Supplemental Material for:

Heritability of working memory brain activation

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This file includes:

Task activation and performance

Supplementary Table 1 shows the means and standard deviations for task-related brain response (i.e. BOLD t-score for 2>0-back contrast) at group analysis peak activation coordinates, and for performance measures. Most areas activated during the task did not show significant effects of zygosity on means or variances. One small cluster of 162 voxels in middle occipital gyrus (R: [36, −75, 21], [45, −75, 6]) and middle temporal gyrus (R: [42, −54, 15], [42, −69, 15], [51, −51, 12]) showed a significant zygosity effect on the mean, and one cluster of 559 voxels in inferior frontal gyrus (R: [30, 9, 30]) and precentral gyrus (R: [27, 21, 27]) showed a significant zygosity effect on the variance. There were no mean or variance differences between zygosity groups for task performance. Birth order effects (means not shown) on means and variances were also generally not significant. No significant clusters (height threshold $p < 0.05$, extent threshold 147 voxels) were found for the birth order effect on the mean. Two small cluster totaling 461 voxels in caudate nucleus (L: [−18, 6, 21]) and putamen (L: [−21, 15, 9]), inferior frontal gyrus (R: [39, 30, 12]), middle frontal gyrus (R: [27, 51, 6], [33, 9, 45], [36, 27, 33]) and superior frontal gyrus (R: [24, 57, 12]), showed a birth order effect on the variance. There were no birth order effects on means and variances for task performance. Sex influenced voxel activation means, accuracy ($d = 0.42$, $p < 0.001$) and reaction time ($d = -0.25$, $p < 0.05$) in the 0-back condition, and accuracy in the 2-back condition ($d = 0.39$, $p < 0.01$), with males generally having stronger activation (**Supplementary Table 1**, and Figure 4 in main text), and performing slightly better than females respectively. No significant sex effects on the variance were present, although two clusters totaling 494 voxels in superior parietal lobule, including precuneus (R: [6, −42, 45], [9, −51, 60], [9, −63, 51], [9, −72, 45], [18,

−48, 51], [24, −72, 48]), inferior frontal gyrus (R: [33, 18, 24], [36, 21, 27], [42, 3, 27]), middle frontal gyrus (R: [27, 24, 39], [33, 15, 48], [36, 21, 33], [39, 12, 45]) and precentral gyrus (R: [39, 0, 33], [45, 6, 36]) showed a significant sex effect on the covariance.

-----Insert Supplementary Table 1 about here-----

Twin correlations

Maximum likelihood twin correlations for the group analysis peak activation coordinates are shown in **Supplementary Table 2**. MZ correlations for the majority of the local maxima were significant and greater than the respective DZ correlation, suggesting additive genetic control of task-related brain activation. The 95% confidence intervals (CIs) for MZ and DZ correlations for task-related brain activation are shown in **Supplementary Figure 2**. The CIs for task-related brain activation are wide and include zero for many regions (especially for the DZ twins) and show that there is a degree of overlap in the estimates for the MZ and DZ groups.

-----Insert Supplementary Table 2 about here-----

-----Insert Supplementary Figure 2 about here-----

Reproducibility

The 95% CIs and corresponding *p*-value maps for the test-retest ICCs are shown in **Supplementary Figure 3**. As expected, CIs are generally narrowest for areas with the highest activation intensity in the group random effects analysis.

-----Insert Supplementary Figure 3 about here-----

It should be mentioned that test-retest reliability differed slightly between females and males, being somewhat lower in females for both the voxel values and the performance measures. The paired samples *t*-test showed 2 voxels [−6, −18, 12] significantly different for males ($p < 0.05$, FWE-corrected), and 13 voxels (peak locations x,y,z: [−3, 6, 60], 2 voxels; [30, −63, 57], 4 voxels; [48, −24, 33], 5 voxels; [60, −51, 0], 1 voxel; and [−36, −30, 33], 1 voxel) significantly different for females ($p < 0.05$, FWE-corrected). This can be explained by the fact that females showed lower activation and performance initially. The differential test-retest reliability for males and females emphasizes the potential importance of estimating heritability in males and females separately. Not only may different sets of genes be involved in explaining individual differences in task-related brain activation, it may be the case that task-related brain activation is more suitable as an endophenotype in males than in females.

Phenotypic correlations among measures

Task performance measures, accuracy and reaction time (RT) were moderately correlated and both were moderately correlated with FIQ as shown in **Supplementary Table 3**. Consistent with the general finding that working memory is moderately to strongly related to cognitive ability (e.g., (Buehner, 2005)), the phenotypic correlations between 2-back performance measures and FIQ (accuracy: $r = 0.43$; RT: $r = -0.20$) were significant and similar to those reported in previous twin studies (Ando et al., 2001; Luciano et al., 2001) (0.20–0.41).

-----Insert Supplementary Table 3 about here-----

-----Insert Supplementary Figure 4 about here-----

Supplementary Figure 4 shows the phenotypic correlations between task performance measures and brain activation. In just 17.1% of voxels in the group activation area did 0-back performance accuracy correlate significantly with task-related brain activation. The strongest positive correlations between 0-back performance accuracy and voxel activation values to survive cluster thresholding were found in inferior frontal gyrus (R: [39, 9, 27]), supramarginal gyrus (R: [42, -33, 39]), superior parietal lobule, including precuneus (L: [−18, −66, 54], [−15, −60, 42], [−12, −66, 51], [−9, −60, 60], [−6, −51, 63]; R: [9, −57, 60], [21, −54, 54]), middle temporal gyri (L: [−45, −60, 6], R: [45, −57, 6]), superior temporal gyrus (R: [54, −45, 12]), and middle occipital gyrus (R: [42, −75, 6]), with *r* ranging between 0.20 and 0.32 for these coordinates. No negative correlations survived cluster thresholding.

In just 21.7% of voxels in the group activation area did 0-back RT correlate significantly. RT on the 0-back condition showed the strongest significant negative correlations with brain activation (i.e. faster response, higher activation) in inferior frontal gyrus (pars opercularis) (R: [54, 12, 27]), middle frontal gyrus (L: [−27, 3, 60]), precentral gyrus (R: [45, 6, 30], [48, 9, 39]), superior parietal lobule, including precuneus (L: [−24, −66, 51], [−24, −72, 48], [−9, −60, 60], [−6, −60, 51]; R: [6, −66, 54], [9, −60, 57], [15, −57, 51]), middle temporal gyrus (L: [−48, −63, 3]), and occipital cortex (R: [54, −66, 0]), with *r* ranging between −0.21 and −0.32. Slower responses were most strongly associated with higher activation in SMA (R: [12, 24, 54]), superior medial gyrus (L: [−3, 36, 39], R: [9, 33, 45]) and anterior cingulate cortex (L: [9, 39, 21]), with *r* ranging between 0.21 and 0.26.

In just 35.2% of voxels in the group activation area did 2-back performance accuracy correlate significantly, and in a mere 20.0% of voxels did 2-back accuracy significantly predict activation (Figure 4 main text). For performance accuracy on the 2-back condition, we found the strongest significant negative correlations in inferior frontal gyrus (pars triangularis) (L: [−54, 18, 9], [−48, 21, 15]), middle frontal gyrus (L: [−39, 15, 36]), SMA (Brodmann area 6) (L: [−3, 21, 57]), anterior cingulate cortex (L: [−3, 33, 24]) and superior medial gyrus (L: [−3, 30, 48]), with *r* ranging between −0.20 and −0.25. These correlations might partly be attributable to error monitoring processes (Carter et al., 1998). The strongest significant positive correlations were found in anterior ventral bank of intraparietal sulcus (R: [33, −51, 42], [36, −42, 42]), superior parietal lobule, including precuneus (R: [6, −57, 51], [9, −54, 48], [21, −57, 54]), middle temporal gyrus (R: [48, −60, 6], [39, −57, 12]), and caudate nucleus (L: [−18, 15, 12], [−15, 24, 3]), with *r* ranging between 0.25 and 0.33.

In just 2.4% of voxels in the group activation area did 2-back RT correlate significantly. Similar to the 0-back RTs, RT on the 2-back condition showed significant positive correlations with brain activation (slower responses, higher activation) in the anterior cingulate cortex (L: [−6, 24, 27]; R: [3, 30, 27], [3, 36, 21]), and superior medial gyrus (L: [−6, 18, 42]), with *r* ranging between 0.21 and 0.25. No negative correlations survived cluster thresholding for 2-back RT.

-----Insert Supplementary Figure 5 about here-----

Supplementary Figure 5 shows the phenotypic correlations of FIQ and gray matter volume with brain activation. In just 13.4% of voxels in the group activation area did FIQ correlate significantly with task-related brain activation, and in a mere 3.1% of voxels did FIQ significantly predict activation (Figure 4 main text). The highest positive correlations between FIQ and activation were found in superior frontal gyrus (R: [18, 9, 57], [21, 6, 54]), angular gyrus (L: [−45, −81, 15]; R: [48, −72, 15], [51, −57, 12]), superior parietal lobule, including precuneus (L: [0, −63, 51]; R: [3, −60, 54], [9, −54, 51], [21, −51, 63]), occipital cortex (hOC5) (R: [51, −66, 3]), hippocampus (L: [−21, −42, 6], [−18, −39, 9]; R: [21, −36, 9]), and thalamus (L: [−15, −27, 12]), with *r* ranging between 0.20 and 0.25. No negative correlations survived cluster thresholding.

In just 23.7% of voxels in the group activation area did we detect a correlation with gray matter volume. The highest negative correlations between gray matter volume and task-related brain activation were found in SMA (L: [−3, 21, 57]), and superior medial gyrus (L: [0, 36, 42]; R: [9, 36, 42], [12, 30, 45]), with *r* ranging between −0.22 and −0.25). The highest positive correlations between gray matter volume and activation were found in inferior frontal gyrus (pars opercularis) (R: [51, 12, 27], [60, 12, 12]), middle frontal gyri (L: [−21, 6, 54]; R: [36, 3, 57]), superior frontal gyri (L: [−18, 0, 51]; R: [24, 3, 60]), precentral gyri, including Brodmann area 6 (L: [−45, 0, 48]; R: [36, −3, 48], [48, 6, 45]), middle cingulate cortex (R: [3, 18, 33]), superior parietal lobule, including precuneus and cuneus (L: [−15, −72, 48], [15, −63, 54], [−3, −60, 51]; R: [3, −57, 54], [6, −54, 51], [18, −72, 45], [21, −66, 36]), middle temporal gyrus (L: [−42, −66, 9]), insula lobe (R: [42, 15, −3]), middle occipital gyrus (L: [−39, −72, 6], [−39, −78, 12]; R: [36, −75, 36]), and superior occipital gyrus (R: [27, −72, 45]), with r ranging between 0.20 and 0.37.

Gestational age and birth weight were highly correlated, but neither correlated with FIQ or task performance (**Supplementary Table 3**). Other than some weak inverse correlations between birth weight and task-related activation in the caudate nucleus (R: [12, 6, 12], [12, 18, 0], [15, −3, 15], [18, 6, 15]) and pallidum (R: [18, 6, 3]) (r ranging between −0.14 and −0.22), neither correlated with voxel activation values. Birth weight correlated 0.15 ($p < 0.01$) with gray matter volume. Socio-economic index did not correlate with brain activation or any of the other variables ($p > 0.05$).

Multiple linear regression analyses of task-related brain activation on age, sex, performance measures, FIQ, GM volume, gestational age, birth weight, and socio-economic index (SEI) detected the following ranges of effect (mean ± s.d. negative unstandardized regression coefficient; mean ± s.d. positive unstandardized regression coefficient) on task-related brain activation: age: −0.110 to +0.072 t-contrast score difference per year (−0.016±0.013; +0.011±0.011); sex: −0.315 to +0.696 deviation for males as compared to females (−0.041±0.040; +0.082±0.077); 0-back accuracy: −0.011 to +0.011 per percent accuracy (−0.0018±0.0016; +0.0018±0.0015); 0-back RT: −0.004 to +0.002 per ms (−0.0006±0.0006; +0.0004±0.0003); 2-back accuracy: −0.008 to +0.010 per percent accuracy (−0.0015±0.0013; +0.0017±0.0013); 2-back RT: −0.0006 to +0.0016 per ms (−0.0001±0.0001; +0.0002±0.0002); FIQ: −0.009 to +0.010 per IQ point (−0.0017±0.0014; +0.0017±0.0015); GM volume: −0.003 to +0.003 per ml

(−0.0033±0.0032; +0.0040±0.0037); gestational age: −0.057 to +0.061 per week gestation (−0.007±0.006; +0.009±0.008); birth weight: −0.0004 to +0.0003 per gram (−0.00006±0.00006; +0.00003±0.00003); SEI: −0.006 to +0.004 per point (−0.0008±0.0008; +0.0007±0.0006). Although the range of regression coefficients for 0-back performance accuracy is greater than that for 2-back accuracy, overall, the effect of 2-back performance accuracy is stronger.

Supplementary Table 4 shows the regression coefficients for the covariates sex, age, 2-back response accuracy, and FIQ in the group analysis peak activated voxels. This table demonstrates the range of effects across the brain and clearly shows that the effect of sex is strongest.

-----Insert Supplementary Table 4 about here-----

Supplementary Table 1. Descriptives for task-related brain activation and performance.

Brain area		MNI coordinates x	y	z	MZ (n = 162 individuals)	DZ (n = 157 individuals)	Females (n = 199 individuals)	Males (n = 120 individuals)	Total (n = 319 individuals)
R Inferior Temporal Gyrus		51	−54	−9	0.35 (±0.28)	0.31 (±0.29)	0.31 (±0.27)	0.36 (±0.31)	0.33 (±0.29)
R Middle Temporal Gyrus		54	−51	−6	0.36 (±0.31)	0.34 (±0.30)	0.35 (±0.28)	0.35 (±0.34)	0.35 (±0.30)
R Lateral Orbitofrontal Gyrus		33	24	−6	1.02 (±0.42)	1.04 (±0.45)	1.00 (±0.43)	1.08 (±0.44)	1.03 (±0.43)
L Insular Cortex		−33	21	−3	0.86 (±0.46)	0.87 (±0.40)	0.84 (±0.43)	0.91 (±0.42)	0.86 (±0.43)
R Inferior Frontal Gyrus		51	18	3	0.62 (±0.38)	0.61 (±0.34)	0.61 (±0.36)	0.63 (±0.36)	0.62 (±0.36)
R Inferior Frontal Gyrus		51	15	12	0.67 (±0.40)	0.67 (±0.40)	0.62 (±0.39)	0.75 (±0.41)**	0.67 (±0.40)
R Caudate Nucleus		18	6	15	0.36 (±0.27)	0.34 (±0.28)	0.33 (±0.28)	0.37 (±0.27)	0.35 (±0.28)
R Angular Gyrus		57	−39	18	0.46 (±0.36)	0.47 (±0.32)	0.39 (±0.31)	0.6 (±0.34)***	0.47 (±0.34)
L Caudate Nucleus		−18	3	18	0.31 (±0.24)	0.32 (±0.27)	0.30 (±0.25)	0.34 (±0.26)	0.31 (±0.26)
R Middle Frontal Gyrus		42	39	21	0.91 (±0.47)	0.96 (±0.53)	0.89 (±0.48)	1.00 (±0.53)*	0.93 (±0.50)
L Inferior Frontal Gyrus		−45	9	24	0.68 (±0.42)	0.69 (±0.43)	0.64 (±0.41)	0.76 (±0.45)*	0.68 (±0.42)
R Inferior Frontal Gyrus		45	12	27	1.04 (±0.55)	1.02 (±0.57)	0.94 (±0.52)	1.17 (±0.59)***	1.03 (±0.56)
L Middle Occipital Gyrus		−27	−69	30	0.64 (±0.42)	0.60 (±0.43)	0.56 (±0.41)	0.72 (±0.43)**	0.62 (±0.42)
L Inferior Frontal Gyrus		−45	6	33	0.73 (±0.43)	0.75 (±0.46)	0.74 (±0.45)	0.73 (±0.43)	0.74 (±0.45)
R Middle Occipital Gyrus		36	−69	36	0.88 (±0.51)	0.80 (±0.47)	0.74 (±0.44)	1.01 (±0.53)***	0.84 (±0.49)
L Superior Parietal Gyrus		−24	−63	42	0.75 (±0.49)	0.71 (±0.46)	0.66 (±0.46)	0.85 (±0.49)***	0.73 (±0.48)
L SupraMarginal Gyrus		−42	−42	42	0.85 (±0.45)	0.76 (±0.43)	0.77 (±0.42)	0.87 (±0.47)	0.81 (±0.44)
R Superior Frontal Gyrus		6	24	42	1.12 (±0.49)	1.08 (±0.48)	1.05 (±0.44)	1.18 (±0.55)*	1.10 (±0.49)
R SupraMarginal Gyrus		33	−57	45	0.88 (±0.45)	0.80 (±0.47)	0.77 (±0.44)	0.96 (±0.47)***	0.84 (±0.46)
R SupraMarginal Gyrus		45	−39	45	1.03 (±0.46)	1.01 (±0.47)	0.98 (±0.46)	1.09 (±0.47)*	1.02 (±0.46)
R Superior Parietal Gyrus		30	−63	48	1.00 (±0.50)	0.99 (±0.57)	0.90 (±0.50)	1.16 (±0.56)***	1.00 (±0.54)
R Angular Gyrus		36	−54	48	1.02 (±0.5)	0.92 (±0.58)	0.89 (±0.52)	1.11 (±0.55)***	0.97 (±0.54)
R Middle Frontal Gyrus		27	12	51	1.13 (±0.52)	1.2 (±0.51)	1.1 (±0.46)	1.27 (±0.59)**	1.16 (±0.52)
L Precuneus		−9	−60	54	0.96 (±0.54)	0.92 (±0.56)	0.78 (±0.49)	1.21 (±0.55)***	0.94 (±0.55)
R Precuneus		9	−57	54	1.21 (±0.62)	1.13 (±0.62)	1 (±0.51)	1.47 (±0.68)***	1.17 (±0.62)
L Middle Frontal Gyrus		−27	6	54	0.84 (±0.49)	0.83 (±0.45)	0.77 (±0.39)	0.94 (±0.55)**	0.84 (±0.47)
Performance measure									
0-back	Accuracy (%)				87.6 (±10.9)	89.2 (±10.5)	86.7 (±11.1)	91.0 (±9.5)***	88.3 (±10.7)
	RT (ms)				442.8 (±62.6)	440.7 (±56.2)	447.3 (±59.9)	432.5 (±57.7)*	441.7 (±59.4)
2-back	Accuracy (%)				73.3 (±18.0)	69.6 (±19.7)	68.8 (±18.6)	76.0 (±18.6)**	71.5 (±18.9)
	RT (ms)				258.4 (±116.1)	248.6 (±111.2)	249.8 (±117.0)	259.8 (±108.0)	253.5 (±113.6)

Abbreviations: DZ, dizygotic; L, Left Hemisphere; MNI, Montréal Neurological Institute; ms, milliseconds; MZ, monozygotic; R, Right Hemisphere; RT, Reaction Time; s.d., standard deviation. Means (± s.d.) for *t*-contrast difference 2>0-back at group random effects analysis local maxima, and for performance measures. T-tests: * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Supplementary Table 2. Twin correlations at group random effects analysis local maxima.

Brain Area	r_{MZ} (95% CI)	r_{DZ} (95% CI)	r_{MZF} (95% CI)	r_{MZM} (95% CI)	r_{DZF} (95% CI)	r_{DZM} (95% CI)	r_{DZOS} (95% CI)
R Inferior Temporal Gyrus	0.32 (0.05,0.53)*	0.13 (−0.14,0.38)	0.38 (0.05,0.62)*	0.22 (−0.21,0.56)	0.14 (−0.26,0.49)	0.53 (−0.03,0.84)	−0.09 (−0.63,0.53)
R Middle Temporal Gyrus	0.34 (0.11,0.53)*	0.04 (−0.21,0.28)	0.09 (−0.20,0.36)	0.59 (0.27,0.77)*	0.02 (−0.34,0.38)	0.34 (−0.23,0.74)	−0.10 (−0.59,0.44)
R Lateral Orbitofrontal Gyrus	0.36 (0.15,0.54)*	0.12 (−0.11,0.34)	0.12 (−0.18,0.40)	0.24 (−0.13,0.55)	0.13 (−0.23,0.45)	−0.54 (−0.84,0.04)	0.61 (0.20,0.83)*
L Insular Cortex	0.16 (−0.07,0.38)	0.29 (0.07,0.49)*	0.30 (−0.02,0.55)	−0.02 (−0.35,0.33)	0.25 (−0.10,0.53)	0.25 (−0.34,0.71)	0.08 (−0.41,0.53)
R Inferior Frontal Gyrus	0.33 (0.12,0.50)*	−0.09 (−0.32,0.16)	0.41 (0.14,0.62)*	0.21 (−0.15,0.51)	−0.38 (−0.65,−0.03)	0.48 (−0.09,0.81)	−0.08 (−0.56,0.45)
R Inferior Frontal Gyrus	0.46 (0.25,0.62)*	0.19 (−0.05,0.41)	0.42 (0.14,0.64)*	0.49 (0.12,0.71)*	−0.01 (−0.35,0.34)	0.61 (0.11,0.88)*	0.15 (−0.38,0.61)
R Caudate Nucleus	0.32 (0.10,0.51)*	0.03 (−0.21,0.27)	0.14 (−0.17,0.43)	0.50 (0.20,0.72)*	−0.22 (−0.54,0.16)	0.25 (−0.39,0.75)	0.34 (−0.16,0.70)
R Angular Gyrus	0.35 (0.13,0.53)*	0.26 (0.00,0.47)*	0.18 (−0.10,0.45)	0.59 (0.29,0.77)*	0.15 (−0.25,0.48)	0.31 (−0.32,0.74)	0.49 (0.04,0.80)*
L Caudate Nucleus	0.21 (−0.05,0.45)	−0.02 (−0.26,0.22)	0.35 (0.03,0.60)*	0.07 (−0.34,0.45)	−0.10 (−0.43,0.25)	−0.16 (−0.71,0.59)	0.19 (−0.31,0.60)
R Middle Frontal Gyrus	0.29 (0.06,0.49)*	0.27 (0.03,0.47)*	0.13 (−0.18,0.40)	0.54 (0.19,0.75)*	0.27 (−0.10,0.58)	−0.05 (−0.56,0.51)	0.51 (0.03,0.79)*
L Inferior Frontal Gyrus	0.20 (−0.03,0.41)	0.27 (0.02,0.49)*	0.04 (−0.27,0.34)	0.39 (0.06,0.64)*	0.27 (−0.10,0.58)	0.29 (−0.34,0.73)	0.70 (0.33,0.88)*
R Inferior Frontal Gyrus	0.23 (0.00,0.44)*	0.09 (−0.15,0.32)	−0.04 (−0.34,0.26)	0.49 (0.17,0.71)*	0.09 (−0.26,0.42)	0.01 (−0.58,0.59)	0.15 (−0.35,0.58)
L Middle Occipital Gyrus	0.46 (0.24,0.62)*	0.16 (−0.09,0.39)	0.43 (0.18,0.64)*	0.53 (0.13,0.75)*	0.32 (−0.03,0.60)	0.35 (−0.28,0.75)	−0.25 (−0.67,0.30)
L Inferior Frontal Gyrus	0.09 (−0.14,0.31)	0.21 (−0.03,0.43)	0.08 (−0.20,0.34)	0.11 (−0.26,0.45)	0.42 (0.08,0.67)*	0.23 (−0.38,0.70)	−0.01 (−0.47,0.46)
R Middle Occipital Gyrus	0.25 (0.02,0.44)*	−0.07 (−0.07,0.20)	0.16 (−0.13,0.42)	0.37 (−0.03,0.62)	−0.15 (−0.50,0.23)	0.36 (−0.21,0.77)	−0.18 (−0.60,0.29)
L Superior Parietal Gyrus	0.37 (0.16,0.55)*	0.28 (0.02,0.50)*	0.36 (0.09,0.58)*	0.40 (0.02,0.67)*	0.36 (0.01,0.63)*	−0.04 (−0.58,0.53)	0.25 (−0.25,0.64)
L SupraMarginal Gyrus	0.30 (0.08,0.48)*	0.29 (0.02,0.52)*	0.35 (0.08,0.58)*	0.27 (−0.09,0.56)	0.30 (−0.05,0.58)	0.33 (−0.34,0.77)	0.24 (−0.52,0.74)
R Superior Frontal Gyrus	0.20 (−0.04,0.41)	0.26 (0.02,0.47)*	0.19 (−0.12,0.46)	0.19 (−0.19,0.51)	−0.03 (−0.36,0.31)	0.52 (−0.04,0.82)	0.74 (0.41,0.90)*
R SupraMarginal Gyrus	0.12 (−0.11,0.33)	0.08 (−0.17,0.31)	−0.02 (−0.30,0.28)	0.30 (−0.05,0.57)	0.06 (−0.31,0.40)	0.05 (−0.49,0.59)	0.19 (−0.19,0.60)
R SupraMarginal Gyrus	0.33 (0.11,0.52)*	−0.01 (−0.27,0.26)	0.39 (0.12,0.61)*	0.25 (−0.12,0.55)	−0.24 (−0.55,0.14)	−0.04 (−0.61,0.55)	0.22 (−0.50,0.73)
R Superior Parietal Gyrus	0.15 (−0.08,0.36)	0.11 (−0.14,0.34)	−0.08 (−0.37,0.22)	0.41 (0.10,0.65)*	0.06 (−0.30,0.40)	0.15 (−0.42,0.63)	0.43 (−0.10,0.76)
R Angular Gyrus	0.25 (0.02,0.45)*	0.10 (−0.14,0.33)	0.28 (−0.02,0.53)	0.20 (−0.20,0.53)	0.22 (−0.24,0.54)	0.22 (−0.36,0.72)	0.21 (−0.31,0.60)
R Middle Frontal Gyrus	0.38 (0.17,0.56)*	0.02 (−0.22,0.25)	0.28 (0.00,0.52)*	0.47 (0.12,0.70)*	0.08 (−0.27,0.41)	−0.39 (−0.71,0.28)	0.02 (−0.45,0.48)
L Precuneus	0.26 (−0.00,0.44)	0.18 (−0.04,0.45)	0.18 (−0.12,0.45)	0.29 (−0.06,0.58)	0.24 (−0.12,0.54)	0.17 (−0.39,0.64)	0.13 (−0.38,0.58)
R Precuneus	0.47 (0.23,0.62)*	0.28 (0.07,0.53)*	0.22 (−0.09,0.48)	0.61 (0.32,0.79)*	0.20 (−0.17,0.51)	0.26 (−0.34,0.70)	0.61 (0.13,0.85)*
L Middle Frontal Gyrus	0.36 (0.14,0.54)*	0.27 (0.00,0.49)*	0.14 (−0.15,0.41)	0.55 (0.25,0.74)*	0.38 (0.03,0.64)*	0.46 (−0.10,0.80)	0.03 (−0.51,0.57)

Maximum likelihood twin correlations (95% confidence intervals [CI]) for *t*-contrast difference 2>0-back at group random effects analysis local maxima. See Supplementary Table 1 for MNI coordinates. * $p < 0.05$.

Supplementary Table 3. Phenotypic correlations.

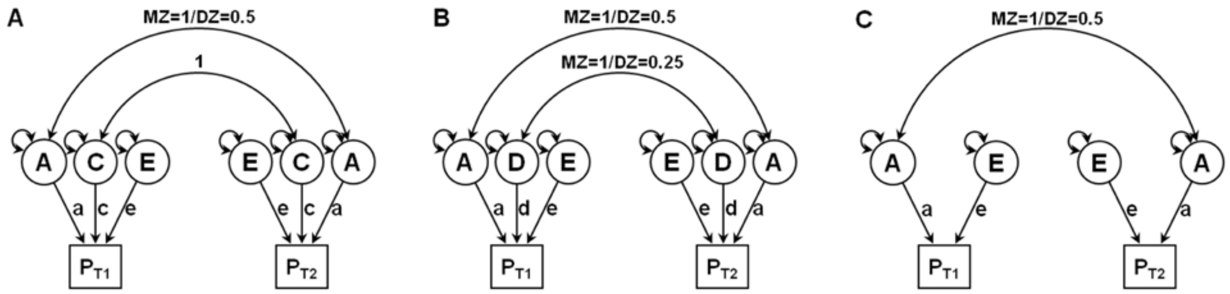
Brain area		0-back Accuracy	0-back RT	2-back Accuracy	2-back RT	FIQ	GM Volume	Gestational Age	Birth Weight	SEI
R Inferior Temporal Gyrus		0.05	−0.13*	0.18**	−0.03	0.05	0.04	−0.09	−0.08	−0.03
R Middle Temporal Gyrus		0.04	−0.06	0.15**	−0.04	0.07	−0.03	−0.04	−0.02	−0.03
R Lateral Orbitofrontal Gyrus		0.07	0.04	0.04	0.10	−0.07	−0.02	0.06	−0.01	−0.08
L Insular Cortex		0.04	0.02	−0.06	0.14*	−0.03	0.05	0.03	−0.05	0.06
R Inferior Frontal Gyrus		−0.06	0.13*	−0.09	0.04	−0.11*	−0.03	0.00	−0.05	−0.07
R Inferior Frontal Gyrus		0.00	0.02	0.04	−0.02	−0.06	0.07	0.01	0.03	0.06
R Caudate Nucleus		0.04	0.02	0.11*	0.05	0.06	0.03	−0.06	−0.14*	0.06
R Angular Gyrus		0.15**	−0.11	0.19***	−0.01	0.09	0.27***	0.01	−0.01	0.02
L Caudate Nucleus		0.11*	−0.07	0.12*	−0.04	0.07	0.06	0.00	0.01	0.05
R Middle Frontal Gyrus		0.04	−0.04	0.07	0.06	0.05	0.04	0.07	−0.03	0.01
L Inferior Frontal Gyrus		0.14*	−0.15**	0.00	0.01	0.02	0.05	0.05	−0.01	0.09
R Inferior Frontal Gyrus		0.18**	−0.17**	0.18**	−0.04	0.18**	0.2***	−0.05	0.01	0.13*
L Middle Occipital Gyrus		0.08	−0.20***	0.05	0.09	0.06	0.19***	−0.06	−0.01	−0.02
L Inferior Frontal Gyrus		0.11*	−0.10	0.00	0.08	0.04	0.01	0.06	−0.02	0.09
R Middle Occipital Gyrus		0.01	−0.12*	0.13*	0.07	0.08	0.26***	0.04	0.02	0.02
L Superior Parietal Gyrus		0.07	−0.26***	0.05	0.05	0.08	0.18**	0.02	−0.06	0.08
L SupraMarginal Gyrus		0.08	−0.19***	−0.01	−0.03	0.12*	0.16**	−0.02	−0.12*	−0.01
R Superior Frontal Gyrus		0.06	0.03	0.07	0.05	0.09	0.09	0.00	0.00	−0.09
R SupraMarginal Gyrus		0.12*	−0.16**	0.15**	0.06	0.07	0.13*	0.03	−0.06	0.06
R SupraMarginal Gyrus		0.13*	−0.11	0.10	−0.01	0.10	0.09	−0.02	−0.08	0.01
R Superior Parietal Gyrus		0.07	−0.16**	0.15**	0.03	0.09	0.19***	0.06	0.00	0.08
R Angular Gyrus		0.15**	−0.16**	0.20***	0.07	0.11	0.17**	−0.01	−0.12*	0.01
R Middle Frontal Gyrus		0.06	−0.07	0.15**	0.04	0.10	0.15**	0.05	0.07	−0.02
L Precuneus		0.21***	−0.20***	0.16**	0.11*	0.13*	0.29***	0.04	0.04	0.05
R Precuneus		0.25***	−0.25***	0.23***	0.04	0.15**	0.3***	0.00	0.08	0.02
L Middle Frontal Gyrus		0.14*	−0.15**	0.09	0.12*	0.12*	0.16**	−0.02	−0.02	−0.07
0-back	Accuracy (%)	1								
	RT (ms)	−0.50**	1							
2-back	Accuracy (%)	0.29**	−0.18**	1						
	RT (ms)	0.07	0.19**	−0.26**	1					
FIQ		0.24**	−0.35**	0.43**	−0.20**	1				
GM Volume		0.19***	−0.26***	0.20***	−0.003	0.37***	1			
Gestational Age (weeks)		0.01	0.04	0.06	0.03	−0.10	0.02	1		
Birth Weight (grams)		0.08	−0.01	0.04	−0.01	−0.08	0.15**	0.65**	1	
SEI		0.07	−0.04	0.08	−0.02	0.08	0.09	−0.01	0.04	1

Abbreviations: FIQ, Full-scale Intelligence Quotient; GM, gray matter; ms, milliseconds; L, Left Hemisphere; R, Right Hemisphere; RT, Reaction Time; SEI, Socio-Economic Index. Phenotypic correlations (Pearson, 2-tailed) for *t*-contrast difference 2>0-back at group random effects analysis local maxima, performance measures, FIQ, whole brain GM volume, birth information, and SEI. See Supplementary Table 1 for MNI coordinates. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

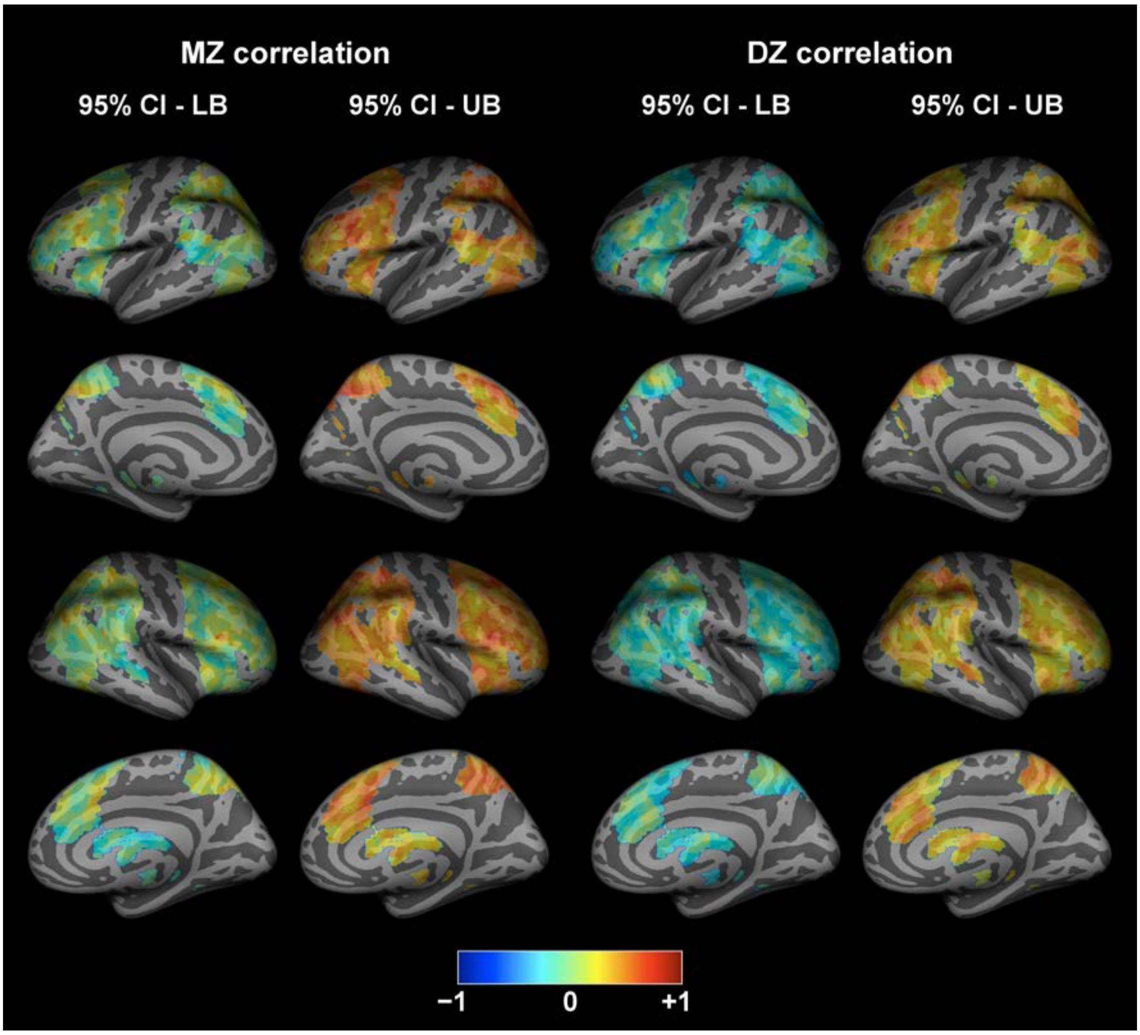
Supplementary Table 4. Covariate effects at group random effects analysis local maxima.

	Regression Coefficients							
Brain Area	**Sex**		**Age**		**2-back Accuracy**		**FIQ**	
	B	**β**	**B**	**β**	**B**	**β**	**B**	**β**
R Inferior Temporal Gyrus	0.0245	0.0412	0.0111	0.0698	0.0028**	0.1856**	−0.0004	−0.0184
R Middle Temporal Gyrus	−0.0281	−0.0449	−0.0008	−0.0047	0.0022	0.1377	0.0008	0.0305
R Lateral Orbitofrontal Gyrus	0.0744	0.083	0.0146	0.0611	0.0018	0.0792	−0.0039	−0.1072
L Insular Cortex	0.0912*	0.1038*	0.0004	0.0016	−0.0015	−0.067	−0.0005	−0.0134
R Inferior Frontal Gyrus	0.0316	0.0426	0.0137	0.0693	−0.0012	−0.0617	−0.0024	−0.0779
R Inferior Frontal Gyrus	0.1318*	0.1601*	−0.0068	−0.031	0.0011	0.0527	−0.0041*	−0.122*
R Caudate Nucleus	0.0332	0.0585	−0.0107	−0.071	0.0014	0.0979	−0.0003	−0.0124
R Angular Gyrus	0.1873***	0.2682***	−0.0089	−0.0477	0.0024	0.135	−0.0003	−0.01
L Caudate Nucleus	0.0333	0.0628	−0.0197	−0.139	0.0014	0.1017	−0.0001	−0.0041
R Middle Frontal Gyrus	0.1024	0.0989	0.0348*	0.1261*	0.0015	0.0583	0.0012	0.0279
L Inferior Frontal Gyrus	0.1331*	0.1519*	−0.0297*	−0.127*	−0.0001	−0.0048	−0.0009	−0.0241
R Inferior Frontal Gyrus	0.1929**	0.1674**	−0.0079	−0.0256	0.0035*	0.1178*	0.0042	0.0882
L Middle Occipital Gyrus	0.164**	0.1894**	−0.0161	−0.0696	0.0006	0.0277	0.0002	0.0058
L Inferior Frontal Gyrus	0.0017	0.0018	−0.0369*	−0.151*	−0.0006	−0.0243	0.001	0.0258
R Middle Occipital Gyrus	0.2544***	0.252***	−0.0341**	−0.1268**	0.0023	0.0872	−0.0008	−0.0202
L Superior Parietal Gyrus	0.2062**	0.2105**	−0.0175	−0.0671	−0.0004	−0.0144	0.0014	0.0342
L SupraMarginal Gyrus	0.1059	0.1164	−0.0285	−0.1173	−0.0015	−0.0662	0.0036	0.0956
R Superior Frontal Gyrus	0.0969	0.0968	0.0017	0.0064	0.0006	0.0241	0.0024	0.0586
R SupraMarginal Gyrus	0.1829**	0.1931**	−0.0166	−0.0656	0.0031	0.126	−0.0011	−0.0294
R SupraMarginal Gyrus	0.1014	0.106	−0.0175	−0.0685	0.0009	0.0369	0.0024	0.06
R Superior Parietal Gyrus	0.2543**	0.2304**	−0.0284	−0.0964	0.0032*	0.1139*	−0.0008	−0.0167
R Angular Gyrus	0.1788**	0.1605**	−0.014	−0.047	0.0046**	0.16**	0.0001	0.0016
R Middle Frontal Gyrus	0.1451	0.1365	−0.0267	−0.0941	0.0031	0.1126	0.0007	0.017
L Precuneus	0.4075***	0.3577***	−0.0206	−0.0679	0.0024	0.082	0.0011	0.0233
R Precuneus	0.4296***	0.3348***	−0.0363	−0.1061	0.006**	0.1826**	0.0013	0.0247
L Middle Frontal Gyrus	0.1689**	0.1758**	−0.0351*	−0.1369*	0.0006	0.0251	0.0029	0.0743

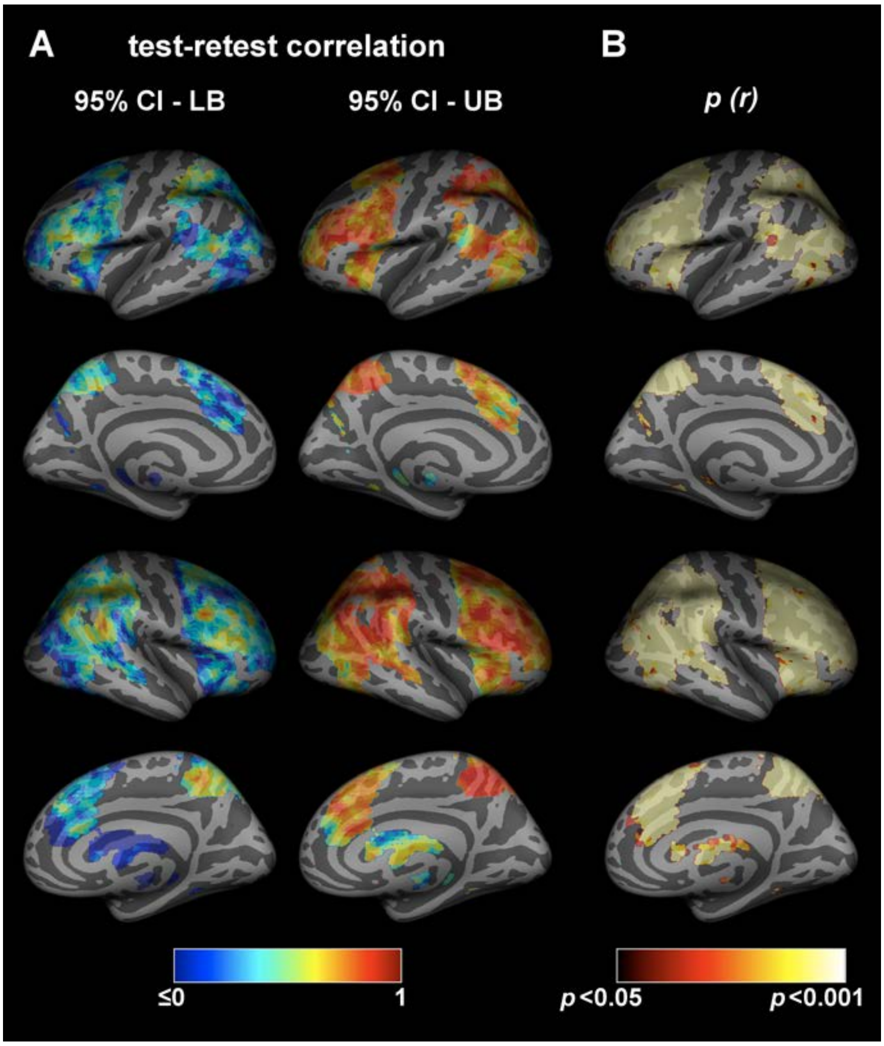
Unstandardized (B) and standardized (β) regression coefficients for the effects of the covariates sex, age, 2-back response accuracy, and FIQ on the *t*-contrast difference 2>0-back at group random effects analysis local maxima. See Supplementary Table 1 for MNI coordinates. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.



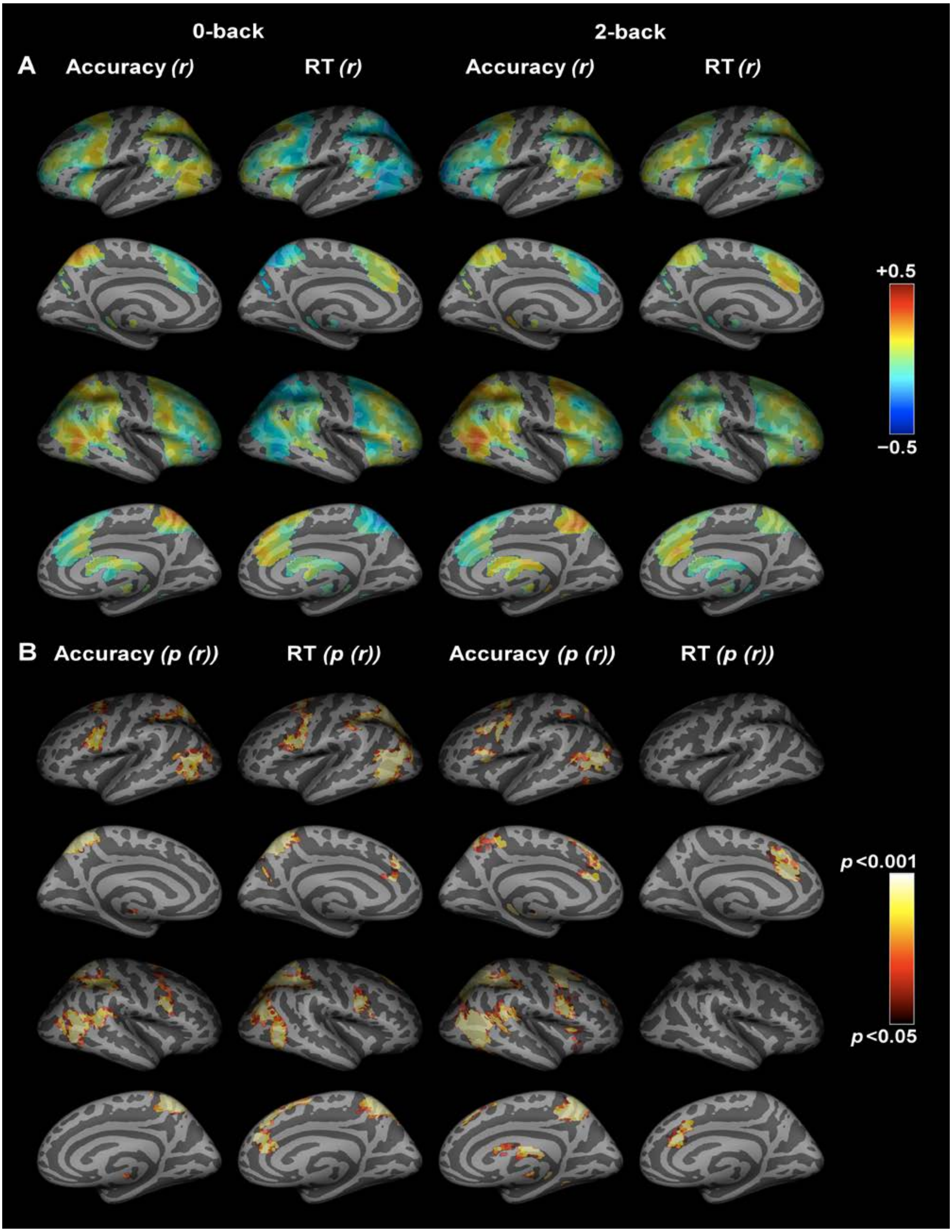
Supplementary Figure 1. Path diagrams depicting twin models. (***A***) ACE model, (***B***) ADE model, and (***C***) AE model, where P = phenotype; T1 = twin 1 of a pair; T2 = twin 2 of a pair; MZ = monozygotic; DZ = dizygotic; A = additive genetic influences; C = common environmental influences; D = dominance genetic influences; E = unique environmental influences; a = additive genetic partial regression coefficient; c = common environmental partial regression coefficient; d = dominance genetic partial regression coefficient; e = unique environmental partial regression coefficient. Circles represent latent, unobserved variables; squares represent observed phenotypes; single-headed arrows represent influences of latent on observed variables; double-headed arrows represent (co)variances. In the classical twin design (***A***), the observed variance in a trait is typically decomposed into three possible sources of variance—additive genetic (A), common or shared environmental (C), and unique or non-shared environmental (E) components, which include measurement error, differentiated by the relationships between factors for co-twins (Neale and Maes, 2004). However, variance due to genetic dominance (D) may also be estimated (***B***), but with MZ and DZ twins reared together it is not possible to determine the effects of both C and D in the same model; although one or the other source can be assumed absent depending on whether the DZ twin correlation is greater (d = 0) or less (c = 0) than half the MZ correlation. Correlations between additive genetic factors are fixed at 1 for MZ twin pairs, as they share 100% of their genes, and 0.5 for DZ pairs as they share, on average, 50% of their genes. In the classical twin model (ACE model), for common environmental factors (e.g., socioeconomic status or parental rearing style) correlations between co-twins are fixed at 1 for both MZ and DZ pairs, based on the rigorous and frequent testing that has supported the assumption that environments for MZ and DZ twins are comparable. On the other hand, in the genetic dominance model (ADE model), correlations between dominance genetic factors are fixed at 1 for MZ pairs, but fixed at 0.25 for DZ pairs. By definition, in all models non-shared environmental factors (e.g., illness, prenatal or postnatal traumas, peer groups) are left uncorrelated.



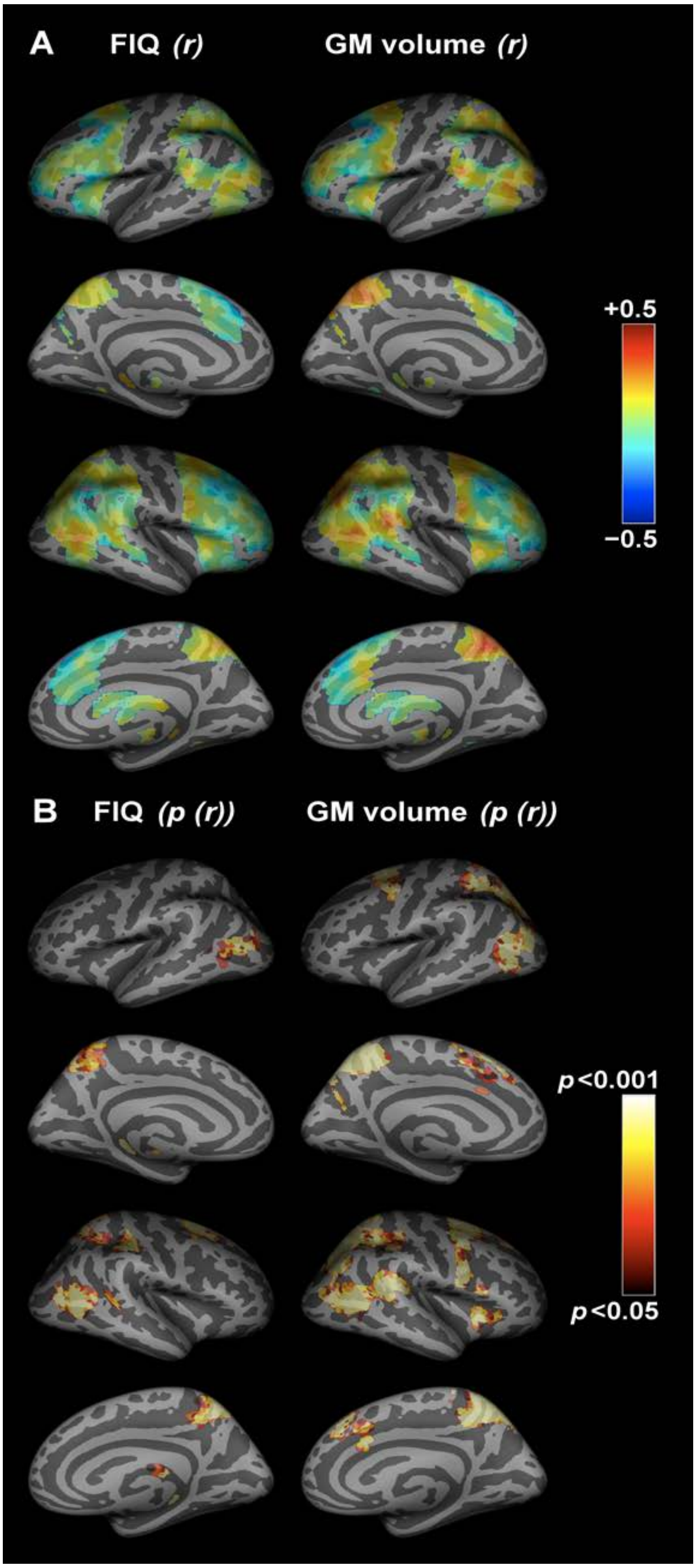
Supplementary Figure 2. Confidence intervals for the twin correlations. 95% confidence intervals for the MZ and DZ maximum likelihood twin correlations. Abbreviations: CI, Confidence Interval; LB, Lower Bound; UB; Upper Bound.



Supplementary Figure 3. Confidence intervals and significance for the test-retest correlations. (***A***) 95% confidence intervals and (***B***) height- and cluster-thresholded *p*-value maps for the test-retest intra-class correlations. Abbreviations: CI, Confidence Interval; LB, Lower Bound; UB; Upper Bound.



Supplementary Figure 4. Phenotypic correlations for task performance with task-related brain activation. (***A***) Phenotypic correlations for task performance measures 0-back response accuracy, 0-back RT, 2-back response accuracy, and 2-back RT, with task-related brain activation, and (***B***) corresponding height- and cluster-thresholded *p*-value maps. Abbreviations: RT, Reaction Time.



Supplementary Figure 5. Phenotypic correlations for task performance with Full-Scale IQ and gray matter volume. (***A***) Phenotypic correlations for FIQ and GM volume, with task-related brain activation, and (***B***) corresponding height- and cluster-thresholded *p*-value maps. Abbreviations: FIQ, Full-Scale IQ; GM, gray matter.

Supplementary References

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