Effects of baclofen on the directional selectivity of transient neurons in the catfish retina.

Sung-Jong Lee and Sun-Ho Bai*

Physics and Biophysics Section, Department of Natural Sciences, College of Medicine, The Catholic University of Korea, Seoul 137-701, Korea.

Abstract

Effects of baclofen on the directional selectivity of the inner retinal neurons were studied using conventional intracellular recording techniques and computer simulations. Baclofen suppressed sustained components, but enhanced transient components of third-order neurons in the catfish retina. In addition, directional selectivity of transient neurons was enhanced by the application of baclofen. The simplified network model was tested to account for the details of directional selectivity observed in the inner retina. Results suggest that the directional selectivity in fish retina could be evoked by the asymmetric distribution of GABAergic third-order neurons.

Key Words: Baclofen, GABAb receptors, Directional selectivity, Catfish retina

1. Introduction

Directional selectivity is a dynamic property of the receptive field, formed by retinal microcircuits. Directionally selective third-order neurons respond strongly to the motion of a bar stimulus moved across their receptive field in the preferred direction, which evokes little

response to the same stimulus moved in the opposite direction. Several models have been proposed to explain the cellular origin and mechanism of the directional selectivity. Starburst amacrine cells are well situated to account for the details of the mechanism, since they have been shown to release both acetylcholine and GABA onto the bistratified dendrites of the direction selective ganglion cells [4]. GABAergic inhibitory system is known to play a key role in the mechanism of directional selectivity. It has been reported that the blockade of GABAa receptors leads to the loss of directional selectivity [1]. However, following the infusion of baclofen (GABAb receptor agonist) into the retina, the directional selectivity of third-order neurons is enhanced in the amphibian retina [2]. The GABAb system has been known to open potassium channels on third-order neurons, and close calcium channels on bipolar and ganglion cells [3]. Consequently, baclofen hyperpolarizes the membrane potentials and produces a selective suppression of portions of the light response while GABA and glycine suppress all components of the light response.

Retinal third-order neurons are dichotomized into transient and sustained cells according to their light responses. It has been proposed that transient cells carry information in the direction of motion, while sustained cells carry information on steady-state conditions, such as color or spatial acuity. Interestingly, baclofen seems to make a transition from sustained to transient in propensity by the suppression of sustained components, and the enhancement of transient components of third-order neurons.

Therefore, we have explored the effects of baclofen on directional selectivity from the physiological recordings and computer simulation, to discern the functional roles of GABAb receptors on transient neurons in the inner retinal microcircuit.

2. Methods

The catfish (Ictalurus punctatus) retina was investigated by using the intracellular

recording techniques. The stimuli were generated by a computer monitor, which was imaged through an optical system onto the retina. They consisted of moving bars of various sizes and directions. The same stimuli were repeated on a slave monitor during the experiment. The preferred-null axis was empirically determined as that plane that showed the greatest asymmetry in amplitude to back and forth movement of the bar. A gravity driven perfusion system was used to super fuse the solutions and a piece of absorbent tissue with a hole large enough to expose the retina was centered over the eyecup to serve as a wick to draw off the super-fusate. The resistance of the microelectrode for the intracellular recordings was approximately 150 MΩ. A model of the transient neuron was described in terms of the Hodgkin-Huxley kinetic model based on electrophysiological measurements. The network model was tested for its ability to account for the details of directional selectivity induced by GABAb receptor system in the inner retina. Simulations were carried out using NEURON package.

3. Results & Discussion

Perfusion experiments were performed to show the effects of baclofen on neurons in the catfish inner retina. The action of baclofen (0.1mM) on third-order neurons is illustrated in Fig.1. When the retina was exposed to baclofen, sustained components of the ON-sustained cell were suppressed and spiking discharges of putative ganglion cell were reduced (A & B). The square pulses below the voltage trace indicate the timing of light stimuli. Baclofen hyperpolarized the dark membrane potential, suppressed sustained component and enhanced transient component of the ON-sustained cell with large transient component, but did not affect the surrounding antagonism of the cell (C). The application of baclofen was mainly associated with a suppression of sustained component and an enhancement of transient components. The responses were recovered after returning to the control solution.

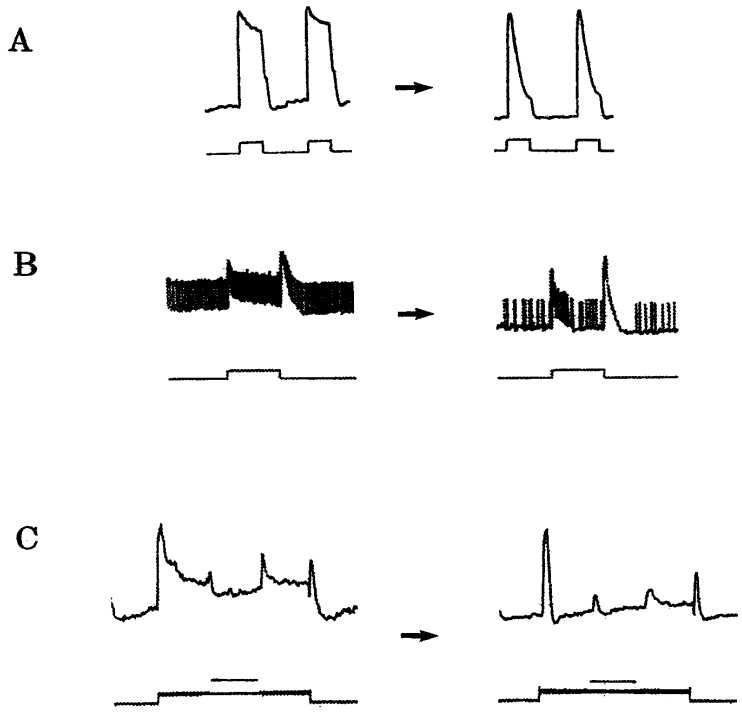

Fig.1. Intracellular recordings from third-order neurons exposed to baclofen. Baclofen application was mainly associated with a suppression of sustained components and an enhancement of transient components.

To show the effects of baclofen for the transient components under moving stimulation, we applied a single light bar with appropriate width and speed (Fig.2). In response to a single moving bar of light, transient neurons generated symmetrical patterns of EPSP that were dependent on the direction of the stimulus movement. The scan produced two groups of EPSP as the leading edge and trailing edges of the bar traversed the receptive field. Under control conditions, the responses give vague indication of directional selectivity (A).However, after the retina was treated with baclofen, the cell showed a preference for motion of the slit in the 135° direction and a weak response to the opposite direction (B). The results suggest that the directional selectivity is mediated by GABAb receptors in the catfish inner retina. Accordingly, the network model was proposed to interpret the directional selectivity induced by baclofen (Fig.3). The simulations show a consistency with the experimental data, however, the direct

physiological and anatomical bases for the baclofen induced directional selectivity are not presently known.

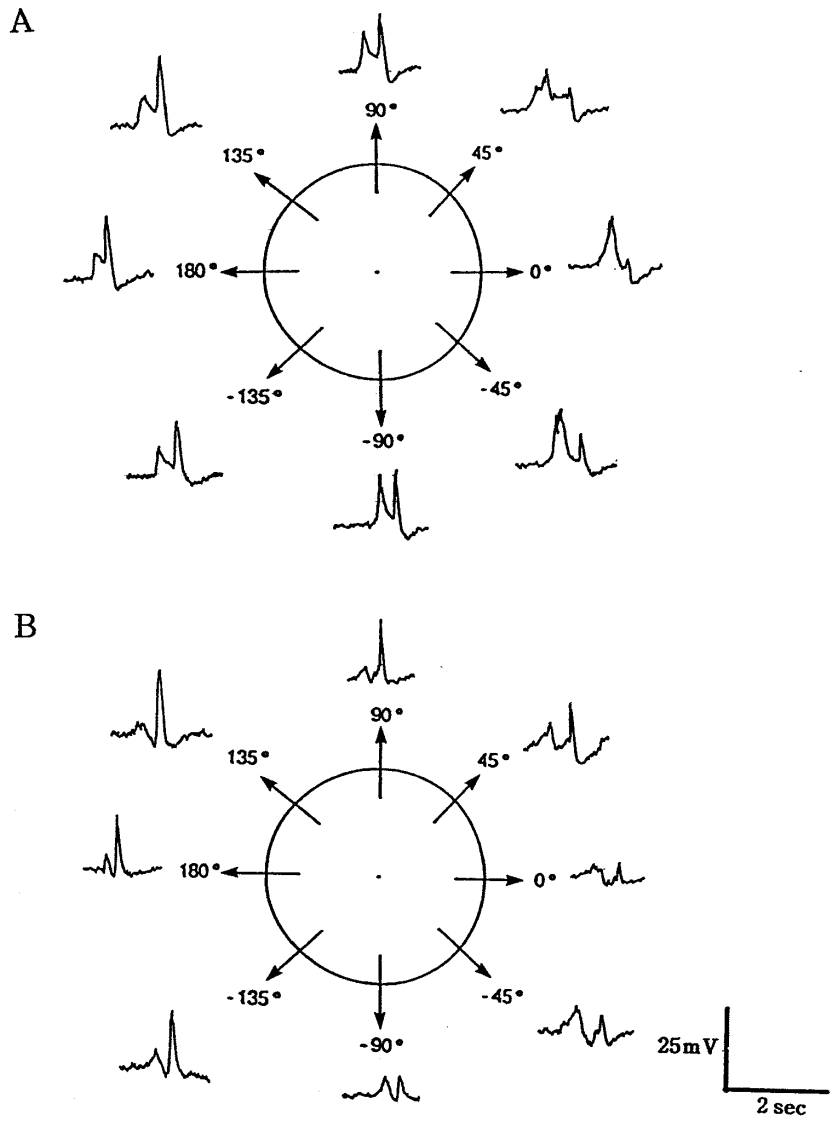

Fig. 2. Responses of an ON-OFF transient cell to a 350㎛-wide light slit moving across the retina in the directions indicated by the arrows. The long axis of the slit was orthogonal to the direction of motion.

Therefore, it is presumed that the dynamic properties of third-order neurons are modulated by baclofen, and asymmetric GABA inhibition and its nonlinear integration are essential parts of the mechanism of directional selectivity.

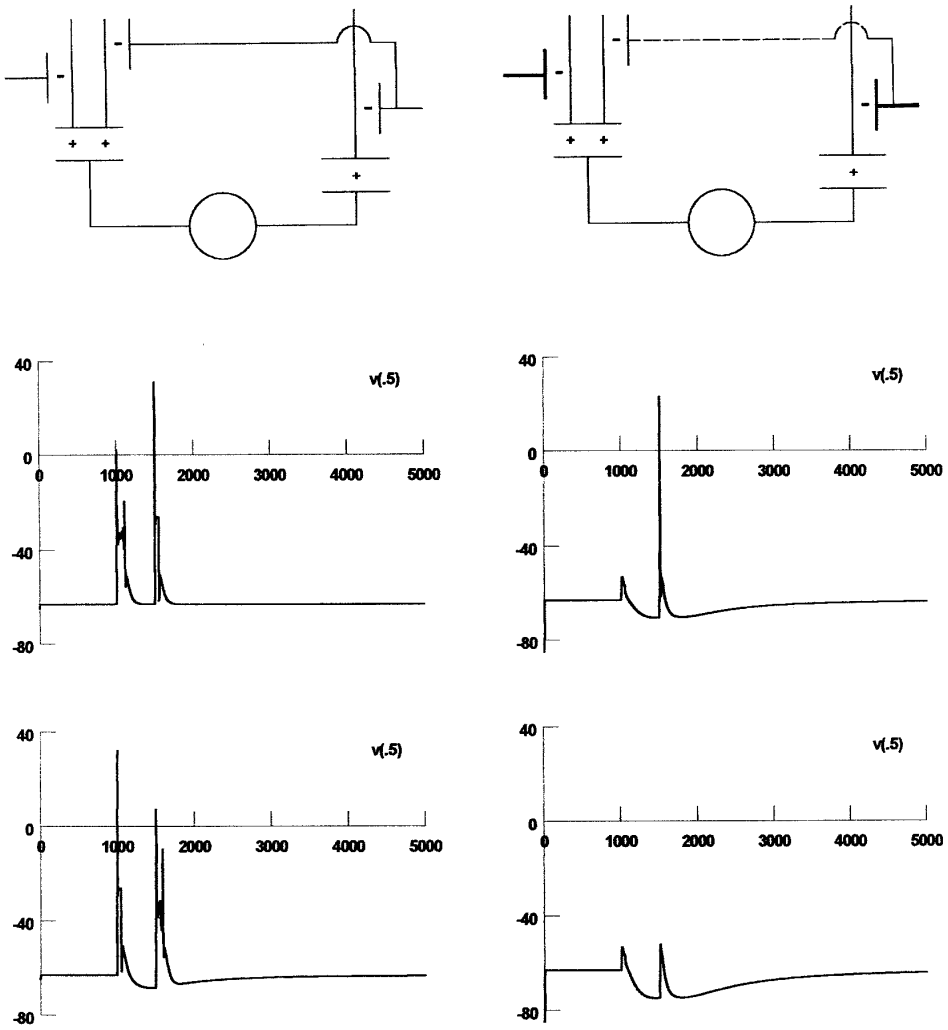

Fig. 3. The model of baclofen induced directional selectivity and the simulated responses of the transient neurons.

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Figure Explanations

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* Corresponding author. Physics and Biophysics Section, Department of Natural Sciences, College of Medicine, The Catholic University of Korea, Seoul 137-701, Korea. Tel.:+ 82-2-590-1256; fax: + 82-2-535-1270

E-mail address: sunhobai@cmc.cuk.ac.kr (S-H. Bai).