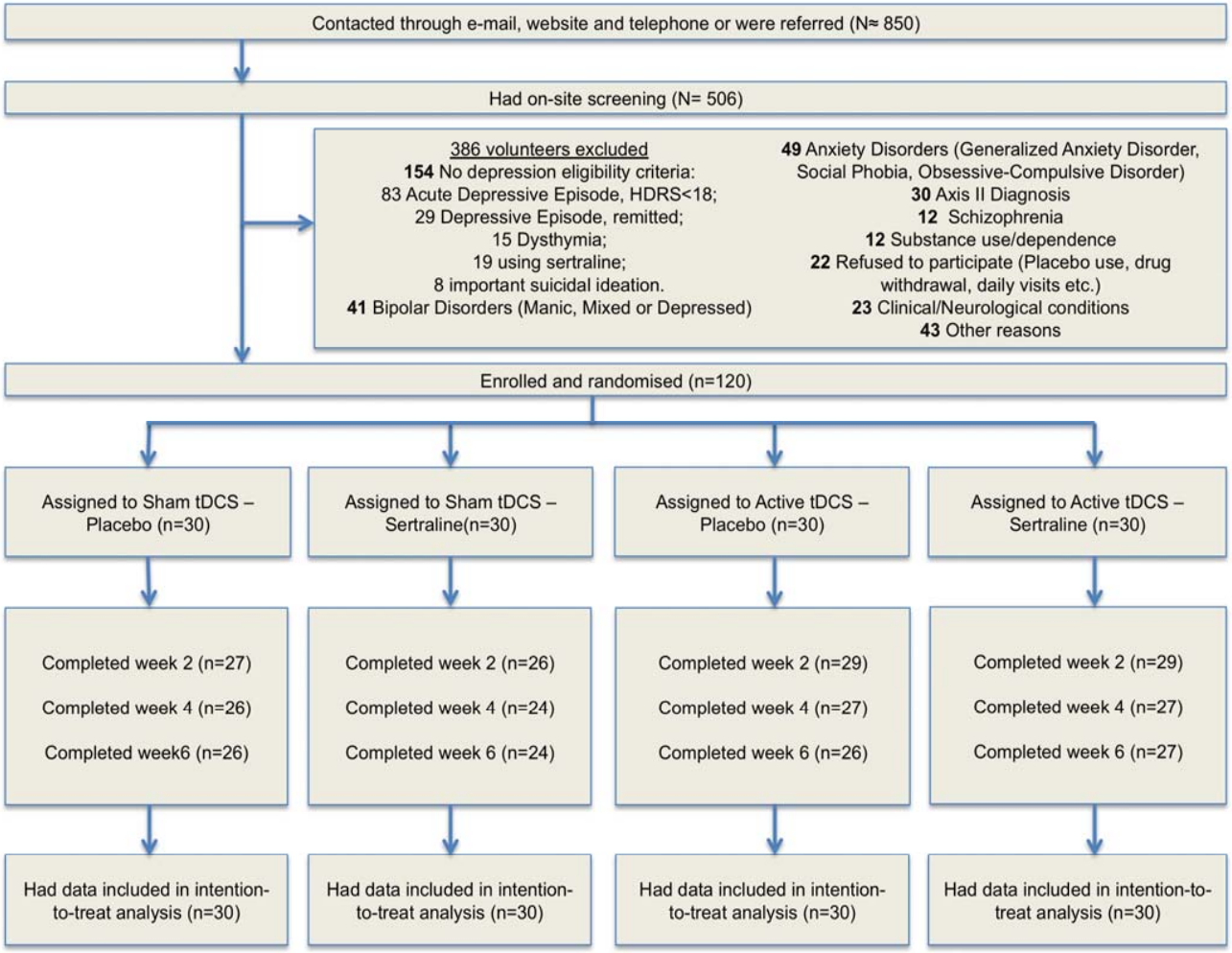
Supplementary Online Content

Brunoni AR, Valiengo L, Baccaro A, Zanão TA, de Oliveira JF, Goulart A, Boggio PS, Lotufo PA, Benseñor IM, Fregni F. The Sertraline vs Electrical Current Therapy for Treating Depression Clinical Study: results from a factorial, randomized, controlled trial. *JAMA Psychiatry*. Published online February 6, 2013. doi:10.1001/2013.jamapsychiatry.32.

This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure. Flow diagram for participants. tDCS refers to transcranial direct current stimulation, HDRS refers to the 17 item Hamilton Depression Rating Scale.



eTable 1. Baseline clinical and demographic characteristics of the study sample.

	Sham tDCS - Placebo	Sham tDCS - Sertraline	Active tDCS - Placebo	Active tDCS - Sertraline	*p*	Total
Demographic characteristics						
Age, years (SD)	46.4 (14)	41 (12)	41 (12)	41 (13)	0.24	42 (12)
Women, n (%)	20 (67)	17 (56)	21 (70)	24 (80)	0.28	82 (68)
Years at school, mean (SD)	13 (4)	14.6 (4)	13.5 (3)	14 (4)	0.51	13.7 (4)
Depression subtypes, n(%)						
Atypical	13 (43)	14 (46)	17(57)	19(63)	0.38	63 (52)
Melancholic	7 (23)	10 (30)	8 (26)	6 (20)	0.76	31 (26)
Treatment-resistant depression, n(%)						
≤ 1 failed trial	18 (60)	15 (50)	17 (56)	17 (56)	0.93	67 (56)
> 2 failed trials	5 (17)	9 (30)	8 (27)	4 (13)	0.31	26 (21)
Characteristics of depressive episode, median (IQR)						
Previous episodes	3(2-5.5)	3 (2-5)	2 (2-5)	3 (2-5)	0.45	3 (2-5)
Episode duration (weeks)	6 (3-20)	12 (5-24)	13(8-24)	9 (6-12)	0.34	12(5-20)
Psychiatric comorbidities, n (%)						
Dysthymia	9 (30)	9 (30)	7 (23)	6 (20)	0.76	31 (26)
GAD	11 (36)	15 (50)	15 (50)	18 (62)	0.28	60 (50)
Social Phobia	4 (13)	5 (17)	3 (10)	3 (10)	0.85	15 (12)
Panic Disorder	7 (23)	3 (10)	5 (16)	2 (7)	0.27	17 (14)
Clinical comorbidities, n (%)						
Hypertension	8 (27)	6 (20)	9 (30)	4 (13)	0.42	27 (22)
Hypothyroidism	4 (13)	3 (10)	6 (20)	3 (10)	0.63	16 (13)
Current smokers	7 (23)	7 (23)	3 (10)	4 (13)	0.41	21 (17)
Baseline scores, mean (SD)						
MADRS	31 (5.3)	30.5 (6)	31 (5.8)	30.7 (7)	0.99	30.6 (6)
HDRS17	22 (4.2)	22 (3.8)	21(3.8)	22.3 (3)	0.5	21.8 (4)
BDI	33 (7.5)	34 (9.5)	31 (8.6)	33(10.3)	0.39	32.7 (9)
CGI	4.5 (0.7)	4 (1.1)	4.5 (1)	4.5 (0.9)	0.13	4.4 (1)

GAD, Generalized Anxiety Disorder; MADRS, Montgomery-Asberg depression rating scale; HDRS17, Hamilton depression rating scale, 17 items; BDI, Beck Depression Inventory; CGI, Clinical Global Impressions severity of illness. *P* values represent the significance of one-way ANOVAs or Chi-Square tests.

eTable 2. Endpoint score changes in HDRS17, CGI and BDI measures.

	CGI	**HDRS17**	**BDI**
Group	% (SE)	% (SE)	% (SE)
Sham tDCS - Placebo	-18.2 (5.3)	-16.7 (4.7)	-29.6 (5.4)
Sham tDCS - Sertraline	- 29.8 (6.7)	-28.9 (6.4)	-36.5 (6.6)
Active tDCS - Placebo	-39.5 (6.2)	-36.6 (5.3)	-38 (7.5)
Active tDCS- Sertraline	-55.6 (5)	-49.1 (5)	-56.4 (5.1)
p	**0.02**	**<0.01**	**0.03**

tDCS; transcranial direct current stimulation; CGI, clinical global impression severity of illness; BDI, Beck depression inventory; % represents percentage of change, calculated as (endpoint – baseline) / baseline; SE, standard error of the mean. *P* values represent results for the mixed model ANOVA time x group interaction; values in **bold** represent significant interactions at a $p \leq 0.05$ level.

eTable 3. Summary of adverse events.

	Week 2			Week 6		
	Sham	**Active**	***p***	**Sham**	**Active**	***p***
tDCS questionnaire						
Headache	10 (19%)	12 (22%)	0.81	7 (14%)	7 (14%)	1
Neck pain	5 (9.5%)	7 (13%)	0.76	7 (14%)	3 (6%)	0.2
Scalp pain	6 (11%)	10 (19%)	0.41	2 (4%)	7 (14%)	0.16
Tingling	5 (9%)	7 (13%)	0.76	8 (16%)	4 (7.8%)	0.23
Itching	13 (25%)	20 (37%)	0.21	9 (18%)	17 (34%)	0.11
Skin redness	4 (8%)	13 (25%)	**0.03**	4 (8%)	11 (22%)	0.09
Sleepiness	15 (29%)	24 (44%)	0.11	17 (35%)	15 (29%)	0.67
Trouble concentrating	12 (23%)	11 (20%)	0.81	16 (32%)	8 (16%)	0.06
Acute mood change	9 (17%)	7 (13%)	0.6	12 (25%)	8 (16%)	0.32
SAFTEE (*)	**Placebo**	**Sertraline**		**Placebo**	**Sertraline**	
Insomnia	16 (30%)	16 (30%)	1	14 (27%)	15 (31%)	0.66
Sedation	12 (22%)	11 (21%)	1	10 (19%)	12 (25%)	0.63
Shakiness	2 (4%)	11 (21%)	**<0.01**	4 (8%)	8 (16%)	0.22
Headache	21 (39%)	19 (36%)	0.84	11 (21%)	16 (33%)	0.26
Dry mouth	18 (33%)	19 (36%)	0.84	14 (27%)	18 (37%)	0.28
Nausea	8 (15%)	11 (21%)	0.45	8 (15%)	8 (15%)	1
Constipation	10 (19%)	6 (12%)	0.41	6 (11%)	8 (17%)	1
Diarrhea	11 (20%)	15 (29%)	0.37	6 (12%)	6 (12%)	1
Increased Appetite	9 (17%)	7 (14%)	0.78	7 (13%)	9 (18%)	0.6
Decreased Appetite	8 (15%)	11 (21%)	0,45	7 (13%)	9 (18%)	0,6

tDCS, transcranial direct current stimulation; SAFTEE, Systematic Assessment for Treatment Emergent Effects. (*) Only side effects with >15% prevalence are shown; other side effects did not present statistically significant differences from sertraline vs. placebo. *P* values are the results of Chi-Square tests; values in **bold** represent significant interactions at a $p \leq 0.05$ level.

eTable 4. Summary of scores for the cognitive assessments performed at trial baseline and endpoint.

	Sham tDCS - Placebo			Sham tDCS - Sertraline			Active tDCS - Placebo			Active tDCS - Sertraline		
	Baseline	**Week 6**	***p***	**Baseline**	**Week 6**	***p***	**Baseline**	**Week 6**	***p***	**Baseline**	**Week 6**	***p***
MMSE	28.6 (1.2)	28.3 (1.4)	0.39	28.8 (1.7)	27.4 (5.5)	0.21	28.5 (1.3)	28.6 (1.7)	0.81	28.5 (1.8)	28.2 (1.9)	0.35
MOCA	25.8 (3.3)	24.9 (3)	0.21	24.8 (3.2)	26.5 (2.8)	**0.02**	24.7 (3.2)	25.5 (3.8)	0.16	24.8 (3.1)	26.1 (2.3)	**0.02**
Trail Making												
A	46.7 (14.9)	41 (15.4)	0.08	42 (13.3)	34 (15.6)	**<0.01**	43 (16.7)	39.1 (12.2)	**0.03**	49.9 (25.5)	39.4 (12)	**<0.01**
B	94.4 (46.5)	78 (48.8)	0.11	72 (27.6)	69.2 (27.2)	0.44	79.2 (34.1)	82.4 (47.7)	0.73	89 (50.3)	80.5 (51.2)	0.13
Digit Span												
Forward	8.7 (1.7)	9.4 (1.9)	0.09	9.9 (3.2)	10.6 (2.8)	0.17	8.3 (2.4)	10.1 (5.3)	0.07	8.9 (2.7)	9.5 (2.8)	0.15
Backward	5.7 (1.9)	5.9 (2.3)	0.8	6 (2.3)	6.8 (2)	0.06	5.1 (1.6)	5.4 (1.6)	0.32	5.6 (2)	6.2 (2.3)	0.07
Stroop												
Color	18.7 (6.2)	17.1 (4.7)	0.11	14.5 (2.3)	13.9 (2.1)	0.28	16.7 (4.4)	15.9 (4.4)	0.32	17 (5.3)	15 (3.3)	**<0.01**
Word	21.2 (5)	22 (10)	0.6	18.8 (6.1)	16.8 (3.6)	**0.04**	20.4 (6.1)	19.3 (5)	**0.16**	19.6 (5.2)	18 (4.3)	**<0.01**
Interference	31.9 (10.4)	27.6 (8.8)	**<0.01**	29 (11.4)	24.1 (6.7)	**<0.01**	33.6 (11.5)	28.3 (7.8)	**<0.01**	33.3 (14.5)	27.4 (9.9)	**<0.01**

tDCS, transcranial direct current stimulation. MMSE, Mini-Mental State Examination; MOCA, Montreal Cognitive Assessment. Values represent mean (SD) scores. For all assessments, with the exception of Stroop and Trail Making tests, higher numbers represent a better performance. *P* values are the results of paired *t* tests; values in **bold** represent significant interactions at a $p \leq 0.05$ level

eTable 5. Predictors of response.

Predictor variable	Main Effect		Interaction w/ tDCS		Interaction w/ sertraline		3-way interaction	
	F	**p**	**F**	**p**	**F**	**p**	**F**	**p**
Baseline severity	5.94	**0.01**	0.82	0.36	0.05	0.82	8.27	**<0.01**
Age (yrs)	0.01	0.91	0.83	0.36	0.36	0.55	0.01	0.99
Gender	0.47	0.49	0.03	0.87	1.85	0.17	2.01	0.16
Using AD when screened	0.05	0.82	0.2	0.65	2.7	0.11	1.28	0.26
Using benzodiazepines	2.38	0.12	0.49	0.48	0.04	0.83	4.91	**0.03**
Washout length (days)	0.01	0.95	0.94	0.33	0.04	0.83	0.41	0.52
Duration of index episode (wk)	3.29	0.07	0.69	0.4	1.43	0.23	1.83	0.17
Number of previous episodes	0.65	0.42	2.59	0.11	1.44	0.23	1.4	0.24
Duration of MDD (yrs)	0.04	0.83	0.01	0.92	0.38	0.53	0.01	0.9
Treatment-resistance								
0-1 vs. >1 failed trials	6.2	**0.01**	0.34	0.55	0.29	0.58	0.02	0.89
0-2 vs. >2 failed trials	2.35	0.12	0.14	0.71	0.11	0.74	0.33	0.56
Melancholic depression	0.29	0.58	4.7	**0.03**	0.48	0.49	0.22	0.64
Atypical depression	0.23	0.63	0.09	0.76	0.02	0.89	0.21	0.64
Dysthymia	2.7	0.11	2.29	0.13	0.1	0.75	0.05	0.83
Comorbid anxiety disorder	0.2	0.65	0.59	0.44	0.1	0.74	0.08	0.78

AD, antidepressant; tDCS, transcranial direct current stimulation. *P* values represent the significance of the interaction between the variable's main effect and also with tDCS, sertraline and both (the dependent variable is the difference between endpoint and baseline depression scores per MADRS). Significant *p* values are in bold. Results are not corrected for multiple comparisons, since the analyses are exploratory.

eTable 6. Integrity of blinding.

Considering all completers, patients correctly guessed sertraline use (χ^2= 11.4, p<0.01) and tDCS use (χ^2= 5.1, p=0.03). For both interventions participants were moderately confident of their choices (mean rate of 3.6 in a 1 to 5 Likert Scale).

tDCS			
Guessed group	True group		
	Sham tDCS	Active tDCS	Total
Sham tDCS	18	9	27
Active tDCS	31	44	75
Total	49	53	χ^2= 5.1, p=0.03
Sertraline			
Guessed group	True group		
	Placebo	Sertraline	Total
Placebo	39	21	60
Sertraline	13	29	42
Total	52	50	χ^2= 11.4, p<0.01

However, considering only the subsample of patients who were "almost" or "absolutely" sure of the intervention (rates 4 and 5), tDCS use was not guessed correctly (χ^2=2.8 p=0.09), although sertraline use remained significant (χ^2 =9.9, p<0.01).

tDCS			
Guessed group	True group		
	Sham tDCS	Active tDCS	Total
Sham tDCS	9	4	13
Active tDCS	21	28	49
Total	30	32	χ^2= 2.8, p=0.09
Sertraline			
Guessed group	True group		
	Placebo	Sertraline	Total
Placebo	24	13	37
Sertraline	6	19	25
Total	30	32	χ^2= 10, p<0.01

In addition, participants who presented clinical response with tDCS correctly guessed their group (χ^2= 6.03, p=0.01) whereas those who did not present response were not able to correctly guess their group (χ^2= 0.16, p=0.69). This first group also rated their choice more confidently than the second one (p=0.04).

No clinical response			
Guessed group	True group		
	Sham tDCS	Active tDCS	Total
Sham tDCS	14	21	35
Active tDCS	8	15	23
Total	22	36	χ^2= 0.16 p=0.69
Clinical response			
Guessed group	True group		
	Sham tDCS	Active tDCS	Total
Sham tDCS	4	10	14
Active tDCS	1	29	30
Total	5	39	χ^2= 6.1, p=0.01