Brain Lithium and Sodium Concentration in Lithium-treated Euthymic Bipolar Disorder Subjects

F. E. Boada[1], M. Phillips[2], Y. Qian[3], and D. Kupfer[2]
[1]Radiology and Bioengineering, University of Pittsburgh, Pittsburgh, PA, United States, [2]Psychiatry, University of Pittsburgh, Pittsburgh, PA, United States, [3]Radiology, University of Pittsburgh, Pittsburgh, PA, United States

INTRODUCTION

Lithium carbonate treatment is one of the preferred means for treating Bipolar Disorder (BPD). Lithium has remarkable mood-regulating properties, but also presents with dangerous and life-threatening side effects. Management of such side effects requires using a dose-escalation procedure aimed to establish a serum lithium concentration (SLC) in the range of 0.5-1.0mM. This procedure, however, is only of limited success and, consequently, means to directly or indirectly monitor brain lithium concentration (BLC) have been actively sought for. Whole brain MRS protocols had been the mainstay for non-invasive BLC measurement at clinical field strengths (<3T) [1,2,3]. Such whole-brain MRS protocols are, however, limited by excessive partial-voluming effects and lack of spatial information. There is evidence that lithium competes with sodium trans-membrane channels and that lithium treatment leads to regulation of otherwise abnormal intracellular sodium concentration [4,5]. Consequently, normalization of brain sodium concentration (BSC) might be a surrogate marker for lihitum's effects in the brain. We demonstrate an Ultra-High-Field (UHF) imaging protocol for concurrent mapping of BLC and BSC in BPD subjects. Our results suggest normal BSC on lithium-treated euthymic BPD subjects.

METHODS

Subjects were scanned on a whole body Magnetom TIM 7 Tesla scanner (Siemens AG, Erlangen, Germany) using an approved Institutional Review Board (IRB) protocol. Each session commenced with the acquisition of standard Gradient recalled (GRE) and high-resolution T1 (MPGRAGE) proton images used for co-registration and volumetric measurements, respectively. The lithium data acquisition took place using a single-tuned, 8-channel RF coil (Stark Contrast, Erlangen, Germany) and the sodium acquisition took place using a single-tuned, home-built, 16-channel RF coil. Acquisition of the sodium images (TE/TR=0.3/100ms, Voxel=0.008cc, 12 minutes) was performed using a twisted projection acquisition (TPI, Fig. 1, left) [6] while lithium images (TE/TR=0.8/1000ms, Voxel=3.75cc, 32 minutes) were obtained using an acquisition-weighted stack of spirals sequence (AWSOS, Fig. 1, right) [7]. Lithium multi-channel images were obtained as the sum of squares with no coil uniformity corrections. Lithium spectra as well as phantom images were also obtained for all subjects in order to estimate longitudinal relaxation effects and molar content, respectively.

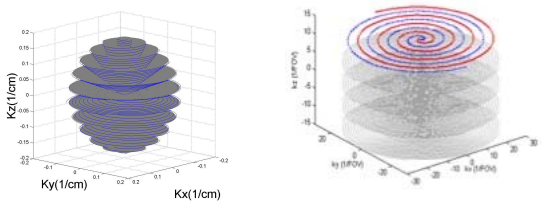

Figure 1: k-space trajectories for the (left) *TPI and (right) AWSOS sequences.*

RESULTS

Figure 2 presents selected partitions from the GRE (top row), lithium (middle row) and sodium (bottom row) images acquired on one of the subjects in the study. The partitions correspond to the same spatial location and document significant heterogeneity in the BLC. Notably, the concentration of lithium in the cerebrospinal fluid (CSF) spaces and the scalp is very high. Comparison of *in vivo* data with phantom data using the same coil and data acquisition ruled out RF inhomogeneity as the cause of this BLC heterogeneity. Sodium images, on the other hand, documented a normal BSC for this small euthymic subject pool.

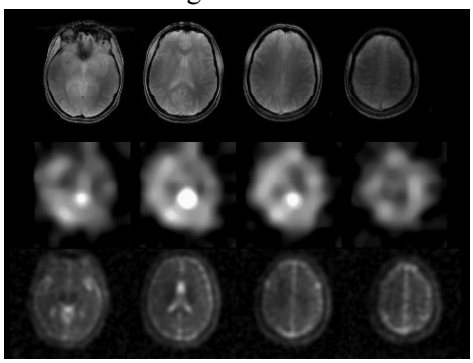

Figure 2: *Selected partitions from GRE (top), lithium (middle) and sodium (bottom) images acquired on one of the study subjects.*

CONCLUSIONS

Our results to date demonstrate that UHF MRI techniques can be used effectively for measuring BLC *in vivo* in BPD subjects and that concurrent measurement of BLC and BSC is suitable for the practical constraints an *in vivo* imaging study. The BSC distribution in euthymic BPD subjects on Lithium Carbonate was found to be close to that of human volunteers. Further improvements in image quality are still possible through the use of larger k-space coverage per RF excitation as well as self-calibrated trajectories such as TPI.

REFERENCES: [1] Gonzalez RG, et al., AJNR, **14**:1027, 1993. [2] Soares JC, et al., Biol. Psychiatry, **49**:437, 2001. [3] Forester BP, et al., Bipolar Disord., **10**:691, 2008. [4] El-Mallakh RS, et al., Biol. Psych., **37:** 235, 1995. [5] Huang X, et al., Bipolar Disord., **9**:298, 2007 [6] Boada FE et al., MRM, **37:**706, 1997. [7] Qian Y, et al., MRM, **60**:135, 2008. **Supported in part by PHS Grant R01-MH088370-01.**