EFFECTS OF ACETAZOLAMIDE ON THE ELECTRORETINOGRAM OF THE SKATE, (RAJA OSCELLATA)

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The electroretinogram (ERG) is the electrical response measured across the retina to light stimuli. It has been found to be valuable in the clinical evaluation of retinal function. The most prominent part of the ERG is the b-wave as shown in figure 1. This is thought to be generated by radial currents arising in the retina due to depolarization of the Muller fibers, which are glial cells (Newman & Odette, J. Neurophysiol. 51:164-182, 1984).

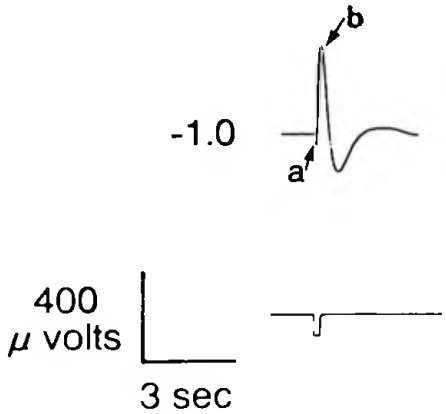

Figure 1. Electroretinogram recorded from the skate, showing the negative a-wave (a) and the positive b-wave (b) in response to a 200 msec flash of 500 nm light, 4 log units above threshold.

The depolarization is believed to be due to the release of potassium into the extracellular space by other retinal neurons. We have shown that the Muller fibers of the skate contains significanat amounts of the enzyme carbonic anhydrase (Cohen & Linser Invest. Ophthal. & Vis. Sci. Suppl. 28:404, 1987). This enzyme is important in the control of intracellular pH. The objective of this study was therefore to determine what effect inhibition of this enzyme would have on retinal function as measured by the b-wave of the electroretinogram.

Eyes were removed from skates (Raja oscellata) under dim red light. The anterior section of the eye, including the cornea, and lens was removed. The remaining eyecup was placed into a lucite chamber. A reference electrode was underneath the eyecup. The electrode was a chlorided silver wire. Oxygenated elasmobranch saline flowed continuously over the eyecup at the rate of 2 ml/min. ERG's were then recorded during superfusion in

normal saline and in saline containing different concentrations of acetazolamide, an inhibitor of carbonic anhydrase. The pH of all solutions was adjusted to 7.6 before the start of each experiment. The light stimulus consisted of 200 msec flashes of 500 nm light.

Following superfusion of the eyecup with 100 μM acetazolamide there was a significant decrease in the amplitude of the b-wave. Over a range of 5 log units of stimulus intensities the b-wave was depressed 36% to 48% (SEM=12%, n=5).

To insure that the effects seen with acetazolamide was not the result of effects on the photoreceptor cells, 20 mM aspartic acid was added to the superfusate. Aspartic acid has been shown to depolarize all cells proximal to the photoreceptors, thus allowing only the receptor potential to be recorded (Cervetto & MacNichol, Science 178:767-768, 1972). Treatment with doses up to 2 mM acetazolamide had no effect on the receptor potential compared to control values. Thus, the attenuation of the b-wave was not due to any action of acetazolamide on photoreceptor function.

These results suggest that inhibition of the enzyme carbonic anhydrase depresses the amplitude of the b-wave of the ERG. Carbonic anhydrase has been proposed to be involved in regulation of pH and cation transport, possibly potassium (Carter, Biol. Rev. 47:465-513, 1972; Ripps & Witkovsky, Prog. Retinal Res. 4:181-219, 1985). Since the b-wave is thought to involve a potassium current arising in the Muller fibers following stimulation of the retina with light, inhibition of carbonic anhydrase may result in a depression of the potassium current flow, thus causing a reduction in the amplitude of the b-wave.

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