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THEORETICAL ANALYSIS OF THE RELATIONSHIP BETWEEN CHANGES IN RETINAL PERFUSION AND TISSUE METABOLIC DEMAND

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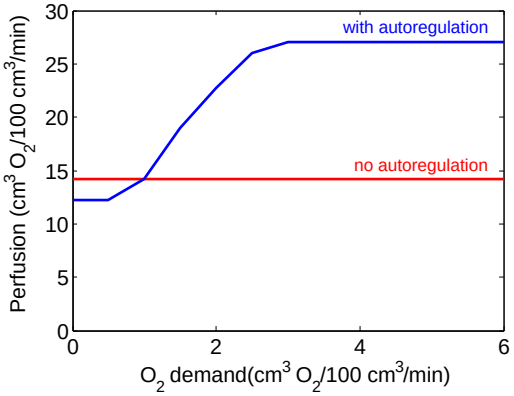
Alterations in retinal perfusion are associated with many ocular and systemic diseases such as glaucoma, age-related macular degeneration and diabetes [1, 2]. The retina is capable of metabolic autoregulation, which is the ability to adjust perfusion in response to altered tissue demand. In cases of exercise or flicker stimulation, the metabolic demands of the retina are observed to increase, whereas in pathological cases, retinal perfusion may not meet oxygen demand. Here, a mathematical model is used to investigate the relationship between retinal perfusion and tissue demand.

The retinal vasculature is represented by compartments for the central retinal artery (CRA), large arterioles, small arterioles, capillaries, small venules, large venules, and the central retinal vein (CRV). The blood flow is driven by systemic pressures, and is modulated by variable resistances accounting for nonlinear effects due to blood flow autoregulation, direct effect of intraocular pressure (IOP) on vessels and IOP-induced compression of the lamina cribrosa on CRA and CRV. The model is based on passive and active length-tension relationships of smooth muscle that determine arteriolar diameters. Passive tension is described by an exponential function, and active tension is represented by the product of maximally active tension (given by a Gaussian function) and a factor between zero and one that indicates the level of smooth muscle activation. When all mechanisms of blood flow autoregulation are functioning, arterioles are assumed to respond to changes in pressure, shear stress, carbon dioxide, and the downstream metabolic state. If autoregulation is not functioning, arteriolar vascular tone is assumed to be constant. Overall the model consists of a system of coupled ordinary differential equations.

When autoregulation is functional, the model predicts that retinal perfusion increases

nearly two-fold in response to a three-fold increase in oxygen demand. The model predicts a 14% decrease in perfusion if demand is decreased by 50%, and a 33% increase in perfusion if demand is increased by 50%. In the absence of autoregulation, the model shows a constant level of perfusion that does not respond to changes in oxygen demand (see Figure).

The model results suggest that impaired autoregulation might increase the risk of retinal ischemic damage in conditions of elevated demand (as in flicker stimulation), since the vasculature is unable to adequately respond to the increase in demand. The model also suggests that autoregulation allows for a greater degree of compensation for increased demand than for decreased demand. In particular, the model predicts only a moderate decrease in perfusion in response to a decrease in metabolic demand (as in retinal ganglion cell loss).



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