Reprinted from the Archives of Ophthalmology
July, 1931, Vol. 6, pp. 104-111

THE RETINA AS A NERVOUS CENTER *

RAGNAR GRANIT, M.D.
PHILADELPHIA

It is well known that anatomically the retina is not only a receptor organ but a "true nervous center," to use the words of Ramón y Cajal, who discovered and traced its synaptic connections. However, there has been little appreciation of the part this synaptic structure plays in the mechanism of vision. This is due in part to the fact that the method of approach to visual problems has been chiefly by the interpretation of sensory data, which used alone do not allow of any differentiation between retinal happenings and processes in the brain; and in part to the fact that the attractive simplicity of the theory of duplicity has focused attention on the mechanism of the rods and cones and has hidden from many workers the real complexity of the problem. Recent progress in two related fields of physiology, however, emphasizes the importance of the synaptic functions of the retina, and in so doing indicates problems the solution of which will yield valuable information regarding some of the more fundamental aspects of vision. It is my purpose to outline in this paper the conception of the retina as a nervous center and to report some recent researches that show how this point of view may be used to advantage in a study of visual phenomena.

Of first importance to an understanding of the synaptic interaction between neurons is the work of Sir Charles Sherrington and his group of co-workers. Their brilliant work on reflex phenomena is gradually bringing order out of the chaos surrounding the mechanism of the central nervous system, and as far as the retina possesses many of the characteristic properties of the central nervous system, their work must be considered of basic importance to the science of ophthalmology. A second field of research that bears directly on the problems of vision is the recent series of researches by Prof. E. D. Adrian and his associates, in which they have recorded by means of vacuum tube amplifiers the action potentials in sensory nerves stimulated through their end-organs. In collaboration with R. Matthews,[1] he has employed his

* From the Eldridge Reeves Johnson Foundation for Medical Physics, University of Pennsylvania.

1. Adrian, E. D., and Matthews, R.: J. Physiol. **63**:378, 1927; **64**:279, 1927; **65**:273, 1928.

remarkable technic for recording the nerve impulses in the long optic nerve of the Conger eel when the retina was stimulated with light. He thus found that on stimulation the retina discharged a series of impulses into the optic nerve the magnitude of which was independent of the strength of the stimulus, as was to be expected since nerve fibers act according to an "all-or-none" principle. However, there were two characteristics of the discharge that varied with the intensity of the stimulus: (1) the frequency of the impulses increased with the intensity of the light, and (2) the latent period of the outburst of impulses decreased with the strength of the stimulus. The first phenomenon has further been shown by Adrian and his successive collaborators to be a characteristic of the discharge from all sense organs as well as of the central nervous structures discharging reflexly (Adrian and Bronk [2]). This variation in frequency is an important determinant of the intensity of sensation and is one of the factors regulating the intensity of the motor response. However, the shortening of the latent period of discharge was found to be a better measure of the intensity of the physiologic processes in the retina than the frequency variation, because the large number of fibers in the optic nerve makes it difficult, if not almost impossible, to record the actual frequency of the individual units of the nerve responding.

By using the decrease in the latent period of discharge as the measure of increased intensity of retinal response, Adrian and Matthews [3] found that an increase in the area of the retina stimulated gave the same effect as an increase in the intensity of the light. The correct explanation of this spatial effect was obtained later,[4] when it was shown to be due to a synaptic reaction of the type generally known as spatial summation.[5] They proved this fact by studying the effect of four separated areas of illumination on the action potential in the nerve. When each area was stimulated alone, it was found that the latent period of discharge in the optic nerve was much longer than when all four areas were stimulated simultaneously. It was thus shown that the effects of the four separated areas interacted somewhere in the retina in such a way as to increase the intensity of the physiologic process that preceded the appearance of the discharge in the nerve. The simultaneous stimulation of four separated patches instead of one therefore gave an effect equivalent to that resulting from an increase in area.

---

2. Adrian, E. D., and Bronk, D. W.: J. Physiol. **66**:81, 1928.

3. Adrian and Matthews (footnote 1, first reference).

4. Adrian and Matthews (footnote 1, third reference).

5. In nervous centers spatially separated stimuli give a greater effect than each stimulus gives alone (Sherrington, C. S.: Integrative Action of the Central Nervous System, New York, Charles Scribner's Sons, 1906, p. 114).

The rods and cones are separated, but there is a dense net of lateral junctions furnished by the horizontal cells, the amacrines and the cells of the ganglionic layer, and by these paths separated stimuli may be able to reenforce each other through the process of summation. If this is the correct explanation, one would expect to find that the interaction between the four spots, resulting in an increased intensity of the physiologic process and a consequent reduction of the latent period, should be enhanced by the application of strychnine to the retina, which is known to increase synaptic interaction. This was definitely found to be the case. Adrian and Matthews therefore inferred that the process was identical with the familiar phenomenon of spatial summation as displayed by any central nervous structure with several paths converging on a common neuron. As pointed out by Sherrington,[6] on the basis of statistical considerations the amount of convergence should increase with the number of neurons activated; hence, an increase in the area stimulated would be equivalent to an increase in intensity.

These experiments have far-reaching consequences in the physiology of vision. They give a clear picture of interaction in the visual process, and because they were performed on the excised eye and the optic nerve, they show this to take place in the retina. However, an important question is to what extent these phenomena are reproduced by the entire mechanism, including sensation. As for the similar effects of area and intensity, it has indeed long been known that at the threshold of vision an increase in area may compensate for insufficient intensity of stimulation. Although by analogy with the similar results on the excised eye it is reasonable to suggest that they have a similar explanation in the basis of retinal summation, it must be pointed out that the phenomenon can and has been explained in a different way. However, if it is possible to repeat Adrian and Matthews' four spot experiment with sensory criteria and if it is possible to correlate the results with the structure of the retina and the general concepts of reflex physiology, the case for retinal interaction and spatial summation in the process of human vision would be much clearer.

In testing for this interaction between four separated areas of the human retina, it was not possible to use ordinary photometric methods based on an equalization of adjoining stimuli, since the effect to be looked for is mutual and hence would be eliminated by a procedure involving a comparison of brightness between two or more areas. The intensity of the retinal effect in the four stimulated areas was therefore measured by determining the fusion frequency of a flickering light. It is well known that this fusion frequency increases with the intensity of the stimulus and consequently measures the intensity of the physiologic process underlying the perception of brightness. The question to

6. Sherrington, C. S.: Proc. Roy Soc., s. B, London **105**:332 (Sept. 2) 1929.

be tested experimentally, then, is whether the fusion frequency for four separated areas stimulated simultaneously is higher than the value for any one of the areas illuminated separately.

The accompanying table shows typical results. The intensities were 94 and 0.94 meter candles, respectively, and the four illuminated spots were 1 degree in diameter, lying symmetrically on an imaginary circle 3 degrees in diameter. Experiments have been performed with central fixation and with the fixation point 10 degrees toward the periphery. The light was flickered by revolving a sectored disk in the beam.

A large number of well controlled experiments, as well as the one reported in the table, show that the four spots stimulated simultaneously give a higher fusion frequency than the areas stimulated singly. Here, then, as in the case of the experiments on the eel's eye, there is interaction between separated regions of the retina, the interaction producing a retinal effect equivalent to that resulting from an increase in the

Results of Experiments on Fusion Frequency *

	Central Fixation		Peripheral Fixation	
Intensity, Meter Candles	Fusion Frequency of Single Spots, Revolutions per Second	Fusion Frequency of all Simultaneously Illuminated, Revolutions per Second	Fusion Frequency of Single Spots, Revolutions per Second	Fusion Frequency of all Simultaneously Illuminated, Revolutions per Second
94.00	22.84	23.07	19.88	22.76
0.94	13.28	13.31	12.10	12.69

* From Granit, R.: Am. J. Physiol. **94**:41, 1930.

intensity of illumination. It is interesting to note that this phenomenon is especially marked in the periphery, which is anatomically similar to the eel's retina. In the eel's retina, the retinal connections are all particularly well developed, and many receptors converge on the ganglion cells, whereas in the human fovea the path from the receptor to the optic nerve fiber is more isolated. Indeed,

> Anatomically, the periphery of the human eye seems to be the nearest approach to that prototype of nervous pattern, which on evidence derived from work on motor neurones by Sherrington and his co-workers must be expected to display summation *par preference*.[7]

As previously pointed out, summation may be looked on as the physiologic expression of anatomic convergence of a number of paths to a common neuron. This view has here been put to an experimental test, and I think confirmed on the human eye in which different degrees of convergence can be obtained by varying the retinal location of the stimuli.

7. Granit, R.: Am. J. Physiol. **94**:41, 1930.

In central fixation there is less summation than in the periphery, but the power is by no means lacking. The foregoing experiment shows the amount of interaction in the fovea to be negligible, but more sensitive experimental tests reveal a definite effect. In certain experiments two semicircular areas of stimulation have been employed the distance of separation of which could be varied. With small distances between the two areas, an appreciable amount of summation was found in the center as well as in the periphery (Granit and Harper [8]). It is noteworthy that in such experiments the summative power frequently reached its maximum value when the two semicircular portions were still so far apart that the resolving power was not interfered with.

Since four separated areas of stimulation in the human retina interact to give summation of response, as indicated by an increase in fusion frequency, it should follow as a corollary that an increase in the area stimulated should also raise the fusion frequency. This has been shown to be the case by Miss Harper and me.[8]

The relation between fusion frequency of the flickering light and the area illuminated is given by the formula:

$$n = c \log A + d$$

in which n = fusion frequency, A = area, and c and d are constants. It will be seen that this expression closely resembles the well known Ferry-Porter law relating intensity and fusion frequency:

$$n = a \log I + b$$

In both cases the true curves represented by the equations are probably S-shaped, there being marked deviation from linearity at high and low intensities and large and small areas. The similarity of these two equations again emphasizes the fact that the fusion frequency varies with area of stimulus in the same general way as it does with intensity, although there are, of course, quantitative differences. What is more important, however, is that the variation of fusion frequency with area is decidedly greater in the periphery than in the center, whereas the variation of fusion frequency with intensity is less influenced by retinal location.

The statements in the preceding paragraph have indicated that peripheral vision is far more dependent on the area stimulated than is central vision. The two sets of experiments with variations in intensity and area offer a basis for a tentative explanation of this difference between central and peripheral vision, in which physiologic considerations are well substantiated by anatomic evidence. The general outline of the argument has already been set forth. The greater number of lateral connections in the peripheral retina makes the synaptic factor relatively more important in peripheral vision. Depending on the degree of summation, the peripheral sensitivity to light in daylight vision may be lower, equal to or higher, than the central sensitivity. There is therefore no absolute difference between the values of fusion frequencies

8. Granit, R., and Harper, P.: Am. J. Physiol. **95**:211, 1930.

for the center and the periphery,[8] as these frequencies are a function of both the area and the intensity of the test object used. With a sufficiently large area of stimulation and a relatively high intensity, the summation in peripheral vision may even overcompensate for its lower sensitivity. The following statement by Parsons[9] is therefore easily explained by our results:

> There is overwhelming proof, derived from peripheral luminosity curves, minimal field and minimal time luminosity curves, that peripheral vision behaves in exactly the same manner as central vision but with diminished sensitivity. Greater stimuli are required to produce similar responses, but if the stimuli are sufficiently great, the differences disappear, including even qualitative differences so that the fields of vision for colors extend to the extreme periphery.

Evidently, the theory of duplicity, the aim of which is to account for regional differences in the field of vision by the different distribution of rods and cones in the retina, is too great a simplification of retinal physiology. The synaptic aspect enters as a serious complication, but nevertheless one that can be profitably attacked.

Consider, for instance, the influence of the spatial factor on the mechanism of local adaptation. Although fairly conclusive evidence (Granit and von Ammon[10]) shows this phenomenon to be chiefly determined by processes in the receptors, let us see what influence the synaptic structure may have on this mechanism? It is well known that the rate of local adaptation in the fovea is low and that it is much greater in the periphery—so much greater, in fact, that the large decrease in apparent brightness during the first few seconds as a result of the adaptation is easily measurable by the flicker method. We have investigated the effect of area on the rate of peripheral adaptation and have found that there is a considerable drop in apparent brightness (decrease in fusion frequency) during a fixation time of 3 seconds, but that by increasing the area of illumination the intensity does not drop to as low a final level of equilibrium as with a small area. In terms of the synaptic concepts of retinal function, this may be explained by saying that the decrease in excitability of the receptors through adaptation is to a certain extent compensated for by an input over lateral channels. For the larger the area stimulated the more efficiently is any one neuron within the stimulated area charged by virtue of the effect of adjacent neurons. The excitatory state is better sustained the greater the number of paths converging on the neuron, and thus the adaptive effect is retarded and checked. The synaptic system in this case serves as a "buffer." The rapid adaptation of the peripheral receptors would seriously hamper peripheral daylight vision if it were not for the buffering effect with

9. Parsons, J. H.: Theory of Perception, London, Cambridge University Press, 1927, p. 177.

10. Granit, R., and von Ammon, W.: Am. J. Physiol. **95**:229, 1930.

large areas. It is indeed well known that small areas do disappear altogether if fixated for a few seconds, and in the same way differences of detail are smoothed over.

By virtue, then, of its great summative power the peripheral eye is in a remarkable manner able to cooperate with the fovea at high intensities, whereas at low intensities dark adaptation makes it especially sensitive to light. The two processes, summation and dark adaptation, make the periphery an efficient organ throughout the enormous range of intensities within which vision is possible. The fovea, as is well known, is a special organ for the upper part of that range only, is blind in darkness and has properties with regard to refraction and isolated conduction which meet the demands for discrimination of brightness and visual acuity. On the other hand, "the peripheral retina is adapted to the limitations set to it by the refractive system. It has little visual acuity and great summative power" (Granit, Hohenthal and Uoti [11]). It is the more primitive organ, but it is admirably well equipped for the elementary function of perceiving gross differences of light under all conditions of illumination. As it is much larger than the fovea, it can afford to be dependent on stimuli of greater area for proper evaluation of the peripheral brightness conditions. In short, the two regions, periphery and center, are extremely different as regards the adaptability and sensitivity and could not cooperate at all in daylight vision if it were not for the stabilizing and sensitizing influence of the synapses. There may indeed be pathologic conditions in which these synaptic influences are impaired, and it should be possible to detect these conditions if clinical tests were designed to ascertain the amount of summative power instead of merely measuring, as at present, the visibility regardless of how it is brought about.

Increased emphasis on the synaptic concept in the physiology of vision leads to many problems suggested by the facts and theories of reflex physiology. Several have already been discussed: Of the many remaining, I shall consider briefly the so-called temporal summation of subliminal stimuli. For instance, it is well established that a number of successive stimuli that individually are incapable of eliciting a scratch reflex may do so if repeated for some time. Eccles and Sherrington [12] have employed this phenomenon as a means for studying the time course of excitation in the spinal cord. They employed two subliminal stimuli separated by varying intervals of time, and the amount of reflex contraction elicited by the second stimulus was taken as a measure of the "central excitatory state" left by the first. Repeated tests showed that neither of them was sufficiently strong to elicit any contraction alone.

---

11. Granit, R.; Hohenthal, T., and Uoti, A.: Acta ophth. **8**:137, 1930.

12. Eccles, J. C., and Sherrington, C. S.: J. Physiol. **69**:1, 1930.

In collaboration with W. A. Davis, I have recently been performing similar experiments on the human eye.[13] Two subliminal stimuli have been used, and the time interval between them has been varied. It has been found that when this interval is lengthened, it is necessary to increase the second stimulus in order that it may be sufficient to raise the remaining subliminal state of excitation above the threshold of perception. As the interval between the two increases, the second stimulus must be increased until it finally reaches a liminal value. For instance, in the dark-adapted periphery it is found that the state of excitation reached with the first subliminal stimulus may remain at a nearly constant level for as long as 0.045 second and that it then falls off gradually, being still appreciable at about 0.135 second, at which time the second stimulus has to be made as strong as the first. The maximal duration of an effective residual excitatory state, that is, the maximum interval within which two subliminal stimuli will sum, has not yet been established. It must be obvious that such data may be used to trace the time course of excitation and give interesting information regarding the nature of the threshold of vision. In common with many other visual investigations suggested by synaptic considerations, such experiments yield valuable information for the student of reflex physiology and neurology.

Because the retina has a synaptic structure similar to that of the central nervous system but simpler in both arrangement and function, it may be hoped that the ophthalmologist may be able to contribute much to the elucidation of the difficult problems of nervous function. About thirty years ago an attempt was made by Braunstein[14] to use the flicker method for clinical work. His results showed that the fusion frequency decreased in certain pathologic conditions and suggest that with the methods of analysis presented in this paper it should be possible to arrive at a more detailed understanding of the nature and retinal localization of the physiologic processes underlying the general symptom of decreased visibility.

---

13. Granit, R., and Davis, W. A.: Am. J. Physiol., to be published.
14. Braunstein, E. P.: Ztschr. f. Psychol. **33**:171 and 241, 1903.