A network model of inhibitory effect induced by transcranial magnetic stimulation

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Abstract

We studied inhibitory effects of transcranial magnetic stimulation (TMS) on neural population. TMS can affect the electromagnetic activities inside our brain with high temporal resolution and without any invasions. Due to these advantages, TMS is widely used as a powerful tool not only in cognitive neuroscience field but also as a clinical treatment. However, the neural mechanisms underlying the effect, especially in theoretical aspect, are quite unclear. In this study, we employed a simple neural population model and computationally analyzed their responses to a TMS-like brief pulsed perturbation. Aplying the perturbation, the averaged network activity transiently increased, and then decreased for relatively long lasting period followed by loss of a localized activity pattern. When afferent input has a strong transient component and weak sustained component, there exists a critical latency period in which the perturbation completely suppresses the network activity. These results suggest that inhibitory effects typically observed in TMS studies can be yielded by dynamical interaction in neural population.

Key words: Transcranial magnetic stimulation; Inhibitory effect; Network model; Perturbation

1 Introduction

TMS is a stimulator of the human brain by a brief magnetic pulse yielded by the coil placed on the scalp. TMS can stimulate our neurons in completely noninvasive way with high accuracy in temporal domain. Due to these outstanding characteristics, TMS has been widely used in experimental researches of human functions, such as motor, memory, and perception.

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Typically, TMS causes inhibitory effects on those functions, e.g. TMS applied to motor area suppresses EMG, and that applied to visual cortex created visual field deficit contralateral to the stimulated site. However, the neural substrates underlying these inhibitory effects are totally unknown.

Several biophysical studies have demonstrated the spike generation by magnetic stimulation on a long straight axon model[10]. Recently, biophysical modeling were conducted to address the cortical stimulation. Nagarajan showed the spike generation in finite cable model[9], and Kamitani demonstrated the long inhibitory period after the initial burst firing in realistic compartmental models of neocortical neurons[7].

These all studies are based on the external magnetic field effects on a single cellular level. In real situation, however, spatial extent of magnetic field induced by a TMS coil is so large compared to dimension of a single neuron that large number of neurons should be stimulated simultaneously in the region close to the coil. Therefore, in addition to the analysis of an isolated single neuron, it is necessary to take into account the effect onto the neural population and analyze the time course of their activities through their dynamical interactions.

One of the key issues to be considered in population level is how the optimal timing of TMS to cause a suppressive effect is generated. Most of the past TMS studies except repetitive stimulation demonstrated that there is a certain period in order to cause a suppressive effect by TMS. It is quite conceivable that this temporal relationship between stimulus onset and TMS is determined by the dynamical state of neural population after the afferent input.

In this paper, we employ a simple analog neural network model with lateral inhibitory connections and quasi-linear output function, and analyze the response of the network to a TMS-like brief pulsed perturbation, especially focusing on the optimal timing and the effective range of the perturbation to suppress the network activity.

2 Methods

We employed a simple analog neural network model (Eq.1–4) that is well analyzed as a model for a sensory feature detector system. Details of this model are described in the literatures [4][5].

$$\tau_m \frac{d}{dt} m(\theta, t) = -m(\theta, t) + g[h(\theta, t)] \tag{1}$$

$$h(\theta,t) = \frac{1}{\pi}\int_{-\pi/2}^{\pi/2} J(\theta-\theta')m(\theta',t)d\theta' + h_{ext}(\theta,t) \tag{2}$$

$$J(\theta-\theta') = -J_0 + J_2\cos 2(\theta-\theta') \tag{3}$$

$$h_{ext}(\theta,t) = c(t)[1-\epsilon+\epsilon\cos 2\theta] \tag{4}$$

$m(\theta,t)$ is the output of neuron θ and $g[f]$ is the quasi-linear output function that is inactivated if $f < T$(T:threshold) and saturated if $f > T + 1/\beta$, and it works as $\beta(h-T)$ between them. $h(\theta,t)$ denotes the input to the neuron θ. Generally, integral range is defined by the extent of connections of neuron θ. Here, for simplicity, we assume that $m(\theta,t)$ has a periodic boundary condition ($-\pi/2 \le \theta \le \pi/2$), so that connections among each neurons are limited in this periodic range. Afferent input, denoted by $h_{ext}(\theta,t)$, has a maximal amplitude $c(t)$ at $\theta = 0$. ϵ is an afferent tuning coefficient that means how the input to the target population has been already localized ($0 \le \epsilon \le 1/2$).

Synaptic weight and afferent input have only the 0th and 2nd order fourier components, so that dynamics of $m(\theta,t)$ can be fully described by the 0th and 2nd order fourier coefficients of $m(\theta,t)$ ($m_0(t)$ and $m_{2\cos}(t)$, respectively). $m_0(t)$ is the averaged activities of the whole neurons and $m_{2\cos}(t)$ is the degree of localization of an activity profile. They are the order parameter of this network model.

Spatial extent of the neuronal population dealt here is so small that the induced electric field is almost uniform in such a limited area. Therefore, we assume that TMS perturbation would be constant for all neurons, and simply modify the input function as $\hat{h}(\theta,t) = h(\theta,t) + I_{TMS}(t)$. Because I_{TMS} is constant for all neurons regarding to specific time t, this additional term directly affect the 0th order fourier component only, and the order parameter equations can be simply modified by replacing h into $\hat{h}$. Here, we employ a rectangular input (amplitude: I_{TMS}, duration: W_{TMS}) as a TMS-like perturbation.

3 Results

In order to evaluate whether the TMS-like perturbation is effective to suppress the activity or not, we examine the final equilibrium state ($t \to \infty$). However, if the intesity of afferent input is constant ($c(t) = \text{const}$), there is only one attractor in the analog neural network we deal here. If a system has only one attractor, the final state of the system is uniquely defined by the intensity of afferent input, even though any strong perturbations are delivered.

In order to achieve a dependence on the past input, we adopt relatively higher

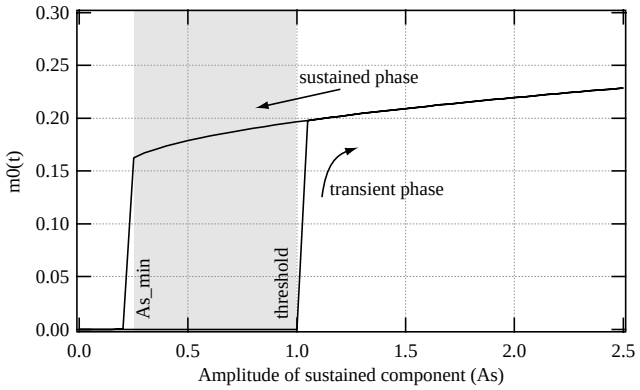

Fig. 1. Bistability embeded in the network. When the transient component is sufficiently large ($W_t = 30\tau_m$ and $A_t = 5$ for this graph), the final state is defined by the sustained component. For A_s in the gray region, the network hold the zero and non-zero attractors. The network parameters used here are, $\epsilon = 0.1, \beta = 0.25, J_0 = 73, J_2 = 110, T = 1$ (see also [4]).

β and allow the network to exibit non-linearity. In this regime, the network shows bistability of zero and non-zero attractors if an appropriate afferent input is given, and it converges to the either of them depending on the past input.

As one of the typical example of the afferent input showing bistability, we employ the simplest one that consisted of suprathreshold transient component (amplitude: $A_t > T$, duration: W_t) and subthreshold sustained component (amplitude: $A_s < T$). If the gain β is large, the network activity can still maintain even if the afferent input disappears. Here, we took the relatively small β but in non-linear range, so that minimum value of A_s showing bistability is bounded to non-zero value (Fig.1). Time course of this afferent input model is shown in the bottom of the Fig.2a. This type of time course of afferent input is commonly observed in the brain, for example, LGN and visual cortex.

The network dynamics after the afferent input in the bistable regime is illustrated in Fig.2a and Fig.2b. Because the network state is fully described by m0 and m2c, it can be depicted as a trajectory in m0-m2 plane. In the early period after the afferent input, the network goes to the attractor made by the transient component and then back to the relatively weak but stable attractor made by the sustained component, where is the final state of the network.

Applying a brief perturbation into the network, the trajectory deviates from the control condition (Fig.2b). It is shown that the final state of the network critically depends on the timing of perturbation. These two perturbations have the same intensity and duration. Only the difference is the delay from the onset of the afferent input (stimulus onset asynchrony, SOA). If the network is perturbed in the early period of transient phase, it cannot reach the non-zero

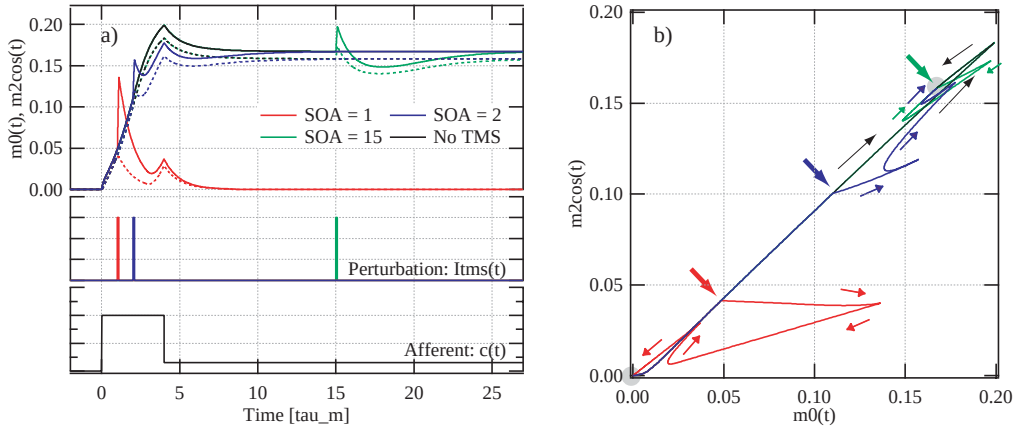

Fig. 2. The network response to a brief pulsed perturbation. a) Time course of the order parameters with the perturbation. m_0 (solid line) transiently increased and then decreased for relatively long lasting period followed by reduction of $m_{2\cos}$ (dotted line). b) The network state in m_0-$m_{2\cos}$ plane. Thin arrows indicate the direction of the state. Thick arrors indicate the onset of the perturbation. There are two attractors indicated gray disk. Depending on the timing of the perturbation, the network converges either of them. The parameters used here is, $A_t = 2, W_t = 4\tau_m, I_{TMS} = 15, W_{TMS} = 0.1\tau_m$. Other paratemers are the same as Fig.1.

state, and finally drops to the zero attractor. However, if the network is perturbed in the late period including sustained phase, the trajectory temporary turns away but it can still maintain the activity and finally converges to the non-zero attractor.

These results indicate that there must be a critical SOA range where the perturbation can completely suppresses the network activity. In addition, it is easily imagined that the susceptibility to the perturbation is not uniform in the critical period and there might be the best timing when the perturbation acts most effectively. These characteristics can be measured by the minimum intensity of the perturbation that is required to suppress the network activity in each SOA (Fig.3). The minimum requirement of the perturbation enough to suppress the activity, of course, depends on the power of the afferent input, so that the $I_{TMS_{min}}$ - SOA curves totally shifts to the upward. Even though, the profile of these curves itself have consistently basin shapes which have a bottom around SOA =0, regardless of the intensity of the transient components. Inside these basin curves, the perturbation succeeds to suppress the activity, so that the horizontal width of these basins means the length of a critical SOA range. It reaches up to 10 times of the membrane constant if the intensity of the transient component is relatively low.

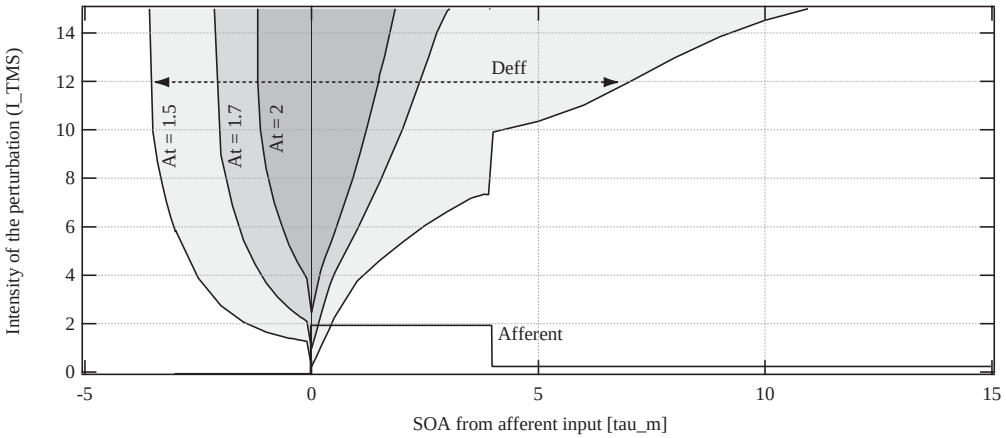

Fig. 3. The minimum intensity of the perturbation to suppress the network activity. The width of these curves is the effective range of SOA (D_{eff}). For example, in case of $A_t = 1.5$ and $I_{TMS} = 12$, the perturbation delivered within SOA from -3.5 to 7 (so that, $D_{eff} = 10.5\tau_m$) is possible to suppress the network. The parameters are the same as Fig.2.

4 Discussions

We observed the suppressive effects in the analog network model induced by a TMS-like brief perturbation. There is a critical period that the perturbation can suppress the network activity to the same level without afferent input.

Assuming that the membrane constant τ_m is 10ms, the duration of the perturbation would be 1ms. This is consistent of a typical TMS spec commercially available, including both very brief positive phase and relatively long lasting negative phase of the induced electric field. The length of the critical SOA range would be about 130ms at most. This is also consistent with typical experimental data of SOA range to cause inihibitory effects[1][6][3].

Parametric studies [8] showed that the degree of suppression depends on TMS intensity and the brightness of stimulus. In our simulation study, it was also difficult to suppress the network activity when the transient component of the afferent input is strong. Amassian said that the suppression cannot be elicited if the characters are read too easily [2]. Therefore, possibly, the afferent input to the neural population (in this case, neurons in visual cortex) might be slightly above the threshold. In our simulation, it means A_t should be limited slightly above T, and it is indeed the condition that the critical SOA range reached the large value over 100ms that is comparable to experimental data. These results suggest that inhibitory effects observed in TMS studies can be brought by interactions in neural population level.

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