Evaluation of a new quantitative BOLD approach to map local blood oxygen saturation in healthy rat

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Introduction

Quantitative BOLD (Blood Oxygen Level Dependent) has been proposed to map brain oxygenation levels using MRI [1]. This approach yields tissular SO2 (oxygen saturation) estimates, i.e. a mean SO2 across the microvascular network in the MRI voxel. To improve the accuracy and the spatial resolution of SO2MR maps, an approach which combines a steady-state Blood Volume fraction (BVf) measurement scheme, B0 and T2 mapping techniques, and a simpler mathematical model has recently been proposed [2]. In this study, we evaluate the proposed acquisition scheme in healthy rats while varying the inspired oxygen fraction and using a complete physiological monitoring.

Materials and Methods

Experiments were performed at 4.7 T on a Bruker Avance 3 console using volume/surface cross coil configuration.

Study 1. Wistar rats (n=12), anaesthetized using isoflurane, mechanically ventilated, were equipped with catheters in the femoral vein and in the superior longitudinal sinus. By varying the inspired oxygen fraction (FiO2) in N_2, rats were submitted to hyperoxia (PaO2= 351mmHg), normoxia (PaO2= 150mmHg), moderate (PaO2= 65mmHg) and severe (PaO2= 40mmHg) hypoxia. For each FiO2 level, blood samples were analyzed.

Study 2. Wistar rats (n=17), ventilated as above, were submitted to the same PaO2 levels as in Study 1. For each PaO2 level, SO2MR was mapped at 4.7T and blood samples from the femoral vein and from the femoral artery were analyzed. All data were acquired with the same geometry (7 contiguous, 1mm-thick slices, FOV=30x30mm; matrix=64x64), except for B0 mapping (3D GE sequence, FOV= 30x30x8mm, matrix= 128x128x40, TR= 100ms TEs= 4 and 12ms). Acquisition protocol was: brain shimming, B_0 mapping, T2 mapping (TR= 1500ms, 20 spin-echoes, ΔTE= 12ms), T2* mapping (TR=1500ms, 30 gradient echoes, ΔTE=2.5ms), Blood Volume fraction (BVf) mapping (multiple gradient-echoes TR= 6000ms; ΔTE= 3ms, before and 3min after injection of 200µmol/kg of iron oxide particles (P904, Guerbet, France)). Nominal spatial resolution was 470x470x1000 µm3. For one inspired oxygen fraction, the MR session lasted less than 30min. BVf was computed from the change in T2* before and after injection of iron oxide particles (The change in blood magnetic susceptibility induced by the presence of these particles in the vasculature was set to 0.28ppm [3]). SO2MR was computed from the difference between 1/T2 and 1/T2*, measured prior to the injection of iron oxide particles. To compute SO2MR, we used a hematocrit of 0.42 and a difference in magnetic susceptibility between fully oxygenated and fully deoxygenated hemoglobin of ΔX_0= 0.264ppm. Eventually, the mean SO2MR was measured in a large cortical region of interest.

Results

For both studies, PaCO2, hemoglobin levels, and arterial pressure were similar and stable across PaO2 levels (not shown).

Study 1 yielded a linear relation (R^2>0.95) between SvO2 (SO2 in the femoral vein) and SsO2 (SO2 in the superior longitudinal sinus) (Fig 2a).

Study 2. SvO2 values obtained in this study were converted into SsO2 values using the linear relation found in Study 1. BVf was stable across PaO2 levels (not shown). A linear relation was obtained between SO2MR and SvO2 (R^2=0.843, Fig 2b) as well as between SO2MR and SsO2 (R^2=0.840). A Bland-Altman analysis indicated that, although all values are within the ±2 standard deviation range, SO2MR slightly overestimates SsO2 in severe hypoxic condition and slightly underestimates SsO2 in hyperoxic condition (Fig. 2c). Results also lead to SO2MR=0.65SaO2+0.24SvO2. This relation is in good agreement with the one obtained using Near InfraRed Spectrometry in the piglet brain (SO2NIRS =0.75SvO2+0.24, when considering SaO2=95%) [3].

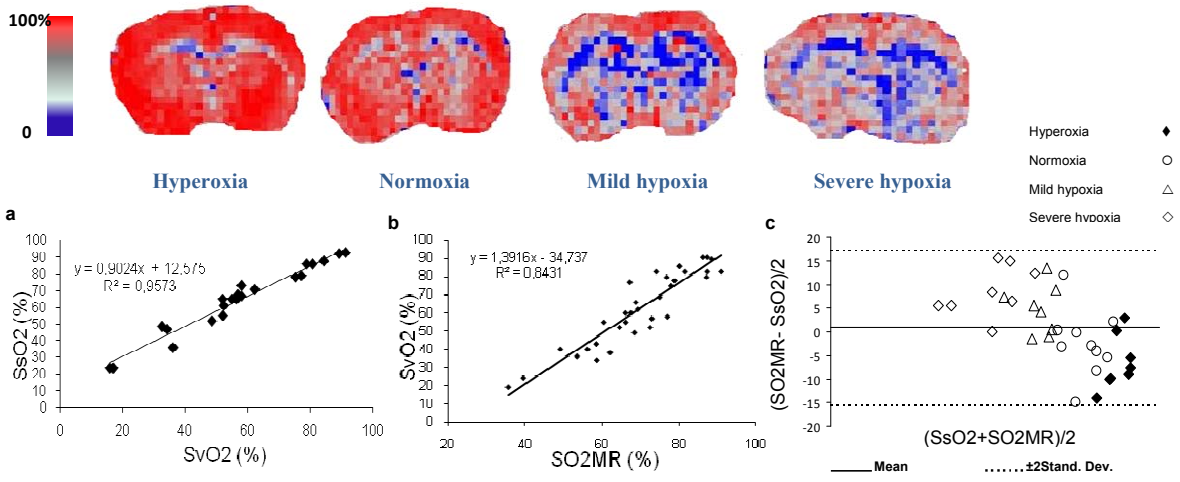

Figure 1. Typical quantitative SO2MR maps obtained in the rat brain at 4.7T. One typical map per inspired FiO2 level is displayed.

Figure 2. (a) Correlation between SsO2 and SvO2. **(b)** Correlation between SvO2 and $SO2_{MR}$ measured in a cortical ROI. **(c)** Bland-Altmann graph of $SO2_{MR}$ versus SsO2.

Discussion/Conclusion

Values of SO2MR obtained while breathing air under mechanical ventilation are similar to those reported by [1] and are consistent with tissular SO2 measured by NIRS in the brain [4]. In gray matter, the variations in SO2MR are in excellent agreement with the SsO2 or the SvO2. In the corpus callosum, SO2MR estimate is not accurate. This could be ascribed to the specific properties of the local microvascular network (e.g. preferential orientation) or of the tissue microstructure (e.g. heterogeneous magnetic susceptibility) [5].

This study shows that microvascular characteristics (blood volume fraction) and tissular blood oxygen saturation can be collected within a single MR exam, with good spatial resolutions. The characterization of tissular blood oxygen saturation is a very promising tool to characterize and monitor brain pathologies.

References

(1) He et al. MRM 2007 (2) Christen et al. NMR in biomed, In Press. (3) Valable et al. NMR in biomed 2008 (4) Hueber et al. Phys Med Biol 2001. (5) Zhong et al. Neuroimage 2008.