Effect of Anesthetic and Blood Oxygenation in Migraine Animal Model at 21.1 T

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Introduction

The anesthetic isoflurane is regularly used during MR imaging of animals and can dramatically affect the results (1). Here we report how the proton ultra high magnetic field MR signal reveals progressive rat brain de-oxygenation during anesthesia sessions, as well as during the initiation of migraine. MR experiments at ultra high magnetic field provide enhanced sensitivity to the minor adaptations in blood oxygenation through the deviations in magnetic susceptibility of blood. The resulting changes are proportional to the magnetic field and represent a direct consequence of shift in the oxygen content of hemoglobin, a major component of red blood cells (Fig. 1).

Experimental

For *in vivo* experiments, rats (n=3) were anesthetized with 2 % isoflurane. Nitroglycerine (NG, 10 mg/Kg) was IP administered 30 min after the start of MR measurements. NG injection was done remotely without repositioning the animal. The resonance frequency of proton MR signal from rat head was detected each minute by single pulse sequence. Experiments were performed using Bruker Avance III MRI system (PV5.1 software) and 21.1 T magnet (^{1}H freq = 900 MHz), designed and constructed at NHMFL, Tallahassee, Florida.

Results and Discussion

Under anesthesia, oxygenation of the rat brain gradually decreases. During this time, blood becomes more paramagnetic (Fig. 1) and, consequently, proton resonance frequency steadily increases with the rate of 0.61 ± 0.02 Hz/min (Fig. 2). Induction of migraine by exposure to nitroglycerine produces a sharp decrease in oxygenation detectable with an exponential rate of MR frequency increase ~5 Hz/min. The level of de-oxygenation is reaching its maximum plato in ~10 minutes.

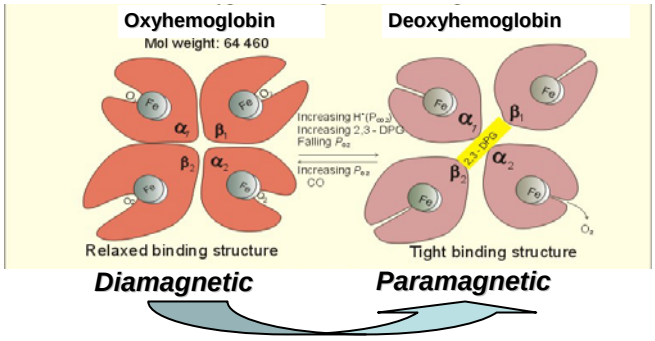

Fig. 1. Decline of hemoglobin oxygenation in red blood cells makes it paramagnetic and, thus, detectable by magnetic resonance.

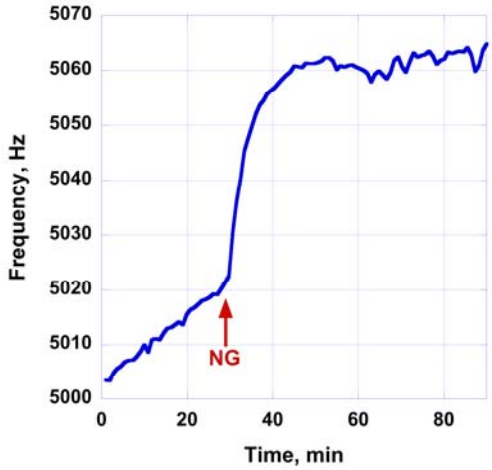

Fig. 2. Time course of MR signal frequency from rat head as a result of blood de-oxygenation due to exposure to anesthetic (0 – 30 min) and initiation of migraine (NG).

Conclusions

Ultra high magnetic fields provide enhanced sensitivity to alterations in brain functioning. The long anesthetic exposure or major interventions, as migraine, may lead to extreme changes in brain oxygenation and energy metabolism, which is detectable as a saturation of the MR response. Altogether, non-invasive global oximetry may be helpful for drug development and can increase success rates in the discovery of new medicine.

Acknowledgements

The study was supported by NIH grant R01NS072497 and performed at NHMFL (Tallahassee) supported by National Science Foundation Cooperative Agreement No. DMR-1157490, the State of Florida, and the U.S. Department of Energy.

References

[1] Boretius, S., *et al*., NeuroImage, **69**, 244-255 (2013).