2-4mm lateral to the midline) [16]. Saline (5%) was used to avoid the cortex desiccating and body temperature was maintained at approximately 38°C throughout the experiments.

C. Optical Stimulation

980nm LED infrared (Associated Opto-Electronics Corp., Chongqing, China) was used to irradiate the exposed primary motor cortex of SD rat. The infrared light was delivered to the cortex through a silica optical fiber, which was with a numerical aperture (NA) of 0.22 and the core diameter of 105μm. The fiber was pointed to durotomy window, and the fiber tip was placed above 700-1000μm from the cortex surface. Trained infrared pulse was used for INS, which was controlled by constant current source (AB2D6B, Changchun New Industries, Changchun, China) and LabVIEW software and National Instruments hardware (Fig. 2). The single pulse width was 250μs and the repetition rate was 200Hz. The infrared pulse train last for 500ms and a 4.5-second rest interval was assigned between two infrared pulse trains. Each trail lasted 125s. The radiant exposure varied between 1.45 and 1.81 J/cm^2.

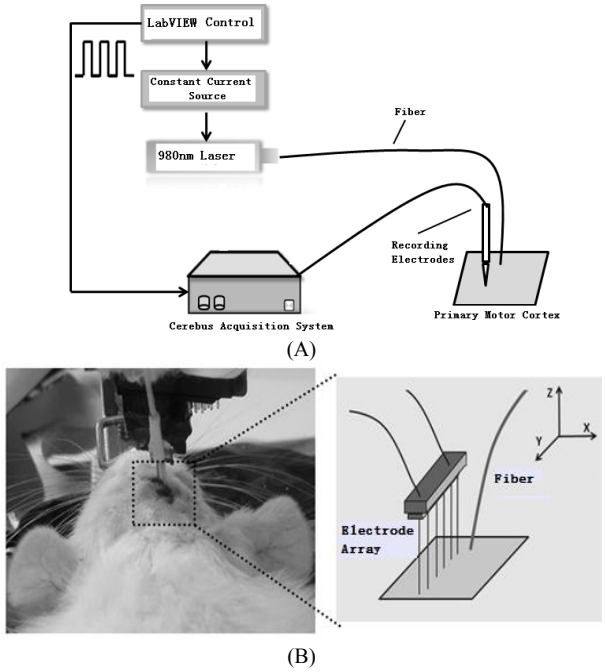

Fig. 2 Conceptual illustration (A) and experiment scene (B) of the 980nm optical stimulation and its neural response recording in primary motor cortex.

D. Electrophysiological recordings

The single unit response to infrared neural stimulation were recorded with a nicochrome electrode array (1-3MΩ, Global Biotech INC., China) inserted into cortex at depth of 500-1000μm corresponds to the layers Ⅲ-Ⅴ. The electrodes was placed 1mm away from the fiber optic, and the angle between the electrodes and fiber was fixed to 20° to avoid aiming the laser directly at the electrodes. A multichannel physiological signal acquisition system, Cerebus (Cerebus 6.01, Blackrock Microsystems, USA) was employed for spike recording with a passband of 250-5000Hz and sampled rate of 30 kHz. The synchronization signal of the optical stimulus was collected for off-line data analysis.

E. Electrophysiological analysis

To examine whether the 980nm INS has effect on the neuronal firing rate, we divided every trails into sequential 25 segments, and every segment consisted of 1-second pre-stimulation, 500-ms infrared stimulation and 3.5-second post-stimulation. By visual inspection, the artifact was eliminated due to its waveform differed from neural spike caused by laser pulses. And then a Post-stimulus time histogram (PSTH; 50ms bin width) was generated by averaging the firing rate of 25 segments for each trail. All data were analyzed offline in Matlab R2009a (7.8.0.347，MathWorks, USA). A paired t- test was used to determine the significance of spike rate observed in the PSTH related to infrared pulse train (SPSS statistics 19, IBM, USA). The statistical testing was performed with a significance level of p=0.05.

III. Results and Discussion

A. The heating model

To simplify the calculations we only consider the single pulse irradiation. Fig.3 showed the temperature distribution along the fiber axis in the cortex, in which the temperature decreased with the depth increment in cortex tissue. In accordance with reports from Thompson [17], the 1875nm INS induced temperature decreased very quickly when depth increased, however, the temperature of 980nm INS decreased slowly. Cayce et al [9] reported that 1875nm INS can penetrate 300-600μm into somatosensory cortex, where the temperature changed from 0.53℃to 0.16℃ in our simulation result (Fig.3). Then, if the 0.16℃can be considered as a temperature threshold for effective INS, the 980-nm INS can reach the threshold 0.16℃ around 1.27mm depth in M1 tissue. Based on the above statements, we can speculate that 980nm can effect on the deeper layers of cortex, which resulted from the temperature decreased more gently with increasing depth than 1875nm INS.

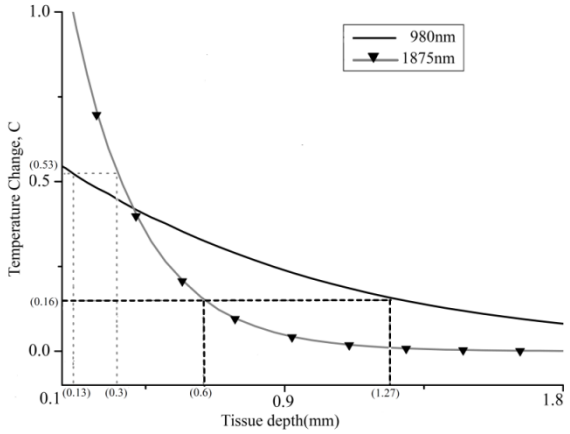

Fig.3 Simulation results. temperature changed from 0.53℃ to 0.16℃ in the depth of 300- 600μm induced by 1875nm INS(pulse duration:250μs, power:2.76.W), correspondingly, 980nm INS (pulse duration:250μs, power:7W) can penetrate into the depth from 130μm to 1.27mm.

B. Neural response to INS

To verify the hypothesis whether 980nm infrared pulse can evoke neural response in the deeper cortex layers which was predicted by the model (Fig. 3). We recorded single unit firing across five rats. For each rat, neural spikes was recorded in shallow layers (500-600 μ m) and deep layer (800-1000 μ m), respectively. The population average PSTH response in different depths was shown in Fig.4.

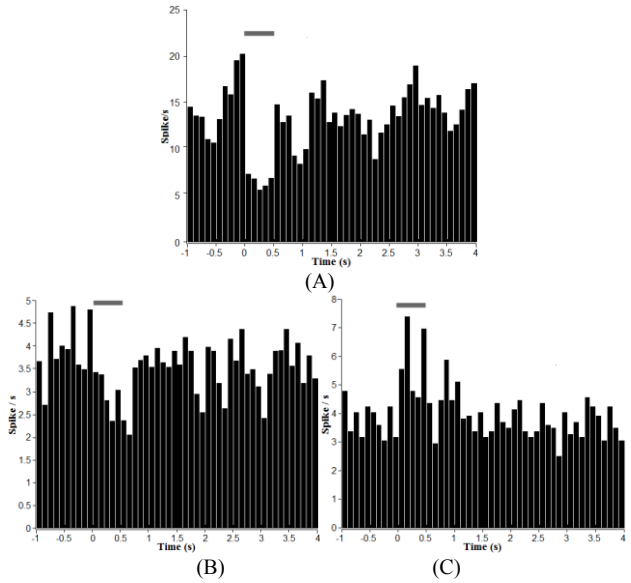

Fig.4 The PSTH summation of trails. Inhibition response in shallow layers (500-600 μ m)(A) and in deep layers (800-1000 μ m)(B), part of trails show excitation effect of INS in deep layers (C).

As illustrated in Fig.4 A, the 980-nm INS decreased neural activities in shallow layer (500-600 μ m) of M1, and the mean neural firing rate during INS was significant lower than that of pre–stimulation in most of trails (9/12) ($p<0.05$). Interestingly, 9/18 trails showed inhibited neural activity in deep layer (800-1000 μ m) (see Fig.4 B), however, INS increased neural firing sometimes (4/18 trails) (see Fig.4 C).

IV. CONCLUSION

The present work is to explore whether the 980nm INS has effect on the neuronal firing rate in the primary motor cortex of rats. Simulation suggested that 980nm may be able to evoke response of neurons deep into approximate 1.2mm in the primary motor cortex. By detecting the neural spike at the depth about 600 μ m, the results showed that INS induced an inhibitory effect in shallow layer, while both inhibitory and excitatory effects were observed in the deep layer. Shapiro et al. [18] recently reported that the photothermal effect of INS resulted in a change in the electrical capacitance of cell membrane, which can lead to depolarization of neurons. Then, the evoked excitatory responses can be recorded if excitatory neurons being depolarized; if the inhibitory neurons were activated, the pyramidal neurons would be suppressed, and decreased spikes can be observed in the central nervous system [9]. In our experiment, the infrared light penetrated into the primary motor cortex where both excitatory and inhibitory neurons coexisted [19]. The capacitance of both types of cells may alter and depolarize during a transient temperature raise. And then, depolarization of excitatory neurons would produce more spikes, whereas depolarized inhibitory neurons would depress the neural activation and firing rate would be degraded.

On other hand, previous researches suggest that the INS can promote the activation level of inhibitory neurons when INS-induced temperature increases in central neural tissues. Feng et al. reported that the temperature increment of infrared irradiation enhanced the release of GABAergic in the cultured cortical neurons; the raised GABAergic facilitated the spontaneous inhibitory postsynaptic currents and caused inhibitory response thereafter [20]. In our studies, the infrared pulse induced temperature rise significantly in the shallow layer of primary motor cortex, which may led to more release of GABAergic and marked inhibitory response. Then, the neural spikes would be depressed, which was similar to the previous reports [9]. However, the temperature induced by INS decreased quickly when the depth increased in primary motor cortex tissue, and INS-induced temperature field did not affect the GABAergic activities in deeper layer of primary motor cortex; then, the 980-nm INS only induced weak inhibitory effect around 800-1000 μ m depth. Moreover, previous experiments electrical stimulation of primary motor cortex demonstrated that enhanced stimulation intensity frequently recruited the synaptically interconnected network and transmitted inhibition [19]. In our studies, due to the absorption and scatter of infrared light in neural tissue, the photothermal energy in the deep layer was weaker than that in the shallow layer. The inhibitory networks could not be activated easily in deeper layer, and INS just induced slight inhibitory effect accordingly.

In this work, we found INS may induce different response in the central neural system. However, due to the limited power level of the used light source and the diameter size of

fiber, verification of the effect of stimulation parameters was not performed. So, further work is needed to study the mechanism of excitation and inhibition neural responses induced by INS, and construct optimal INS model for cortex stimulation.

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