Published in final edited form as:
Magn Reson Med. 2009 November ; 62(5): 1338–1341. doi:10.1002/mrm.22133.

Sodium Long-Component T_2^* Mapping in Human Brain at 7 Tesla

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Abstract

Sodium (^{23}Na) MRI may provide unique information about the cellular and metabolic integrity of the brain. The quantification of tissue sodium concentration from ^{23}Na images with nonzero echo time (TE) requires knowledge of tissue-specific parameters that influence the single-quantum sodium signal such as transverse (T_2) relaxation times. We report the sodium (^{23}Na) long component of the effective transverse relaxation time T_2^* values obtained at 7 T in several brain regions from six healthy volunteers. A two-point protocol based on a gradient-echo sequence optimized for the least error per given imaging time was used (TE_1 = 12 ms; TE_2 = 37 ms; averaged N_1 = 5; N_2 = 15 times; pulse repetition time = 130 ms). The results reveal that long T_2^* component of tissue sodium (mean ± standard deviation) varied between cerebrospinal fluid (54 ± 4 ms) and gray (28 ± 2 ms) and white (29 ± 2 ms) matter structures. The results also show that the long T_2^* component increases as a function of the main static field B_0, indicating that correlation time of sodium ion motion is smaller than the time-scale defined by the Larmor frequency. These results are a prerequisite for the quantification of tissue sodium concentration from ^{23}Na MRI scans with nonzero echo time, will contribute to the design of future measurements (such as triple-quantum imaging), and themselves may be of clinical utility.

Keywords

brain; sodium; high magnetic field; MR imaging; transverse relaxation time

Brain tissue sodium concentration provides an indicator of cellular and metabolic integrity and ion homeostasis in pathologic conditions such as tumors and acute cerebral ischemia (1). However, the application of sodium MRI (^{23}Na-MRI) is limited by the lower concentration and sensitivity of the ^{23}Na nucleus compared to ^{1}H. The increasing availability of magnets operating at 7 T for human imaging may help overcome these limitations by providing higher signal-to-noise ratio (SNR). The quantification of tissue sodium concentration has to take into account various instrumental- (2) acquisition- (3,4) and tissue-specific parameters that influence the single-quantum sodium signal such as longitudinal (T_1) and transverse (T_2*) relaxation times.

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Long T_2^* components have been measured in humans at lower fields (3,9,10); therefore, the aim of this study was to measure sodium long T_2^* relaxation times in several human brain regions at 7 T using the method similar to that of Bartha and Menon (3). The short T_2^* component maps of the sodium signal decay cannot be reliably measured due to low SNR (associated with fast signal decay) and technical limitations (3). Nonetheless, knowledge of the long sodium T_2^* component will aid in the quantification of tissue sodium concentration and in the design of future quantitative measurements such as triple-quantum sodium mapping (11,12) and might become of diagnostic utility on its own.

MATERIALS AND METHODS

Six healthy volunteers (three males) with a mean age of 30 (range: 24–35) years were consecutively enrolled in this study. Approval for this study was obtained from the Institutional Board of Research Associates of New York University Medical Center, and informed consent was obtained from all subjects.

All experiments were performed on a whole-body 7-T Magnetom scanner (Siemens AG, Erlangen, Germany) with a custom-built, transmit-receive, dual-tuned, $^{1}H/^{23}Na$ head coil (XLR Imaging, London, ON, Canada). The coil comprises ∅28 × 21 cm 16-rung proton and ∅28 × 19 cm eight-rung sodium quadrature hybrid birdcage coils. Transmitter reference voltage (voltage needed to achieve 180° excitation pulse in 1 ms) for the sodium part of the coil varied subject to subject between 450 and 500 V. A vendor-provided shimming procedure based on a dual-echo steady state sequence was performed iteratively five to 10 times till it converged and yielded whole-head water line width of 34 ± 4 Hz full width at half maximum.

The MRI protocol included (a) a T_1-weighted, magnetization-prepared, rapid-acquisition, gradient-echo sequence with echo time (TE)/pulse repetition time/inversion time: 2.6/2250/1100 ms; 192 1.0 mm slices, 256 × 256 matrix with 240 × 240 mm^2 field of view; and (b) a three-dimensional gradient-recalled echo sequence with a nonselective excitation for single-quantum sodium images, with a field of view of 240 × 240 × 240 mm^3, with 5 × 5 × 8 mm^3 voxels. The T_2^* maps were obtained using the Fleysher et al. method (13), assuming monoexponential relaxation optimized for a literature T_2^* value of ~20 ms at 4 T (3). More specifically, two sodium images were acquired with TE values set to TE_1 = 12 ms and TE_1 = 37 ms. Images at each TE were averaged N_1 = 5 and N_2 = 15 times, respectively. Receiver bandwidth was set to 2.4 kHz. The pulse repetition time was set to 130 ms and the flip angle was set to 80° which was specific-absorption-rate-limit optimized (14) for a 1-ms nonselective excitation pulse and sodium T_1 value of ~50 ms (5). At these settings, the scan time for the short TE was 15 min 36 sec and 46 min 48 sec for the long one, yielding total acquisition time just under 63 min. Note that even though the protocol was optimized for a guessed T_2^* value, the error in the resultant T_2^* measurements remains relatively constant over a wide range T_2^* values between 15 and 50 ms (see for example Fig. 1 in Fleysher et al. (13)). The T_1-weighted, magnetization-prepared, rapid-acquisition, gradient-echo images were resampled to 8-mm slice thickness to match the sodium images.

The sodium T_2^* relaxation times were computed in vivo in each voxel using:

$$T_2^* = (TE_2 - TE_1) / ln(S_1/S_2) \quad [1]$$

where S_1 and S_2 are the average image intensities at short (TE_1) and long (TE_2) TEs. T_2^*s were calculated in regions of interest in the following brain regions: cerebropsinal fluid (CSF) at the level of the lateral ventricles, thalamus, putamen, and occipital and frontal gray matter;

splenium of the corpus callosum and periventricular, occipital, frontal, and cerebellar white matter. To minimize partial volume contamination, the regions of interest of variable size, as dictated by the anatomic region, were placed on the T_1-weighted, magnetization-prepared, rapid-acquisition, gradient-echo images and overlaid automatically on the corresponding sodium T_2^* parametric map using Image J (http://rsb.info.nih.gov/ij/). To exclude interobserver and to minimize intraobserver variability with respect to the region of interest placement, each subject data set was reviewed by two experienced observers at the same time. The average T_2^*s were recorded for each region bilaterally (except for CSF and corpus callosum) from the sodium T_2^* parametric maps.

A special remark should be made regarding potential bias in the measurement. Since it is known that sodium signal from gray and white matter structures exhibits biexponential decay, ignorance of the short T_2^* component in the measurement may lead to a biased estimate of the long T_2^* component. Another contributor to the possible bias is the measurement noise. The bias due to both of these effects can be estimated using simulations. To do this, an ideal biexponential signal at TE = 12 ms was used as a parameter to Rice (15) distribution in 10^7 drawings. The second parameter of the Rice distribution was set to produce an SNR of 10 (as expected in the actual measurement). Then, the simulated data were processed as described above and compared with the true answer to estimate possible measurement bias. For expected physical parameters of $T_{2\text{long}}^*=20$ ms and $T_{2\text{short}}^*<4$ ms and the contribution to due to long component of 40% to the total signal, the bias in the measurement was less than 8%. For tissues where larger fractions of slow-decaying sodium are observed (5), this bias will be less than 3%. Similar evaluation can be done for expected bias in CSF where $T_2^*=60$ ms, which yielded bias of less than 2%. This expected accuracy in long T_2^* measurement is similar to that provided by a multi-TE method (3).

RESULTS

In vivo T_1-weighted anatomic images, together with corresponding sodium images and T_2^*–decay parametric maps from a single subject, are shown in Fig. 1. Even though only three slices are shown, 30 slices were acquired from each subject. The SNR in the brain tissue at TE_1 was about 10, which theoretically provides 12% coefficient of variation for white matter structures and about 21% for the gray matter structures (13). The measured mean coefficients of variation for the tissue types with the corresponding standard errors of the mean were $CV_{white\ matter}$ = 14.3 ± 1.4% and $CV_{gray\ matter}$ = 20.3 ± 4.2%, respectively, which are in good agreement with the theoretically predicted values based on image SNRs. The T_2^* from the studied regions are compiled in Table 1 and reveal similar T_2^* values among the gray matter and white matter structures studied. The mean ± standard errors of the mean global T_2^* values among the six subjects were 29 ± 2 ms for the white matter and 28 ± 2 ms for the gray and 54 ± 4 ms for CSF. Bias analysis was based on the assumptions that at least 40% of total sodium signal exhibits long decay and that $T_{2\text{short}}^*<4$ ms leads to accuracy in gray/white matter T_2^* values better than 9% and better than 2% in CSF.

DISCUSSION

It has been shown that reliable in vivo measurements of the short T_2^* component of the sodium nuclear magnetic resonance signal are difficult due to low SNR and high line broadening (3). Therefore, the goal of this study was to quantify the long component of the decay rate in a healthy human brain at 7 T. For this purpose, we devised a protocol that provided the highest possible precision for measuring long T_2^* components.

The measured T_2^* values varied considerably between CSF and the gray and white matter. Since signal due to quadrupolar splitting from sodium ions in dilute water solutions is removed by "motion averaging", sodium CSF transverse relaxation rate should be similar to that of saline. Indeed, the CSF T_2^* value of 54 ± 4 (ms) found in this work is consistent with 54 (ms) saline T_2 measurements at 8.3 T (9). The similarity of T_2^* values for the gray (28 ± 2 ms) and white (29 ± 2 ms) matter suggests that the sodium ion environment in these two tissue types is similar despite the differences in the sodium concentrations. It is important to emphasize that even though statistically significant differences between values of the long T_2^* component between gray and white matter or even among anatomic structures within a tissue type may exist, these differences alone are not likely to produce strong contrast on sodium T_2^*–weighted images acquired with TE less than 20 ms.

We compared our measurements of sodium long T_2^* values at 7T with those reported in the literature at 1.5 T and 4 T. Magnetic field dependence of the long T_2^* and T_2 component compiled from Bartha and Menon (3), Perman et al. (9), Winkler et al. (10), and this work is presented in Fig. 2. The plot shows that the long T_2^* component increases in gray and white matter structures as a function of the main magnetic field, which indicates that neither macroscopic residual field gradients nor sodium diffusion has an appreciable contribution to the decay rate and that the correlation time of the random sodium ion motion is much smaller compared to the time scale defined by the Larmor frequency. Thus, according to the Bloembergen Purcell Pound theory (16) one could expect that sodium T_2 value should be close to its T_1. This is in agreement with previous sodium T_1 and T_2 measurements (5,9).

Great care has been taken in designing the measurements so that the contributions due to random errors are minimized. A note should be made about the accuracy of the measurement and possible remaining biases which could have affected the measurement. For example, making TE_1 small could lead to a considerable bias in T_2^* measurement due to short T_2^* component contribution. To "protect" against such an error, we selected a large TE_1 value (we used TE_1 = 12 ms). Setting TE_1 too small would have led to an underestimation of T_2^* values. On the other hand, TE_1 cannot be made too long because images with TE_2 ($TE_2 > TE_1$) could have very low SNR. Low SNR in TE_2 images could shift T_2^* values toward higher values. This is because noise distribution in the magnitude images is Rician and deviates significantly from the Gaussian for SNR less than 3 (15). Because the data were averaged several times, the SNR in these images was above 5, which indicates absence of the bias in the measurement. If this effect were appreciable, the true T_2^* would be even higher than measured. Quantitatively, for the selected acquisition parameters possible bias in long component T_2^* measurement was less than 9% for gray and white matter structures and less than 2% for CSF. These estimates of the bias were made assuming that the short T_2^* component was less than 4 (ms) and that the long T_2^* component contributed at least 40% to the total signal at zero TE. Thus, the accuracy in long T_2^* measurement is similar to that provided by a multi-TE method (3). Based on these considerations, it is unlikely that the observed increase in T_2^* values as a function of main magnetic field was caused by instrumental effects. Nonunique to this work, partial-volume effects could significantly degrade the quality of T_2^* measurements (especially in the voxels with significant partial CSF volume).

CONCLUSIONS

Sodium T_2^* values at 7 T were measured on a voxel-by-voxel basis using an optimal protocol that minimizes random errors and systematic biases for the fixed imaging time. The T_2^* values of CSF were similar to previous reports at 1.5 and 4 T, while the T_2^* values for gray and white

matter structures increase as a function of the magnetic field strength. The obtained T_2^* values will aid the quantification of sodium concentration in studies with nonzero TE values. In addition, future studies will investigate whether sodium long T_2^* or T_2 component maps have some diagnostic potential in pathologic conditions such as brain tumors, head trauma and multiple sclerosis.

Acknowledgments

The authors thank Enzo Barberi and Robert Pinkerton for their help in hardware development.

Grant sponsor: National Institutes of Health; Grant numbers: R01NS051623, R01NS029029, and R01NS 39135.

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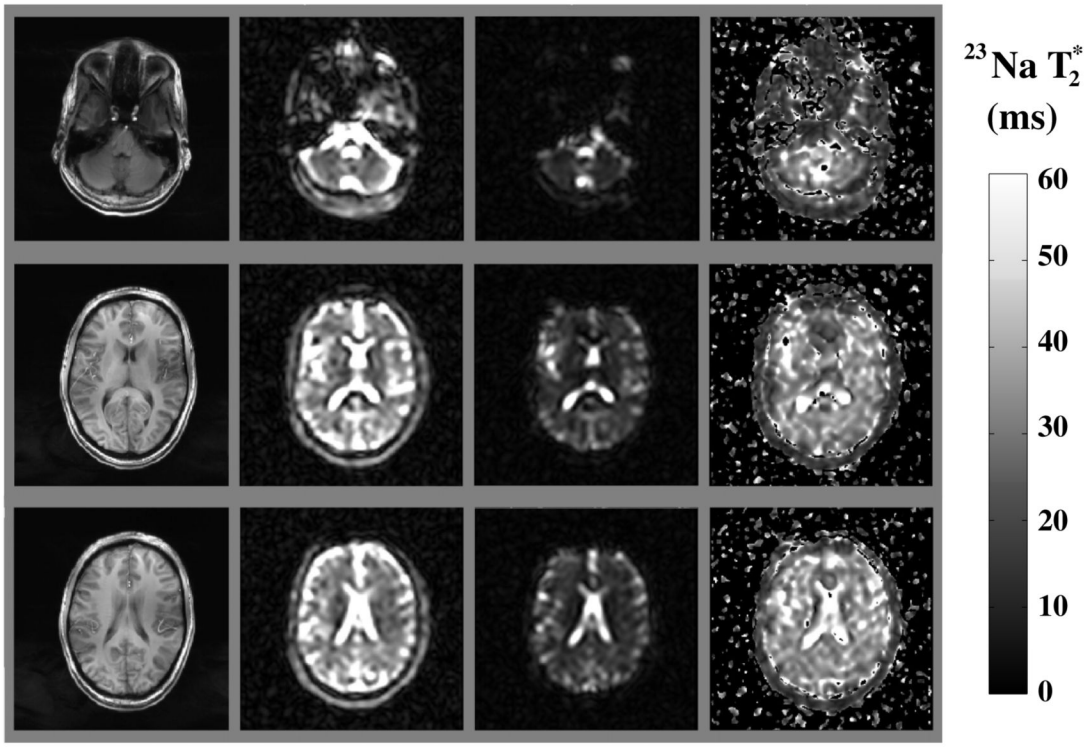

FIG. 1.

T_1-weighted axial brain images (8 mm thick) from a healthy volunteer at 7 T (left column), single-quantum sodium images of the corresponding slices at TE = 12 ms and TE = 37 ms (center columns), and T_2^* parametric map of the selected brain slices (right column). The short TE images were acquired once, while the long TE images were averaged three times, yielding total acquisition time of 63 min (see Materials and Methods section).

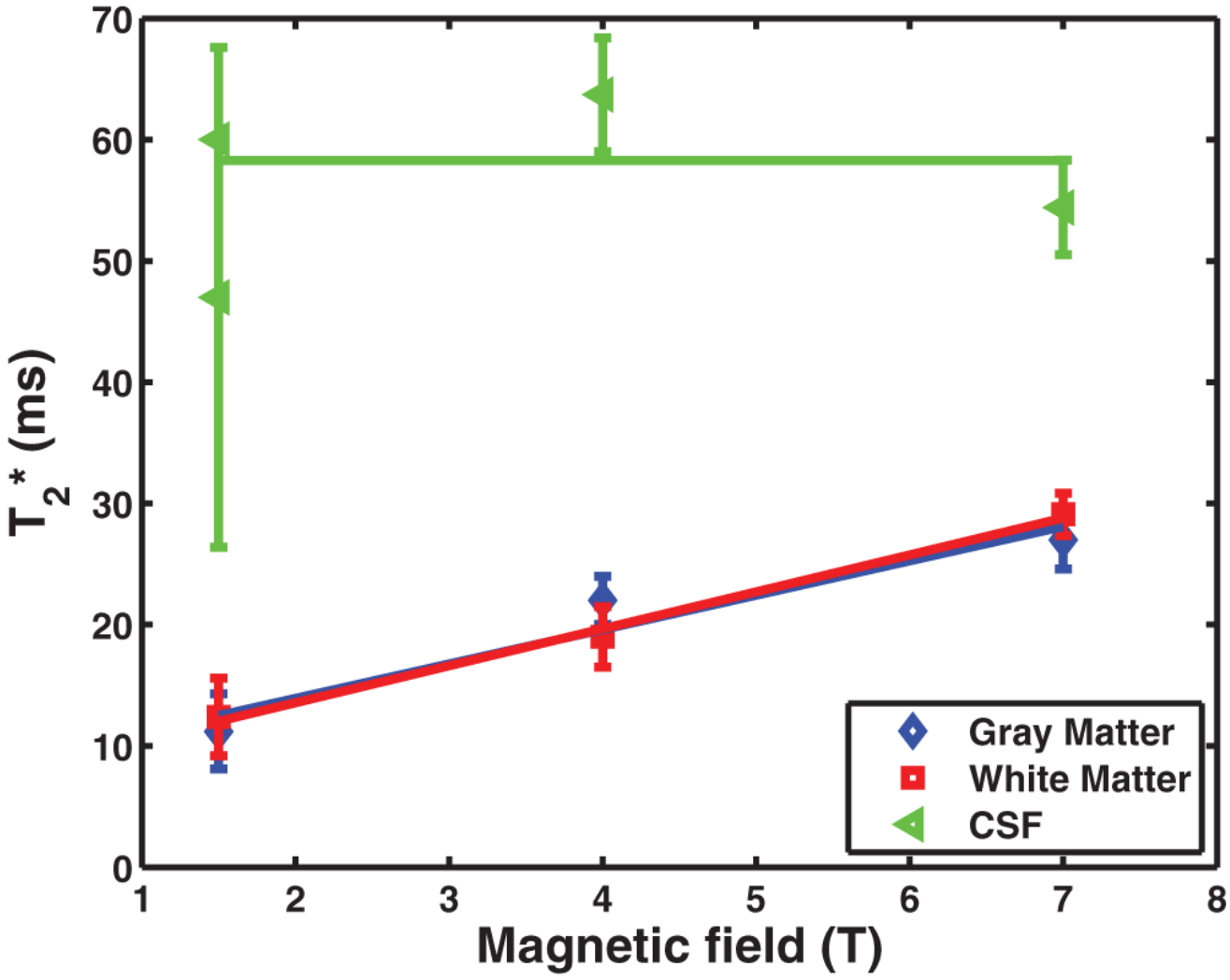

FIG. 2.

The plot shows the sodium long T_2^* component dependency on magnetic field strength in gray matter, white matter, and CSF. Mean values and corresponding standard errors on the mean are reported for the three tissue types. The values at 1.5 T and 4 T field strengths are taken from the literature (3,9,10). T_2^* values at 7 T are from Table 1.

Table 1

Mean ± SEM Sodium T_2^* Relaxation Times (Milliseconds) at 7 T in the Various Gray Matter (GM) and White Matter (WM) Brain Regions[a]

		T_2^* (ms)		
		Right	**Left**	**Average**
GM	Frontal cortex	27 ± 3	28 ± 4	27 ± 2
	Occipital cortex	29 ± 1	29 ± 1	29 ± 1
	Putamen	21± 2	24 ± 2	23 ± 2
	Thalamus	32 ± 3	32 ± 3	32 ± 2
	Average	28 ± 2		
WM	Frontal WM	32 ± 1	31 ± 3	31 ± 1
	Occipital WM	28 ± 1	29 ± 1	28 ± 1
	Periventricular WM	37 ± 2	32 ± 2	34 ± 1
	Cerebellum	25 ± 1	24 ± 1	24 ± 1
	Splenium of CC	28 ± 2		
	Average	29 ± 2		
CSF		53 ± 5	56 ± 7	54 ± 4

[a] CC: corpus callosum.