Effect of hematocrit on MR estimates of BVf, VSI and local blood oxygen saturation. An in vivo study.

T. Christen[1], B. Lemasson[1], N. Pannetier[1], R. Farion[1], C. Segebarth[1], C. Remy[1], and E. L. Barbier[1]
[1]INSERM U836, Grenoble, France

Introduction

Using MRI and a contrast agent (CA), one can assess numerous characteristics of the microvasculaure: Blood Volume fraction (BVf), Vessel Size Index (VSI), or local SO_2 (lSO_2) [1] [2]. These MRI methods rely on infinite cylinders to model the vessels that contain the CA. In the vessel, one assumes that the CA is homogeneously distributed [3]. The contribution of red blood cells is at best taken into account using a constant scaling factor (hematocrit). There is however no evidence that red blood cells affect MRI estimates linearly. To evaluate the contributon of hematocrit to MRI estimates of BVf, VSI, and lSO_2, hematocrit was experimentally modified in rats. MRI estimates were compared to values obtained from quantitative histology or blood gas analysis.

Material and methods

Male Wistar rats (n=17) were anaesthetized using isoflurane (2%). The femoral vein and artery were equipped with a catheter. Three groups of animal were studied:

- Control group (n=8): rats were used as control.
- Hemodilution group (n=5): Isovolemic hemodilution was produced by the withdrawal (1h prior MRI) of 5 mL of arterial blood (rate of 1 mL/min), which were concurrentely replaced by the same volume of serum albumin injected at the same rate.
- Hypoxia group (n=6): For 14 consecutive days before MR session, the rats were housed in custom-made hypoxia chamber and submitted to change in inspired O_2 fraction (FiO_2) with a period of 1 min (40s at FiO_2=5% followed by 20s at FiO_2=21%) and repeated for 8 h during daytime [4].

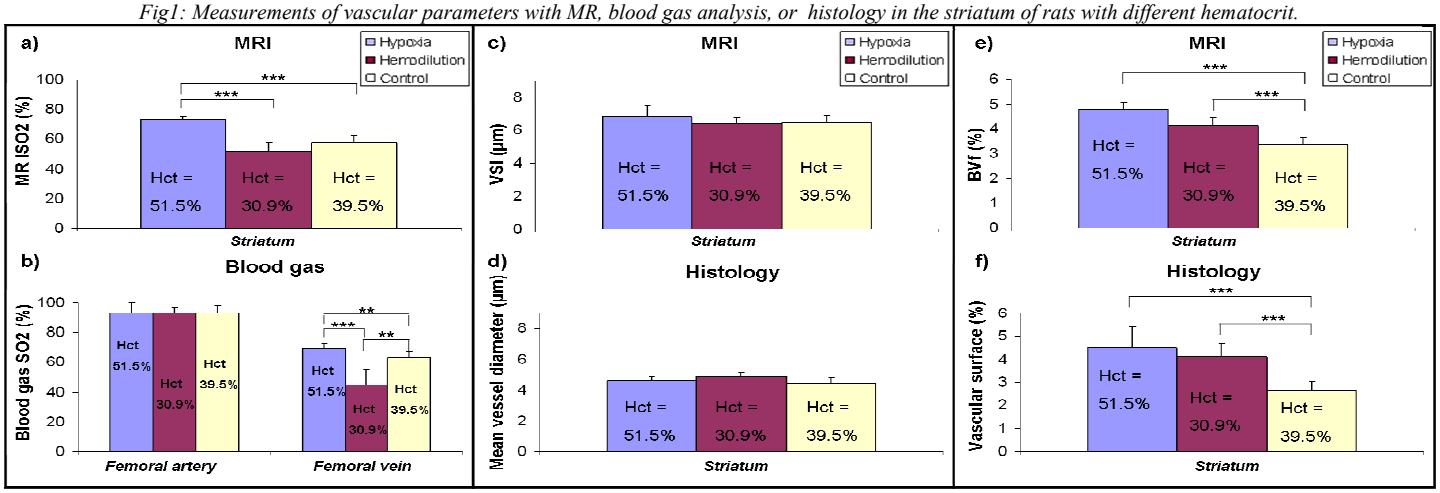
MR imaging was performed at 4.7T on a Bruker Avance 3 console using volume/surface cross coil configuration. All data were acquired with the same geometry (7 contiguous, 1mm-thick slices, FOV=30x30mm; matrix=128x128), except for B_0 mapping (3D GE sequence, FOV=30x30mm, matrix=256x256x40, TR=100ms TEs=4 and 12ms). Acquisition protocol was: brain shimming, B_0 mapping, T_2 mapping (TR=1500ms, 20 spin-echoes, ΔTE=12ms), multiple gradient-echoes spin-echo sequence, before and 3min after injection of 200µmol/kg of iron oxide particles (USPIO: Combidex®/Sinerem®, Amag Pharmaceuticals/Guerbet): TR=6000ms; ΔTEGE=3ms; TESE=60ms). BVf/VSI were estimated using formula in [1]. Local SO_2 was estimated using a quantitative bold approach similar to that described in [2]. The entire MRI protocol lasted 1h15 per animal.

At the end of the imaging session, analysis of venous and arterial blood oxygen saturations of haemoglobin (femoral SvO_2, SaO_2) and hematocrit (Hct) were performed in blood samples of less than 0.1 ml (ABL 510, Radiometer, Copenhagen, Denmark). Animals were then sacrificed, brains were collected and cryo-preserved for collagen IV immunostaining. Vascular surface and mean diameter of vessels were estimated using ImageJ as described in [5].

Data, averaged across rats in each group, are presented for a region of interest (striatum). Student t-tests were used to assess differences (**:p<0.01, ***:p<0.001).

Results

Fig1: Measurements of vascular parameters with MR, blood gas analysis, or histology in the striatum of rats with different hematocrit.



Hct measured in the femoral vein varied from 39.5% in the control group to 30.9% and 51.5% in the hemodilution and hypoxia groups respectively. These values have been reported on each graph of Fig1**.** The local blood oxygen saturation estimated by MR decreased in the hemodilution group and increased in the hypoxia group (consistent with stable tissue oxygenation level) (Fig1a). This trend was also found in blood gas estimates of SvO_2 (Fig1b). The SaO_2 remains stable between groups. Neither VSI assessed by MR nor mean vessel diameter assessed by histology were affected by hematocrit variations (Fig1c,d). BVf were significantly higher in the group submitted to intermittent hypoxia and in the hemodilution group than in the control group (Fig1e). These observations have also been noticed in the histological estimates of vascular surface (Fig1f).

Conclusion

Using either hypoxia or hemodilution, we induced significant hematocrit changes in healthy rats. The physiological perturbations on BVf, VSI and lSO_2 have been measured with MR. Despite changes in hematocrit, MRI and biology remain correlated. While the effect of hematocrit on MR estimates seems to be linear, the effect of hematocrit on the absolute values obtained by MR remain to be quantified. It is worth to notice that VSI seems to be an estimate independent of hematocrit.

References

[1] I Troprès et al, Magn Reson Med, 2001. [2] T Christen, ISMRM09, #213. [3] Yablonskiy and Haacke, Magn Reson Med, 1994. [4] Joyeux-Faure et al, J Apl Physiol, 2005. [5] S Valable et al, NMR Biomed, 2008.