Functional MRI (BOLD) at 3 Tesla in the brain of fetal sheep: the relationship to maternal blood oxygenation during hypoxia and methodological aspects

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Introduction: Intrauterine growth restriction (IUGR) is associated with an increased risk of perinatal mortality, morbidity, and impaired neurodevelopment (1-3). Thus methods to assess fetal tissue oxygenation would be desirable to detect the fetus at risk with the option to initiate precautionary or therapeutic measures (e.g. induction of preterm delivery). There is currently no non-invasive method available which provides direct information on fetal oxygenation. The blood oxygen level dependent (BOLD) effect, which measures changes in the deoxyhemoglobin concentration (4-5), provides a possible mechanism for non-invasive fetal oxygenation measurements. Although BOLD MRI is used primary to detect relatively small changes due to functional activation in adult brain, it can also be used to observe changes in other contexts. The aim of this study was to quantify the dependence of the fetal brain BOLD signal on maternal blood oxygenation ($MatSO_2$).

Methods: The brains of singleton fetuses of five anaesthetized sheep were subjected to single-shot-EPI sequences (TE 45 ms, FOV 180 mm, resolution 1.4 x 1.4 mm, matrix 80X80, slice thickness 5 mm, flip angle 90°) of BOLD measurements 3T MR-scanner (Intera Philips Medical Systems, Best, the Netherlands). $MatSO_2$ and maternal heart rate were recorded continuously. After a normoxic phase, hypoxia was induced by reduction of oxygen in the ventilated gas mixture (Fig. 1). ROI were placed in the cerebrum (Fig. 2) and in the cerebellum. BOLD SI% were calculated from mean values of steady state BOLD signal intensities (SI) of control and hypoxic plateaus:

$$\text{BOLD SI\%} = \frac{SI_{hypoxia}}{SI_{control}} \cdot 100.$$

BOLD SI% were correlated with $MatSO_2$, and linear regression analysis (slope) was performed.

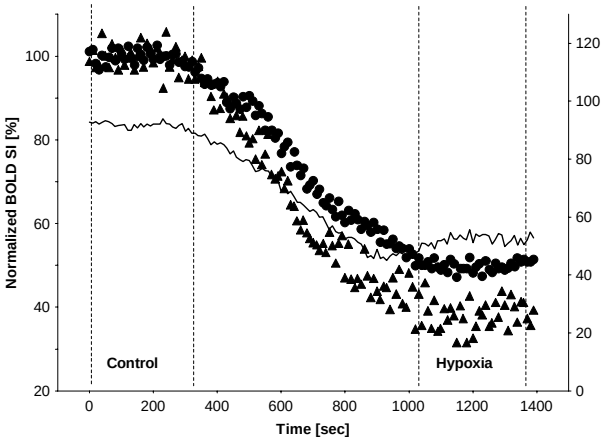

Figure 1: Scatterplot of a hypoxic phase with an initial control period and hypoxia after reduction of the $MatSO_2$. Time course of normalized BOLD signal intensities of the cerebrum (●), cerebellum (▲) and $MatSO_2$ (–).

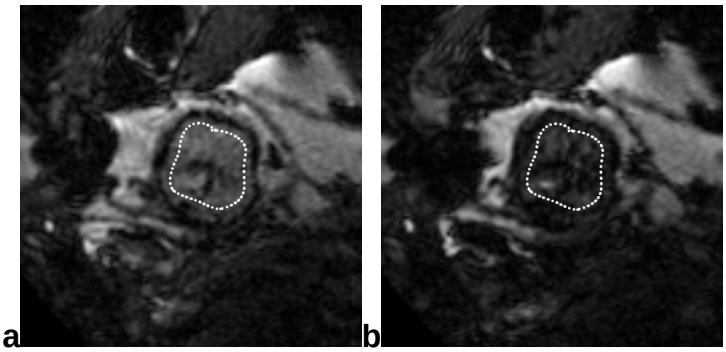

Figure 2 a, b: BOLD images of the fetal cerebrum in transversal orientation. The left image (a) is during the control period with 92% and the right image (b) during the hypoxic plateau with 53% maternal oxygen saturation. The signal decrease of 50% during hypoxia is clearly visible.

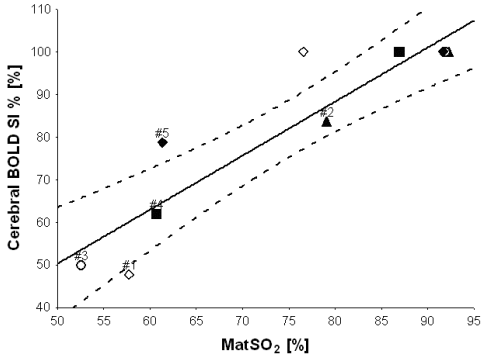

Figure 3: Linear regression of BOLD SI% for cerebrum with maternal oxygen saturation ($MatSO_2$). Mean values of the hypoxic plateaus are marked for each animal (animal #1: ◇, #2: ▲; #3: ○; #4: ■; #5: ◆). Dotted lines indicate the 95% confidence interval of the regression line.

Results: Control $MatSO_2$ was 88%O_2[80-96] [mean(95%CI)]. During hypoxia $MatSO_2$ was reduced to 62%[50-75] and fetal BOLD SI% decreased to 64%[44-85] in the cerebrum and significantly more distinct to 56%[32-80] in the cerebellum. Correlation and regression between BOLD SI% and $MatSO_2$ were: cerebrum: r^2=0.84;slope=1.27 SI%/$MatSO_2$[1.17-1.36] (Fig. 3); cerebellum: r^2=0.83; slope=1.54 [1.44-1.63].

Discussion and Conclusions: We conclude that fetal BOLD MRI is a possible tool to detect changes in the fetal brain tissue oxygenation following changes in maternal oxygen saturation. A reduction of the fetal BOLD signal intensity was observed with maternal hypoxia in all experiments, but there was a large variation of the regression coefficients with a difference between the cerebrum and cerebellum. It is to be expected that fetal BOLD signal intensities will be more closely associated with fetal oxygenation parameters than with maternal parameters. BOLD signal changes might also be influenced by blood volume changes in the fetal brain during hypoxia (6-7). In the future, animal studies should investigate whether and how reliable changes of fetal oxygenation can be predicted by functional MR imaging.

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References:

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