Principles and Practice of Clinical Electrophysiology of Vision

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14

The M-Wave

Chester Karwoski
Laura J. Frishman

Like the proximal negative response (PNR), the M-wave is a light-evoked field potential that can be recorded in the proximal retina. It was named and most fully described in amphibians by Karwoski and Proenza,[10, 11] although possibly related responses have been reported by several groups since the studies of Arden and Brown[1] and Byzov.[2] The M-wave consists of a slow, negative-going response at both light onset and offset to a small, well-centered spot (see Fig 13–1). Annular and diffuse illumination elicit complex waveforms, sometimes dominated by the b-wave. The M-wave has recently been described in detail in the cat,[13] and thus is likely to be a general feature in the vertebrate retina.

Because the M-wave has maximum amplitude at the same depth as the PNR,[8] it is likely that it originates from events in the inner plexiform layer. In amphibians, the time course and stimulus dependence of the M-wave are similar to that of intracellular Müller cell responses as well as to light-evoked increases in $[K^+]_o$ in the inner plexiform layer.[8, 11] This led to the model of M-wave generation that is schematized in Figure 13–1. Here, light evokes responses in proximal neurons, K^+ is released into the extracellular space, and this K^+ generates currents due to spatial buffering in Müller cells. The model explains most intraretinal features of the M-wave, including its negative polarity. Figure 14–1 shows that certain key features of this model also hold for the M-wave in the cat.[4, 13] The model receives additional support from experiments in amphibian retinas with the K^+ channel blocker barium (Ba^{2+}): Ba^{2+} has minor effects on light-evoked neural activity and the increase in $[K^+]_o$ in the proximal retina, but it blocks Müller cell K^+ conductance, K^+ spatial buffering by Müller cells, and the M-wave.[7, 9]

As is the case with the PNR, any contribution of the M-wave to the transretinal electroretinogram (ERG) would be important as an index of proximal retinal activity. The M-wave can be recorded in the thin layer of residual vitreous after most has been drained,[6, 11] but the nature of M-wave contribution to the normal transretinal ERG in amphibians is uncertain. In superfused amphibian eyecups, computer averaging of the responses elicited by a small, dim light spot and recorded in the superfusate reveals a negative-going PNR followed by a slow, positive potential (C.J. Karwoski, unpublished observation). The origin of this positive potential has not yet been explored.

In the cat, the M-wave may contribute a small negativity to the flash ERG, but any such contribution is small, in part because a diffuse flash is a poor stimulus for the M-wave.[13] Under light-adapted conditions in response to small spots, the M-wave is the most prominent potential that can be recorded intraretinally in the cat. However, even under these stimulus conditions, the contribution of the M-wave, as a negative potential, is small relative to that of PII, which dominates the ERG as a positive potential.[13] (Under dark-adapted conditions, another proximal retinal response, the scotopic threshold response (STR), also contributes a negative potential to the ERG. The STR is described in Chapter 15.)

The contribution of the M-wave to the ERG may be greater when periodic stimuli (such as grating

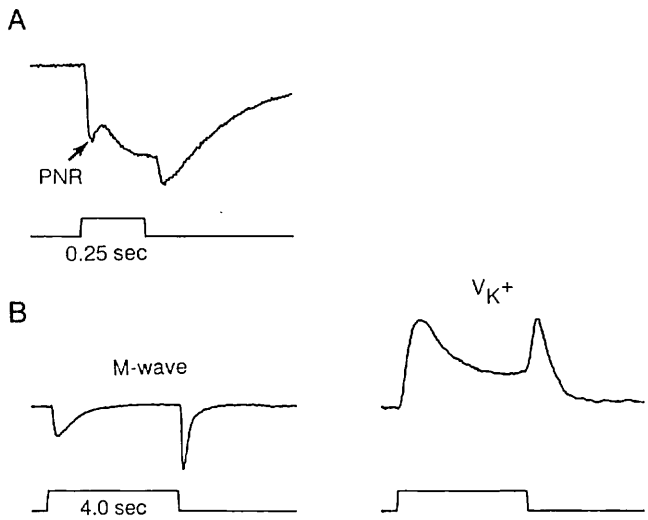

FIG 14–1.
The PNR, M-wave, and light-evoked increases in extracellular potassium concentration ($[K^+]_o$) recorded in the proximal retina of the cat. **A,** Recording of the M-wave with an unusually large initial transient following stimulus onset that has the appearance of the PNR in cold-blooded animals *(arrow)* (flash diameter, 0.8 degrees; background illumination, 9.7 log q $deg^{-2}s^{-1}$; flash illumination, 10.8). (Adapted from Sieving PA, Frishman LJ, Steinberg RH: *J Neurophysiol* 1986; 56:1039–1048.) **B,** M-wave and V_{K^+} recorded simultaneously with a double-barreled K^+-selective microelectrode. The maximum K^+ increase was about 0.18mM for the on response. Other details are similar to **A.** (Adapted from Frishman LJ, Sieving PA, Steinberg RH: *Vis Neurosci* 1988; 1:307–315.)

patterns that stimulate large regions of retina) are used. Sieving and Steinberg[14] presented evidence that the M-wave is tuned to a spot diameter similar to the bar width of the optimal spatial frequency for the intraretinal pattern ERG in the cat, and they suggested that the M-wave contributes to the pattern ERG.

The light-adapted diffuse flash ERG of several mammals (e.g., the cat,[5] rabbit,[12] and monkey[3, 12]) contains negative potentials at light onset and offset, and these have a time course similar to the M-wave of the proximal retina. However, these responses sum spatially over a much larger area than the M-wave.[5] Moreover, the negative on response generally is not affected by 2-amino-4-phosphonobutyric acid (APB),[5, 12] which blocks the transmission of photoreceptor signals to on bipolar cells.[16] This indicates that the response arises in the photoreceptors. Analysis with scotopically matched red and blue filters in the cat shows that it is the rod-receptor potential.[5] (An exception in the cat occurs at very high background illuminations where APB reduces the amplitude of a transient cone-dominated negative on response.[5])

The negative off component of the light-adapted ERG is abolished by APB in the rabbit and substantially reduced in the monkey[12] and the cat,[5] which suggests that the offset of PII (rod and cone) contributes to this component. The negative off response that remains is cone dominated in the cat. It originates proximal to the photoreceptors in the off pathway because it is abolished by aspartate,[5] which isolates the photoreceptor response.[15] The exact locus of origin of the cone off response (and of the cone-dominated negative on response in cats) is currently unknown.

Note: Oakley et al. have provided evidence for the M-wave in toads having an origin involving K^+ spatial buffering in Muller cells, and for the M-wave appearing as a positive-going potential in the ERG recorded in the vitreous humor.

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