terone and etiocholanolone propionate.

Our results show that neonatally administered 5α-dihydrotestosterone propionate and estradiol benzoate are almost as efficient as testosterone propionate in programming hepatic steroid metabolism. The relatively specific nature of this imprinting phenomenon is obvious from the fact that epitestosterone propionate and etiocholanolone propionate were almost without effect. The fact that the nonaromatizable androgen 5α-dihydrotestosterone is active as an imprinting agent indicates that the mechanism involved is different from that behind the androgen-induced development of persistent estrous syndrome and acyclic gonadotropin secretion. The involvement of different mechanisms is further supported by the fact that *o,p'*-DDT, administered in doses similar to those inducing persistent vaginal estrus (*8*), did not have a masculinizing effect on hepatic steroid metabolism. Further studies are needed to determine whether different regions of the hypothalamus are involved in control of hepatic metabolism and estrus, respectively.

The question may be raised as to why the hepatic metabolism of steroid hormones in the rat is sex-differentiated by specific neonatal programming of the hypothalamus by testicular androgens. It seems reasonable to assume that the specific regulation of the hepatic enzymes is associated with a specific function of the steroid metabolites that are formed by the action of these enzymes. Thus, the male-specific products of hepatic steroid metabolism (for example, 3β- and 17α-hydroxy-C_{19} steroids) may act as androgen effectors in target organs yet to be defined.

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Specific Effects of Neurotransmitter Antagonists on Ganglion Cells in Rabbit Retina

Abstract. *Directionally sensitive ganglion cells in rabbit retina lose their directional sensitivity when picrotoxin, an antagonist of the inhibitory neurotransmitter γ-aminobutyric acid, is infused into the retinal blood supply. Strychnine, an antagonist of glycine, does not produce this effect. Other receptive field types are affected by strychnine but not picrotoxin. Inhibitory transmitters therefore have specific functions in information processing in the retina.*

The rabbit retina contains ganglion cells with a great variety of receptive fields. As well as cells with center-surround receptive fields, there are directionally sensitive cells, which respond most vigorously to stimulus motion in a particular direction (the preferred direction), and local edge detectors, which respond to small moving stimuli without any preference for direction of motion (*1*). Other types of receptive field are found in smaller quantities.

A number of synaptic transmitters are found in the rabbit retina, as in most retinas, and it seems likely that each performs a different function (*2*). Our purpose in this work was to find out whether particular transmitters might be implicated in the functions of known receptive field types.

Responses of ganglion cells in the right eye were recorded extracellularly with tungsten-in-glass electrodes inserted through the sclera (*3*, *4*). A particular re-

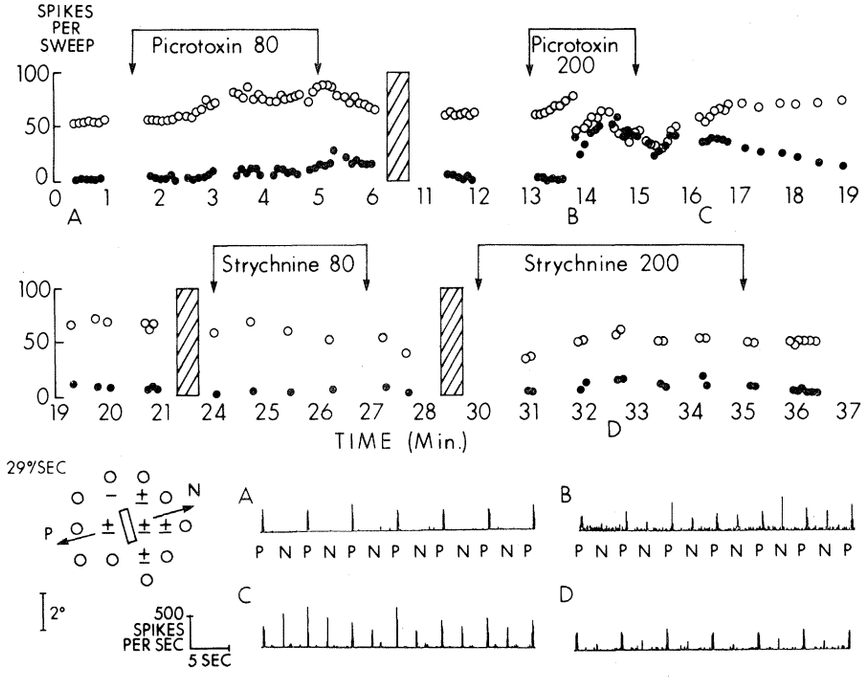

Fig. 1. Effect of picrotoxin and strychnine on an "on-off" directionally sensitive cell. Inset at lower left shows the preferred (*P*) and null (*N*) directions and the size of the stimulus in relation to the receptive field. The graphs at the top show the total number of action potentials per sweep for movement in the preferred direction (○) and null direction (●). Infusion rates are given in micrograms per minute. (A to D) Some of the data from which the graphs were obtained (number of action potentials per bin of 66-msec width): (A) before application of drugs; (B) about 1 minute after starting infusion of picrotoxin at 200 μg/min; (C) about 1 minute after ending infusion of picrotoxin at 200 μg/min; and (D) about 2½ minutes after starting infusion of strychnine at 200 μg/min.

ceptive field was analyzed with bars and spots of light moved across or flashed on a tangent screen (*4*). Various drugs, believed to be antagonists of particular transmitters, were then infused into the right internal maxillary artery. This was accomplished by upstream injection into the right external maxillary artery, with the right lingual, temporal, and internal carotid arteries clamped off (*5*). The receptive field was then studied again, care being taken to detect any change in organization. Results were obtained from 61 units in 14 animals. Many cells were isolated and held for several hours, so that the effects of more than one drug on a single cell could be compared and various dosages could be tested.

The effect of picrotoxin [which antagonizes the inhibitory transmitter γ-aminobutyric acid (GABA) at several sites within the central nervous system (*6*)] on directionally sensitive cells is dramatic. Initially the response in the preferred direction increases slightly; then the response in the preferred direction drops and the response in the null direction increases, so that the cell becomes equally responsive to preferred and null directions of movement (Fig. 1). This occurs rapidly, within 2 minutes of the start of drug infusion (Fig. 1B). It is also reversible: the cells become directionally sensitive again a few minutes after drug infusion is discontinued (Fig. 1C). The two classes of directionally sensitive cells, "on-off" and "on" types [so called because of their responses to flashed spots of light (*3*)], both become nondirectional with picrotoxin.

Picrotoxin also affects the specificity of directionally sensitive cells for small spots (Fig. 2). The cell in Fig. 2 was an "on" type, which responded to a spot but not a bar for motion in the preferred direction, and to neither for motion in the null direction. After infusion of picrotoxin, the cell responded to both a spot and a bar moved in either direction. This cell was a rather extreme example in that there was no response to a bar moved in the preferred direction. Most directionally sensitive cells in the rabbit retina respond equally well to a spot or a bar moved in the preferred direction, but better to a spot than a bar moved in a direction 45° or 90° to the preferred direction (*4*). The effect of picrotoxin on this size specificity varied from cell to cell, and occasionally size specificity was less affected than directional sensitivity. In general, however, both directional sensitivity and size specificity were reduced, supporting the hypothesis that the same lateral connections give rise to both properties (*4*).

The dosage of picrotoxin required for these effects was about 200 μg/min infused

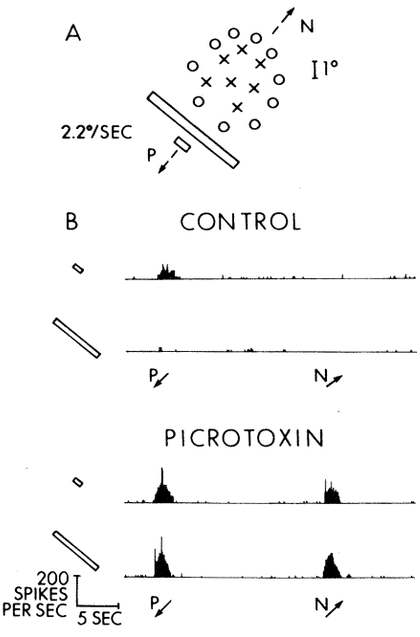

Fig. 2. Effect of picrotoxin on an "on" directionally sensitive cell. (A) Plot of receptive field, showing size and speed of stimuli. (B) Responses (printout of number of spikes per 66-msec bin) to movement of spot and bar, before and during infusion of picrotoxin (200 μg/min for 3 minutes).

for about 2 minutes. Occasionally a smaller dosage sufficed, and where a larger dosage was necessary the preparation was usually found to be poor (*7*).

Strychnine, an antagonist of the inhibitory transmitter glycine (*6*), does not abolish the directional sensitivity of these cells (Fig. 1) when applied in the same range of concentrations as picrotoxin. It does increase spontaneous activity (as does picrotoxin) and the general responsiveness of the cell. However, strychnine affects some other types of cell that are not affected by picrotoxin. A local edge detector was found to lose its specificity for small stimuli after infusion of strychnine, but not of picrotoxin. The "on" response, obtained from the surround of an off-center center-surround cell stimulated with an annulus of light, was found to increase more with strychnine than with picrotoxin. These effects of strychnine were seen with dosages lower than those which failed to affect directional sensitivity, which supports the idea that directional sensitivity is selectively sensitive to picrotoxin.

Many more experiments will be required before specific transmitter substances can be assigned to specific synapses within the receptor fields of these cells. While picrotoxin is relatively specific for GABA, this is not always the case (*6*). Picrotoxin affects the response of Y cells in the cat retina (*8*), and more detailed studies of center-surround cells in the rabbit retina may also show some effects there.

However, the results do fit together neatly with experiments on the pharmacological localization of transmitter substances in the retina, and with what is known about the physiology of directionally sensitive cells. Both GABA and glycine are found in the retinas of many species (*2*). In rabbit retina, both substances have been localized to amacrine cells, each to a limited population of amacrine cells (*9*). Directional sensitivity in the rabbit retina is believed to result from asymmetric lateral inhibition (*3, 4*) and it has been suggested that the specificity for stimulus size found in these cells results from the same inhibitory connections (*4*). Our results suggest that the transmitter for this lateral inhibition is GABA, and therefore support the hypothesis that these inhibitory connections are made by amacrine cells in the inner plexiform layer (*4, 10*) rather than by horizontal cells (*3*). In general, the results also support the hypothesis that there are separate classes of amacrine cell, each with a different transmitter, associated with different functional classes of ganglion cell.

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