Brain Abnormalities in Bipolar Disorder Detected by Quantitative T1ρ Mapping

Casey P. Johnson, PhD[1], **Robin L. Follmer, MS**[2], **Ipek Oguz, PhD**[3], **Lois A. Warren, BSW**[2], **Gary E. Christensen, DSc**[3], **Jess G. Fiedorowicz, MD, PhD**[2,4,5], **Vincent A. Magnotta, PhD**[1,2], and **John A. Wemmie, MD, PhD**[2,6]

[1]Department of Radiology, University of Iowa, Iowa City, IA

[2]Department of Psychiatry, University of Iowa, Iowa City, IA

[3]Department of Electrical and Computer Engineering, University of Iowa, Iowa City, IA

[4]Department of Epidemiology, University of Iowa, Iowa City, IA

[5]Department of Internal Medicine, University of Iowa, Iowa City, IA

[6]Veteran Affairs Hospital Center, Iowa City, IA

Abstract

Abnormal metabolism has been reported in bipolar disorder, however these studies have been limited to specific regions of the brain. To investigate whole-brain changes potentially associated with these processes, we applied a magnetic resonance imaging technique novel to psychiatric research, quantitative mapping of T1 relaxation in the rotating frame (T1ρ). This method is sensitive to proton chemical exchange, which is affected by pH, metabolite concentrations, and cellular density with high spatial resolution relative to alternative techniques such as magnetic resonance spectroscopy and positron emission tomography. Study participants included 15 patients with bipolar I disorder in the euthymic state and 25 normal controls balanced for age and gender. T1ρ maps were generated and compared between the bipolar and control groups using voxel-wise and regional analyses. T1ρ values were found to be elevated in the cerebral white matter and cerebellum in the bipolar group. However, volumes of these areas were normal as measured by high-resolution T1- and T2-weighted magnetic resonance imaging. Interestingly, the cerebellar T1ρ abnormalities were normalized in participants receiving lithium treatment. These findings are consistent with metabolic or microstructural abnormalities in bipolar disorder and draw attention to roles of the cerebral white matter and cerebellum. This study highlights the potential utility of high-resolution T1ρ mapping in psychiatric research.

Corresponding Authors: Vincent A. Magnotta, PhD, Roy J. and Lucille A. Carver College of Medicine, University of Iowa, Iowa City, IA 52242, Tel: 319-356-8255, Fax: 319-353-6275, vincent-magnotta@uiowa.edu, John A. Wemmie, MD, PhD, Roy J. and Lucille A. Carver College of Medicine, University of Iowa, Iowa City, IA 52242, Tel: 319-384-3173, Fax: 319-384-3176, john-wemmie@uiowa.edu.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

INTRODUCTION

Although the pathophysiological mechanisms of bipolar disorder are largely unknown, accumulating evidence is beginning to link the disease to abnormal metabolism. Magnetic resonance (MR) spectroscopy studies have found evidence for reduced intracellular pH, N-acetyl-aspartate, phosphocreatine, and phosphomonodiesters and elevated lactate, glutamate, choline, and myo-inositol in euthymic people with bipolar disorder compared to matched controls, particularly in the frontal lobes and basal ganglia.[1] These factors suggest increased anaerobic metabolism as well as altered phospholipid metabolism.[1] Mitochondrial dysfunction has been hypothesized to be a common thread between these various findings.[1, 2] This view is buttressed by genetic evidence of abnormal mitochondria gene expression in bipolar disorder[3–5] as well as the presence of white matter abnormalities that may have a metabolic source such as hyperintensities[6–8] and dysconnectivity.[9, 10] Metabolic abnormalities may also result in an inflammatory response, which may lead to synaptic pruning,[11] loss of oligodendrocytes,[12, 13] and ultimately disease progression[14] and cognitive decline in bipolar disorder.[15] These various observations suggest parenchymal brain abnormalities in bipolar disorder including acidosis, altered metabolite concentrations, and loss of cellular density.

New imaging tools are needed to further investigate potential abnormalities in bipolar disorder. Magnetic resonance (MR) spectroscopy has proven useful for detecting metabolically-derived signals in the brain, with its primary advantage being that it can probe specific metabolites.[16] However, MR spectroscopy is limited by coarse spatial resolution (~8.0 cm^3 per voxel), incomplete brain coverage (single voxel or single slice), and long acquisition times (>5 min for a single voxel). Positron emission tomography has also been used to study metabolism,[17] but it is limited by dependence on radiolabelled markers as well as coarse spatial and temporal resolution. An alternative imaging modality that may be particularly useful to investigate bipolar disorder is quantitative MR mapping of T1 relaxation in the rotating frame (T1ρ).[18] The T1ρ signal is sensitive to chemical exchange between protons and other molecules largely via amide and hydroxyl groups.[19] T1ρ is increased by acidic pH, reduced cellular density, and reduced concentrations of metabolites such as glucose,[20–24] all of which have been suggested from studies of participants with bipolar disorder in the euthymic state. In contrast to MR spectroscopy, quantitative T1ρ mapping can be performed with an order of magnitude higher spatial resolution and whole-brain three-dimensional (3D) coverage in less than 10 minutes, which provide the ability to efficiently probe for abnormalities throughout the brain and not just in targeted regions.

In light of the previous suggestions of abnormal metabolism and cellular damage in bipolar disorder and the potential sensitivity of T1ρ to these processes, we hypothesized that T1ρ would be elevated in bipolar I disorder. To test this hypothesis, we used whole-brain quantitative T1ρ mapping to compare people with bipolar I disorder in the euthymic state to healthy controls balanced for age and gender. Our results suggest T1ρ mapping may be a valuable strategy for investigating bipolar disorder and its underlying mechanisms.

MATERIALS AND METHODS

Participants

Fifteen participants with a DSM-IV diagnosis of bipolar I disorder in the euthymic state (Young Mania Rating Scale 12 and Montgomery-Asberg Depression Rating Scale <10) and a normal control group of 25 participants balanced for age and gender with no known psychiatric history were enrolled into this study after providing written informed consent in accordance with the local Institutional Review Board. Euthymic participants consisted of individuals whose mood state had cycled from either depression or mania within the past two years. All participants completed a medical and psychiatric history including current medications. Sample demographic and clinical features are tabulated in Table 1.

Data Collection

Participants were imaged using a 3T Siemens Tim Trio MRI system (Magnetom; Siemens Healthcare; Erlangen, Germany) and a vendor-provided 12-channel receiver head coil. Whole-brain T1- and T2-weighted anatomical acquisitions with 1.0 mm isotropic spatial resolution were acquired first, and the quantitative T1ρ acquisition followed. The T1-weighted acquisition used a 3D magnetization-prepared rapid gradient echo sequence with the following parameters: coronal orientation; field-of-view = $25.6 \times 25.6 \times 25.6$ cm^3; sampling matrix = $256 \times 256 \times 256$; TR/TE/TI = 2530/2.8/909 ms; flip angle = 10°; bandwidth = 180 Hz/pixel; and R=2 GRAPPA. The T2-weighted acquisition used a 3D turbo spin echo with variable flip angle sequence with the following parameters: sagittal orientation; field-of-view = $26 \times 22.8 \times 17.6$ cm^3; sampling matrix = $256 \times 230 \times 176$; TR/TE = 4000/406 ms; bandwidth = 592 Hz/pixel; and R=2 GRAPPA. The T1ρ acquisition used a segmented 3D gradient echo sequence with the following parameters: coronal orientation; field-of-view = $22 \times 22 \times 20$ cm^3; sampling matrix = $128 \times 128 \times 40$; TR/TE = 5.6/2.5 ms; segment block time = 1500 ms; views per segment = 24; flip angle = 10°; bandwidth = 260 Hz/pixel; R=2 GRAPPA; and 7/8 partial Fourier. The T1ρ spin-lock preparation used a self-compensating spin-lock cluster[25] with spin-lock frequency = 330 Hz and spin-lock times (TSLs) = 10 and 55 ms.

Additional data were acquired to investigate factors that may affect T1ρ. Respiratory rate and heart rate were recorded using a physiological monitoring system (Biopac Systems, Inc; Goleta, CA) either during or following the T1ρ acquisition. Additionally, for all participants except four controls, blood samples were collected on the same day as the MRI exam (with the exception of four participants with bipolar disorder whose blood was collected during a visit 10 to 16 months prior to the exam) to measure the levels of 14 peripheral inflammatory markers (C-reactive protein, interleukin (IL)-1β, IL-1RA, IL-4, IL-6, IL-10, IL-17, IL-18, IL-18BP, interferon γ, tumor necrosis factor (TNF)-α, TNF-R1, TNF-R2, and monocyte chemotactic protein 1).

Data Analysis

BRAINS (Brain Research: Analysis of Images, Networks, and Systems) AutoWorkup[26] was used to align the T1- and T2-weighted anatomical images for each participant to a common brain atlas (NAC HNCMA Atlas 2013).[27] During this process, a deformable transformation

was calculated using Advanced Normalization Tools (ANTs)[28] to warp each participant's anatomical images to the common brain atlas, which includes a set of manually-defined tissue classification labels for cerebral and cerebellar gray and white matter and subcortical structures.[27] Another atlas with labels for 48 white matter tracts (ICBM-DTI-81 White Matter Labels Atlas)[29] was also registered to the common brain atlas space to provide a more detailed segmentation of the white matter. These transformations and atlas labels were subsequently used to regionally measure T1ρ values. Additionally, using segmentation voxel counts generated from BRAINS AutoWorkup, volumes of brain regions of interest were calculated relative to intracranial volume.

For each participant, a T1ρ map was calculated by fitting the 10 and 55 ms spin-lock time (TSL) image signals (S) according to the relationship:

$$S(TSL) = S(0)e^{-TSL/T1\rho}. \quad [1]$$

Using the TSL=55 ms image as a reference, the T1ρ map was aligned to the anatomical T1-weighted image using Analysis of Functional NeuroImages (AFNI).[30] The T1ρ map was then interpolated to 1.0 mm isotropic resolution to match that of the anatomical T1-weighted image, and the deformable transformation calculated during the BRAINS AutoWorkup processing was used to subsequently warp the T1-aligned T1ρ map to the common brain atlas. For visualization and group-wise comparisons, the warped T1ρ map was masked to only include voxels corresponding to brain tissue in the atlas.

Statistical Analysis

A voxel-wise comparison was performed to investigate brain tissue T1ρ differences between the bipolar and control groups and identify regions of interest for further evaluation. For this analysis, the groups' mean T1ρ maps were calculated and compared voxel-wise using an independent samples two-tailed *t*-test ($p < 0.05$) corrected for multiple comparisons by cluster thresholding (α=0.05). Calculations were performed using AFNI.

Two approaches were then used to investigate regional T1ρ differences between the euthymic bipolar and normal control groups in specific regions of interest identified using the voxel-wise comparison. First, label-specific histograms were generated for each group's mean T1ρ map. Twelve common brain atlas labels were available for investigation: cerebral and cerebellar gray and white matter; putamen; hippocampus; globus pallidus; amygdala; nucleus accumbens; caudate; thalamus; and pons. Only voxels with a T1ρ value between an expected range of 50 and 100 ms[31] in both maps were included in the analysis to reduce the influence of outliers (e.g., due to cerebral spinal fluid partial volume artifacts). The Pearson's correlation *r* between the two groups' voxel-paired mean T1ρ values in each label was also calculated. Second, the median T1ρ relaxation times in the common brain atlas labels of interest and all 48 white matter tract labels were calculated for each individual participant T1ρ map. The median T1ρ values for each label were then compared between the bipolar and control groups using a one-way ANOVA with a significance threshold of $p < 0.05$. Sub-threshold differences with significance level $p < 0.1$ were also recorded to determine if regions were trending toward significance. Calculations were performed using R statistical software.[32]

Potential covariates of the group T1ρ differences include respiratory rate, heart rate, medication use, regional brain volumes, and inflammatory marker levels. To assess whether respiratory rate, heart rate, and regional brain volumes were potential covariates of group T1ρ differences, euthymic bipolar and normal control group mean values of each were compared using a two-tailed *t*-test ($p<0.05$). Each of the 14 inflammatory markers were similarly assessed using a Wilcoxon rank sum test ($p<0.05$). The relationship between T1ρ values and respiratory rate and heart rate were also considered using a one-way ANOVA as above for each common brain atlas region of interest with significance level $p<0.05$. A similar ANOVA was performed to evaluate the influence of broad medication classes (lithium, anticonvulsants, antidepressants, antipsychotics, and sedative hypnotics) on T1ρ values within the euthymic bipolar group. Although there may be a relationship between T1ρ, age, and gender,[31] these factors were not evaluated as potential covariates since they were balanced in this study. Calculations were performed using R.

RESULTS

To explore the potential utility of whole-brain high-spatial-resolution T1ρ mapping in bipolar disorder, we quantified and compared T1ρ values between a euthymic group of participants with bipolar I disorder and a normal control group balanced for age and gender (Table 1). First we generated and averaged T1ρ maps for the euthymic bipolar and normal control groups. Voxel-wise comparison between these maps revealed significantly ($p<0.05$, corrected) greater T1ρ values in the cerebral white matter and cerebellum of the euthymic bipolar group (Fig. 1a). This finding was supported by histogram analyses for which we plotted the number of voxels versus T1ρ values in these regions of interest as defined by the common brain atlas labels[27] (Fig. 1b). Although the patterns of these histograms were very similar and showed a strong correlation between groups (r 0.90), the curves were shifted to the right in the bipolar group, suggesting a general increase in T1ρ across each region. A between-group analysis of variance (ANOVA) of T1ρ values in the cerebral white matter and cerebellar regions of interest also revealed an increase in the bipolar group, although these findings were not statistically significant after correction for multiple comparisons (Table 2). Sub-dividing the cerebral white matter into regions defined by the white matter tract atlas labels[29] consistently revealed increased T1ρ values in the bipolar group, although these differences were also not significant after correction for multiple comparisons.

One potential source of elevated T1ρ values in the euthymic bipolar group is inflammation. To investigate this possibility, we compared serum levels of 14 inflammatory markers between the bipolar and control groups. None of the inflammatory marker levels were significantly different between the two groups. Although the extent to which these markers in peripheral blood reflect inflammation in the brain is unknown,[33] this finding suggests that the T1ρ differences are not due to active systemic inflammatory processes.

Another potential source of elevated T1ρ is cellular loss, perhaps due to prior inflammation or injury. To explore this potential explanation for the observed T1ρ abnormalities, we compared regional brain volumes of the cerebral and cerebellar gray and white matter as a percentage of intracranial volume between the bipolar and control groups. No regional volume differences were found (cerebral white matter: $p=0.68$, 35.7 ± 1.3 vs. $35.8 \pm 1.7\%$;

cerebellar white matter: $p=0.15$, 4.55 ± 0.40 vs. $4.74 \pm 0.38\%$; cerebellar gray matter: $p=0.39$, 4.95 ± 0.52 vs. $4.80 \pm 0.53\%$), suggesting an absence of extensive cellular loss.

We have previously shown that respiratory rate and CO_2 inhalation can alter T1ρ throughout the brain.[22] However, we monitored respiratory rate in these studies and did not find a difference between the groups ($p=0.9$: 15.5 ± 2.8 vs. 15.4 ± 3.0 breaths/min). We did detect a general increase in heart rate in the bipolar group ($p=0.03$: 70.0 ± 11.1 vs. 62.7 ± 8.6 beats/min), suggesting cardiovascular deconditioning. Nevertheless, general physiological parameters such as these are unlikely to cause the focal T1ρ changes observed here, and the heart rate increase did not correlate with the region of interest median T1ρ values.

Because medications might also potentially influence T1ρ values, we assessed whether broad medication classes (Table 1) were associated with T1ρ abnormalities in the euthymic bipolar group. Analysis of variance (ANOVA) did not reveal any significant relationships between T1ρ and use of anticonvulsants, antidepressants, antipsychotics, or sedative hypnotics in the key regions of interest, the cerebral white matter and cerebellum. Note that the statistical power of this analysis was limited by small sample sizes. Interestingly, however, we did detect an effect of lithium in the cerebellum. T1ρ values in the cerebellum were elevated in participants in the bipolar group not taking lithium (Li−), whereas T1ρ values in the cerebellum were normal in their counterparts who were taking lithium (Li+) (Fig. 2). Similar results were observed in voxel-wise comparisons between the average T1ρ maps for the Li−, Li+, and control groups (Fig. 3). The Li− and Li+ groups were of similar age (mean=40.9 ± 16.6 and 40.0 ± 13.4 years, respectively) and gender (male/female=4/5 and 3/3, respectively). These findings suggest that medications were unlikely to cause the elevated T1ρ values in the bipolar group. Moreover, they suggest that lithium may have a normalizing effect on T1ρ values in the cerebellum. If so, then T1ρ may be sensitive to biological processes that contribute to bipolar disorder and that are corrected by lithium.

DISCUSSION

To our knowledge, this is the first study to apply quantitative T1ρ mapping to a psychiatric disorder. By mapping T1ρ relaxation times throughout the brain with high spatial resolution, we found cerebral white matter and cerebellum abnormalities in a group of euthymic participants with bipolar I disorder compared to a normal control group, suggesting a potential role for these regions in the pathophysiology of the disease.

Our findings provide new evidence for widespread white matter alterations in bipolar disorder. Whereas prior imaging studies of white matter in bipolar disorder have largely focused on the frontal-limbic networks associated with emotion processing,[9, 34–36] our findings include abnormalities in the corpus callosum, sagittal striatum, superior longitudinal fasciculus, and cerebellar peduncle. There is evidence for white matter inflammation, tissue loss, and altered metabolism in bipolar disorder,[13, 14, 34, 37] all of which may have a broad effect and could be reflected in the T1ρ findings. However, we did not find evidence for peripheral inflammation or white matter volume loss in the bipolar group, which lends some support that our white matter findings may reflect abnormal metabolism. If the elevation of T1ρ is in fact due to metabolic factors, then our finding is consistent with

reduced pH and reduced glucose concentration.[20, 22–24] Others have found evidence for both reduced pH and abnormal glucose metabolism in the white matter of bipolar disorder,[6, 38–40] which further supports a metabolic interpretation of our results. Our T1ρ findings suggest a need to focus on these white matter regions and on the cerebellum in future studies, for example by targeting MR spectroscopy specifically to these areas.

Our T1ρ data also point to the cerebellum as a key region of interest. Although prior studies have not widely appreciated that the cerebellum may be critical in bipolar disorder, the cerebellum has been suggested to play an important role in emotion processing.[41, 42] Indeed, some prior studies have detected cerebellar abnormalities in bipolar disorder, including structural deficits,[43] reduced cerebellar blood volume,[44, 45] and dysfunction as assessed by eyeblink, posture, and finger tapping tests.[46–48] Finding that lithium alters T1ρ in the cerebellum adds to this evidence and is consistent with our interpretation that abnormal metabolism underlies the observed T1ρ abnormalities. Lithium is unlikely to reverse cellular loss but it has been suggested to change glucose consumption in the cerebellum,[49, 50] perhaps through its effects on glycogen synthase kinase-3 or calcium signaling.[51]

Primary advantages of T1ρ mapping include sensitivity, spatial resolution, whole brain coverage, and quantification, but specificity remains a challenge. We attempted to address some of the potential factors that may have influenced T1ρ to better understand the source of the abnormalities observed here. The T1ρ abnormalities may very well reflect abnormal metabolism rather than inflammation or cellular loss. However, at present we cannot rule out local changes in tissue structure or water content. These possibilities could be investigated in future studies by using complementary mapping of T2,[52] adiabatic T1ρ and T2ρ,[53] and T1ρ dispersion.[54]

Other limitations of this study can also be addressed in future work. First, although our sample size was sufficient to detect statistically significant differences across groups, we were powered to detect only relatively large effects. In particular, increasing the sample size could improve the power to estimate effects of medications. Second, although we examined patients in the euthymic state, we cannot presently rule out effects of lingering mood states or their consequences. Future studies examining T1ρ in different mood states would provide important additional insight. Third, given previously detected imaging abnormalities in the frontal, subcortical, and cerebral gray matter regions in bipolar disorder,[55] it was somewhat surprising that T1ρ did not detect changes in these areas. T1ρ may not be sensitive to these same abnormalities or technical factors may have prevented their detection, including: (i) distortion from frontal sinus susceptibility artifacts; (ii) partial volume averaging of cerebral gray matter with cerebral spinal fluid and increased variability in gray matter due to lower spatial resolution (5.0 mm) in the slice-encode direction; or (iii) limited T1ρ fitting precision due to use of only two TSLs to reduce acquisition time. In the future, pulse sequence advances such as T1ρ preparation with reduced sensitivity to field inhomogeneity,[56, 57] variable flip angle schemes coupled with corrective methods for T1 contamination to enable higher spatial resolution and faster acquisitions,[58] and more optimal selection of TSLs for improved T1ρ map precision[59] would be beneficial. Finally, we did not assess whether the white matter and cerebellar abnormalities are specific to bipolar disorder, although it will be

important in future studies to determine if these abnormalities are shared by patients suffering from other diseases such as schizophrenia and depression.

The findings presented in this paper potentially represent an important advance in the study of bipolar disorder. Using an imaging strategy novel to psychiatric illness, we identified abnormalities in cerebral white matter and cerebellum that have not been previously observed and may reflect locally altered metabolism and consequences of lithium action. This work points to T1ρ mapping as an important new tool for studying psychiatric disorders, which combined with existing techniques may lead to improved insight into mechanisms and treatment of severe mental illnesses.

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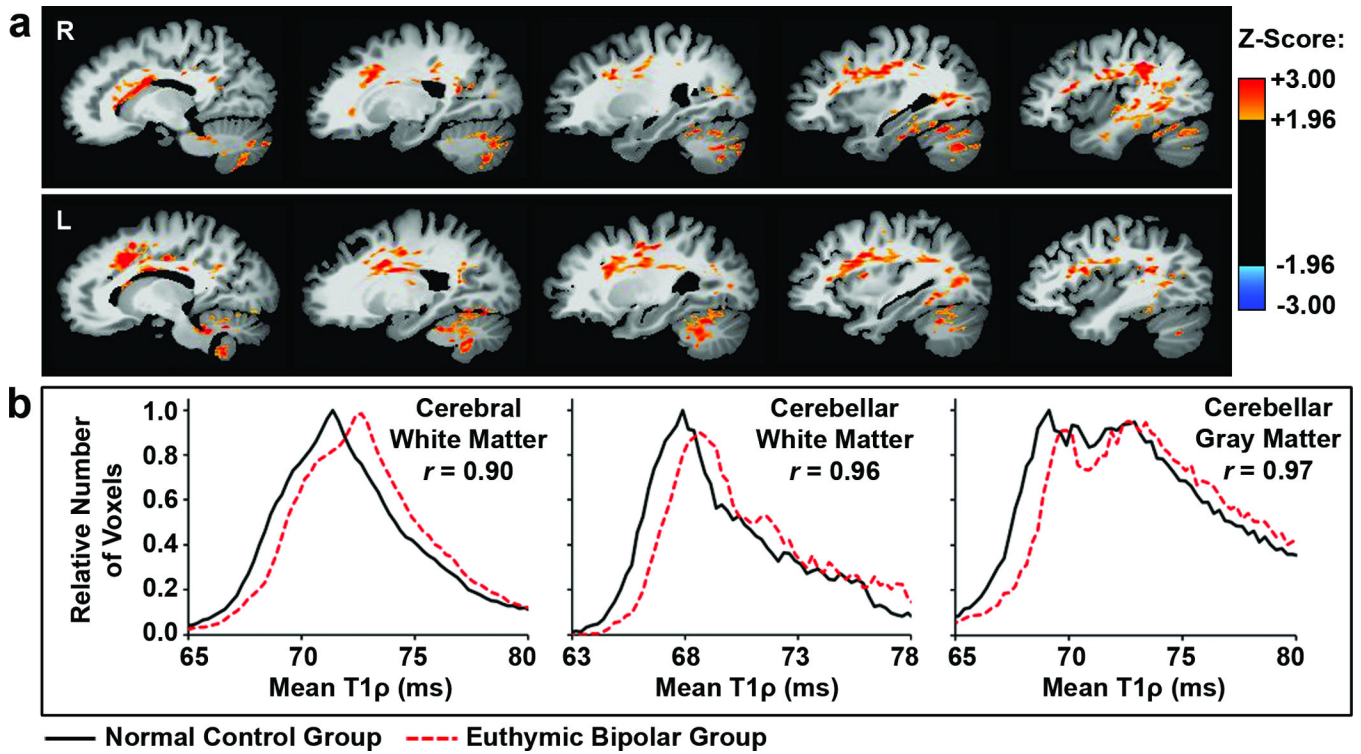
Fig. 1.

T1ρ values are elevated in the euthymic bipolar group in the cerebral white matter and cerebellum. (**a**) Statistical maps of the voxel-wise differences for the right (R) and left (L) brain hemispheres. Z-scores are thresholded at a significance level of $p<0.05$ with correction for multiple comparisons. A positive Z-score indicates the mean T1ρ value for the bipolar group was greater than that of the control group at that voxel. The statistical map is overlaid on the average common-atlas-aligned T1-weighted image for all participants. (**b**) Histograms of each group's T1ρ values in these regions of interest. Pearson's correlation coefficient r between the groups' T1ρ values is indicated for each label. The bipolar group histograms are shifted to the right, which indicates a general increase in T1ρ compared to the controls.
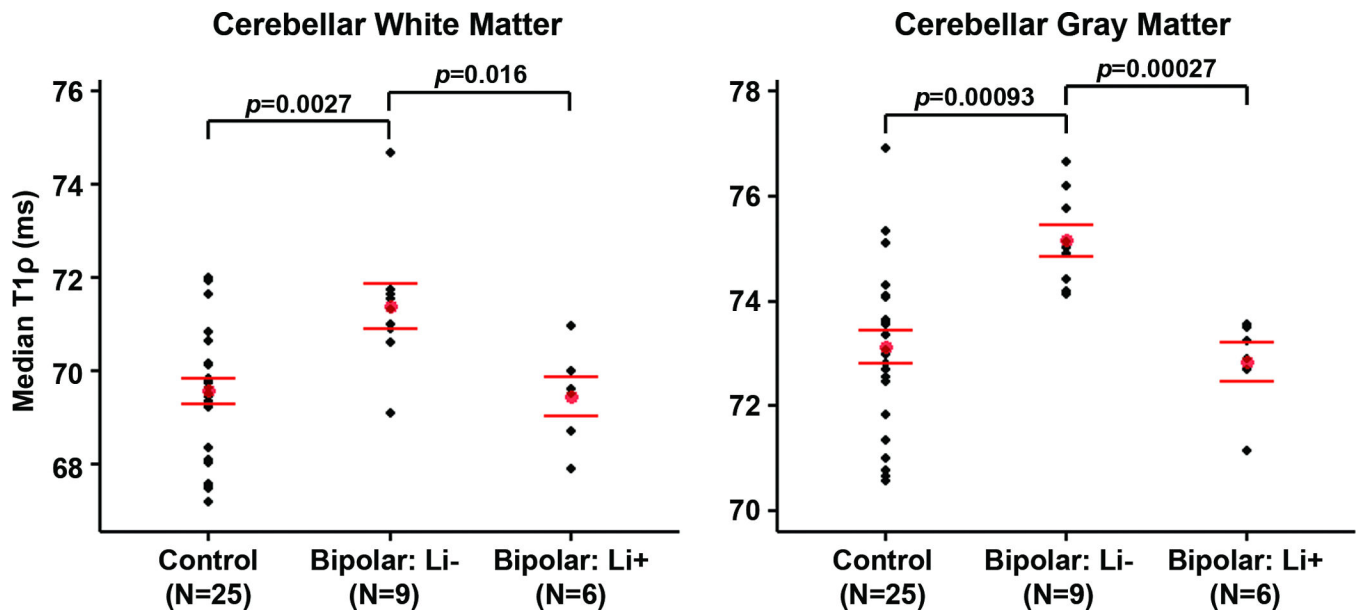
Fig. 2.
Cerebellar T1ρ values appear normalized with lithium use. Median T1ρ relaxation times for each participant in the cerebellar white and gray matter regions of interest are grouped by normal control participants, euthymic bipolar participants who were not using lithium (Li−), and euthymic bipolar participants who were using lithium (Li+). The average median value for each group is indicated by the red dot, and the red bars show the standard error. The Li− participants have significantly higher T1ρ values than the normal control and Li+ participants, whereas the normal control and Li+ participants have similar values.
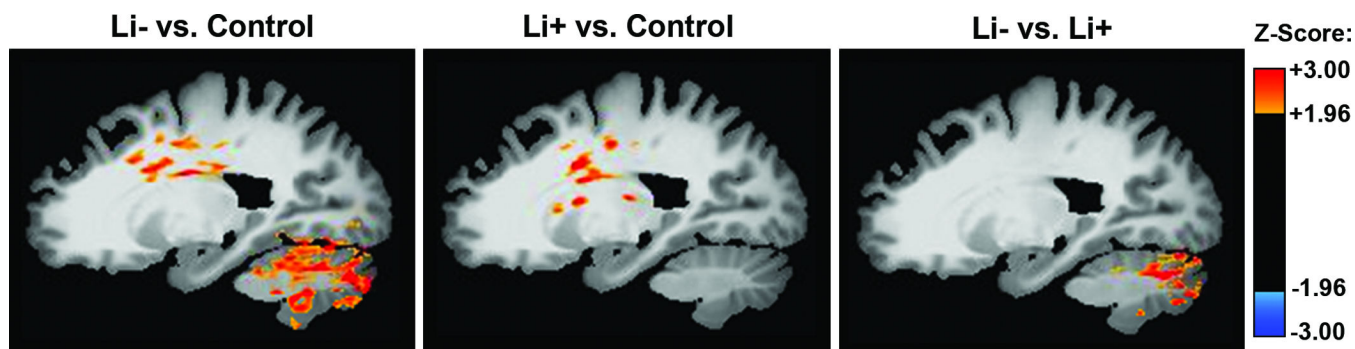
Fig. 3.
The effect of lithium on T1ρ values is unique to the cerebellum. Mean T1ρ map differences between bipolar participants not using lithium (Li−), those using it (Li+), and all controls indicate that lithium use is associated with normalized T1ρ values in the cerebellum but not the cerebral white matter. Statistical maps of the voxel-wise differences are shown for one slice, but the effect is seen throughout the brain. Z-scores were thresholded at a significance level of *p*<0.05 with correction for multiple comparisons.

Table 1

Euthymic bipolar and normal control group demographic and clinical features.

	Euthymic Bipolar Group	Normal Control Group
Participants		
N (Male/Female)	15 (7/8)	25 (13/12)
Age Mean ± SD	40.5 ± 14.9	41.5 ± 12.7
Age Range	21–66	21–62
Medications (N)		
Lithium	6	0
Anticonvulsants	6	0
Antidepressants	6	0
Antipsychotics	4	0
Sedative Hypnotics	7	0
None	2	25

Table 2

ANOVA of euthymic bipolar vs. normal control group T1ρ values in the cerebral white matter and cerebellar regions of interest as defined by the common brain and white matter tract atlas labels. Only those white matter tract labels with *p*<0.1 (uncorrected) are shown.

	Euthymic Bipolar Group: T1ρ Mean ± SD (ms)	Normal Control Group: T1ρ Mean ± SD (ms)	*p*	*F*
Common Brain Atlas Labels				
Cerebellar white matter	70.6 ± 1.6	69.6 ± 1.4	0.039	4.6
Cerebellar gray matter	74.2 ± 1.5	73.1 ± 1.6	0.032	4.9
Cerebral white matter	72.4 ± 1.9	71.5 ± 1.1	0.061	3.7
White Matter Tract Labels				
Body of corpus callosum	73.7 ± 2.0	72.5 ± 1.1	0.022	5.7
Left superior corona radiata	74.9 ± 2.5	73.5 ± 1.3	0.024	5.5
Right superior longitudinal fasciculus	72.7 ± 2.1	71.5 ± 1.4	0.025	5.4
Left cingulum	76.1 ± 2.4	74.5 ± 1.9	0.034	4.9
Left superior longitudinal fasciculus	72.3 ± 2.5	71.0 ± 1.3	0.037	4.7
Middle cerebellar peduncle	74.5 ± 2.3	72.9 ± 2.2	0.038	4.6
Right sagittal striatum	71.6 ± 2.2	70.0 ± 2.4	0.046	4.3
Right posterior thalamic radiation	75.2 ± 2.4	73.8 ± 1.9	0.046	4.3
Left posterior limb of internal capsule	72.7 ± 2.6	71.4 ± 1.4	0.046	4.2
Splenium of corpus callosum	74.6 ± 1.9	73.6 ± 1.6	0.062	3.7
Left superior cerebellar peduncle	77.4 ± 2.8	76.0 ± 2.0	0.063	3.7
Right inferior cerebellar peduncle	76.5 ± 2.1	75.0 ± 2.8	0.070	3.5
Left posterior thalamic radiation	74.6 ± 2.5	73.3 ± 1.8	0.071	3.4
Right medial lemniscus	69.0 ± 2.0	67.4 ± 2.9	0.073	3.4
Right fornix and stria terminalis	72.7 ± 2.0	71.7 ± 1.4	0.073	3.4
Left tapetum	86.0 ± 2.5	84.2 ± 3.1	0.077	3.3
Genu of corpus callosum	73.1 ± 2.9	71.8 ± 1.6	0.078	3.3
Right superior cerebellar peduncle	81.2 ± 2.5	79.5 ± 3.1	0.080	3.2
Left posterior corona radiata	76.2 ± 2.2	75.2 ± 1.6	0.090	3.0
Left sagittal stratum	72.0 ± 2.7	70.8 ± 1.7	0.098	2.9
Right superior corona radiata	74.5 ± 2.2	73.6 ± 1.3	0.099	2.9