ANALYSIS OF A POTENTIAL NEW MODEL FOR NEUROVASCULAR COUPLING IN RETINA AND ITS RELATION TO THE RETINAL RELAXING FACTOR

Name: MAENHAUT N.

Affiliation institution: Ghent University, Dept. Pharmacology

Promotor: VAN DE VOORDE J.

Background and aim(s) of the project (max 10 lines):

Neurovascular coupling is extensively studied in brain. However, much less is known about the neurovascular coupling in retina.
Recently, we have observed that electrical field stimulation (EFS) of bovine retinal arteries surrounded by adherent retinal tissue elicits a rapid and reversible vasorelaxation. This can be due to the presence of retinal tissue. To confirm this hypothesis, we repeated the experiment on isolated bovine retinal arteries which were carefully cleaned of surrounding retinal tissue. No effect was seen on these preparations. These experiments suggest that this experimental set-up can be used as a potential in vitro model for investigating neurovascular coupling in retinal circulation.
The aim of the present project is to characterize this vasorelaxing effect, which may lead to a better understanding of neurovascular coupling in retina.

Development of the project (max 25 lines):

Experiments will be performed using isolated bovine retinal arteries with adherent retinal tissue mounted for isometric tension measurements in a wire myograph. Ring segments of a vessel will be placed in an organ bath filled with an oxygenated physiological solution at 37°C. Two wires are guided through the lumen of the vessels. One wire is fixed on a holder connected to a micrometer, the other one fixed on a holder connected to a force transducer that measures isometric tension changes in the ring segment. After precontraction of the preparations EFS will be applied by a stimulator via two parallel platinum electrodes on each side of the retinal artery.
In a first series of experiments we will investigate the link between the EFS characteristics and the EFS induced vasorelaxation. By these experiments we can validate our model. We will also validate this model by checking the involvement of neurons in the EFS-induced vasorelaxation, using neurotoxic agents.
Furthermore, we want to investigate whether glial cells are involved in the EFS-induced relaxation. In neurovascular coupling in brain, it is known that neurons can communicate with astrocytes through the release of glutamate. Glutamate-mediated $[Ca^{2+}]_i$ elevations in astrocytes trigger the release of gliotransmitters to adjust blood flow to neuronal activity (1). Therefore, we will block the binding or uptake of glutamate in glial cells. In addition, we will use a selective glial toxic agent.
Finally, we will address the question what vasoactive molecule(s) is (are) involved in the EFS-induced relaxing response. A first possibility, is the involvement of the retinal relaxing factor (RRF). About one decade ago our research group discovered an as yet unknown retinal relaxing factor (RRF) (2).

To investigate the involvement of the RRF, we will use a RRF-blocker. Besides RRF many other neurotransmitters (such as NO, ACh) and gliotransmitters (3) (for example prostaglandins, epoxyeicoatrienoic acids, CO, K^+) can be considered as potential mediators of EFS-induced relaxation. Therefore, we will also investigate the involvement of these vasoactive mediators using selective blockers.

REFERENCES

(1) ZONTA M., ANGULO M.C., GOBBO S., ROSENGARTEN B., HOSSMANN K.A., POZZAN T., CARMIGNOTO G. – Neuron-to-astrocyte signaling is central to the dynamic control of brain microcirculation. *Nat Neurosci* 2003 January; 6 (1): 43-50.

(2) DELAEY C., VAN DE VOORDE J. – Retinal arterial tone is controlled by a retinal-derived relaxing factor. *Circ Res* 1998 October 5; 83 (7): 714-20.

(3) METEA M.R., NEWMAN E.A. – Glial cells dilate and constrict blood vessels: a mechanism of neurovascular coupling. *J Neurosci* 2006 March 15; 26 (11): 2862-70.

.