JANUARY 1974 Vol. 13/1
investigative ophthalmology
A Journal of Clinical and Basic Research

Editorials on Recent Advances

Vision and graded potentials in vertebrate retinas

Responses of single ganglion cells were first recorded from vertebrate retinas over thirty years ago. It was then evident that the understanding of vision and retinal function could be greatly advanced by extending single-cell recording to include all classes of retinal cells. But the retina gives up its secrets grudgingly. To satisfactorily analyze the response of cells in the distal retina, it proved necessary to penetrate these cells with ultrafine micropipettes, record their intracellular response, and then identify the cell of origin by intracellular injection of dye.[1] It took about twenty years of successive approximations to perfect the required techniques. Then in 1965, the response of single receptors was first clearly described and about three years later, intracellular methods were judiciously and widely applied to the large-celled retina of the mudpuppy.[2] The cells of the distal retina-receptors, bipolars, and horizontals—did not respond with a discharge of all-or-none impulses, but rather gave slow potentials whose amplitude increased in a graded manner with the intensity of incident illumination.[3] These cardinal findings have since triggered a flurry of research from which it now seems possible to further sketch some important relations between basic aspects of vision and the electrophysiology of the distal retina.[4]

The processes of adaptation allow the visual system to operate efficiently over an enormous range of ambient illumination and have thus been the object of experimentation and theory for decades. In addition to providing the first studies of adaptation in single receptors, intracellular recording has confirmed earlier contentions that the PIII component of the electroretinogram is the extracellular manifestation of the receptor response. This is particularly important because PIII, isolated by sodium aspartate or by clamping, can be recorded over a wider range of species and conditions than is yet possible for the intracellular response. The two recording modes are thus usefully complementary. Previous psychophysical and electrophysiologic work has shown that dark adaptation proceeds in two phases—an initial rapid phase in which sensitivity increases within a minute or so, and a slow phase which may continue for an hour or more. The origin of both has been subject to much lively speculation. Recordings of receptor potentials in several species have now provided direct evidence that both phases are largely of receptor origin. In light adaptation, the fundamental observation is Weber's law:

intensity discrimination remains nearly constant over a very large range of prevailing illumination. In the last three years, quantitative studies of receptor potentials from cones of monkey, carp, and mudpuppy and from rods of skate and gekko retinas have all shown remarkedly close agreement with Weber's law. So the thrust of recent work indicates that the main features of light and dark adaptation are established at the first stage of the visual system. It is a challenging task for the future to determine the nature of the mechanisms which regulate the sensitivity of the receptor potential.

The duplicity principle of vision is well established but a basic question still remains: are the measured differences between rod and cone vision due to intrinsic differences in the receptors or to differences in the neural pathways which carry rod and cone signals? Evidence for intrinsic differences at the receptor level is now at hand: in the mudpuppy, rods have been found to be about ten times more sensitive than cones. Rods are also saturated by intense background illumination while cones are not, a finding which may account for the rod saturation effect known from psychophysical work on human vision. The well-known generalization that the temporal resolution of cone vision is superior to that of rod vision also seems initiated at the receptor level: in both monkey and mudpuppy, the time course of the cone-receptor potential has been found to be faster than that of the rod-receptor potential.

Antagonistic interaction between central and surrounding regions of the receptive field, long recognized from work on ganglion cells as a basic neural mechanism for spatial vision, was found in the initial recordings from bipolar cells in the mudpuppy. This important finding has now been repeatedly confirmed in mudpuppy and clearly shown in frog and fish. New observations suggest that this antagonistic organization in bipolar cells may lie at the root of the sensitizing effects of background illumination found in human vision.

It is likely that the antagonistic effects evoked by surround illumination are carried by horizontal cells which then act upon bipolar cells. But recent work indicates that horizontal cells may also feed back antagonistic effects upon receptors. This was convincingly shown in the turtle by recording from a cone with one electrode while hyperpolarizing a neighboring horizontal cell with a second electrode, and strongly supported by the later finding that sodium aspartate abolishes the response of horizontal cells and the feedback effect in cones. This is provocative because it implies that receptor cells, to some extent, can no longer be treated as a mosaic of functionally independent elements. This in turn raises questions about possible interactions between rods and cones and between cones of different spectral types, so it is important to determine the nature and magnitude of horizontal-receptor interaction in various species. At present, observations suggesting horizontal-receptor feedback may be found in work on monkey receptor potentials and in recent intracellular work in fish, mudpuppy, gekko, and cat.

The study of horizontal cell function with the L-type S potential, a response known for many years and found in all classes of vertebrates, has received a boost from work on intracellular staining which conclusively shows that the response arises from horizontal cells in cat, turtle, amphibians, and fish. Coupling between horizontal cells has been elegantly demonstrated by showing that a dye or electrical current injected in one cell spreads to neighboring horizontal cells in the dogfish. This coupling is presumably a factor behind the very general finding that horizontal cells respond to illumination within a very large field on the retina, but tests for coupling in other species are needed. It has recently been shown that injecting a weak current in a single horizontal cell can evoke a ganglion cell discharge in fish retinas and the detailed form of the dis-

charge varies with the polarity of the applied current. These findings add a new dimension to the accumulated evidence that horizontal cells modulate the transmission of visual information through the distal retina.

After the frustrating uncertainties of the fifties and the dramatic strides of the mid-sixties, research on the function of the distal cells of the retina is now proceeding at a brisk pace. Within this decade, we may reasonably expect to see the intracellular approach increase our insight into the roots of the psychophysics and electrophysiology of human vision, strengthen the correlation between retinal structure and function, sharpen our perspective of central neural networks, and begin to unravel the ionic mechanisms of transduction and synaptic transmission in the retina.

Dwight A. Burkhardt
Minneapolis, Minn.

REFERENCES

1. William H. Miller discusses the methods and significance of intracellular staining in a recent editorial: Miller, W. H.: INVEST. OPHTHALMOL. 12: 317, 1973.
2. For reviews of this work, see Tomita, T.: Quart. Rev. Biophys. 3: 179, 1970; Dowling, J. E.: INVEST. OPHTHALMOL. 9: 655, 1970; Dowling, J.E., and Werblin, F. S.: Vision Res. Suppl. 3: 1, 1971.
3. In a recent editorial, William W. Dawson discusses some implications of these findings for brain function: Dawson, W. W.: INVEST. OPHTHALMOL. 12: 398, 1973.
4. The sketch given here is drawn from the efforts of over fifty individuals. Much of this research has been presented at the 1972 and 1973 meetings of the A.R.V.O. Some of it has now been published and may be found primarily in J. Neurophysiol., J. Physiol., Vision Res., J. Gen. Physiol., and Science.

Laser treatment for glaucoma

Lasers (light amplification by stimulated emission radiation) have been available for the last 10 years. A laser works by stimulating electrons into orbit so that their emissions are simultaneously released and amplified in a resonating chamber or crystal.[1] The solid-state lasers depend upon polished surfaces on either end to resonate back and forth. The gas lasers use an ionized gas within a chamber and mirrors, one of which is incompletely silvered that allows a small per cent of the lased light to continuously leave through it. The duration of a gas laser such as an argon laser can be controlled by a shutter or by pulsing the tube with repetitive strobe flashes. The solid-state lasers such as the ruby or neodymium are pulsed or pumped with a strobe unit and can be Q-switched (quality switched). In this process, a mirror, dye, or other method of stopping the resonation is placed within the unit such that a very high intensity builds up until the switch is released and the quality of the pulse is changed from a longer duration (microsecond) pulse of a few watts to an ultra short (nanosecond) pulse of very high wattage (megawatts).

The use of lasers in the treatment of retinal diseases has received much atten-