

# MRSI Study of Brain Lithium Followed by Missed Doses

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## Introduction

Lithium and its salts continue to be a major prophylactic drug of manic depressive or bipolar illness (1). Effective prophylactic treatment requires strict compliance with the prescribed doses. However the effect of missed doses on brain lithium is not known. The effect of missed doses on lithium concentration in the CNS is an important determining factor in the treatment of bipolar disorder. To date there are no studies that attempt to examine the significance of missed doses on lithium levels in discrete brain regions. Following the preliminary feasibility study of Li observation in an animal tissue (2), studies using the modern high field instruments have made it possible (3, 4) to significantly improve the imaging of lithium in brain regions. It is the aim of this study to use <sup>7</sup>Li MR on a mammalian model to explore the changes that may occur in brain Li due to missed doses.

## Methods

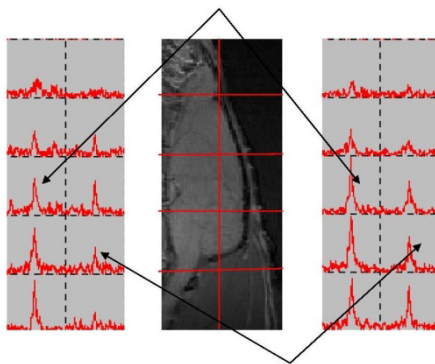
In the present study, 4 groups of 4 male Sprague Dawley rats weighing ~200gms were used. Each rat was administered a 2.0 meq/kg dose of lithium chloride (LiCl) as an IP dose. The control rats were injected once in the morning and once in the evening on the first and second days and the final dose was administered in the morning of the 3<sup>rd</sup> day. The remaining three groups were so treated that they missed the 2<sup>nd</sup> or the 3<sup>rd</sup> or the 4<sup>th</sup> dose as required for the study. The rat groups were studied for brain lithium by the <sup>7</sup>Li MRSI technique developed by us (4, 5).

**<sup>1</sup>H and <sup>7</sup>Li MR studies:** All MR studies were performed on the Bruker 7T animal imager operating at 300.0 MHz for <sup>1</sup>H and 116.6 MHz for <sup>7</sup>Li nucleus. <sup>1</sup>H scout images were acquired using spin-echo pulse sequence. The <sup>7</sup>Li spectroscopic imaging (SI) images were collected as 8x8 data matrix using a 52° flip angle, a sinc pulse of 578μs and TR of 1sec. The total data accumulation time for 64 averages was ~1 hr.

## Results and Discussion

Since the MR data were recorded in exactly the same manner for both control rats and those that missed a dose, a comparative study of the Li intensities in the two rat groups could be performed. As can be seen from Figure 1, the Li intensities in the brain voxels were generally lower in intensity in the rats that missed the dose. Intensity changes in brain voxels were also seen in other groups that missed a dose.

Figure 1: <sup>7</sup>Li SI data for the rat missing the 4<sup>th</sup> dose (A) and a control (C) that received all 5 doses. The image in the middle (B) is the <sup>1</sup>H sagittal slice of the rat head. The arrows point to changes in peak intensities.



## Conclusions

The <sup>7</sup>Li MRSI data on the brain show differences between the missed dose group and that which received all five doses of Li. Such data were obtainable conveniently in

about 1hr of data accumulation time with signal to noise ratio in the neighborhood of 10. Our studies clearly identify the brain regions which show decreases in lithium concentration and demonstrate that it can be studied effectively by in vivo magnetic resonance spectroscopic imaging technique.

## Acknowledgements

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## References

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