# Oxygen Saturation Changes During Hyperoxic and Hypercapnic Stimuli Measured by Near Infrared Spectroscopy (NIRS) Cerebral Oximetry

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## Purpose

Respiratory stimuli are commonly used in calibrated fMRI techniques. The most commonly used forms are mild hypercapnia and hyperoxia. It is usually assumed that these challenges have negligible impact on oxygen metabolism, although there is some debate about this.[1] However the Davis model[2,3] is reliant on certain assumptions about the effects they have on CBF, and $SvO_2$, and it implicitly assumes that the arterial oxygen saturation ($SaO_2$) is 1.0. In general, it is assumed that hyperoxia has a negligible effect on $SaO_2$, but a pronounced effect on the partial pressure ($PaO_2$), while hypercapnia has no effect on either $SaO_2$ or $PaO_2$ and only affects the CBF and thereby the venous saturation ($SvO_2$). Near-infrared spectroscopy (NIRS) is capable of non-invasively measuring the relative concentrations of oxygenated and deoxygenated haemoglobin via a term called the tissue saturation ($StO_2$), and in a completely independent approach to MRI. $StO_2$ is effectively the oxy:deoxyhaemoglobin ratio averaged over the total blood volume. We have tested the impact of a simple dual-gas respiratory paradigm on arterial and tissue saturations.

## Methods & Results

Ten healthy subjects were recruited (6 male, mean age 24±3 years) and monitored during a 16.5 minute hypercapnia/hyperoxia paradigm identical to that used in calibrated fMRI experiments.[4] A 2-channel NIRS cerebral oximeter (Casmed Fore-Sight, CT, USA) was used to measure tissue saturation in the frontal lobes at 2 second intervals, by placing sensors on the foreheads of the supine subjects. A finger-clip Nonin 7500FO pulse oximeter (Nonin, MN, USA) was used to acquire simultaneous arterial saturation values, which were sampled with a Powerlab data acquisition module (ADInstruments, Dunedin, New Zealand). The gases were delivered and sampled through a 2-tube nasal cannula and monitored by an ADInstruments Gas Analyser connected to the Powerlab. The gas paradigm consisted of 2 mins hypercapnia/1 min air/3 mins hyperoxia/2 mins air, repeated twice, and preceded by 40secs air (see Fig. 2). All gases were delivered at a flow rate of 8 l/min. Gas mixtures consisted of medical air (21% $O_2$, balance nitrogen); 10% $CO_2$ for hypercapnia (with 21% $O_2$ and balance nitrogen), and 100% $O_2$ for hyperoxia; resulting in an inspired $CO_2$ fraction of ~ 4%; and inspired $O_2$ fraction of ~ 50% due to mixing with room air.

Data were averaged across all subjects at each time point. NIRS readings ($StO_2$) were temporally smoothed (25sec kernel) and then converted into venous oxygen saturation ($SvO_2$) using the $SaO_2$ measured by the pulseox as follows: $SvO_2 = (StO_2 - 0.3 \times SaO_2)/0.7$. This expression assumes that the arterial and venous compartments occupy 30% and 70% of the blood pool respectively, as is commonly assumed by NIRS manufacturers.[5] Arterial saturation ($SaO_2$) values were similarly averaged and smoothed and are shown in red in Fig. 1. The group averaged $StO_2$ time-course also showed the effect of the gas paradigm, independently of the $SaO_2$ measures. Fig. 2 shows the end-tidal derived $SaO_2$ from a *single* representative subject, and has not been averaged or smoothed. Fig. 2 also shows the timings of the gas paradigm. The data shown in Fig. 2 needs to be treated with caution, as without an accurately calibrated gas monitor, and exact knowledge of the atmospheric pressure, the alveolar–arterial (A-a) gradient and the haemoglobin concentration of the individual subject this cannot be calculated with sufficient accuracy. However it clearly demonstrates that the trends seen in the NIRS and pulseox data are also present in the end-tidal trace.

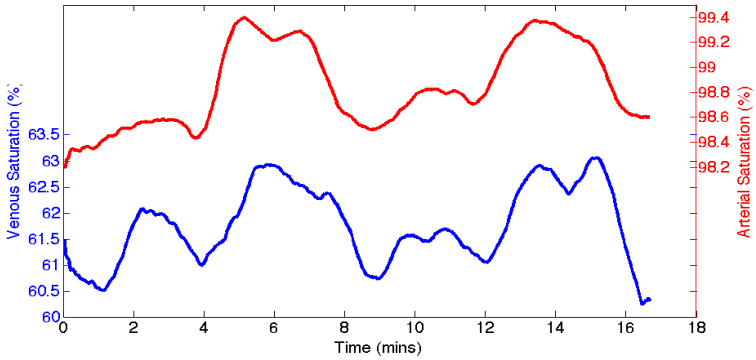


**Fig. 1**. Group mean time courses of the arterial and venous oxygen saturations from the pulseox (red) and NIRS (blue).

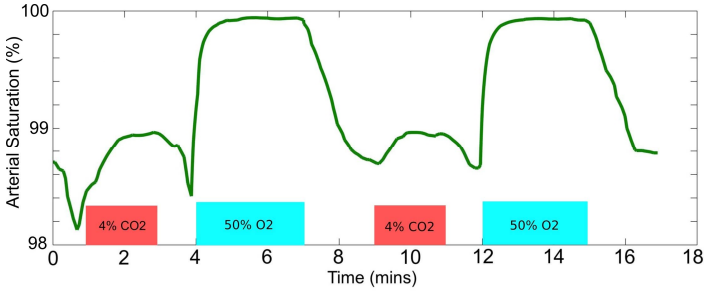


**Fig. 2.** Arterial oxygen saturation time course for a single subject, calculated from the end-tidal oxygen measurements

## Discussion & Conclusions

Although changes in saturation were too small to be seen on an individual subject level (both NIRS and pulse oximeter readings were only given to the nearest 1%), the mean time-courses clearly show increases in both arterial and venous saturations during hyperoxia and, to a lesser extent, during hypercapnia. On average a hyperoxic stimulus of $FiO_2$ ~0.5 induces a change in $SvO_2$ of ~2% and $SaO_2$ of ~1%, whereas a hypercapnic stimulus of $FiCO_2$ ~0.04 causes an increase in $SvO_2$ of ~1% and $SaO_2$ of ~ 0.5%. This implies that a non-negligible amount of BOLD signal change induced by these stimuli happens on the arterial side. This also impacts any calculation of OEF as the saturation is changing on both sides of the vasculature. These changes are too small to measure in a single subject using a pulse-oximeter or NIRS, or to infer from end-tidal measurements.

This result has implications for gas-calibrated fMRI approaches based on the Davis model. The scale of the effect is reasonably small and can likely be ignored under most circumstances. However for studies requiring a high-level of accuracy, and particularly for signal modelling, this should be taken into account. Incorporating the effects seen here into the detailed BOLD signal model[6] to estimate the size of the effect indicated that a hypercapnic stimulus inducing a 50% CBF increase would induce a BOLD change of 4.2% with no change in $SaO_2$, but would be 4.6% if the $SaO_2$ changes by 0.5%. This could introduce an error in OEF of up to 0.05.

## References

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