7 T ^{87}Rb MRI to assess K^+ dynamics in ischemic rat brain in vivo

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INTRODUCTION

A change in brain tissue potassium concentration, $[K^+]_{br}$, has been suggested as an index of progressive ischemic damage (1). To monitor K^+, partial K replacement with its congener ^{87}Rb, which possesses higher MRI-sensitivity, and, thus, a possibility of ^{87}Rb MRI in vivo, have been demonstrated (2). MRI quantification of ^{87}Rb in the brain still poses a significant challenge, however, because of its very short T_2 (~0.4 ms), natural abundance of only 28%, and, therefore, relatively low tissue concentration. In this study our goals are to: 1) perform the first ^{87}Rb MRI in a rat model of focal ischemic stroke; and 2) prove the suitability of ^{87}Rb MRI at high fields (7 T) to obtain quantitative data on the $[K^+]_{br}$ dynamics in this model.

METHODS

Six normally fed male Sprague-Dawley rats weighing 310 ± 39 g were given 40 mM RbCl in the drinking water for 14 days (2). Permanent focal cerebral ischemia was produced by middle cerebral artery transection and bilateral common carotid artery occlusion (MCAT) (3) under isoflurane (in 30% O_2, 70% N_2O) anesthesia. For ^{87}Rb/^{1}H MRI, a dedicated dual-tuned, 35-mm-diameter transmit/receive coil has been designed and constructed to accommodate the animal with a recirculating water bed and fittings for anesthesia gas supply. Calibration standards (10, 20 and 50 mM RbCl in 10% agarose gel) were placed next to the animal's head. Images were obtained on a 7 T Siemens Magnetom scanner using GRE and SE pulse sequences (for ^{1}H), and a spiral ultrashort-TE sequence with TR/TE of 3/0.07 ms and a voxel size of 3.8 mm^3 (for ^{87}Rb), and analyzed using AMIDE software (4). The infarct size and location were assessed by ADC maps reconstructed from ^{1}H single-scan trace diffusion-weighted multislice spin-echo images (*b*-factors of 0, 200, 500, and 800 s/mm^2), and further verified by the change in surface reflectivity of ischemic tissue and MAP2 immunohistochemistry (5).

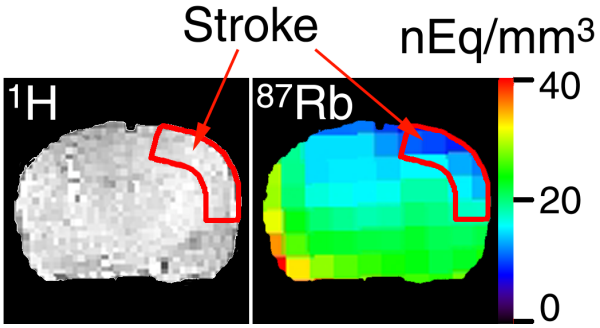

Fig. 1. Left: a coronal anatomic GRE image featuring an ischemic lesion ROI (outlined); right: a ^{87}Rb MRI in the same plane obtained in 13.1 min at 5.8 hours after MCAT and showing lower $[Rb^+]_{br}$ in the ischemic ROI.

RESULTS AND DISCUSSION

Fig. 1 shows the first ^{87}Rb MRI of ischemic rat brain, which demonstrates a drop in brain tissue rubidium concentration, $[Rb^+]_{br}$ in ischemic rat cortex after MCAT. For MRI to provide a quantitative measure of $[Rb^+]_{br}$, the MRI protocol utilized ultra-short TE (0.07 ms) to minimize a quantitation bias caused by the ^{87}Rb fast biexponential relaxation, and the use of calibration standards with T_1 and T_2 characteristics approximating those in brain tissue. To obtain $[Rb^+]_{br}$ concentrations, average ^{87}Rb MR image intensities over selected ROIs in the brain were referenced to those from ROIs placed over the reference tubes (6). The changes in $[Rb^+]_{br}$ after MCAT were analyzed in the ipsilateral and homotopic cortex. In agreement with an earlier flame photometry report (2), $[Rb^+]_{br}$ data showed a decrease in ischemic brain, and no statistically significant changes in contralateral ROIs over time were observed (Fig. 2). To convert $[Rb^+]_{br}$ into physiologically meaningful values of $[K^+]_{br}$ + $[Rb^+]_{br}$, different degrees of Rb^+/K^+ replacement in different animals were taken into account (2). The average dynamics of $[K^+]_{br}$ + $[Rb^+]_{br}$ in all animals (Fig. 3) displays the net K^+ efflux from the ischemic brain, in agreement with K^+ dynamics studied earlier by traditional techniques (1).

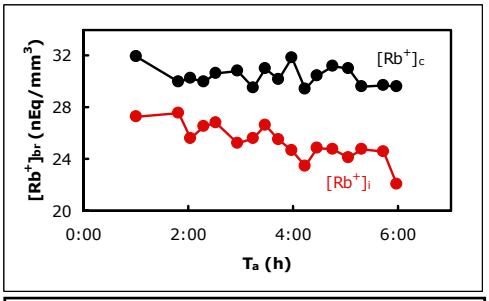

Fig. 2. $[Rb^+]_{br}$ in the ischemic cortex ROI ($[Rb^+]_i$, red) and homotopic normal cortex ROI ($[Rb^+]_c$, black) in the rat #2. T_a, time after MCAT.

CONCLUSIONS

These findings represent the world's first successful ^{87}Rb MRI in vivo co-registered with anatomic images. These data demonstrate the potential of 7 T ^{87}Rb MRI to assess the dynamics of K^+ efflux from the ischemic brain with 13-min temporal resolution in a single animal. This technique may become a unique tool to approach the mechanisms of the progression of ischemic damage, as well as to address a need for novel early biomarkers of tissue viability and for therapy monitoring.

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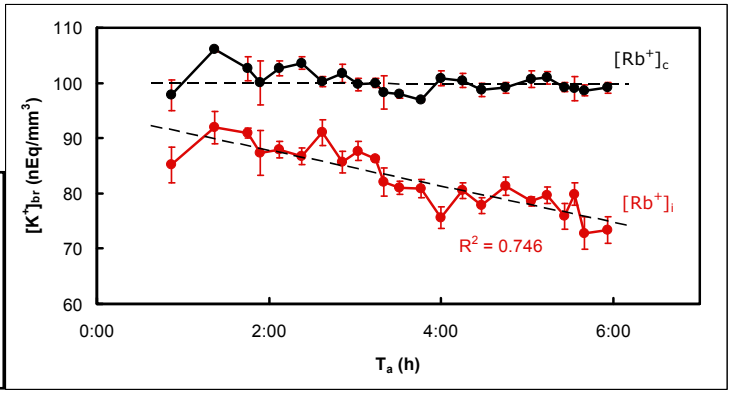

Fig. 3. $[K^+]_{br}$ efflux from the ischemic cortex ($[K^+]_i$, red) after MCAT assessed by ^{87}Rb MRI in vivo. $[Rb^+]_c$, black, shows $[K^+]_{br}$ in the homotopic normal cortex. The data are averaged over all 6 animals. T_a, time after MCAT. Error bars are SEM.