

Supplementary Table S1. Comparison of LTL between patients with TRD and controls in a subsample of patients and controls matched for age.

	LTL, median (IQR)	Unadjusted analyses		Analyses adjusted for age	
		U	p	Quade's F	p
Patients with TRD (n=147)	0.77 (0.30)	5,567	< 0.0001	58.92	< 0.0001
Controls (n=147)	1.03 (0.48)				
Patients with MDD (n=121)	0.79 (0.28)	4,698	< 0.0001	47.91	< 0.0001
Controls (n=147)	1.03 (0.48)				
Patients with BD (n=26)	0.70 (0.45)	869	< 0.0001	22.81	< 0.0001
Controls (n=147)	1.03 (0.48)				

LTL was compared between a subsample of 147 patients with TRD (median age: 56 years, IQR = 19 years) and 147 controls (median age: 54 years, IQR: 20 years) who were matched based on age using the Case Control Matching function in SPSS v. 26. A tolerance factor of 3 years was applied in order to minimize the loss of cases while still obtaining two groups of cases and controls that did not show a statistically significant difference in age (Mann Whitney's U = 9610, p = 0.10).

Abbreviations: IQR, interquartile range; LTL, leukocyte telomere length; TRD, treatment-resistant depression.

Supplementary Table S2. Comparison of LTL between responders and non-responders to ECT in patients with TRD stratified based on psychiatric diagnosis.

		Unadjusted analyses		Analyses adjusted for age	
	LTL, median (IQR)	U	p	Quade's F	p
Patients with MDD					
Responders at T1 (n=102)	0.79 (0.27)	598	0.57	0.30	0.59
Non-Responders at T1 (n=13)	0.86 (0.25)				
Responders at T2 (n=59)	0.77 (0.31)	598	0.17	0.94	0.34
Non-Responders at T2 (n=25)	0.89 (0.24)				
Remitters (n=47)	0.75 (0.30)	605	0.10	1.93	0.17
Non remitters (n=33)	0.88 (0.26)				
Patients with BD					
Responders at T1 (n=17)	0.65 (0.33)	5	0.67	0.39	0.54
Non-Responders at T1 (n=1)	-				
Responders at T2 (n=6)	0.76 (0.44)	3	0.43	0.47	0.52
Non-Responders at T2 (n=2)	0.60 (-)				
Remitters (n=6)	0.76 (0.44)	3	0.43	0.47	0.52
Non remitters (n=2)	0.60 (-)				
	Median (IQR)	Spearman's rho	p	partial corr. coeff.	p
Patients with MDD					
Delta % MADRS T1-T0	75.00 (21.22)	-0.13	0.15	-0.15	0.11
Delta % MADRS T2-T0	74.08 (55.75)	-0.19	0.09	-0.18	0.12
Patients with BD					
Delta % MADRS T1-T0	79.22 (31.16)	0.15	0.56	0.18	0.50
Delta % MADRS T2-T0	94.17 (41.81)	0.22	0.60	0.19	0.69

Abbreviations: BD, bipolar disorder; corr. coeff, correlation coefficient; IQR, interquartile range; LTL, leukocyte telomere length; MADRS, Montgomery Asberg Depression rating scale; MDD, major depressive disorder.

Supplementary Table S3. Comparison of LTL between responders and non-responders to ECT in patients with TRD stratified based on intake of clonazepam.

		Unadjusted analyses		Analyses adjusted for age	
	LTL, median (IQR)	U	p	Quade's F	p
Not treated with clonazepam					
Responders at T1 (n=91)	0.78 (0.30)	437	0.49	0.28	0.60
Non-Responders at T1 (n=11)	0.81 (0.31)				
Responders at T2 (n=55)	0.77 (0.36)	426	0.38	0.72	0.40
Non-Responders at T2 (n=18)	0.89 (0.26)				
Remitters at T2 (n=44)	0.75 (0.30)	423	0.11	0.53	0.12
Non remitters at T2 (n=25)	0.89 (0.27)				
Treated with clonazepam					
Responders at T1 (n=27)	0.75 (0.26)	10	0.03	0.24	0.14
Non-Responders at T1 (n=3)	0.98 (-)				
Responders at T2 (n=10)	0.75 (0.32)	40	0.72	0.05	0.83
Non-Responders at T2 (n=9)	0.77 (0.28)				
Remitters at T2 (n= 9)	0.75 (0.30)	41	0.78	0.18	0.68
Non remitters at T2 (n=10)	0.76 (0.29)				
	Median (IQR)	Spearman's rho	p	partial corr. coeff.	p
Not treated with clonazepam					
Delta % MADRS T1-T0	75.34 (21.74)	-0.01	0.93	-0.06	0.54
Delta % MADRS T2-T0	80.00 (44.58)				
Treated with clonazepam					
Delta % MADRS T1-T0	75.53 (24.31)	-0.36	0.048	-0.23	0.23
Delta % MADRS T2-T0	73.53 (80.29)				

Abbreviations: corr. coeff, correlation coefficient; IQR, interquartile range; LTL, leukocyte telomere length; MADRS, Montgomery Asberg Depression rating scale.

Supplementary Table S4. Assessment of overrepresentation between SNPs and genes associated with response to ECT and LTL.

Number of SNPs nominally associated with LTL	Number of SNPs nominally associated with response	Overlap between SNPs associated with LTL and response	p
SNP associated with LTL: 185,410	SNPs associated with response at T1: 128,228	6,021	p = 1
	SNPs associated with response at T2: 144,770	6,222	p = 1
	SNPs associated with remission: 145,795	6,803	p = 1
	SNPs associated with Delta % T0-T1: 179,239	8,312	p = 1
	SNPs associated with Delta % T0-T2: 177,725	8,134	p = 1
Number of genes nominally associated with LTL	Number of genes nominally associated with response	Overlap between genes associated with LTL and response	p
Genes associated with LTL: 885	Genes associated with response at T1: 608	39	p = 0.11
	Genes associated with response at T2: 651	26	p = 0.93
	Genes associated with remission: 602	26	p = 0.85
	Genes associated with Delta % T0-T1: 849	45	p = 0.44
	Genes associated with Delta % T0-T2: 810	48	p = 0.17

Abbreviations: LTL, leukocyte telomere length; SNP, single nucleotide polymorphism.

Supplementary Table S5. Association between SNP previously associated with LTL and response to ECT.

			Response at T1			Delta % T0-T1		Response at T2		Remission		Delta % T0-T2		LTL in current sample	
Chr	SNP	Closest gene	A1	OR	P	Beta	P	OR	P	OR	P	Beta	P	Beta	P
1	rs3219104	PARP1	A	0.95	0.93	0.80	0.81	0.64	0.33	0.78	0.58	-7.37	0.33	-0.03	0.41
3	rs2613954	RP11-572M11.4	C	1.26	0.72	2.97	0.35	2.47	0.10	1.48	0.38	12.70	0.09	-0.02	0.60
3	rs10936600	LRRC34 (TERC)	T	0.55	0.21	-0.29	0.91	0.69	0.33	0.65	0.26	-2.64	0.69	0.00	0.94
4	rs60160057	DCLK2	A	2.33	0.26	3.80	0.18	0.41	0.045	0.42	0.06	-16.63	0.02	0.00	0.94
4	rs4691895	NAF1	G	0.76	0.63	0.40	0.90	2.20	0.12	1.34	0.51	-0.90	0.90	-0.02	0.68
5	rs2853677	TERT	G	1.20	0.71	-3.55	0.15	1.38	0.37	1.72	0.13	4.87	0.38	-0.01	0.61
6	rs2736176	PRRC2A	C	1.22	0.69	0.32	0.90	0.53	0.11	0.84	0.64	-9.44	0.12	-0.01	0.86
7	rs59294613	POT1	A	1.15	0.76	2.70	0.26	1.11	0.77	1.25	0.51	3.61	0.50	-0.02	0.47
8	rs57415150	CSMD1	A	1.00	1.00	-5.07	0.39	0.92	0.92	1.53	0.64	-4.57	0.75	0.00	0.97
10	rs9419958	STN1 (OBFC1)	T	0.47	0.13	-4.60	0.14	1.38	0.52	1.20	0.69	4.37	0.54	-0.06	0.08
11	rs228595	ATM	G	1.79	0.23	2.36	0.33	0.78	0.49	0.82	0.56	-2.28	0.69	0.05	0.11
12	rs7311314	SMUG1	A	3.45	0.06	-0.16	0.95	1.41	0.39	1.67	0.18	4.41	0.46	0.01	0.74
14	rs2302588	DCAF4	C	0.59	0.36	-6.87	0.05	1.28	0.64	1.09	0.86	-1.56	0.85	0.03	0.49
15	rs12909131	ATP8B4	T	0.61	0.38	-1.38	0.68	0.79	0.60	0.88	0.78	-7.73	0.30	0.00	0.92
16	rs3785074	TERF2	G	0.60	0.31	-4.29	0.13	1.26	0.60	0.95	0.90	1.35	0.84	0.00	0.92
16	rs7194734	MPHOSPH6	C	1.36	0.58	4.23	0.12	0.39	0.032	0.72	0.42	-13.05	0.05	0.07	0.04
18	rs2124616	TYMS	A	1.03	0.97	3.43	0.44	0.59	0.42	0.74	0.64	-2.49	0.82	0.01	0.88
19	rs8105767	ZNF208	G	0.44	0.07	-7.19	0.003	0.73	0.41	0.49	0.07	-11.26	0.07	0.01	0.78
20	rs75691080	STMN3	T	1.39	0.69	0.60	0.88	2.00	0.27	3.37	0.05	13.68	0.13	0.01	0.76
20	rs932827	ZBTB46	T	0.85	0.76	2.30	0.43	0.72	0.46	0.60	0.25	-0.79	0.91	-0.04	0.29
20	rs73624724	ZBTB46	C	NA	NA	0.99	0.86	0.29	0.09	0.32	0.13	-19.26	0.12	0.07	0.31

Abbreviations: A1, effect allele; Chr, chromosome; LTL, leukocyte telomere length; NA, not available, OR, odds ratio; SNP, single nucleotide polymorphism.