The effect of vasoactive drugs on the BOLD signal change: Implications for neuropharmacological fMRI

K. Scheffler[1], E. Seifritz[2], J. Hennig[1], E.W. Radü[3], D. Bilecen[3]

[1]Medical Physics, University of Freiburg, Germany

[2]Department of Psychiatry and [3]Diagnostic Radiology, University of Basel, Switzerland

Introduction

The T_2^*–weighted signal change in response to neuronal activation depends on the change in local blood oxygenation, blood volume (rCBV) and blood flow (rCBF). A pathologically or pharmacologically induced change of these parameters can reduce or increase the BOLD signal change [1,2]. The aim of this study was to calculate the relationship between the BOLD signal change and the baseline rCBF. The resulting Flow–BOLD–Dependence (FBD) curve was used to model the reduced BOLD signal change caused by the vasodilating effects of ethanol [3].

BOLD signal change and blood flow

The MR–signal change for a gradient echo experiment with echo time TE is given by

$$S(TE) \sim \exp(-TE(\frac{1}{T_2} + R_2^*)). \quad (1)$$

The relaxivity R_2^* is a function of rCBV and the fraction Y of oxygenated blood within the imaging voxel,

$$R_2^* = \frac{4}{3}\pi\gamma\Delta\chi_B B_0(1-Y)rCBV. \quad (2)$$

$\Delta\chi_B$ is the susceptibility difference between deoxygenated and oxygenated blood, and B_0 the main magnetic field [4]. A pharmacologically induced increase of rCBF will increase the resting oxygenation level and the resting blood volume. The relation between rCBF and oxygenation Y is governed by Fick's law [5]

$$CMRO_2 = H(1-Y)rCBF \quad (3)$$

where $CMRO_2$ is the cerebral metabolic rate of oxygen. Blood volume and blood flow are related via [6]

$$\left(\frac{rCBV}{rCBV_{\text{rest}}}\right)^{0.38} = \frac{rCBF}{rCBF_{\text{rest}}}. \quad (4)$$

According to equation (3) and (4), an increase in blood flow will thus increase the baseline of the BOLD signal due to an increased level of oxygenated blood. This relation has also been observed experimentally by Bruhn [2] who used intravenous acetazolamide as vasodilator. As a result, the BOLD signal change in response to neuronal stimulation will be reduced compared to the BOLD signal change without pharmacologically induced blood flow increase. The dependence of the BOLD signal change induced by neuronal activation as a function of an overall increase of the baseline blood flow can be calculated by means of eqs. (2–4), and is shown in Fig. 1.

Experiments

The effects of ethanol on acoustically stimulated BOLD response in healthy subjects were examined and compared to the calculated FBD curve (Fig. 1). The BOLD signal change reaching 3% for the placebo experiment was reduced by about 20% after ethanol intake as depicted in Fig. 2. Applied to the FBD curve shown in Fig. 1, the vasodilation–induced reduction in BOLD signal change corresponds to a 15% increase in baseline rCBF. The numbers given in literature on perfusion increase after ethanol are, however, only about 10% [7].

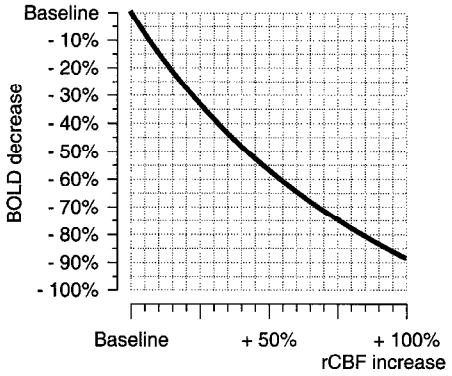

Fig. 1: FBD curve: dependence of BOLD signal change and baseline rCBF change. An increase in baseline blood flow reduces the BOLD signal change.

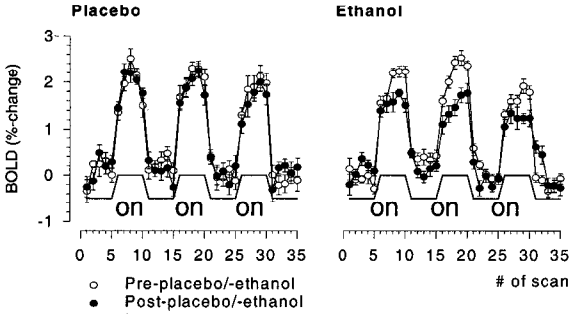

Fig. 2: Vasodilatation induced by ethanol reduces BOLD signal change by about 20%.

Conclusion

The influence of drugs that change the baseline rCBF such as anesthetics, CO_2, acetazolamide, or ethanol on the BOLD signal change was described by the FBD curve and compared to experimental results. In case of ethanol, the signal decrease was greater than that induced by pure vasodilatation. The data thus suggest that the reduction of BOLD signal change after ethanol reflects some suppression of neuronal activity. Although our model needs empirical validation, its cautious implementation appears to be helpful if fMRI is used in combination with vasoactive drugs.

References

[1] Davis TL et al. *PNAS.* **95**, 1834, 1998.

[2] Bruhn H et al. *Cereb. Blood Flow Methab.* **14**, 742, 1994.

[3] Seifritz E., et al. *Psych. Res. Neuroimaging Sec.* accepted 1999.

[4] Yablonskiy D.A. et al. *Magn. Reson. Med.* **32**, 749, 1994.

[5] Schwarzbauer C et al. *Magn. Reson. Med.* **41**, 537, 1999.

[6] Grupp RL et al. *Stroke* **5**, 630, 1974.

[7] Mathew RJ et al. *Stroke* **17**, 1156, 1986.