

Centrifugal and antidromic effects on the retina

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Antidromic stimulation means to stimulate nerves backwards so that the electrical impulse (in the present case), enters the retina from behind. It can be picked up in the usual way by a microelectrode on the retinal ganglion cell. I have used cats and the stimulating electrode has been on the end branches of optic nerve fibres in the brain (chiefly pretectum and colliculus superior). One begins by locating an active ganglion cell, stimulating with light in the usual way, and then proceeds to find the place in the brain which excites it antidromically. The crucial test consists in making the artificial antidromic impulse collide with the natural one elicited by light.

In such experiments it was discovered that whilst the impulse, as is well known, reaches the blind spot in 1-1.2 milliseconds, it is greatly delayed as it spreads over the retina. This spread may be studied by picking ganglion cells further and further away from the blind spot. Those along the edge of the retina are delayed from 4-5 msec. and the explanation of the lowered conduction velocity is the sudden loss of the myelin sheath of the optic nerve at the blind spot. Maximum conduction velocity in the optic nerve is of the order of 70 metres per second; within the retina it will be something of the order a few metres per second depending upon whether one traces large or small ganglion cells. These relations are now being systematically worked out in our laboratory by Dr. E. Dodt (Freiburg, i. Br.). If one considers that the fastest optic nerve impulses to light reach the visual area of the cortex in about 10-12 milliseconds, provided very high light intensities be used, one quarter to maximally one half of this time may be spent in tra-

versing the distance within the retina to the blind spot. Consequently, in a moving eye, space differences are translated into considerable time differences. This space-time grid may well provide important "local signs", it being known from the work of Riggs and his colleagues and Ditchburn (presenting his facts at this meeting, with references) that images in stopped eyes tend to fade out. From this it is concluded that the small saccadic eye movements play a role in normal vision and, hence, that the space-time grid actually is put into operation. From the informational point of view there is a close analogy in acoustics where the ear is well known to localize sound with the aid of minute time differences of the wave front as between the two ears.

If one then, having found a large ganglion cell responding antidromically, proceeds to stimulate it backwards for a while (3-30 seconds), preferably at frequencies around 200-300 shocks per second, the cell is found to have become "potentiated" in the sense that it afterwards fires for some 15-20 seconds at higher frequencies than before. To put it in visual terms: if the ganglion cell to a test light of 5 lux has responded with a certain low spike frequency, it may, after antidromic stimulation, fire with the higher frequency corresponding to an increase of the (as such constant) test light to 600 lux (as measured by an ordinary luxmeter). Technically this effect is described as a post-tetanic potentiation but as such it is unique because antidromic post-tetanic potentiations have not been found in other nerve cells. Only normally directed or orthodromic potentiations have been described. The antidromic post-tetanic potentiation is strictly confined to the retinal cell that has been driven from above at the high frequency used. If driving ceases, there is no post-tetanic potentiation. This can be simply demonstrated by slightly withdrawing the stimulating electrode from the fibre end in the brain. Other fibres may then be driven from above but the one recorded from is not stimulated and so responds normally, that it, as before tetanization.

It is difficult to interpret this phenomenon as a reflex action through a loop within the brain and then down to centrifugal fibres because aspiration of the lateral geniculate ganglion and adjacent portions with consequent interruption of the whole fibre supply to pretectum and superior colliculus does not destroy a potentiation from the optic tract further down.

Accordingly there are only three alternatives left: (i) optic nerve fibres are provided with recurrent loops running into the retina; (ii) there is stimulation of the centrifugal fibres of Ramón y Cajal or (iii) dendritic transfer. The most attractive possibility is (i), yet there is no anatomical evidence for such recurrent loops in the retina (though they are well known from other structures in brain and spinal cord). It is impossible to exclude (ii) but on this view it is difficult to understand the necessity for driving the large ganglion cell. There is a 1:1 ratio of optic ganglion cells to optic nerve

fibres which suggests that the centrifugal fibres, if they exist at all in the optic tract, must be very fine ones and hence neither stained by ordinary methods nor easily stimulated at the thresholds for the large optic nerve fibres. Cajal gave beautiful pictures of efferent fibres entering the retina, among mammals in the dog, but they may, of course, be recurrent collaterals. The only difficulty here is that Cajal, who in so many other instances described recurrent collaterals, actually characterized these fibres as true centrifugals. Alternative (iii) cannot be excluded but, in view of what is known about antidromic stimulation, must be regarded as unattractive because improbable.

This, however, was followed up by a search for other places in the brain where similar phenomena might be detectable *without* driving. Such places were actually found within the mesencephalic reticular substance, as is interesting because we have shown that another sense organ, the muscle spindle, can be controlled from this region by means of well-known centrifugal fibres (Granit and Kaada, 1952). Now, a high-frequency repetitive stimulation was found to stimulate the retina in a similar slow drawn-out fashion, although no driving occurred, as was easily checked from the records. The mesencephalic reticular substance is known to receive optic nerve projections so that driving of the smallest fibres might have occurred in places which were not below the microelectrode. At any rate, the large cell isolated by the microelectrode was not driven, yet responded with facilitation. In neither type of experiment (with or without driving) was it possible to influence small ganglion cells in a definite fashion.

In both types of experiment, the antidromic as well as the reticular one, cases occurred when inhibition (depression) dominated or even was the only result of stimulation. There is always a brief inhibitory pause after cessation of stimulation but this is a different matter. The true depressions occurring after tetanization were long-lasting ones, often up to a minute.

Now, is the reticular potentiation (without visible driving) a true centrifugal neural effect or not? On this point it is still necessary to entertain some doubt. One reason for this is that in our laboratory Ingvar has seen reddening of the retina in response to a reticular stimulation which also causes visible vasodilation in the superficial vessels of the brain. This explanation at the moment suffers from the difficulty that no potentiation was obtained when the microelectrode isolated small ganglion cells. Often small and large ganglion cells were isolated together and then only the large one responded in the way described. There remains the possibility of a hormonal chemical effect of some kind, as recently found by Dell and his collaborators (1954) upon tetanic stimulation of the brain stem in the manner of the present experiments. On the other hand, Cajal was a great histologist and after studying his pictures as well as the confirmatory ones of Polyak (1941) it seems to me

impossible to deny that the centrifugal path exists. The only possible way out of this dilemma is to regard the centrifugal fibre as a recurrent collateral within the retina (branching off somewhere within blind spot and ganglion cells) as an alternative to accepting the centrifugal path as an independent one all the way from the brain to the eye. There are better staining methods for very thin fibres to-day and so its to be hoped that someone will take up this problem for re-investigation. In the meantime, here is an array of new and curious facts of considerable neurophysiological interest. The visual interest arises from the fact that independently of whether the centrifugal fibres are recurrent collaterals or come all the way from the brain, the results obtained point to the existence of positive and negative feedback control of some of the retinal ganglion cells from which the optic nerve fibres arise. It is under all circumstances a far-fetched notion to explain the effects resulting from antidromic driving as hormonal chemical ones, even if this explanation might be applicable to the reticular case.

The results obtained have been described in a paper accepted for publication by the Journal of Neurophysiology (1955) as well as in Ch. III of a book (Granit, 1955) which also in considerable detail discusses the general problem of centrifugal control of other sense organs. [*Addendum*. They have since been confirmed by *Dodt, I. Physiol.*, 1955. 128.12 P.].

REFERENCES

- (1) - BONVALLET M., DELL P. & HIEBEL G., *EEG Clin. Neurophysiol.*, 1954, 6, 119.
- (2) - GRANIT R., *J. Neurophysiol.*, 1955 18, 388-411.
- (3) - GRANIT R., *Receptors and Sensory Perception*. Silliman Lectures. Yale University Press, New Haven 1955.
- (4) - POLYAK S., *The Retina*. Chicago University Press, Chicago 1941.
- (5) - RAMON Y CAYAL S., *Die Retina der Wirbeltiere*. Bergmann, Wiesbaden, 1894.