Abstract

To accomplish sufficient blood flow in the brain, the functioning of the cerebral regulatory mechanisms is of great importance. Cerebral autoregulation, the control mechanism that accounts for blood pressure variations, and neurovascular coupling, the regulatory system that adjusts blood flow to the local metabolic need, are mainly responsible for an adequate cerebral blood flow under diverse circumstances. Both mechanisms may be disturbed by (part of) pathological processes underlying hypertension, preeclampsia and Alzheimer’s disease. Examination of these regulatory mechanisms could provide helpful diagnostic, predictive and therapeutic information. Nevertheless, proposed methods to evaluate cerebral blood flow regulation show a large spread in outcomes and were unable to differentiate sufficiently between normal and pathological functioning. Therefore, assessment of the regulatory mechanisms is still under investigation and hence, not (yet) implemented in daily clinical practice.

In a recent study, neurovascular coupling function has been assessed in former (pre)eclamptic patients by ultrasound measurement of the blood flow through the visual cortex during visual stimulation. The resulting visually-evoked blood flow response (VEFR) revealed that three different types of responses can be distinguished, based on their course as well as on quantitative parameter values. One type can be identified as the usual ‘normal’ response, since it has also been described by other authors. The other two types, however, have not been reported before. Although they were mainly found in former patients (but not in all), these response types can only hypothetically be considered as pathological with probably one type being the more severely affected and the other the result of moderate disorder.

The results of this study are the starting point for the clinical project described in this report. The project has originated from the idea that more insight in the underlying (patho-)physiology is required to interpret the observed response types. This has lead to the more concrete objective to develop a tool that provides the possibility to simulate the visually-evoked blood flow response and that can be used to study the effect of different possible pathological conditions on this response.

Vascular modeling is chosen as approach to realize the project goal. In the development of this kind of model, physiological features as well as anatomical structure of the blood vessels can be taken into account. Applying this on the vasculature of the visual cortex, a simple vascular lumped parameter model has been developed which consists of an arterial compartment representing the only supplying vessel for the visual cortex and a microcirculatory compartment representing the microcirculation of the visual cortex. With this model, it should be possible, at least in theory, to investigate the effect of changes at microcirculatory level on the supplying artery level where the measurement are acquired.

To test the practical utility of the model, a few simple tests have been carried out to simulate (the effect of) visual stimulation, i.e., the working of the neurovascular coupling mechanism. To this end, first model parameter values have been assessed under baseline conditions, i.e., when no visual stimulus is applied. Then, visual stimulation has been incorporated simply by variation of the microcirculatory resistance. The results of these tests prove that with this model the effect of a change in microcirculatory parameters on the flow response in the supplying artery can be studied. Therefore, it may be concluded that the fundamentals for realization of a link between VEFR curves and (patho-)physiology have been established. As a next step, more complex hypotheses regarding the functioning of the neurovascular coupling mechanism under normal and pathological conditions can be implemented in the model. In conclusion, this simulation tool can bring us a step closer to (patho-)physiological explanation of the measured visually-evoked response types and hence, to the application of neurovascular coupling assessment as an additional clinical tool.