Limitation of Glucose Consumption in Rat Head Detected by Labeled Glucose-^{17}O

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Introduction

The rate of glucose metabolism can be determined by MR using a time course of the labeled glucose alterations. Experiments using ^{17}O labeled glucose were conducted with the ultimate goal of using such experiments to differentiate tumor cells from the normal cells in future. The question arose whether the rate of glucose metabolism may remain relatively unchanged in normal tissue, while during the same time the concentration of glucose in the body varies several times after bolus injection. The experiments were conducted with rats using a range of doses for injected glucose to analyze such observations.

Experimental

Intravenous tail bolus administrations of glucose-6-^{17}O (abundance 47%) were explored by detecting ^{17}O MR signal from a rat head at 21.1 T. The MR experiments were performed using Bruker MRI Avance III console (PV 5.1 software). The *in vivo* RF probe has a double tuned ^{17}O/^{1}H volume RF coil covering the whole rat head. The time course of the MR ^{17}O signal changes was detected using 90^{o} RF pulse of 160 μs, TR time of 90 ms and NA = 166. Thus, the time course had a resolution of 15 s/point. Glucose injection doses were in the range of 3 - 15 μmole/g of animal weight. The *in vivo* experiments were performed using 6 male Fisher 344 rats (~ 200 g) anesthetized by isoflurane 1.5%. All animal experiments were conducted according to protocols approved by The Florida State University ACUC.

Results and Discussion

Glucose consumption was determined by ^{17}O-water signal without prior determination of CBF [1] The same MR experiments allowed monitoring changes of glucose concentration through direct observation of the glucose-6-^{17}O MR signal peak positioned separately at -12.3 ppm relative to the ^{17}O water peak. The direct detection of glucose-^{17}O in a rat head demonstrates a large change of glucose concentration during the time after the bolus injection (**Fig. 1**). These changes could be manyfold till the time when glucose is distributed evenly around the rat body and partially consumed. At the same time the detected level of the metabolized ^{17}O-water was linear increasing with the rate of 0.14 **±** 0.02 %/min. The rate is expressed in percent relative to the natural concentration of ^{17}O-water (20.7 mM). The rate of metabolized water increase represents a consistent glucose consumption CMR_{glc} = 0.43 ± 0.06 μmol/g tissue/min. This $CMRG_{glc}$ rate was found unchanged during alteration of the glucose concentration in the bolus injection. This observation correlates with others specifying that glucose-6-phosphate (G-6-P) does not accumulate in hyperglycemia [2]. The hexokinase which is driving glucose phosphorylation only in one direction serves as a gate. It can be inhibited by the excess amount of G-6-P, which eventually, limits glucose consumption.

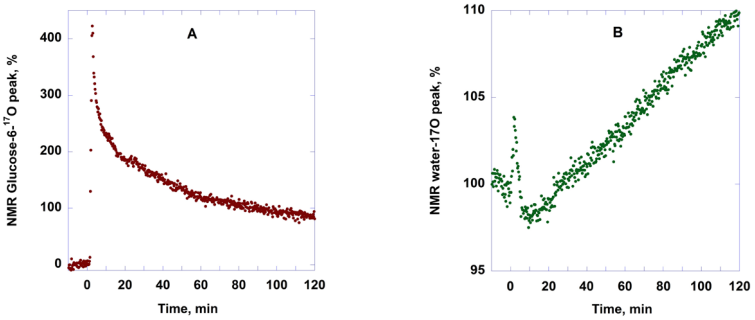

Fig.1. Time course of ^{17}O NMR glucose concentration (A) and water peak (B) in rat head after IV injection of glucose-6-^{17}O.

Conclusions

The rate of glucose metabolism in a normal rat head remains unchanged during a large variation of the glucose injected doses and a large alteration of glucose concentration after bolus injection. The phosphorylation of glucose by hexokinase may serve as a limiting factor for the rate of glucose metabolism during hyperglycemia.

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References

[1] Fiat D., *et al.,* Neurological Research, **15(7)**, 7-22 (1993).
[2] Siesjo, B.K., Brain Energy Metabolism, John Wiley & Sons, New York (1978).