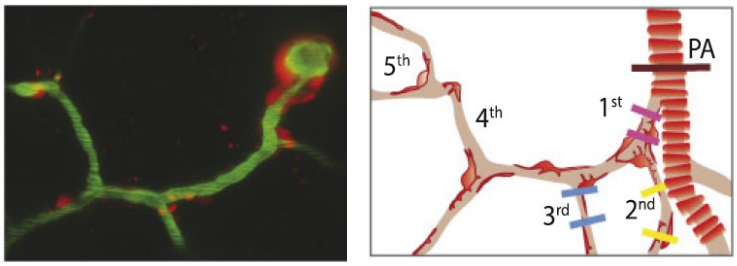
Student project

Do capillary sphincters exist in the human brain?



Mouse experiments: A penetrating arteriole (PA) with capillary branches. Green: the vessels, with the sphincter at the entrance of the first capillary. Red: pericytes. [1]

Background: Blood flow to our brain is tightly regulated, such that all of our brain cells receive enough oxygen and nutrients. Such regulation is impaired in a variety of conditions. Thus, in acute ischemic stroke, blood flow is interrupted by a clot in one of the cerebral arteries, with devastating consequences. We further suspect that in various forms of dementia, impaired blood flow adds to the disease progression, with slow but no less devastating consequences.

Blood flow is regulated by vasoconstriction and dilation of blood vessels. But which vessels? There are two opinions: the classic concept is that regulation is performed in small arteries by smooth muscle cell contraction, with the capillaries being static, 'boring tubes'. Yet an ancient theory that has been revived states that capillaries regulate flow, through contractile pericytes, with the arteries being the boring part.

While there is a lot of evidence for both thoughts, such evidence is mostly based on experiments in mice (see figure). Yet, humans are not mice. So how is this in humans? This is where you come in!

Project: You will investigate the structure of the human cerebral microvasculature, with special focus on the existence or not of so-called capillary sphincters. These are highly contractile entrance points of capillaries, with the contraction driven by pericytes or pericyte-like cells. We envision that you will cut and process human brain samples that contain complete units of penetrating arteries with their arteriolar and capillary side branches. The challenge is to cut tissue blocks that are thick enough to image these structures in 3D while still allowing for immunostaining and microscopic imaging. This will allow you identifying the various vessel types and testing whether indeed such sphincters exist, and if they exist, what their dimensions are and whether pericytes are involved.

You: Are a Bachelor's or Master's student in biomedical sciences or a related study. We will tune the program to your level of education, length of internship and any requirements by your study program.

Starting date and duration: Starting date is flexible, duration is flexible but should be at least 4 months.

Daily supervision: Judith de Vos and Moeed Khokhar

Final responsibility: Inge Mulder and Ed van Bavel

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1 Khennouf L, Gesslein B, Brazhe A, Octeau JC, Kutuzov N, Khakh BS, Lauritzen M (2018) Active role of capillary pericytes during stimulation-induced activity and spreading depolarization. Brain 141: 2032-2046 Doi 10.1093/brain/awy143