Link between impaired cerebral hemodynamics and cognitive deficits in patients with asymptomatic internal carotid artery stenosis – a multi-parametric MRI study –

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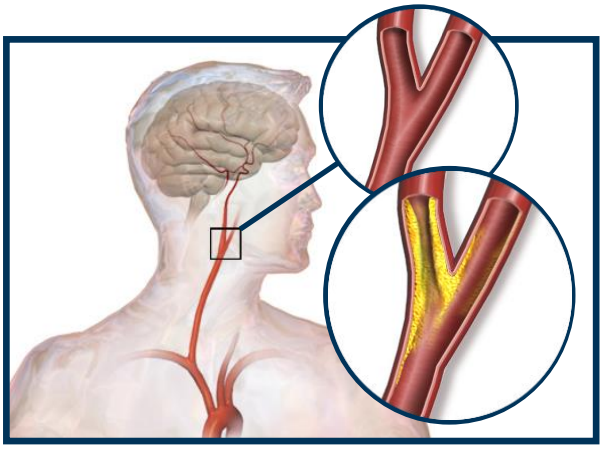
Project description



Internal Carotid Artery Stenosis (ICAS) is a major public health concern, accounting for 10-15% of all ischemic strokes. Conventionally, ICAS patients without transient or permanent neurological deficits are deemed clinically 'asymptomatic'. This, however, ignores a frequently observed gradual cognitive decline in these patients, which may eventually lead to severe dementia. The underlying mechanisms of this cognitive decline are poorly understood.

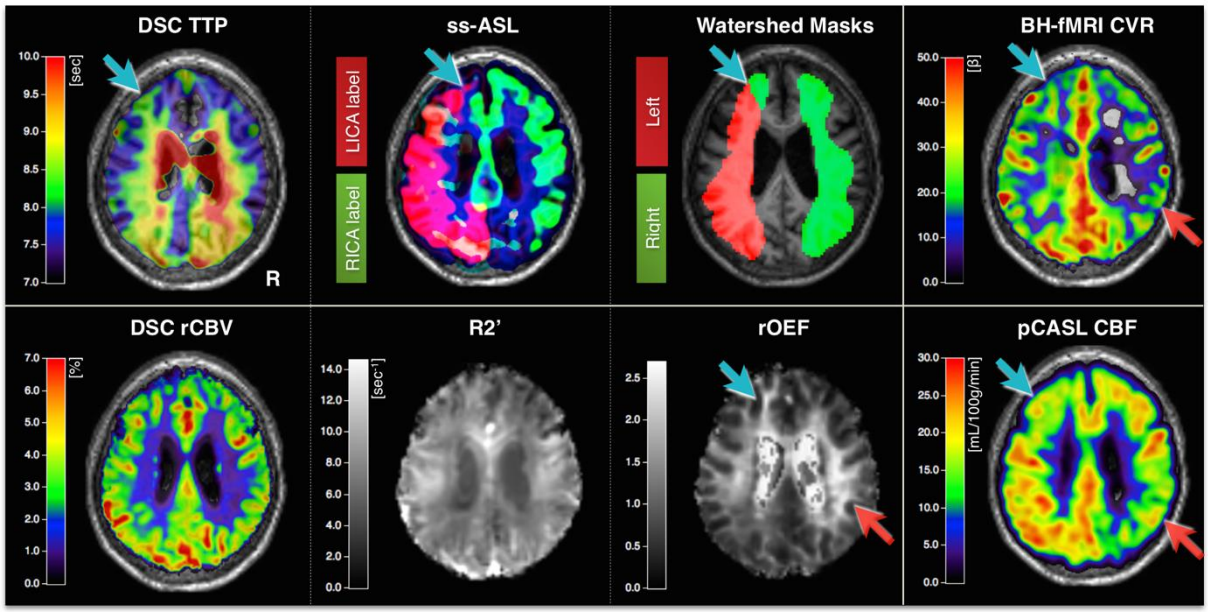
Our research aims at understanding the complex pathophysiological mechanisms underpinning cognitive decline in ICAS patients. A seminal observation from our previous study is that alterations of cerebral hemodynamics in ICAS patients are intricately linked with attention deficits (Göttler et al., 2020; Schmitzer et al., 2021). This finding is particularly profound for patients without explicit neurological deficits but enduring detrimental hemodynamic impairments.

This project is designed to further investigate the association between hemodynamic impairments, white matter structural alterations and cognitive performance in patients with high-grade asymptomatic ICAS. The multi-parametric MRI protocol has been developed by our interdisciplinary research group. Applied methods are state-of-the-art and developed in close collaboration with Philips Healthcare and internationally renowned experts, e.g., Prof. van Osch (Leiden University). This includes cerebral perfusion MRI (based on contrast agent and arterial spin labeling), diffusion tensor imaging, and cerebrovascular reactivity mapping via CO_2 inhalation in the scanner. To increase sensitivity for subtle hemodynamic alterations, we thereby delineate individual cerebral watershed areas by a procedure developed by our group (Kaczmarz et al., 2018). Moreover, comprehensive neuro-cognitive evaluation of study participants will be performed to discern mild cognitive deficits across various domains in ICAS patients.

An innovative facet of our approach lies in machine learning, aiming to elucidate correlations between white matter alterations, hemodynamic shifts, and potential trajectories of progression and cognitive deterioration in subsequent assessments. Additionally, machine learning-assisted segmentations, focusing on regions like white matter hyperintensities and adjacent tissues, aim to unveil subtle, yet crucial, insights into white matter structural alteration that remain elusive in current scientific discourse.

Preliminary results

In a previous multi-parametric study in ICAS patients, we observed significant hemodynamic alterations (Göttler et al., 2019) that were pronounced in individual watershed areas (Kaczmarz et al., 2018&2020; Schmitzer et al. 2021) and related to reductions in BOLD functional connectivity (Schneider et al., 2022,2023). In particular, we observed associations between hemodynamic impairments and cognitive decline (Göttler et al., 2020) and used machine learning to predict ICAS (Gleißner et al. 2024).



Feasibility (max 500 characters)

The study is DFG funded and ethics approval exists. Data acquisition has already started, major data processing pipelines exist and preliminary results are promising. Our interdisciplinary research group has excellent expertise in conducting clinical studies, data analysis and supervising students.

Related funding (max 500 characters)

CP, JG & SK received DFG grants to study hemodynamics, structural alternations and their impact on cognition in patients with asymptomatic ICAS (project numbers 395030489 & 547 163 214).

Track record of successful graduations

Our research group has an excellent track record of successful graduations, several with honours: Dr. rer. nat. Anne Kluge, Dr. med. Vanessa Griese, Dr. rer. nat. Stephan Kaczmarz, Dr. rer. nat. Ronja Berg, Dr. med. Miriam Reichert, Carina Gleißner (Dr. med. cand., dissertation submitted), Jan Kufer (Dr. med. cand.), Lena Schmitzer (Dr. med. cand.), Franziska Richter (Dr. med. cand.).

Project related own publications

Gleißner C, **Kaczmarz S**, Kufer J, Schmitzer L, Kallmayer M, Zimmer C, Wiestler B, **Preibisch C**, **Göttler J.** (2023) Hemodynamic MRI parameters to predict asymptomatic unilateral carotid artery stenosis with random forest machine learning. Front Neuroimaging. 12;1:1056503. doi: 10.3389/fnimg.2022.1056503.

Göttler J, Kaczmarz S, Kallmayer M, Wustrow I, Eckstein HH, Zimmer C, Sorg C, **Preibisch C**, Hyder F. (2019) Flow-metabolism uncoupling in patients with asymptomatic unilateral carotid artery stenosis assessed by multi-modal magnetic resonance imaging. J Cereb Blood Flow Metab. 39(11):2132-2143

Göttler J, Kaczmarz S, Nuttall R, Griese V, Napiórkowski N, Kallmayer M, Wustrow I, Eckstein HH, Zimmer C, **Preibisch C**, Finke K, Sorg C. (2020) The stronger one-sided relative hypoperfusion, the more pronounced ipsilateral spatial attentional bias in patients with asymptomatic carotid stenosis. J Cereb Blood Flow Metab. Feb;40(2):314-327.

Kaczmarz S, Göttler J, Petr J, Hansen MB, Mouridsen K, Zimmer C, Hyder F, **Preibisch C**. (2021) Hemodynamic impairments within individual watershed areas in asymptomatic carotid artery stenosis by multimodal MRI. J Cereb Blood Flow Metab. 41(2):380-396.

Kaczmarz S, Griese V, **Preibisch C**, Kallmayer M, Helle M, Wustrow I, Petersen ET, Eckstein HH, Zimmer C, Sorg C, **Göttler J.** (2018) Increased variability of watershed areas in patients with high-grade carotid stenosis. Neuroradiology. 60(3):311-323.

Schmitzer L, Sollmann N, Kufer J, Kallmayer M, Eckstein HH, Zimmer C, **Preibisch C**, **Kaczmarz S, Göttler J.** (2021) Decreasing Spatial Variability of Individual Watershed Areas by Revascularization Therapy in Patients With High-Grade Carotid Artery Stenosis. J Magn Reson Imaging. 54(6):1878-1889.

Schneider SC, Archila-Meléndez ME, **Göttler J, Kaczmarz S**, Zott B, Priller J, Kallmayer M, Zimmer C, Sorg C, **Preibisch C**. (2022) Resting-state BOLD functional connectivity depends on the heterogeneity of capillary transit times in the human brain A combined lesion and simulation study about the influence of blood flow response timing. Neuroimage. 255:119208. doi: 10.1016/j.neuroimage.2022.119208.

Schneider SC, **Kaczmarz S, Göttler J,** Kufer J, Zott B, Priller J, Kallmayer M, Zimmer C, Sorg C, **Preibisch C**. (2023) Stronger influence of systemic than local hemodynamic-vascular factors on resting-state BOLD functional connectivity. Neuroimage. 281:120380. doi: 10.1016/j.neuroimage.2023.120380.