# Principles and Practice of Clinical Electrophysiology of Vision


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# 13

# The e-Wave and Proximal Negative Response

Chester Karwoski

## e-WAVE

The e-wave is a delayed-off field potential that was first recorded in the frog retina[14] and has since been reported in the tadpole,[3] mudpuppy (C.J. Karwoski, unpublished observations), and trout.[4] Because delayed-off neuronal responses have been reported in the cat,[16] the e-wave may be present in mammals. The e-wave is recorded transretinally only on occasion.[12] The e-wave has attracted interest over the years because of its long latency (2 to over 60 seconds) following light offset.[12] Also, delayed-off responses in general are of interest because they likely are related to the perceptual phenomenon of afterimages.

Because the e-wave is present only in dark-adapted retinas, rod activity must play a role in its origin, and in fact, Tomita et al.[17] have argued that the e-wave is simply a scotopic d-wave. In response to relatively intense light, rods generate their hyperpolarizing receptor potential, but at light offset, this hyperpolarization returns back to baseline slowly and is delayed (rod aftereffect).[9] Changes in intracellular potential of the photoreceptors initiate responses through the rest of the retina, and it is thought that the delayed decay of the rod aftereffect initiates responses in other retinal cells that generate the e-wave. Karwoski and Newman[9] presented several experiments indicating that the e-wave arises from delayed-off activity in the proximal retina and specifically that at least a portion of the e-wave arises from Müller cells via spatial buffer currents induced by $K^+$ released by neurons in the proximal retina.

## PROXIMAL NEGATIVE RESPONSE

The proximal negative response (PNR) is a light-evoked field potential that can be recorded in the proximal retina. It was named and most fully described by Burkhardt,[1, 2] although recordings similar to it had been reported by a few groups since the pioneering studies of Tomita on the "intraretinal action potential."[18, 19] The PNR consists of a sharp, negative-going transient at both the onset and offset of a small light spot (Fig 13–1). The spot must be centered precisely about the microelectrode tip. Annular and diffuse illumination elicit complex waveforms that are sometimes dominated by positive-going responses.[2, 13] The PNR can be recorded in all vertebrate retinas, including the cat[15] and primate.[13]

Dye marking shows that the PNR is maximal in the inner plexiform layer.[7, 8, 10] Several lines of evidence suggest that the PNR in amphibians arises from on/off neurons,[10] probably amacrine cells.[2] Burkhardt's proposal is supported by the finding in the rabbit that the PNR is normal in retinas in which ganglion cell degeneration had been induced by optic nerve section (see R.F. Miller, D.A. Burkhardt, and R. Dacheux, unpublished observations[11]). The PNR in primates[13] and cats[15] may arise from on and

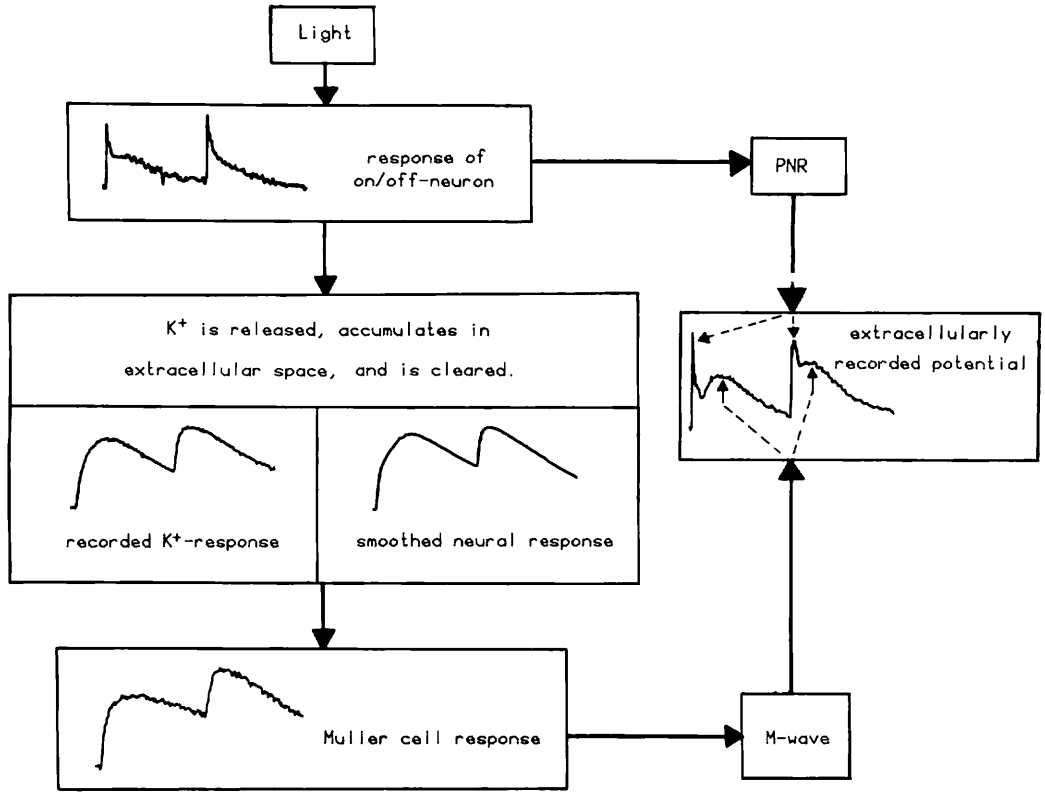


**FIG 13–1.**
Summary of events underlying generation of the PNR and M-wave in the proximal retina of the mudpuppy. A well-centered small-diameter light stimulus evokes depolarizing responses in on/off neurons *(top)* whose extracellular currents generate the PNR. The PNR is seen in the extracellularly recorded potential to the *right* as initial, sharp voltage transients at light onset and offset (negative is up in the extracellular potential). The neurons also release $K^+$, which accumulates in extracellular space and, in turn, depolarizes the Müller cells *(bottom)*. Müller cell extracellular currents generate the M-wave, which is seen to the *right* as slower negative transients at light onset and offset.

off cells, because these retinas contain relatively few on/off neurons.

Any PNR contribution to the transretinally recorded electroretinogram (ERG) would be important since it would provide an index of proximal retinal activity. In amphibian eyecups drained of vitreous humor, the PNR can be easily recorded in the thin layer of residual vitreous.[6, 10] However, the nature of any PNR contribution to the normal transretinal ERG is uncertain and probably small. This is because the PNR, which is best developed intraretinally in response to a small spot, is shunted through adjacent low-resistance regions of the retina that are not activated by the light. This results in little potential drop in the vitreous. Nevertheless, with extensive computer averaging, a negative-going PNR with a normal waveform can be recorded in the superfusate flowing over a frog eyecup (C.J. Karwoski, unpublished observations). In addition, it has been claimed that the PNR contributes to the vitreal-negative $a_2$ component of the frog ERG.[5] Finally, one should not yet exclude the possibility of a PNR contribution to the pattern ERG.

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