

# Supplemental Material

## Supplementary Tables

Table S1: Pairwise correlations between the standardized scores of all cognitive tests instances, obtained from all participants who were brain scanned and genotyped. (A) first touchscreen test; (B) second touchscreen test; (C) third touchscreen test; (D) web-based test. All measures were standardized.

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)
(1) g	1.00													
(2) Fluid intelligence (A)	0.66	1.00												
(3) Fluid intelligence (B)	0.68	0.65	1.00											
(4) Fluid intelligence (C)	0.69	0.64	0.69	1.00										
(5) Fluid intelligence (D)	0.67	0.60	0.61	0.62	1.00									
(6) Numeric memory (A)	0.55	0.32	0.38	0.34	0.29	1.00								
(7) Numeric memory (D)	0.65	0.29	0.29	0.32	0.30	0.43	1.00							
(8) Reaction time (A)	-0.40	-0.12	-0.16	-0.12	-0.12	-0.05	-0.09	1.00						
(9) Reaction time (B)	-0.41	-0.13	-0.15	-0.13	-0.13	0.02	-0.10	0.57	1.00					
(10) Reaction time (C)	-0.41	-0.14	-0.15	-0.15	-0.13	-0.07	-0.09	0.51	0.56	1.00				
(11) Visual memory (A)	-0.42	-0.19	-0.21	-0.19	-0.18	-0.08	-0.09	0.12	0.09	0.10	1.00			
(12) Visual memory (B)	-0.39	-0.19	-0.19	-0.19	-0.18	-0.04	-0.08	0.11	0.09	0.10	0.22	1.00		
(13) Visual memory (C)	-0.41	-0.16	-0.16	-0.20	-0.16	-0.05	-0.09	0.10	0.09	0.13	0.22	0.21	1.00	
(14) Visual memory (D)	-0.42	-0.13	-0.15	-0.17	-0.19	-0.08	-0.11	0.09	0.11	0.09	0.19	0.19	0.20	1.00

Table S2: Pairwise correlations between key variables in the analysis

		(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)
(1)	Brain volume	1.00												
(2)	Fluid IQ	0.21	1.00											
(3)	Numeric memory	0.14	0.36	1.00										
(4)	Reaction time	-0.11	-0.17	-0.10	1.00									
(5)	Visual memory	-0.07	-0.28	-0.13	0.17	1.00								
(6)	G-factor	0.22	0.78	0.65	-0.47	-0.60	1.00							
(7)	EA	0.14	0.31	0.14	-0.08	-0.08	0.25	1.00						
(8)	Male	0.62	0.08	0.09	-0.09	0.00	0.10	0.09	1.00					
(9)	Age at scan	-0.04	-0.05	-0.09	0.29	0.19	-0.23	-0.05	0.07	1.00				
(10)	Height	0.59	0.16	0.12	-0.14	-0.07	0.18	0.11	0.73	-0.07	1.00			
(11)	PC1	-0.07	-0.12	-0.03	0.05	0.08	-0.09	0.04	0.01	-0.09	-0.03	1.00		
(12)	PC2	0.06	0.08	0.01	-0.01	-0.02	0.05	-0.04	-0.01	0.05	0.06	-0.20	1.00	
(13)	PC3	-0.03	-0.01	-0.01	0.04	0.04	-0.00	0.02	0.04	-0.01	0.01	-0.02	0.14	1.00
(14)	PC4	0.02	-0.05	-0.00	0.05	0.02	-0.03	-0.06	-0.02	-0.00	0.00	-0.05	0.05	-0.04

Table S3: Descriptive statistics of the study sample

VARIABLES	mean (sd)
Standardized values of fluid intelligence score	0.00 (1.00)
Educational attainment in US-schooling year equivalents	15.47 (4.74)
Brain volume	1,568.04 (145.74)
Male	0.47 (0.50)
Age at scan	61.61 (6.98)
Height	169.28 (9.16)
Observations	13,608

Table S4: Brain size and fluid intelligence: differences between measurement instances

Ordinary least squares (OLS) regression with *fluid intelligence* as dependent variable, for individuals who completed all four instances of the test. Table reports standardized beta coefficients and 95% confidence intervals in parentheses. Regressions include all control variables, including genetic controls. Coefficients for control variables not displayed.

	All tests	recruitment	1st repeat measure	screening visit	online
Brain volume	0.20*** (0.09 - 0.27)	0.17** (0.06 - 0.26)	0.15** (0.05 - 0.25)	0.13* (0.03 - 0.22)	0.23*** (0.12 - 0.32)
$R^2$	0.19	0.16	0.18	0.19	0.21
$N$	708	708	708	708	708

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S5: Brain volume and fluid intelligence, controlling for Townsend social deprivation index and place of birth

Ordinary least squares (OLS) regression with *fluid intelligence* as the dependent variable. Table reports 95% confidence intervals in parentheses. Total brain volume is in cm<sup>3</sup>, control variables include Townsend index, geographic North-East coordinates for place of birth as dummy variables (the results hold when dummy variables for all interactions of north / east coordinates are used instead), sex, age at scan in years, average age at IQ testing sessions (dummy coded) and its interactions with sex, height in cm and participant specific IQ testing sessions (dummy coded). Coefficients for control variables except the Townsend index are not displayed.

	Standardized betas	Marginal effects (dy/dx)
Brain volume	0.19*** (0.17 - 0.21)	0.0013*** (0.0012 - 0.0015)
Townsend index	-0.03*** (-0.05 - -0.02)	-0.01*** (-0.02 - -0.01)
$R^2$	0.19	0.19
$N$	12,822	12,822

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S6: Brain size and fluid intelligence, without height as a control

Ordinary least squares (OLS) regression with *fluid intelligence* as the dependent variable. The analysis replicates the regression in Table 1 from the main text, excluding height as a control variable.

	Excluding genetic controls		Including genetic controls	
	Standardized betas	Marginal effects (dy/dx)	Standardized betas	Marginal effects (dy/dx)
Brain volume	0.23*** (0.21 - 0.26)	0.0016*** (0.0015 - 0.0018)	0.21*** (0.19 - 0.23)	0.0015*** (0.0013 - 0.0016)
$R^2$	0.10	0.10	0.13	0.13
$N$	13,608	13,608	13,608	13,608

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S7: Robustness check with UKB-derived brain size variable

Ordinary least squares (OLS) regression with *fluid intelligence* (two left columns) and educational attainment (two right columns) as dependent variables. Table reports 95% confidence intervals in parentheses. Brain volume measurement (in cm<sup>3</sup>) was derived by UKB Imaging Working Group, and is composed of only grey and white matter volume. Regressions include all control variables specified in Table 1 (for fluid intelligence) and Table 2 (for educational attainment), and include controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	Fluid intelligence		Educational attainment	
	Standardized beta	Marginal effect (dy/dx)	Standardized beta	Marginal effect (dy/dx)
Brain volume (UKB-derived)	0.18***	0.0017***	0.10***	0.0042***
	(0.16 - 0.20)	(0.0015 - 0.0018)	(0.08 - 0.12)	(0.0033 - 0.0051)
$R^2$	0.13	0.13	0.05	0.05
$N$	13,409	13,409	13,409	13,409

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S8: Brain size and educational attainment, controlling for Townsend index of social deprivation and place of birth

Ordinary least squares (OLS) regression with *educational attainment* as the dependent variable. Table reports 95% confidence intervals in parentheses. Total brain volume is in cm<sup>3</sup>, control variables include Townsend index, geographic North-East coordinates for place of birth as dummy variables (the results hold when dummy variables for all interactions of north / east coordinates are used instead), sex, age at scan, body height, birth year (dummy coded) and its interactions with sex. Coefficients for control variables except the Townsend index are not displayed.

	Standardized betas	Marginal effects (dy/dx)
Brain volume	0.11*** (0.08 - 0.13)	0.0035*** (0.0027 - 0.0042)
Townsend index	-0.05*** (-0.07 - -0.03)	-0.09*** (-0.12 - -0.06)
$R^2$	0.14	0.14
$N$	12,822	12,822

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S9: Brain size and fluid intelligence, by sex

Ordinary least squares (OLS) regression with *fluid intelligence* as the dependent variable, stratified by sex. Table reports 95% confidence intervals in parentheses. Brain volume is in cm<sup>3</sup>. Regression includes all control variables specified in Table 1, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	Females		Males	
	Standardized betas	Marginal effects (dy/dx)	Standardized betas	Marginal effects (dy/dx)
Brain volume	0.16*** (0.14 - 0.18)	0.0013*** (0.0011 - 0.0015)	0.15*** (0.13 - 0.17)	0.0011*** (0.0010 - 0.0013)
$R^2$	0.13	0.13	0.14	0.14
$N$	7,183	7,183	6,425	6,425

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S10: Interaction between sex and brain size

Ordinary least squares (OLS) regression with *fluid intelligence* as the dependent variable. Table reports 95% confidence intervals in parentheses. Brain volume is in cm<sup>3</sup>, baseline category for sex is female. Regression includes all control variables specified in Table 1, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	Fluid intelligence	Educational attainment
Brain volume	0.21*** (13.38)	0.14*** (8.43)
Male × brain volume	-0.13 (-1.06)	-0.18 (-1.46)
$R^2$	0.14	0.06
$N$	13,608	13,608

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S11: Brain size and fluid intelligence - by age groups

Ordinary least squares (OLS) regression with *fluid intelligence* as the dependent variable, by age groups. Table reports 95% confidence intervals in parentheses. Brain volume is in cm<sup>3</sup>. Regression includes all control variables specified in Table 1, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	<50yrs	50<=yrs<57	57<=yrs<62	>=62yrs
Brain volume	0.22*** (0.18 - 0.26)	0.20*** (0.16 - 0.24)	0.21*** (0.17 - 0.25)	0.15*** (0.10 - 0.19)
$R^2$	0.16	0.14	0.15	0.13
$N$	3,434	3,540	3,278	3,356

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S12: Brain size and educational attainment - by sex

Ordinary least squares (OLS) regression with *educational attainment* as the dependent variable, by sex. Table reports 95% confidence intervals in parentheses. Brain volume is in cm<sup>3</sup>. Regression includes all control variables specified in Table 2, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	Females		Males	
	Standardized betas	Marginal effects (dy/dx)	Standardized betas	Marginal effects (dy/dx)
Brain volume	0.11*** (0.08 - 0.13)	0.0047*** (0.0036 - 0.0057)	0.09*** (0.07 - 0.12)	0.0035*** (0.0025 - 0.0044)
$R^2$	0.06	0.06	0.04	0.04
$N$	7,183	7,183	6,425	6,425

Table S13: Brain size and educational attainment - by age groups

Ordinary least squares (OLS) regression with *educational attainment* as the dependent variable, by age groups. Table reports 95% confidence intervals in parentheses. Brain volume is in cm<sup>3</sup>. Regression includes all control variables specified in Table 2, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	<50yrs	50<=yrs<57	57<=yrs<62	>=62yrs
Brain volume	0.13*** (0.08 - 0.17)	0.11*** (0.06 - 0.15)	0.12*** (0.08 - 0.17)	0.12*** (0.07 - 0.16)
$R^2$	0.06	0.06	0.09	0.08
$N$	3,434	3,540	3,278	3,356

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Note: Table reports standardized beta coefficients and 95% confidence intervals in parentheses. Coefficients for control variables are not displayed.

Table S14a: Brain size and general cognitive ability ( $g$ ), principal component analysis

Ordinary least squares (OLS) regression. The dependent variable is general cognitive ability ( $g$ ), proxied using the first unrotated principal component of the four cognitive tests available in the UKB. Table reports 95% confidence intervals in parentheses. Brain volume is in  $\text{cm}^3$ . Regression includes all control variables specified in Table 1, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	Excluding genetic controls		Including genetic controls	
	Standardized beta	Marginal effect (dy/dx)	Standardized beta	Marginal effect (dy/dx)
Brain volume	0.19*** (0.16 - 0.22)	0.0013*** (0.0011 - 0.0015)	0.18*** (0.15 - 0.21)	0.0012*** (0.0010 - 0.0014)
$R^2$	0.13	0.13	0.15	0.15
$N$	7,511	7,511	7,511	7,511

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S14b: Brain size and general cognitive ability ( $g$ ), as measured by Lyall et al. (2016)

Ordinary least squares (OLS) regression. The dependent variable is general cognitive ability ( $g$ ), as measured by Lyall et al. (2016). Table reports 95% confidence intervals in parentheses. Brain volume is in  $\text{cm}^3$ . Regression includes all control variables specified in Table 1, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	Excluding genetic controls		Including genetic controls	
	Standardized beta	Marginal effect (dy/dx)	Standardized beta	Marginal effect (dy/dx)
Brain volume	0.18*** (0.10 - 0.27)	0.0013*** (0.0007 - 0.0018)	0.18*** (0.09 - 0.26)	0.0012*** (0.0007 - 0.0018)
$R^2$	0.14	0.14	0.18	0.18
$N$	1,017	1,017	1,004	1,004

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S14c: Brain size and general cognitive ability ( $g$ ), factor analysis

Ordinary least squares (OLS) regression. The dependent variable is general cognitive ability ( $g$ ), proxied by performing factor analysis of a single factor on the four cognitive tests available in the UKB. Table reports 95% confidence intervals in parentheses. Brain volume is in  $\text{cm}^3$ . Regression includes all control variables specified in Table 1, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	Excluding genetic controls		Including genetic controls	
	Standardized betas	Marginal effects (dy/dx)	Standardized betas	Marginal effects (dy/dx)
Brain volume	0.22*** (0.19 - 0.25)	0.0015*** (0.0013 - 0.0017)	0.21*** (0.18 - 0.24)	0.0014*** (0.0012 - 0.0016)
$R^2$	0.12	0.12	0.15	0.15
$N$	7,511	7,511	7,511	7,511

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S14d: Brain volume and g excluding fluid intelligence

Ordinary least squares (OLS) regression. The dependent variable is general cognitive ability ( $g$ ), proxied using the first unrotated principal component of the three cognitive tests available in the UKB (all tests except *fluid intelligence*). Table reports 95% confidence intervals in parentheses. Brain volume is in  $\text{cm}^3$ . Regression includes all control variables specified in Table 1, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	Excluding genetic controls		Including genetic controls	
	Standardized betas	Marginal effects (dy/dx)	Standardized betas	Marginal effects (dy/dx)
Brain volume	0.10*** (0.08 - 0.13)	0.0007*** (0.0005 - 0.0009)	0.10*** (0.07 - 0.12)	0.0007*** (0.0005 - 0.0009)
$R^2$	0.14	0.14	0.16	0.16
$N$	7,511	7,511	7,511	7,511

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S15: Brain volume and different measures of cognitive performance

Ordinary least squares (OLS) regression. The dependent variables are the different cognitive measures in the UKB (except *fluid intelligence*). Table reports 95% confidence intervals in parentheses. Brain volume is in cm<sup>3</sup>. Regression includes all control variables specified in Table 1, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	Numeric memory		Reaction time		Visual memory	
	Standardized betas	Marginal effects (dy/dx)	Standardized betas	Marginal effects (dy/dx)	Standardized betas	Marginal effects (dy/dx)
Brain volume	0.11*** (0.08 - 0.14)	0.0008*** (0.0006 - 0.0010)	-0.02 (-0.04 - 0.00)	-0.0001 (-0.0003 - 0.0000)	-0.05*** (-0.07 - -0.03)	-0.0003*** (-0.0005 - -0.0002)
$R^2$	0.05	0.05	0.13	0.13	0.08	0.08
$N$	7,722	7,722	13,608	13,608	13,292	13,292

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

Table S16: Brain volume predicted from cognitive tests

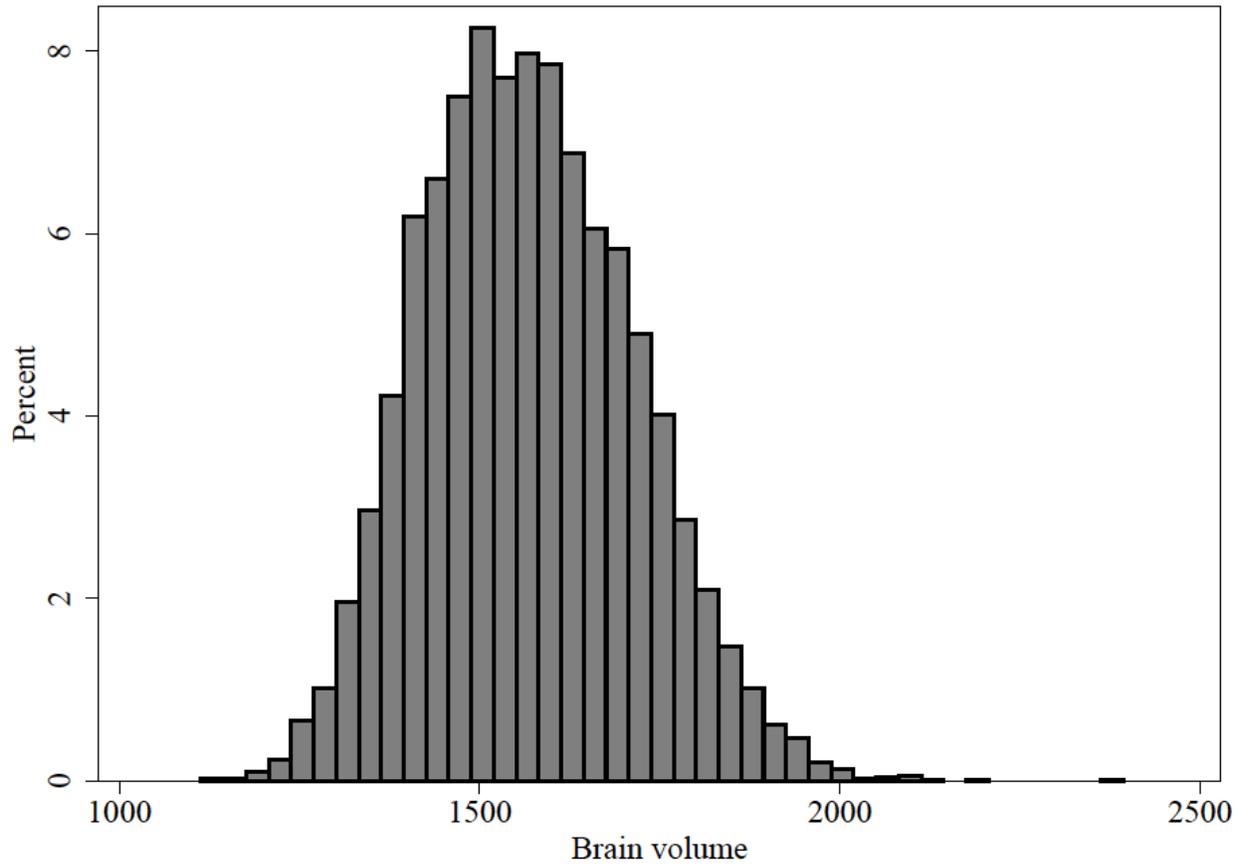
Ordinary least squares (OLS) regression. The dependent variable is total brain volume in cm<sup>3</sup>. Table reports 95% confidence intervals in parentheses. Regression includes all control variables specified in Table 1, including controls for population structure using the first 40 principal components of the genome. Coefficients for control variables are not displayed.

	Excluding EA	Including EA
<i>Fluid Intelligence</i>	0.13*** (0.11 - 0.15)	0.12*** (0.10 - 0.14)
<i>Numeric memory</i>	0.03** (0.01 - 0.04)	0.03** (0.01 - 0.04)
<i>Reaction time</i>	-0.00 (-0.02 - 0.02)	-0.00 (-0.02 - 0.02)
<i>Visual memory</i>	0.01 (-0.01 - 0.03)	0.01 (-0.01 - 0.03)
<i>Educational attainment</i>		0.03** (0.00 - 0.01)
$R^2$	0.45	0.46
$N$	7,511	7,511

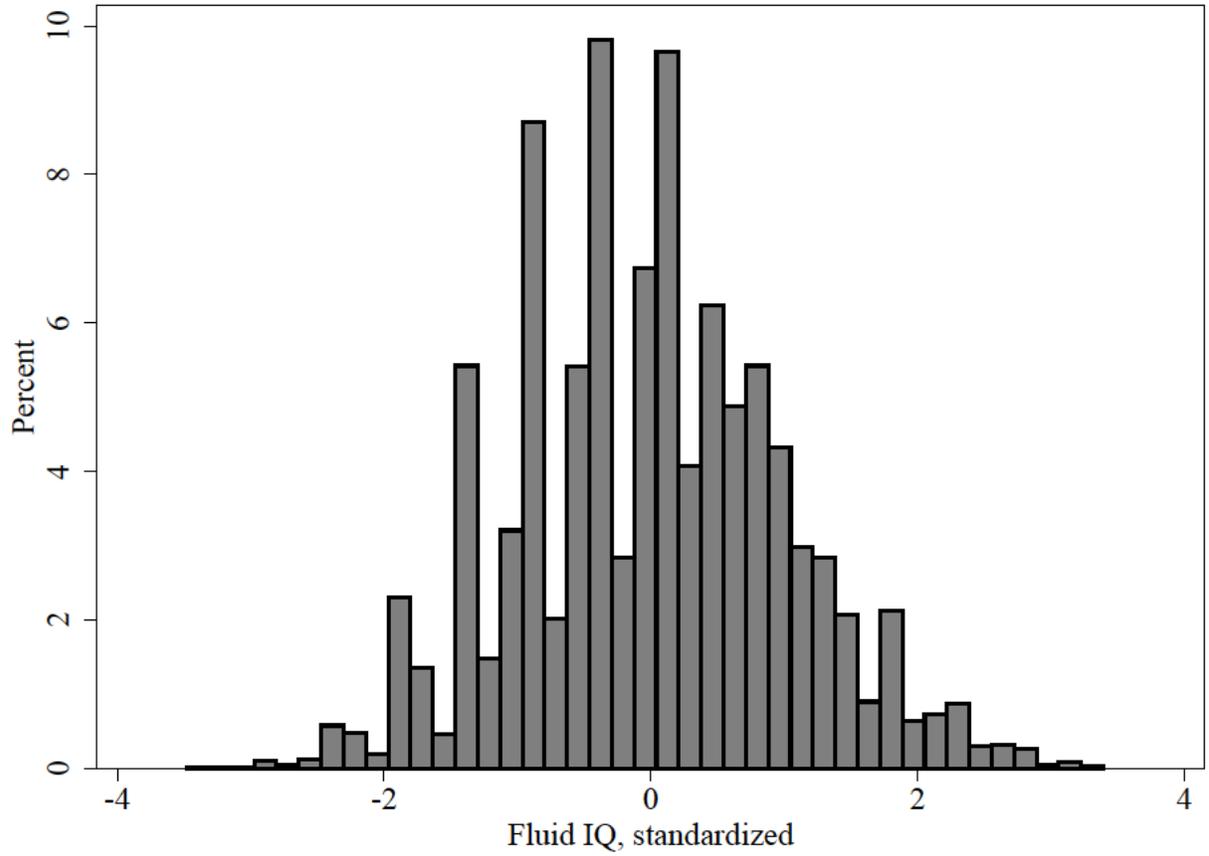
\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$

## Supplementary Figures

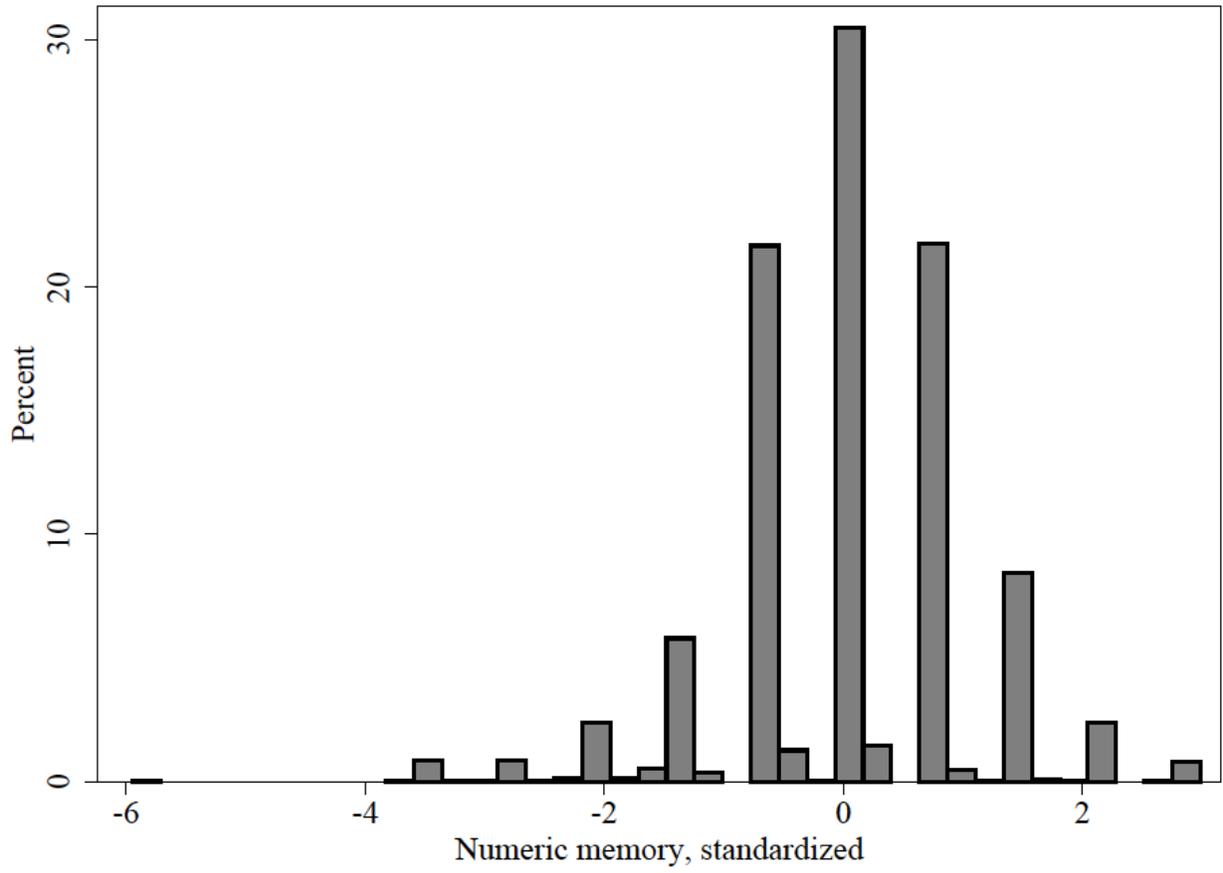
**Figure S1:** Total brain volume (cm<sup>3</sup>) distribution in the study sample



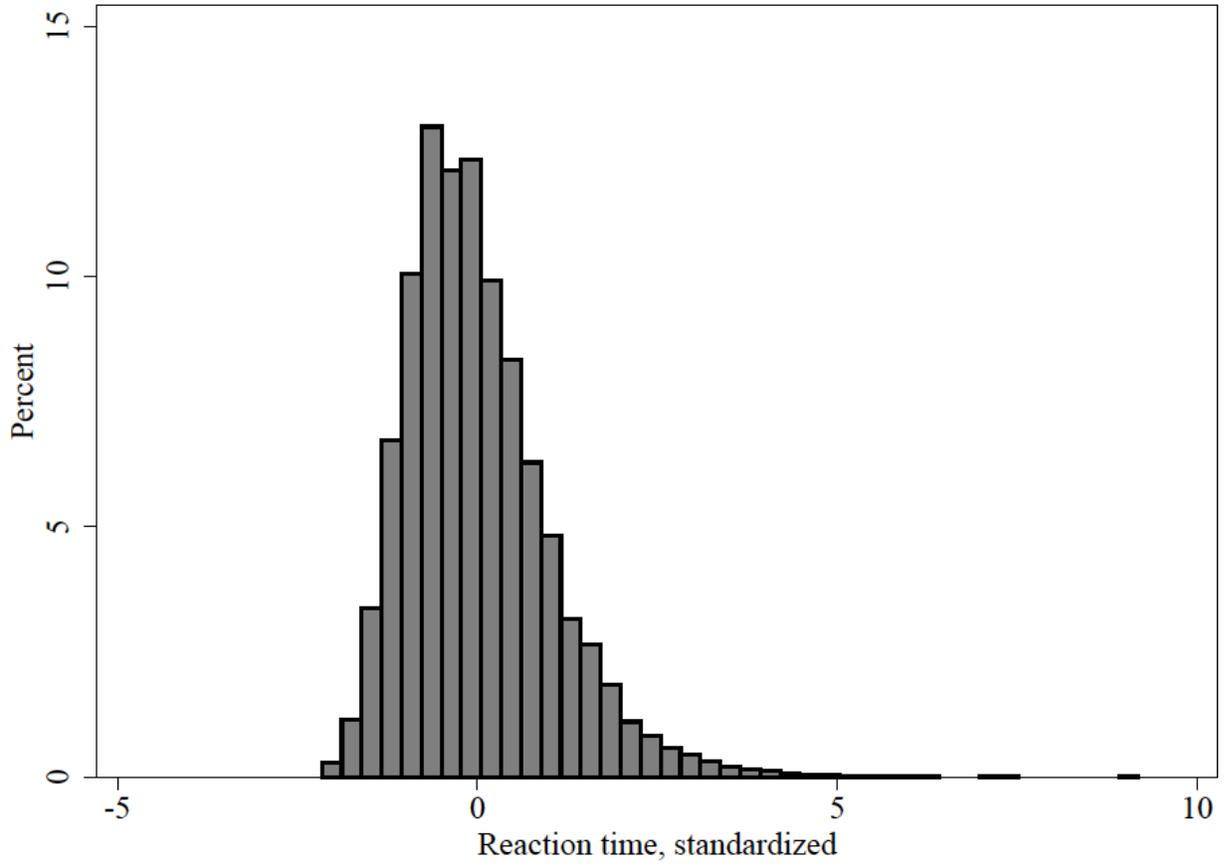
**Figure S2:** Fluid intelligence scores distribution in the study sample (standardized)



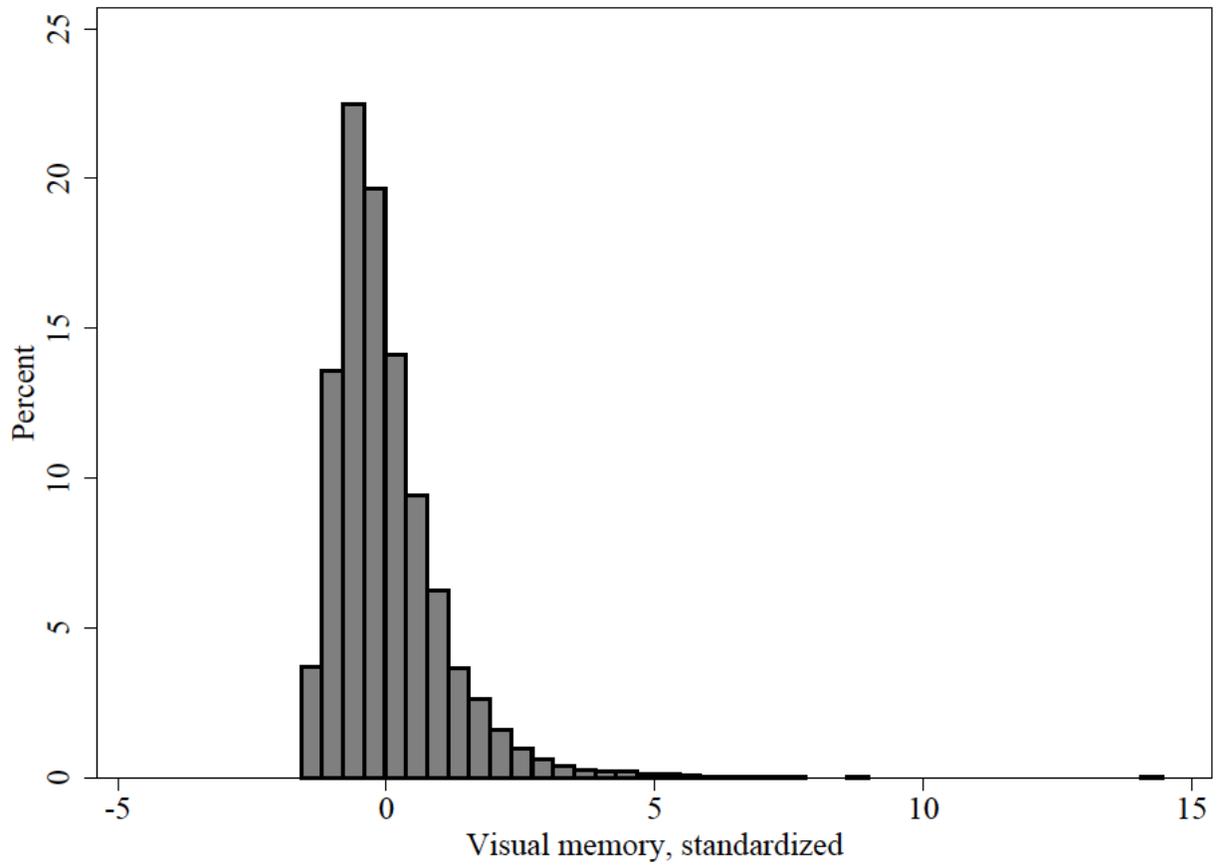
**Figure S3:** Numeric memory score distribution in the study sample (standardized)



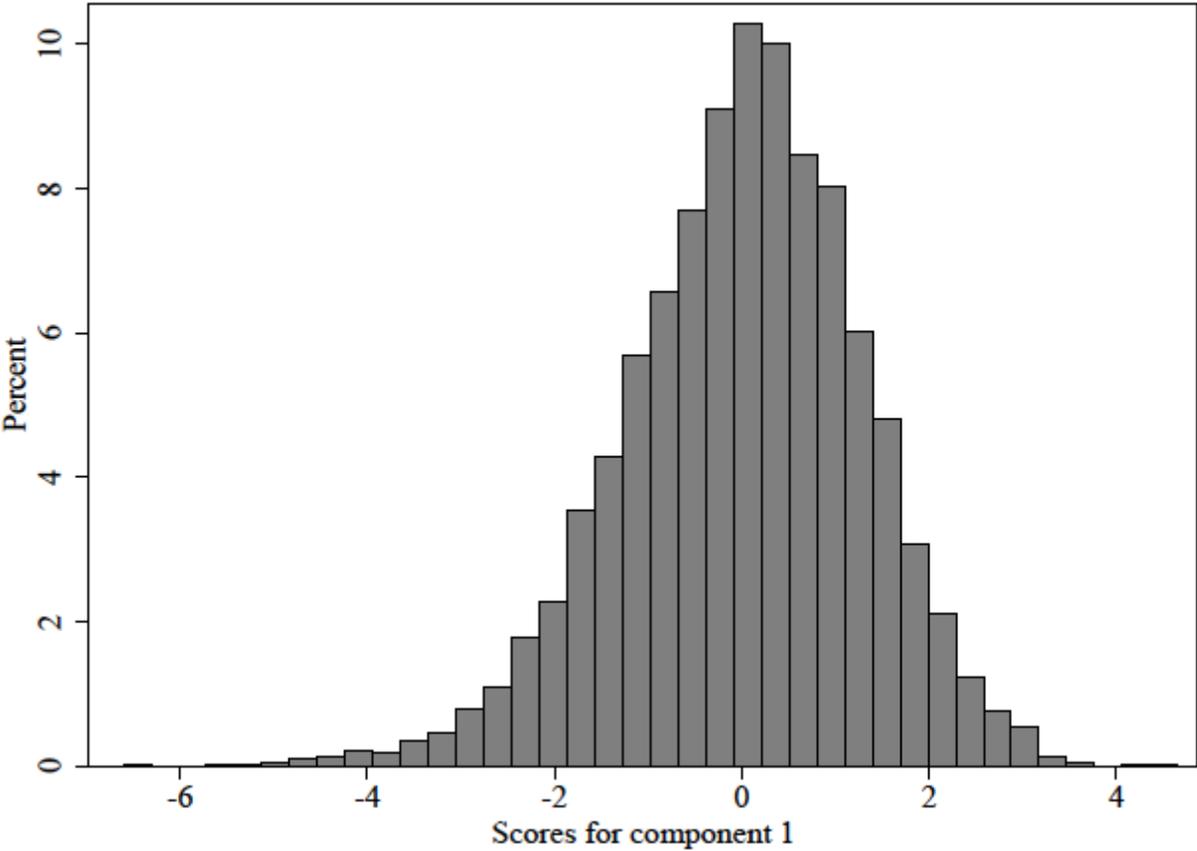
**Figure S4:** Reaction time task scores distribution in the study sample (standardized)



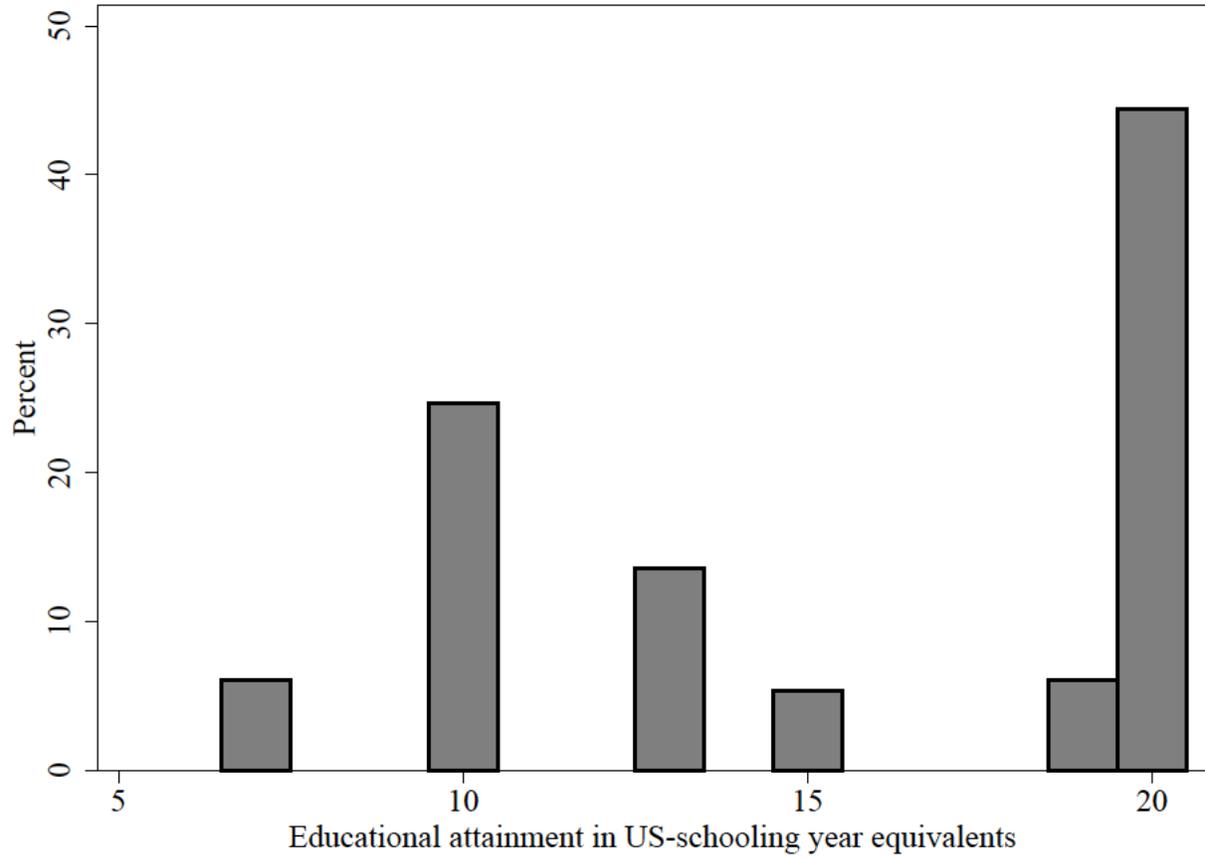
**Figure S5:** Visual memory task scores distribution in the study sample (standardized)



**Figure S6:** Distribution of general intelligence ('g') scores in the study sample (standardized), obtained by extracting the first unrotated principal component of the four measures of cognitive performance in the UKB



**Figure S7:** Educational attainment (in US-schooling year equivalents) distribution in the study sample



## Fluid intelligence test in the UK Biobank

1. Add the following numbers together: 1 2 3 4 5 – is the answer?

Select from:

- 13
- 14
- 15
- 16
- 17
- Do not know
- Prefer not to answer

2. Which number is the largest?

Select from:

- 642
- 308
- 987
- 714
- 253
- Do not know
- Prefer not to answer

3. Bud is to flower as child is to?

- Grow
- Develop
- Adult
- Old
- Do not know
- Prefer not to answer

4. 11 12 13 14 15 16 17 18

Divide the sixth number to the right of twelve by three. Is the answer?

Select from:

- 5
- 6
- 7
- 8
- Do not know
- Prefer not to answer

5. If Truda's mother's brother is Tim's sister's father, what relation is Truda to Tim?

Select from:

- Aunt
- Sister
- Niece
- Cousin
- No relation
- Do not know
- Prefer not to answer

6. If sixty is more than half of seventy-five, multiple twenty-three by three. If not subtract 15 from eighty-five. Is the answer?

Select from:

- 68
- 69
- 70
- 71
- 72
- Do not know
- Prefer not to answer

7. Stop means the same as?

Select from:

- Pause
- Close
- Cease
- Break
- Rest
- Do not know
- Prefer not to answer

8. If David is twenty-one and Owen is nineteen and Daniel is nine years younger than David, what is half their combined age?

Select from:

- 25
- 26
- 27
- 28
- 29
- Do not know
- Prefer not to answer

9. Age is to years as height is to?

Select from:

- Long
- Deep
- Top
- Metres
- Tall
- Do not know
- Prefer not to answer

10. 150...137...125...114...104...

What comes next?

Select from:

- 96
- 95
- 94
- 93
- 92
- Do not know
- Prefer not to answer

11. Relaxed means the opposite of?

Select from:

- Calm
- Anxious
- Cool
- Worried
- Tense

- Do not know
- Prefer not to answer

12. 100...99...95...86...70...

What comes next?

Select from:

- 50
- 49
- 48
- 47
- 46
- 45
- Do not know
- Prefer not to answer

13. If some flinks are plinks and some plinks are stinks then some flinks are definitely stinks?

Select from:

- False
- True
- Neither true nor false
- Do not know
- Prefer not to answer

14. If 'Anne' is thirty-four and 'John' is forty-seven, what number is 'that'?

Select from:

- 49
- 50
- 51
- 52
- 53

Question 14 was only asked in the online follow-up, not in the original touchscreen version.