Retinal physiology

A foot in the vitreous fluid

from A. R. Gardner-Medwin

A PAPER by Newman on page 155 of this issue documents a striking property of the glial cells in the vertebrate retina: their membrane permeability, which is almost exclusively a permeability to potassium, is largely concentrated at the end which has membrane expansions ('endfeet') facing the vitreous fluid of the eye[1]. Indirect arguments in support of the idea of regional specialization of the glial membranes had already been put forward by Tomita and his colleagues[2,3] and by Newman himself[4,5] on the basis of experiments on the frog retina. Newman's new experiments provide a particularly direct demonstration of the phenomenon for glial cells isolated from the salamander retina. The elegance of the experiments may help to stimulate a reconsideration of the role of the glial cells in the vertebrate retina.

Like glial cells throughout the nervous system, Müller cells — the principal glial cells of the retina — do not, so far as is known, participate directly in the processing of neural information. As the only cells that span the full depth of the retina (see the figure), Müller cells are in a position to influence, or to be influenced by, the environment of all the neurone and receptor types of the retina as well as the vitreous fluid.

The principal issue for debate in Müller cell electrophysiology has been the part the cells play in the generation of the electroretinogram — that is, the changes in potential generated across the retina and the eye in response to light. Miller and Dowling[6] suggested that the vitreal positive 'b' wave of the electroretinogram might be due to a build-up of extracellular potassium in the retina following neural activity and to the consequential currents flowing through the Müller cell. That suggestion seemed unlikely to be correct when measurements with ion-selective electrodes showed that potassium is largely built up close to the vitreal surface of the retina[7-9]; on the assumption that the permeability of the Müller cell is uniformly distributed, this would lead one to expect voltage changes opposite in sign to those observed for the b wave. But with evidence of the asymmetry of the permeability of Müller cells[1-5] it becomes possible to account for the observed polarity of the b wave even for contributions coming from increases in potassium concentration close to the vitreal surface. In fact, the greatest contribution to the electroretinogram will come from the changes in potassium concentration that occur furthest from the vitreal surface, since for these the current loop through the Müller cells passes through the greatest extracellular resistance. The distal increase of potassium concentration is more transient than the proximal increase, partly because of uptake of potassium into the photoreceptors. This seems adequately to explain why the b wave is substantially briefer than the depolarization measured within Müller cells[4,5]. Thus the potassium hypothesis for generation of the b wave looks as if it may be substantially correct.

A more important issue than the generation of the electroretinogram is the possible effect that Müller cells may have on retinal neurones. In other tissues it has become clear that glial cells have a significant role in dispersing potassium from regions of the neural environment where it has built up (see review in ref.10). This is the so-called 'spatial buffer' action. Newman suggests that in the retina, the specialized endfeet of Müller cells serve to transfer potassium not to other regions of nervous tissue but specifically to and from the large reservoir of vitreous fluid. Since the retina is only 0.2 mm thick and often subject to uniform stimulation, there may be little undisturbed neural tissue following retinal stimulation and the fluid bordering the retina may represent the chief reservoir of extracellular fluid available for buffering. Newman's proposal is therefore attractive. It remains to be established, though, whether the effect on the neuronal environment is substantial. Using data from Fig. 7 of Newman's current-density analysis[4,5] it is possible to calculate that the cumulative effect of current flowing in the loops shown in the figure during the first 2 seconds of the b wave would diminish the extracellular potassium concentration by approximately 0.15 mM, on average, throughout the retina. The decrease would be two to three times greater (0.3–0.5 mM) in the localized regions of potassium build-up where the current enters the Müller cells. These changes, if confirmed experimentally, seem likely to be large enough to have a significant effect on retinal neurones.

If direct and rapid clearance of potassium through the Müller cells into the vitreal fluid turns out to be important for the homeostasis of the retinal environment, it should stimulate consideration of similar mechanisms in other tissues. It may also stimulate a reconsideration of some data obtained from retinal preparations in which the vitreal fluid has been removed. □

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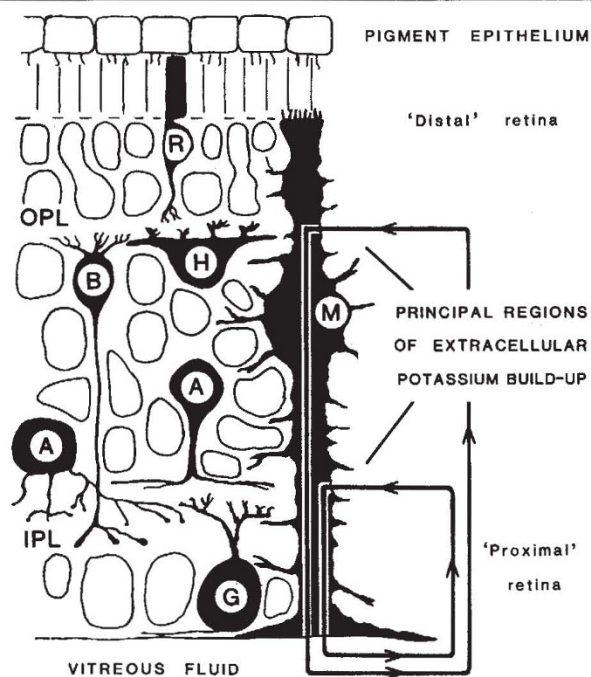
The principal cell types and the principal paths of current flow due to potassium build-up following light stimulation in the vertebrate retina. The current is carried largely by potassium within and across the membranes of the Müller cells and largely by sodium and chloride in the extracellular space: it serves to transfer potassium from the extracellular space to the vitreous fluid. A, amacrine; B, bipolar; G, ganglion; H, horizontal; M, Müller cells; R, receptor cells; IPL and OPL, inner and outer plexiform layers. (After refs 4,5 and 11.)