Resting-State Connectivity and Its Association With Cognitive Performance, Educational Attainment, and Household Income in UK Biobank

Supplementary Information

Supplementary Methods

Participants

The UK Biobank covers an age range from 40 to 70 at the initial visit, and by the time of the imaging assessment, the age range was from 45 to 75, because the imaging assessment took place after the initial visit. The imaging sample was selected within the overall sample for predominantly healthy participants to achieve a selection of population-based sample. The UK Biobank sample chose mainly white people with European ancestry. The education level was comparatively high, with a proportion of 53.15% received college or university level degree.

Clustering of 55*55 matrix

The clustering for the whole-brain analyses on 55*55 connectivity matrix was for better illustration, using hierarchical clustering approach described in: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0076315. The number of cluster was user-defined as n=5.

Educational attainment and household income

For educational attainment, participants could choose at least one of the following options: College or university degree, A levels/AS levels or equivalent, O levels/GCSEs or equivalent, CSEs or equivalent, NVQ or HND or HNC or equivalent, other professional qualifications, none of the above, and prefer not to answer.

For household income, available choices were: <£18,000, £18,000 to £30,999, £31,000 to £51,999, £52,000 to £100,000, >£100,000, do not know and prefer not to answer. An ordinal variable from 1 to 5 was created to determine the level of household income (<£18,000 as 1, >£100,000 as 5).

PCA analysis for cognitive performance, educational attainment and household income

As the results in the main text showed that the regions involved in the three traits were highly overlapping, we have conducted a PCA analysis to extract the first unrotated latent component of the three traits, and used the scores for the factor to test the resting-state-network associations with the common variance of all three traits.

PCA was conducted using princomp in R (https://stat.ethz.ch/R-manual/R-devel/library/stats/html/princomp.html). Results are shown in supplementary results and Figure S5.

Permutation test

As we now have an updated sample of 7,144 people (from the latest data release), we have now additionally conducted two further sets of analyses to validate our results.

First we performed permutation test on half-sized sample (N=3,572) and tested the distributions of the p values for the significant connections found in 55*55 matrix described in our initial findings. After 1,000 times of randomly selecting half of our sample, conducting analyses on them, we found that the distributions of p values for over 90% of the significant connections found in our initial results were lower, compared with the mean p value for the rest of connections (Figure S7-S9).

Second, another permutation test was performed to test whether the results found in a training subsample can predict the results in a separate testing sample. We cut the sample in halves, and used the first half as a training dataset and the second half as a testing dataset. We extracted the effect sizes for the 55*55 connectivity matrix acquired from the training sample and applied them on the testing dataset to calculate a neural connectivity score for the trait. And then we used the neural connectivity score to predict the variances for the traits in the testing sample. For instance, we used the effect sizes of cognitive performance in the training sample ($\beta_{training}$), and calculated the sum of $\beta training*Connectivity_{testing}$ as the neural-network score of cognitive performance in the testing sample. We then used this score to predict the cognitive performance, educational attainment and household income in the testing sample. Age, age^2, gender, scanner positions and mean motion were controlled. Likewise permutation tests were conducted to use the neural associations of educational attainment or household income to predict other traits in the testing sample. Results are shown in Figure S10.

Supplementary Results

Phenotypic associations

The mean test performance score for the VNR was 6.92 (SD = 2.15). Age and sex both showed significant associations with VNR score (age: β=-0.07, p=3.50×10^{-5}, sex: β=0.19, p=3.18×10^{-9}; Male=1, Female=0).

In total, 1,801 participants reported having obtained a college/university-level degree (43.29% of the overall sample). The mean age of people with a college/university-level degree was 61.62 (SD=7.49), which was significantly lower than the group without (Mean age=62.65, SD=7.58, t=4.37, p=1.27×10^{-5}). Men reported a significantly higher proportion of college degrees (48.80%) than women (39.73%), χ^2=34.8, df=1, p=3.65×10^{-9}. Educational attainment showed positive association with cognitive performance, with age, age2 and sex controlled (β=0.457, p<2×10^{-16}).

The proportion of people who reported having household income at each level is shown in Figure S1. The income band of £31,000 to £51,999 contained the highest proportion (29.98%) of individuals, and the band >£100,000 contained the lowest proportion (6.06%). Both age and sex showed significant associations with household income (age: β=-0.29, p<2×10^{-16}; sex: β=0.20, p=1.04×10^{-9}). Higher household income was associated with better cognitive performance (β=0.167, p<2×10^{-16}), with age, age2, and sex controlled in the model.

PCA analysis of cognitive performance, educational attainment and household income

The first latent component (g) of the three traits explains a major portion of total variance (75.6%), it was heavily loaded on cognitive performance (correlation loadings: cognitive performance: 0.998, educational attainment: 0.261, household income: 0.220).

We have conducted an additional analysis using the first latent component as a predictor and tested the shared component of cognitive performance, educational attainment and household income on the resting-state networks (see supplementary methods). Results are shown in Figure S7. As expected, the regions involved with stronger connections with latent g of the three traits were mainly located in default mode network areas and lateral prefrontal cortex.
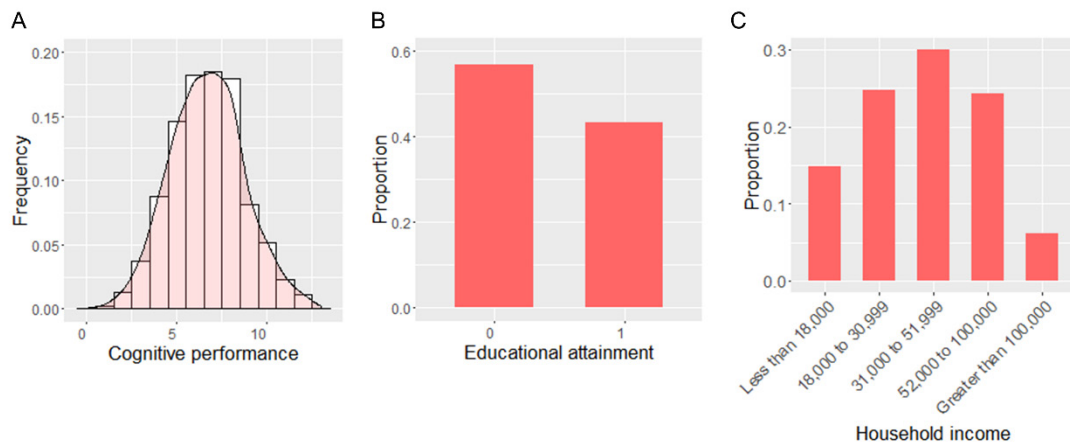
Figure S1. Descriptive statistics of (a) cognitive performance on the verbal-numerical reasoning test; (b) educational attainment (those with [0] and without [1] a college degree; and (c) household income (GBP per annum).
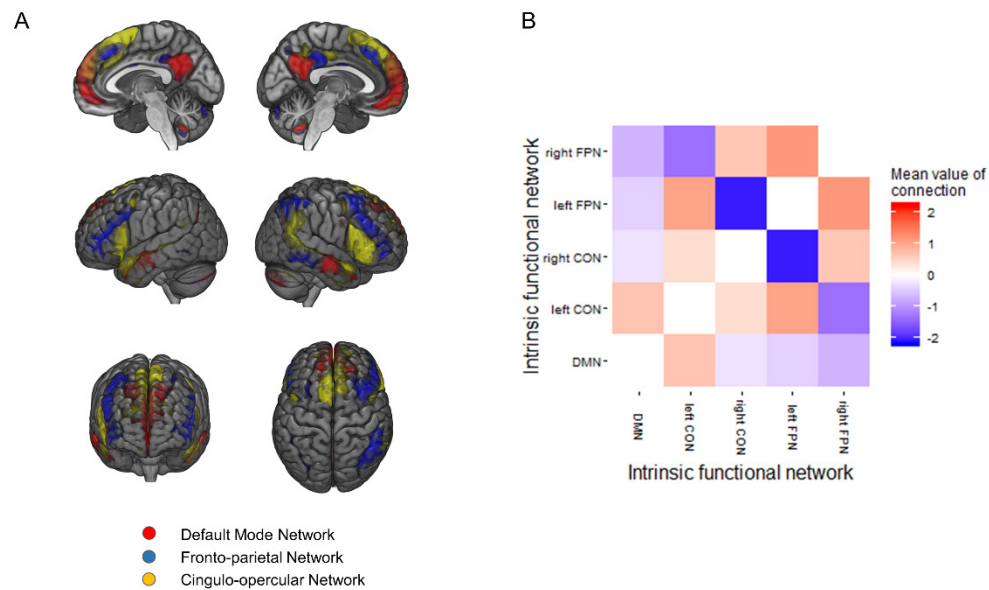
Figure S2. (A) Five intrinsic functional networks selected from the 21 components generated by low-dimension ICA (see Methods, Imaging data). Component 1 was identified as the default mode network (DMN, red). Component 13 and 21 were left and right cingulo-opercular network (CON) respectively (yellow). And finally, component 5 and 6 were identified as right and left fronto-parietal network (FPN, blue). (B) The mean values of couplings of networks of interest. The values are standardised temporal correlation coefficient between networks of interest. A higher absolute value indicates a higher strength, and the sign indicates the directionality of the connection. A negative value means an anti-correlated connection, whilst a positive value indicates a positive connection. Mean values and 95% confident intervals of the connections can be viewed in Table 1.
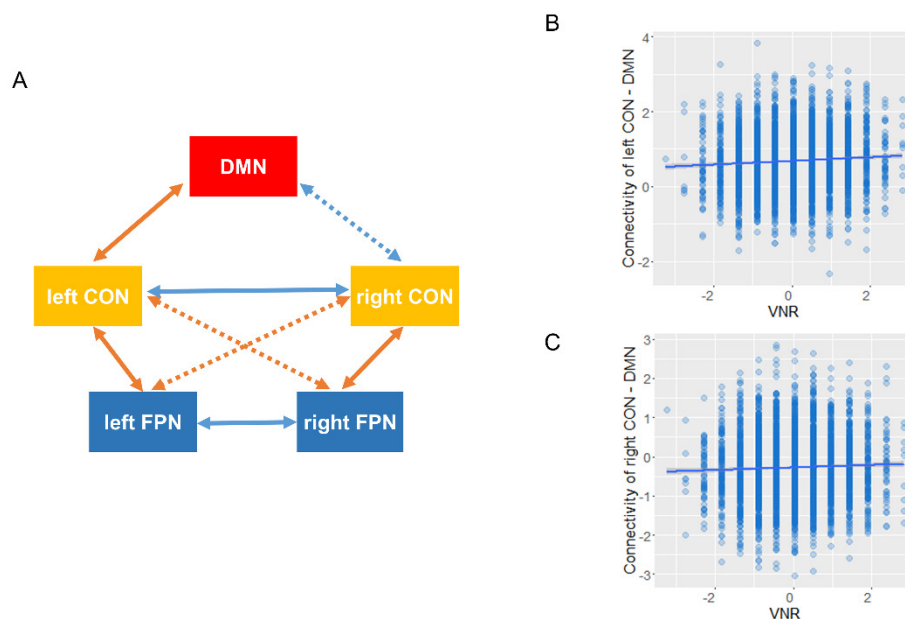
Figure S3. (A) Significant network couplings associated with cognitive performance in verbal-numerical reasoning (absolute β ranged from 0.034 to 0.063, all effect sizes of the significant connections are reported in Table 1). An orange arrow means positive association between cognitive ability with the absolute strength of a connection, whilst a blue arrow indicates decreased absolute strength of a connection with better cognitive performance. Solid arrows are positive connections and dashed ones are negative. An orange arrow reflects positive associations between cognitive ability with the absolute strength of a connection, whilst a blue arrow indicates decreased absolute strength of a connection with better cognitive performance. (B) and (C) represent the association of cognitive performance in verbal-numerical reasoning and the connection between left/right CON (β=0.061 and -0.045 respectively for left/right CON) and DMN (β=-0.045). Y-axis represent the normalised correlation coefficient between temporal modulations of networks. Better cognitive performance was associated with more positive connections between DMN and bilateral CON. The spatial maps of the functional networks can be found in Figure S2.
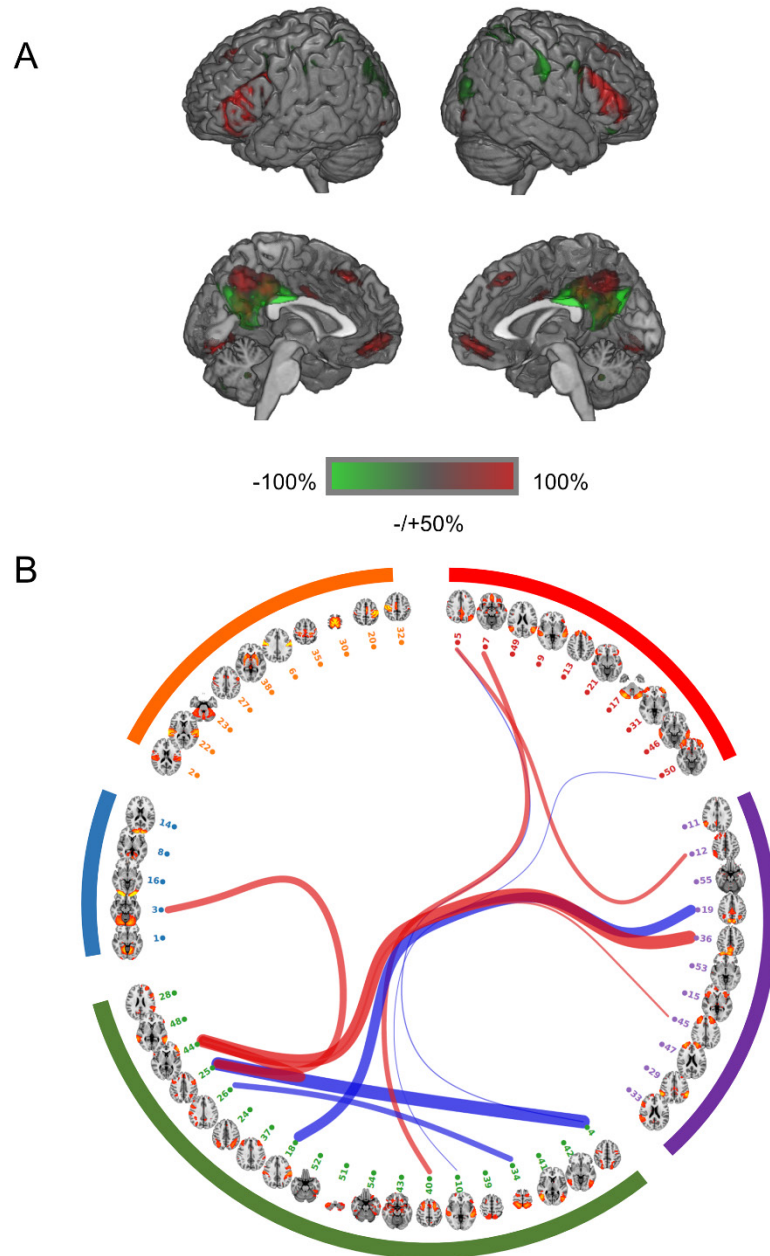
Figure S4. Results for whole-brain analysis of non-binary proxy for educational attainment. Three levels were set, which included: college or university level, A or AS level, and all other levels.
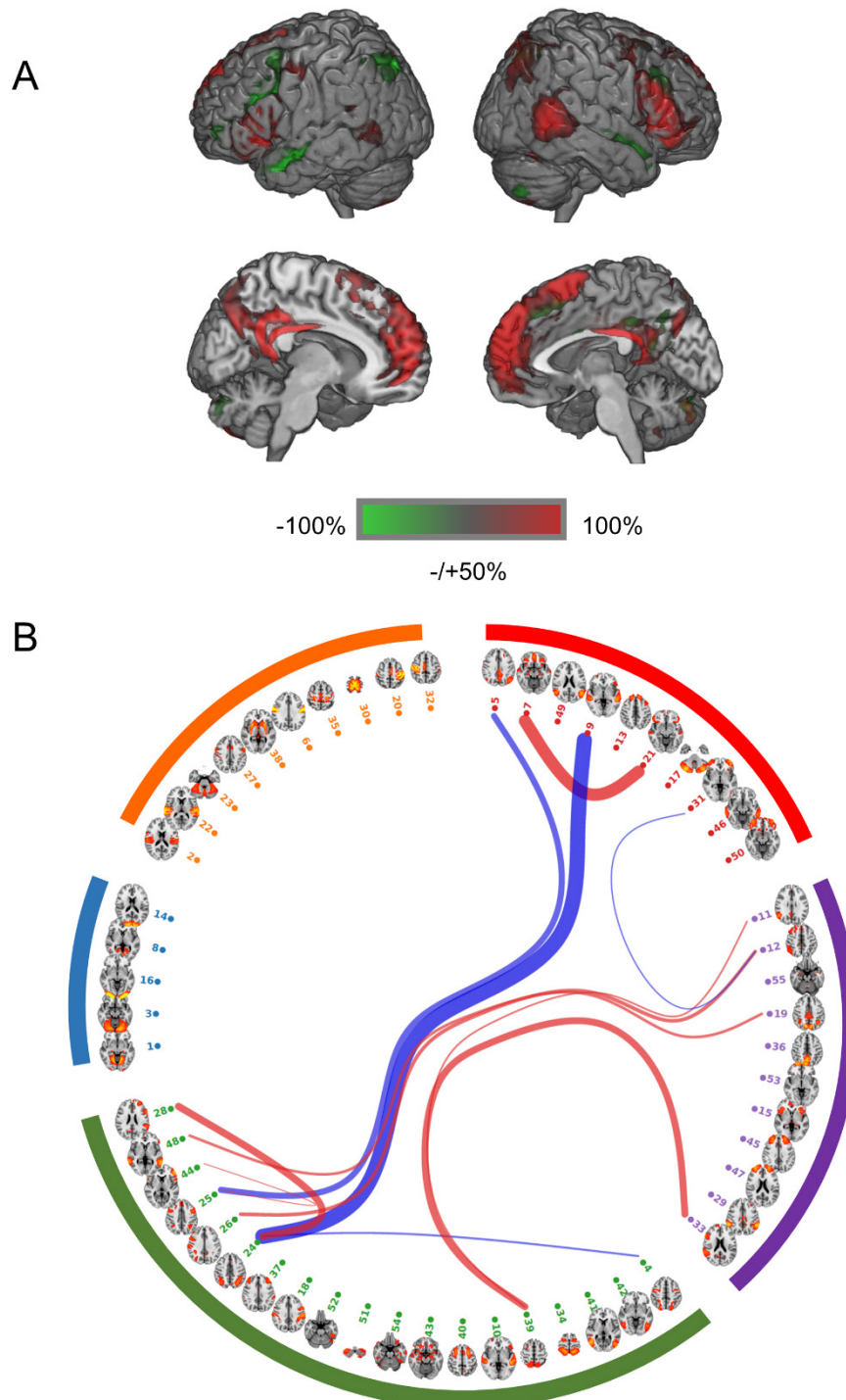
Figure S5. Results for whole brain analysis of the first latent component of cognitive performance (VNR), educational attainment and household income. The first latent component was extracted from unrotated PCA by using princomp in R (https://stat.ethz.ch/R-manual/R-devel/library/stats/html/princomp.html). This component explains 75.6% of total variance. Correlation loadings for the factor are: cognitive performance: 0.998, educational attainment: 0.261, household income: 0.220.

A

VNR

β = 0.064

β = 0.247

rFPN-rCON

c′ = 0.005

c = 0.021

Educational attainment

B

VNR

β = -0.037

β = 0.246

DMN-rCON

c′ = -0.04

c = -0.049

Educational attainment
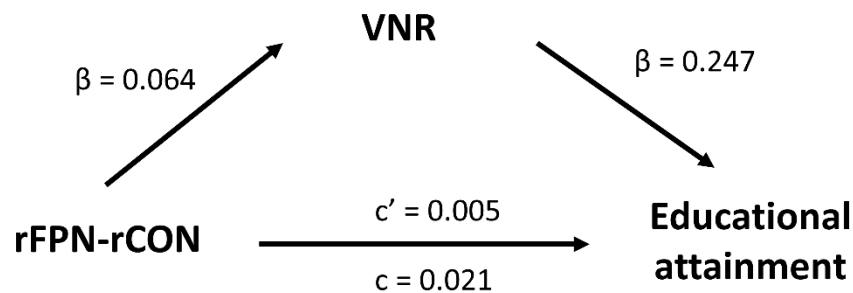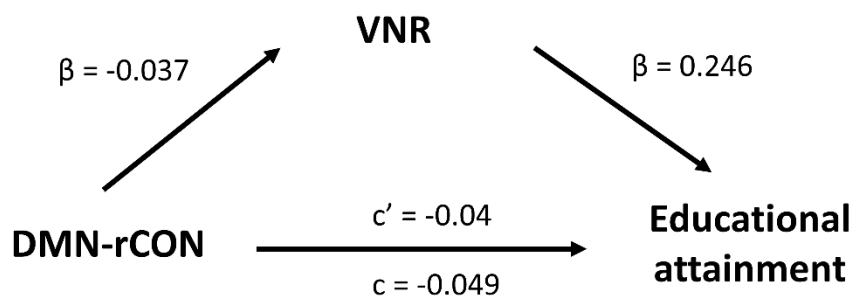
Figure S6. Mediation analysis for NOI results. Network connectivity was set as the predictor, and educational attainment as the dependent variable. Mediator was set as cognitive performance. We tested on two network connections that were significant for both educational attainment and cognitive performance. The association between rFPN-rCON and rCON-DMN connectivity and educational attainment was mediated by cognitive performance (18.4% and 76.2% of direct path mediated by indirect path respectively for each model, CFI = TLI = 1).
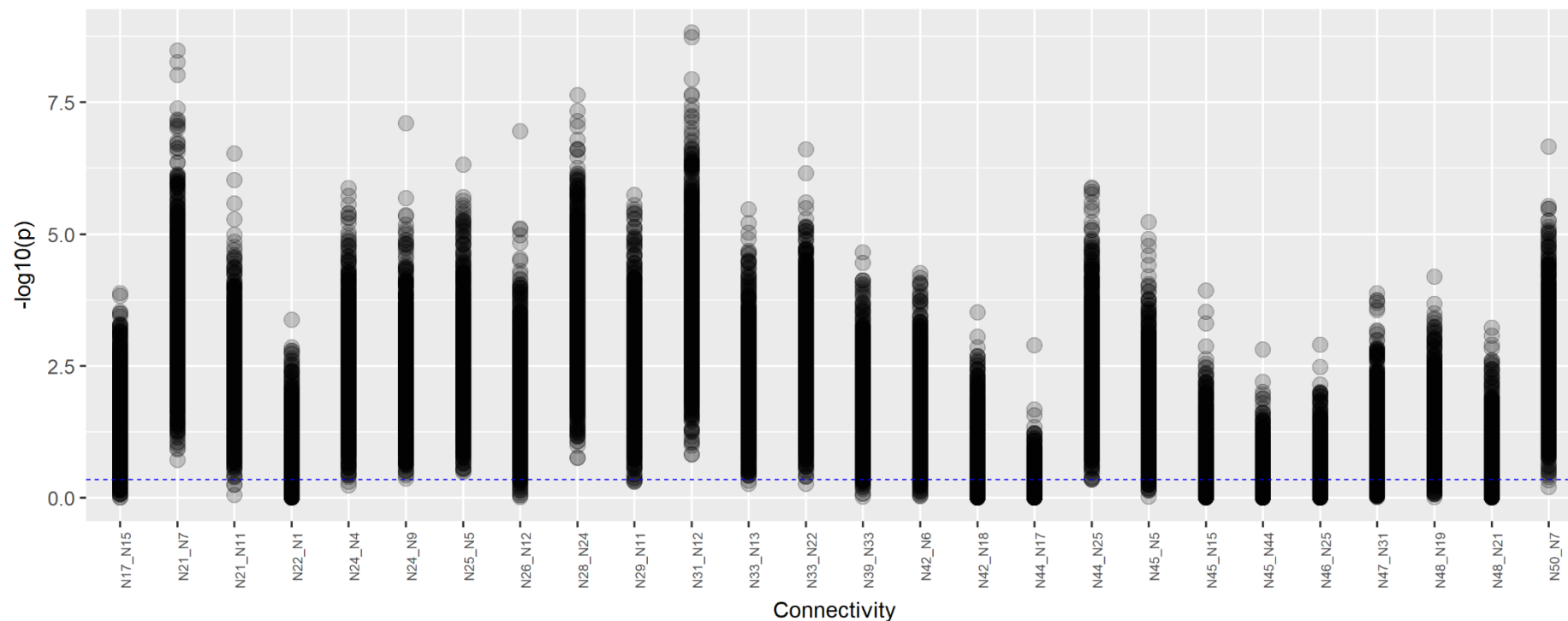
Figure S7. Permutation test on cognitive performance (VNR). X axis shows the connections, and y axis shows the uncorrected p value transformed by -log10 function. T-test was performed on the p-value distributions for each connection that was found associated with VNR to test whether these tested connections have significantly lower p values compared to the non-significant connections in the initial finding. The dashed blue line is the mean uncorrected p value of all other connections. Two connections' p values were not significantly lower than the mean p value of all other connections (N44-N17: t(999)=18.25, p<1E-16, and N45-N44: t(999)=6.95, p=6.50E-12). All other connections have lower p values compared to the non-significant ones, which takes up 92.3% of all 26 connections (t-test p<1E-16).
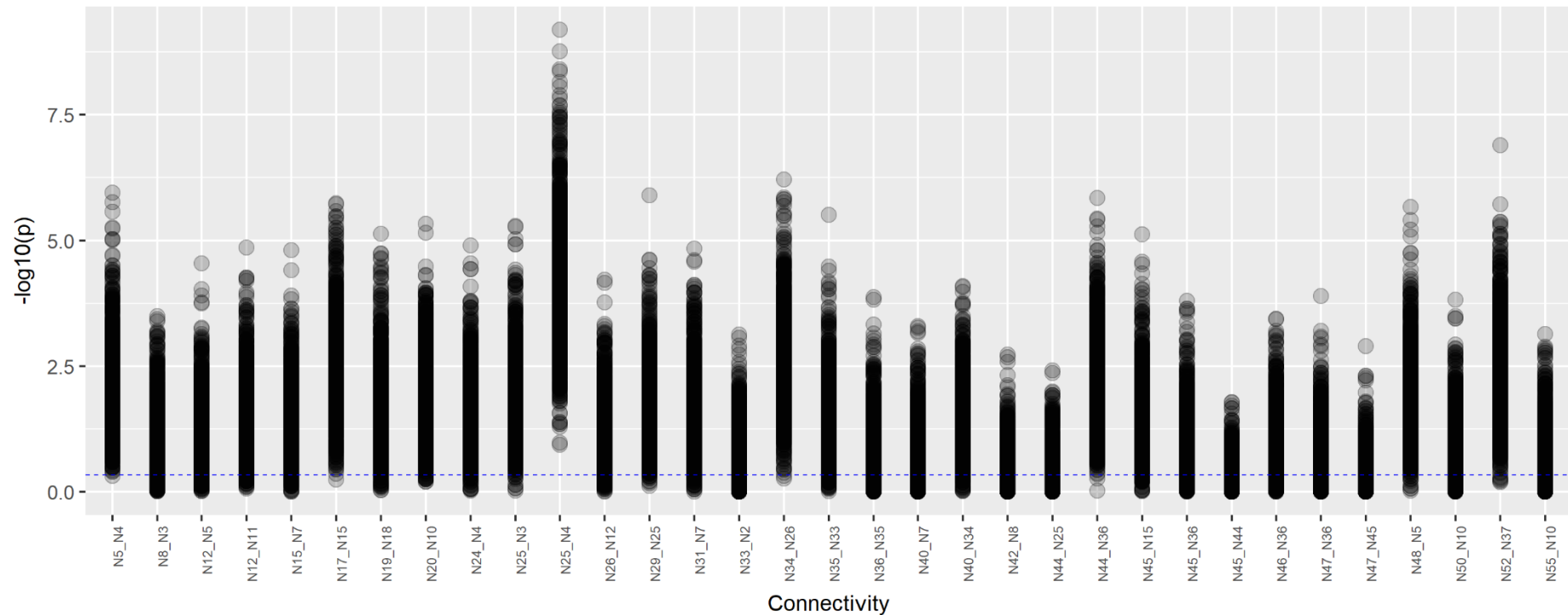
Figure S8. Permutation test on educational attainment. X axis shows the connections, and y axis shows the uncorrected p value transformed by -log10 function. T-test was performed on the p-value distributions for each connection that was found associated with educational attainment to test whether these tested connections have significantly lower p values compared to the non-significant connections in the initial finding. The dashed blue line is the mean uncorrected p value of all other connections. Three connections' p values were not significantly lower than the mean p value of all other connections (N44-N25: t(999)=1.22, p=0.22, N45-N44: t(999)=11.55, p<1E-16, and N47-N45: t(999)=4.98, p=7.34E-7). All other connections have lower p values compared to the non-significant ones, which takes up 90.0% of all 33 connections (t-test p<1E-16).
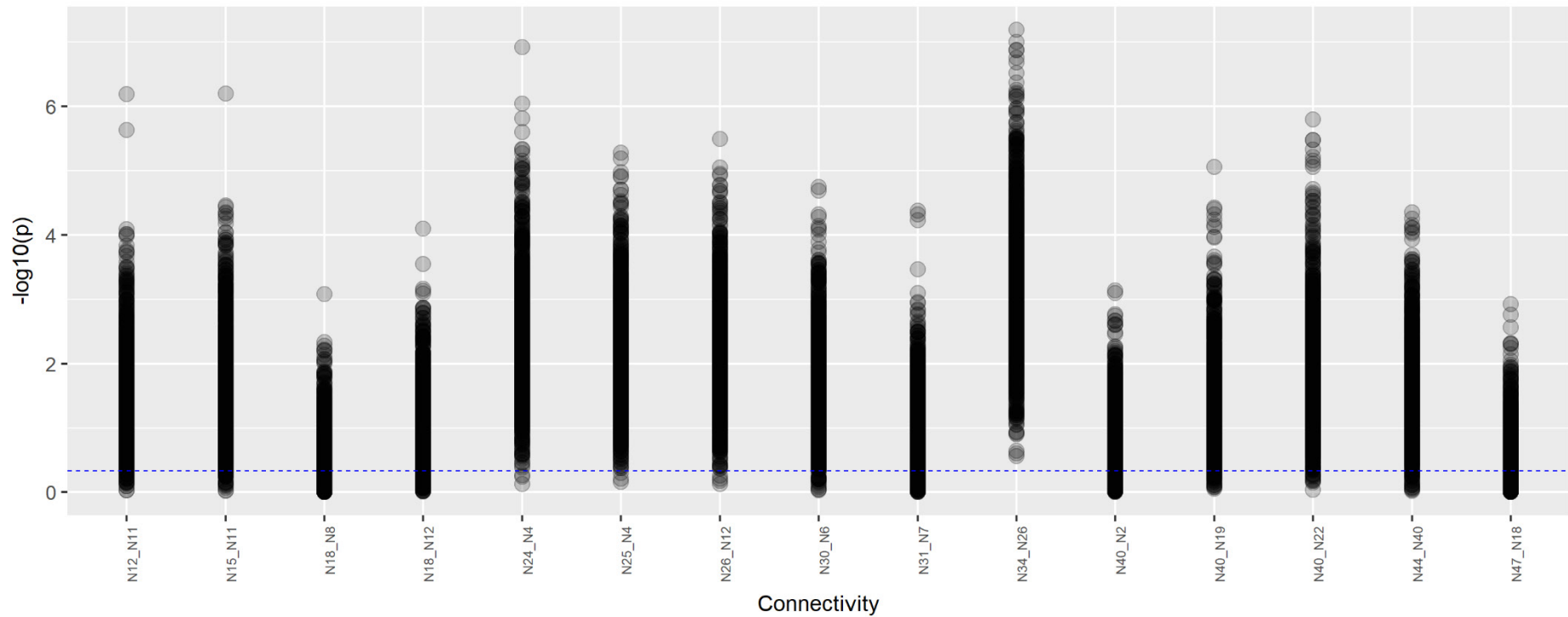
Figure S9. Permutation test on household income. X axis shows the connections, and y axis shows the uncorrected p value transformed by -log10 function. T-test was performed on the p-value distributions for each connection that was found associated with household income to test whether these tested connections have significantly lower p values compared to the non-significant connections in the initial finding. The dashed blue line is the mean uncorrected p value of all other connections. All the connections have lower p values compared to the non-significant ones (t-test p<4.91E-8).
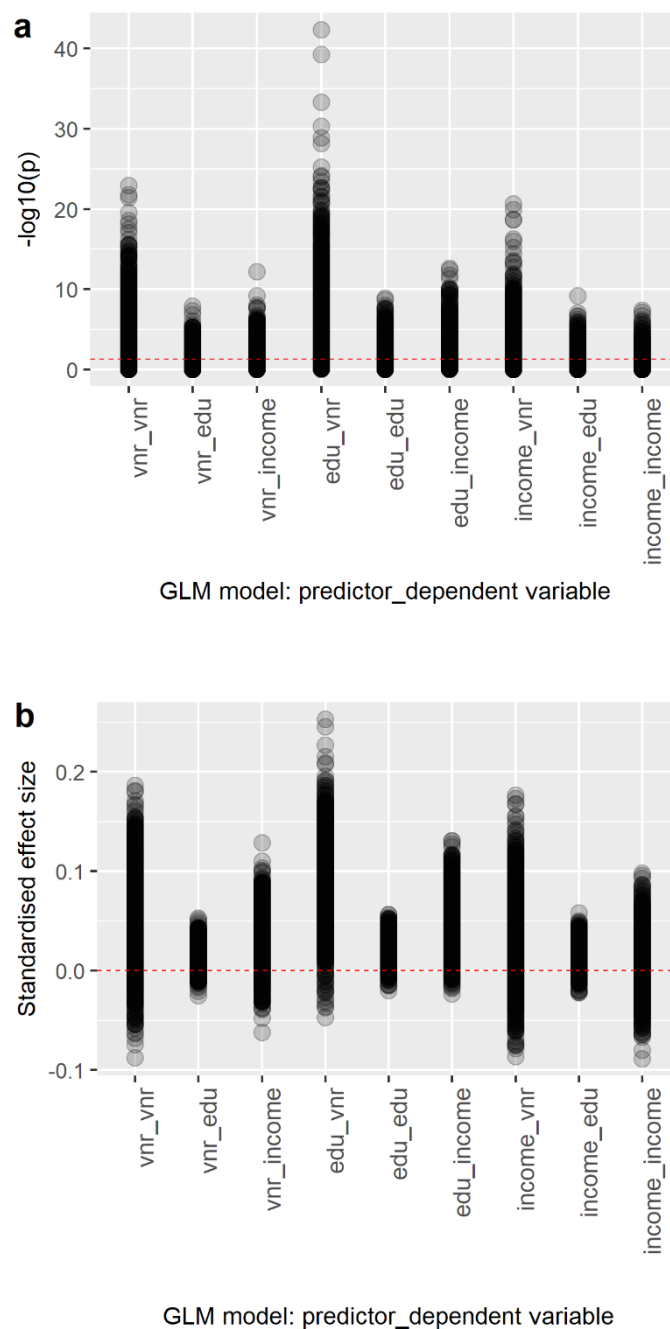
Figure S10. Using the model built by the training sample to predict the traits in the testing sample. The x axis is the models of using predictors derived from training sample to predict the trait as the dependent variable in the testing sample. In panel a, the y axis is the uncorrected p value transformed by -log10. In panel a, the red dashed line is the p=0.05 significance line, as there is no baseline mean p value to compare with like in Figure S6-8. In Figure b, the y axis is the standardised effect size. We also conducted t-test to compare the effect sizes with 0, and all models showed significant difference from 0 (income_income: p = 0.009, for all other models: $p < 1 \times 10^{-16}$).

Table S1. Connections that showed significant association with cognitive performance in VNR on 55*55 partial correlation matrix. All reported betas are standardised effect sizes. The regression model was applied to test the association between VNR and absolute strength of connections, which was achieved by multiplying values of connections with the sign of their mean value (see Methods). The spatial maps of the nodes in the table indicated by numbers can be found in Figure 2.

	Beta	Standard error	t.value	p	p.corrected	Valence of connection	95% CI of value of connection	
N17_N15	0.054	0.016	-3.403	6.73E-04	0.038	+	1.215	1.275
N21_N11	0.062	0.016	3.901	9.72E-05	0.014	-	-1.939	-1.881
N21_N7	0.097	0.016	6.140	9.09E-10	0.000	+	3.746	3.829
N22_N1	0.061	0.016	-3.789	1.53E-04	0.018	-	-0.561	-0.510
N24_N4	-0.066	0.016	-4.092	4.37E-05	0.007	-	-1.136	-1.075
N24_N9	-0.083	0.016	5.196	2.14E-07	<0.001	+	0.319	0.363
N25_N5	-0.072	0.016	4.488	7.39E-06	0.002	-	-0.639	-0.579
N26_N12	0.081	0.016	5.036	4.96E-07	0.000	+	3.746	3.829
N28_N24	0.076	0.016	4.737	2.25E-06	0.001	+	0.151	0.206
N29_N11	0.059	0.016	3.671	2.45E-04	0.021	+	0.762	0.830
N31_N12	-0.066	0.016	-4.109	4.06E-05	0.007	+	1.234	1.300
N33_N13	0.060	0.016	-3.751	1.78E-04	0.018	-	-0.702	-0.649
N33_N22	0.055	0.016	3.412	6.52E-04	0.038	+	0.649	0.701
N39_N33	0.074	0.016	-4.580	4.80E-06	0.001	-	-0.561	-0.510
N42_N18	0.055	0.016	3.445	5.77E-04	0.037	+	1.671	1.737
N42_N6	-0.056	0.016	3.516	4.43E-04	0.031	-	-0.594	-0.548
N44_N17	0.054	0.016	3.425	6.21E-04	0.038	+	0.276	0.314
N44_N25	0.071	0.016	4.477	7.78E-06	0.002	+	2.321	2.383
N45_N15	0.059	0.016	3.682	2.34E-04	0.021	+	1.233	1.291
N45_N44	0.055	0.016	-3.494	4.81E-04	0.032	-	-1.264	-1.217
N45_N5	-0.058	0.016	-3.625	2.93E-04	0.024	+	0.026	0.095

	Beta	Standard error	t.value	p	p.corrected	Valence of connection	95% CI of value of connection	
N46_N25	-0.057	0.016	-3.543	4.00E-04	0.030	+	0.002	0.046
N47_N31	0.059	0.016	3.766	1.68E-04	0.018	+	1.096	1.159
N48_N19	0.061	0.016	-3.780	1.59E-04	0.018	-	-0.679	-0.627
N48_N21	-0.061	0.016	-3.804	1.44E-04	0.018	+	0.005	0.053
N50_N7	0.057	0.016	-3.591	3.33E-04	0.026	-	-0.251	-0.213

Table S2. Connections that showed significant association between their absolute strength with educational attainment on the whole brain proxied by 55*55 partial correlation matrix. The spatial maps of the nodes in the table indicated by numbers can be found in Figure 2.

	Beta	Standard error	t.value	p	p.corrected	Valence of connection	95% CI of value of connection	
N5-N4	-0.103	0.031	3.290	1.01E-03	0.045	-	-0.720	-0.660
N8-N3	-0.119	0.031	-3.809	1.42E-04	0.018	+	0.903	0.994
N12-N5	0.132	0.031	-4.201	2.71E-05	0.007	-	-2.111	-2.036
N12-N11	0.106	0.031	3.394	6.94E-04	0.040	+	6.507	6.608
N15-N7	0.122	0.031	3.949	7.96E-05	0.015	+	0.875	0.929
N17-N15	0.121	0.031	-3.905	9.59E-05	0.015	-	-0.825	-0.784
N19-N18	-0.136	0.031	4.338	1.47E-05	0.005	-	-0.747	-0.689
N20-N10	-0.109	0.031	3.488	4.91E-04	0.038	-	-0.443	-0.399
N24-N4	-0.108	0.031	-3.428	6.15E-04	0.038	+	0.588	0.651
N25-N3	0.137	0.031	-4.355	1.36E-05	0.005	-	-0.264	-0.223
N25-N4	-0.161	0.031	-5.150	2.73E-07	<0.001	+	0.995	1.059
N26-N12	0.108	0.031	3.457	5.51E-04	0.038	+	3.746	3.829
N29-N25	0.108	0.031	-3.440	5.88E-04	0.038	+	0.180	0.241
N31-N7	0.125	0.031	-3.995	6.57E-05	0.014	-	-1.939	-1.881
N33-N2	-0.103	0.031	-3.294	9.96E-04	0.045	+	0.257	0.310
N34-N26	-0.133	0.031	-4.254	2.14E-05	0.006	+	0.320	0.378
N35-N33	0.108	0.031	-3.452	5.63E-04	0.038	-	-0.075	-0.035
N36-N35	0.105	0.031	-3.363	7.79E-04	0.041	-	-0.636	-0.596
N40-N7	0.118	0.031	-3.761	1.72E-04	0.020	-	-0.694	-0.648
N40-N34	0.122	0.031	-3.888	1.03E-04	0.015	-	-0.479	-0.429
N42-N8	-0.108	0.031	3.439	5.89E-04	0.038	-	-0.756	-0.699
N44-N25	0.112	0.031	3.589	3.35E-04	0.029	+	2.321	2.383

	Beta	Standard error	t.value	p	p.corrected	Valence of connection	95% CI of value of connection	
N44-N36	0.139	0.031	-4.431	9.61E-06	0.005	-	-1.469	-1.424
N45-N15	0.117	0.031	3.717	2.05E-04	0.022	+	1.233	1.291
N45-N36	0.105	0.031	3.348	8.20E-04	0.041	+	0.617	0.662
N45-N44	0.105	0.031	-3.403	6.74E-04	0.040	-	-1.264	-1.217
N46-N36	0.110	0.031	-3.509	4.54E-04	0.037	-	-0.935	-0.890
N47-N36	0.105	0.031	3.358	7.93E-04	0.041	+	0.721	0.766
N47-N45	0.110	0.031	3.590	3.35E-04	0.029	+	2.071	2.130
N48-N5	-0.114	0.031	3.641	2.75E-04	0.027	-	-0.123	-0.055
N50-N10	-0.121	0.031	3.861	1.15E-04	0.015	-	-0.606	-0.569
N52-N37	0.104	0.031	3.343	8.37E-04	0.041	+	0.303	0.344
N55-N10	-0.105	0.031	3.337	8.53E-04	0.041	-	-0.063	-0.034

Table S3. Connections that showed significant association between their absolute strength with household income on the whole brain proxied by 55*55 partial correlation matrix. The significant connections presented in the table is identical with those connections shown in Figure 2.

	Beta	Standard error	t.value	p	p.corrected	Valence of connection	95% CI of value of connection	
N12_N11	0.072	0.017	4.208	2.64E-05	0.010	+	6.507	6.608
N15_N11	0.082	0.017	-4.806	1.60E-06	0.002	-	-1.246	-1.185
N18_N8	0.064	0.017	3.720	2.02E-04	0.033	+	0.216	0.267
N18_N12	0.067	0.017	-3.909	9.42E-05	0.020	-	-2.099	-2.035
N24_N4	-0.067	0.017	-3.908	9.49E-05	0.020	+	0.588	0.651
N25_N4	-0.062	0.017	-3.629	2.88E-04	0.039	+	0.995	1.059
N26_N12	0.078	0.017	4.531	6.04E-06	0.004	+	3.746	3.829
N30_N6	0.062	0.017	3.634	2.83E-04	0.039	+	0.350	0.411
N31_N7	0.062	0.017	-3.603	3.19E-04	0.039	-	-1.939	-1.881
N34_N26	-0.073	0.017	-4.269	2.01E-05	0.010	+	0.320	0.378
N40_N2	0.060	0.017	-3.526	4.27E-04	0.042	-	-1.806	-1.752
N40_N19	0.060	0.017	-3.539	4.06E-04	0.042	-	-1.136	-1.075
N40_N22	-0.061	0.017	3.554	3.84E-04	0.042	-	-0.548	-0.506
N44_N40	0.065	0.017	-3.812	1.40E-04	0.026	-	-0.509	-0.460
N47_N18	0.068	0.017	-3.967	7.42E-05	0.020	-	-0.724	-0.679

Table S4. Regions involved in the significant connections of VNR. The regions were extracted using the "result" function of SPM (http://www.fil.ion.ucl.ac.uk/spm/). Clusters that were above 50% of the highest global intensity and cluster size above 20 are reported in the following tables. The coordinates and AAL labels indicate the peak of the reported cluster.

Positive connections

No	Coordinate of peak region	AAL label	Number of voxels	Intensity of peak region
1	-22, -74, -26	Cerebelum_Crus1_L	2804	6.4319
2	36, -72, -40	Cerebelum_Crus2_R	2661	4.765
3	-12, -48, -42	Cerebelum_9_L	159	3.0327
4	50, 4, -38	Temporal_Inf_R	157	3.0399
5	2, -68, -32	Vermis_8	36	2.5446
6	56, 34, 0	Frontal_Inf_Tri_R	35023	6.9587
7	-48, -54, -12	Temporal_Inf_L	313	2.8549
8	26, -20, -14	Hippocampus_R	58	3.2229
9	10, 0, 14	Caudate_R	78	3.1414
10	-10, -4, 16	Caudate_L	35	2.8065
11	4, -20, 8	Thalamus_R	29	2.6283
12	-40, -46, 40	Parietal_Inf_L	713	3.1276
13	-24, -10, 50	Frontal_Sup_L	147	2.5947
14	34, -2, 60	Frontal_Mid_R	54	2.053

Negative connections

No	Coordinate of peak region	AAL label	Number of voxels	Intensity of peak region
1	32, -70, -48	Cerebelum_7b_R	351	-3.5296
2	8, -74, -24	Cerebelum_Crus1_R	1982	-3.4538
3	-2, -52, -34	Cerebelum_9_L	225	-2.4617
4	-22, -34, -42	Cerebelum_10_L	56	-2.3538
5	48, -60, -8	Temporal_Inf_R	2456	-3.9686
6	-28, -74, 22	Occipital_Mid_L	8857	-8.2862
7	30, -64, -28	Cerebelum_6_R	147	-2.8812
8	-46, 14, -14	Temporal_Pole_Sup_L	26	-1.8379
9	-8, 38, -12	Frontal_Med_Orb_L	275	-2.3001
10	-30, 26, -2	Insula_L	988	-3.4967
11	34, 38, -8	Frontal_Inf_Orb_R	144	-3.0886
12	32, 26, -2	Insula_R	260	-3.2563
16	-50, -12, 30	Postcentral_L	6311	-4.4245
17	26, 52, -2	Frontal_Mid_R	338	-2.4291
19	32, -72, 22	Occipital_Mid_R	3881	-7.9954
22	-10, -40, 34	Cingulum_Mid_L	1340	-3.8093

No	Coordinate of peak region	AAL label	Number of voxels	Intensity of peak region
23	-8, 0, 12	Caudate_L	51	-2.1585
24	-34, -32, 20	Insula_L	20	-1.757
25	36, -30, 18	Insula_R	23	-1.7716
26	6, 4, 56	Supp_Motor_Area_R	71	-2.3897
27	-4, 6, 54	Supp_Motor_Area_L	31	-1.6887
28	12, -32, 66	Paracentral_Lobule_R	32	-1.8698

Table S5. Regions involved in the significant connections of educational attainment. The coordinates and AAL labels indicate the peak of the reported cluster.

Positive connections

No	Coordinate of peak region	AAL label	Number of voxels	Intensity of peak region
1	12, -46, -44	Cerebelum_9_R	311	8.8438
2	-38, -66, -42	Cerebelum_Crus2_L	3413	11.1
3	-2, -68, -34	Vermis_8	29	4.7242
4	2, -58, -24	Vermis_6	22	5.1606
5	58, -6, -14	Temporal_Mid_R	402	8.8827
6	-26, -36, -16	Fusiform_L	75	6.8778
7	-24, -20, -16	Hippocampus_L	55	7.7283
8	0, -58, 44	Precuneus_L	13050	15.5606
9	22, 28, 46	Frontal_Sup_R	8148	14.3976
10	-20, 30, 38	Frontal_Mid_L	6549	14.9328
11	-32, 36, -10	Frontal_Inf_Orb_L	421	10.9456
12	-60, -12, -10	Temporal_Mid_L	212	7.2928
13	-54, -46, -12	Temporal_Inf_L	55	6.1464
14	-20, -84, -10	Fusiform_L	739	6.1887
15	56, -40, -10	Temporal_Mid_R	40	4.8633
16	24, -76, -6	Lingual_R	187	6.9006
17	-8, 4, 6	Caudate_L	40	7.5075
18	8, 6, 4	Caudate_R	73	7.6276
19	-48, -24, 6	Temporal_Sup_L	56	5.9954
20	36, -84, 10	Occipital_Mid_R	25	4.1809
21	-46, -48, 12	Temporal_Mid_L	26	4.5143
22	50, -44, 26	SupraMarginal_R	1413	6.1332
23	34, -26, 18	Insula_R	37	5.3353
24	30, -74, 20	Occipital_Mid_R	26	4.8628
25	38, -14, 20	Insula_R	20	5.6089
26	-34, -18, 42	Postcentral_L	189	7.0578
27	-50, -40, 46	Parietal_Inf_L	343	5.4355
28	-16, -4, 68	Frontal_Sup_L	40	5.1036

Negative connections

No	Coordinate of peak region	AAL label	Number of voxels	Intensity of peak region
1	-10, -72, -26	Cerebelum_Crus1_L	453	-5.7127
2	34, -70, -48	Cerebelum_7b_R	77	-5.1072
3	-16, -42, -46	Cerebelum_9_L	109	-6.2768
4	18, -42, -46	Cerebelum_9_R	114	-7.2587
5	10, -84, -38	Cerebelum_Crus2_R	60	-4.8257
6	-2, -52, -34	Cerebelum_9_L	78	-6.9646
7	10, -74, -24	Cerebelum_6_R	27	-4.779
8	-16, -58, 16	Precuneus_L	15001	-15.7718
9	24, -20, -16	Hippocampus_R	43	-4.5335
10	-22, -22, -16	Hippocampus_L	25	-4.972
11	56, -4, -18	Temporal_Mid_R	110	-5.2959
12	-34, 36, -12	Frontal_Inf_Orb_L	111	-5.2593
13	32, 38, -8	Frontal_Inf_Orb_R	851	-6.4684
14	50, -58, -6	Temporal_Inf_R	366	-6.3365
15	-40, -66, -6	Occipital_Inf_L	689	-6.7649
16	8, 52, -10	Frontal_Med_Orb_R	35	-4.3472
17	-10, 46, -6	Frontal_Med_Orb_L	30	-4.1374
18	40, -18, 0	Insula_R	22	-4.7318
19	38, 0, 14	Insula_R	35	-5.385
20	-46, -22, 20	Rolandic_Oper_L	111	-5.0322
21	-38, -4, 16	Insula_L	38	-7.1293
22	60, -26, 32	SupraMarginal_R	106	-4.2938
23	50, 4, 34	Precentral_R	151	-4.4223
24	-20, 28, 38	Frontal_Sup_L	144	-5.3051
25	-38, -24, 60	Precentral_L	373	-7.4667
26	-26, -8, 48	Precentral_L	89	-4.6457

Table S6. Regions involved in the significant connections of household income. The coordinates and AAL labels indicate the peak of the reported cluster.

Positive connections

No	Coordinate of peak region	AAL label	Number of voxels	Intensity of peak region
1	24, 26, 50	Frontal_Sup_R	21182	5.4614
2	12, -72, -48	Cerebelum_8_R	394	2.7072
3	64, -16, -16	Temporal_Mid_R	1409	3.2367
4	42, 18, -36	Temporal_Pole_Mid_R	41	1.8175
5	54, 10, -32	Temporal_Pole_Mid_R	21	2.0982
6	28, -70, -24	Cerebelum_6_R	182	2.1569
7	-16, -62, -22	Cerebelum_6_L	56	2.2845
8	10, 44, -20	Rectus_R	35	2.7192
9	40, -2, 16	Insula_R	7530	5.667
10	-38, -4, 16	Insula_L	6699	6.2029
11	-42, -44, -14	Temporal_Inf_L	38	1.8629
12	-24, 42, -14	Frontal_Sup_Orb_L	116	2.5622
13	-38, 48, 2	Frontal_Mid_L	1066	2.6366
14	-46, -68, 8	Temporal_Mid_L	381	2.5717
15	-10, -16, 10	Thalamus_L	121	2.7542

Negative connections

No	Coordinate of peak region	AAL label	Number of voxels	Intensity of peak region
1	-28, -70, -50	Cerebelum_8_L	89	-1.7068
2	-14, -52, -48	Cerebelum_9_L	20	-1.5
3	-6, -74, -40	Cerebelum_7b_L	147	-1.8434
4	22, -38, -44	Cerebelum_10_R	34	-1.7134
5	-20, -36, -44	Cerebelum_10_L	31	-1.6446
6	6, -76, -34	Cerebelum_Crus2_R	42	-1.6713
7	-2, -52, -34	Cerebelum_9_L	33	-1.7678
8	-40, -72, -28	Cerebelum_Crus1_L	29	-1.5027
9	-28, -62, -30	Cerebelum_6_L	52	-1.994
10	30, -64, -28	Cerebelum_6_R	21	-1.5615
11	32, -46, -8	Fusiform_R	227	-2.5744
12	52, -16, 6	Temporal_Sup_R	1372	-2.9145
13	44, -56, -6	Temporal_Inf_R	270	-2.3303
14	-40, -32, 10	Temporal_Sup_L	922	-3.1724
15	34, 36, -10	Frontal_Inf_Orb_R	43	-1.6368
16	-28, -60, -8	Fusiform_L	165	-2.5173
17	-40, -66, -6	Occipital_Inf_L	319	-2.3311

No	Coordinate of peak region	AAL label	Number of voxels	Intensity of peak region
18	32, 28, 0	Insula_R	39	-1.5766
19	-28, -74, 22	Occipital_Mid_L	3066	-5.032
20	32, -70, 24	Occipital_Mid_R	4320	-5.2122
21	46, 6, 24	Frontal_Inf_Oper_R	793	-2.1462
22	-34, 8, 28	Frontal_Inf_Oper_L	413	-1.8625
23	8, 16, 50	Supp_Motor_Area_R	58	-1.5919
24	-24, -4, 50	Frontal_Mid_L	707	-2.2576
25	-14, -42, 48	Cingulum_Mid_L	20	-1.436
26	16, -40, 48	Paracentral_Lobule_R	33	-1.5304
27	-6, 16, 48	Supp_Motor_Area_L	29	-1.5881

Table S7. Network-of-interest (NOI) results for cognitive performance (VNR) and educational attainment. The significant between-network connections were shown in the results below.

				VNR					
Type	Connections	Beta	Std	t.value	p	p_{corrected}	Mean value of connection	95% CI of value of connection	
inter-hemisphere	left FPN - right FPN	-0.040	0.016	-2.493	1.27E-02	0.018	1.156	1.127	1.185
	right CON - left CON	-0.063	0.016	-3.923	8.89E-05	6.67E-04	0.379	0.356	0.402
CON - FPN	left CON - right FPN	0.034	0.016	-2.106	3.52E-02	0.044	-1.359	-1.387	-1.330
	right CON - left FPN	0.043	0.016	-2.714	6.68E-03	0.011	-2.088	-2.122	-2.054
	left CON - left FPN	0.044	0.016	2.732	6.33E-03	0.011	1.043	1.018	1.067
	right CON - right FPN	0.051	0.016	3.200	1.38E-03	0.005	0.648	0.620	0.676
DMN-related	left CON - DMN	0.061	0.016	3.824	1.33E-04	6.67E-04	0.675	0.652	0.698
	right CON - DMN	-0.045	0.016	2.797	5.18E-03	0.011	-0.275	-0.300	-0.250

				EDUCATION					
Type	Connections	Beta	Std	t.value	p	p_{corrected}	Mean value of connection	95% CI of value of connection	
CON - FPN	right CON - right FPN	0.086	0.031	2.736	6.24E-03	0.021	0.648	0.620	0.676
DMN-related	right FPN - DMN	0.104	0.031	-3.335	8.59E-04	0.004	-0.710	-0.738	-0.682
	right CON - DMN	-0.149	0.031	4.761	1.99E-06	1.99E-05	-0.275	-0.300	-0.250

Table S7. Correlation matrix between average motion during resting-state assessment, first four genetic principal components, cognitive performance (VNR), educational attainment and household income. Motions and genetic principal components showed very weak correlations with VNR, educational attainment and household income.

	Age	Sex	Motion	VNR	Edu	Income
Age	1	0.085	0.155	-0.061	-0.021	-0.28
Sex	0.085	1	0.147	0.081	0.071	0.079
Motion	0.155	0.147	1	-0.085	-0.094	-0.113
VNR	-0.061	0.081	-0.085	1	0.257	0.202
Edu	-0.021	0.071	-0.094	0.257	1	0.237
Income	-0.28	0.079	-0.113	0.202	0.237	1

Table S8. Replication analyses on the (1) unrelated sample, which related people were removed (N=3,253), and (2) updated unrelated sample (N=7,144). Three connections turned null in both unrelated 4k sample and unrelated 7k sample, which takes up 4.05% of 74 significant connections found in the main results. None of the significant connections showed opposite direction of effect in the additional analyses.

	Connection	Main model			Unrelated people (N~=4k)		Unrelated people (N~=7k)	
		Beta (std)	$P_{uncorrected}$	$P_{corrected}$	Beta (std)	$P_{uncorrected}$	Beta (std)	$P_{uncorrected}$
VNR	N17_N15	0.054 (0.016)	6.73E-04	3.85E-02	0.053 (0.018)	3.36E-03	0.049 (0.012)	7.30E-05
	N21_N7	0.097 (0.016)	9.09E-10	1.35E-06	0.09 (0.018)	5.38E-07	0.074 (0.012)	2.71E-09
	N21_N11	0.062 (0.016)	9.72E-05	1.44E-02	0.067 (0.018)	2.28E-04	0.058 (0.012)	3.14E-06
	N22_N1	0.061 (0.016)	1.53E-04	1.77E-02	0.051 (0.018)	4.99E-03	0.025 (0.012)	4.66E-02
	N24_N4	-0.066 (0.016)	4.37E-05	7.21E-03	-0.064 (0.018)	4.36E-04	-0.052 (0.013)	3.71E-05
	N24_N9	-0.083 (0.016)	2.14E-07	1.59E-04	-0.073 (0.018)	6.33E-05	-0.059 (0.012)	2.45E-06
	N25_N5	-0.072 (0.016)	7.39E-06	1.65E-03	-0.084 (0.018)	3.57E-06	-0.057 (0.012)	3.75E-06
	N26_N12	0.081 (0.016)	4.96E-07	2.45E-04	0.061 (0.018)	7.47E-04	0.052 (0.012)	2.57E-05
	N28_N24	0.076 (0.016)	2.25E-06	8.35E-04	0.081 (0.018)	1.01E-05	0.074 (0.013)	4.02E-09
	N29_N11	0.059 (0.016)	2.45E-04	2.14E-02	0.057 (0.018)	1.71E-03	0.055 (0.013)	9.99E-06
	N31_N12	-0.066 (0.016)	4.06E-05	7.21E-03	-0.079 (0.018)	1.47E-05	-0.074 (0.012)	3.61E-09
	N33_N13	0.06 (0.016)	1.78E-04	1.77E-02	0.05 (0.018)	5.90E-03	0.043 (0.012)	5.67E-04
	N33_N22	0.055 (0.016)	6.52E-04	3.85E-02	0.055 (0.018)	2.76E-03	0.055 (0.013)	1.11E-05
	N39_N33	0.074 (0.016)	4.80E-06	1.43E-03	0.046 (0.018)	1.23E-02	0.047 (0.013)	1.78E-04
	N42_N6	-0.056 (0.016)	4.43E-04	3.13E-02	-0.057 (0.018)	1.80E-03	-0.044 (0.013)	4.75E-04
	N42_N18	0.055 (0.016)	5.77E-04	3.73E-02	**0.035 (0.018)**	**5.63E-02**	0.025 (0.012)	4.60E-02
	N44_N17	0.054 (0.016)	6.21E-04	3.84E-02	0.041 (0.018)	2.33E-02	**<0.001, >-0.001 (0.012)**	**9.68E-01**
	N44_N25	0.071 (0.016)	7.78E-06	1.65E-03	0.057 (0.018)	1.48E-03	0.054 (0.012)	1.19E-05
	N45_N5	-0.058 (0.016)	2.93E-04	2.42E-02	-0.045 (0.018)	1.28E-02	-0.05 (0.012)	7.09E-05
	N45_N15	0.059 (0.016)	2.34E-04	2.14E-02	0.037 (0.018)	4.03E-02	0.039 (0.012)	1.72E-03
	N45_N44	0.055 (0.016)	4.81E-04	3.25E-02	**0.034 (0.018)**	**5.71E-02**	**0.019 (0.012)**	**1.27E-01**
	N46_N25	-0.057 (0.016)	4.00E-04	2.97E-02	-0.039 (0.018)	3.18E-02	**-0.02 (0.012)**	**1.09E-01**
	N47_N31	0.059 (0.016)	1.68E-04	1.77E-02	0.056 (0.018)	1.87E-03	0.034 (0.012)	5.23E-03
	N48_N19	0.061 (0.016)	1.59E-04	1.77E-02	0.046 (0.018)	1.10E-02	0.041 (0.013)	1.14E-03
	N48_N21	-0.061 (0.016)	1.44E-04	1.77E-02	-0.057 (0.018)	1.75E-03	-0.021 (0.012)	8.73E-02
	N50_N7	0.057 (0.016)	3.33E-04	2.60E-02	0.059 (0.018)	1.18E-03	0.057 (0.012)	4.27E-06
Educational attainment	N5_N4	-0.103 (0.031)	1.01E-03	4.54E-02	-0.056 (0.018)	2.28E-03	-0.045 (0.013)	3.91E-04
	N8_N3	-0.119 (0.031)	1.42E-04	1.75E-02	-0.056 (0.018)	2.34E-03	-0.036 (0.013)	4.51E-03
	N12_N5	0.132 (0.031)	2.71E-05	6.71E-03	0.056 (0.018)	2.25E-03	0.033 (0.013)	8.67E-03
	N12_N11	0.106 (0.031)	6.94E-04	3.97E-02	**0.032 (0.018)**	**7.50E-02**	0.038 (0.012)	2.24E-03
	N15_N7	0.122 (0.031)	7.96E-05	1.48E-02	0.041 (0.018)	2.35E-02	0.044 (0.012)	4.66E-04
	N17_N15	0.121 (0.031)	9.59E-05	1.53E-02	0.046 (0.018)	1.21E-02	0.054 (0.012)	1.65E-05
	N19_N18	-0.136 (0.031)	1.47E-05	5.47E-03	-0.058 (0.019)	1.74E-03	-0.039 (0.013)	1.99E-03
	N20_N10	-0.109 (0.031)	4.91E-04	3.80E-02	-0.071 (0.018)	1.28E-04	-0.043 (0.013)	6.06E-04

Connection	Main model			Unrelated people (N~=4k)		Unrelated people (N~=7k)	
	Beta (std)	$P_{uncorrected}$	$P_{corrected}$	Beta (std)	$P_{uncorrected}$	Beta (std)	$P_{uncorrected}$
N24_N4	-0.108 (0.031)	6.15E-04	3.80E-02	-0.049 (0.018)	7.95E-03	-0.038 (0.013)	2.33E-03
N25_N3	0.137 (0.031)	1.36E-05	5.47E-03	0.068 (0.018)	2.36E-04	0.042 (0.013)	8.17E-04
N25_N4	-0.161 (0.031)	2.73E-07	4.06E-04	-0.081 (0.018)	1.06E-05	-0.077 (0.013)	8.59E-10
N26_N12	0.108 (0.031)	5.51E-04	3.80E-02	**0.029 (0.018)**	**1.12E-01**	0.032 (0.013)	1.05E-02
N29_N25	0.108 (0.031)	5.88E-04	3.80E-02	0.042 (0.018)	2.29E-02	0.038 (0.013)	2.75E-03
N31_N7	0.125 (0.031)	6.57E-05	1.39E-02	0.039 (0.018)	3.21E-02	0.038 (0.012)	2.19E-03
N33_N2	-0.103 (0.031)	9.96E-04	4.54E-02	-0.064 (0.018)	5.00E-04	**-0.024 (0.013)**	**6.05E-02**
N34_N26	-0.133 (0.031)	2.14E-05	6.37E-03	-0.051 (0.018)	5.55E-03	-0.059 (0.013)	2.69E-06
N35_N33	0.108 (0.031)	5.63E-04	3.80E-02	0.055 (0.019)	3.26E-03	0.037 (0.013)	3.41E-03
N36_N35	0.105 (0.031)	7.79E-04	4.09E-02	0.055 (0.018)	2.59E-03	0.027 (0.013)	3.49E-02
N40_N7	0.118 (0.031)	1.72E-04	1.96E-02	0.06 (0.018)	1.24E-03	**0.019 (0.013)**	**1.46E-01**
N40_N34	0.122 (0.031)	1.03E-04	1.53E-02	0.049 (0.018)	7.75E-03	0.044 (0.013)	4.62E-04
N42_N8	-0.108 (0.031)	5.89E-04	3.80E-02	-0.052 (0.018)	4.56E-03	**-0.018 (0.013)**	**1.55E-01**
N44_N25	0.112 (0.031)	3.35E-04	2.93E-02	0.047 (0.018)	9.83E-03	**0.012 (0.012)**	**3.30E-01**
N44_N36	0.139 (0.031)	9.61E-06	5.47E-03	0.071 (0.018)	1.09E-04	0.044 (0.013)	4.38E-04
N45_N15	0.117 (0.031)	2.05E-04	2.17E-02	**0.028 (0.018)**	**1.33E-01**	0.037 (0.013)	3.59E-03
N45_N36	0.105 (0.031)	8.20E-04	4.09E-02	0.061 (0.018)	1.07E-03	0.031 (0.013)	1.46E-02
N45_N44	0.105 (0.031)	6.74E-04	3.97E-02	**0.036 (0.018)**	**5.18E-02**	**0.008 (0.013)**	**5.02E-01**
N46_N36	0.11 (0.031)	4.54E-04	3.74E-02	0.047 (0.018)	1.09E-02	0.029 (0.013)	1.91E-02
N47_N36	0.105 (0.031)	7.93E-04	4.09E-02	0.046 (0.018)	1.29E-02	0.028 (0.013)	2.42E-02
N47_N45	0.11 (0.031)	3.35E-04	2.93E-02	**0.029 (0.018)**	**1.02E-01**	**0.016 (0.012)**	**1.88E-01**
N48_N5	-0.114 (0.031)	2.75E-04	2.72E-02	-0.061 (0.018)	8.06E-04	-0.046 (0.013)	2.78E-04
N50_N10	-0.121 (0.031)	1.15E-04	1.55E-02	-0.059 (0.018)	1.31E-03	-0.029 (0.013)	2.30E-02
N52_N37	0.104 (0.031)	8.37E-04	4.09E-02	0.052 (0.018)	4.74E-03	0.043 (0.013)	5.31E-04
N55_N10	-0.105 (0.031)	8.53E-04	4.09E-02	-0.074 (0.018)	6.83E-05	-0.027 (0.013)	3.32E-02
N12_N11	0.072 (0.017)	2.64E-05	9.80E-03	0.063 (0.019)	9.81E-04	0.043 (0.013)	1.17E-03
N15_N11	0.082 (0.017)	1.60E-06	2.38E-03	0.082 (0.019)	1.91E-05	0.043 (0.013)	1.21E-03
N18_N8	0.064 (0.017)	2.02E-04	3.34E-02	0.06 (0.02)	2.40E-03	**0.019 (0.013)**	**1.50E-01**
N18_N12	0.067 (0.017)	9.42E-05	2.01E-02	0.047 (0.02)	1.69E-02	0.035 (0.013)	9.10E-03
N24_N4	-0.067 (0.017)	9.49E-05	2.01E-02	-0.062 (0.02)	1.65E-03	-0.052 (0.013)	1.23E-04
N25_N4	-0.062 (0.017)	2.88E-04	3.89E-02	-0.065 (0.02)	9.67E-04	-0.056 (0.013)	2.66E-05
N26_N12	0.078 (0.017)	6.04E-06	4.49E-03	0.074 (0.019)	1.54E-04	0.062 (0.013)	3.55E-06
N30_N6	0.062 (0.017)	2.83E-04	3.89E-02	0.049 (0.02)	1.24E-02	0.039 (0.013)	3.19E-03
N31_N7	0.062 (0.017)	3.19E-04	3.94E-02	0.049 (0.019)	1.09E-02	0.035 (0.013)	7.45E-03
N34_N26	-0.073 (0.017)	2.01E-05	9.80E-03	-0.079 (0.02)	5.35E-05	-0.071 (0.013)	1.25E-07
N40_N2	0.06 (0.017)	4.27E-04	4.23E-02	0.041 (0.019)	3.63E-02	**0.024 (0.013)**	**7.07E-02**
N40_N19	0.06 (0.017)	4.06E-04	4.23E-02	0.051 (0.019)	8.10E-03	0.044 (0.013)	8.49E-04
N40_N22	-0.061 (0.017)	3.84E-04	4.23E-02	-0.073 (0.02)	2.14E-04	-0.051 (0.013)	1.51E-04
N44_N40	0.065 (0.017)	1.40E-04	2.59E-02	0.062 (0.019)	1.58E-03	0.042 (0.013)	1.58E-03
N47_N18	0.068 (0.017)	7.42E-05	2.01E-02	0.053 (0.02)	6.36E-03	**0.024 (0.013)**	**7.24E-02**

Household income (vertical label for bottom section)