A network model of inhibitory effects induced by transcranial magnetic stimulation

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Abstract

We have studied the inhibitory effects of transcranial magnetic stimulation (TMS) on a neural population. Because TMS can affect the electromagnetic activities inside our brain with high temporal resolution and noninvasively, it is widely used as a powerful tool both in the field of cognitive neuroscience and for clinical treatment. However, the neural mechanisms underlying these effects remain unclear, especially from a theoretical perspective. In our study, we employed a simple neural population model and computationally analyzed the responses to a TMS-like perturbation. When the perturbation was applied, the mean activity of the network transiently increased, and then decreased for a relatively long period followed by the loss of a localized activity pattern. When the afferent input had a strong transient component and a weak sustained component, there was a critical latency period during which the perturbation completely suppressed the network activity. These results suggest that the inhibitory effects typically observed in TMS studies can be yielded through dynamical interaction in a neural population.

Key words: TMS; Inhibitory effect; Network model; Perturbation

1 Introduction

Transcranial magnetic stimulation (TMS) can noninvasively stimulate our neurons with high temporal resolution through a brief magnetic pulse generated by a coil placed on the scalp. Because of these outstanding characteristics, TMS has been widely used in experimental research regarding human functions, such as motor, memory, and perception. Typically, TMS has inhibitory effects on those functions; for example, TMS applied to a motor area

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suppresses EMG [5], and that applied to the visual cortex creates a visual field deficit [1][6]. However, the neural substrates underlying these inhibitory effects are totally unknown.

Several biophysical studies have demonstrated the spike generation resulting from magnetic stimulation on a long straight axon model [10]. Recently, biophysical approaches were also used to examine cortical stimulation. Nagarajan described the spike generation in a finite cable model [9], and Kamitani demonstrated the long inhibitory period after the initial burst firing in realistic compartmental models of neocortical neurons [7]. All of these studies were based on the magnetic field effects on a single cellular level. In a real situation, however, the spatial extent of the magnetic field induced by a TMS coil is so large compared to the dimensions of a single neuron that a large number of neurons would be simultaneously stimulated under the coil. Therefore, we need to take into account the effect on the neural population and analyze the time course of the neural activity through their dynamical interactions.

A key issue to be considered at the population level is how to generate the optimal TMS timing to cause a suppressive effect. Most single pulse TMS studies have demonstrated that there is a certain period during which TMS has a suppressive effect. It is quite conceivable that the temporal properties of TMS interference are determined by the dynamical state of the neural population after the afferent input. In this work, we have analyzed the response of a simple analog neural network model to a TMS-like perturbation. We focused especially on the optimal timing and the effective range of the perturbation in suppressing network activity.

2 Methods

The simple analog neural network model we used here is represented by Eq.1–4, which has been well analyzed as a model for a sensory feature detector system [4].

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

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

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

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

Here, $m(\theta, t)$ is the output of neuron θ and $g[h]$ is the quasi-linear output function that is inactive (g=0) if h<T (T: threshold), saturated (g=1) if h>T+$1/\beta$, and linearly operative as $\beta(h - T)$ between these points. $h(\theta, t)$ denotes the input to the neuron θ. Generally, the integral range is defined by the extent of the connections of neuron θ. Here, for simplicity, we assume that $m(\theta, t)$ has a periodic boundary condition ($-\pi/2 \leq \theta \leq \pi/2$), so that connections among each of the neurons are limited in this periodic range. Afferent input, $h_{ext}(\theta, t)$, has a maximal amplitude $c(t)$ at $\theta = 0$. ϵ measures the degree of modulation of afferent input to the target neural population ($0 \leq \epsilon \leq 1/2$).

Synaptic weight and afferent input have only the zero- and second-order Fourier components, so that the dynamics of $m(\theta, t)$ can be fully described by the zero- and second-order Fourier coefficients of $m(\theta, t)$ ($m_0(t)$ and $m_{2c}(t)$, respectively). $m_0(t)$ represents the mean activity of the entire network and $m_{2c}(t)$ represents the degree of localization of an activity profile. These are the order parameters of this network model.

The spatial extent of the neural population that we deal with is supposed to be so small that the induced electric field will be almost uniform in such a limited area. Therefore, we assumed that TMS perturbation would be constant for all neurons and simply modified the input function as $\hat{h}(\theta, t) = h(\theta, t) + I_{TMS}(t)$. Hence, the order parameter equations can be also 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

To evaluate whether the TMS-like perturbation can suppress the network activity, we examined the equilibrium state of the network ($t \to \infty$). However, if the intensity of the afferent input is constant ($c(t) = \text{const}$), there is only one attractor in this simple neural network. If the network has only one attractor, the final state of the network will be uniquely defined by the intensity of the afferent input even if any strong perturbations are delivered.

Thus, to achieve dependence on the past input, we adopted a large β and allowed the network to exhibit non-linearity. If an appropriate afferent input is given under this regime, the network will show bistability and converge either of the active state that the network holds a local excitation or the silent state that the whole network activity is zero. As a typical example of afferent input showing bistability, we can use the simplest input which consists of a suprathreshold transient component (amplitude: A_t>T, duration: W_t) and a subthreshold sustained component (amplitude: A_s<T). Here, we took a relatively small β but still in the non-linear range, so that the minimum

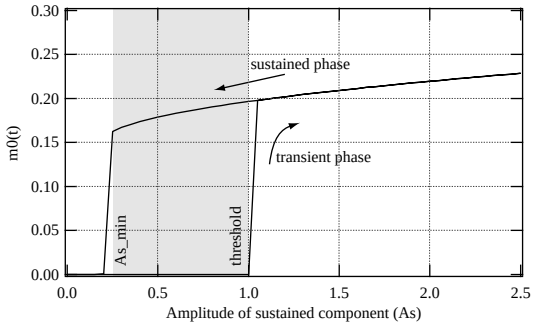

Fig. 1. Bistability of the network. If the transient component is sufficiently large, the final state simply depends on the sustained component. For A_s in the gray region, the network hold two attractors of the active and silent states. The network parameters used here were ϵ=0.1, β=0.25, J_0=73, J_2=110, T=1 (see also [4]).

value of A_s showing bistability was bounded to a non-zero value (Fig.1). The time course of this afferent input model is shown at the bottom of Fig.2a. This kind of time course of neural activity is commonly observed in the LGN, visual cortex, and other brain areas.

The network dynamics after the afferent input are illustrated in Figs. 2a and 2b. In the early period after the afferent input, the network goes to the attractor made by the transient component and then turns back to the relatively weak but stable attractor made by the sustained component, which is the final state of the network without the perturbation. When we applied the perturbation, the trajectory deviated from the control condition and converged either of the active or silent states depending on the timing of the perturbation. If the network was perturbed during the early period of the transient phase (SOA = 1), it could not reach the active state, and finally dropped to the silent state. However, if the network was perturbed during the late period (SOA = 2, 15), the trajectory temporarily turned away but could still maintain the activity and finally converged to the active state.

These results indicate that there must be a critical SOA range where the perturbation can completely suppress the network activity. In addition, we can easily imagine that the susceptibility to the perturbation was not uniform in the critical period and there might be an optimal timing that maximizes the suppression effect of the perturbation. These characteristics can be measured through the minimum intensity of the perturbation needed to suppress the network activity for each SOA (Fig. 3). The minimum perturbation needed to suppress the network activity depended on the power of the afferent input, so that the $I_{TMS_{min}}$-SOA curves fully shifted upward when a strong afferent input was given. Even so, the profiles of these curves consistently had basin shapes with a bottom at SOA = 0 regardless of the intensity of the transient components. Inside these basin curves, the perturbation suppresses the activity, so the horizontal width of each basin represents the length of a critical

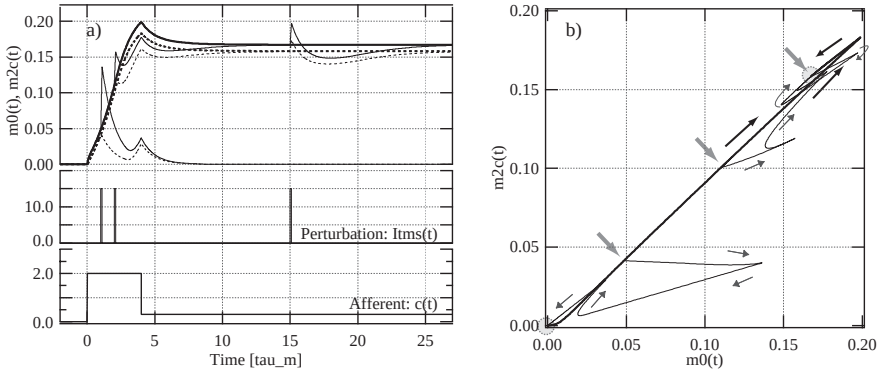

Fig. 2. a) Time course of the order parameters with the perturbation. The results for SOA (stimulus onset asynchrony) = 1, 2, and 15 (thin lines) and the control condition without the perturbation (thick line) are shown. m_0 (solid line) transiently increased and then decreased for a relatively long period followed by a reduction of m_{2c} (dotted line). b) The network state in the m_0-m_{2c} plane. Thin arrows indicate the direction of the network state. Thick arrows indicate the onset of the perturbation. The gray disks indicate the two attractors of the network. Depending on the timing of the perturbation, the network converged on either of the attractors. Parameters used here were A_t=2, W_t=4τ_m, I_{TMS}=15, W_{TMS}=0.1τ_m. Other parameters were the same as for Fig. 1.

SOA range. This length was over 10 times the time constant τ_m when the intensity of the transient component was relatively low.

4 Discussion

By observing the suppressive effects induced by a TMS-like perturbation in an simple neural population model, we have found that there is a critical period during which the perturbation can completely suppress network activity.

If we assume that the time constant τ_m is 10 ms, the duration of the perturbation would be 1 ms. This is consistent with the typical specification of commercially available TMS systems. The length of the critical SOA range would be over 100 ms at most. This is also consistent with typical experimental data of occipital TMS concerning the SOA range that can cause inhibitory effects on visual perception [1][3][6].

Parametric studies of occipital TMS [8] have shown that the degree of visual suppression depends on the TMS intensity and the brightness of the stimulus. In our computational study, we also found it difficult to suppress the network activity when the afferent input was strong. Amassian also reported that the suppression cannot be elicited if the characters are read too easily [2]. Therefore, the afferent input to the neural population (in this case, neurons in the visual cortex) might be slightly above the threshold. With regard to our

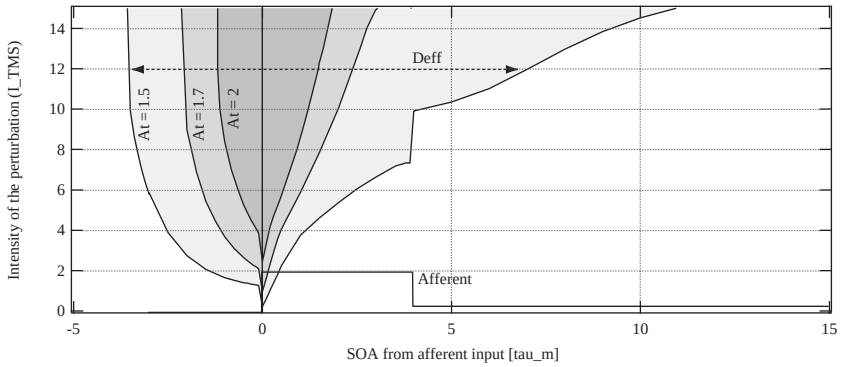

Fig. 3. Minimum perturbation intensity needed to suppress network activity. The width of each curve represents the SOA range (D_{eff}) within which network activity is suppressed. For example, when $A_t = 1.5$ and $I_{TMS} = 12$, the perturbation delivered within an SOA range from -3.5 to 7 (i.e., $D_{eff} = 10.5\tau_m$) can suppress network activity. The parameters were the same as for Fig. 2.

simulation, it means that A_t should be limited to slightly above T, which was the condition under which the critical SOA range reached a large value (over 100 ms) comparable to the experimental data. These results suggest that the inhibitory effects observed in TMS studies can be attributed to interactions at the neural population level.

References

[1] Amassian VE, Cracco RQ, Maccabee PJ, Cracco JB, Rudell A, Eberle L, *Electroencephalogr Clin Neurophysiol* **74** (1989) 458-62.

[2] Amassian VE, Cracco RQ, Maccabee PJ, Cracco JB, *in: Handbook of Transcranial Magnetic Stimulation* Pascaul-Leone A, Davey NJ, Rothwell J, Wasserman EM, Puri BK, ed., Arnold Publisher, (2002) 323-34.

[3] Beckers G, Zeki S, *Brain* **118** (1995) 49-60.

[4] Ben-Yishai R, Bar-Or RL, Sompolinsky H, *Proc Natl Acad Sci USA* **92** (1995) 3844-8.

[5] Inghilleri M, Berardelli A, Cruccu G, Manfredi M, *J Physiol* **466** (1993) 521-34.

[6] Kamitani Y, Shimojo S, *Nat Neurosci* **2** (1999) 767-71.

[7] Kamitani Y, Bhalodi VM, Kubota Y, Shimojo S, *Neurocomputing* **38-40** (2001) 697-703.

[8] Kammer T, Nusseck HG, *Neuropsychologia* **36** (1998) 1161-6.

[9] Nagarajan SS, Durand DM, Warman EN, *IEEE Trans Biomed Eng* **40** (1993) 1175-88.

[10] Roth BJ, Basser PJ, *IEEE Trans Biomed Eng* **37** (1990) 588-97.