Physiological properties of the pupil light reflex in healthy and diseased eyes

Figure 1. Physiological principles of the pupil light reflex in mammalian species. The pupil light reflex in healthy retinas is primarily driven by photoreceptor activity (red pathway – photoreceptor mediated response). The second (late) component of the pupil light reflex is mediated by melanopsin containing retinal ganglion cells (blue pathway – melanopsin mediated response).
How you can utilize Melan-100 to help you establish a proper diagnosis for your patients?

1. Sudden acquired retinal degeneration (SARD)
Characteristics: sudden onset of blindness, normal fundus appearance, complete absence of retinal electrical activity (no ERG amplitudes), slow and delayed pupil light reflex can always be elicited with very bright light source.

**Figure 2.** Sudden acquired retinal degeneration (SARD) is characterized by acute onset of blindness due to photoreceptor damage. Stimulation of the pupil light reflex in SARD patients with red light does not provide any response (no pupil constriction). Stimulation with blue light provides almost complete pupil constriction due to activation of melanopsin-containing retinal ganglion cells.

**Figure 3.** Spectral pupillary light reflex analysis in the SARD patient – no response to the red light, good response to the blue light.
2. Optic neuritis

Characteristics: usually sudden onset of blindness, swollen optic nerve head appearance on fundus examination, normal retinal electrical activity, can be associated with other signs neurological disease (proprioceptive deficits, ataxia, nystagmus…), the pupil light reflex is usually absent.

Figure 4. No pupil light reflex can be detected with blue or red light in optic neuritis patients.
3. Immune mediated retinitis (“pupillary dissociation syndrome”)
Characteristics: Clinical picture is identical to SARD patients – sudden onset of blindness, normal fundus appearance, no neurological or other systemic abnormalities, no pupil light reflex (or barely detectable) with red light, good pupil light reflex with blue light. Unlike SARD patients, electroretinogram amplitudes are normal or near normal. This condition is responsive to medical treatment.

**Figure 5.** Patients with “pupillary dissociation syndrome” have normal photoreceptor electrical activity, however electrical signals are not transmitted to retinal ganglion cells, which results in the absence of photoreceptor-mediated pupil light reflex (no response to red light).
4. Retinal degeneration
Characteristics: Usually early clinical symptoms are decreased vision in dim light conditions (rare exceptions are primary cone degenerations – vision is decreased during bright light conditions) and slow and incomplete pupil light reflex. Special ERG routines are frequently needed to establish diagnosis in the early stage of disease.

Figure 6. Due to decreased/inadequate input of photoreceptors to the retinal ganglion cells, the pupil light response to the red light is completely absent (advanced retinal degeneration) or decreased with pupillary escape (early retinal degeneration). The pupil light response to blue light (melanopsin-mediated response) is usually normal in early retinal degeneration or decreased with pupillary escape in advanced retinal degeneration, which is suggestive of the inner retina structural and organizational remodeling and retinal ganglion cell degenerative changes.
5. Retinal detachment

Characteristics: Frequently associated with a history of “sudden onset of blindness”. The pupil light reflex is usually slow, delayed, incomplete or sometimes completely absent.

![Retinal detachment diagram](image)

**Figure 8.** Due to the photoreceptor (outer segments) damage, the photoreceptor-mediated pupil light response (red light) is usually absent, while melanopsin-mediated response (blue light) is present. In the cases of steroid-responsive retinal detachment, both spectral components (red and blue) of the pupil light reflex can be absent. End stage retinal degeneration after chronic presence of retinal detachment (usually longer than 5 weeks) can also result in the complete loss of the red and blue responses.
Limitations to the successful evaluation of the retina and optic nerve disease by using spectral properties of the pupil light reflex:

- severe iris atrophy
- severe uveitis causing miosis
- glaucoma (causing ischemia of the iris sphincter)
- ophthalmoplegia interna/externa
- presence of intracranial neoplastic or inflammatory disease causing lack of the physiological synaptic inhibition in subcortical regions
- recent use of pharmacological agents causing miosis or mydriasis
- general anesthesia (subcortical inhibition)
- heavy sedation (subcortical inhibition)

*Disclaimer* - presented data present the most frequently observed pupil responses in different types of ocular diseases, however differences may exist between different patients due to individual patient variations, stage of disease or presence of multiple diseases affecting visual system simultaneously.

*Note: The images and data courtesy of Dr. Sinisa Grozdanic.*
References