Data Supplement for Widge et al., Electroencephalographic Biomarkers for Treatment Response Prediction in Major Depressive Illness: A Meta-Analysis. Am J Psychiatry (doi: 10.1176/appi.ajp.2018.17121358)

Supplementary Methods

Search Strategy and Article Selection

We searched PubMed for articles published anytime before November 28, 2017 whose title and/or abstract contained keywords matching the query:

(electroencephalogram OR electroencephalography OR EEG OR QEEG OR event-related potential OR ERP OR cordance OR coherence OR spectral OR spectrum OR alpha OR beta OR theta OR delta OR gamma OR N1 OR P2 OR P300 OR N200 OR SSVEP OR VEP OR AEP OR evoked potential OR oscillation OR electrical activity)
AND
(depression OR depressive OR major depression OR major depressive disorder OR major depressive episode OR depressed OR antidepressant OR mood disorder)
AND
(differential OR predictor OR prediction OR predict OR biomarker OR marker OR phenotype OR response index)
AND
(response OR remission OR treatment response OR responsiveness OR nonresponse OR non-response OR responder OR non-responder OR therapeutic OR outcome OR treatment resistance OR comparative effectiveness OR effectiveness OR treatment selection OR efficacy)

The search was limited to articles in English and to human studies.

We then added additional articles known to one of the authors or identified through the references of recent reviews. We did not attempt to discover un-published data, as there is no single reasonable point of contact as there would be with a drug or therapeutic device manufacturer. Unpublished data from the authors of individual published studies may have technical flaws, as the acquisition and analysis of EEG is not straightforward.

All abstracts that appeared to involve EEG, treatment prediction, and some form of depressive illness were retained for further review. We did not consider abstracts or articles published as book chapters rather than in peer-reviewed journals. We removed an article from the analysis if, on detailed reading, it did not attempt to predict treatment response. We also removed two articles that, on careful inspection, were reports of the same marker as another article using a highly overlapping dataset. For these pairs (Cook2009 vs [1], Leuchter2009 vs. [2]), we retained the article with the larger sample size. We retained articles that attempted prediction but found a non-significant result. We accepted one article that used magneto-encephalography (MEG) instead of EEG (Heikman 2001) on the grounds that the two techniques measure very similar signals.

This protocol was not pre-registered.

Data Extraction

10 articles did not directly report the necessary information to reconstruct a 2x2 table enumerating false/true positives and negatives (Noda et al., 2017 ; van Dinteren et al., 2015 ; Arns et al., 2014 ; Widge et al., 2013 ; Narushima et al., 2010 ; Mulert et al., 2002 ; Pizzagalli et al., 2001 ; Bruder et al., 2001 ; Cook and Leuchter, 2001 ; Heikman et al., 2001). They did, however, provide sufficient additional information (e.g., a high-resolution ROC plot or all-subjects scatterplot) to infer it. For these studies, we computed diagnostic odds ratio (DOR) at every indicated point on the ROC, then assigned the study the 2x2 values that maximized its DOR. This gives each study the maximum "benefit of the doubt" in the meta-analysis. For studies that reported no association between any target QEEG feature and treatment response, we imputed table values assuming positive and negative predictive values equal to the prior probabilities of the patient sample. We did not identify discrepancies during this that required contact with the original investigators. We accepted each article's individual definition of (non)response, the threshold for which varied between authors. As with most of our design choices, this was meant to bias the meta-analysis in favor of detecting a signal if one exists.

For descriptive analysis, we extracted the type of treatment and the specific biomarker being studied. We coded treatments as medication vs. non-medication, rTMS vs. not, and SSRI vs. any other type of treatment. We further noted articles that used citalopram or venlafaxine as their primary medication, as these were the two most common treatments in the overall sample. For biomarkers, we classified them as resting state vs. task-based, and as calculated in cortical source space vs. sensor space. We coded which articles involved the most common biomarkers in our sample: event-related potentials, auditory evoked potentials, oscillatory asymmetry, oscillatory

power amplitude (theta and alpha), cordance, and the Antidepressant Treatment Response index. Each of these was studied in multiple papers, several by multiple investigators.

For study quality reporting, we extracted the total sample size (N), whether the analysis corrected for multiple hypothesis tests, and whether the analysis used any out-of-training-set cross-validation. N was the N reported for each study's EEG analysis, which often differed slightly from that reported in the abstract due to technical difficulties with a small number of EEG recordings. Any type of correction to the significance threshold was considered acceptable. We only required multiple-testing correction if the authors explicitly stated that they tested multiple frequency bands or biomarkers for their correlation with treatment response. For studies reporting analysis of a single biomarker at a single timepoint, we again granted the investigators the benefit of the doubt and treated these as hypothesis-driven studies. Similarly, any type of cross-validation was sufficient to count an article as positive, as long as the cross-validated results were reported in the body of the article. We explicitly chose not to rate articles against the QUADAS [3] or STARD [4] quality framework. Those models are designed to assess whether a new diagnostic test is being accurately compared against a gold standard. All of our articles used effectively the same gold standard: whether patients achieved a given percent change in a clinician-rated scale.

In a supplemental analysis, we repeated the main study extracting the standardized mean difference (Cohen's d) from each of the studied articles. When an article reported QEEG marker means and standard deviations for responders/non-responders, we used these directly. For articles reporting an area under the curve, we converted this to d using a published formula[5]. We

did the same for articles reporting a linear correlation coefficient (Pearson's r) between a depressive rating scale and the QEEG biomarker, again using a published formula[6]. Finally, when neither of these were available, we estimated d from the 2x2 table using an online calculator[7]. We note that d and other standardized mean differences are not recommended by any statistical authority for use in meta-analysis of diagnostic markers. Collapsing sensitivity and specificity into a single marker ignores the tradeoff/negative correlation between those outcomes. In the case of d, it further assumes a normal distribution. We report this additional analysis mainly for comparison with other reports, e.g. Pizzagalli et al. 2011.

We did not explicitly extract or code details of the EEG recording (number of channels, the specific amplifier, sampling rate). There is no *a priori* reason why any of these should be related to a study's findings, assuming basic investigator competency. We did not explicitly code whether studies used a "pure" MDD sample vs. any type of depressive diagnosis, nor did we stratify them by response threshold. Depression is a heterogeneous diagnosis, and we have no clear evidence that MDD, "depression NOS", or depressed episodes in bipolar disorder differ in their neurobiology.

Meta-Analysis Procedures

Diagnostic Odds Ratio (DOR), sensitivity, and specificity all may become undefined for studies with zero false positives/negatives. To prevent this, we added 0.5 to all 2x2 table values for all studies (including those that did not report a "perfect" discriminator).

Although we extracted data for specific subclasses of medications, our meta-regression considered only "Medication", "rTMS", and "Other" as treatment classes. More detailed models could not be fit to the dataset.

For standardized mean differences, we fit a univariate mixed-effects meta-analysis with inverse variance weighting, using metafor's "rma" function. The funnel plot for this regression plotted effect size against the reciprocal square root of sample size (1/sqrt(n)), as funnel plots based on this method are more robust against false-positive detection of asymmetry[8].

Supplementary Figures

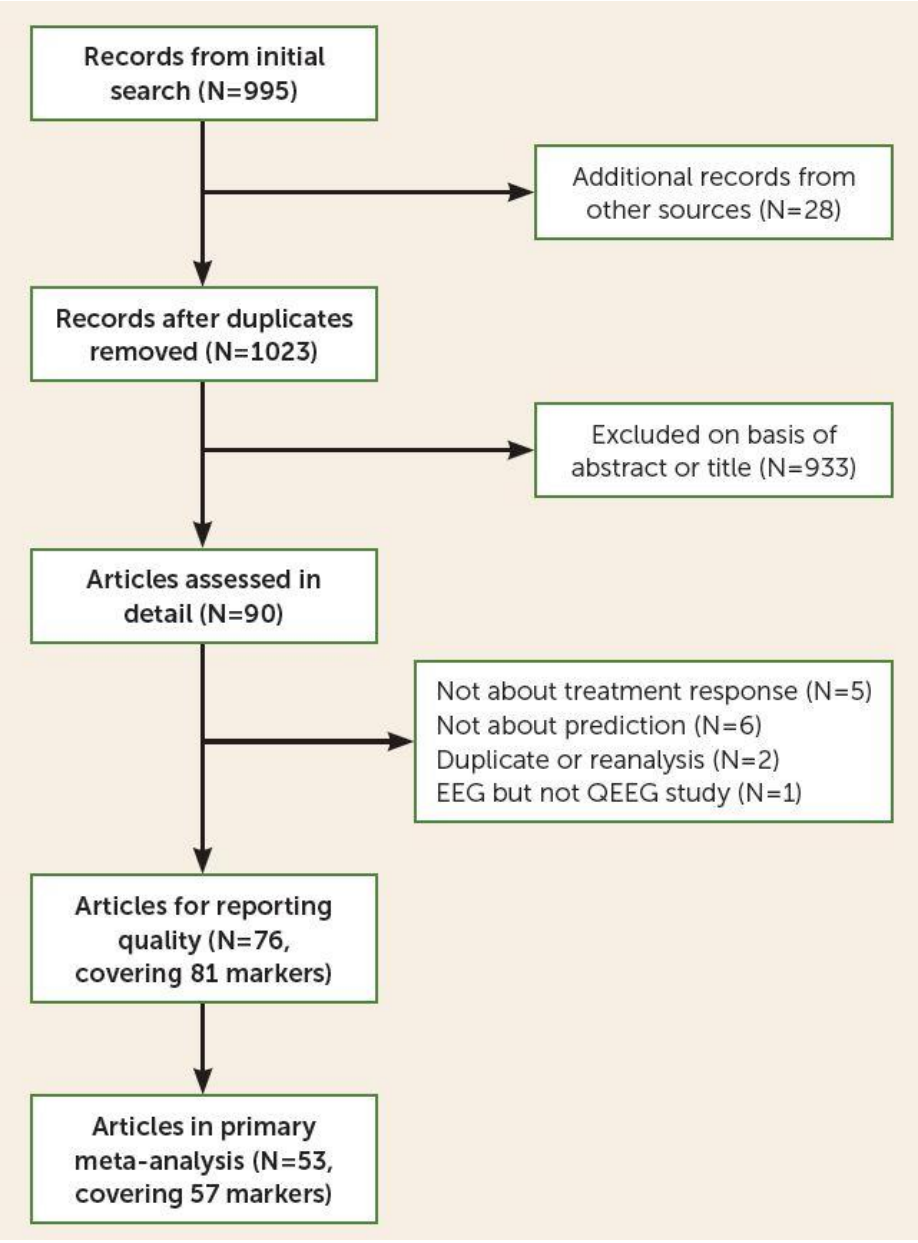

FIGURE S1. PRISMA Diagram for a Meta-Analysis of Quantitative EEG (QEEG) Biomarkers in Depression Treatment

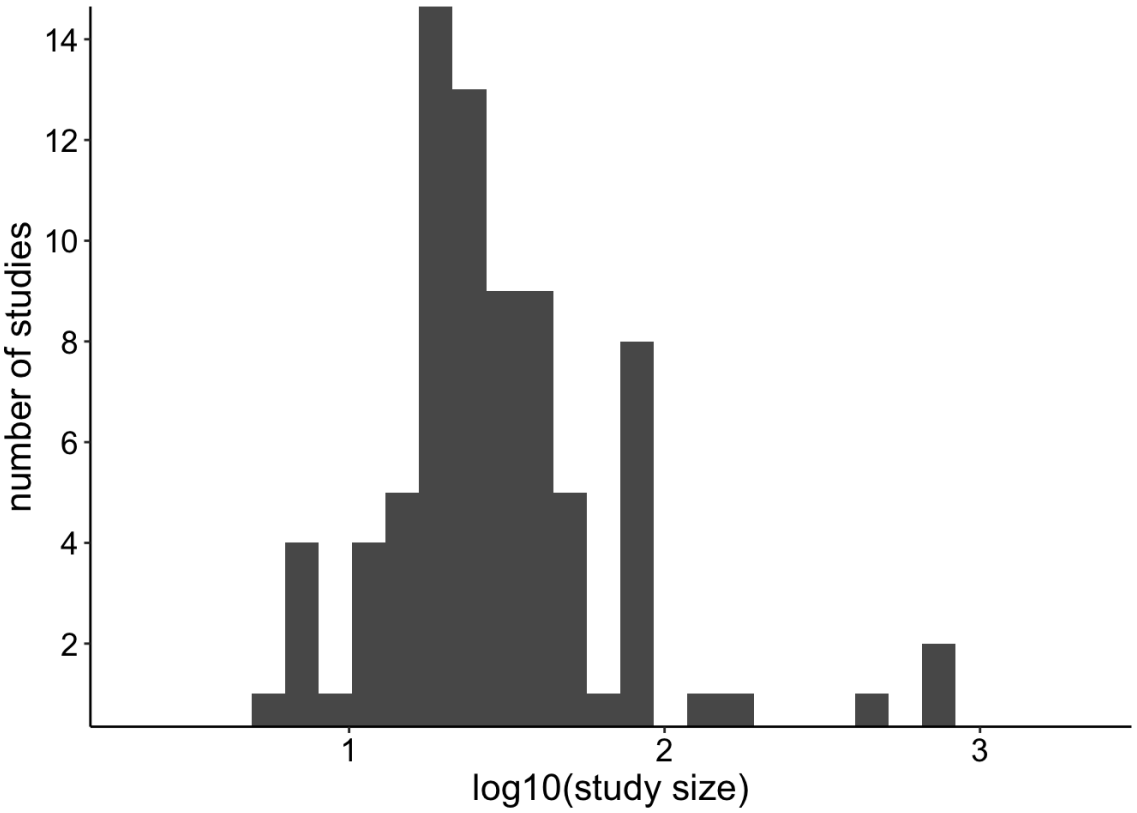

FIGURE S2. Histogram of study sizes, plotted on log scale due to presence of a few very large studies. Most were small, with the bulk of the distribution below N=100 and the two largest modes at N=22 and N=85.

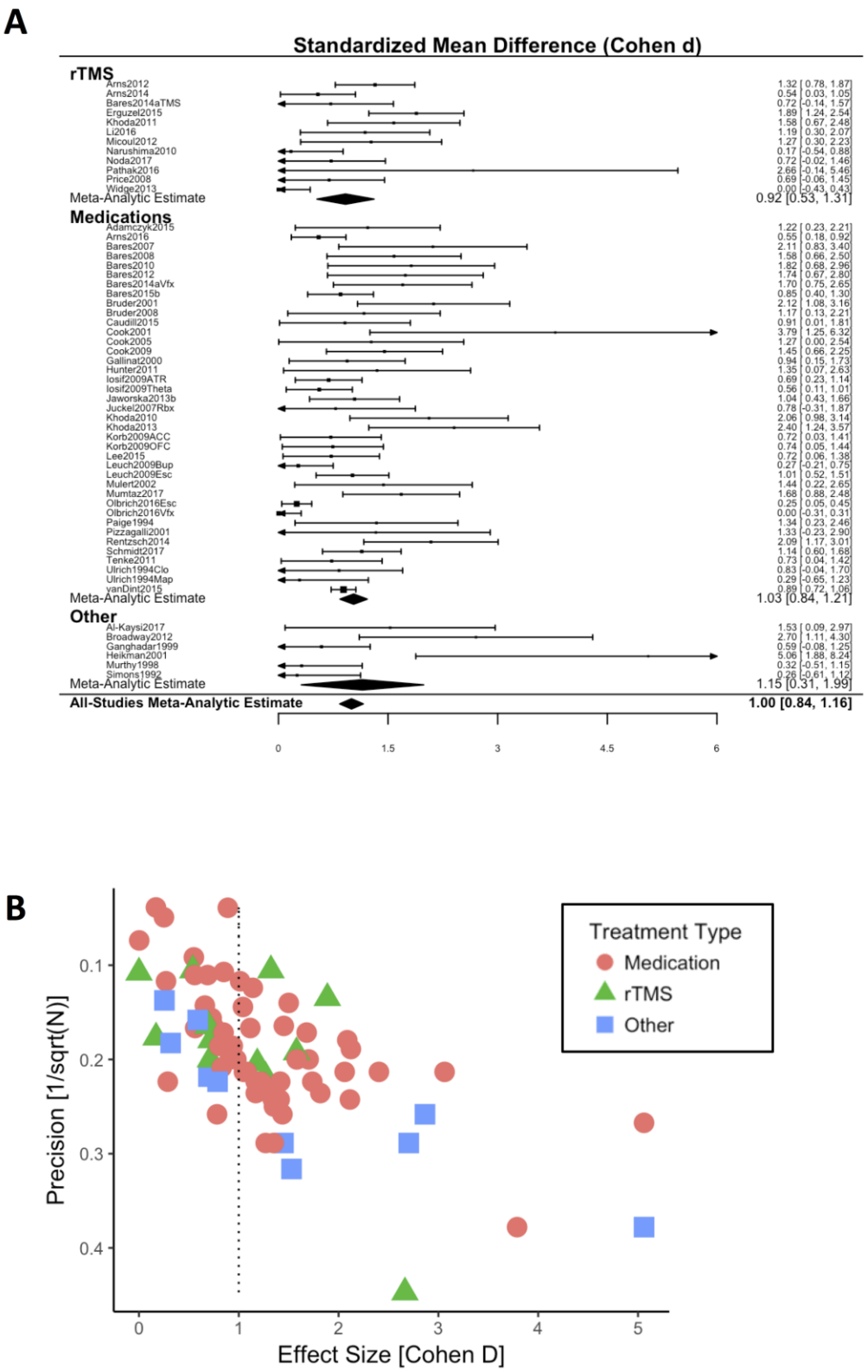

FIGURE S3. Meta-analysis of QEEG standardized mean differences (Cohen's d) between responders and non-responders. Data were extractable from 67 articles covering 72 putative

biomarkers. Most articles (21/24, 87.5%) that did not include 2x2 table information for the main meta-analysis did include information sufficient to compute d. Individual studies and their values are reported in Table S2 below. (**A**), forest plot. The meta-analytic estimate of d=1 (CI 0.84 to 1.16) is consistent with a "large" effect size and similar to that estimated by Pizzagalli (2011) for rostral theta power. (**B**), funnel plot of effect size vs. precision (reciprocal of root of sample size). There is a strong asymmetry, with under-representation of studies having lower precision and correspondingly low effect sizes. Meta-regression of effect size vs. precision (analogue of Egger's test) had p=5.87e-7, consistent with the asymmetry in the main analysis.

Supplementary Tables

TABLE S1. Studies included in meta-analysis, with report of quality metrics, study size, and predictive values. Empty cells represent data that were not reported and could not be imputed.

First Author	Year	Journal	Treatment	Marker	Population	Mult Corr	Cross Val	N	TP	FP	TN	FN	Sens	Spec	AUC
van Dinteren	2015	European Neuropsychopharmacology	Escitalopram, sertraline, or venlafaxine-XR (iSPOT-D)	ERP latency and amplitude	MDD	N	N	655	316	100	139	100	0.76	0.58	
Arns	2016	Clinical Neurophysiology	Escitalopram, sertraline, or venlafaxine-XR (iSPOT-D)	occipital alpha power & frontal alpha asymmetry	MDD	Y	N	119	31	15	47	26	0.54	0.76	0.64
Woźniak-Kwaśniewska	2015	Journal of Affective Disorders	rTMS	prefrontal theta and beta power	MDD/BP	Y	N	18							
Arns	2015	European Neuropsychopharmacology	Escitalopram, sertraline, or venlafaxine-XR (iSPOT-D)	frontal and rostral anterior cingulate (rACC) theta	MDD	N/A	N	667							
Lee	2015	International Journal of Molecular Sciences	Escitalopram, sertraline, or paroxetine	LDAEP, source localized	MDD	N/A	N	41	16	5	11	9	0.64	0.69	
Caudill	2015	Clinical EEG and Neuroscience	Reboxetine	ATR 4.1	MDD	N/A	N	25	12	1	7	5	0.71	0.88	0.74
Canali	2014	Bipolar Disorders	Sleep deprivation	Cortical excitability to TMS	BP	N/A	N	21							
Bares	2015b	European Archives of Psychiatry and Clinical Neurosciences	Any antidepressant	Prefrontal theta cordance	MDD	N	N	87	40	7	32	8	0.83	0.82	0.91

Bares	2015a Vfx	Clinical EEG and Neuroscience	Venlafaxine	Prefrontal theta cordance	MDD	N/A	N	25	10	4	11	0	1.00	0.73	0.89
Bares	2015a TMS	Clinical EEG and Neuroscience	low frequency TMS	Prefrontal theta cordance	MDD	N/A	N	25	9	6	10	0	1.00	0.63	0.75
Arns	2014	Clinical Neurophysiology	rTMS	Non-linear complexity metrics, alpha band	MDD	N/A	N	90	70	15	5	0	1.00	0.27	0.70
Quraan	2014	Neuropsychopharmacology	Cg25 Deep brain stimulation	Theta and alpha frontal asymmetry	MDD	Y	N	12							
Widge	2013	Brain Stimulation	rTMS	ATR 4.1	MDD	N/A	N/A	86	19	19	24	24	0.50	0.50	0.50
Hunter	2013	Journal of Neuropsychiatry and Clinical Neurosciences	Sertraline	rACC theta current density (LORETA)	MDD	N/A	N	22							
Khodayari-Rostamabad	2013	Clinical Neurophysiology	Any SSRI	Multi-marker weighted	MDD	N/A	Y	22	6	1	14	1	0.81	0.95	
Jaworska	2013a	European Neuropsychopharmacology	Escitalopram, bupropion, or both	auditory oddball ERP	MDD	Y	N	49							
Jaworska	2013b	Progress in neuro-psychopharmacology and biological psychiatry	Escitalopram, bupropion, or both	LDAEP	MDD	Y	N	48	15	3	22	8	0.65	0.88	
Arns	2012	Brain Stimulation	rTMS	Multi-marker weighted	MDD or dysthymia	Y	N	90	63	9	11	7	0.90	0.55	0.81
Khodayari-Rostamabad	2011	Conference Proceedings: Annual International Conference of the IEEEEngineering in Medicine and Biology Society	rTMS	Multi-marker weighted	MDD	N	Y	27	7	3	15	2	0.78	0.83	
Micoulaud-Franchi	2012	Journal of Affective Disorders	rTMS	alpha power	MDD/BP	Y	N	21	12	3	6	0	1.00	0.66	0.82
Bares	2012	Journal of Psychiatric Research	Any antidepressant	Prefrontal theta cordance	BP	N/A	N	20	7	2	10	1	0.88	0.83	0.80

Tenke	2011	Biological Psychiatry	SSRI or SI	multi-electrode alpha power	MDD, dysthymia, or dep NOS	N/A	N	41	14	1	12	14	0.50	0.92	
Khodayari-Rostamabad	2010	Conference Proceedings: Annual International Conference of the IEEEEngineering in Medicine and Biology Society	Any SSRI	Multi-marker weighted	MDD	N	Y	22	7	2	12	1	0.88	0.86	
Spronk	2011	Journal of Affective Disorders	Any antidepressant	Theta power, auditory ERP	MDD	N	N	25							
Bares	2010	European Neuropsychopharmacology	Bupropion	prefrontal EEG theta cordance	MDD	N/A	N	18	9	1	6	2	0.82	0.86	
Salvadore	2010	Neuropsychopharmacology	Ketamine	Pregenual ACC activity and connectivity	MDD	N/A	N	15							
Narushima	2010	Journal of Neuropsychiatry and Clinical Neurosciences	rTMS	subgenual ACC theta power	Vascular Depression	N	N	32	3	0	16	10	0.88	0.86	0.55
Wang	2009	Chinese Medical Journal	Any antidepressant	Auditory ERP	Any depression	N	N	36							
Cook	2009	Psychiatry Research	Fluoxetine or venlafaxine	frontal theta cordance and power	MDD	N	N	37	10	10	16	1	0.90	0.60	0.76
Leuchter	2009 Esc	Psychiatry Research	Escitalopram	ATR 4.1	MDD	N/A	N	73	22	3	32	16	0.58	0.91	0.77
Leuchter	2009 Bup	Psychiatry Research	Bupropion	ATR4.1	MDD	N/A	N	73	20	18	25	10	0.88	0.86	
Iosifescu	2009 Theta	European Neuropsychopharmacology	SSRI or venlafaxine	Theta Cordance	MDD	N/A	N	82	28	16	21	17	0.62	0.57	0.66
Iosifescu	2009 ATR	European Neuropsychopharmacology	SSRI or venlafaxine	ATR 4.1	MDD	N/A	N	82	37	17	20	8	0.82	0.54	0.72
Korb	2009 OFC	Clinical Neurophysiology	Fluoxetine, venlafaxine, or placebo	mOFC theta current density	MDD	N/A	N	37	16	6	9	6	0.73	0.60	0.69
Korb	2009 ACC	Clinical Neurophysiology	Fluoxetine, venlafaxine, or placebo	rACC theta current density	MDD	N/A	N	37	14	5	10	8	0.64	0.67	0.71

				(LORETA)											
Price	2008	Clinical EEG and Neuroscience	rTMS	alpha power, frequency, asymmetry	MDD	N/A	N/A	37	5	13	14	5	0.50	0.52	
Spronk	2008	Clinical EEG and Neuroscience	rTMS	Auditory oddball and alpha asymmetry	MDD	N	N	8							
Bares	2008	European Psychiatry	Venlafaxine	Prefrontal theta cordance	MDD	N	N	25	11	5	8	1	0.92	0.62	
Bruder	2008	Biological Psychiatry	Fluoxetine	Alpha power and asymmetry, occipital	Any depression	N/A	N	18	9	2	5	2	0.82	0.71	
Mulert	2007	Journal of Affective Disorders	Citalopram or reboxetine	rACC theta current density, LDAEP	MDD	N	N	17							
Bares	2007	Journal of Psychiatric Research	Any antidepressant	theta cordance	MDD	N/A	N	17	5	2	10	0	1.00	0.83	
Linka	2005	Pharmacopsychiatry	Reboxetine	LDAEP	Any depression	N/A	N	14							
Linka	2004	Neuroscience Letters	Citalopram	LDAEP	MDD	N	N	16							
Kalayam	2003	American Journal of Psychiatry	Citalopram	frontal error-related negativity	Geriatric MDD	Y	N	22							
Mulert	2002	Clinical Neurophysiology	Citalopram	LDAEP, source localized	MDD	N/A	N	15	9	1	4	1	0.90	0.80	0.88
Pizzagalli	2001	American Journal of Psychiatry	Nortriptyline	rACC theta current density (LORETA)	MDD	N	N	18	16	0	2	0	1.00	1.00	
Gallinat	2000	Psychopharmacology	any SSRI	LDAEP	MDD	N/A	N	29	9	6	11	3	0.75	0.65	
Olbrich	2016 Esc	Journal of Psychiatric Research	escitalopram or sertraline	Vigilance (VIGALL)	MDD	N/A	N	414	192	91	60	71	0.73	0.40	
Olbrich	2016 Vfx	Journal of Psychiatric Research	Venlafaxine	Vigilance (VIGALL)	MDD	N/A	N	184							
Adamczyk	2015	Journal of	any	theta	Any	N/A	N	20	5	1	11	3	0.63	0.92	0.90

		Psychiatric Research	antidepressant	cordance	depression										
Erguzel	2015	Psychiatry Investigation	rTMS	delta and theta cordance	MDD	N/A	Y	55	28	5	20	2	0.93	0.80	0.89
Rentzsch	2014	European Archives of Psychiatry and Clinical Neuroscience	any antidepressant	source-localized power	MDD	Y	N	31	9	0	20	2	0.82	1.00	0.93
Hunter	2011	Journal of clinical neurophysiology	Fluoxetine	ATR 4.1	MDD	N/A	N	12	12	4	8	0	1.00	0.67	0.83
Juckel	2007 Cit	Journal of Clinical Psychiatry	Citalopram	LDAEP, source localized	MDD	N/A	N/A	20							
Juckel	2007 Rbx	Journal of Clinical Psychiatry	reboxetine	LDAEP, source localized	MDD	N/A	N/A	15	3	4	5	3	0.50	0.56	
Cook	2005	Journal of Psychiatric Research	any medication	Prefrontal theta cordance	MDD	N/A	N	12	5	2	4	1	0.83	0.67	
Bruder	2001	Biological Psychiatry	Fluoxetine	alpha asymmetry	MDD, female	N/A	N	28	20	2	5	1	0.95	0.71	
Cook	2001	Seminars in clinical neuropsychiatry	SSRI or venlafaxine	Prefrontal theta cordance	MDD	N/A	N	7	4	0	3	0	1.00	1.00	
Heikman	2001	Journal of ECT	ECT	delta and theta MEG power and scalp ratios	MDD	N	N	7	5	0	2	0	1.00	1.00	
Knott	2000	Pharmacopsychiatry	paroxetine	power and coherence, multiple bands	MDD	N	N	51							
Broadway	2012	Neuropsychopharmacology	Cg25 Deep brain stimulation	theta cordance	MDD or bipolar II	N/A	N	12	5	0	6	1	0.83	1.00	0.97
Al-Kaysi	2017	Journal of Affective Disorders	tDCS	Multi-marker weighted	MDD	N	Y	10	4	1	4	1	0.76	0.76	
Li	2016	Cerebral Cortex	rTMS	Prefrontal theta power after task	MDD	N/A	N	24	10	3	9	2	0.83	0.77	0.80
Mumtaz	2017	PLoS ONE	Any SSRI	Multi-marker weighted	MDD	N/A	Y	34	15	4	14	1	0.95	0.80	
Noda	2017	Clinical Neurophysiology	rTMS	Gamma power, theta-gamma	MDD	Y	N	31	10	3	12	6	0.65	0.82	0.70

				coupling											
Pathak	2016	Frontiers in Neural Circuits	rTMS	Gamma and delta power and connectivity	MDD	N	N	5	4	0	1	0	1.00	1.00	
Schmidt	2017	Scientific Reports	Any antidepressant	Vigilance (VIGALL)	MDD	N/A	N	65	22	9	27	7	0.77	0.74	0.79
Ganghadar	1999	Journal of Affective Disorders	ECT	Fractal dimension post-ECT	MDD, melancholic	N/A	N	40	18	4	11	7	0.714	0.727	0.773
Staedt	1998	Journal of Affective Disorders	Tricyclic antidepressant	Sleep architecture (cluster disturbance)	MDD	N	N	20							
Murthy	1998	Journal of Affective Disorders	Sudarshan Kriya Yoga	auditory oddball ERP	MDD or dysthymia	N/A	N	30	11	4	4	11	0.50	0.50	
Knott	1996	Journal of Affective Disorders	Imipramine	Multi-electrode multi-band power	MDD	N	N	29							
Luthringer	1995	Biological Psychiatry	MAO or SSRI	Mean frequency of spectral peak	MDD	N	N	0							
Ulrich	1994 Clo	Journal of Affective Disorders	Clomipramine	Alpha power distribution	MDD/BP	N	N	23	6	2	9	6	0.50	0.82	
Ulrich	1994 Map	Journal of Affective Disorders	Maprotiline	Alpha power distribution	MDD/BP	N	N	20	3	4	9	4	0.43	0.69	
Paige	1994	Neuropsychobiology	Multiple antidepressant	LDAEP	MDD	N/A	N	17	8	0	6	3	0.73	1.00	0.848
Kupfer	1989	Psychiatry Research	Clomipramine	Delta power during sleep	MDD	Y	N	0							
Kasper	1988	Psychiatry Research	Sleep deprivation	Auditory ERP	Any depression	Y	N	20							
Frank	1984	Psychiatry Research	Imipramine and interpersonal therapy	REM latency	Any depression	N	N	34							
Kupfer	1981	American Journal of Psychiatry	Amitriptyline	REM latency	MDD	N	N	0							
Paige	1995	Psychopharmacology Bulletin	Bupropion	LDAEP	MDD	N/A	N	8							
Simons	1992	Journal of Consulting and Clinical Psychology	cognitive-behavioral therapy	REM latency	endogenous MDD	N/A	N	33	20	13	10	10	0.67	0.43	

Mult Corr, study reported (or did not report) correction for multiple hypothesis testing.

Cross Val, study did (or did not) use cross validation to verify proposed biomarkers.

ACC, anterior cingulate cortex. ATR, Antidepressant Treatment Response index. BP, bipolar disorder. ECT, electroconvulsive therapy. EEG, electroencephalogram. ERP, event-related potential. iSPOT-D, International Study to Predict Optimized Treatment of Depression. LDAEP, loudness dependence of the auditory evoked potential. LORETA, low resolution electrical tomography. MDD, major depressive disorder. MEG, Magnetoencephalography. NOS, not otherwise specified. rACC, rostral anterior cingulate cortex. rTMS, repetitive transcranial magnetic stimulation. SNRI, selective norepinephrine reuptake inhibitor. SSRI, selective serotonin reuptake inhibitor. TMS, transcranial magnetic stimulation.

TABLE S2. Studies included in meta-analysis of standard mean differences (Cohen's d), with necessary input variables when available. Abbreviations follow Table S1. Resp, responder. NResp, non-responder.

First Author	Year	Journal	Treatment	Marker	Resp Mean	Resp SD	NResp Mean	NResp SD	Cohen's d
van Dinteren	2015	European Neuropsychopharmacology	Escitalopram, sertraline, or venlafaxine-XR (iSPOT-D)	ERP latency and amplitude					0.890
Arns	2016	Clinical Neurophysiology	Escitalopram, sertraline, or venlafaxine-XR (iSPOT-D)	occipital alpha power & frontal alpha asymmetry					0.550
Woźniak-Kwaśniewska	2015	Journal of Affective Disorders	rTMS	prefrontal theta and beta power	2260.000	961.332	3260.000	613.769	1.240
Arns	2015	European Neuropsychopharmacology	Escitalopram, sertraline, or venlafaxine-XR (iSPOT-D)	frontal and rostral anterior cingulate (rACC) theta					0.170
Lee	2015	International Journal of Molecular Sciences	Escitalopram, sertraline, or paroxetine	LDAEP, source localized	1.470	0.830	0.950	0.590	0.722
Caudill	2015	Clinical EEG and Neuroscience	Reboxetine	ATR 4.1					0.910
Canali	2014	Bipolar Disorders	Sleep deprivation	Cortical excitability to TMS					0.696
Bares	2015b	European Archives of Psychiatry and Clinical Neurosciences	Any antidepressant	Prefrontal theta cordance	0.070	0.200	-0.100	0.200	0.850
Bares	2015a Vfx	Clinical EEG and Neuroscience	Venlafaxine	Prefrontal theta cordance	-0.130	0.100	0.040	0.100	1.700
Bares	2015a TMS	Clinical EEG and Neuroscience	low frequency TMS	Prefrontal theta cordance	-0.130	0.100	0.030	0.300	0.716
Arns	2014	Clinical Neurophysiology	rTMS	Non-linear complexity metrics, alpha band	-0.002	0.007	0.002	0.005	0.540
Quraan	2014	Neuropsychopharmacology	Cg25 Deep brain stimulation	Theta and alpha frontal asymmetry	0.360	0.710	-0.600	0.612	1.448
Widge	2013	Brain Stimulation	rTMS	ATR 4.1					
Hunter	2013	Journal of Neuropsychiatry and Clinical Neurosciences	Sertraline	rACC theta current density (LORETA)	0.370	0.340	1.310	0.270	3.062
Khodayari-Rostamabad	2013	Clinical Neurophysiology	Any SSRI	Multi-marker weighted	0.189	0.081	0.348	0.066	2.404

Jaworska	2013a	European Neuropsychopharmacology	Escitalopram, bupropion, or both	auditory oddball ERP	10.000	4.589	7.000	4.500	0.660
Jaworska	2013b	Progress in neuro-psychopharmacology and biological psychiatry	Escitalopram, bupropion, or both	LDAEP	4.750	2.700	2.350	1.825	1.041
Arns	2012	Brain Stimulation	rTMS	Multi-marker weighted					1.322
Khodayari-Rostamabad	2011	Conference Proceedings: Annual International Conference of the IEEE Engineering in Medicine and Biology Society	rTMS	Multi-marker weighted					1.578
Micoulaud-Franchi	2012	Journal of Affective Disorders	rTMS	alpha power					1.268
Bares	2012	Journal of Psychiatric Research	Any antidepressant	Prefrontal theta cordance					1.737
Tenke	2011	Biological Psychiatry	SSRI or SI	multi-electrode alpha power					0.728
Khodayari-Rostamabad	2010	Conference Proceedings: Annual International Conference of the IEEEEngineering in Medicine and Biology Society	Any SSRI	Multi-marker weighted					2.061
Spronk	2011	Journal of Affective Disorders	Any antidepressant	Theta power, auditory ERP					0.976
Bares	2010	European Neuropsychopharmacology	Bupropion	prefrontal EEG theta cordance					1.817
Salvadore	2010	Neuropsychopharmacology	Ketamine	Pregenual ACC activity and connectivity					2.865
Narushima	2010	Journal of Neuropsychiatry and Clinical Neurosciences	rTMS	subgenual ACC theta power					0.171
Wang	2009	Chinese Medical Journal	Any antidepressant	Auditory ERP					0.563
Cook	2009	Psychiatry Research	Fluoxetine or venlafaxine	frontal theta cordance and power	-1.140	0.770	-0.030	0.760	1.451
Leuchter	2009 Esc	Psychiatry Research	Escitalopram	ATR 4.1	59.000	10.200	49.800	7.800	1.013
Leuchter	2009 Bup	Psychiatry Research	Bupropion	ATR4.1	50.100	10.300	53.000	11.100	0.271
Iosifescu	2009 Theta	European Neuropsychopharmacology	SSRI or venlafaxine	Theta Cordance	21.100	4.400	23.700	4.900	0.558

Iosifescu	2009 ATR	European Neuropsychopharmacology	SSRI or venlafaxine	ATR 4.1	56.100	11.400	48.700	10.100	0.687
Korb	2009 OFC	Clinical Neurophysiology	Fluoxetine, venlafaxine, or placebo	mOFC theta current density	-1.932	0.253	-2.107	0.216	0.744
Korb	2009 ACC	Clinical Neurophysiology	Fluoxetine, venlafaxine, or placebo	rACC theta current density (LORETA)	-1.890	0.228	-2.046	0.207	0.716
Price	2008	Clinical EEG and Neuroscience	rTMS	alpha power, frequency, asymmetry	0.140	0.240	-0.030	0.250	0.694
Spronk	2008	Clinical EEG and Neuroscience	rTMS	Auditory oddball and alpha asymmetry					
Bares	2008	European Psychiatry	Venlafaxine	Prefrontal theta cordance					1.581
Bruder	2008	Biological Psychiatry	Fluoxetine	Alpha power and asymmetry, occipital	1.750	0.470	1.200	0.470	1.170
Mulert	2007	Journal of Affective Disorders	Citalopram or reboxetine	rACC theta current density, LDAEP					1.410
Bares	2007	Journal of Psychiatric Research	Any antidepressant	theta cordance					2.113
Linka	2005	Pharmacopsychiatry	Reboxetine	LDAEP					5.060
Linka	2004	Neuroscience Letters	Citalopram	LDAEP					1.352
Kalayam	2003	American Journal of Psychiatry	Citalopram	frontal error-related negativity	-4.840	1.840	-8.120	4.010	1.051
Mulert	2002	Clinical Neurophysiology	Citalopram	LDAEP, source localized	1.530	0.890	0.410	0.650	1.437
Pizzagalli	2001	American Journal of Psychiatry	Nortriptyline	rACC theta current density (LORETA)	-3.350	0.060	-3.430	0.060	1.333
Gallinat	2000	Psychopharmacology	any SSRI	LDAEP					0.940
Olbrich	2016 Esc	Journal of Psychiatric Research	escitalopram or sertraline	Vigilance (VIGALL)					0.250
Olbrich	2016 Vfx	Journal of Psychiatric Research	Venlafaxine	Vigilance (VIGALL)					0.002
Adamczyk	2015	Journal of Psychiatric Research	any antidepressant	theta cordance	-2.030	0.870	-2.840	0.350	1.222
Erguzel	2015	Psychiatry Investigation	rTMS	delta and theta cordance					1.887
Rentzsch	2014	European Archives of Psychiatry and Clinical Neuroscience	any antidepressant	source-localized power					2.087
Hunter	2011	Journal of clinical neurophysiology	Fluoxetine	ATR 4.1					1.349
Juckel	2007 Cit	Journal of Clinical Psychiatry	Citalopram	LDAEP, source localized					1.169

Juckel	2007 Rbx	Journal of Clinical Psychiatry	reboxetine	LDAEP, source localized					0.782
Cook	2005	Journal of Psychiatric Research	any medication	Prefrontal theta cordance					1.270
Bruder	2001	Biological Psychiatry	Fluoxetine	alpha asymmetry					2.123
Cook	2001	Seminars in clinical neuropsychiatry	SSRI or venlafaxine	Prefrontal theta cordance	-0.465	0.099	0.090	0.182	3.788
Heikman	2001	Journal of ECT	ECT	delta and theta MEG power and scalp ratios					5.060
Knott	2000	Pharmacopsychiatry	paroxetine	power and coherence, multiple bands					1.500
Broadway	2012	Neuropsychopharmacology	Cg25 Deep brain stimulation	theta cordance					2.703
Al-Kaysi	2017	Journal of Affective Disorders	tDCS	Multi-marker weighted					1.529
Li	2016	Cerebral Cortex	rTMS	Prefrontal theta power after task					1.185
Mumtaz	2017	PLoS ONE	Any SSRI	Multi-marker weighted					1.680
Noda	2017	Clinical Neurophysiology	rTMS	Gamma power, theta-gamma coupling					0.721
Pathak	2016	Frontiers in Neural Circuits	rTMS	Gamma and delta power and connectivity					2.665
Schmidt	2017	Scientific Reports	Any antidepressant	Vigilance (VIGALL)					1.141
Ganghadar	1999	Journal of Affective Disorders	ECT	Fractal dimension post-ECT	1.070	0.086	1.030	0.043	0.588
Staedt	1998	Journal of Affective Disorders	Tricyclic antidepressant	Sleep architecture (cluster disturbance)					1.415
Murthy	1998	Journal of Affective Disorders	Sudarshan Kriya Yoga	auditory oddball ERP	7.400	3.800	7.600	5.000	0.317
Knott	1996	Journal of Affective Disorders	Imipramine	Multi-electrode multi-band power					0.806
Luthringer	1995	Biological Psychiatry	MAO or SSRI	Mean frequency of spectral peak	6.910	1.750	8.500	2.420	1.115
Ulrich	1994 Clo	Journal of Affective Disorders	Clomipramine	Alpha power distribution					0.829
Ulrich	1994 Map	Journal of Affective Disorders	Maprotiline	Alpha power distribution					0.289
Paige	1994	Neuropsychobiology	Multiple antidepressant	LDAEP	0.301	0.183	0.076	0.151	1.341
Kupfer	1989	Psychiatry Research	Clomipramine	Delta power during sleep					

Kasper	1988	Psychiatry Research	Sleep deprivation	Auditory ERP					0.787
Frank	1984	Psychiatry Research	Imipramine and interpersonal therapy	REM latency					0.847
Kupfer	1981	American Journal of Psychiatry	Amitriptyline	REM latency					1.079
Paige	1995	Psychopharmacology Bulletin	Bupropion	LDAEP					
Simons	1992	Journal of Consulting and Clinical Psychology	cognitive-behavioral therapy	REM latency					0.255

TABLE S3. Meta-regression coefficients for the bivariate meta-analytic model, estimating differential effects of specific biomarkers. p-values are from Z-test on regression coefficients. Two coefficients reach significance for being more specific than QEEG overall. The Akaike Information Criterion increases, however, from -115.66 for the all-studies model to -104.11 for this meta-regression model. This indicates that the significant coefficient represent over-fitting rather than a true effect.

Marker	Sens	Sens (SE)	Sens (p)	Spec	Spec (SE)	Spec (p)
Intercept	0.691	0.042	**0.000**	0.567	0.050	0.213
Alpha Power	0.041	0.347	0.636	0.050	0.337	0.589
Alpha Asymmetry	-0.011	0.356	0.910	0.089	0.339	0.367
ATR	-0.029	0.337	0.721	0.089	0.327	0.283
Cordance	0.120	0.336	0.065	0.170	0.314	**0.015**
LDAEP	-0.010	0.344	0.906	0.153	0.330	0.096
Multivariate	0.128	0.359	0.167	0.250	0.320	**0.005**
Theta Power	0.013	0.346	0.879	0.128	0.331	0.161

Sens, sensitivity ; Spec, specificity ; SE, standard error of regression coefficient; p, p-value.

TABLE S4. Meta-regression coefficients for the bivariate meta-analytic model, estimating differential ability of QEEG to predict the response to specific treatments. p-values are from Z-test on regression coefficients. The coefficients for medication and rTMS are non-significant, suggesting no greater predictive power for either treatment class.

Marker	Sens	Sens (SE)	Sens (p)	Spec	Spec (SE)	Spec (p)
Intercept	0.678	0.064	**0.032**	0.631	0.078	0.173
Medication	0.045	0.337	0.565	0.067	0.343	0.470
rTMS	0.059	0.349	0.507	0.011	0.355	0.919

Sens, sensitivity ; Spec, specificity ; SE, standard error of regression coefficient; p, p-value.

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