Dynamics of cerebral lactate during acute hypoxia

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Introduction

The role of cerebral lactate is debated, as there is evidence that it is also used as an energy source by neurons rather than simply being a by-product of anaerobic metabolism [1]. There is also controversy about cerebral metabolism during hypoxia, with some groups showing perhaps counter-intuitive results of cerebral metabolism increasing during hypoxia [1,2]. In this study, we investigate the temporal dynamics of lactate during acute hypoxia using edited MRS. The goal of this study is to describe cerebral lactate dynamics when exposed to acute hypoxia and the recovery after returning to normoxia.

Methods

Three subjects each underwent 4 MRS scanning sessions. The protocol consisted of 10 min normoxia (baseline), 20 min hypoxia and 10 min normoxia (recovery). Dynamic end-tidal forcing was used [3] to maintain end-tidal CO_2 ($PetCO_2$) at the subject's specific resting level and hypoxia was defined as a reduction in end-tidal PO_2 ($PetO_2$) of 60 mmHg from baseline to a minimum of 50 mmHg $PetO_2$. Resting values were determined after the subject had acclimatized to the experimental set-up but prior to the beginning of the MRS protocol.

Imaging was performed at 3 T (GE HDx) with an 8-channel phased-array receive-only head coil using a 40×40×60 mm^3 voxel (majority white matter) in the left hemisphere. A MEGA-PRESS acquisition was used (TR/TE=2000 ms/140 ms, spectral width=5 kHz, 40 min acquisition). The 40 min acquisition was separated into 12 time periods to analyse the temporal dynamics of lactate. Lactate quantification was based on previous methods [4]. Briefly, using temporal averages across all data, a lactate model was based on a Gaussian doublet fit to the difference of the lactate spectra during hypoxia and normoxia. Secondly, a macromolecule model was developed using the mean spectrum, including the lactate doublet in combination with Gaussian peaks at 1.24 ppm and 1.43 ppm for co-edited macromolecules. The linear combination of the lactate and the macromolecule models was used to quantify lactate in each time period for each subject.

Results

Temporally resolved, quantified lactate data was acquired (Fig 1). Due to subject movement, one trial was discarded from subject 3. Table 1 shows mean lactate for baseline normoxia for each subject and the average lactate during the last 10 min of hypoxia. Lactate is significantly increased in the last 10 min of hypoxia (*t*-test, $p < 0.001$). Fig 2 shows the time course of lactate evolution for each subject averaged over the 4 trials. While the majority of the lactate changes occur in the first 10 min of hypoxia, it is not clear if subjects have reached a steady state after 20 min. The median time of lactate peak was at 13.3 min (range 10 min to 23.3 min after start).

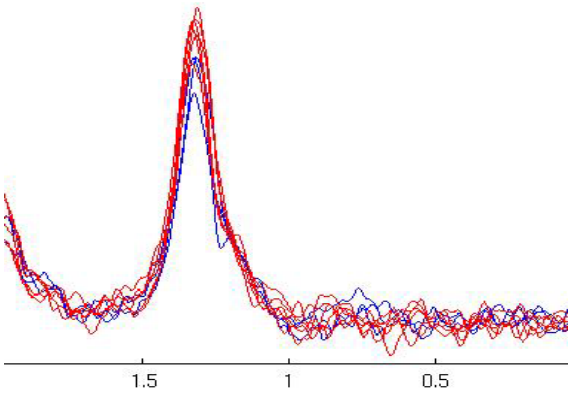

Fig 1. Sample lactate spectra from one trial. Blue = baseline normoxia, red = hypoxia

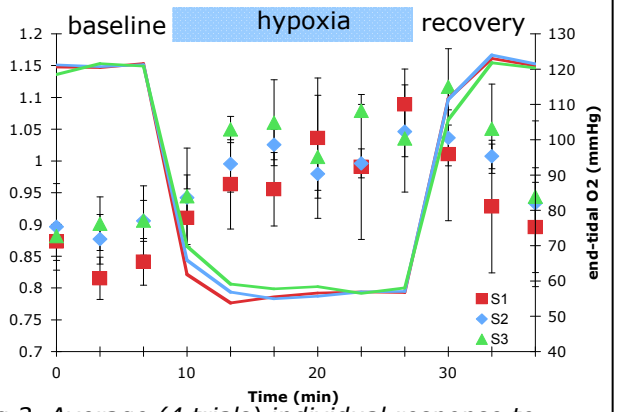

Fig 2. Average (4 trials) individual response to hypoxia (standard error shown) and lines indicating end-tidal O_2.

Discussion

As designed the experiment has sufficient signal-to-noise to investigate the temporal dynamics of lactate. The accumulation of lactate appears to happen over the course of several minutes and is variable between trials, with the peak lactate appearing as early as 10 min after the beginning of hypoxia and as late as 23.3 min, which was after the beginning of the normoxic recovery. The dynamics of lactate during hypoxia and after the return to normoxia indicate lactate accumulation and clearance is a complex and variable process. This may be a result of systemic lactate circulation in combination with lactate production in the brain. However, circulating lactate has been shown not to alter cerebral MRS lactate measurements [6]. Future investigations will examine these dynamics and the relationship with blood lactate measurements.

Table. Mean and standard error during baseline normoxia and the last 10 min across subjects.

	baseline mean (i.u.)	Last 10 min Hypoxia (i.u.)
S1	0.843±0.025	1.038±0.083
S2	0.922±0.043	1.037±0.021
S3	0.877±0.035	1.180±0.062
mean	0.881±0.034	1.085±0.055

References

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