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Electrophysiological Analysis of GABA and Glycine Action on Neurons of the Catfish Retina

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= ABSTRACT=

Vertebrate retinal neurons, like brain tracts, form complex synaptic relations in the outer and inner plexiform layers which are equivalent to the central nervous system nuclei. The effects of γ-aminobutyric acid (GABA) and glycine on retinal neurons were explored to discern the mechanisms of action of neurotransmitters. Experiments were performed in the superfused retina-eyecup preparation of the channel catfish, *Ictalurus punctatus*, using intracellular electrophysiological techniques.

The roles of GABA and glycine as inhibitory neurotransmitters are well established in the vertebrate retina. But, we found that the depolarizing action of GABA and glycine on third-order neurons in the catfish retina. GABA and glycine appeared to act on retinal neurons based on the observations that: (1) effects on photoreceptors were not observed, (2) horizontal cells were either hyperpolarized (~33%) or depolarized (~67%), (3) bipolar cells were all hyperpolarized, (4) amacrine and ganglion cells were either hyperpolarized (~37%) or depolarized (~63%), (5) GABA and glycine may be working to suppress presynaptic inhibition.

The results suggest that depolarization of third-order neurons by GABA and glycine is due to at least two mechanisms; a direct postsynaptic effect and an indirect effect. Therefore, in the catfish retina, a mechanism of presynaptic inhibition or disinhibition including the direct postsynaptic effect may exist in the third-order neurons.

Key Words: Catfish retinal neurons, Eyecup, GABA, Glycine, Disinhibition

INTRODUCTION

The first intracellular recordings from the vertebrate retina were made with glass micropipettes by Svaetichin (1953). Because the vertebrate retina is embryologically derived from the same neural crest tissue that gives rise to the brain, neurophysiologists have become interested in the use of retina as "nature's own brain slice" in the study of the nervous system.

The vertebrate retina consists of two functionally different layers: an outer retina where first-order neurons (photoreceptors) interact with second-order neurons (bipolar and horizontal cells), and an inner retina where bipolar cells feed into third-order neurons (amacrine and ganglion cells). In the outer retina, there is a second synaptic interaction involving the photoreceptors. This interaction is an inhibitory feedback from the horizontal cells in some cones, but feedback from horizontal cells onto rods has not been found (Baylor et al, 1971;

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Fain 1975; Fain et al, 1978).

Bipolar cells, like photoreceptors and horizontal cells, respond to light with sustained graded potentials. In all species, bipolar cells can be classified into two types according to their response patterns: those that hyperpolarize in response to illumination of the center of cell's receptive field and those that depolarize in response to center illumination (Werblin & Dowling, 1969; Kaneko, 1970; Matsumoto & Naka, 1972; Schwartz, 1974; Dacheux & Miller, 1981). The former calls are called hyperpolarizing or off-center (OFF) bipolar cells, and the latter are called depolarizing or on-center (ON) bipolar cells.

In the inner retina, two types of amacrine cells have been described according to light responses: transient and sustained amacrine cells, although in most retinas many more transient amacrine cell responses than sustained amacrine cell responses are recorded (Kaneko, 1971; Matsumoto & Naka, 1972; Toyoda et al, 1973; Naka & Ohtsuka, 1975). Transient amacrine cells have an extremely narrow intensity-response function. Sustained amacrine cells resemble those of the distal retinal neurons, especially those of the horizontal and bipolar cells, and have some properties of transient amacrine cells (Sakuranaga & Naka, 1985).

Most reports describe basically two kinds of ganglion cells: those that give sustained on-center (ON) or off-center (OFF) responses and show an antagonistic surround, and those that respond to flashes of light with transient ON-OFF responses at both onset and cessation of illumination. ON-OFF ganglion cells resemble the transient amacrine cell in terms of the transient nature of its responses and receptive field organization, whereas the sustained ganglion cell resembles the bipolar cell in terms of its sustained responses and center-surround antagonistic receptive field organization.

In the retina, the central pathway consists of 'photoreceptor→bipolar cell' and 'bipolar cell→ganglion cell' synapses whereas the lateral pathway consists of the input and output synapses of horizontal cells and amacrine cells. In the central pathway the neurotransmitter used by synapses is probably glutamate (Slaughter & Miller, 1981 & 1983), and in the lateral pathway mainly γ-aminobutyric acid (GABA) and glycine (Marc et al, 1978). The best studied neurotransmitters in the lateral synaptic pathway are GABA and glycine.

GABA acts at two distinct membrane sites, which have been classified as $GABA_A$ and $GABA_B$ receptors (Bormann, 1988). The $GABA_A$ receptor opens a chloride conductance (Cohen et al, 1989) while the $GABA_B$ receptor modulates two different conductances: the opening of a potassium channel (Slaughter & Bai, 1989; Bai & Slaughter, 1989) and the closing of a calcium channel (Maguire et al, 1989). Potassium always, and chloride usually, have reversal potentials which are more negative than the resting membrane potential. Therefore, opening these channels tends to hyperpolarize the cell. In this paper, we show depolarizing actions of GABA and glycine in catfish retinal neurons.

The purpose of the present study is to examine in detail the light-evoked responses of catifish retinal neurons and to discern the mechanisms of GABA's and glycine's action. An initial report of this work has been previously published (Bai et al, 1992).

METHODS

Retina-eyecup preparation

Experiments were performed in the superfused retina-eyecup preparation of the channel catfish, *Ictalurus punctatus,* using standard electro-physiological techniques. One of the reasons we chose the channel catfish is because its retina contains only a single class of cone (red sensitive, maximal absorbance 625 nm; Naka, 1969). The animals were decapitated and pithed before the eye, and the surrounding tissue was removed from the skull. The retina was exposed by excising the cornea, iris, and vitreous. 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 superfusate. This preparation rested on a wad of cotton soaked in Ringer in contact with an Ag/AgCl reference electrode and was placed in a chamber inside a light-tight Faraday cage.

Solutions and drugs

A pipette was placed at the rim of the eyecup over the retina. The perfusate consisted of a control solution of Ringer: 126 mM NaCl, 4.0 mM KCl, 3.0 mM $CaCl_2$, 1.0 mM $MgCl_2$, 15 mM glucose, 2.0 mM HEPES, and adjusted to pH 7.4 (Shingai & Christensen, 1986). The solution was continuously bubbled with 100% O_2.

The different perfused solutions were contained in a series of bottles which were connected through separate Teflon-lined valves and tubing to a mixing chamber. A short length of polyethylene tubing, that served as the common exit from the mixing chamber, was fed into the perfusion pipette near the retina. This system permitted the addition of two or more solutions to the retina simultaneously, and the exchange time on switching solutions (due to dead space in the lines) was about 30 sec.

Stimulation and recording

Our animals were maintained under normal day/night light cycles, and dissections were done under bright light. The retina eye-cups were then placed in a dark Faraday cage where they adapted to a mesopic state. Diffuse light stimuli were generated by red or green light-emitting diodes (LEDs) positioned above the eyecup (Nygaard & Frumkes, 1982). Intracellular recordings were made with the use of borosilicate glass micropipettes fashioned from "omega dot" capillary tubing (0.6 mm ID, 1.2 mm OD; Glass Company of America) filled with 2 M potassium acetate and having resistances of about 100-200 MΩ. Capacitative "buzzing" was used to facilitate cell impalement. As shown in Fig. 1, voltage recordings were obtained using an amplifier (Intra 767, WPI Inc., USA) and amplified signals were recorded on a storage oscilloscope (Tektronix 5113, USA), a penwriter (Brush 260, Gould Inc., USA), and a Data Recorder (RM-40, Fukuda Denshi Co., Japan).

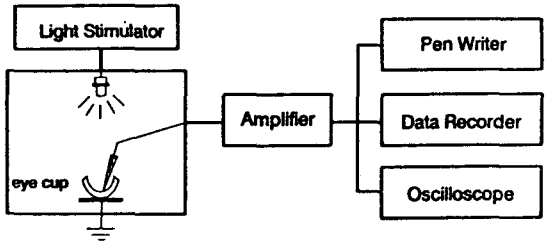

Fig. 1. Schematic diagram of the experimental equipment for intracellular recording from retinal neurons.

Cell indentification

There is much evidence for cell identification of retinal neurons in vertebrate animals (Werblin & Dowling, 1969; Kaneko, 1970; Naka & Ohtsuka, 1975; Werblin 1977). Particularly, in the catfish, morphological and functional identification of retinal neurons has been performed by Naka and his co-workers (Naka & Carraway, 1975; Naka & Ohtsuka, 1975; Naka et al, 1975; Sakai & Naka, 1988).

In our experiment, based on the above findings, cells were identified according to their intracellular light responses, and by the depth of recording.

RESULTS

When we examined the effects of GABA and glycine of first-order neurons in the catfish retina, we found no evidence that GABA or glycine produced a hyperpolarization of the dark membrane potential or a decrease in the light response. As illustrated in the top 2 traces (A & B) in Fig. 2, for example, 5 mM GABA and 5 mM glycine did not alter the light response amplitude or waveform of cone cells (4 tested). In another cone cell shown in the bottom trace (Fig. 2C), the waveform of the cell was altered by the prolongation of interstimulus interval

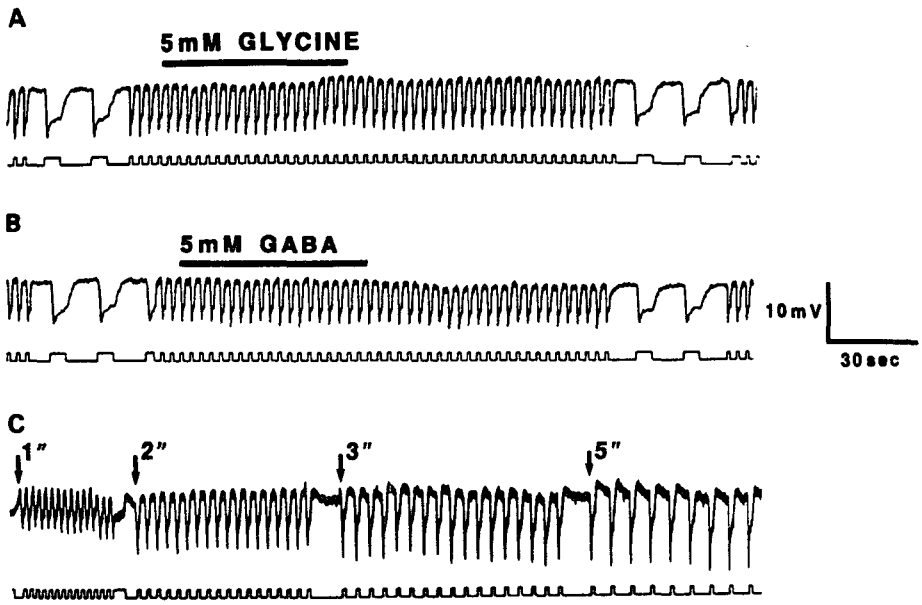

Fig. 2. Intracellular recording from a cone cell. 5 mM GABA (A) and 5 mM glycine (B) did not produce any obvious change in the light-evoked response characteristics of the cell. The dark bar above the voltage trace indicates drug application. The light stimuli for the top 2 traces were red diffuse illumination having durations of 1 sec and an interstimulus interval of 2 sec as indicated by the square-wave pulses at the bottom of the voltage trace (A & B). In the bottom trace (C) showing the cone cell responses to various durations (marked in seconds with arrows at top) of the dark, the amplitude of the responses became progressively larger and the time course of the response rise time became comparatively longer.

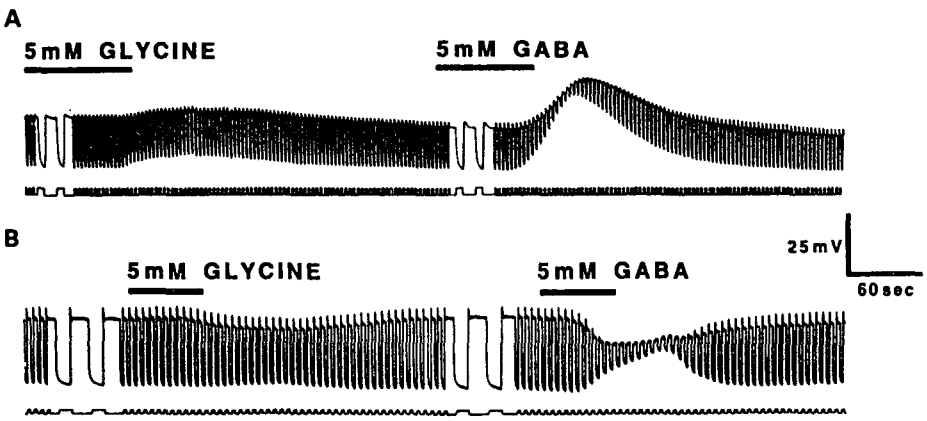

Fig. 3. Intracellular recording from a retinal horizontal cell. A: 5 mM glycine depolarized the cell by ~4 mV, whereas 5 mM GABA depolarized the same cell by ~20 mV. B: 5 mM glycine hyperpolarized the cell by ~4 mV, Whereas 5 mM GABA hyperpolarized the same cell by ~10 mV. The light stimuli were diffuse light, red (upward pulse).

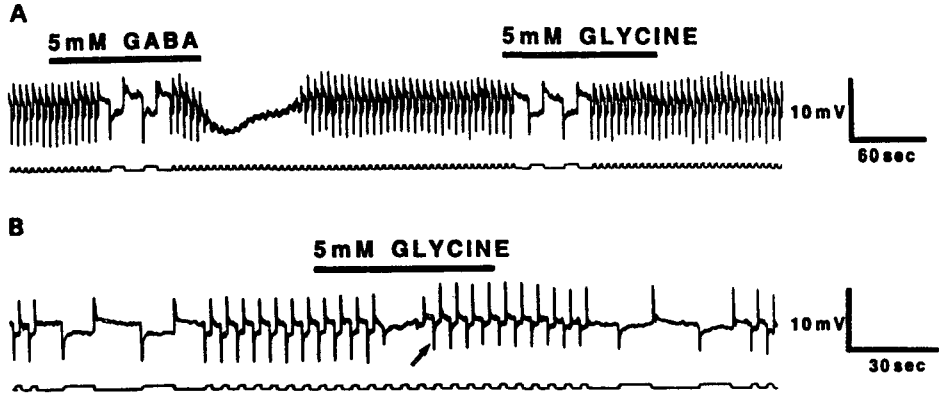

Fig. 4. Intracellular recording from a bipolar cell, exposed to GABA and glycine. In the upper trace, 5 mM GABA hyperpolarized the cell by ~6 mV with a loss of the light-evoked potential and 5 mM glycine produced relatively little effect (A). In the lower trace, another bipolar cell produced a loss of the light-evoked potential with a little hyperpolarization. In spite of the presence of glycine, this cell returned to the control environment (desensitization) (arrow in B). Red diffuse light stimuli.

(prolonged darkness). As the prolonged darkness was increased, the response rise time was progressively longer than that of the shortened darkness and the magnitude of the light-evoked potential was comparatively enhanced in cone responses.

The actions of GABA and glycine on horizontal cells are illustrated in Fig. 3. It appeared that the effects of GABA and glycine on horizontal cells were variable. GABA and glycine depolarized 64 (~67%) of 96 cells, and hyperpolarized 32 cells (~33%). Fig. 3A shows the depolarizing actions by the inhibitory neurotransmitters. In the upper trace, 5 mM glycine depolarized the cell by ~4 mV and 5 mM GABA depolarized the same cell by ~20 mV. Glycine usually acted similarly to GABA, but produced a much smaller effect GABA and glycine were musch more effective at depolarizing than hyperpolarizing the horizontal cells. Fig. 3B shows a cell in which the GABA and glycine hyperpolarization is particularly greater than normal. In the other cell shown in the lower trace, 5 mM glycine hyperpolarized the cell by ~4 mV and 5 mM GABA hyperpolarized the same cell by ~10 mV.

GABA and glycine hyperpolarized bipolar cells and reduced the light-evoked response in the catfish retina. An example of this inhibitory action is shown in the OFF bipolar cell in Fig. 4. The GABA hyperpolarization was very marked, while the effect of glycine was indistinguishable (Fig. 4A). In the upper trace of this figure, 5 mM GABA hyperpolarized the cell by ~6 mM with a loss of the light-evoked potential whereas 5 mM glycine produced considerably less effect. Another bipolar cell in the lower trace of Fig. 4 showed a hyperpolarization with a loss of the light-evoked potential, but this cell returned to the control environment (arrow in Fig. 4B) in spite of the presence of glycine (desensitization).

We found that GABA and glycine, acted as excitatory neurotransmitters on the third-order neurons in the catfish retina. Of 54 third-order neurons studies, 34 were excited while 20 of these inhibited by GABA and glycine application. An example of inhibitory action is demonstrated in the cell shown in Fig. 5. On the other hand, although it is well known that GABA and glycine are the inhibitory neurotransmitters in the vertebrate retina, GABA and glycine depo-

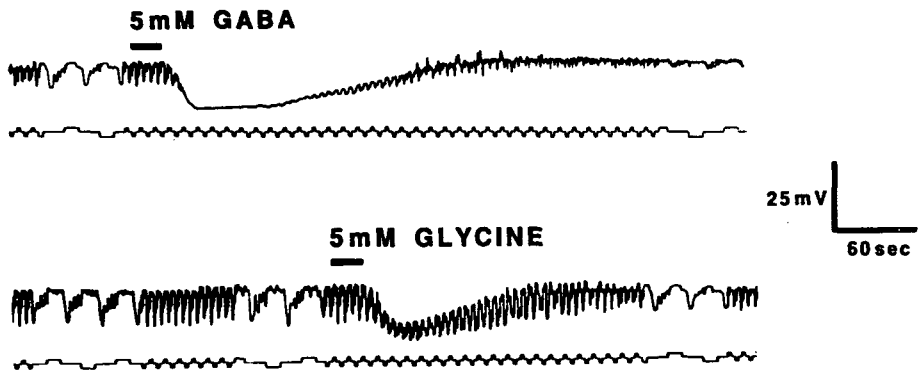

Fig. 5. Hyperpolarizing action (~37%) of GABA and glycine on a third-order neuron which was not frequently found in the catfish retina in contrast to depolarizing action (~63%). Red (up) and green (down) diffuse light stimuli.

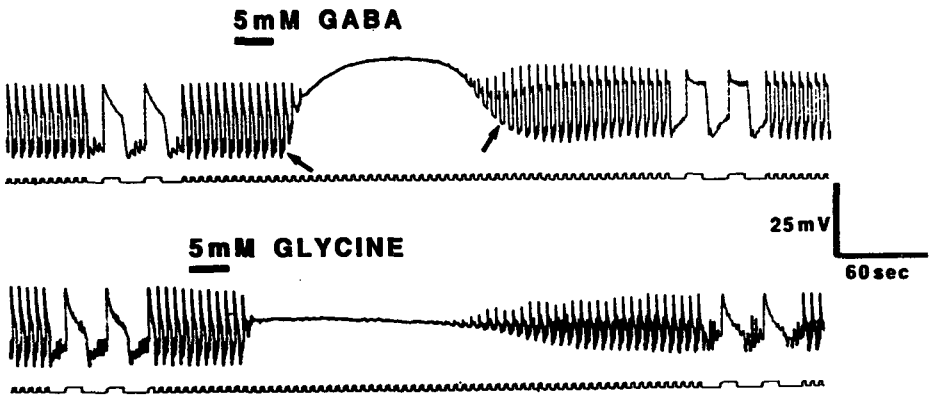

Fig. 6. Depolarizing actions of GABA and glycine on third-order neurons in the catfish retina. GABA almost always has a greater effect than glycine. In the ON sustained cell shown at the upper trace, 5 mM GABA depolarized the dark membrane potential by ~30 mV and abolished the light-evoked potential. Arrows indicate the oscillatory potentials before (first arrow) and after (second arrow) GABA administration. In the lower trae, 5 mM glycine depolarized the cell by ~14 mV and abolished the light-evoked potential. Red diffuse light stimuli.

larized the third-order neurons in the catfish retina. In an ON sustained cell (Fig. 6), 5 mM GABA produced ~30 mV depolarization while 5 mM glycine produced ~14 mV. But GABA and glycine abolished the light-evoked response. In the upper trace of this figure, the dark membrane noise decreased very significantly during GABA treatment (compare oscillation at first and second arrow). In a series of experiments to test for a dose-dependent effect (not shown), it did not make any difference in depolarization without the dose-response.

The depolarizing action of GABA and glycine is demonstrated in another ON sustained cell with a pronounced OFF-transient EPSP (excitatory postsynaptic potential) shown in

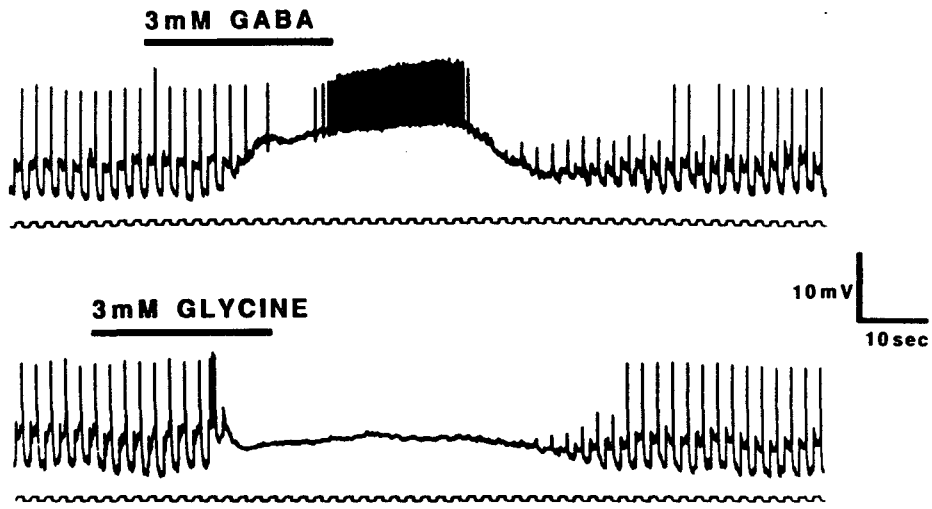

Fig. 7. Excitatory actions of GABA on third-order neurons in the catfish retina. In an ON sustained cell with pronounced OFF-transient EPSP, 3 mM GABA depolarized the dark membrane potential by ~9 mV and produced spike-firing during the depolarization. 3 mM glycine depolarized the same cell by ~4 mV, in the lower trace, but did not produce any spikes. Red diffuse light stimuli.

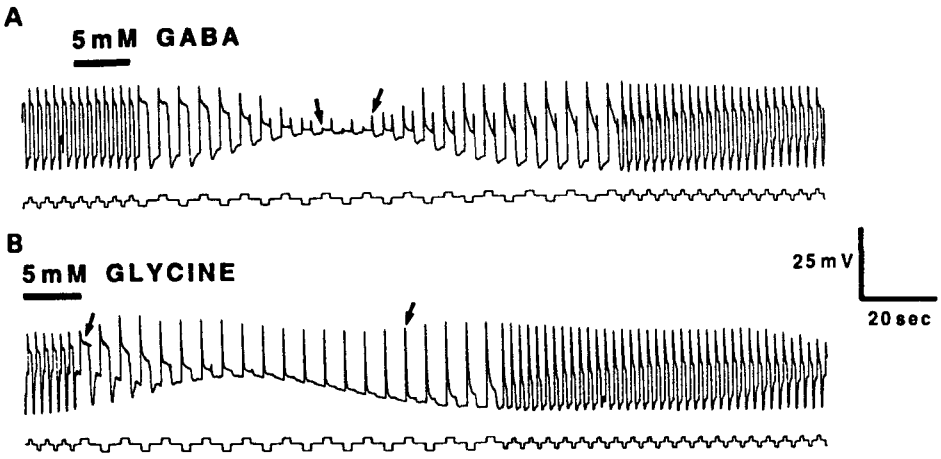

Fig. 8. Another ON sustained cell in which GABA and glycine hyperpolarized the light-evoked potential, but the effects on the dark membrane potentials were variable. A: 5 mM GABA depolarized the dark membrane potential by ~10 mV, while it hyperpolarized the light-evoked potential by ~10 mV. GABA suppressed the ON transient responses (first arrow) with ON sustained potentials producing OFF transient responses (second arrow) in the upper trace. B: 5 mM glycine depolarized the same cell by ~12 mV. Glycine suppresed the ON sustained responses (first arrow) and the light responses were altered to ON transient responses (second arrow) in the lower trace. Red (up) and green (down) diffuse light stimuli.

Fig. 7. Strikingly, 3 mM GABA made the cell produce a series of spike-firing during the depolarization as illustrated in the upper trace. But, 3 mM glycine did not cause this excitatory action accompanied with spike activity as shown in the lower trace.

Fig. 8 illustrates recording from an ON sustained cell with a pronounced ON transient EPSP, in which both GABA and glycine depolarized the dark membrane potential but hyperpolarized the light-evoked potential. In the cell illustrated in the upper trace, 5 mM GABA depolarized the dark membrane potential by ~10 mV while it hyperpolarized the light-evoked potential by ~10 mV. In the ON sustained cell of Fig. 8A, light stimulation initially produced a tonic EPSP. 5 mM GABA caused a depolarization of the cell, and the light response was converted to a small, transient depolarization (first arrow) at light onset and a large, transient depolarization (second arrow) at light offset. In the same cell shown in the lower trace of Fig. 8, 5 mM glycine caused the cell to depolarize by ~12 mV and the light response was altered from a tonic depolarization (first arrow) throughout the light period to a very large, transient EPSP (second arrow) at light onset. In an ON-OFF transient cell we observed that 5 mM GABA abolished the ON transient response and maintained the OFF response whereas 5 mM glycine conserved the ON transient response and abolished the OFF response.

DISCUSSION

In the catfish retina, we found no evidence that both 5 mM GABA and 5 mM glycine had an effect on photoreceptors (Fig. 2A & B). This result is supported by the findings of Miller and his co-workers (1981) who showed that GABA and glycine caused no detectable change in the membrane potential or amplitude of the light-evoked response in the mudpuppy retina. But, certain studies have indicated that GABA hyperpolarizes cones in the carp retina (Murakami et al, 1972; Wu & Dowling, 1980). In this paper, the failure of photoreceptors to respond to GABA and glycine is perhaps due to an inactivation mechanism for GABA or an offset action between direct and indirect synaptic influences.

Yang and Wu (1989) indicated that the amplitude of cone responses was slightly increased by prolonged light exposure in tiger salamander retina. As a different attempt from the above result, we applied a series of dark durations to the catfish cone cells with a constant light exposure (1 sec). We found that prolongation of dark duration speeds up the rise time course and also the amplitude of the cone light responses is increased (Fig. 2C). Therefore, in the catfish cone cell, it one should apply 1-sec light stimuli and 2-sec dark duration or more.

The effect of GABA and glycine on the catfish horizontal cells was either hyperpolarization (~33%) or depolarization (~67%) (Fig. 3). Horizontal cells are the primary neurons in the outer retina that contain GABA. In many species, a subset of horizontal cells appear to be GABAergic (Massey & Redburn, 1987; Yazulla, 1986). The presence of GABA and glycine receptors on horizontal cells seems to be a species-specific phenomenon in vertebrate retinas. For example, goldfish and carp do not appear to have GABA receptors (Wu & Dowling, 1980; Murakami et al, 1982) whereas they are prominent in the skate retina (Lasater et al, 1984). Results obtained with the catfish suggests that may of the horizontal cells are much more sensitive to GABA, but glycine is usually less effective than GABA. In the horizontal cell shown in Fig. 3A, GABA significantly depolarized the cell and glycine did slightly. Based on results obtained from amphibian retina, Stockton et al. (1988) have shown that horizontal cells can be depolarized by GABA and glycine. The depolarizing action of GABA on horizontal cells is presumably due to either an electrogenic uptake mechanism (Kehoe, 1975) or an ionic mechanism (Gallagher et al, 1978; Miller et al, 1981; Stockton & Slaughter, 1991). It seems relevant to consider that, if the chlo-

ride equilibrium potential (E_{Cl}) is more positive than the dark membrane potential (V_m), the depolarizing action of GABA will be blocked by removal of external chloride ions.

It has been known that the effect of the photoreceptor transmitter on many ON bipolar cells is to close ionic channels, whereas its action on the OFF bipolar cells and the horizontal cells is to open channels (Saito & Kaneko, 1983; Saito et al, 1979). Thus, a difference in the postsynaptic receptors on these cells is to be expected. In the present paper, GABA intensively hyperpolarized an OFF bipolar cell while the effects of glycine were very weak or almost negligible in the catfish retinal neurons (Fig. 4A). This finding is in agreement with the results of Muller and Marc (1990) who showed that glycinergic receptors on bipolar cells are extremely rare. However, the efficacy of GABA could be potent in the catfish bipolar cells, but that of glycine is likely to be insensitive. Moreover, we were able to observe a desensitization effect (Katz & Thesleff, 1957) of glycine in another OFF bipolar cell (Fig. 4B). It seems to be relevant that the postsynaptic membrane became significantly less responsive to applied neurotransmitter over time (arrow in Fig. 4B).

It is interesting that, in the catfish retina, many third-order neurons were depolarized (Fig. 6-8) by GABA and glycine while the remainder were hyperpolarized (Fig. 5). GABA and glycine are widespread but clearly separated anatomically and have different physiological roles in the inner retina. It has been shown that amacrine cells make chemical synapses on bipolar cell axon terminals in most vertebrate retinas (Dowling & Werblin, 1969) and GABAergic amacrine cells appear to primarily inhibit the ON ganglion cells but not the OFF cells in the catfish and skate (Lasater & Lam, 1984, Cohen, 1985). In the third-order neuron (Fig. 6), the reduction of dark membrane noise during GABA treatment might indicate that GABA was opening many channels on the cell, thus reducing the input resistance, which decreased the voltage noise. Also ON sustained cells were much more sensitive to GABA compared with glycine (Fig. 6 & 7). These results could be concerned with the observation that, in the goldfish, approximately 50% of the somas in the amacrine cell layer are GABAergic while roughly 30% are glycinergic (Marc et al, 1978). Looking at the ON sustained cell (Fig. 8), it seems that GABA suppresses ON channels of the cells while glycine suppresses OFF channels significantly in the catfish retina. These findings are in agreement with the results of Miller et al. (1981) who reported that the OFF pathway is more glycinergic than the ON pathway in the mudpuppy retina.

Concerning the dual effect of GABA, Andersen et al. (1980) have reported a depolarizing and a hyperpolarizing effect of GABA in hippocampal CA1 neurons; that is, they observed that iontophoretic application of GABA to the dendritic region depolarized the CA1 neuron, while application to the cell soma hyperpolarized the membrane potential. On the other hand, Bai and Slaughter (1989) have reported that the paradoxical effect of baclofen ($GABA_B$ agonist) producing a hyperpolarization of the third-order neurons and an enhancement of synaptic responses due to at least two mechanisms in the mudpuppy retina. What is the mechanism of depolarization by the inhibitory neurotransmitters? The effect could be achieved by direct depolarization of the inhibited cell, by inhibition of the inhibitory interneurons, or by a combination of both. Thus, although many problems remain to be solved, it is likely to involve two types of mechanisms; one is an ionic effect and the other is a network effect.

As for the ionic mechanism, in the inner retina, it seems that GABA and glycine open chloride channels and then mediate alterations in Cl^- permeability of the membrane. If the chloride equilibrium potential is more positive than the dark membrane potential and requires an inwardly directed chloride pump, chloride-dependent depolarization by the inhibitory neurotransmitter could be occur. This possibility seems to be supported by the result of

Gallagher et al. (1978) who observed that depolarization was produced when GABA was applied to the primary afferent neurons iontophoretically.

'GABAergic amacrine→ganglion cell' synapses, along with the 'GABAergic amacrine→bipolar cell' synapses, form a network of lateral connections in the inner plexiform layer that are responsible for mediating the antagonistic surround responses of retinal ganglion cells (Ishida & Cohen, 1988). As for the network mechanism, although the cellular organizations of vertebrate retinal synapses are complex, let us imagine a basic signal channel of a simple series of retinal neurons; a non-GABAergic bipolar cell (BC)→GABAergic amacrine cell (AM)→non-GABAergic ganglion cell (GC). It is estimated that the application of GABA induces the inhibitory activation of BC and subsequent inactivation of AM, which then results in the excitatory activation of GC. This possibility of depolarizing actions by GABA and glycine could be supported by the immunocytochemical observation of Chun (1993). He indicated that, in the guinea pig retina, GABAergic amacrine cells inhibit GABAergic amacrine cells which synapse onto the non-GABAergic ON- and OFF-ganglion cells causing disinhibition. Thus, there seems to be little doubt that GABA and glycine are working to suppress presynaptic inhibition or disinhibition. Consequently, the present study suggests that there are both presynaptic inhibitory effects and also direct postsynaptic effects of GABA and glycine on the third-order neurons in the catfish retina.

REFERENCES

Andersen P, Dingledine R, Gjestad L, Langmoen IA & Mosfeldt Laursen A (1980) Two different responses of hippocampal pyramidal cells to application of gamma-aminobutyric acid. *J Physiol* **305,** 279-296

Bai S-H & Slaughter MM (1989) Effects of baclofen on transient neurons in the mudpuppy retina: electrogenic and network actions. *J Neurophysiol* **61,** 382-390

Bai S-H, Jung C-S & Lee S-J (1992) Depolarizing actions of GABA and glycine on neurons in the catfish retina (Abstract). *Kor J Physiol* **26,** 185

Baylor DA, Fuortes MGF & O'Bryan PM (1971) Receptive fields of single cones in the retina of the turtle. *J Physiol* **214,** 256-294

Bormann J (1988) Electrophysiology of $GABA_A$ and $GABA_B$ receptor subtypes. *Trends Neurosci* **11,** 112-116

Chun M-H (1993) Personal communication.

Cohen BN, Fain GL & Fain MJ (1989) GABA and glycine channels in isolated ganglion cells from goldfish retina. *J Physiol Lond* **417,** 53-82

Cohen JL (1985) Effect of glycine and GABA on ganglion cells of the retina of the skate Raja crinacca. *Brain Res* **332,** 169-173

Dacheux RF & Miller RF (1981) An intracellular electrophysiological study of the ontogeny of functional synapses in the rabbit retina. I. Receptors, horizontal and bipolar cells. *J Comp Neurol* **198,** 307-326

Dowling JE & Werblin F (1969) Organization of the retina of the mudpuppy, *Necturus maculosus.* I. Synaptic structure. *J Neurophysiol* **32,** 315-338

Fain GL (1975) Interaction of rod and cone signals in the mudpuppy retina. *J Physiol* **252,** 735-769

Fain GL, Quandt FN, Bastian BL & Gerschenfeld HM (1978) Contribution of a caesium-sensitive conductance increase to the rod response. *Nature* **272,** 467-469

Gallagher JP, Higashi H & Nishi S (1978) Characterization and ionic bases of GABA-induced depolarizations recorded *in vivo* from cat primary afferent neurones. *J Physiol* **275,** 263-282

Ishida AT & Cohen BN (1988) GABA-activated whole cell currents in isolated retinal ganglion cell. *J Neurophysiol* **60,** 381-396

Kaneko A (1970) Physiological and morphological identification of horizontal, bipolar, and amacrine cells in the goldfish retina. *J Physiol* **207,** 623-633

Kaneko A (1971) Physiological studies of single retinal cells and their morphological identification. *Vision Res Suppl* **3,** 17-26

Katz B & Thesleff S (1957) A study of the "desensitization" produced by acetylcholine at the motor end-plate. *J Physiol* **138,** 63-80

Kehoe JS (1975) Electrogenic effects on neutral

amino acids on neurons of *Aplysia californica*. *Cold Spring Harbor Symp Quant Biol* **40**, 145-156

Lasater EM & Lam DMK (1984) The identification and some functions of GABAergic neurons in the distal catfish retina. *Vision RES* **24**, 497-506

Maguire G, Maple B, Lukasiewicz P & Werblin F (1989) Gamma-aminobutyrate type B receptor modulation of L-type calcium channel current at bipolar cell terminals in the retina of the tiger salamander. *Proc Natl Acad Sci USA* **86**, 10144-10147

Marc RE, Stell WK, Bok D & Lam DMK (1978) GABAergic pathways in the goldfish retina. *J Comp Neurol* **182**, 221-246

Massey SC & Redburn DA (1987) Transmitter circuits in the vertebrate retina. *Prog Neurobiol* **28**, 55-96

Matsumoto N & Naka K-I (1972) Identification of intracellular responses in the frog retina. *Brain Res* **42**, 59-71

Miller RF, Frumkes TE, Slaughter MM & Dacheux RF (1981) Physiological and pharmacological basis of GABA and glycine action on neurons of mudpuppy retina. I. Receptors, horizontal Cells, bipolar, and G-cells. *J Neurophysiol* **45**, 743-763

Muller JF & Marc RE (1990) GABA-ergic and glycinergic pathways in the inner plexiform layer of the goldfish retina. *J Comp Neurol* **291**, 281-304

Murakami M, Ohstu K & Ohtsuka K (1972) Effects of chemicals on receptors and horizontal cells in the retina. *J Physiol, Lond* **227**, 899-913

Murakami M, Shimoda Y, Nakatami K, Miyachi E & Watanabe S (1982) GABA mediated negative feedback and color opponency in the carp retina. *Jpn J Physiol* **32**, 927-935

Naka K-I (1969) Computer assisted analysis of S-potentials. *Biophys J* **9**, 855-899

Naka K-I & Carraway RG (1975) Morphological and functional identification of catfish retinal neurons. I. Classical morphology. *J Neurophysiol* **38**, 53-71

Naka K-I & Ohtsuka T (1975) Morphological and functional identifications of catfish retinal neurons. II. Morphological identification. *J Neurophysiol* **38**, 72-91

Naka K-I, Marmarelis PZ & Chan RY (1975) Morphological and functional identification of catfish retinal neurons. III. Functional identification. *J Neurophysiol* **38**, 92-130

Nygaard RW & Frumkes TE (1982) LEDs: Convenient, inexpensive sources for visual experimentation. *Vision Res* **22**, 435-440

Saito T & Kaneko A (1983) Ionic mechanisms underlying the responses of off-center bipolar cells in the carp retina. I. Studies on responses evoked by light. *J Gen Physiol* **81**, 589-601

Saito T, Kondo H & Toyoda J (1979) Ionic mechanisms of two types of on-center bipolar cells in the carp retina I. The responses to central illumination. *J Gen Physiol* **73**, 73-90

Sakai HM & Naka K-I (1988) Neuron network in catfish retina: 1968-1987. *Prog Ret Res* **7**, 149-208

Sakuranaga M & Naka K-I (1985) Signal transmission in the catfish retina. II. Transmission to type-N cell. *J Neurophysiol* **53**, 390-410

Schwartz EA (1974) Responses of bipolar cells in the retina of the turtle. *J Physiol* **217**, 71-91

Shingai R & Christensen BN (1986) Excitable properties and voltage-sensitive ion conductances of horizontal cells isolated from catfish (*Ictalurus punctatus*) retina. *J Neurophysiol* **56**, 32-49

Slaughter MM & Bai S-H (1989) Differential effects of baclofen on sustained and transient cells in the mudpuppy retina. *J Neurophysiol* **61**, 374-381

Slaughter MM & Miller RF (1981) 2-Amino-4-phosphonobutyric acid: a new pharmacological tool for retina research. *Science* **211**, 182-185

Slaughter MM & Miller RF (1983) Bipolar cells in the mudpuppy retina use an excitatory amino-acid neurotransmitter. *Nature* **303**, 537-538

Stockton RA & Slaughter MM (1991) Depolarizing actions of GABA and glycine on amphibian retinal horizontal cells. *J Neurophysiol* **65**, 680-692

Stockton RA, Bai S-H & Slaughter MM (1988) Depolarizing actions of GABA and glycine upon retinal horizontal cells of mudpuppy and tiger salamander (Abstract). *Invest Ophthalmol 29*, Suppl: 101

Svaetichin G (1953) The cone action potential. *Acta Physiol* **29**, 565-600

Toyoda J, Hashimoto H & Ohtsu K (1973) Bipolar-

amacrine transmission in the carp retina. *Vision Res* **13,** 295-307

Werblin FS (1977) Regenerative amacrine cell depolarization and formation of on-off ganglion cell responses. *J Physiol* **264,** 767-785

Werblin FS & Dowling JE (1969) Organization of the retina of the mudpuppy, *Necturus maculosus.* II. Intracellular recording. *J Neurophysiol* **32,** 339-355

Wu SM & Dowling JE (1980) Effects of GABA and glycine on the distal cells of the cyprinid retina. *Brain Res* **199,** 401-414

Yang X-L & Wu SM (1989) Effects of prolonged light exposure, GABA, and glycine on horizontal cell responses in tiger salamander retina. *J Neurophysiol* **61,** 1025-1035

Yazulla S (1986) GABAergic mechanisms in the retina. *Prog Retina Res* **5,** 1-52