Monitoring Brain Potassium with ^{87}Rb MRI

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Introduction

An abrupt change in brain tissue potassium concentration, $[K^+]_{br}$, has been suggested as an index of progressive ischemic damage [1]. To monitor K^+ by MRI, partial K replacement with ^{87}Rb [2] or with ^{133}Cs [3] has been considered based on the properties of Rb^+ and Cs^+ as congeners for K^+ in tissues and their much better MRI-sensitivity. The use of Cs^+ as a probe of K^+ is limited to intracellular cations. Whereas Rb^+ resembles tissue K^+ more closely, ^{87}Rb MRI has never been attempted in vivo. For ^{87}Rb MRI in vivo to be feasible, high and safe replacement levels are needed. However, existing data on the $[Rb^+]_{br}$ after dietary and i.p. RbCl administration in pharmacological studies are scarce and inconclusive [4]. The effects of such substitution on ion balance in ischemic brain have not been studied previously. A purpose of the present study was to develop an MR-suitable protocol of dietary RbCl administration, to verify that it does not interfere with the process of K^+ dynamics in the ischemic brain, and to prove the possibility of ^{87}Rb MRI in the rat brain.

Methods

Thirty normally fed male Sprague-Dawley rats weighing 230-380 g were given 5-80 mM RbCl in the drinking water for 6 to 75 days. In 15, focal cerebral ischemia was produced by MCA transection and bilateral common carotid artery occlusion (MCAT) [5]. Na, K and Rb content in 1-mg samples of cortical brain were determined by emission flame photometry at 589, 766 and 791 nm for Na, K and Rb, respectively, and corrected for the mutual interference effects. The samples were punched from the ischemic core and contralateral area using the change in surface reflectivity of ischemic cortex as a guide. For multinuclear ^{87}Rb/^{23}Na/^{1}H MRI, a surface coil and a prototype 50 mm diameter parallel cosine (PCOS) [6] transmit/receive coils have been built and tested. The animal cradle with a recirculating water bed and fittings for anesthesia gas supply was designed to accommodate the PCOS coil with the tuning/matching circuit schematics external to the conductors (i.e., no capacitors in the rungs) allowing triple tuning of the coil. The SNR of the PCOS coil measured with an HP 8573C network analyzer was greater than 250 when loaded with a saline and RbCl phantom comparable to the load of a rat. Images were obtained on a 3 T GEMS scanner using conventional GRE and SE pulse sequences for ^{1}H, and a Twisted Projection Imaging scheme [7] with TR/TE of 15/0.4 ms (for ^{87}Rb) and 100/0.4 ms (for ^{23}Na), and analyzed using AMIDE software [8].

Results

Fig. 1 shows that $[Rb^+]_{br}$ increased with the duration of intense treatment up to 25 mEq/kg (representing the degree of Rb/(K+Rb) replacement of 0.26) over 17 days, the total of [K]+[Rb] being approximately constant at 94 mEq/kg (SD=9 mEq/kg). In agreement with earlier reports, Rb/(K+Rb) in the brain was 2.1-2.8 times lower than those in liver and skeletal muscle [4]. Body weight increased steadily in all animals during the course of treatment. No significant changes in behavior were noted upon initiation and in the course of RbCl feeding. The minor adverse effects were a topical skin irritation and/or hair loss (in 15 animals), a transient interruption in gaining weight at high RbCl dosage, and low tolerance to isoflurane anesthesia observed in two rats with the highest brain Rb/(K+Rb) replacement ratios (above 0.25). Thus, the degree of Rb/(K+Rb) replacement of at least 0.18 in the rat brain may be achieved with virtually insignificant toxic effects of Rb.

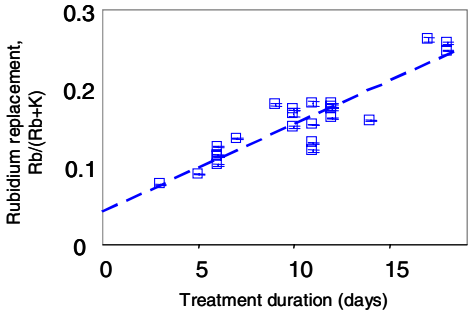

Fig. 1. Degree of Rb/(K+Rb) replacement in the normal cortex of the rat brain plotted against the duration of intense treatment (i.e., the number of days when the animal ingested drinking water not less than 40 mM RbCl) in 23 rats. For 8 to 10 samples taken from each individual brain, the SEM bar is less than the symbol size on the plot.

The $[K^+]_{br}$+$[Rb^+]_{br}$ data reproduced the $[K^+]_{br}$ fall in ischemic cortex before 3 h and the subsequent sharp drop in $[K^+]_{br}$ at 3-4 h after MCAT (Fig. 2), which we observed previously in animals without Rb/K substitution [1]. In all of these observations, the Rb replacement ratio, Rb/(K+Rb), increased over time in ischemic areas ($R=0.76$, $p<0.05$): by 6% before 3 h, by 15% at 4 h, and by as much as 40% at 7 h. This indicates that Rb^+ is retained in brain slightly more than K^+, and is consistent with other data from electrophysiology and transport studies showing a tendency of Rb^+ to lag behind K^+ because of its larger molecular size. Overall, the data indicate that Rb^+ itself does not significantly change the pattern of $[K^+]_{br}$ decrease in ischemic cortex over time.

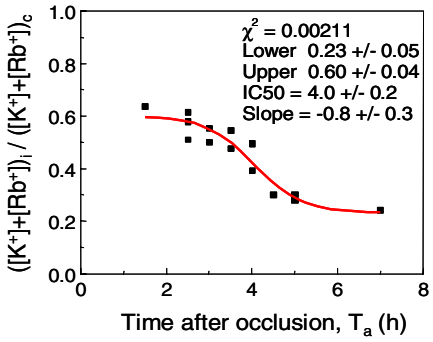

Fig. 2. $[K^+]+[Rb^+]$ in 15 animals after MCAT and bilateral CCAO. Data are normalized to the contralateral cortex. The sigmoidal fit showed a transition point at 4 h; other parameters of the fit are given in the box.

Preliminary ^{23}Na and ^{87}Rb experiments on a number of phantoms and several rats have been performed using the TPI method. Fig. 3 shows three images of the phantom most closely simulating a head of a RbCl-fed rat: a 1.5-ml tube containing a solution of RbCl attached to the inner surface of a bigger tube approximately of the size of a head. Both tubes contain 0.9% NaCl to closely approximate the coil load in an animal experiment. The bulk saline and walls of the small tube are clearly seen on both ^{1}H and ^{23}Na images, whereas the ^{87}Rb image (obtained within 10 min) shows only the compartment containing RbCl. Preliminary animal ^{87}Rb MRI with a surface coil and standard solutions as concentration references yielded an estimate of $[Rb^+]_{br}$ of 20-25 mEq/kg wet weight (n=2) in normal cortex of RbCl-fed rats.

Conclusions

Feeding of rats with RbCl in the drinking water is a suitable way to prepare them for ^{87}Rb MRI of the brain. The data support the conclusion that $[Rb^+]_{br}$ of at least 17 mEq/kg wet weight can be safely obtained in normal brain.

Rb replacement is an effective method to monitor K^+ changes. This approach does not interfere with ion balance in ischemia progression, thus enabling ^{87}Rb MRI studies of K^+ in this particular pathological process.

Preliminary scans prove the technical possibility and practicability of ^{87}Rb MRI of the rat brain with a PCOS coil.

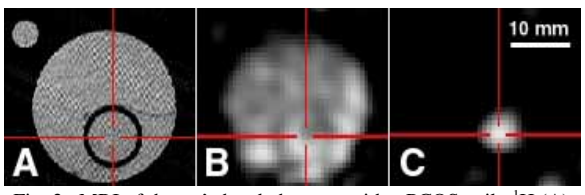

Fig. 3. MRI of the rat's head phantom with a PCOS coil. ^{1}H (A), ^{23}Na (B), and ^{87}Rb (C) images show a small tube with 100 mM RbCl in saline inside the bigger vial with saline. A small circle in the upper left corner of the ^{1}H image is a reference tube. Scale bar is in the upper right corner.

References

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