

Magnetic Resonance Techniques Applied to the Study of Mouse Brain Complications in Sepsis

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Impact and Significance: Brain dysfunctions are often considered an important manifestation of sepsis pathogenesis⁽¹⁾, as long-term cognitive problems contribute to a severe reduction of quality of life. Additionally, acute impairment of brain function can influence hemodynamic, immune and endocrine functions in septic patients. However, the mechanism related to the development of sepsis-associated encephalopathy and a better characterization of this syndrome is lacking⁽²⁾. We propose that magnetic resonance imaging techniques can benefit the understanding of sepsis-induced neurological complications.

Methods: We used a 7T Bruker Biospin system for magnetic resonance imaging and spectroscopy to monitor the response of the mouse brain in the first 24 hours of a cecal ligation and puncture (CLP) model of sepsis. In particular, T₂-weighted imaging was used to assess gross morphologic changes that may occur during sepsis. Apparent diffusion coefficient (ADC) mapping was implemented in an attempt to bring additional *in vivo* data to the determination of the respective contributions of cytotoxic or vasogenic processes⁽³⁾ in sepsis-induced cerebral edema. Finally, proton spectroscopy was used to gather information on the relative amounts of choline and creatine containing metabolites and N-acetyl aspartate (NAA) in the septic mouse brain.

Results: The brains of the septic mice were observed before and 6 or 24 hours after surgery through magnetic resonance imaging of axial slices with T₂ weighting. Some animals developed the distinctive feature of a hyperintense area visible in the vicinity of the large vessels present at the base of the brain (figure 1). This phenotype was strongly correlated to animal death in the first 24 hours. The ADCs in the brain tissue of septic animals were compared with sham-operated animals. In general, septic animals were found to have a diffuse decrease in their ADC. Decreases in the ADC values in the cortical and thalamic areas had a noticeable correlation with absence of survival (figure 2). The T₂ hyperintense area seen in some animals was also found to be hyperdiffusive. Localized spectroscopy results revealed that septic animals experienced a decrease in NAA accompanied by relatively little changes in either creatine or choline.

Conclusions: Significant changes were detected in the metabolic profile, brain basal vasculature integrity and tissue ADC of septic animals. These endpoints add valuable insight into sepsis pathologic processes. More studies are required and may reveal a mechanistic link between oxidative stress and tissue and cellular damage.

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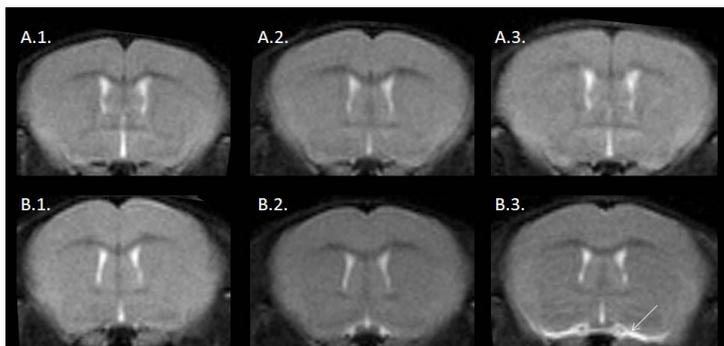


Figure 1: T₂-weighted axial MR images of sham-operated (A) and CLP-operated (B) mice brains. 1: baseline, 2: 6 hours post-surgery, 3: 24 hours post surgery. Accumulation of edematous fluid is visible as hyperintense area emanating from the blood vessels at the base of the brain (B.3., arrow).

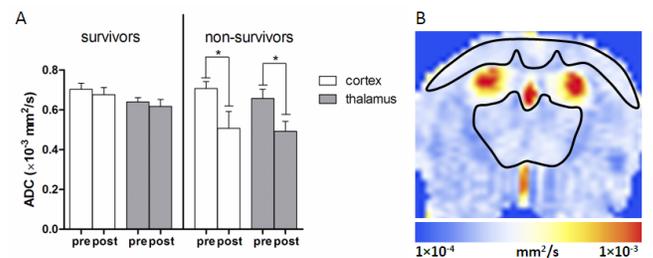


Figure 2: Apparent diffusion coefficients. A: Average apparent diffusion coefficients (ADC) measured in the cortex and thalamus of mice before ("pre") or 6 hours after CLP ("post"). Animals were segregated according to their survival to septic challenge. * indicates significance of student t-test to the P<0.05 level. B: Representative ADC map as calculated from diffusion-weighted axial images. The regions of interest for cortex and thalamus are represented.