Apparent Diffusion Coefficient of Extra- and Intracellular Sodium in Rat Skeletal Muscle: Effects of Prolonged Ischemia

A. Babsky[1], H. Zhang[1], S. K. Hekmatyar[1], N. Bansal[1]
[1]Radiology, Indiana University, Indianapolis, Indiana, United States

Introduction

Ischemia causes a decrease in cellular energy status, acid accumulation, poor washout of metabolites, and an increase in intracellular (IC) Na^+. Ischemic damage to tissue microvasculature may lead to changes in the volume of extracellular (EC) water. Intracellular water may also change because of alterations in membrane permeability and ion transport processes across the cell membrane. All of these changes may alter the mobility of water in damaged tissue. Self diffusion of water and sodium in tissue can be noninvasively measured as apparent diffusion coefficient (ADC) by using ^1H or ^{23}Na MRS. The major advantage of ^{23}Na MRS is the possibility of simultaneously monitoring the ADC of Na^+ in IC and EC compartments with the help of a shift reagent (SR). In this study, the effects of prolonged ischemia on ADCs of water and Na^+ in IC and EC were monitored in the rat skeletal muscle using *in vivo* ^{23}Na and ^1H MRS.

Methods

The *in vivo* SR, $TmDOTP^{5-}$ (80 mM), was infused through a jugular vein at a rate of 1-4 ml/h in order to separate intra- and extra-cellular sodium (Na^+_i and Na^+_e respectively) signals from the rat leg skeletal muscle (n = 7). Severe total ischemia was induced by sacrificing the animal by an embolism through the same vein used for SR infusion. MR experiments were conducted on a Varian 9.4 Tesla, 31-cm horizontal bore system using a 10-mm diameter surface coil dual-tuned to ^{23}Na and ^1H. Water, Na^+_i, and Na^+_e ADC and ^{23}Na spectra were acquired before and 1, 2, 3, and 4 hours after ischemia. Six interleaved *b*-factors (*b* = 10, 100, 200, 400, 600 and 800 s/mm^2) were used for Na^+ ADC measurements (Fig. 1) and eight interleaved *b*-factors (*b* = 10, 100, 200, 400, 600, 800, 1200 and 1600 s/mm^2) were used for the water ADC measurements.

Results and Discussion

$TmDOTP^{5-}$ shifted the Na^+_e signal by ~3 ppm after 40-50 min of SR infusion without altering the blood oxygen tension or heart rate as measured by a pulse oximeter (Nonin, Plymouth, MN). Ischemia caused a 2.5-time increase in Na^+_i, a 25% decrease in Na^+_e, and a 3.5-time increase in Na^+_i/Na^+_e ratio in the skeletal muscle 4 hours after the onset of ischemia. The ischemia-induced increase in Na^+_i was caused most likely by energy failure of the Na^+/K^+-ATPase. The decrease in Na^+_e signal intensity could be caused by movement of Na^+ from EC to IC space, and/or by a decrease in EC space as a result of blood washout from the tissue.

Before ischemia, the Na^+ ADCs in both the IC and EC compartments were similar and higher than water ADC. It is commonly expected that water ADC is lower in IC space compared to EC space due to high concentration of macromolecules in IC space. However, our results are in agreement with Duong et al. (1) who showed that ADC of 2-[^{19}F]fluoro-2-deoxyglucose-6-phospate in IC and EC spaces of the brain are similar. ADC of Na^+_e decreased by 30-40% after 2-4 hours of ischemia (Fig. 2). The most reasonable explanation of this effect is an increase in the tortuosity of EC space. Cellular swelling, which is associated with ischemia-induced cell injury, presses cell membranes closer together in the EC space and thereby increases the tortuosity of this space (1). It is interesting to note that Na^+_i and total water ADC remained mostly unchanged during 4 hours of ischemia (Fig. 2). These data are in agreement with the data reported by Liess et al. (2) which showed that ADC of water in isolated and KCl-arrested rat hearts is unchanged during and after total global ischemia. It seems that ischemia-induced changes in IC space leading to an increase in ADC, such as influx of water and dissociation of IC molecules, are counterbalanced by ADC reducing factors, such as a decrease in energy-dependent cytoplasmic motion. Further studies are needed to determine why tissue Na^+ ADC is higher than water ADC, while in both saline and agarose phantoms, Na^+ ADC was 45% lower than water ADC.

References

(1) Duong TQ et al. MRM 1998; 40: 1-13.
(2) Liess C et al. MRM. 2000; 44: 208-214.

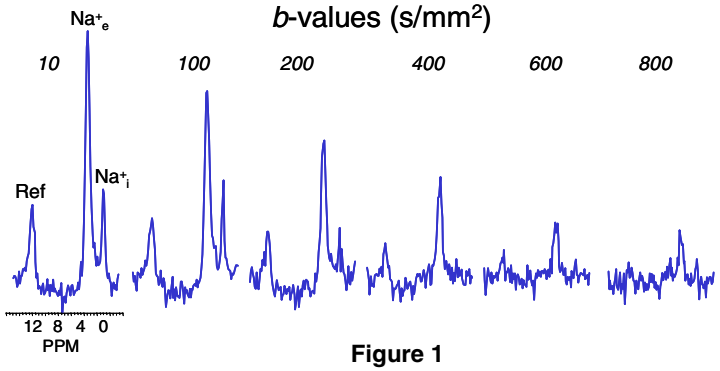

Figure 1

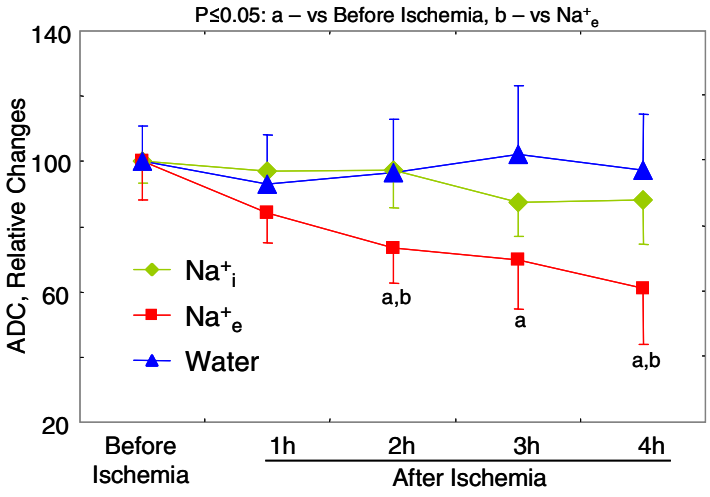

Figure 2