A study of cerebral energetics and pH_i in the visual cortex using ^{31}P MRS during stimulation ot reduced blood oxygen saturation levels

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Introduction

Demand of energy substrates to the brain is met by supply via cerebral blood flow (CBF). Increased neuronal activity is associated with a mismatch between the amount of O_2 delivered and consumed in brain parenchyma (1). To date, the physiological reasons for the mismatch are not fully understood. It has been proposed that O_2 diffusion in the brain parenchyma limits delivery for mitochondria leading to a disproportional high CBF response relative to $CMRO_2$ (2) . Recent evidence from human brain activations show, however, that CBF responses are not influenced by mild hypoxic hypoxia (3,4). Therefore, assuming that O_2 diffusion in the brain parenchyma is restricted, brain energetics can be expected to be vulnerable to activations in hypoxia, which would lead to anoxic energy failure during increased neuronal work. To explore this hypothesis, we have used ^{31}P MRS to study brain energy state and intracellular pH (pH_i) in the visual cortex in both euoxia and hypoxia during visual activations.

Methods

The protocol was approved by the Human Ethical Committee of the University of Birmingham. Eight healthy adults (3 females, 5 males) enrolled the study and gave informed consent. Inspired O_2 content (FIO_2) was either 21% (i.e. euoxia) or 12% (hypoxic hypoxia, in a non-rebreathing circuit). Oxygen saturation (Y_{sat}) and pulse rate were monitored with a pulse oximeter. MR scans were acquired on a Philips Achieva 3T system using a transmit/receive body coil for ^1H imaging and a ^{31}P surface coil for MRS. B/W checkerboard (8 Hz) was projected on a screen for visual stimulation.^{31}P MR spectra were collected from a volume (40x30x30 mm^3) encompassing primary visual cortex and adjacent cerebral structures, using the ISIS method. TR 4308ms, SW 3kHz, 1k data points, blocks of 48 scans were acquired. Spectra were analysed with jMRUI, zerofilled to 4k data points and line apodized to 25 Hz prior to FT. Peak areas were determined using AMARES from the jMRUI platform in the frequency domain. Prior knowledge of metabolite ppm values were used to improve accuracy in quantifying metabolite peak areas. pH_i was determined from the chemical shift difference between PCr and P_i using the calibration by Taylor et al (5). Paired t-test was used for statistical analysis of spectral results.

Results

Activation of the occipital lobe was confirmed by the presence of strong BOLD responses (signal increase by 5.3 ± 2%) in the visual area. Y_{sat} decreased from 0.99±0.01 to 0.88±0.35 at FIO_2 of 12%. Typical ^{31}P spectra are shown for euoxia (top panels) and hypoxia (bottom panel) both in baseline (left panels) and during visual stimulations (right panels) (Fig. 1). Individual PCr/γ-ATP ratios for each subject are shown as a function of Y_{sat} (Fig 2) in both baseline and activated states. It is evident that the PCr/γ-ATP ratio did not change during visual activations in either euoxia or hypoxia. pH_i of 7.02±0.03 did not change during activations in euoxia. There was a small alkaline shift to 7.05±0.04 during baseline in hypoxia, however, visual activation did not cause a further change in pH_i (Fig. 3).

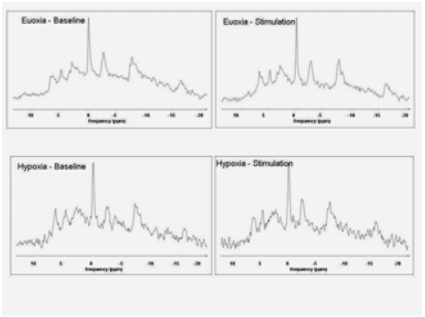

Fig 1 Typical ^{31}P MRS in both euoxic and hypoxic conditions.

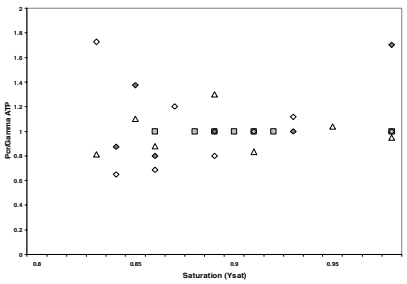

Fig 2 PCr/γ-ATP ratios for each subject across different saturation levels and conditions.

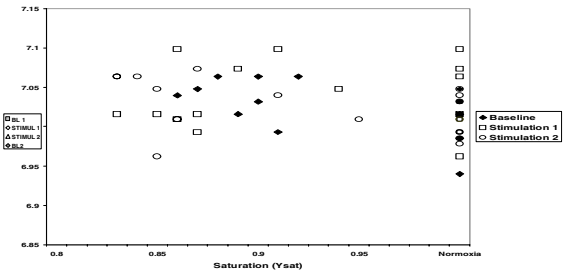

Fig 3 pH_i responses across all saturation levels for each subject at different conditions.

Conclusions

The present ^{31}P MRS data show that both PCr/γ-ATP and pH_i are not affected by visual stimulation within the Y_{sat} range studied. These observations suggest directly that (a) O_2 delivery to the brain under baseline and stimulated conditions is in excess to the demand by the energy metabolism and conversely, that (b) cerebral energy state may not be involved in eliciting the haemodynamic response for oxygen delivery

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References

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