Quantitative Lithium Spectroscopy in the Normal Human Brain on a 3T Clinical Scanner

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Introduction:

Lithium (Li) is the principal treatment for numerous neuropsychiatric conditions and for conditions such as bipolar disorder is generally effective at serum concentrations of 0.8mmol/L[1]. Since the safe serum range of Li is relatively narrow, regular monitoring by blood testing is required to prevent toxicity. However, serum levels are thought to be a poor indicator of the concentration of Li in brain tissue[1]. Magnetic resonance spectroscopy (MRS) has previously been used to detect ^{7}Li in the human brain in patients with bipolar disorder but adequate signal to noise levels have been limited by long scan times when full localisation has been attempted[2] or localisation has been limited to essentially whole brain voxels[3]. Here we report development of a quantitative ^{7}Li spectroscopic imaging (SI) protocol using a clinical 3T scanner, with 1D spatially localised measurements of ^{7}Li obtained in a complete examination time of less than 20 minutes, and determine the T_1 of ^{7}Li in human brain at 3 Tesla.

Methods:

Subjects: Seven healthy male subjects (age 22±4years) were recruited and given lithium carbonate (mean dose = 942 ± 97.6 mg, duration = 11±1days). The study was approved by the local ethics committee and all patients gave written informed consent.

Scanner & Coil: ^{7}Li spectroscopy was performed using a 3T Philips Achieava scanner equipped with a second broadband channel for non-proton nuclei. An 8cm diameter circular surface coil (tuned to 49.6MHz) was constructed in-house which incorporated an internal reference marker. This marker contained an aqueous solution of 50mM LiCl solution with 135mM $DyCl_3$ added as a shift reagent, which was found to be the most stable preparation for a surface concentration standard (T_1 17s).

T1 measurement: To determine the optimal scan conditions for *in vivo* ^{7}Li spectroscopy at 3 Tesla, T_1 was measured in the brain using non-localised, steady-state saturation measurements with adiabatic half passage excitation and 20 repetition times ranging between 0.5 and 10 seconds. The theoretical spatial B_1 distribution of the surface coil[4] was used in a Bloch simulation of the adiabatic pulse sequence in order to determine the reliability of the saturation with depth from the coil and hence estimate error in the T_1 value calculated from these unlocalised measurements. This was further confirmed using experimental T_1 measurements in an extended aqueous lithium phantom.

Quantitative spectroscopic imaging: The surface coil was positioned over the left fronto-parietal region (figure 1). Variation in coil performance between subjects was assessed by measuring the pulse width for 90° excitation of the surface marker (fully relaxed TR=60s, hard pulse, 4 flip angles, 1 average). Spatially localised ^{7}Li data were then acquired using a 1D-SI sequence with the spatial encoding plane positioned parallel to the coil plane (adiabatic half passage excitation, fully relaxed TR 6500ms, 12 encode steps, 12 cm FOV, 3 averages, weighted k-space averaging, total scan time ~4mins). Calculation of ^{7}Li concentration was made using knowledge of the signal variation with depth from the coil together with the signal from the known concentration of the surface marker.

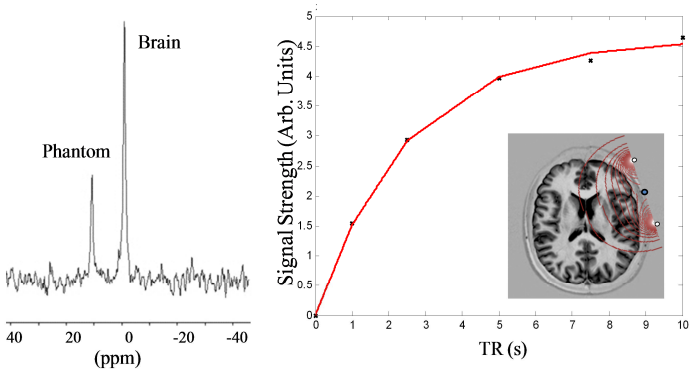

Figure 1: Typical unlocalised spectrum (*left*) and steady-state saturation curve (*right*) from which T_1 was calculated. *Inset* shows coil location over frontal-parietal region.

Results:

Figure 1 shows an example spectrum from the T_1 data in one subject. Direct fitting of the steady-state saturation data showed the T_1 of ^{7}Li in human brain at 3T to be 2.0±0.4s (n=7). The simulated flip-angle distribution suggested the maximum error in T_1 from assuming uniform 90° excitation was <5%. Figure 2 shows a plot of Li spectra acquired using the 1D-SI sequence. Across all subjects a mean signal to noise ratio (SNR) of 15 was achievable at 3cm depth from the coil, with signal measurable to 8cm depth. Mean plasma concentration on the day of the study was 0.7±0.3mmol/L while lithium concentration was found to be typically 0.4-0.5mmol/L within brain tissue (~70% of plasma concentration).

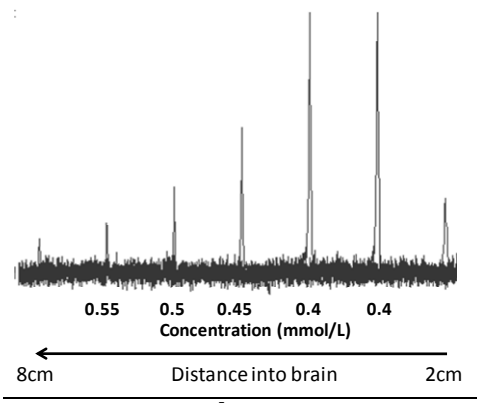

Figure 2: Plot of in vivo ^{7}Li 1D-SI spectra with depth into brain with calculated concentration.

Discussion:

Spatially localised measurements of ^{7}Li concentration were made in the brains of healthy volunteers with good SNR in an examination lasting under 20 minutes. Brain lithium T_1 was measured to be 2.0s which is comparable to recent measurements at high field in rats[5] but lower than previous data at 1.5T[2]. Brain lithium concentration was measured to be approximately 70% of plasma levels in healthy subjects. While this 1D-SI measurement does not provide full localisation, the resolution is sufficient to separate gray and white matter.

Acknowledgements:

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References:

[1] Komoroski, R.A., et al., *NMR in Biomed*, **18**:67-73, (2005).
[2] Girard, F., et al., *MAGMA*, **13**:1-7, (2001).
[3] Forester B.P., et al., *Am J Ger Psych*, **17**:13-23, (2009).
[4] Haase A., et al., *J Magn Reson*, **56**: 401-412, (1984).
[5] Ramprasad S., et al., *Magn Reson Imag*, **23**: 859-863, (2005).