Lithium brain absorption in the elderly versus younger patients with bipolar disease.

Maria Otaduy[1], Ivan Aprahaiam[2], Rodolfo Ladeira[2], Rodrigo Machado-Vieira[3,4], Claudia Leite[5], Wagner Gattaz[6], and Orestes Forlenza[2]

[1]Laboratory of Magnetic Resonance in Neuroradiology, LIM 44, Institute and Department of Radiology, University of São Paulo, São Paulo, São Paulo, Brazil, [2]Laboratory of Neuroscience, LIM 27, Institute and Department of Psychiatry, University of São Paulo, São Paulo, São Paulo, Brazil, [3]Laboratory of Neuroscience, LIM 27, Institute and Department of Psychiatry, University of São Paulo, São Paulo, Brazil, [4]Department of Health and Human Services, National Institute of Mental Health, National Institutes of Health, Bethesda, MD, United States, [5]Laboratory of Magnetic Resonance in Neuroradiology, LIM 44, Institute and Department of Radiology, University of São Paulo, Sao Paulo, Brazil, [6]Laboratory of Neuroscience, LIM 27, Institute and Department of Psychiatry, University of São Paulo, São Paulo, Sao Paulo, Brazil

TARGET AUDIENCE: Psychiatrists, neurologists, radiologists and MR spectroscopists will potentially benefit from this information.

PURPOSE: In vivo 7Li-MRS is a unique tool to measure the lithium concentration in the brain and as such it can aim in the understanding which are the factors that influence lithium brain absorption, since clinical response to lithium treatment varies from patient to patient. In this study we wanted to assess how age influences lithium brain absorption. For that purpose we compared a group of young (20-40yrs) to a group of elderly (60-80yrs) patients with bipolar disease (BD) under lithium therapy.

METHODS: A total of 27 of patients with BD (type I and II) were included in the study. Patients were divided in two groups: young (range: 21-34 yrs) and elderly (63-82 yrs). The young group consisted of 15 patients (mean age=27±5 yrs) and the elderly of 12 patients (mean age=73±6 yrs). All patients were under lithium treatment and euthymic at the date of examination. Plasma lithium levels were obtained in the same week of examination. Patients underwent a 7Li-MRS exam with a 3T whole body Intera Achieva scanner (Philips Healthcare, Best, Netherlands) and a double tuned 7Li-1H head coil (RAPID Biomedical). The spectroscopy sequence used was a slice selective ISIS sequence (TE/TR= 95.6μs/5s) with an adiabatic rf pulse exciting a 60mm thick slab, covering most part of the brain from the level of the corpus callosum (Fig. 1). Afterwards the same 7Li-MRS sequence was applied on a 1.0 mmol LiCl water solution doped with gadolinium, to be used as a concentration reference. Axial high resolution 1mm^3 volumetric images were also obtained to be used for tissue segmentation into CSF, grey and white matter within the selected MRS slice. The integral of the single lithium peak was quantified after spectral apodization, zero filling and manual phase correction. After correcting for the different coil load and temperature in the phantom and patient, lithium brain concentration was calculated according to the method proposed by Soares et al.[1]. Lithium brain concentration was compared to lithium plasma levels in order to assess lithium brain absorption by the lithium brain to plasma ratio Li brain/Li plasma.

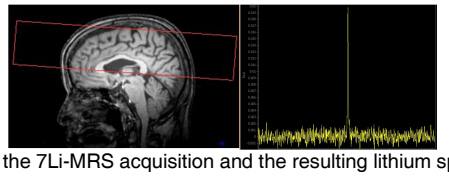

Figure 1. Brain slice selected in the 7Li-MRS acquisition and the resulting lithium spectrum showing a single peak.

RESULTS: The mean Li brain/Li plasma was equal for both groups (young: 0.53±0.22 and elderly: 0.50±0.09; p=0.72). Figure 2 (left) displays the correlation between brain and plasma lithium concentration. Both groups presented a similar (Z=-1.5; p=0.134) positive correlation between brain and plasma lithium concentration (young: r=0.70; p=0.004 and elderly: r=0.91; p=4e-5), but we can note a higher dispersion of the data in the young group (blue data points). By observing the influence of age within the groups (Figure 2 right), we noted that in the young group the Li brain/Li plasma shows a negative correlation with age, while the same is independent on age in the elderly group.

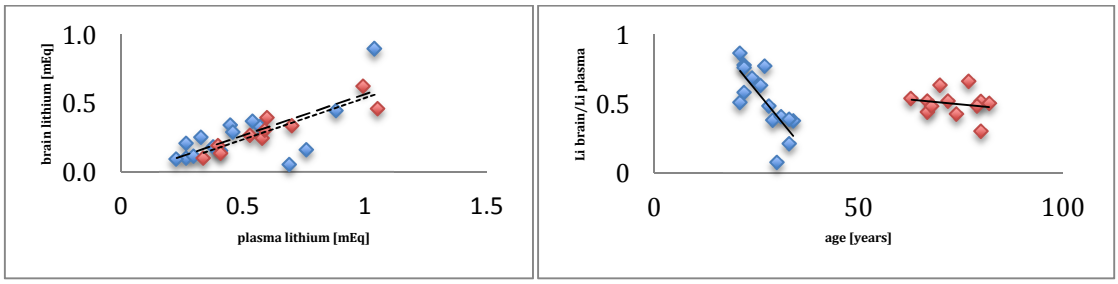

Figure 2. Left: Correlation between brain and plasma lithium concentration in young (blue) and elderly (red) patients with BD. Right: Correlation of the lithium brain to lithium plasma ratio with age for young (blue) and elderly (red) patients with BD.

DISCUSSION:

Moore et al.[2] studied the influence of age in lithium brain absorption for the age span of 7 to 52 years old and with lithium serum levels ranging from 0.5 to 1.3 mEq. They observed a positive correlation of lithium brain absorption with age, suggesting that children and adolescents may need higher maintenance serum lithium concentrations than adults. In our study, we compared elderly to younger patients (age range: 20-80 years) and we did not find differences in the mean lithium brain absorption, when looking at a lithium plasma level ranging from 0.2 to 1.1 mEq. Our results suggest that the reported increase of lithium brain absorption with age is valid only for the younger period of life, and that this absorption does not increase further above 40 years. Noteworthy, as we plot the individual data points as a function of age, we found very different correlations for our young and elderly groups. A larger study with a larger sample size and including patients in the range of 40-60 years need to be conducted in order to corroborate this effect. A possible bias in our study is that our elderly patients were under lithium treatment for a longer period of time than the younger patients, who took lithium only for 6 weeks before performing the examination. However, Riedl et al.[3] already reported that there is no difference in the lithium brain to plasma ratio with duration of treatment. Our preliminary results indicate that more studies are needed in order to understand fully how lithium absorption works in the brain.

CONCLUSION: With 7Li-MRS we found a different age effect on lithium absorption for young and elderly patients. More studies including a larger number of patients and covering all age ranges need to be conducted in order to corroborate these findings. 7Li-MRS represents a promising tool to elucidate the mechanisms of lithium in the brain.

REFERENCES: **1.** Soares JC, Boada F, Spencer S, Mallinger AG, Dippold CS, Wells KF, Frank E, Keshavan MS, Gershon S, Kupfer DJ. Brain lithium concentrations in bipolar disorder patients: preliminary (7)Li magnetic resonance studies at 3 T. Biol Psychiatry. 2001; 49(5): 437-43. **2.** Moore CM, Demopulos CM, Henry ME, Steingard RJ, Zamvil L, Katic A, Breeze JL, Moore JC, Cohen BM, Renshaw PF. Brain-to-serum lithium ratio and age: an in vivo magnetic resonance spectroscopy study. Am J Psychiatry. 2002 Jul;159(7):1240-2. **3.** Riedl U, Barocka A, Kolem H, Demling J, Kaschka WP, Schelp R, Stemmler M, Ebert D. Duration of lithium treatment and brain lithium concentration in patients with unipolar and schizoaffective disorder--a study with magnetic resonance spectroscopy. Biol Psychiatry. 1997 Apr 15;41(8):844-50.