

## Supplementary

**Table S1** Outliers

id.exposure	SNP	effect_allele.exposure	other_allele.exposure	effect_allele.outcome	other_allele.outcome
ebi-a-GCST006948	rs12729445	T	C	T	C
ebi-a-GCST006948	rs9879090	C	T	C	T
ebi-a-GCST006950	rs57462170	A	G	A	G
ebi-a-GCST006952	rs10218528	A	T	A	T
ebi-a-GCST006952	rs2097247	T	C	T	C
ukb-a-230	rs57838764	C	T	C	T

id.exposure, identifier for exposure; SNP, single nucleotide polymorphism.

**Table S2** Results of the two-sample MR analysis and sensitivity analysis

GWAS ID	Exposure	Method	nsnp	b	SE	P value	lo_ci	up_ci	or	or_lci95	or_uci95	Q	Q_df	Q_P value	egger_intercept	P value
ebi-a-GCST005232	Neuroticism	Inverse variance-weighted (multiplicative random effects)	54	0.136410526	0.061086504	0.03	0.016680979	0.256140074	1.146152323	1.016820883	1.291933681	53.404851	53	0.46	0.0015287	0.94
ebi-a-GCST005232	Neuroticism	MR-Egger	54	0.093175728	0.599408759	0.88	-1.081665439	1.268016895	1.097654607	0.339030421	3.553798015	53.399452	52	0.42	-	-
ebi-a-GCST005232	Neuroticism	Weighted median	54	0.199484	0.084375949	0.02	0.03410714	0.364860861	1.220772677	1.034695458	1.44031359	-	-	-	-	-
ukb-a-230	Neuroticism score	Inverse variance-weighted (multiplicative random effects)	53	0.103118405	0.038115964	0.007	0.028411115	0.177825695	1.108622668	1.028818561	1.194617075	55.81815	51	0.30	-0.008147	0.60
ukb-a-230	Neuroticism score	MR-Egger	53	0.244432072	0.272922609	0.37	-0.290496241	0.779360385	1.276895922	0.74789234	2.18007741	56.117494	52	0.32	-	-
ukb-a-230	Neuroticism score	Weighted median	53	0.095257363	0.054157054	0.08	-0.010890464	0.201405189	1.099941903	0.989168623	1.223120266	-	-	-	-	-
ebi-a-GCST006944	Experiencing mood swings	Inverse variance-weighted (multiplicative random effects)	34	0.341816615	0.171790029	0.047	0.005108158	0.678525072	1.407502159	1.005121227	1.970968551	31.100431	33	0.56	-0.027326	0.19
ebi-a-GCST006944	Experiencing mood swings	MR-Egger	34	2.122310812	1.332360692	0.12	-0.489116144	4.733737768	8.350411442	0.613168107	113.7198273	29.282544	32	0.60	-	-
ebi-a-GCST006944	Experiencing mood swings	Weighted median	34	0.438713792	0.253326546	0.08	-0.057806238	0.935233821	1.550711397	0.943832809	2.547809119	-	-	-	-	-
ebi-a-GCST006942	Feeling lonely	Inverse variance-weighted (multiplicative random effects)	4	1.796094453	0.532193733	<0.001	0.752994737	2.839194169	6.026066359	2.123349377	17.10197867	3.326265	3	0.34	-0.051095	0.46
ebi-a-GCST006942	Feeling lonely	MR-Egger	4	5.00120646	3.594598487	0.30	-2.044206574	12.04661949	148.5923217	0.129482884	170521.9819	2.3640353	2	0.31	-	-
ebi-a-GCST006942	Feeling lonely	Weighted median	4	2.277697987	0.620585882	<0.001	1.061349657	3.494046316	9.754200247	2.890269231	32.91887878	-	-	-	-	-
ebi-a-GCST006943	Feeling miserable	Inverse variance-weighted (multiplicative random effects)	25	-0.143016064	0.185923584	0.44	-0.507426288	0.22139416	0.866740145	0.602043072	1.247815172	18.942219	24	0.76	0.0024184	0.86
ebi-a-GCST006943	Feeling miserable	MR-Egger	25	-0.290120519	0.880594981	0.74	-2.016086682	1.435845644	0.748173393	0.133175605	4.203197915	18.912642	23	0.71	-	-
ebi-a-GCST006943	Feeling miserable	Weighted median	25	-0.259376908	0.285575953	0.36	-0.819105776	0.30035196	0.771532172	0.440825675	1.350333988	-	-	-	-	-
ebi-a-GCST006950	Feeling worry	Inverse variance-weighted (multiplicative random effects)	27	0.455340584	0.210066588	0.03	0.04361007	0.867071097	1.576710293	1.044574964	2.379930051	29.189911	26	0.30	-0.006275	0.80
ebi-a-GCST006950	Feeling worry	MR-Egger	27	0.852608487	1.586038095	0.60	-2.256026179	3.961243154	2.345757758	0.10476598	52.52257904	29.115489	25	0.26	-	-
ebi-a-GCST006950	Feeling worry	Weighted median	27	0.500788495	0.284449019	0.08	-0.056731583	1.058308572	1.650021791	0.944847649	2.881493027	-	-	-	-	-
ebi-a-GCST006946	Worry too long after an embarrassing experience	Inverse variance-weighted (multiplicative random effects)	12	0.280735233	0.300702251	0.35	-0.308641178	0.870111645	1.324102979	0.734444257	2.387177354	11.540381	11	0.40	-0.037537	0.28
ebi-a-GCST006946	Worry too long after an embarrassing experience	MR-Egger	12	2.678411656	2.123420139	0.24	-1.483491817	6.840315129	14.56194554	0.226844205	934.7836655	10.212382	10	0.42	-	-
ebi-a-GCST006946	Worry too long after an embarrassing experience	Weighted median	12	0.453844748	0.396536872	0.25	-0.323367521	1.231057017	1.574353557	0.723707827	3.424847748	-	-	-	-	-
ebi-a-GCST006947	Feeling fed-up	Inverse variance-weighted (multiplicative random effects)	21	0.234590549	0.261689479	0.37	-0.27832083	0.747501929	1.264390957	0.757053897	2.1117182	28.33047	20	0.10	0.0054748	0.81
ebi-a-GCST006947	Feeling fed-up	MR-Egger	21	-0.099635601	1.38890227	0.94	-2.82188405	2.622612849	0.9051672	0.059493748	13.77165989	28.241067	19	0.08	-	-
ebi-a-GCST006947	Feeling fed-up	Weighted median	21	0.435102289	0.318634415	0.17	-0.189421165	1.059625743	1.545121099	0.827437945	2.885290946	-	-	-	-	-
ebi-a-GCST006945	Feeling guilty	Inverse variance-weighted (multiplicative random effects)	10	-0.053493558	0.320880229	0.87	-0.682418806	0.575431691	0.947912048	0.505393065	1.777897864	9.3288645	9	0.41	-0.008881	0.80
ebi-a-GCST006945	Feeling guilty	MR-Egger	10	0.487975642	2.148058509	0.83	-3.722219035	4.69817032	1.629015171	0.024180251	109.7461883	9.2534904	8	0.32	-	-
ebi-a-GCST006945	Feeling guilty	Weighted median	10	-0.028654432	0.428427537	0.95	-0.868372405	0.811063541	0.971752213	0.419633988	2.250300002	-	-	-	-	-
ebi-a-GCST006948	Feeling nervous	Inverse variance-weighted (multiplicative random effects)	23	-0.059559322	0.245488603	0.81	-0.540716984	0.421598341	0.94217964	0.582330581	1.524396114	29.530583	22	0.13	-0.002782	0.89
ebi-a-GCST006948	Feeling nervous	MR-Egger	23	0.110131048	1.262606292	0.93	-2.364577285	2.584839381	1.116424366	0.093989023	13.26115892	29.50416	21	0.10	-	-
ebi-a-GCST006948	Feeling nervous	Weighted median	23	-0.165818146	0.310251639	0.59	-0.77391136	0.442275067	0.847200287	0.461205595	1.556243752	-	-	-	-	-
ebi-a-GCST006952	Feeling tense	Inverse variance-weighted (multiplicative random effects)	17	-0.086479696	0.24818527	0.73	-0.572922824	0.399963432	0.917154171	0.563874921	1.491770146	16.112038	16	0.45	-0.030028	0.39
ebi-a-GCST006952	Feeling tense	MR-Egger	17	1.779555107	2.128961231	0.42	-2.393208906	5.95231912	5.927218854	0.091336124	384.644342	15.316608	15	0.43	-	-
ebi-a-GCST006952	Feeling tense	Weighted median	17	-0.034722084	0.341635694	0.92	-0.704328044	0.634883876	0.965873811	0.494440705	1.886803026	-	-	-	-	-
ebi-a-GCST006941	Irritable mood	Inverse variance-weighted (multiplicative random effects)	30	0.474916213	0.203192271	0.02	0.076659363	0.873173064	1.607879473	1.079674237	2.394496703	34.497754	29	0.22	0.019983	0.47
ebi-a-GCST006941	Irritable mood	MR-Egger	30	-0.793333938	1.761778545	0.66	-4.246419886	2.659752011	0.452334225	0.014315393	14.29274422	33.862451	28	0.21	-	-
ebi-a-GCST006941	Irritable mood	Weighted median	30	0.332468834	0.268198271	0.22	-0.193199778	0.858137445	1.39440644	0.824317277	2.358763274	-	-	-	-	-
ebi-a-GCST006951	Feeling hurt	Inverse variance-weighted (multiplicative random effects)	24	0.582556864	0.282586861	0.04	0.028686616	1.136427111	1.79061093	1.02910204	3.115616703	39.64272	23	0.02	-0.068142	0.02
ebi-a-GCST006951	Feeling hurt	MR-Egger	24	5.042521795	1.786484011	0.010	1.541013133	8.544030456	154.8600483	4.669318516	5136.003138	30.750709	22	0.10	-	-
ebi-a-GCST006951	Feeling hurt	Weighted median	24	0.684179776	0.340365955	0.044	0.017062503	1.351297048	1.982145364	1.017208899	3.862432043	-	-	-	-	-

MR, Mendelian randomization; GWAS ID, genome-wide association study identifier; nsnp, number of single nucleotide polymorphisms; SE, standard error; lo\_ci, lower confidence interval of the regression coefficient b; up\_ci, upper confidence interval of the regression coefficient b; or, odds ratio; or\_lci95, odds ratio lower confidence interval at 95%; or\_uci95, odds ratio upper confidence interval at 95%; Q, Q-value of the Q test; Q\_df, Q statistic degrees of freedom; Q\_P, Q statistic P value.

**Table S3** The results of the pleiotropy test using MR-PRESSO

Exposure	Global test RSSobs	Global test P value
Experiencing mood swings	33.06842427	0.58
Feeling fed-up	31.76094347	0.08
Feeling guilty	11.33693522	0.43
Feeling hurt	43.16208	0.02
Feeling lonely	5.820765	0.44
Feeling miserable	20.65213	0.75
Feeling nervous	32.19791	0.13
Feeling tense	18.36476	0.43
Feeling worry	31.43784	0.32
Irritable mood	36.90099	0.23
Neuroticism	55.24939	0.50
Worry too long after an embarrassing experience	13.50418309	0.43
Neuroticism score	58.26299518	0.33

MR-PRESSO, Mendelian randomization pleiotropy residual sum and outlier; RSSobs, the observed residual sum of squares.