



Benefits and risks of light entering the eye.

Age-related macular degeneration (AMD) is the most common cause of blindness in the developed world and affects over 35 per cent of persons over the age of 75. It is characterized by the progressive degeneration of the retina, retinal pigmented epithelium (RPE) and choroid. In about ten per cent of all cases, the formation of choroidal neovascularization membranes and vessel leakage (wet form of AMD) adds to the degeneration of retinal and choroidal tissues and exacerbates the course of the disease. To date, there is no efficient cure or prevention method. The pathogenesis of AMD is poorly understood, but may be linked to stress caused by radical oxygen species in macular photoreceptor cells and proximate retinal pigment epithelium cells (RPE). Both cell types are non-replicating (post-mitotic) and must respond to a lifetime of oxidative insult including light-induced oxidative stress. In consequence, retinal mechanisms for preventing and forestalling oxidative insult begin to break down by middle-age, which can increase the susceptibility of the retina to accumulated damage.

In the **photoreceptor outer segments (POS)**, photopigments absorb light, the photoreceptor cell bleaches and becomes unavailable for light absorption. The tips of the POS are shed daily and phagocytized and metabolized by the adjacent RPE cells. This process includes recycling of the bleached photopigment through a lengthy metabolic pathway called the visual cycle.

Visible light absorbed by photoreceptors, especially short wavelengths, is a significant factor in the production of **radical oxygen species**, thus contributing to the formation of AMD, and the risk of retinal damage from light is also termed "the blue light hazard" with the greatest hazard peaking at wavelength of 440 nm. The generation of radicals combined with high polyunsaturated fatty acid content in the POS form radical oxygen species, which oxidize proteins (like advanced glycation endproducts-AGEs, advanced lipoxidation endproducts – ALEs and oxysterols). The extent of photonic damage is proportional to the amount of light absorbed by the photo-pigments, and blue light potentiates the retina for a much greater degree of photo-oxidative damage by increasing the photon catch capacity by short circuiting the metabolic visual cycle through a process of photoreversal.

In dependence upon blue light exposure, **RPE cells** are challenged with oxidized POS, and the more such

oxidized products accumulate over time, the more toxic endproducts like the lipofuscin component A2E are formed in the RPE cells. In addition, cytochromes of the respiratory chain all adsorb light within the 410-440 nm range, e.g. blue light induces ROS production in the mitochondria of RPE cells, which results in RPE cell dysfunction and death and consequently also affects photoreceptor cells.

The macular area (point of highest visual acuity) is most affected by these processes, because no inner retinal (neural) layers may filter harmful short wave lengths [15]. To shelter macular photoreceptors, the macula is enriched in anti-oxidative molecules like β -carotene, vitamin E, zeaxanthine, lycopene and lutein.

Concerning the quality of light, short wavelength (blue) light is believed to be a major pathogenetic factor in AMD. In contrast to this, infrared (IR) light was found to possess a regenerative potential in many situations of tissue repair.

The following has been recorded: an acceleration of wound healing, improved recovery from ischemic injury and attenuation of the degeneration of the injured optic nerve. Regarding the cellular effects of IR light, many hints point to a stimulation of the respiratory chain in mitochondria.

Because in our group many experiments were performed regarding the functional morphology of mitochondria we assessed the "rescue capacity" of IR light after damage to the mitochondria, and cell metabolism (including reactive oxygen species – ROS – production) with blue light in a retinal ganglion cell line.

With different methods probing the functional and energy status as well as the life-death (apoptosis) of a retinal cell line, we were able to show that IR light can rescue the decreased mitochondrial membrane potential and cellular energy status significantly. In addition, the blue light induced enhanced ROS production was reduced by IR light. All indicators of apoptosis and necrosis point to reduction of cell death by IR light.

Conclusion. Our results point to a convincing rescuing capacity of IR light for cells which have been damaged by blue light. It remains elusive if this is exclusively a result of triggering the respiratory chain, or if other factors including gene and protein regulation are responsible. This is the subject of our ongoing research.