Progress in Nuclear Magnetic Resonance Spectroscopy 59 (2011) 319–335

Contents lists available at ScienceDirect

Progress in Nuclear Magnetic Resonance Spectroscopy

journal homepage: www.elsevier.com/locate/pnmrs

In vivo oxygen-17 NMR for imaging brain oxygen metabolism at high field

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ARTICLE INFO

Article history:
Received 3 March 2011
Accepted 14 April 2011
Available online 23 April 2011

Keywords:
In vivo ^{17}O NMR
Brain
High field
Cerebral metabolic rate of oxygen utilization
Oxidative metabolism

Contents

Abbreviations: γ, magnetogyric ratio; T_1, longitudinal relaxation time; T_2, transverse relaxation time; T_2^*, apparent T_2; τ_c, rotational correlation time; B_0, magnetic field strength; SNR, signal-to-noise ratio; *Q*, RF coil quality factor; CSI, chemical shift imaging; ATP, adenosine triphosphate; ADP, adenosine diphosphate; Pi, inorganic phosphate; CBF, cerebral blood flow; LDF, laser Doppler flowmeter; BBB, brain–blood-barrier; CMR_{glc}, cerebral metabolic rate of glucose utilization; $CMRO_2$, cerebral metabolic rate of oxygen utilization; PET, positron emission tomography; fMRI, functional magnetic resonance imaging; $C_a(t)$, time-dependent $H_2{}^{17}O$ concentration in excess of the natural abundance $H_2{}^{17}O$ concentration level in the arterial blood; $C_b(t)$, time-dependent $H_2{}^{17}O$ concentration in excess of the natural abundance $H_2{}^{17}O$ concentration level in the brain tissue; $C_v(t)$, time-dependent $H_2{}^{17}O$ concentration in excess of the natural abundance $H_2{}^{17}O$ concentration level in the venous blood; α, ^{17}O enrichment fraction of inhaled $^{17}O_2$ gas; λ, brain/blood partition coefficient.

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doi:10.1016/j.pnmrs.2011.04.002

1. Introduction

The oxygen element is one of the most important components for life on earth because various oxygen containing molecules are present in all levels of biological systems, and oxygen accounts for two thirds of the total human body mass and 90% of the mass of water. However, *in vivo* oxygen-17 (^{17}O) NMR has received very little attention compared to other *in vivo* NMR methodologies, such as ^{1}H, ^{13}C and ^{31}P NMR; even though the ^{17}O NMR signal was first observed in 1951 [1] and utilized since then for many chemical and biochemical applications (see a recent review by Gerothanassis [2,3] and the cited references therein).

It has been demonstrated that *in vivo* ^{17}O NMR can be used to monitor the uptake or washout of an ^{17}O-labeled exogenous agent (e.g. ^{17}O-labeled water) for studying tissue perfusion [4–7] or for detecting oxygen-containing metabolites in living species [8–10]. Nevertheless, the most valuable and unique capability of *in vivo* ^{17}O NMR is to non-invasively determine the metabolic rate of oxygen in live animals or humans (see [11–13] and references cited therein).

In this review article, we attempt to provide an overview of the methodology background and the present status of *in vivo* ^{17}O MR spectroscopy (MRS)/imaging (MRI) approach for imaging the cerebral metabolic rate of oxygen ($CMRO_2$) and studying the central roles of cerebral oxygen metabolism in brain function. The challenges and potentials of this ^{17}O-MR based $CMRO_2$ imaging method will also be discussed.

2. Background

2.1. Importance of oxygen metabolism in brain function and dysfunction

The brain is a highly aerobic organ; it consumes oxygen and glucose extensively in order to generate chemical energy in the form of the adenosine triphosphate (ATP) molecule. A majority of brain energy is used to support the unceasing electrophysiological activities of neurons responsible for inter-neuron transmission and communication throughout the central nervous system. A coupling between neuronal activity and brain energy exists for a wide range

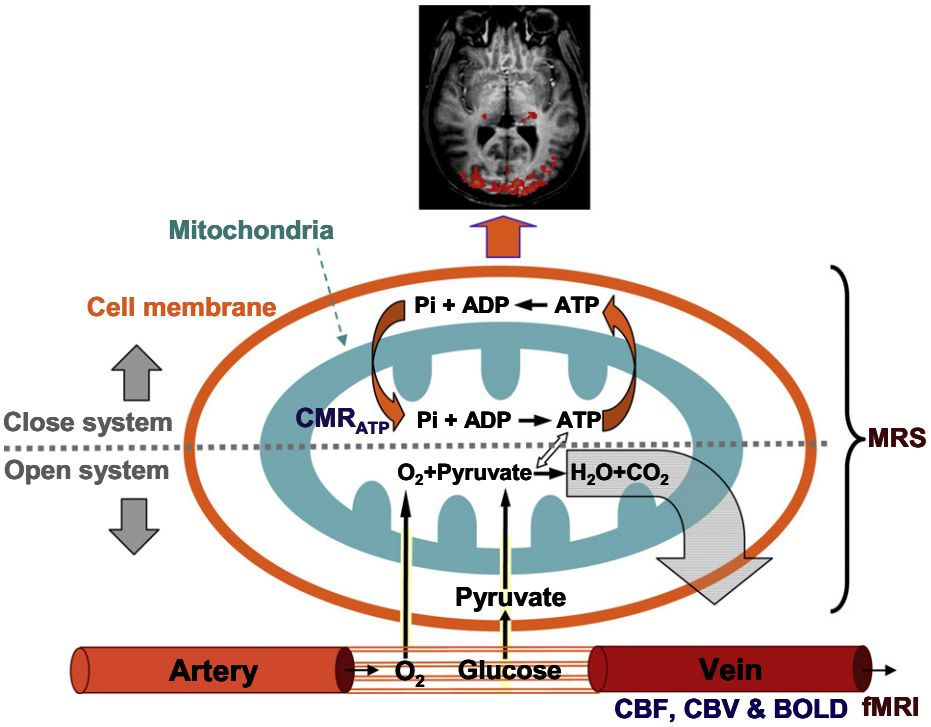

Fig. 1. Key metabolic processes occur in various sub-cellular compartments including both mitochondria and cytosol spaces and the associated vascular or hemodynamic events of the brain.