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					Medication Trials: Lifetime (Current Episode)		
Subject	**Age**	**Gender**	**Axis I**	**Current Medications**	**Antidepressant**	**Mood Stabilizer**	**Antipsychotic**
1	41	F	MDD	Dextroamphetamine 15mg Zolpidem 10mg	7 (6)	0	5 (5)
2	67	F	MDD	Methylphenidate 20mg	2 (2)	1 (1)	1 (1)
3	41	F	Bipolar II, Depressed	Fluvoxamine 400mg Topiramate 100mg Quetiapine 200mg Ziprasidone 160mg Perphenazine 32mg Lorazepam 2mg	4 (4)	1 (1)	4 (4)
4	53	F	MDD	Duloxetine 60mg Bupropion 150mg	5 (2)	0	0
5	26	M	MDD, OCD	Fluoxetine 60mg Bupropion 450mg Topiramate 100mg	2 (2)	1 (1)	0
6	68	F	MDD	Venlafaxine 300mg Citalopram 40mg Clomipramine 50mg Gabapentin 2400mg Clonazepam 0.5mg	3 (3)	1 (1)	0
7	40	M	MDD	Venlafaxine 75mg Bupropion 100mg Lorazepam 1mg	3 (3)	0	0
8	27	F	MDD	None	5 (2)	0	0
9	56	F	MDD	None	2 (2)	1 (1)	1 (1)

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					Medication Trials: Lifetime (Current Episode)		
Subject	**Age**	**Gender**	**Axis I**	**Current Medications**	**Antidepressant**	**Mood Stabilizer**	**Antipsychotic**
10	22	F	MDD	Sertraline 200mg	6 (2)	1 (0)	1 (0)
11	24	F	MDD, OCD	Sertraline 200mg Bupropion 150mg	5 (5)	0	2 (2)
12	21	F	BAD II, Depressed	Lithium 900mg Lamotrigine 200mg Aripiprazole 5mg Pramipexole 6mg Pregabalin 450mg	0 (0)	4 (3)	2 (1)
13	60	F	MDD	Tranylcypromine 40mg Dextroamphetamine 5mg Clonazepam 0.5mg	7 (6)	0	1 (1)
14	32	M	MDD	Fluoxetine 20mg Lamotrigine 50mg Clonazepam 0.5mg (1/wk)	6 (3)	1 (1)	2 (2)
15	27	F	MDD	None	2 (2)	0	2 (2)
16	28	M	MDD	Venlafaxine 150mg Clonazepam 1mg (1/wk) Amphetamine 10mg (1/wk)	8 (3)	2 (0)	1 (0)
17	29	M	MDD, ADHD	Bupropion 150mg Amphetamine 30mg	4 (4)	0	1 (1)
18	62	F	MDD, GAD	Aripiprazole 2mg Lorazepam 1mg	7 (7)	0	4 (4)

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					Medication Trials: Lifetime (Current Episode)		
Subject	**Age**	**Gender**	**Axis I**	**Current Medications**	**Antidepressant**	**Mood Stabilizer**	**Antipsychotic**
19	63	M	MDD	Isocarboxazid 40mg Asenapine 5mg Lorazepam 2mg Zolpidem 5mg	5 (4)	1 (0)	3 (3)
20	25	F	MDD	Lamotrigine 50mg Amphetamine 50mg	4 (4)	2 (2)	1 (1)
21	42	F	MDD	None	3 (1)	3 (1)	0
22	55	M	MDD	Duloxetine 60mg Aripiprazole 10mg Amphetamine 30mg	3 (2)	1 (0)	1 (1)
23	49	F	MDD	Fluoxetine 80mg Trazadone 50mg Clonazepam 1mg	5 (5)	1 (1)	3 (3)

Supplementary Table 1: Age, gender, axis I DSM-IV diagnosis, current medications (total daily dose in milligrams), number of lifetime and current episode trials of adequate dose and duration for antidepressant, mood stabilizer and antipsychotic medication classes.

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		HAMD-24	
Subject	%MT	Baseline	%Change
1	50	31	-19%
2	100	22	-59%
3	81	36	-28%
4	85	27	-44%
5	95	24	-13%
6	86	18	+6%
7	107	28	-29%
8	83	25	-84%
9	50	25	-88%
10	98	37	-54%
11	85	24	-29%
12	109	26	0%
13	80	33	-33%
14	85	27	-15%
15	82	25	-32%
16	92	30	-57%
17	85	22	-55%
18	80	39	-31%
19	83	30	-23%
20	82	37	-59%
21	93	27	-52%
22	100	33	-9%
23	103	35	+6%

Supplementary Table 2: Average stimulation intensity (percent resting motor threshold; %MT) over the left dorsolateral prefrontal cortex during the 5 week course of TMS. Baseline and %Change in HAMD-24 score during the 5 week course of TMS.

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MRS Data Acquisition with the Standard J-editing Sequence

To derive the levels of GABA and Glx with the J-editing technique, a pair of frequency-selective inversion pulses is inserted into the standard PRESS method and applied at the frequency of the GABA C-3 peak at 1.9 ppm on alternate scans (Figure 1C, parts a and b), with TR/TE 1500/68 ms. This results in two subspectra in which the outer lines of the C-4 GABA multiplet resonance at 3.0 ppm are alternatively inverted or not inverted. Subtracting these subspectra yields the GABA difference spectrum, consisting of the GABA C-4 at 3.0 ppm, while the much stronger overlapping total creatine (tCr) resonance is eliminated (Figure 1C, part c). While the J-editing sequence is optimized for GABA detection, it also achieves detection of the Glx resonance at 3.7 ppm (Figure 1C, part c), although with reduced efficiency.

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MRS Data Quality Assessment Criteria and Procedures

In this study, spectral quality assessment, which determined whether the results of individual MRS data sets were ultimately included in and rejected from group analyses, was established using a number of criteria along the spectral data acquisition and processing pipeline. As can be appreciated by examining the sample spectrum presented in Fig. 1C, which is typical of all successful acquisitions, we achieved relatively high spectral quality and signal-to-noise ratios. Therefore, no spectra were rejected strictly due poor quality or SNR. Rather, spectra were rejected because either (a) the shim quality was poor (defined as a full-width at half maximum of the water resonance of more than 20 Hz, and/or spectra with unresolved total creatine and total choline resonances at 3.03 and 3.22 ppm), and (b) there was excessive head motion during a scan. Our criteria for detecting and rejecting motion-degraded spectra were: (1) a very large residual water resonance in the difference or edited spectra due to poor cancelation upon subtracting two subspectra in which the water signal was differentially affected by the head motion; (2) peak phase distortions in all the spectra that could not be automatically adjusted using the phases derived from the

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unsuppressed voxel water resonance, and (3) degraded SNR in the edited spectra due to incoherent summing of subspectra with motion-induced peak phase and position shifts.

All the spectra that met those initial quality assessment criteria were processed as illustrated in Figure 1C (traces [a-f]) to obtain the area under the GABA and Glx peaks, which are proportional to the concentration of each neurotransmitter in the voxel of interest. Briefly, the GABA and Glx resonances in the J-edited difference spectra were modeled as a linear combination pseudo-Voigt lineshape functions and then fitted in the frequency domain using a robust and highly optimized public-domain Levenberg–Marquardt nonlinear least-squares minimization routine, MPFIT (1) (The IDL fitting routine, 'MPFIT', is available at http://purl.com/net/mpfit; Last Modified on 2013-08-14 10:55:25 by Craig Markwardt). The pseudo-Voigt lineshape function enables more precise analysis of lineshapes that consist of mixtures of Lorentzian and Gaussian functions (2), as is often the case for *in vivo* spectra.

At convergence, MPFIT, like all nonlinear least-squares estimation procedures, reports the minimized sum of squared residuals or $\bullet_2$ as the "goodness of fit" (3). A fit is considered

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acceptable if at convergence, $\bullet_2$ is approximately equal number of degrees of freedom -- defined as the difference between the number of spectral data points (N) and the number of estimated parameters (M) -- or if $\bullet_2$ /(N-M), known as reduced $\bullet_2$, is approximately equal to 1. Deviations from these limits generally indicate an incorrect fitting model or failed fit. Due to the relative simplicity and high SNR and quality of the spectra in this study, excellent "good of fit" based on both $\bullet_2$ and visual inspection was consistently obtained, so that no spectra that survived our initial quality assessment criteria were rejected due to poor fit.

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