Magnetic Resonance Imaging to Investigate Cerebrovascular Dysfunction in Experimental Cerebral Malaria

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Abstract

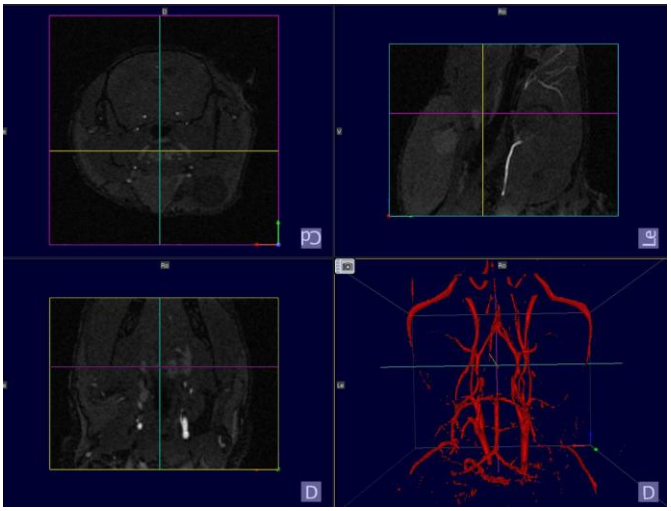
Cerebral malaria (CM) is a severe neurological complication of *Plasmodium falciparum* infection and a major contributor to malaria-related mortality worldwide. The disease is associated with cerebrovascular dysfunction, including vasoconstriction, microvascular obstruction, and impaired cerebral perfusion, leading to neurological damage.

Experimental cerebral malaria (ECM), induced in C57BL/6 mice by infection with *Plasmodium berghei* ANKA, reproduces vascular alterations seen in humans and is a model to investigate mechanisms and therapeutic strategies. Previous work shows that ECM is associated with marked cerebral vasoconstriction and reduced cerebral blood flow, and that restoration of cerebrovascular function can improve recovery and survival in antimalarial-treated mice. However, translational interpretation of these findings remains limited by the lack of quantitative vascular correlates comparable to those obtained in human studies.

Magnetic resonance imaging (MRI) provides a non-invasive approach to investigate cerebral hemodynamics in vivo. In particular, phase-contrast MRI (PC-MRI) enables quantitative measurement of blood flow velocity in individual vessels. In this study, ECM mice were compared with non-infected controls and imaged on a 7T MRI system at day 6 post infection, and after treatment, including early time points after therapy (1 h, 6 h, 24 h). Time-of-flight (TOF) angiography enabled visualization of the murine Circle of Willis and major cerebral arteries, including the middle cerebral artery (MCA), allowing placement of regions of interest for PC-MRI flow quantification.

PC-MRI was then applied to quantify blood flow in the MCA, a major cortical artery analogous to the human MCA. To our knowledge, this represents the first direct quantitative measurement of arterial cerebral blood flow in ECM using PC-MRI, enabling comparison with human data. We hypothesize that ECM mice will exhibit reduced MCA blood flow compared with healthy controls, reflecting cerebrovascular dysfunction associated with experimental cerebral malaria.

This approach provides quantitative, artery-specific measurements of cerebral blood flow and establishes a translational framework to better understand cerebrovascular dysfunction and support the development of vascular targeted therapies in cerebral malaria.



3D time-of-flight (TOF) MR angiography reconstruction of the murine Circle of Willis