

Poster presentation

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## Plasmodium berghei ANKA infection causes brain damage in mice resistant to cerebral malaria

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### Introduction

Severe malaria is a complex multisystem disorder including complications such as cerebral malaria, anemia, acidosis, jaundice, respiratory distress, renal insufficiency, coagulation anomalies and hyperparasitemia. We previously characterized the experimental cerebral syndrome using in vivo MRI and MRS techniques and proved the preponderant role of edema in the fatal outcome of experimental cerebral malaria (CM) [1]. The purpose of the current study was to examine the cerebral effects of *Plasmodium berghei* ANKA (PbA) infection in a mouse strain resistant to CM. We tested the hypothesis that PbA infection could elicit brain injury, despite the absence of experimental CM, and by mechanisms different from those involved in CM.

### Methods

Mice resistant to cerebral malaria (BALB/c strain) were infected with *Plasmodium berghei* ANKA and explored 8 and 15 days later by using in vivo brain MRI and MRS on a 4.7 T horizontal Bruker 47/30 AVANCE Biospec MR system (Bruker), except for angiography which was performed on a on a 11.75 T vertical Bruker AVANCE 500 WB wide-bore MR system. Besides angiography, the MRI protocol included, multi-slice T<sub>2</sub> and T<sub>2</sub>\*-weighted images as

well as diffusion and perfusion MRI of brain. T<sub>1</sub>-weighted images were acquired before and after the injection of Gd-DTPA. In vivo metabolic explorations included <sup>1</sup>H MRS (PRESS sequence with TE = 16 ms and TE = 135 ms) and <sup>31</sup>P MRS. <sup>1</sup>H-MRS of brain extracts was performed on a vertical Bruker AVANCE 500 WB wide-bore MR system operating at 11.75 T.

### Results

The infected mice did not show the lesional and metabolic hallmarks of cerebral malaria. However, we detected brain dysfunction related to anemia, parasite metabolism and hepatic damage in hyperparasitized mice (HP) when compared to controls and to infected mice with low parasitemia (NCM). Indeed, we found a significant increase in cerebral blood flow and a decline in cerebral choline in vivo. In vitro, we measured a reduction in glycerophosphocholine, in myo-inositol, and an increase in glutamine.

### Discussion

Increased blood flow is a compensatory mechanism allowing to temporarily maintaining oxygen supply to brain despite anemia. The brain choline decrease appears related to hyperparasitemia as choline consumption is

necessary for the parasite to proliferate. Finally, glutamine and myo-inositol anomalies together indicate hepatic encephalopathy, a finding in agreement with the liver damage detected in these mice by using biochemical and histological analyses. Our results highlight the vulnerability of brain to malaria infection even in the absence of cerebral malaria [2].

## References

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