Photoreceptors in Pediatric Patients with Usher Syndrome

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Disclosure

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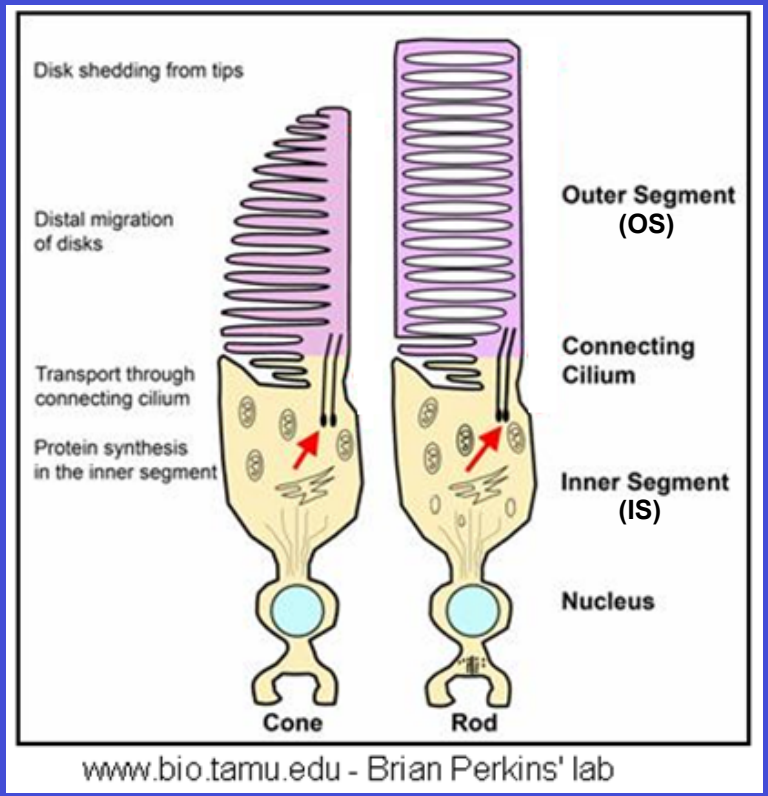
Purpose:

Evaluate retinal cell biology in the living eye

The retinal degeneration of Usher syndrome, all forms, affects both the rod and cone photoreceptors.

Cilia connect the photo-receptor outer segment (the site of phototransduction) to the more proximal inner segment which synapses with the second order retinal neurons.

Cilia are abnormal in Usher syndrome.



Patients with MYO7A and USH2A

We used non-invasive procedures to investigate phototransduction.

Phototransduction proceeds by a cascade of molecular events in the photoreceptor outer segment.

Through these events, light falling on the retina is converted into a neural signal for transmission along the visual pathways.

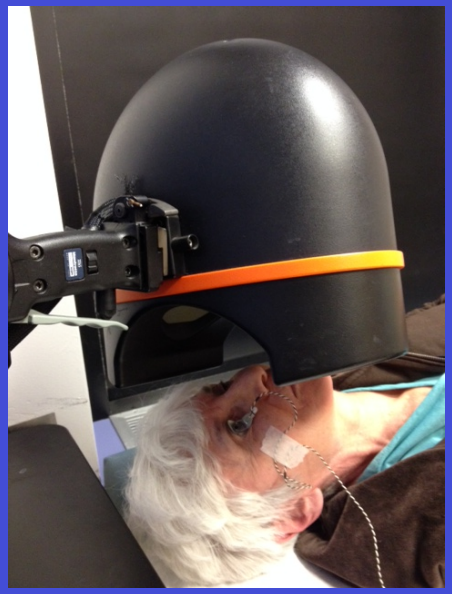
Patients with MYO7A and USH2A

We studied 23 patients (MYO7A, n= 9; USH2A, n=14) in scotopic and photopic conditions.

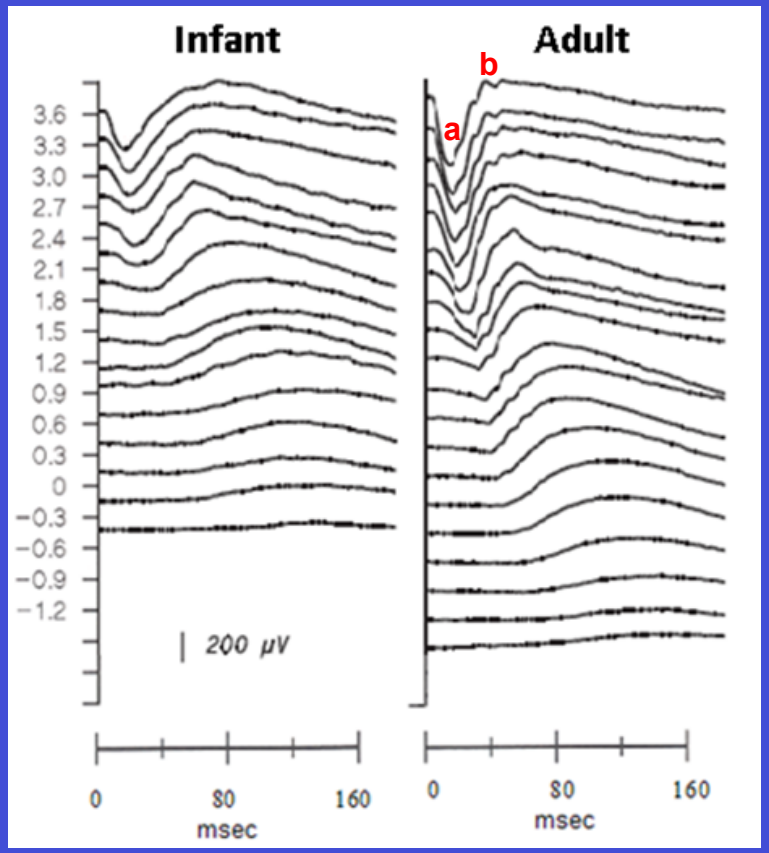
Median age was 6 years (range: 0.8 to 23 years).

Electroretinography (ERG)

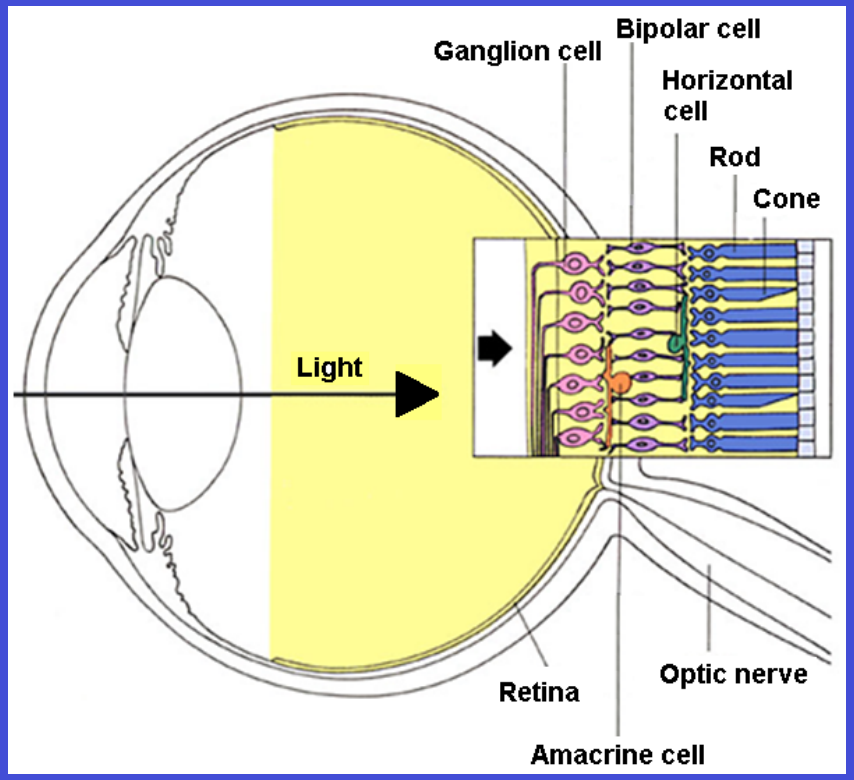
The phototransduction parameters were derived for ERG responses to full field stimuli.



ERG waveforms

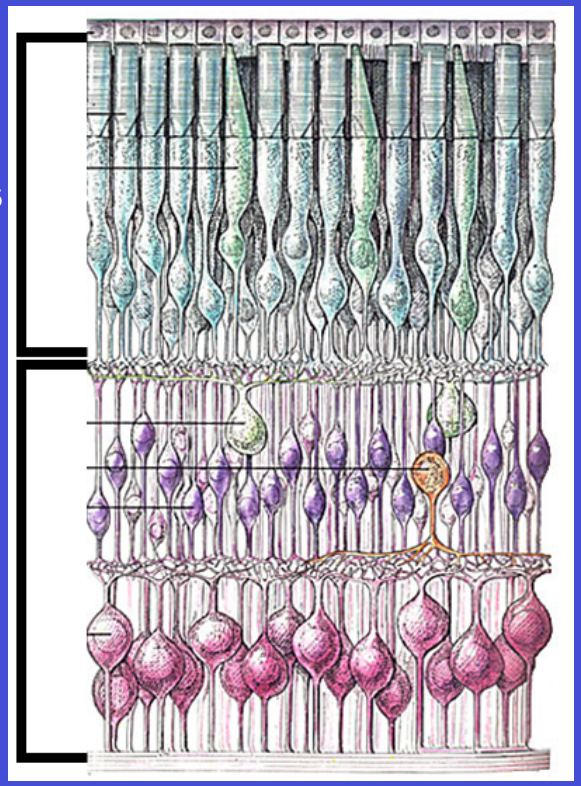


The Eye and Retina



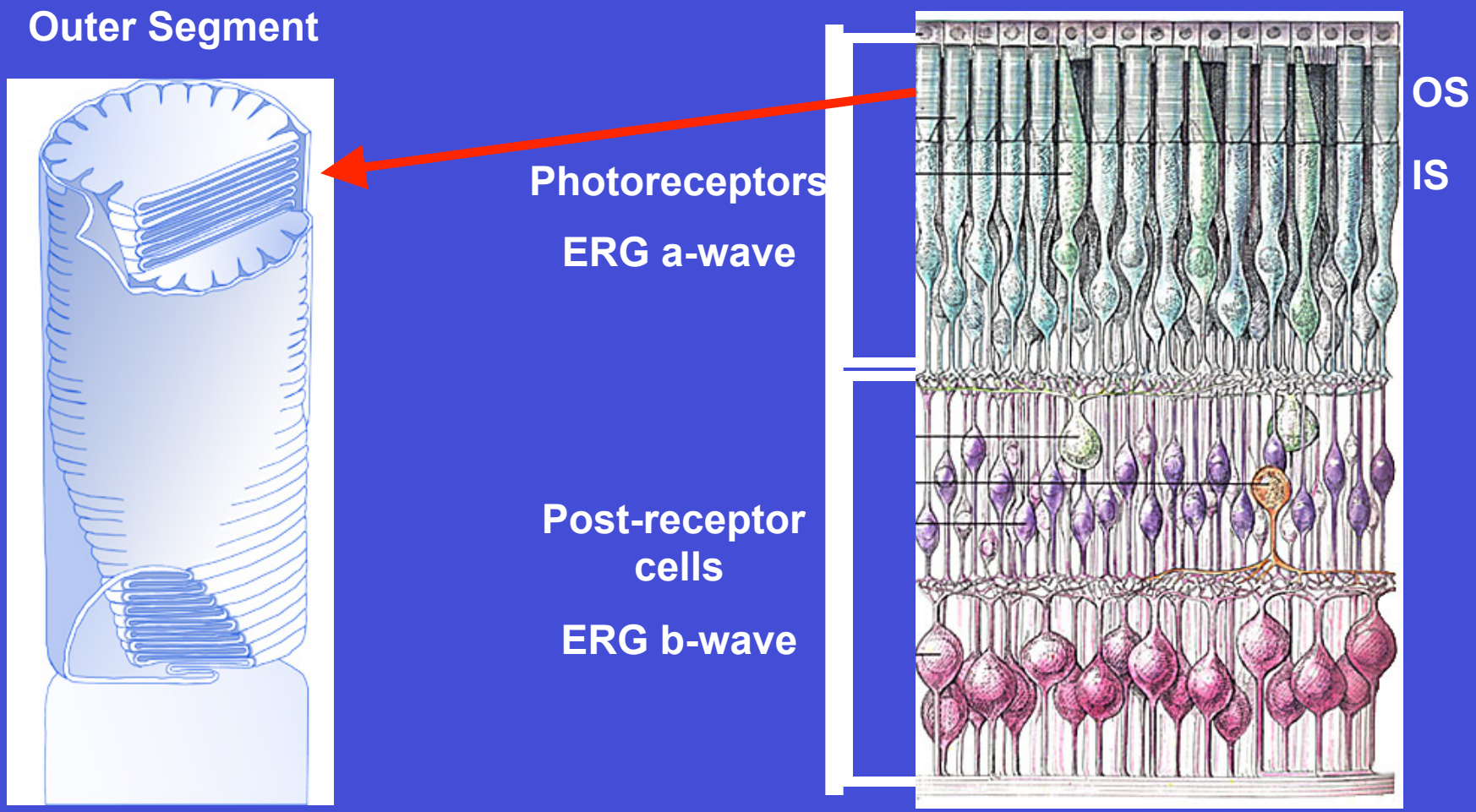
Photoreceptors

Post-Receptor Cells



Hubel, *Eye, Brain and Vision*, 1988

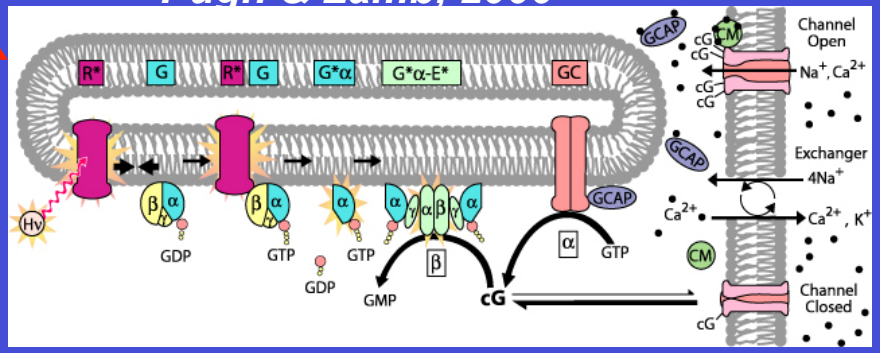
The Photoreceptor



Hubel, *Eye, Brain and Vision*, 1988

The Phototransduction Cascade

Pugh & Lamb, 2000



hν

Rhodopsin → Transducin → PDE → cGMP → Close Channel

Rod Photoresponse

$$R(I,t) = \{1 - \exp[-0.5\ I\ S\ (t-t_d)]\}R$$

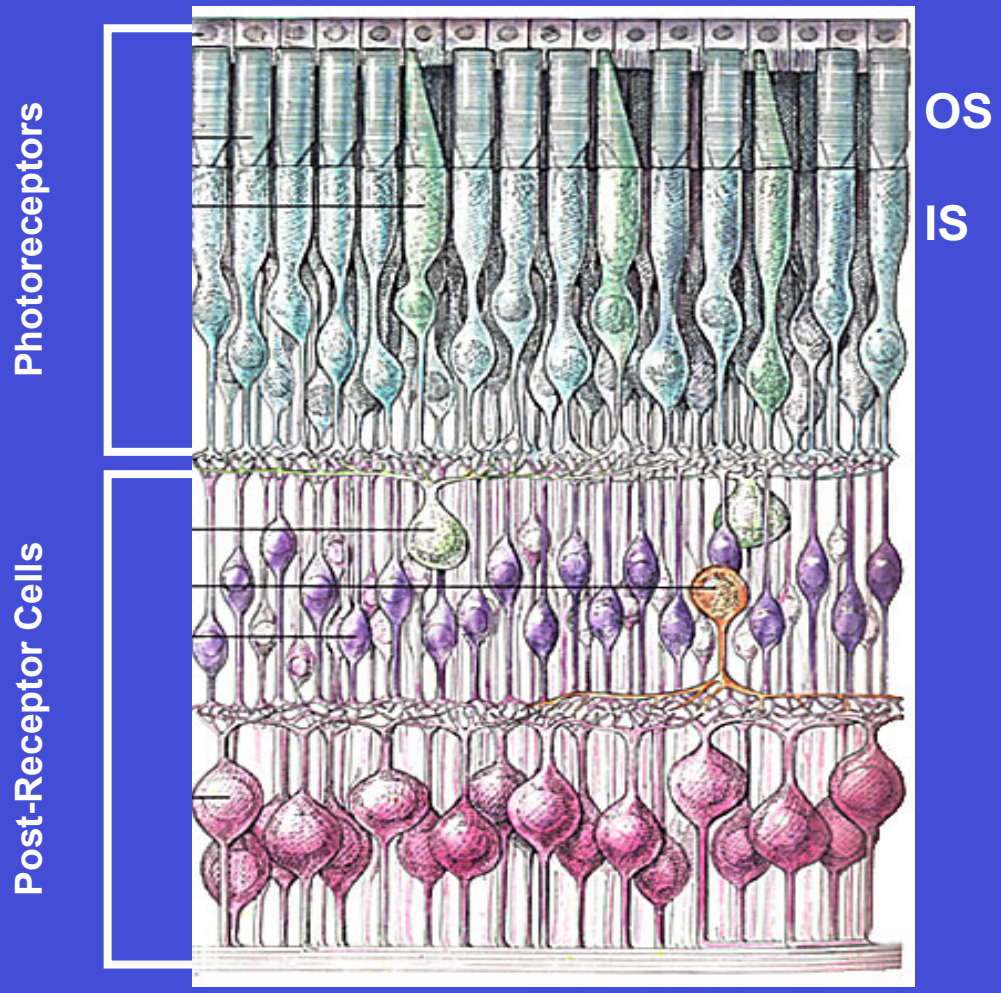
Hood & Birch formulation (1994) of Lamb & Pugh model (1992)

Activation of Phototransduction

Photoreceptor (a-wave) & Post-receptor (b-wave)

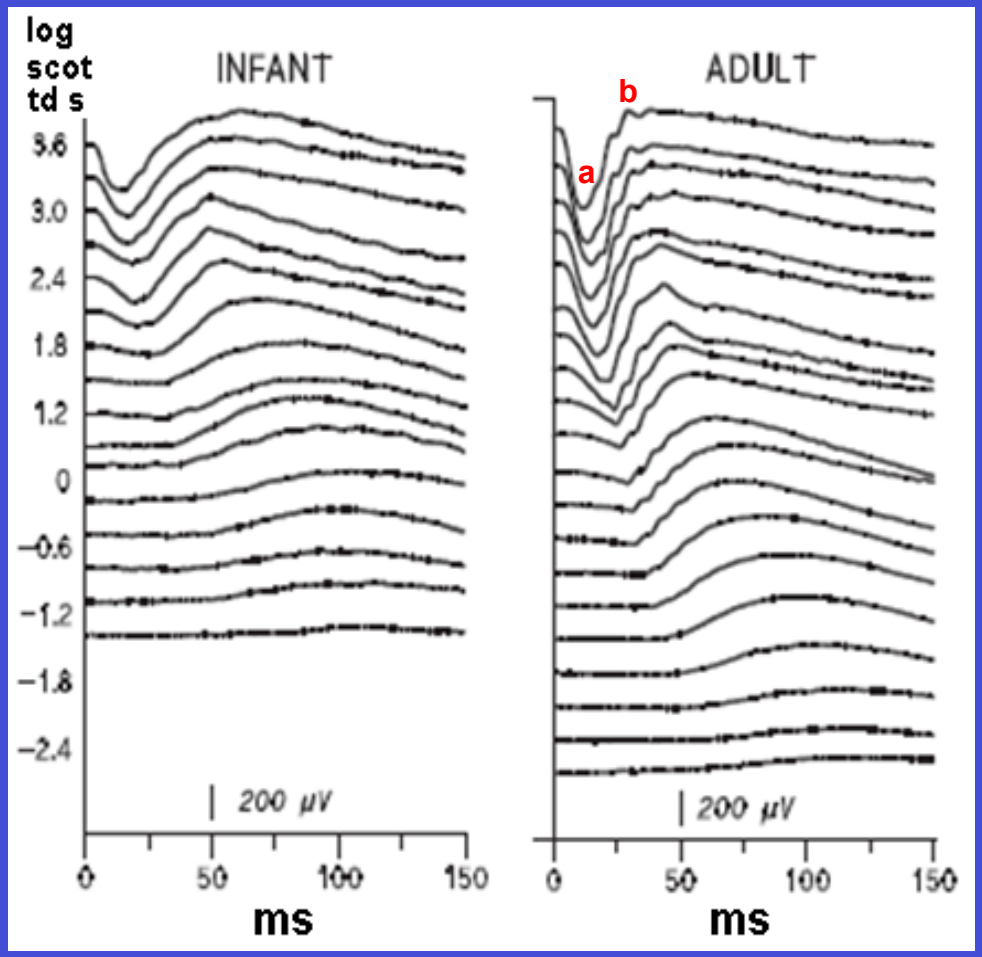
a-wave

b-wave

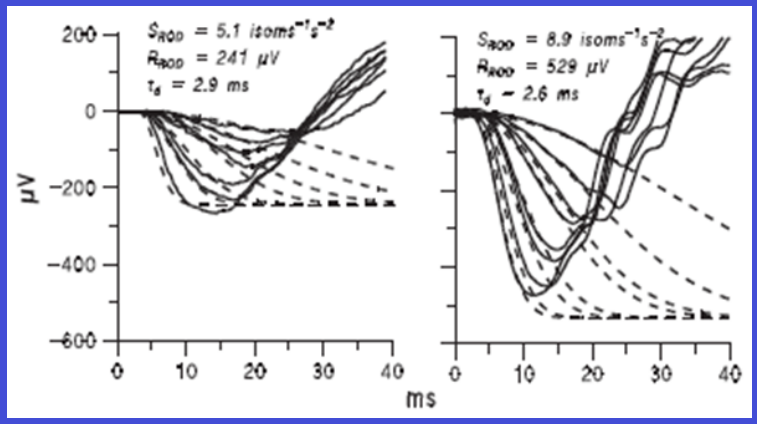


Hubel, *Eye, Brain and Vision*, 1988

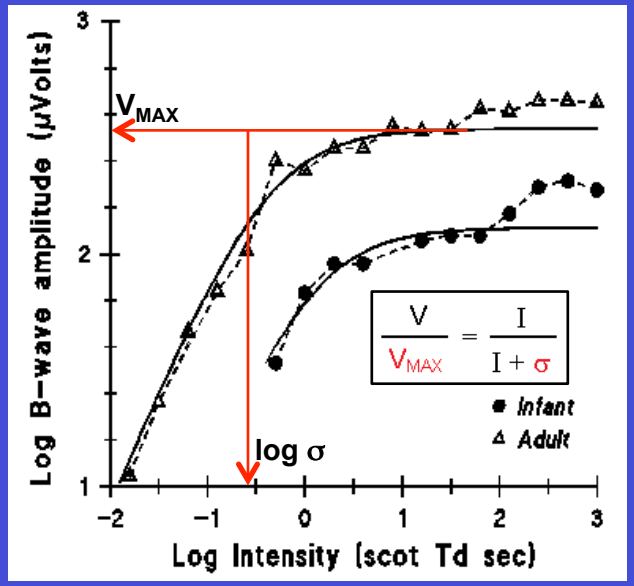
Photoreceptor (a-wave) & Post-receptor (b-wave)



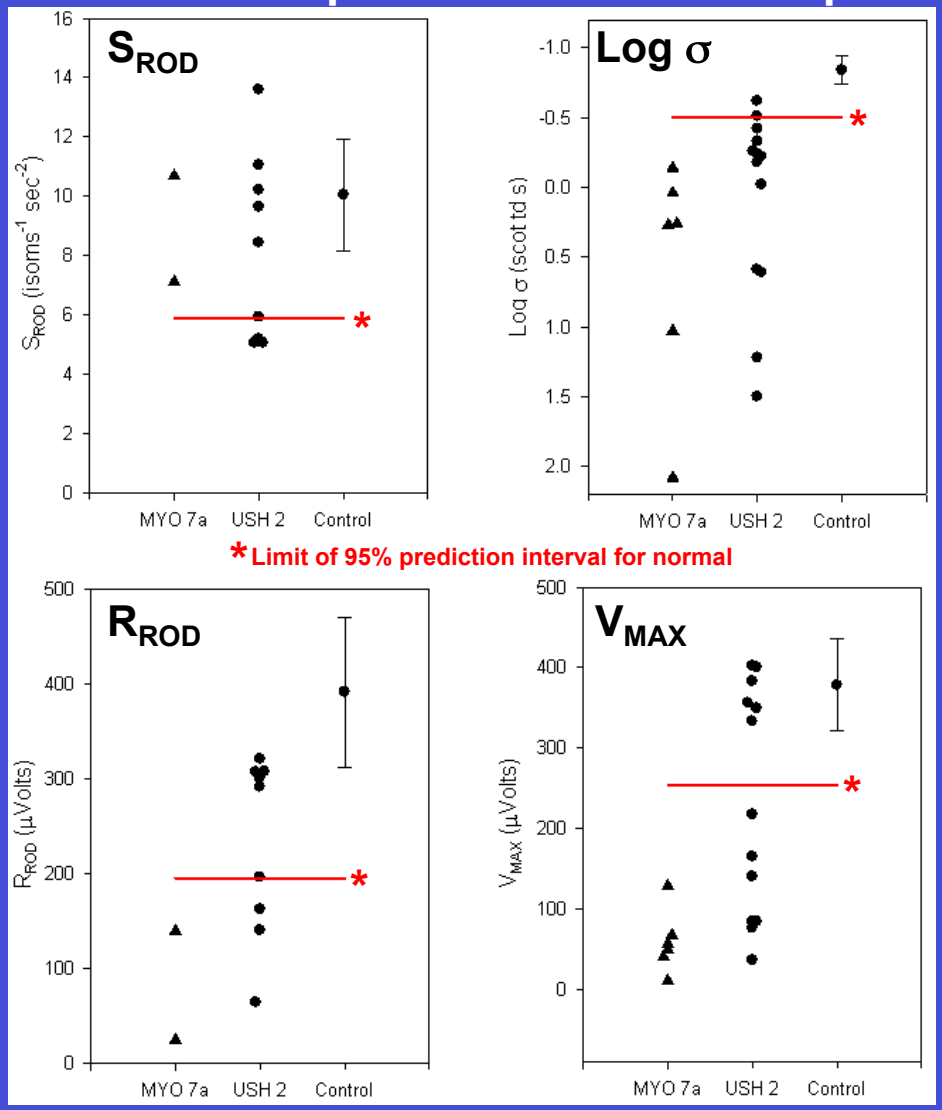
a-wave model fits



b-wave parameters
log σ and V_{MAX}



Scotopic ERG Parameters



In contrast to good photoreceptor sensitivity (S_{ROD}), significant deficits in post-receptor sensitivity (**log** σ) are found.

Log σ depends on transmission of signal from the outer segment, across the cilia, to the post-receptor retinal cells.

Small R_{ROD} is consistent with the thin outer segment layer imaged by optical coherence tomography (OCT). [Mucaj *et al*. ARVO 2014]

Log σ is important because it is correlated with dark adapted *visual* sensitivity in the patients with Usher syndrome. (This significant relationship is shown in a poster by Tavormina *et al.*)