The confounding effects of O_2 on CO_2-induced cerebrovascular reactivity as measured with BOLD MRI

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Introduction:

Cerebrovascular reactivity (CVR) is defined as the changes in cerebral blood flow (CBF) in response to changes in end-tidal partial pressures of CO_2 ($P_{ET}CO_2$). The magnitude of CO_2-induced change in CBF is inferred from corresponding changes in predominantly venous deoxyhemoglobin as measured by BOLD MRI.[1,2] However, the arterial blood oxygen content also affects the deoxyhemoglobin[3] independently of changes in local CBF. The net effect of changes in arterial blood O_2 content and changes in CBF on BOLD signal are unclear. We assessed the effect of changes in end-tidal partial pressures of O_2 ($P_{ET}O_2$) on BOLD signal during the measurement of CO_2-induced CVR.

Methods:

The BOLD response to rapid cyclic changes in $P_{ET}CO_2$ and $P_{ET}O_2$ was mapped in 4 healthy male volunteers using a 3T magnet. $P_{ET}CO_2$ was cycled between 30 and 40 mmHg and $P_{ET}O_2$ was cycled between 100 and 400 mmHg during a 4 min period. The CO_2 and the O_2 cycles were 1 minute out of phase (figure 1) to obtain all combinations of $P_{ET}CO_2$ and $P_{ET}O_2$. A total of 3 cycles were repeated in each subject per session. $P_{ET}O_2$, $P_{ET}CO_2$ and BOLD signal were monitored continuously throughout the session.

Results:

Step changes in $P_{ET}CO_2$ were mirrored by changes in BOLD signal. During high CO_2 stimulus, increases in $P_{ET}O_2$ resulted in an additional increase in BOLD signal beyond that due to CO_2 alone. Data from a representative subject are shown in Figures 1 and 2 below.

Discussions:

Previous studies examining CO_2-induced CVR have ignored the effects of O_2 on BOLD signal intensity. In our study, during high CO_2 stimulus, the apparent increase in BOLD signal following onset of hyperoxia is unlikely to be due to a further increase in blood flow, as hyperoxia classically causes vasoconstriction.[4] A more likely explanation for the increase in BOLD signal with hyperoxia is that a greater initial oxygen content in the arterial blood results in an increased residual oxygen content of the venous blood (assuming unchanged oxygen extraction), resulting in less deoxyhemoglobin. The apparent increase in flow seen during hypercapnic hyperoxia is an epiphenomenon and may mask the vasoconstrictor response to O_2.

Conclusions:

Changes in $P_{ET}O_2$ produce artifactual changes in BOLD signal, probably by affecting the fraction of O_2 dissolved in the plasma. Measurement of CO_2-induced CVR with BOLD therefore requires that the O_2 concentration be kept constant.

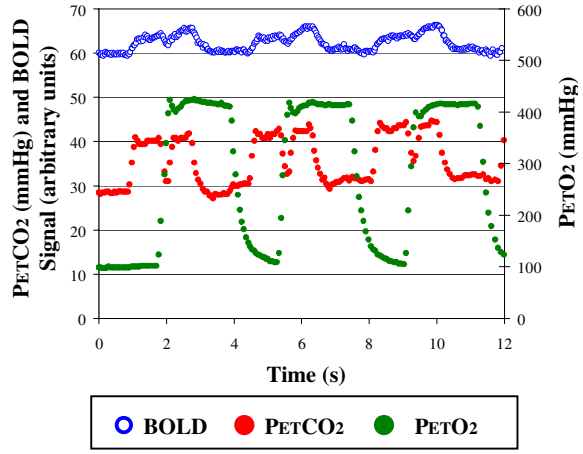

Figure 1 – $PetCO_2$, $PetO_2$ and BOLD data from a representative subject.

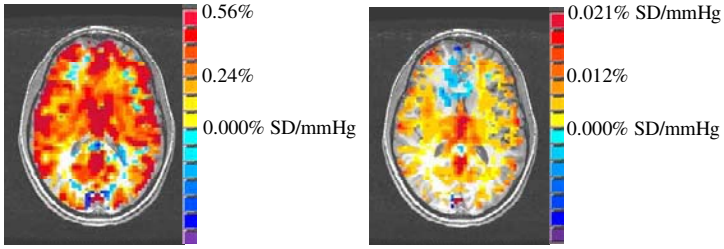

Figure 2 – BOLD CVR maps showing localized reactivity to CO_2 (left) and O_2 (right).

References

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