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RESEARCH PAPER

REGIONAL CEREBRAL RELAXATION TIMES MEASURED BY MAGNETIC RESONANCE IMAGING AT 3.0 TESLA

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ABSTRACT
Brain tissue T_1 and T_2 relaxation times were measured at 3.0 T from a total of 8 (M/F = 5/3) healthy volunteers, selecting 9 regions of interest (ROIs) in the prefrontal, frontal, parietal, occipitoparietal and hippocampal regions. Apart from the prefrontal region, the other four ROIs were selected within the left and right brain hemispheres. The selected ROIs contained either grey matter (GM) or white matter (WM) or both. The T_1 measurements were done using the saturation recovery imaging method at 8 different repetition times (TRs) whereas the T_2 measurements were carried out using the multiple spin-echo imaging method at 12 different echo times (TEs). The average T_1 values (mean ± SE, ms) from 4 (M/F = 2/2) volunteers were: 1942 ± 29 (prefrontal GM), 1203 ± 40 (frontal WM), 1217 ± 21 (parietal WM), 1425 ± 29 (occipitoparietal GM/WM), and 1435 ± 62 (hippocampi). The average T_2 estimates (mean ± SE, ms) from another group of 4 (M/F = 3/1) volunteers were: 147 ± 9 (prefrontal GM), 121 ± 3 (frontal WM), 131 ± 4 (parietal WM), 127 ± 1 (occipitoparietal GM/WM), and 142 ± 8 (hippocampi). Neither T_1 nor T_2 relaxation times differed significantly between the two brain hemispheres by paired t-tests ($p > 0.05$). However, regional T_1 was found to vary significantly ($p < 0.01$) while regional T_2 did not vary significantly ($p = 0.07$) by one-way ANOVA. These findings are consistent with theory and published data for the ROIs studied. The results could thus serve as a reference data set for brain MRI pulse sequence optimisation at 3.0 T and could as well be useful in multicentre data set comparisons aimed at developing a database of in vivo brain relaxation times.

Keywords: *MRI, brain, saturation recovery, spin echo, relaxation time*

INTRODUCTION
The choice of a suitable pulse sequence to achieve a desired image contrast in magnetic resonance imaging (MRI), and the optimisation of any MRI method at 3.0 T or a greater field strength depend on the knowledge of the fundamental nuclear magnetic resonance (NMR) properties of biological tissues at the given field strength (Wansapura *et al*., 1999; Kim *et al.*, 1994). Accurately quantified tissue NMR

relaxation times are important for characterising these tissue NMR properties and for optimising contrast in relatively new imaging methods such as functional MRI, spectroscopic imaging and perfusion imaging (Wansapura *et al*., 1999). The two most important relaxation times that are usually measured *in vivo* in this regard are the spin-lattice (T_1) and spin-spin (T_2) relaxation times.

T_1 relaxation time strongly depends on the external magnetic field strength, B_o (Koenig and Brown, 1984). Even though T_1 may be estimated at any field strength based on theoretical predictions, it is suggested that such derived results will be significantly erroneous and may not be adequate for accurate contrast calculations (Wansapura *et al*., 1999). Brain tissue T_2 relaxation time on the other hand partly depends on B_o but there is no evidence for this behaviour from theory (Wansapura *et al*., 1999; Posse *et al*., 1995). Consequently, quantitative measurements of brain tissue NMR relaxation times at $B_o \geq 3.0$ T are needed and will serve as essential reference data for advanced MR imaging and other quantitative NMR techniques such as MR spectroscopy. Furthermore, reference relaxation data in healthy brain is essential for their diagnostic value as they vary in disease (Laule *et al*., 2007; Whittall *et al*., 1999).

However, it appears from the literature that investigations of relaxation times of human brain tissue at field strengths of 3.0 T and above are limited. Secondly, due to the differences in the chosen regions of interest (ROIs), some brain regions, including those investigated in this report, have been considered by very few research groups. The objective of this study therefore was to accurately measure relaxation times at 3.0 T of both grey matter (GM) and white matter (WM) structures in normal human brain, using saturation recovery and multiple spin-echo imaging methods for T_1 and T_2 measurements, respectively. The measured relaxation times could be applicable in future studies such as those aimed at MRI pulse sequence optimisation and diagnostic MRI (where pathology is associated with changes in relaxation times).

MATERIALS AND METHODS

Subjects

With permission from the West of Scotland Research Ethics Committee 4 (WoSREC4), a total of 8 (5 males, 3 females) healthy subjects participated in the study. Brain tissue T_1 (M/F = 2/2, mean age = 32.0 years) and T_2 (M/F =3/1, mean age = 32.5 years) relaxation times were each measured separately in 4 subjects. The 4 subjects in each one of the two sets of measurements were randomly assigned. Each volunteer gave prior informed written consent. No volunteer had any neurological or psychiatric disorder.

Magnetic resonance imaging

Magnetic resonance imaging for the measurement of both relaxation times were performed on a 3.0 T GE MR scanner equipped with an eight-channel receive-only head coil.

For the measurements of both T_1 and T_2, axial slices covering the whole brain were planned along the hippocampal angle. Each slice was 3 mm thick without slice gaps; and a matrix of 256 x 128 pixels was used to give a reasonable compromise between image resolution and total experimental time. A field of view (FOV) of 25.6 x 25.6 cm^2 was selected to cover the entire axial image, including the hippocampi. For each subject, a high resolution T_1-weighted 3D image of the whole brain was also acquired using an axial slab along the hippocampus. This high resolution axial 3D image gave a better grey/white matter contrast than the corresponding T_1- and T_2-weighted images. These high-resolution 3D MR images served as references during ROI selection in the respective T_1- and T_2-weighted images by co-registration of a given relaxation time weighted image to its corresponding 3D image. Thus all images of any one volunteer acquired within the same scan session for the estimation of either T_1 or T_2 were corrected for rotational errors. The advantage of using axial slices for this study is that in

all acquisitions, they provide access to slices that contain sufficient grey and white matter for the placement of ROIs. Measurements of the T_1 and T_2 relaxation times were performed in separate examination sessions as follows.

T_1 Measurements

T_1 measurements were carried out using a saturation recovery method with a variable *TR* spin-echo imaging sequence. A constant echo time (*TE*) of 11.0 ms was maintained, while axial images (Fig. 1) were acquired at eight successive *TR* times of 200, 350, 550, 750, 1000, 1500, 2000 and 4000 ms.

T_2 Measurements

For T_2 measurements, a multi spin-echo pulse sequence was used. A constant *TR* value of 3000 ms was maintained and twelve T_2-weighted images (Fig. 2) were acquired using the following *TE* values: 16, 25, 30, 32, 48, 50, 60, 64, 75, 90, 100 and 120 ms. The multi spin-echo pulse sequence on the GE MR scanner used for the measurements produces images at four echo times for each user-selected *TE* value. The *TE* values of these acquired images

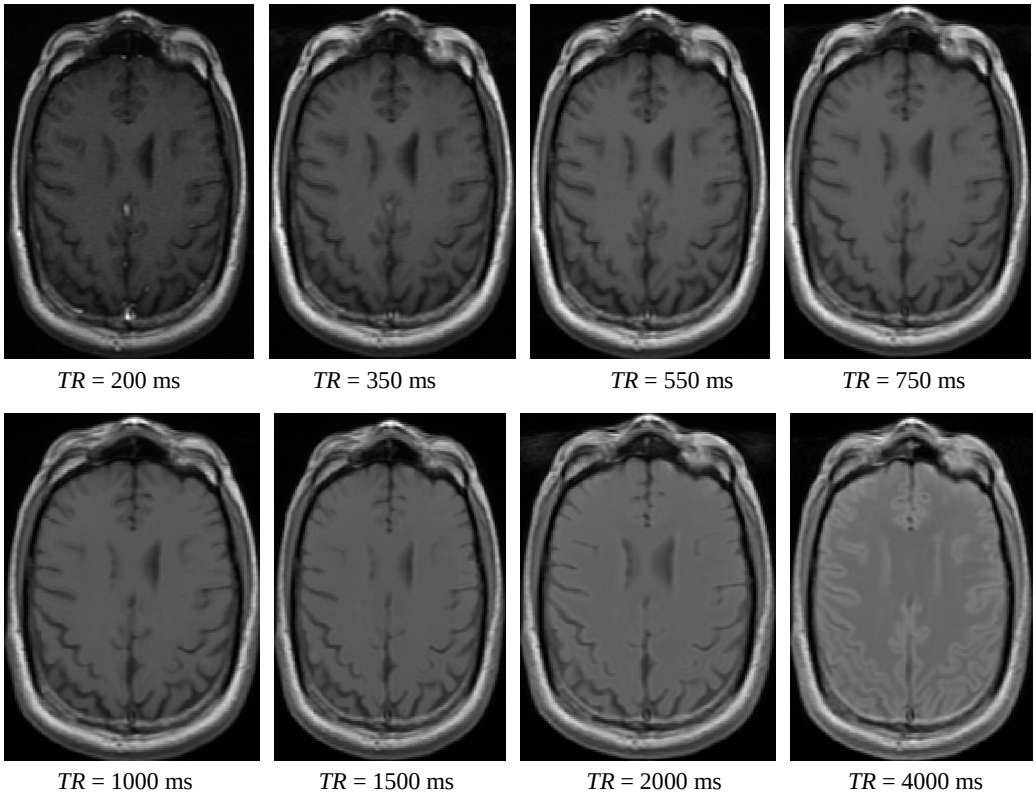

Fig. 1: Stack of axial MR images of a healthy subject acquired at varying repetition times (*TR*) using a constant echo time (*TE*) of 11.0 ms

Note the increasing image intensity as TR increases from 200 ms (top row) to 4000 ms (bottom row). These intensities were measured and the values obtained were then plotted against their respective TR values. A nonlinear least square monoexponential recovery (curve) fitting was then performed on the plot to estimate T_1 relaxation time.

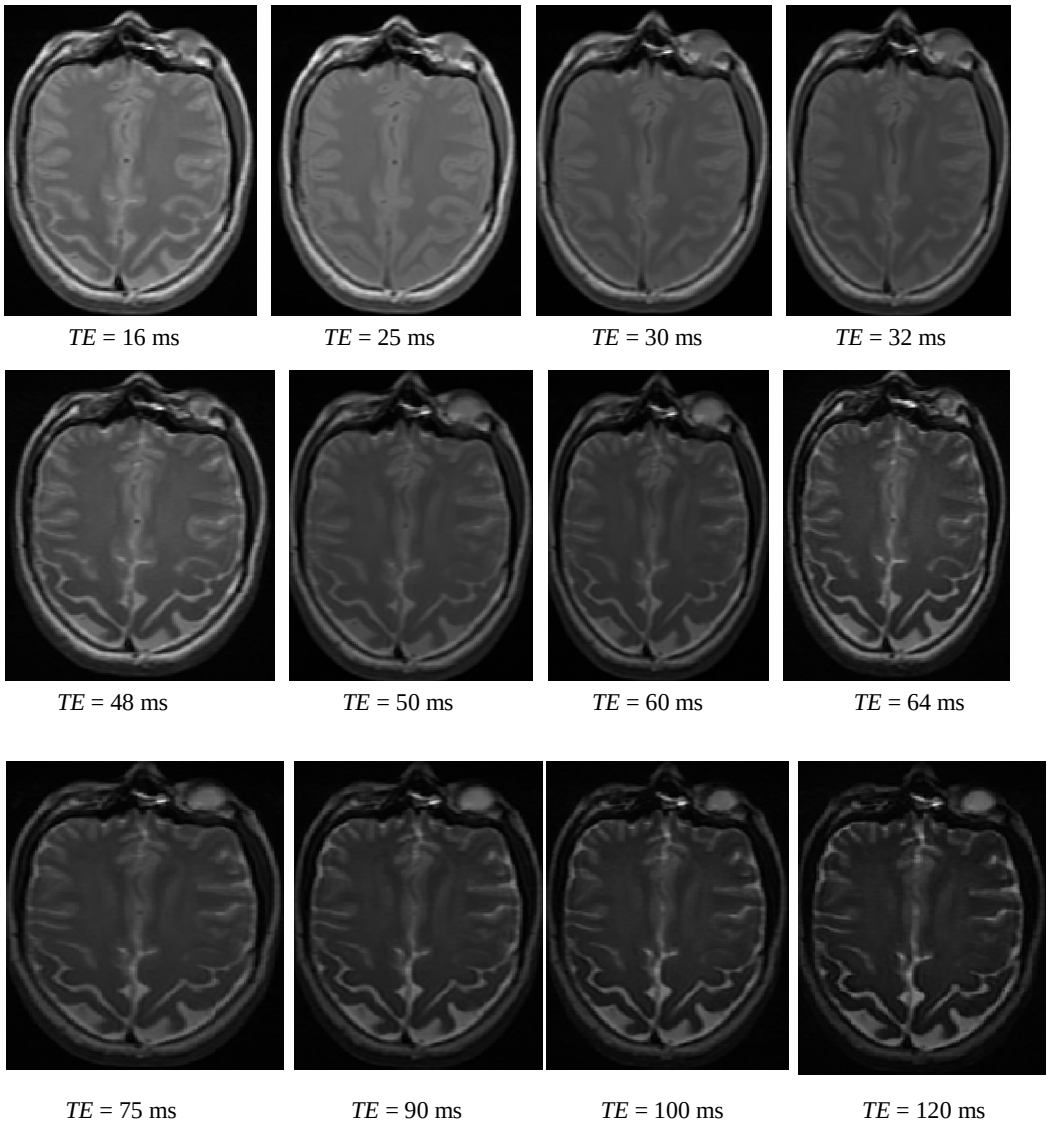

Fig. 2: Stack of axial MR images of a healthy subject acquired at varying echo times (*TE*) using a constant repetition time (*TR*) of 3000 ms

Note the decreasing image intensity as TE increases from 16 ms (top row) through 48 ms (middle row) to 120 ms (bottom row). These intensities were measured and the values obtained were then plotted against their respective TE values. A nonlinear least square monoexponential decay (curve) fitting was then performed on the plot to estimate T_2 relaxation time.

are multiples of the user-selected *TE* value. For the T_2 measurements in this study, three *TE* values were selected: 16, 25 and 30 ms. Thus *TE* = 16 ms produced images at *TE* times of 16, 32, 48 and 64 ms. The *TE* values of 25 and 30 ms also produced four images each, resulting in

twelve image data sets at the above *TE* times.

ROI selection and estimation of relaxation times

Using the T_1- and T_2-weighted images acquired (Figs 1 and 2), four anatomical sites were chosen in each hemisphere, plus one prefrontal region of the brain. This resulted in a total of nine ROIs per subject, as shown in Fig 3a-b. Care was taken in selecting the ROIs, which did not include the ventricles or extra-axial CSF. The shapes of the ROIs were circular, rectangular or freehand-drawn (in the Image-J software, version 1.46r), depending on which shape best-fitted the target area.

Estimates of the brain tissue T_1 relaxation times were obtained from a nonlinear least square monoexponential recovery fit of the image intensities, $A_z(TR)$ (measured from each ROI labelled 1-9 in Fig 3a-b) at their respective *TR* values. The fitting method solved the following equation for T_1:

$$A_z(TR) = A_\infty \times [1 - \exp(-TR/T_1)] \quad (1)$$

where A_∞ is the image intensity at the longest possible *TR* time.

Estimates of the brain tissue T_2 relaxation times on the other hand were obtained from a nonlinear least square monoexponential decay fit of the image intensities, $A(TE)$ (measured from each ROI labelled 1-9 in Fig 3a-b) at their corresponding *TE* times. The fitting method solved the following equation for T_2:

$$A(TE) = A_o \exp(-TE/T_2) \quad (2)$$

where A_o is the maximum image intensity at $TE \approx 0$ ms.

(a) (b)

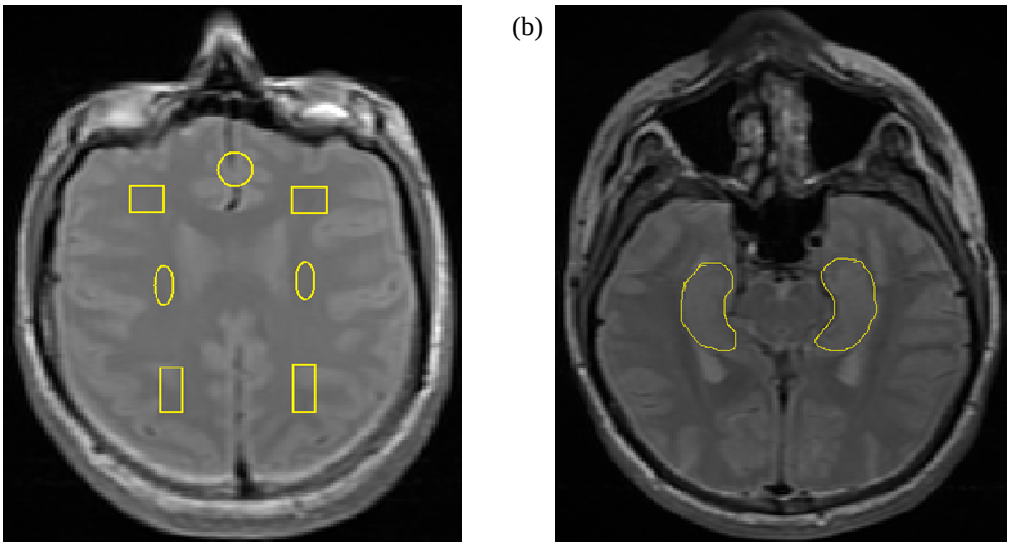

Fig. 3: MRI of an axial slice through the prefrontal brain region (a) and the bilateral hippocampi (b) in a healthy volunteer

The 3 mm thick slices shown in Fig 3a-b are typical of those chosen for all data analysis. The ROIs are indicated by a circle (1), squares (2 and 3), ovals (4 and 5), rectangles (6 and 7) and freehand-drawn (8 and 9) selections. The numbers correspond to the brain structures listed in Tables 1-3.

Curve fitting for the estimation of both T_1 and T_2 relaxation times were performed using the curve fitting toolbox in MATLAB (version 7.8.0.347, R2009a).

Statistical analysis

Measured relaxation times from ROIs drawn in the left and right hemispheres were compared using the *paired t-test*. Assessment of the variations of both relaxation times across the nine ROIs was performed by *one-way ANOVA*. The two statistical tests were chosen after the data was tested to follow a normal distribution using the *Anderson-Darling Normality Test*. All statistical tests were performed using the Minitab software package (version 16, Minitab Inc.). A critical value of $p < 0.05$ was used to accept a statistically significant difference in the comparisons.

RESULTS

Averages of the T_1 and T_2 relaxation times (n = 4 in each case) measured from the nine ROIs drawn in Fig 3a-b are summarised in Tables 1-3. Apart from the prefrontal GM region (Table 1), relaxation times were compared (see fourth columns of Tables 2 and 3) between the left and right hemispheric structures: frontal WM, parietal WM, hippocampus, and occipitoparietal region containing a GM-WM mix. For these four bilateral brain regions, the measured relaxation times were again averaged (see fifth columns of Tables 2 and 3). The uncertainties of all measurements are given in terms of the standard error (SE), calculated as a ratio of the standard deviations of the measurements to the square root of the sample size measured. The goodness of the relaxation curve fits were assessed in terms of their R^2 values generated by the nonlinear least square curve fitting routine in MATLAB; the worst R^2 value was 0.74.

All the T_1 estimates in the left hemisphere were found to be slightly greater than those in the

Table 1: Average relaxation times in the prefrontal GM region

Region [label]	**T_1 [ms (± SE)]**	**T_2 [ms (± SE)]**
Prefrontal GM [1]	1942 (29)	147 (9)

Table 2: T_1 relaxation times compared between left and right hemispheric ROIs drawn within four brain regions

Region [labels]	**Left hemisphere [ms (± SE)]**	**Right hemisphere [ms (± SE)]**	**Comparison (p-value)**	**Average [ms (± SE)]**
Frontal WM [2, 3]	1235 (52)	1170 (64)	0.07	1203 (40)
Parietal WM [4, 5]	1238 (21)	1196 (36)	0.12	1217 (21)
Occipitoparietal GM/WM [6, 7]	1441 (40)	1410 (47)	0.24	1425 (29)
Hippocampus [8, 9]	1439 (96)	1432 (94)	0.64	1435 (62)

Table 3: T_2 relaxation times compared between left and right hemispheric ROIs drawn within four brain regions

Region [labels]	Left hemisphere [ms (± SE)]	Right hemisphere [ms (± SE)]	Comparison (p-value)	Average [ms (± SE)]
Frontal WM [2, 3]	122 (5)	120 (4)	0.49	121 (3)
Parietal WM [4, 5]	128 (4)	134 (8)	0.37	131 (4)
Occipitoparietal GM/WM [6, 7]	127 (1)	127 (2)	0.88	127 (1)
Hippocampus [8, 9]	134 (15)	150 (5)	0.27	142 (8)

right hemisphere but this difference was not statistically significant ($p > 0.05$). The one-way ANOVA results showed that while T_1 varied significantly ($p < 0.01$) across the brain regions, regional T_2 did not vary significantly ($p = 0.07$). The prefrontal GM relaxation times were included in the respective one-way ANOVA tests.

DISCUSSION

Generally, T_2 estimates were only about a tenth of the T_1 estimates, consistent with theoretical predictions. Longest T_1 and T_2 relaxation times were observed in grey matter regions. Both T_1 and T_2 were not significantly different between the two hemispheres of the brain, indicating an approximate equality of relaxation times between contralateral sections of the brain. However, left hemispheric T_1 estimates showed some tendency of higher values than those estimated from the right hemisphere. Intrahemispheric T_1 relaxation times varied widely among the various brain structures. However, T_2 relaxation times did not vary significantly among the brain structures in both hemispheres.

At 4.0 T, Kim *et al* (1994) also observed that the average T_1 of GM was greater in the left than in the right hemisphere, even without performing any significance test on their results. Similarly, Wansapura *et a*l (1999) also observed at 3.0 T that out of nine ROIs in each hemisphere, eight ROIs in the left had greater T_1 estimates than the corresponding regions in the right hemisphere. They only found this difference to reach statistical significance in GM insula. Garber *et al* (1989) also reported higher T_1 values in the left than in the right hemispheres in GM and WM regions at 1.5 T. These findings compare with those reported in this study.

Hemispheric T_2 differences were not significant in all brain regions considered in this study. Even though they did not study the same regions as have been studied in this report, Wansapura *et al* (1999) did not find any difference in T_2 between the two hemispheres for all their nine ROIs. They reported that they could not cite any literature reporting hemispheric T_2 differences. They attributed the T_1 differences they observed between the two hemispheres to non-uniformity of the B_1 field caused by the non-uniform characteristics of brain tissue. Tissue-type differences give rise to standing waves in the head which cause variation in the flip angles across the brain with the application of the RF pulses (Tofts, 2003; Helms, 2008). The extent of the standing wave effect depends on the tissue water proton density of the region of interest. Thus, Wansapura *et al* (1999) did not find differences in the relaxation times between left and right ROIs selected on the image of a uniform $MnCl_2$-doped water phantom.

T_1 values in GM regions were observed to be

greater than those in WM regions. Even though a similar observation has been made previously (Wansapura *et al*., 1999), this difference was not found to be significant in this study. The reason for this insignificant difference in GM/ WM T_1 may be due to the dependence of T_1 on B_o field strength (Bottomley *et al*., 1984; Fischer *et al.,* 1990), so that at high fields ($B_o \geq$ 3.0 T), tissue relaxation rates approach that of water resulting in low GM/WM T_1 contrast (Wansapura *et al*., 1999). In each hemisphere, the hippocampi, which are GM structures, showed the longest average T_2 relaxation time compared to the other structures, while the frontal WM regions had the shortest average T_2 relaxation time. This observation compares with the finding of Wansapura *et al* (1999); they found the highest and lowest T_2 estimates in the occipital GM and frontal WM, respectively. The shorter T_2 relaxation times in WM could be attributable to its high ferric iron content (Drayer *et al*., 1986), which is reported to reduce T_2 relaxation times (Drayer *et al*., 1986; Ye *et al.,* 1996; Vymazal *et al*., 1995; Vymazal *et al*., 1996).

Generally, studies of hemispheric and regional differences in quantitative T_1 and T_2 measurements in the brain are not based on a consistent selection of ROIs or subjected to tests of statistical significance (Wansapura *et al*., 1999). It is therefore difficult to do a more rigorous comparison between the results reported here and those in the literature. Nonetheless, the results of this study are consistent with those reported in the literature for the selected brain regions at the respective field strengths.

CONCLUSION

T_1 and T_2 relaxation times have been accurately measured in nine brain regions of healthy volunteers. Generally, regional brain T_1 was observed to be slightly higher in the left hemisphere but T_2 variation did not show any clear trend between the two hemispheres. The estimates reported here are consistent with theoretical predictions and with published data for relaxation time measurements in the selected anatomical regions at various field strengths. Thus this report provides a comprehensive data set, which may prove useful as a reference for optimisation of pulse sequences for brain imaging at 3.0 T, as well as in multicentre comparisons of measured relaxation times for the anatomical regions studied, especially for purposes of diagnostics.

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LIST OF ABBREVIATIONS

ANOVA = Analysis of Variance
CSF = Cerebrospinal fluid
GM = Grey matter
GE = General Electric
MR/MRI = Magnetic Resonance/ Magnetic Resonance Imaging
NMR = Nuclear magnetic resonance
RF = Radiofrequency
ROI = Region of interest
T_1 = Longitudinal (or spin-lattice) relaxation time
T_2 = Transverse (or spin-spin) relaxation time
TE = Echo time
TR = Repetition time
WM = White matter

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