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Microstrokes and capillary dilations –investigating the effect of single capillary alterations

Monday, 31 May 2021 16:10 (15 minutes)

Capillaries are the most frequent vessel type of the brain's vasculature. The dense and highly interconnected capillary bed is key to ensure a robust blood supply over the entire depth of the cortex, and during baseline and neuronal activation. Besides its relevance our knowledge of structural and functional properties of the capillary bed remains limited. We perform blood flow simulations in realistic microvascular networks and alter individual capillaries to improve our understanding of capillary perfusion and robustness. More precisely, we first investigate the impact of single capillary dilation (1), which has been suggested as a mechanism to contribute to up-regulate flow during neuronal activation. Subsequently, we study flow changes in response to single capillary occlusion (2), because these micro-lesions are linked to dementia and Alzheimer's disease. Both studies provide insights on the role of these alterations but importantly also regarding general characteristics of the cortical capillary bed. Additionally, thanks to our numerical model which tracks 100 thousands of red blood cells (RBCs) (3), we are able to comment on the impact of RBCs on these local changes.

Our results show that a capillary dilation of 10% leads to a flow increase of 23% (per 100 µm) and an increase in the number of RBCs of 20% in the dilated capillary. Interestingly, the precise response depends on the relative bulk flow velocity difference at the upstream divergent bifurcation. As such, single capillary dilation causes a local increase in flow rate and a redistribution of RBCs. However, to increase the total inflow by ~6% in a microvascular network embedded in a tissue volume of 1 mm3 all capillaries need to dilate by 10%. Consequently, capillary dilation is likely relevant for a localized redistribution of flow and RBCs, but is not the driving force to induce an overall flow increase.

Comparable to single capillary dilations, the effects of a microstroke are most pronounced in the direct vicinity of the microstroke capillary (MSC) and the severity is governed by the local vascular topology. The largest changes are observed for a MSC with a convergent bifurcation upstream and a divergent downstream (2-in-2-out). Here, the flow rate drops by 80% in the directly adjacent vessels and is still reduced by 20% in generation ±3 from the MSC. Significantly, smaller changes are observed for a MSC with a divergent bifurcation upstream and a convergent bifurcation downstream (1-in-1-out). Interestingly, MSCs of type 2-in-2-out are considerably less frequent than MSCs of type 1-in-1-out. Moreover, they supply a significantly smaller tissue volume with oxygen and nutrients. Taken together, our results suggest that the perfusion of the capillary bed is inherently robust to single capillary occlusions. Moreover, we hypothesize that the different topological configurations might fulfil distinct structural and functional tasks.

Time Block Preference

Time Block A (09:00-12:00 CET)

References

1. Schmid F, Barrett MJP, Obrist D, Weber B, Jenny P. Red blood cells stabilize flow in brain microvascular networks. PLoS Comput Biol. 2019;15(8):e1007231.
2. Schmid F, Conti G, Jenny P, Weber B. The severity of microstrokes depends on local vascular topology and baseline perfusion. BioRxiv. 2020.

3. Schmid F, Tsai PS, Kleinfeld D, Jenny P, Weber B. Depth-dependent flow and pressure characteristics in cortical microvascular networks. PLOS Computational Biology. 2017;13(2):e1005392.

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