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A neural mechanism of phase-locked responses to sinusoidally amplitude-modulated signals in the inferior colliculus

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ABSTRACT

The central nucleus of the inferior colliculus (ICc) is an auditory region that receives convergent inputs from a large number of lower auditory nuclei. ICc neurons phase-lock to low frequencies of sinusoidally amplitude-modulated (SAM) signals but have a different mechanism in the phase-locking from that in neurons of lower nuclei. In the mustached bat, the phase-locking ability in lower nuclei is created by the coincidence of phase-locked excitatory and inhibitory inputs that have slightly different latencies. In contrast, the phase-locking property of ICc neurons is little influenced by the blocking of inhibitory synapses. Moreover, ICc neurons exhibit different characteristics in the spike patterns and synchronicity, classified here by three types of ICc neurons, or sustained, onset, and non-onset phase-locking neurons. However it remains unclear how ICc neurons create the phase-locking ability and the different characteristics. To address this issue, we developed a model of ICc neuronal population. Using this model, we show that the phase-locking ability of ICc neurons to low SAM frequencies is created by an intrinsic membrane property of ICc neuron, limited by inhibitory ion channels. We also show that response characteristics of the three types of neurons arise from the difference in an inhibitory effect sensitive to SAM frequencies. Our model reproduces well the experimental results observed in the mustached bat. These findings provide necessary conditions of how ICc neurons can give rise to the phase-locking ability and characteristic responses to low SAM frequencies.

1. Introduction

The temporal features of sound are important for a variety of auditory functions including the speech recognition (Shannon et al., 1995), species-specific social communication calls (Stebbins and Moody, 1994), the acoustic identification of objects and events (Bregman, 1990), and specialized functions such as echolocation of bats (Fenton, 1995; Moss and Schnitzler, 1995; Suga, 1988; Kamata et al., 2004). Of the temporal features, amplitude modulation (AM), the change over time of a sound's amplitude envelope, is an important information-bearing parameter carried by communication sounds such as syllabic features in speech (Drullman et al., 1994; Shannon et al., 1995; Steinschneider et al., 1998; Nelken et al., 1999; Füllgrabe et al., 2009) and is thought to be of particular use in segregating sound sources during auditory scene analysis (Bregman, 1990; Yost, 1992; Hu and Wang, 2004). In previous studies, AM stimuli have been used to investigate how neurons in the peripheral and central auditory systems respond to the amplitude modulations in an acoustic stimulus. In laboratory, researchers have used sinusoidal amplitude modulation (SAM) to record the responses from various structures in the auditory nervous system including auditory nerve, cochlea nucleus, superior olive, dorsal nucleus of the lateral lemniscus, inferior colliculus, and primary auditory cortex (see Langner, 1992 and Frisina, 2001 for reviews).

The central nucleus of the inferior colliculus (ICc) is an obligatory relay center for auditory processing, receiving convergent inputs from a large number of lower auditory nuclei. The principle projections to the ICc are from the cochlea nucleus, the lateral and medial superior olives, and the nuclei of the lateral leminiscus (Adams, 1979; Brunso-Bechtold et al., 1981; Oliver and Huerta, 1991; Oliver, 2000; Malmierca et al., 2005; reviewed in Kelly and Caspary, 2005). Many of these projections have excitatory innervation to ICc neurons, and others give inhibitory innervation with GABAergic and glycinergic synaptic connections (Semple and Aitkin, 1980; Glendenning and Baker, 1988;

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Schnerderman et al., 1988; Saint Marie and Banker, 1990; Vater et al., 1992; Winer et al., 1995; González-Hernández et al., 1996; Fubara et al., 1996). Previous studies have shown that there is a marked difference among these nuclei in the upper limit of SAM frequencies that produce synchronous firing of auditory neurons. Neurons in the auditory nerve and most nuclei below the ICc phase-lock to a wide range of SAM frequencies (Javel, 1980; Frisina et al., 1990a,b; Joris and Yin, 1992, 1998; Rohde and Greenberg, 1994; Yang and Pollak, 1997; Huffman et al., 1998), while ICc neurons phase-lock only to low SAM frequencies, typically <300 Hz (Rees and Møller, 1983; Langner and Schreiner, 1988; Schreiner and Langner, 1988; Krishna and Semple, 2000; Walton et al., 2002; Zhang and Kelly, 2003).

In the mustached bat, the medial superior olive (MSO) and the anterior portion of the dorsal nucleus of lateral lemniscus (DNLL), located at the nuclei below the ICc, exhibit the phase-locking to low SAM frequencies <300 Hz. Insights to a mechanism of the phase-locking of the MSO and the DNLL are given by the experimental studies (Grothe, 1994; Yang and Pollak, 1997). The important point is that these nuclei receive inputs that phase-lock to a wide range of SAM frequencies, as in the case for the inputs to the ICc. These studies proposed a phase-locking mechanism in which the phase-locking transformations are created by the coincidence of phase-locked excitatory and inhibitory inputs that have slightly different latencies. In contrast, the experimental study of ICc neurons (Burger and Pollak, 1998) showed that blocking of excitatory and inhibitory inputs provided little changes of discharge patterns of ICc neurons, indicating that the mechanism for the phase-locking of the MSO and the DNLL is not the case for the phase-locking of the ICc. The study by Burger and Pollak (1998) also showed three characteristic discharge patterns to SAM frequencies. The first type is the unit that responds with sustained discharge to a tone burst and phase-locks to SAM frequencies <250 Hz, with low synchronous properties. The second type is the unit that responds with an onset response to a tone burst and phase-locks to SAM frequencies <250 Hz, with remarkable onset responses and higher synchronous properties. The last type is the unit that responds with a weak onset response to a tone burst and phase-locks to SAM frequencies <250 Hz. This type has no remarkable onset property in the phase-locked discharged patterns. The results by Burger and Pollak (1998) raise two questions of how ICc neurons phase-lock to the low SAM frequencies and what are the neuronal factors emerging the difference in the three types of discharge patterns.

To address these issues, we developed a model of ICc neuronal population, which receives inputs from the MSO and the DNLL. We show that the phase-locking of ICc neuron to low SAM frequencies is caused by an intrinsic membrane dynamics of ICc neuron which is produced by inhibitory ion channels embedded in the membrane. The inhibitory channels generate a subthreshold membrane oscillation being resonance with low SAM frequencies, facilitating the phase-locked responses to SAM stimuli. The recovery dynamics by the inhibitory channels limits the phase-locking ability to low SAM frequencies. We also show that the difference in the three types of discharge patterns to low SAM frequencies arises from the difference in an inhibitory effect that is produced by the integration of SAM input. These findings indicate that different inhibitory effects in an ICc neuron may contribute to the phase-locking ability and the generation of characteristic discharge patterns.

2. Model

The model of the ICc consists of a population of ICc neurons, which contains ICc neurons tuned to a frequency of echo sound, as shown in Fig. 1. Each neuron receives an excitatory input from the MSO and an inhibitory input from the DNLL. ICc neuron was modeled with the Izhikevich neuron model (Izhikevich, 2003), given by reducing many biophysically accurate Hodgkin–Huxley neuronal models to a two-dimensional system of ordinary differential equations. The membrane potential of ith ICc neuron, V_i, is given by

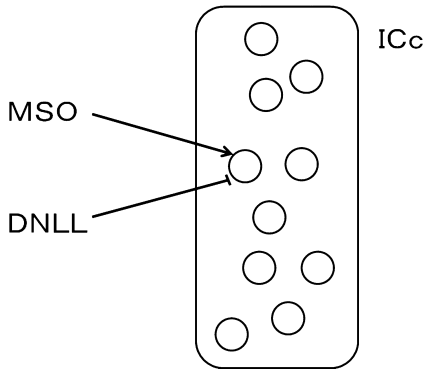

Fig. 1. The model of ICc neuronal population. Each neuron receives an excitatory input from the MSO and an inhibitory one from the DNLL.

$$\frac{dV_i}{dt} = 0.04V_i^2 + 5V_i + 140 - U_i + I_i^{inh} + I_i(t), \tag{1}$$

$$\frac{dU_i}{dt} = a(bV_i - U_i),\ i = 1, 2, ..., N_0, \tag{2}$$

with the auxiliary after-spike resetting,

$$\text{if} V_i \geq 30mV, \text{then} \begin{matrix} V_i \leftarrow c \\ U_i \leftarrow U_i + d. \end{matrix} \tag{3}$$

The variable U_i represents a membrane recovery variable, which accounts for the activation of K^+ ionic currents and inactivation of Na^+ ionic currents, and it provides a negative feedback to V_i. After the membrane potential reaches the threshold value (30 mV), the membrane potential and the recovery variable are reset according to Eq. (3). Here a, b, c and d are the parameters concerning the recovery mechanism and after-spike resetting. N_0 is the number of ICc neurons contained in the population. The input to the ith ICc neuron, $I_i(t)$, is described by

$$I_i(t) = X_i^{MSO}(t) + X_i^{DNLL}(t - t_d) + \xi_i(t), \tag{4}$$

where $X_i^{MSO}(t)$ and $X_i^{DNLL}(t - t_d)$ are an excitatory input from the MSO and an inhibitory input from the DNLL, respectively, each is given by

$$X_i^{MSO}(t) = \frac{X_0^{MSO}}{2}[1 + \sin(2\pi ft)], \tag{5}$$

and

$$X_i^{DNLL}(t - t_d) = \begin{cases} -rX_0^{DNLL} & \text{if} t - t_d \geq 0 \\ 0 & \text{otherwise.} \end{cases} \tag{6}$$

The excitatory input from the MSO, $X_i^{MSO}(t)$, is given by a sinusoidal input with the maximum magnitude X_0^{MSO} and the AM frequency f, which is modulated with the same frequency as the envelope of SAM signal. The input $X_i^{MSO}(t)$ does not contain information of carrier frequency of sound because the ICc model consists of neurons tuned to a best frequency. The input has also all-pass filtering property to SAM frequency, despite that MSO neurons limit the phase-locking property to low SAM frequencies, because ICc neurons receive inputs from several lower nuclei such