Hemodynamic and metabolic response to hypoxia


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Introduction

Cerebral tissue has high metabolic demands, yet has low energy storage, and as a result, it is particularly susceptible to hypoxia. Lactate is a product of anaerobic metabolism and has been localized with MR spectroscopy in many cerebral disorders, including stroke, cancer, and mitochondrial disorders. Lactate also appears to increase during cerebral activation measured at 7 T. Similarly, cerebral blood flow (CBF) increases. Understanding these interactions in healthy subjects will assist in understanding chronic obstructive pulmonary disease, who have increased cerebral lactate.

Methods

Four healthy subjects (3 male) were studied during (a) normoxia and (b) hypoxia, which consisted of 12% inspired O2. Subjects breathed through a tight-fitting facemask throughout the experiment. Blood oxygen saturation (SpO2) was monitored with peripheral pulse oximetry. Subjects acclimatized to each condition for 5 min prior to MR spectroscopy, which was then followed by perfusion imaging.

Imaging was performed at 3 T (Signa HDx, GE) using an 8-channel phased-array receive coil. Lactate spectra were acquired using MEGA-PRESS acquisition from a 40 x 40 x 60 mm3 voxel positioned left of the midline, in a largely white matter region: TR/TE = 2000ms/140ms, 280 acquisitions, 10 min acquisition time. The large voxel size is necessitated by the low concentration of lactate in the healthy normoxic brain, which is typically assumed to be below the detectable threshold of MRS. The edited lactate signal was integrated over a 0.175 ppm range around the signal at 1.3 ppm (Fig 1), and concentration was calculated relative to the unsuppressed water signal from the same volume. CBF was estimated using a single-shot arterial spin labeling PICORE QUIPPSII acquisition (TR/TE = 2000/9.5 ms, 10 cm tag width T1/T2 = 600ms/150ms FOV = 24 cm2, 8 contiguous 6 mm slices, spiral 64 x 64 matrix, 150 reps, 5 min scan time). A grey matter mask was defined using a high-resolution T1-weighted anatomical scan to estimate global grey matter CBF. Results shown as mean ± standard error

Results

High quality edited MRS spectra of lactate were acquired in all subjects. During hypoxia, lactate (Fig 1) and CBF (Fig 2) increased in all four subjects (Fig 3); the average lactate increase was 30.6% ± 5.8% (p = 0.01) and the average CBF increase was 17.6% ± 2.7% (p = 0.01). Three subjects showed greater lactate increases and had lower average SpO2, while the subject with a mild-moderate increase in lactate had a mild desaturation.

Discussion

In spite of an extensive and controversial literature on the physiological role of lactate, MRS has not been widely applied for the quantitation of lactate in the healthy brain, in large part due to the insensitivity of available techniques. To our knowledge this is the first time global lactate and CBF measurements in response to a controlled hypoxic challenge have been demonstrated in humans. Lactate and CBF increase as SpO2 decreases, as expected. However, this relationship appears complex and likely requires a larger cohort to clarify and examine the relative time courses of lactate and CBF increases. Examining the spectra over the acquisition time suggest that lactate accumulates during the 10 min scan (data not shown). However, the degree of circulating lactate compared to that produced locally in the brain remains to be elucidated. The differences in relative lactate and CBF increases are intriguing; for example, Subject 2 had the smallest lactate increase and maintained the highest SpO2, and Subject 3 showed the largest lactate increase and the smallest CBF increase. This suggests that lactate production may be more sensitive to SpO2 than CBF increases. Understanding these interactions in healthy subjects will assist in understanding and treating cerebral pathologies involving impaired oxygen metabolism as well as conditions causing systemic hypoxemia; for example, patients with respiratory failure, i.e., chronic obstructive pulmonary disease, who have increased cerebral lactate.

Acknowledgements: NSERC, MRC

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