Inhibition of Oscillation in A Neuronal Network Model for Tinnitus Management by Sound Therapy

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Abstract: - Tinnitus is a state in which one hears sounds in the ear or head without any external sound. There are many therapeutic approaches for tinnitus and sound therapy is one of the techniques for its treatment that have been proposed. In order to investigate mechanisms of tinnitus generation and the clinical effects of sound therapy from the viewpoint of neural engineering, we have proposed computational models with plasticity and inhibitory feedback using a neural oscillator or model neurons described by simplified Hodgkin-Huxley equations. In the present paper, the improvement of the neuronal network model is described in the reproduction of the clinical results that human auditory system temporarily halts perception of tinnitus following sound therapy.

Key-Words: - tinnitus, sound therapy, neuronal network model, plasticity, oscillation, inhibition

1 Introduction

Tinnitus is a state in which one hears sounds in the ear or head without any external sound [1, 2]. For the cause of tinnitus, contribution of neural plasticity to tinnitus has been discussed [3, 4]. Tinnitus has many subclasses and attempts have been made to categorize tinnitus based on its characteristics that in turn can facilitate the selection of treatment method [5]. Among a number of therapies sound therapy techniques for its treatment have the clinical effect that tinnitus disappears or reduces in its loudness after the sound presentation [6]. The mechanisms of tinnitus and its management by sound therapy, however, are not clear.

To account for those mechanisms from the viewpoint of neural engineering, previously we had proposed a computational model using a neural oscillator [7]. We demonstrated that the model conceptually reproduces tinnitus generation and its inhibition using sound stimuli. It was detected that by providing the model with sinusoidal or noise stimulus that is hypothesized as sound for treatment of tinnitus we can inhibit the oscillations. This was accomplished by incorporating neural plasticity through parameters such that their values can be updated. By hypothesizing that the oscillation and the equilibrium correspond to generation and inhibition of tinnitus, respectively, we reported that these phenomena could explain the fact that the habituated human auditory system temporarily halts perception of tinnitus following sound therapy. However, that model relied on a somewhat conservative simplification of the central auditory pathways and associated central nervous system areas that are relevant to tinnitus.

Next we proposed a different model composed of model neurons described by simplified Hodgkin-Huxley equations [8]. This model is still conceptual since it consists of only three neurons with positive and negative feedbacks, but more realistic than the previous one because it shows time series corresponding to the firings of neurons. We showed that inhibition of the oscillation can be observed in this model as well by constant or pulse train stimuli. It was, however, observed on occasion in the simulation that output pulses of the neurons to their postsynaptic neurons are emitted in spite of no firings.

We modified the model by giving the threshold for output of neurons a higher value and also giving a neuron a bias current in order to remove the inappropriate output pulses keeping the necessary behavior in the network.

In the present paper, the results of computer simulation of the modified model are demonstrated. The results show that the unnecessary output pulses observed in the previous model are almost removed and the inhibition of oscillation can be reproduced, which explains the effect of sound therapy.

2 A neuronal network model

We propose a neuronal network model shown in Fig. 1 in which firing sequences in the nervous system are simulated. This model is a conceptually simplified system of a tinnitus generation network.

It is composed of two excitatory neurons and one inhibitory neuron as shown in Fig. 1. This model includes a positive feedback loop of the excitatory neurons E_1 and E_2 mutually coupled, and a negative feedback loop with the excitatory neuron E_2 and the inhibitory neuron I that are also mutually coupled. The negative feedback loop controls the firing rate. The model can be bistable with a sustained firing state and a non-firing state.

The coupling strength between neurons is denoted by C_{ij} ($i, j \in \{1,2,I\}$). The neuron E_1 receives external stimuli S that is afferent signal due to the acoustic stimuli that are employed in sound therapy.

We express the dynamics of the model by a simplified version of Hodgkin-Huxley equations (HH) [9-11]. We employed it instead of HH to save the time of simulation by reduction of the number of state variables for each neuron from four to two.

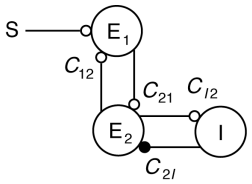

Fig. 1. Basic structure of the present model

2.1 Formulation of the model without plasticity

We describe the basic dynamics of the model as

$$\frac{dv_1}{dt} = \frac{G(v_1, m^{\infty}(v_1), 0.8(1-h_1), h_1) + C_{12}z_2 + D + S}{C_m}, \quad (1)$$

$$\frac{dh_1}{dt} = \alpha_h(v_1)(1-h_1) + \beta_h(v_1)h_1, \quad (2)$$

$$\frac{dv_2}{dt} = \frac{G(v_2, m^{\infty}(v_2), 0.8(1-h_2), h_2) + C_{21}z_1 - C_{2I}z_I}{C_m}, \quad (3)$$

$$\frac{dh_2}{dt} = \alpha_h(v_2)(1-h_2) + \beta_h(v_2)h_2, \quad (4)$$

$$\frac{dv_I}{dt} = \frac{G(v_I, m^{\infty}(v_I), 0.8(1-h_I), h_I) + C_{I2}z_2}{C_m}, \quad (5)$$

and

$$\frac{dh_I}{dt} = \alpha_h(v_I)(1-h_I) + \beta_h(v_I)h_I. \quad (6)$$

where v is the membrane potential and h is the variable associated with activation of potassium ion channel in the neuron E_1, E_2 or I. The functions $G(v,m,n,h)$ and $m^{\infty}(v)$ are expressed as

$$G(v,m,n,h) = \bar{g}_{Na}m^3h(V_{Na}-v) + \bar{g}_K n^4(V_K - v) + \bar{g}_l(V_l - v) \quad (7)$$

and

$$m^{\infty}(v) = \alpha_m(v) \big/ \{\alpha_m(v) + \beta_m(v)\} \quad (8)$$

respectively. The functions $\alpha_m(v)$ and $\beta_m(v)$ in Eq. (8) are expressed respectively as

$$\alpha_m(v) = 0.1(25-v) \big/ \{e^{(25-v)/10} - 1\} \quad (9)$$

and

$$\beta_m(v) = 4\,e^{-v/18} \quad (10)$$

Functions $\alpha_h(v)$ and $\beta_h(v)$ in Eq. (2), (4), (6) are expressed respectively as

$$\alpha_h(v) = 0.07\,e^{-v/20} \quad (11)$$

and

$$\beta_h(v) = 1 \big/ \{e^{(30-v)/10} + 1\}. \quad (12)$$

The parameters of the neuron model were fixed as C_m=1[μF/cm^2], $\bar{g}_{Na} = 120$[mS/cm^2], $\bar{g}_K = 36$[mS/cm^2], $\bar{g}_l = 0.3$[mS/cm^2], V_{Na}=115[mV], $V_K = -12$ [mV], V_l=10.6 [mV], based on the values in Hodgkin-Huxley model.

The output of the neuron to their postsynaptic neurons is denoted by z_j and expressed as function of the membrane potential v_j as

$$z_j = \begin{cases} 1 & (v_j \geq 5) \\ 0 & (v_j < 5) \end{cases}. \quad (13)$$

In Eq. (11) the threshold value is given five. In the previous model, it was unity [8]. It is larger in the present model in order to remove the output pulses that are emitted in the previous model in spite that the neurons do not fire.

The bias term D is introduced in the equation of the membrane v_1 of the neuron E_1, Eq. (1) in order to compensate for the decrease of output pulses due to the larger threshold. The bias may also be introduced in the equations of v_3 and v_I, Eqs. (3) and (5). Here it is given only to Eq. (1) to minimize the change from the previous model.

2.2 Formulation of plasticity

To reproduce the effect of sound therapy, we assume that the coupling strength from the neuron E_1 to the neuron E_2, C_{12}, has plasticity in such a way that it increases when the neurons E_1 and E_2 fires simultaneously, and decreases when the firings of the neurons E_1 and E_2 are not synchronized. This assumption is based on Hebbian hypothesis regarding synaptic plasticity [12]. We describe the dynamics of C_{12} as

$$\frac{dC_{12}}{dt} = \frac{-C_{12} + p(z_1,\ z_2) + C_0}{\tau}, \tag{12}$$

where

$$p(z_1, z_2) = \begin{cases} 0 & (z_1 = z_2 = 0) \\ b(z_1 - 0.5)(z_2 - 0.5) & (otherwise) \end{cases}, \tag{13}$$

In Eq. (12) C_0, b and τ are positive constants. The constant C_0 is associated with the equilibrium of C_{12}. The constants b and τ denote the efficacy of synaptic plasticity and the time constant of C_{12}, respectively.

3 Results

We demonstrate the results of computer simulation of the model. Throughout the simulation the parameter values $D = 11$, $C_{21} = 10$, $C_{2I} = 10$, $C_{I2} = 20$ were employed.

3.1 Analysis of the model without input or plasticity

Without stimulation or plasticity, the model has two stable solutions, an oscillatory state by sustained firings and a non-firing state, which are bistable for a parameter region. We performed the simulation changing the value of the coupling coefficient C_{12} by 0.1 in the range $0 < C_{12} \le 30$.

The non-firing state exists for any value of C_{12} in the range. On the other hand the oscillatory state exists when $C_{12} \ge 1.9$. That is, the two states coexist when $C_{12} \ge 1.9$. The larger C_{12} brings the larger basin of the oscillatory solution in the state space of the model in the region. It corresponds to the clinical fact that a number of patients of tinnitus claim that they do not always hear sound when there is no external sound.

3.2 Analysis of the model with input and plasticity

The inhibition of oscillation by constant input with amplitude I as stimulus S to neuron E_1 was examined with plasticity. The constant input I was applied for 100ms from 200ms to 300ms to the network that is oscillating in the simulation. The parameter value $b = 40$ and $\tau = 50$ [ms] were employed. The value of τ is much smaller than the clinical process. It was given the value so that the simulation is completed in a reasonable time. For each trial the parameter C_0 was changed one by one from 2 to 20. The amplitude I of the input was increased one by one [μA/cm^2]. Stimulation period is 100ms.

Fig. 2 shows an unsuccessful result and Fig. 3 shows a successful result when $C_0 = 10$. As shown in Fig. 2, the constant input with I=3 [μA/cm^2] fails to inhibit the oscillation of the network, while the input with I=4 [μA/cm^2] for 100ms makes the network stop the oscillation after the input is removed. For all the values of C_0, the amplitude I not less than 4 [μA/cm^2] was required for inhibition of oscillation. Longer application of the input did not seem to bring different results.

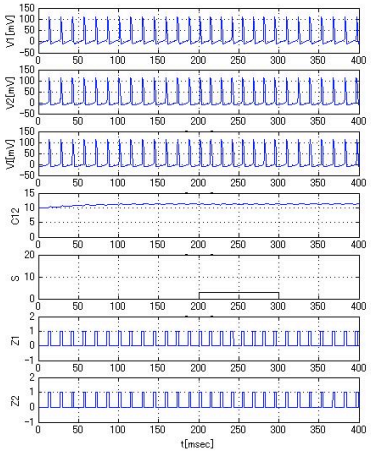

Fig. 2. An unsuccessful simulation result, $I = 3[\mu\text{A/cm}^2]$.

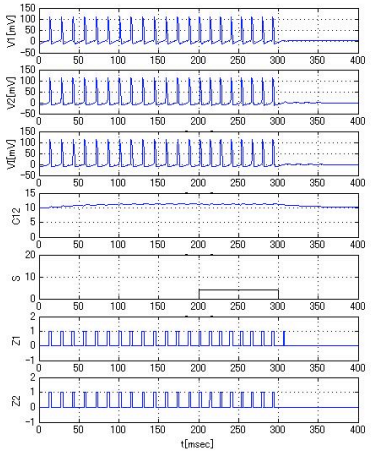

Fig. 3. A successful simulation result, $I = 4[\mu\text{A/cm}^2]$.

In the present study the model has been modified by the change of the threshold for output of the neurons and introduction of bias term D to the neuron E_1. By this modification the outputs to postsynaptic neurons without firing almost disappeared as shown in Fig. 3.

We examined different values of the threshold for output of the neurons. Higher values than a certain value remove unnecessary output. With too high values, however, the network does not oscillate without input. The value five was chosen in order to remove unnecessary output keeping the firings without input for the first 200ms in simulation.

An output pulse of the neuron E_1 is still observed without firing after the stimulation ends. Besides, the coupling coefficient does not decrease during the stimulation, which occurred in the former model. We cannot state in the present model that the inhibition of oscillation is reproduced as the result of synaptic plasticity. The oscillation stops in the present model due to the change of the state of the model by the input. Hence, further investigation of modeling is necessary in order to reproduce the inhibition of oscillation by synaptic plasticity.

4 Conclusion

In this study a conceptual and computational neuronal network model with plasticity in the human auditory system proposed to explain the mechanisms of tinnitus and its management by sound therapy was improved so that the unnecessary output to the postsynaptic neurons are almost removed. Through analysis of this model, it is shown that, similarly to the previous neural oscillator model, oscillation can be inhibited.

However, it is not due to the change of coupling strength between neurons in the model but some change of the state condition of the model by supplying constant input to the model. In order to demonstrate in the modeling that the synaptic plasticity brings the inhibition of oscillation is realized, it is necessary to modify the model.

Our future work will expand this model so that it can more effectively relate to the underlying physiology of tinnitus, and explore better stimulation for its inhibition. This in turn will result in improvement in designing sound therapy techniques and stimuli.

Acknowlegment

Authors thank Susumu Fujii for his help with computer simulation. This work was partly supported by Grant-in-Aid for Scientific Research #21560429 from Japan Society of Promotion of Science.

References:

[1] A. Axelsson and A. Ringdahl,"Tinnitus–a study of its prevalence and characteristics," *British Journal of Audiology*, vol. 23, no. 1, 1989, pp. 53–62.

[2] P. J. Jastreboff, "Phantom auditory perception (tinnitus): mechanisms of generation and perception," *Neuroscience Research*, vol. 8, no. 4, 1990, pp. 221-254.

[3] J. J. Eggermont and L. E. Roberts, "The neuroscience of tinnitus," *Trends in Neurosciences*, vol. 27, no. 11, 2004, pp. 676-682.

[4] A. R. Moller, *Neural plasticity and disorders of the nervous system*, Cambridge: Cambridge University Press, 2006.

[5] R. Tyler, C. Coelho, P. Tao, H. Ji, W. Noble, A. Gehringer, S. Gogel. "Identifying tinnitus subgroups with cluster analysis," American Journal of Audiolology, vol. 17, no. 2, Dec. 2008, pp. S176-184.

[6] J. A. Henry, M. A. Schechter, T. L. Zaugg, S. Griest, P. J. Jastreboff, J. A. Vernont, C. Kaelin, M. B. Meikle, K. S. Lyons and B. J. Stewart, "Outcomes of clinical trial: tinnitus masking versus tinnitus retraining therapy," J. Am. Acad. Audiol., vol. 17, no. 2, 2006, pp. 104-132.

[7] K. Fujimoto, H. Nagashino, Y. Kinouchi, A. A. Danesh and A. S. Pandya, "Oscillation and its inhibition in a neural oscillator model for tinnitus," in *Proc. of the 28th IEEE EMBS Annual International Conference*, 2006, pp. 5547-5550.

[8] H. Nagashino, K. Fujimoto, Y. Kinouchi, A. A. Danesh, A. S. Pandya and J. He, "Oscillation and its inhibition in a neuronal network model for tinnitus sound therapy," in *Proc. of the 30th Annual International Conference of the IEEE EMBS*, 2008, pp. 311-314.

[9] H. Kawakami, *Dynamics of biological rhythmic phenomina— Nonlinear dynamics applied to ME*. Tokyo: Corona, 2001, ch. 7.

[10] J. Rinzel, "Excitation dynamics: Insights from simplified membrane models," *Fed. Proc.*, vol. 15, no. 44, 1985, pp. 2944-2946.

[11] A. L. Hodgkin and A. F. Huxley, "A quantitative description of membrane current and its application to conduction and excitation in nerve," *The Journal of Physiology*, 1952, vol. 117, pp. 500-544.

[12] D. O. Hebb, *The Organization of behavior: A neuropsychological theor.* New York: John Wiley & Sons, 1949.