Measuring the Effect of Hyperoxia and Hypercapnia on R2* and the Balanced SSFP Signal at 3T

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Introduction

The effects of hyperoxia and hypercapnia (i.e. elevated levels of O_2 and CO_2) on the MRI signal are of major diagnostic interest in oncology as they give insight into a wide range of tumor parameters, e.g. the vascular growth, hemodynamic changes in the response to treatments, vasoreactivity, vascular function and vessel maturation [1,2]. The effect of elevated O_2 and CO_2 levels on tissue relaxation rates R2*(=1/T2*) or on R2*-weighted images has been comprehensively discussed in literature [1-5]. Recently, it was demonstrated that balanced SSFP imaging is capable of detecting changes in blood-oxygen levels, in both, vessel and muscle tissue, while providing superior image quality and shorter scan durations [6,7]. To our knowledge, the sensitivity of the balanced SSFP (bSSFP) signal to changing O_2 or CO_2 levels has not yet been investigated. Furthermore, while R2* is predominantly affected by the decreasing amount of deoxygenated blood during inhalation of O_2 through the BOLD effect, the bSSFP contrast dependence on R2 and R1 suggests the use of bSSFP imaging to identify regions of changing oxygenation (R2) as well as increased inflow of unsaturated spins in the presence of elevated flow (apparent R1). This work compares the MR response of R2* and of the bSSFP signal to hyperoxia and hypercapnia in terms of time course and sensitivity, using respiratory challenges in 5 healthy volunteers during MR imaging.

Methods

Scans: All imaging was performed on a 3T clinical scanner (Achieva 3.0T, Philips Medical Systems, Best) using a transmit/receive head-coil to measure a transverse slice through the brain above the ventricle of 5 volunteers, after informed consent was obtained. The effects of hypercapnia and hyperoxia on the MRI signal were investigated in two separate experiments resulting in four dynamic 10min scans (2xbSSFP, 2xR2*) with periods of 3/4/3min of breathing air/gas/air. Room air, Carbogen (95%O_2/5%CO_2) and a CO_2/air gas mixture (5%CO_2/25%O_2/70%N_2) were supplied through a face mask using a demand valve (Draeger Oxidem 3000). The O_2 and CO_2 contents of the in- and exhaled gas mixture were continuously monitored (Invivo Omni-Trak Magnitude 3150/3155) to check tightness of the breathing system. Prior to this study, the bSSFP scan parameters were optimized with regard to sensitivity, banding artifacts and SAR using two samples of venous and fully oxygenated blood. Scan parameters: bSSFP: slice = 5mm, TR/TE = 12/6 ms, flip angle = 45°, 1.4s/frame, and alternating RF pulses. R2*: multi-gradient echo sequence with 12 echoes, spaced by 7.2ms, slice = 5mm, TR=97ms, flip angle = 25°, 2.1s/frame. **Postprocessing**: After motion correction, the dynamic change of R2*, i.e. ΔR2*, was obtained from the ratio of the signal decays during respiratory challenge and baseline [8] to correct for large scale susceptibilities, after the exponential decays were corrected for the effect of apparent differences in T1. The time series of ΔR2* and the relative change of the bSSFP signal were analyzed pixel-wise: periods of baseline and respiratory challenge were compared for significant positive (ΔS_{bSSFP}) or negative (ΔR2*) differences (student's t-test, $p<0.001$) to obtain the regions of response. A mean response function was obtained by averaging the response functions of all pixels in the regions of response.

Results

Fig. 1 shows the maps of ΔR2* and of the relative change in the bSSFP signal as colored overlays in the regions of response of a typical subject. The elevated oxygen supply predominantly affects the cortex and the venous vasculature in the sulci and is less noticeable in white matter regions. Furthermore, the mean response functions of all volunteers are plotted (black dots) with their average (red solid) according to all four experiments. The sensitivity of the response is obtained as the mean signal response during respiratory challenge (Note, that the negative R2* response is plotted for better comparability to the ΔS_{bSSFP}). During hyperoxia R2* decreased by $\Delta R2^* = -2.6 \pm 0.1\ s^{-1}$ (≈-13.2% for an average R2* of $20s^{-1}$), whereas the SSFP signal increased by only $\Delta S_{bSSFP} = 5.3 \pm 0.2$ %. The ΔR2* sensitivity to hypercapnia was only slightly higher than that of the bSSFP signal: $\Delta R2^* = -1.6 \pm 0.1\ s^{-1}$ (-7.9%), $\Delta S_{bSSFP} = +5.0 \pm 0.4$ %.

Discussion and Conclusion

It is well known that in healthy volunteers the predominant effect of breathing hypercapnic gas mixtures is in the increase in the cerebral blood flow (CBF, R1↑↑), which slightly decreases the amount of deoxygenated blood (R2*↓). During inhalation of hyperoxic hypercapnic gas mixtures like Carbogen, the oxygen content counteracts the CO_2-induced increase in the CBF. Those gas mixtures predominantly increase the tissue oxygenation (R2*↓↓) accompanied by a weaker increase in CBF compared with hypercapnia (R1↑). Quantification of ΔR2* with a multi-echo sequence extracts the effect of the changing oxygenation and eliminates the apparent R1 increase that occurs due to the faster inflow of unsaturated spins. ΔR2* was shown to be a very sensitive marker for the changing oxygenation with double sensitivity during hyperoxia than during hypercapnia. Qualitatively, the mean ΔR2* response functions over all responding regions show a similar time course during hypercapnia and hyperoxia. In summary, the R2* response to hypercapnia and hyperoxia is in good agreement with the effects reported by literature [3-5]. The bSSFP signal shows a comparable sensitivity to both respiratory challenges in similar anatomic regions. It thus appears rather insensitive to the elevated oxygen level during hyperoxia. However, interpretation of the bSSFP results is more complex due to the confounding effects of oxygenation and flow that modulate the bSSFP signal through changes in R2 and R1, respectively. We demonstrated that ΔR2* and the bSSFP signal show comparable sensitivity to hypercapnia. With this and the sensitivity of the bSSFP signal to the inflow of unsaturated spins, our study further implies that the bSSFP signal might be suitable to detect hemodynamics changes in response to elevated flow, rather than to act as a pure marker for oxygenation. Further volunteer as well as oncologic studies are required to validate these findings.

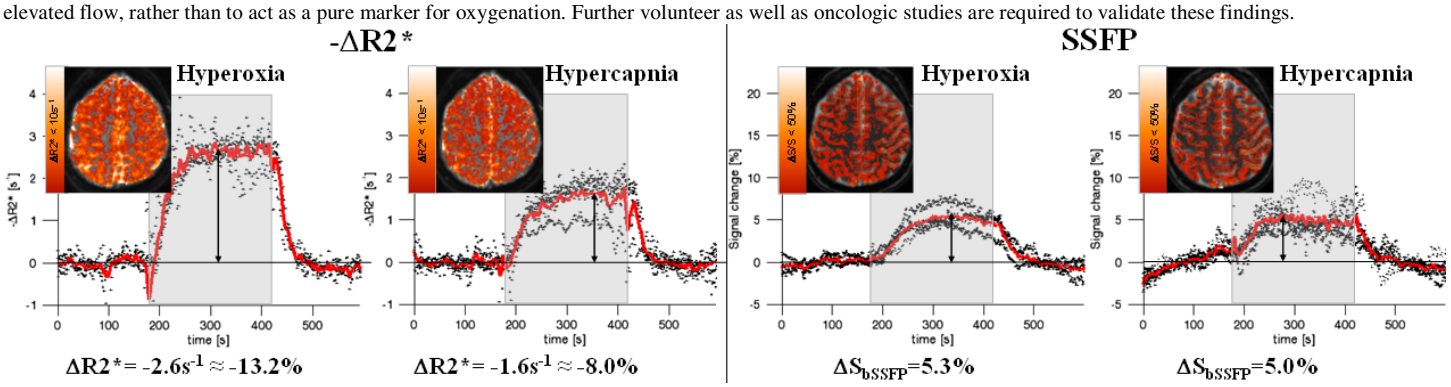

***Figure 1.** : The mean response functions for all volunteers (black dots) and the respective average response function (red solid) for ΔR2* and the relative bSSFP signal change during hyperoxia and hypercapnia. The ΔR2* and bSSFP signal changes are depicted as colored overlays in the areas of significant response for a typical subject. See text for further details.*

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