

Supplementary Information

Genome-wide Association Study of Personality Traits in the Long Life Family Study

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Supplementary Table 1. Transformation formula for the raw NEO-FFI scores

Transformation Formula	Parameters in the Formula
	S = raw NEO-FFI score

This transformation yields sex-specific standardized T-scores with mean=50 and standard deviation of 10.

Supplementary Table 2. Heritability Estimates of the five domains of NEO-FFI in subjects of LLFS, in comparison with Heritability Estimates from SardiNIA (10)

NEO Domains	Heritability Estimates from LLFS (p-value)	Heritability Estimates from SardiNIA (p-value)
Agreeableness	0.176 (1.7×10^{-5})	0.232 (NS)
Conscientiousness	0.300 (1.7×10^{-23})	0.204 (<0.01)
Extraversion	0.318 (3.2×10^{-15})	0.253 (<0.05)
Neuroticism	0.252 (1.7×10^{-15})	0.254 (<0.01)
Openness	0.486 (4.1×10^{-23})	0.328 (<0.001)

Reported are the heritability estimates defined as the ratio between genetic variance and total variance (narrow heritability).

Supplementary Table 3. Results of Replication of LLFS Findings in NECS

Domain	SNP	CHR	Gene	CA	Discovery in LLFS				Replication in NECS			
					CAF	Beta	SE	P	CAF	Beta	SE	P
agree	rs11888210	2	ANKRD44	C	0.14	1.79	0.38	2.23E-06	0.12	-2.9	1.72	0.09
agree	rs2587577	8	-	A	0.16	1.64	0.36	6.53E-06	0.2	2.18	1.28	0.09
agree	rs658912	5	ATP6AP1L	T	0.37	1.22	0.27	6.07E-06	0.39	0.3	1.02	0.77
agree	rs8042694	15	COX5A	G	0.32	-1.29	0.28	5.49E-06	0.31	-0.36	1.15	0.76
consc	rs13397210	2	SCN1A	T	0.21	-1.3	0.27	1.17E-06	0.21	0.35	1.45	0.81
consc	rs1841548	2	SCN1A	C	0.21	-1.3	0.27	1.09E-06	0.21	0.35	1.45	0.81
consc	rs2781564	6	-	A	0.44	0.97	0.22	7.50E-06	0.39	0.73	1.2	0.54
consc	rs3923603	4	-	A	0.39	-1.03	0.22	4.71E-06	0.42	0.07	1.17	0.95
consc	rs6425361	1	-	T	0.26	-1.16	0.25	5.65E-06	0.25	-1.28	1.36	0.35
consc	rs671000	1	-	T	0.25	-1.19	0.26	4.21E-06	0.24	-0.75	1.34	0.58
consc	rs7809940	7	-	G	0.35	-1.04	0.23	4.66E-06	0.37	0.18	1.47	0.9
consc	rs9822730	3	-	A	0.2	-1.2	0.27	7.83E-06	0.18	-2.72	1.58	0.09
extra	rs9832895	3	SCN5A	T	0.48	1.38	0.29	1.73E-06	0.48	0.86	1.14	0.45
neuro	rs178244	11	GRM5	A	0.48	-0.91	0.19	1.82E-06	0.48	-0.57	1.08	0.6
neuro	rs2173324	4	-	G	0.38	0.89	0.2	6.08E-06	0.35	-0.3	1.3	0.82
neuro	rs2189000	7	TWIST1	G	0.14	1.22	0.27	8.28E-06	0.09	2.32	1.96	0.24
neuro	rs4233429	1	-	T	0.29	-0.94	0.21	9.23E-06	0.3	-0.95	1.3	0.46
neuro	rs4725336	7	REPIN1	C	0.15	-1.19	0.27	8.24E-06	0.16	-0.86	1.5	0.57
open	rs10803639	2	-	A	0.26	-1.38	0.31	7.47E-06	0.28	-0.47	1.21	0.7
open	rs10831742	11	MICAL2	G	0.17	1.71	0.36	1.96E-06	0.14	0.6	1.54	0.7
open	rs17039820	2	-	A	0.07	2.31	0.52	8.02E-06	0.08	-0.57	1.98	0.77
open	rs2332838	4	-	A	0.32	1.27	0.29	9.21E-06	0.29	0.33	1.23	0.79

CA: Coded Allele

CAF: Coded Allele Frequency

Of 75 SNPs with p -value $< 10^{-5}$ in the discovery, only 22 SNPs/proxy SNPs were found in the NECS data. Reported are the replication results for these 22 SNPs with corresponding discovery results.

Supplementary Table 4. Results of Replication of LLFS Findings in BLSA

Domain	SNP	CHR	Gene	CA	Discovery in LLFS				Replication in BLSA			
					CAF	Beta	SE	P	CAF	Beta	SE	P
agree	rs10497802	2	ANKRD44	T	0.22	1.51	0.32	2.58E-06	0.22	0.12	0.23	0.61
agree	rs11888210	2	-	C	0.14	1.79	0.38	2.23E-06	0.11	0.17	0.32	0.6
agree	rs16860099	2	-	C	0.14	1.79	0.38	2.31E-06	0.11	0.16	0.32	0.61
agree	rs16860886	2	ANKRD44	C	0.22	1.55	0.32	1.32E-06	0.22	0.11	0.23	0.63
agree	rs16860949	2	ANKRD44	T	0.23	1.5	0.32	2.58E-06	0.22	0.12	0.24	0.6
agree	rs2587559	8	-	A	0.13	1.91	0.39	1.18E-06	0.13	-0.35	0.3	0.25
agree	rs2587561	8	-	G	0.13	1.93	0.39	1.15E-06	0.15	-0.43	0.27	0.11
agree	rs3789332	20	FERMT1	G	0.32	1.3	0.28	4.60E-06	0.31	-0.15	0.22	0.49
agree	rs9650241	8	-	G	0.09	2.89	0.48	1.65E-09	0.1	-0.4	0.31	0.21
consc	rs1020852	2	SCN1A	T	0.21	-1.28	0.27	1.68E-06	0.19	0.51	0.35	0.15
consc	rs13397210	2	SCN1A	T	0.21	-1.3	0.27	1.17E-06	0.12	0.49	0.49	0.32
consc	rs13405797	2	SCN1A	A	0.21	-1.29	0.27	1.30E-06	0.19	0.44	0.35	0.21
consc	rs17029245	3	CMTM8	G	0.12	1.57	0.33	2.64E-06	0.09	-0.61	0.52	0.25
consc	rs17801669	19	-	C	0.24	-1.17	0.25	3.31E-06	0.25	0.24	0.33	0.47
consc	rs1841548	2	SCN1A	G	0.21	-1.3	0.27	1.09E-06	0.19	0.44	0.35	0.21
consc	rs3923603	4	-	T	0.39	-1.03	0.22	4.71E-06	0.36	-0.23	0.29	0.41
consc	rs671000	1	-	T	0.25	-1.19	0.26	4.21E-06	0.24	-0.04	0.33	0.9
consc	rs7809940	7	-	G	0.35	-1.04	0.23	4.66E-06	0.36	0.14	0.28	0.63
extra	rs9832895	3	SCN5A	T	0.48	1.38	0.29	1.73E-06	0.48	-0.16	0.27	0.57
neuro	rs160196	11	GRM5	C	0.48	-0.91	0.19	1.92E-06	0.49	-0.06	0.3	0.85
neuro	rs178244	11	GRM5	A	0.48	-0.91	0.19	1.82E-06	0.49	-0.06	0.3	0.85
neuro	rs8076171	17	ACCN1	G	0.17	-1.17	0.25	4.76E-06	0.17	-0.26	0.46	0.57
open	rs10831742	11	MICAL2	G	0.17	1.71	0.36	1.96E-06	0.12	-0.23	0.46	0.61
open	rs12115280	9	SHC3	T	0.13	-1.95	0.41	2.61E-06	0.11	-0.46	0.53	0.39

CA: Coded Allele

CAF: Coded Allele Frequency

Of 75 SNPs with $p\text{-value} < 10^{-5}$ in the discovery, only 24 SNPs were found in the BLSA data. Reported are the replication results for these 22 SNPs with corresponding discovery results

Supplementary Table 5. Top Findings ($p < 10^{-5}$) from the LLFS

a) Agreeableness

SNP	Chr	Gene	Coded Allele	Non-coded Allele	Coded AF	Beta	SE	Pval
rs9650241	8	-	G	T	0.09	2.89	0.48	1.65E-09
rs2701448	8	-	A	G	0.09	2.87	0.48	1.80E-09
kgp6080058	8	-	A	G	0.09	2.85	0.48	2.44E-09
kgp12343956	2	-	T	G	0.14	1.86	0.38	1.04E-06
rs2587561	8	TRPA1	G	A	0.13	1.93	0.39	1.15E-06
rs2587559	8	TRPA1	A	G	0.13	1.91	0.39	1.18E-06
rs73413011	11	TNNT3	C	T	0.25	-1.48	0.3	1.22E-06
rs16860886	2	ANKRD44	C	T	0.22	1.55	0.32	1.32E-06
rs11888210	2	ANKRD44	C	T	0.14	1.79	0.38	2.23E-06
rs16860099	2	ANKRD44	C	T	0.14	1.79	0.38	2.31E-06
rs16860949	2	ANKRD44	T	C	0.23	1.5	0.32	2.58E-06
rs10497802	2	ANKRD44	T	G	0.22	1.51	0.32	2.58E-06
rs3789332	20	FERMT1	G	A	0.32	1.3	0.28	4.60E-06
rs7497201	15	MPI	A	G	0.32	-1.3	0.28	4.84E-06
rs8042694	15	COX5A	G	A	0.32	-1.29	0.28	5.49E-06
rs658912	5	ATP6AP1L	T	C	0.37	1.22	0.27	6.07E-06
rs6495127	15	C15orf17	C	T	0.32	-1.28	0.28	6.48E-06
rs2587577	8	-	A	G	0.16	1.64	0.36	6.53E-06
rs1501630	3	SLC9A9	C	T	0.41	1.2	0.27	7.13E-06
rs10476618	5	MCTP1	T	C	0.45	1.18	0.26	8.40E-06
rs7596238	2	-	A	G	0.11	-1.9	0.43	9.06E-06

b) Conscientiousness

SNP	Chr	Gene	Coded Allele	Non-coded Allele	Coded AF	Beta	SE	Pval
rs79732200	15	IGDCC3	A	G	0.14	-1.68	0.31	8.73E-08
rs1841548	2	SCN1A	C	T	0.21	-1.3	0.27	1.09E-06
rs13397210	2	SCN1A	T	C	0.21	-1.3	0.27	1.17E-06
rs13405797	2	SCN1A	A	G	0.21	-1.29	0.27	1.30E-06
rs1020852	2	SCN1A	T	C	0.21	-1.28	0.27	1.68E-06
rs56982446	19	-	G	A	0.25	-1.18	0.25	2.38E-06
rs17029245	3	CMTM8	G	A	0.12	1.57	0.33	2.64E-06
rs73173200	22	-	A	G	0.14	-1.49	0.32	3.02E-06
rs535335	1	-	T	C	0.25	-1.21	0.26	3.10E-06
rs17801669	19	-	C	G	0.24	-1.17	0.25	3.31E-06

rs671000	1	-	T	C	0.25	-1.19	0.26	4.21E-06
rs7809940	7	-	G	A	0.35	-1.04	0.23	4.66E-06
rs3923603	4	-	A	G	0.39	-1.03	0.22	4.71E-06
rs73566890	19	-	C	T	0.24	-1.15	0.25	5.20E-06
rs6425361	1	-	T	C	0.26	-1.16	0.25	5.65E-06
rs501915	1	-	C	T	0.25	-1.18	0.26	5.71E-06
rs66528304	21	-	G	A	0.12	-1.55	0.34	5.93E-06
rs56206848	19	-	T	C	0.24	-1.14	0.25	6.95E-06
rs73216895	21	-	G	A	0.12	-1.52	0.34	7.46E-06
rs2781564	6	-	A	C	0.44	0.97	0.22	7.50E-06
rs73223220	21	-	C	T	0.12	-1.53	0.34	7.56E-06
rs9822730	3	-	A	G	0.2	-1.2	0.27	7.83E-06
rs67483822	21	-	A	G	0.12	-1.52	0.34	7.88E-06
rs1485964	11	MICAL2	A	C	0.4	-0.98	0.22	8.09E-06
rs55843704	19	-	A	G	0.2	-1.19	0.27	9.71E-06
rs13383881	2	SCN1A	G	A	0.2	-1.21	0.27	9.73E-06

c) Extraversion

SNP	Chr	Gene	Coded Allele	Non-coded Allele	Coded AF	Beta	SE	Pval
rs9832895	3	SCN5A	T	C	0.48	1.38	0.29	1.73E-06
rs12592645	15	-	A	C	0.18	-1.79	0.39	5.44E-06
rs12196515	6	FLJ22536	A	G	0.13	-1.96	0.43	6.01E-06
rs2598025	7	TXNDC3	A	C	0.33	1.38	0.31	6.78E-06
rs77759768	20	TMEM90B	C	A	0.07	-2.57	0.57	6.81E-06
rs12893426	14	-	C	T	0.24	1.54	0.34	8.03E-06
kgp14702850	2	-	G	A	0.05	2.88	0.65	8.72E-06

d) Neuroticism

SNP	Chr	Gene	Coded Allele	Non-coded Allele	Coded AF	Beta	SE	Pval
rs177389	14	PAPLN	T	G	0.48	-0.97	0.19	5.68E-07
rs178244	11	GRM5	A	G	0.48	-0.91	0.19	1.82E-06
rs160196	11	GRM5	C	G	0.48	-0.91	0.19	1.92E-06
rs57565976	13	-	G	C	0.13	-1.32	0.28	2.98E-06
kgp12000284	5	-	T	G	0.05	2.02	0.44	3.83E-06
rs8076171	17	ACCN1	G	A	0.17	-1.17	0.25	4.76E-06
rs12045704	1	KIRREL	C	T	0.06	1.88	0.41	5.55E-06

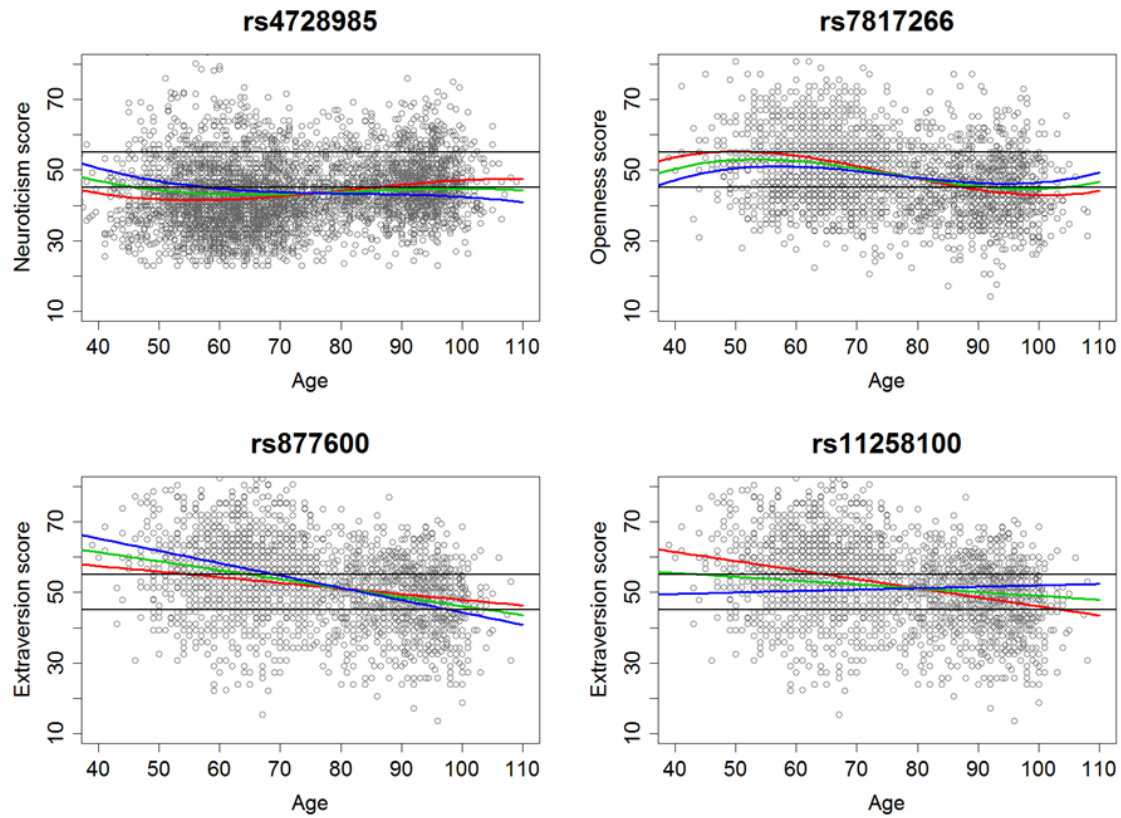
rs2173324	4	-	G	T	0.38	0.89	0.2	6.08E-06
rs2881781	17	ACCN1	A	G	0.17	-1.14	0.25	6.92E-06
rs4725336	7	REPIN1	C	A	0.15	-1.19	0.27	8.24E-06
rs2189000	7	TWIST1	G	A	0.14	1.22	0.27	8.28E-06
rs4233429	1	-	T	G	0.29	-0.94	0.21	9.23E-06

e) Openness

SNP	Chr	Gene	Coded Allele	Non-coded Allele	Coded AF	Beta	SE	Pval
rs10831742	11	MICAL2	G	A	0.17	1.71	0.36	1.96E-06
rs78230823	7	-	C	T	0.13	1.85	0.39	2.28E-06
rs12115280	9	SHC3	T	C	0.13	-1.95	0.41	2.61E-06
rs72812014	17	NXN	A	G	0.08	-2.21	0.48	5.03E-06
rs7287869	22	UPK3A	G	C	0.1	2.05	0.45	5.83E-06
rs10803639	2	-	A	G	0.26	-1.38	0.31	7.47E-06
rs17039820	2	-	A	C	0.07	2.31	0.52	8.02E-06
rs2332838	4	-	A	G	0.32	1.27	0.29	9.21E-06
rs10901809	10	FAM53B	T	C	0.31	-1.29	0.29	9.76E-06

Supplementary Table 6. SNPs associated with *ARNTL* in the LLFS and NECS GWAS.

SNP	CHR	Coded Allele	Coded Allele Frequency	Beta	Pval	Cohort
rs56051850	11	A	0.21	0.73	0.029	LLFS
rs10832020	11	C	0.17	0.78	0.029	LLFS
rs4757142	11	G	0.41	0.58	0.034	LLFS
rs4757145	11	A	0.40	0.56	0.044	LLFS
rs969485	11	G	0.28	-0.59	0.044	LLFS
rs10832030	11	A	0.15	-0.73	0.050	LLFS
rs7941871	11	C	0.17	-3.79	0.005	NECS
rs11022693	11	A	0.31	3.04	0.007	NECS
rs10831990	11	G	0.24	-3.03	0.012	NECS
rs10430831	11	G	0.06	-4.89	0.030	NECS



Supplementary Figure 1. Scatter plots of NEO scores for SNPs with Significant SNP-by-age Interaction. The y-axis reports the T-score for the NEO domains and the x-axis reports the age at the assessment of NEO-FFI. The red, green, and blue lines represent fitted values for individuals with 0, 1, and 2 minor alleles. The area between the two black, horizontal lines indicates the normal range for T-score values.