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Time Courses of Excitation and Inhibition in Retinal Ganglion Cells

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Latencies of the different types of ganglion cell responses to stimulation within a receptive field were measured in guinea pigs. The latency of the response evoked by stimulation of the center or intermediate zone was always less than the response evoked by stimulation of the periphery or intermediate zone. The *on-off* response had latency values as if the responses were independently elicited in the center and periphery. When two light spots were shone in the receptive field at different time intervals, it was found that one could cancel the other if shone in a precise time which was dependent on the latencies of the responses of the receptive field. To account for the observations, it is postulated that the time courses of excitation and inhibition can vary from ganglion cell to ganglion cell.

Introduction

It is now widely accepted that the retinal ganglion cell receptive field is a functional unit, whose final gate is the ganglion cell. The response or lack of response of the ganglion cell is determined by the predominance of either the excitatory or the inhibitory processes that are continuously acting on it. The magnitude of these processes, in turn, is determined by the activity of the receptors in the center and the periphery of the receptive fields. It is not clear whether the periphery exerts its action through the horizontal or amacrine cells, or both (2, 3); but whichever is the case, the peripheral action is always one of inhibition of both the excitation and the inhibition generated in the center (4, 6). However, little attention has been paid to the more precise time courses of the excitatory and inhibitory processes and their inhibition. We have attempted to investigate them by measuring the latencies of the response in different parts of the receptive field and by studying the interactions of two light spots.

Methods

Adult guinea pigs were put in a stereotaxic apparatus after Urethane anesthesia (0.5 ml/100 g), and the eyeballs were fixed by sutures to a ring. Complications from clouding of the cornea were prevented by moistening it with silicone. Micropipettes with a tip diameter of about 1 μ were filled with indium (Wood's metal), and a platinum and gold ball (3–8 μ) was deposited on the tip. The microelectrodes were introduced through a minute opening on the sclera and pushed through the vitreous body until they made contact with the retinal surface. They were connected to a cathode follower and this was connected in turn to an oscilloscope. With this setup, single cell potentials of about 300 μv were recorded for fairly long periods. The responses were stored in a tape recorder and later photographed with a Grass camera.

The animal was looking at a screen in which it was possible to adjust the background illumination. Two Sylvania glow-modulator tubes were used for controlled stimulation of restricted areas of the retina with light spots of variable duration. The spot diameter subtended a visual angle of the order of 15 min. The initiation and duration of the spot were under the control of two synchronized Grass stimulators, and in this way they could be triggered at different time intervals. Signals from the stimulators were introduced to a second beam of the oscilloscope, indicating separately the *on* and *off* of the spots. At least 30 fields were thus analyzed.

Results

In a first series of experiments, we delimited the *on* and *off* zone of ganglion cell receptive fields and selected only those which had a clear *on-off* intermediate zone. In these cells we stimulated the *on-off* zone with a single light spot for several milliseconds and determined the latencies of the *on* and *off* responses. In all cases these latencies were different.[1] After this, by projecting light spots on the center and the periphery of the same cells, we determined the latencies of independently elicited *on* and *off* responses. In all cases these latencies were the same as the corresponding ones determined in the *on-off* zones of the cells (Fig. 1).

In a second series of experiments we directed two light spots to neighboring points in the center (or periphery) of the receptive field, and, by starting them at different intervals or varying their duration, we studied the interactions between the excitation and inhibition that they elicited. In Fig. 2 it is seen that in an *on*-center receptive field, the response to the *on* of the

[1] A quantitative description of the results is not convenient in this case, because the absolute values of the latencies and temporal courses vary greatly from cell to cell, although their general relations are always constant.

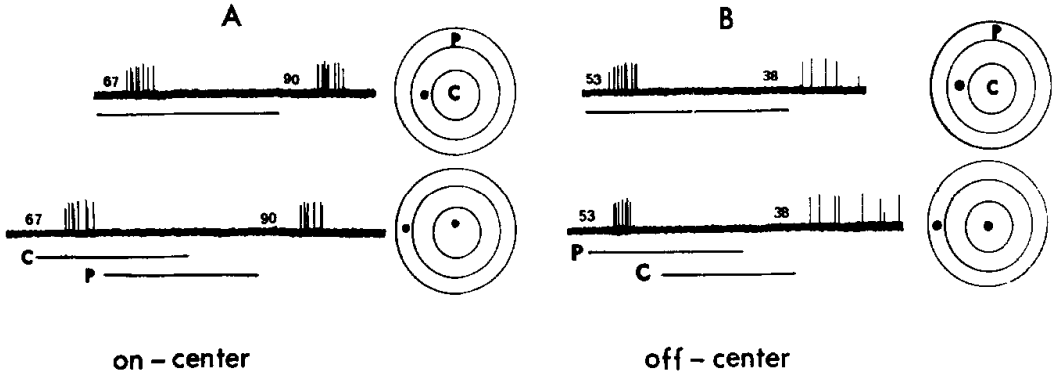

FIG. 1. A. Response of an *on*-center ganglion cell to a light spot shone in its *on-off* zone (upper trace), and to two light spots independently shone in the center (C) and in the periphery (P) of the same cell (lower trace). Latency values are given in msec. The positions of the light spots are indicated by dark dots in the diagram of the receptive field. The lines underneath the traces indicate the stimulus duration. B. Responses of *off*-center ganglion cell under the same conditions as in A. In this and the following two figures the spikes have been retouched for photographic purposes.

second spot of light could be inhibited by the *off* of the first one. This inhibitory action was evident only if the *on* of the second spot followed the *off* of the first one, within a period that was equal to the duration of the first *on* response, and began after a time interval which was equal to the latency of this response. Correspondingly, in an *off*-center receptive field, the re-

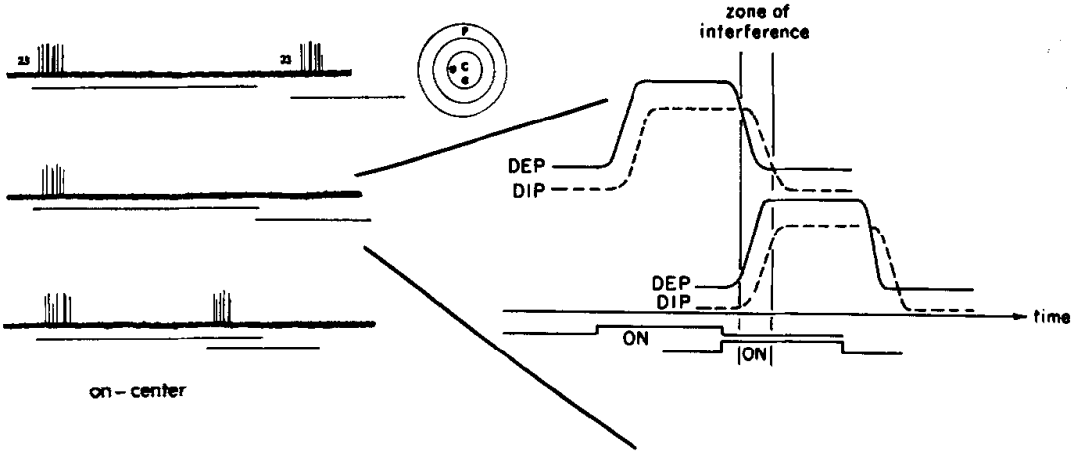

FIG. 2. Responses of an on-center ganglion cell upon stimulation in the center of its receptive field with two light spots shone in different intervals. The lines under the traces indicate the duration of the illumination. The response to the second light spot is suppressed optimally when this begins simultaneously with the *off* of the first spot. This inhibitory action after the *off* of the first light spot is explained according to our interpretation in the right side of the figure: the slower inhibition counteracts the excitation produced by the rising excitation initiated by the second light spot.

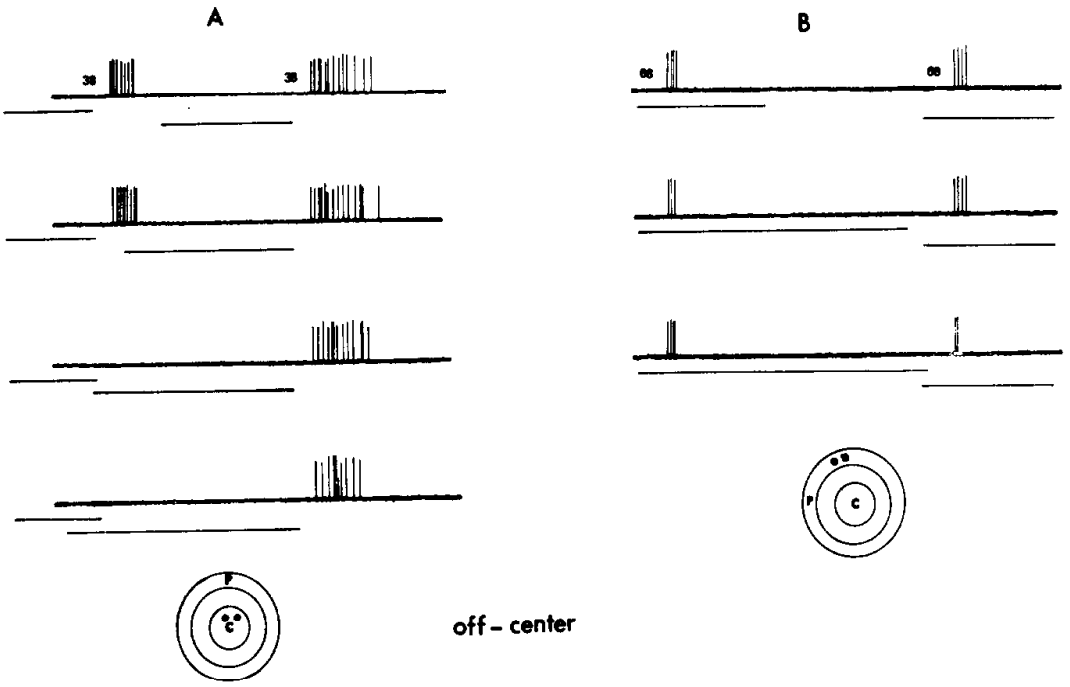

FIG. 3. Responses of an *off*-center ganglion cell upon stimulation with two light spots in the center (A) and in the periphery (B) of its receptive field. The duration of the light spots is indicated by the lines under the traces. The "inhibitory period" (compare to Fig. 4) produced at the *on* of the second light spot in A or at the *off* of the first light spot in B is evidenced. The duration of this inhibitory period does not begin before a time equal to the latency of the response and lasts as long as the burst at the *off*.

sponse to the *off* of the first light spot could be suppressed if this was given after the *on* of the second spot within a period that was equal to the duration of the second *off* response and began after a time equal to the latency of this response (Fig. 3). Similar inhibitory interactions could be obtained in the periphery, and these inhibitory interactions did not begin in a time interval shorter than the difference of latencies between the responses obtained from the center and periphery (Fig. 3).

Discussion

Our results, as well as similar ones reported elsewhere (5), can be easily explained with the following postulate: *The time courses and efficacy of the excitatory and inhibitory processes can differ from ganglion cell to ganglion cell.* The basis for such a postulate is simply the fact that ganglion cells connect with the receptors through the bipolar cells in many different modes, and this implies that the influence the receptors exert on any ganglion cell can be mediated through many different pathways, involving cells and synapses each with different characteristics. In other words, one can

expect the spatiotemporal configuration of the afferent influences to vary from ganglion cell to ganglion cell. Thus, for example, to say that the excitatory process in a ganglion cell receptive field is faster than the inhibitory process, means that, on the average, the excitatory influences reaching the ganglion cell rise (and fall) faster than the inhibitory ones after illumination of the receptive field. Let us brifly describe how this post ulate might, in fact, explain our observations:

Latencies of the Responses. Suppose we illuminate the center of an *on*-center ganglion cell receptive field; the most typical response is a burst after a latency. The illumination activates both the excitatory and the inhibitory processes, but, in our interpretation, the burst is started because the course of the excitation is faster and thus generates an initial preponderance of excitation. However, after a while the increase in inhibition (with a slower time course) brings back the balance of these two processes to a value closer to the one prior to illumination, and the burst is diminished or ended. Whichever stable state of activity the cell adopts during illumination, it will be determined by the difference in efficacy between the excitation and the inhibition. When the periphery is illuminated, both the excitation and the inhibition are diminished by the periphery, but the faster excitation falls first, allowing for a preponderance of the inhibition. At the *off* of the light in the periphery the inhibition of the receptors or bipolar cells (or both) in the center ceases, and their activity increases back to that determined by the background illumination; as a result, as we said for center illumination, the excitation predominates for a while and a burst occurs after a latency (Fig. 4). In general (for both *on*- and *off*-center ganglion cells), because of the intervening lateral system, the latency of the peripheral response (*on* or *off*) is necessarily longer than the latency of the center response.[2]

For an *off*-center ganglion cell receptive field, the time course of the excitation and inhibition should be inverted, that is, the inhibition should have a faster time course. In this case the analysis parallels the one made above almost verbatim (Fig. 4).

The *on-off* response is produced when both the center and the periphery are simultaneously illuminated, either because they overlap or because the spot illuminated both regions. In these cases the peripheral action is activated together with the central excitation and inhibition, but its effects on the ganglion cell output are slower than theirs, because of the participation of the lateral system. Since the description of the analysis of this mode of response is rather long, the reader is referred to Fig. 5.

[2] Notice that this is *not* an assumption, but a conclusion necessarily following the observation that the latency of the periphery-like response is always longer than the latency of the center-like response.

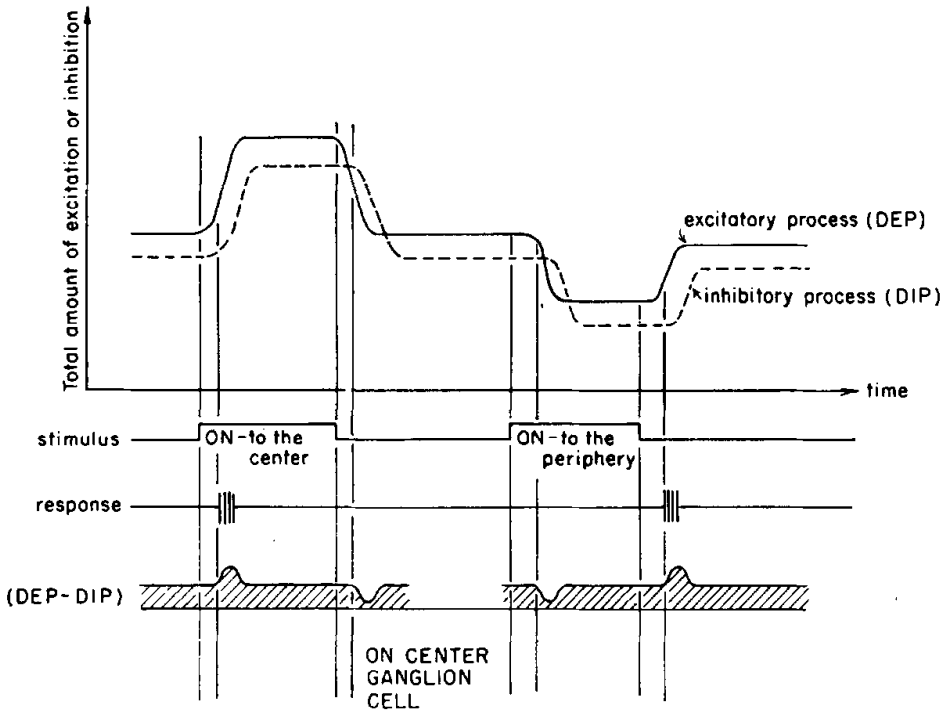

FIG. 4. Diagram of the analysis of the response of an *on*-center ganglion cell when a light is shone in the center (left) or in the periphery (right) of its receptive field. It is assumed that the total amount of excitation (direct excitatory process, DEP) acting on the ganglion cell has a faster time course than the total amount of inhibition (direct inhibitory process, DIP), and that the output of the ganglion cell is a function of the relative weight of this two processes. When the light is turned *on* in the center, both the excitation and the inhibition are activated, but the faster excitation predominates for a while and the cell fires (bottom and middle of the figure) until equilibrium is again attained. When a light is shone in the periphery (right side of the figure), both the excitation and the inhibition are depressed by the inhibitory action of the periphery. As is clear from the figure, in this case the predominance of the excitation will occur at the *off* of light. Notice that in this case the latency of the *off* response is bigger because of the delay caused by the mediation of the lateral system. An entirely similar analysis can be made for an *off*-center ganglion cell in which the inhibition is assumed to have a faster temporal course than the excitation. In this analysis we have assumed that both processes have the same efficacy, and thus there is only phasic response of the cell.

Interactions of Spots. In light of what has been said above, it should be clear that, after a change in illumination, one of the processes predominates with a measurable time course (Fig. 4); thus, two stimuli given at adequate intervals with respect to the time courses of the excitation and inhibition should interfere. As an example of this mode of analysis, we have made a diagrammatic representation of the underlying processes in Fig. 2.

Clearly our interpretation is sufficient but not necessary. However, we think it is attractive because of its simplicity. Final confirmation or rejection of its validity will have to come from direct recordings in excitatory and inhibitory bipolars of the same receptive field.

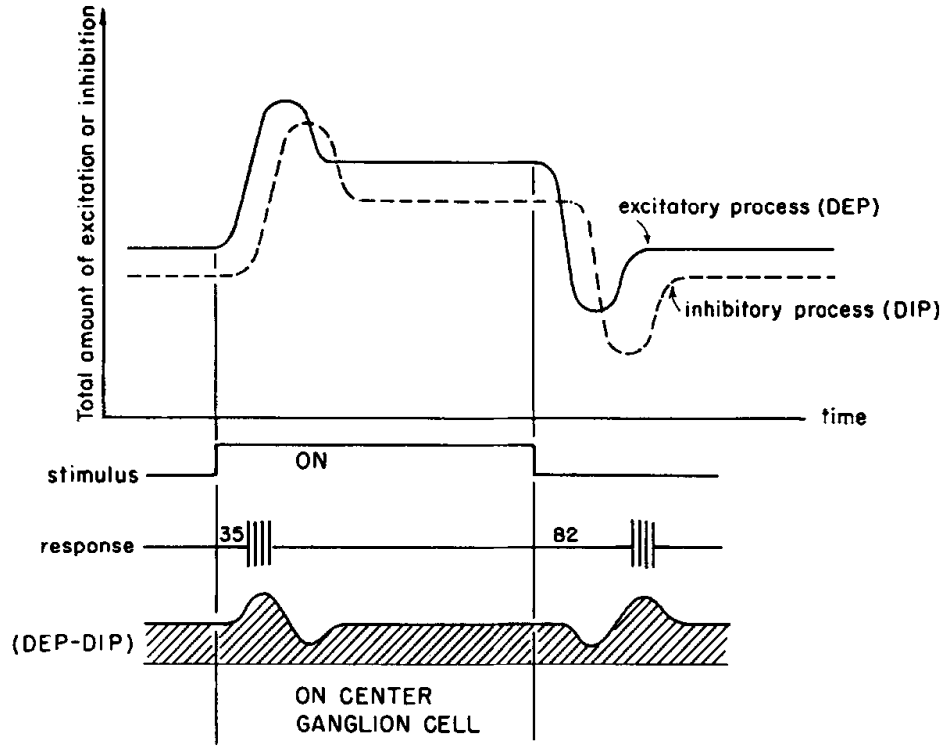

FIG. 5. Diagram of the analysis of the responses of an *on*-center ganglion cell when light is shone in the *on-off* zone of its receptive field. In this case it is assumed that in this area both central and peripheral processes are initiated. Thus, although the central excitation and inhibition are activated by the *on* of light, they are also inhibited by it to some extent with a longer latency by the action of the lateral system. As is clear from the figure, this gives the possibility for an interplay of excitation and inhibition which results in a response to both the *on* and the *off* of light. Notice that because it is an *on*-center ganglion cell, this type of analysis predicts that the response to the off should have a bigger latency than the response to the *on* of light. This is indicated in the figure with data reported by Barlow *et al.* (1). For an *on*-center ganglion cell, the time courses of the excitation and inhibition should be inverted, and, consequently, the relative magnitudes of the latencies should also be inverted. Compare to Fig. 4.

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