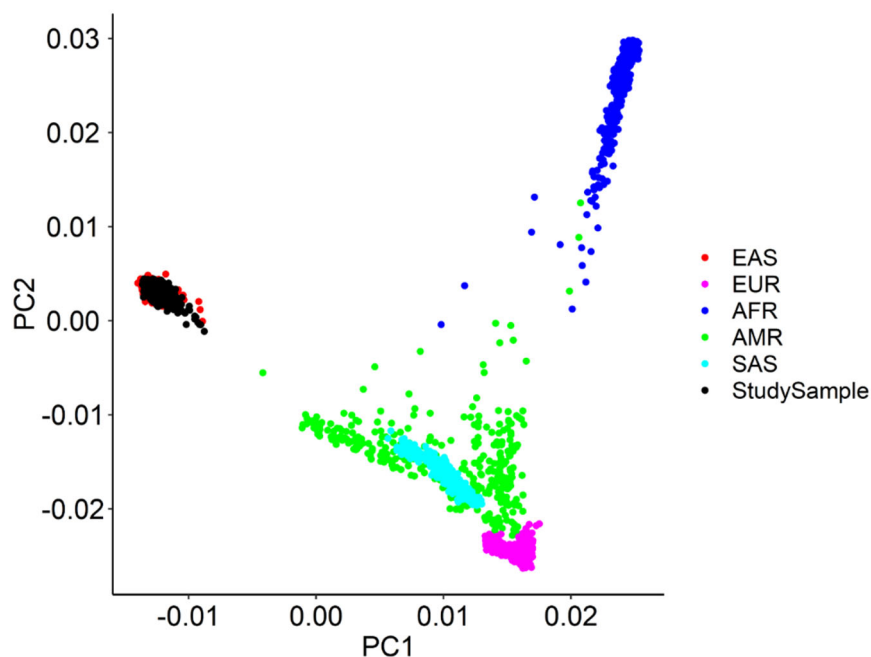


30 voltage-gated cation channel activity ($p = 2.26 \times 10^{-19}$), cation channel activity ($p = 4.44 \times$
31 10^{-19}), channel activity ($p = 8.09 \times 10^{-19}$). In terms of **GO biological process**, these
32 genes showed overrepresentation in synaptic signaling ($p = 2.70 \times 10^{-53}$), anterograde
33 trans-synaptic signaling ($p = 2.70 \times 10^{-53}$), chemical synaptic transmission ($p = 2.70 \times 10^{-$
34 53), trans-synaptic signaling ($p = 9.04 \times 10^{-53}$) and cell-cell signaling ($p = 3.62 \times 10^{-41}$). In
35 terms of **GO cellular component**, the MFG-related genes are mainly enriched for
36 synapse ($p = 8.54 \times 10^{-52}$), neuron projection ($p = 3.49 \times 10^{-40}$), glutamatergic synapse (p
37 $= 9.86 \times 10^{-35}$), synaptic membrane ($p = 1.67 \times 10^{-34}$), and somatodendritic compartment
38 ($p = 1.21 \times 10^{-33}$). For **mouse phenotype**, these genes were enriched for abnormal
39 synaptic transmission ($p = 1.60 \times 10^{-18}$), abnormal CNS synaptic transmission ($p = 1.59 \times$
40 10^{-16}), abnormal nervous system physiology ($p = 1.81 \times 10^{-16}$), abnormal
41 learning/memory/conditioning ($p = 7.39 \times 10^{-16}$), abnormal cognition ($p = 7.39 \times 10^{-16}$). In
42 annotation of **pathway**, these genes showed enrichment in neuroactive ligand-receptor
43 interaction ($p = 6.49 \times 10^{-14}$), calcium signaling pathway ($p = 1.05 \times 10^{-12}$), monoamine
44 GPCRs ($p = 1.78 \times 10^{-8}$), Heterotrimeric G-protein signaling pathway-Gi alpha and Gs
45 alpha mediated pathway ($p = 1.47 \times 10^{-7}$), and axon guidance ($p = 3.06 \times 10^{-7}$). For
46 **disease**, these genes are enriched in schizophrenia ($p = 1.18 \times 10^{-26}$), chronic alcoholic
47 intoxication ($p = 1.43 \times 10^{-15}$), bipolar disorder ($p = 1.43 \times 10^{-15}$), autistic disorders ($p =$
48 1.80×10^{-13}), mental disorders ($p = 3.04 \times 10^{-13}$).

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50 **SCG-related genes** also showed significant enrichment (see Supplementary Data). For
51 **GO molecular functions**: signaling receptor binding ($p = 1.97 \times 10^{-9}$, FDR-BH corrected,
52 hereafter), channel activity ($p = 2.36 \times 10^{-7}$), passive transmembrane transporter activity
53 ($p = 2.36 \times 10^{-7}$), metal ion transmembrane transporter activity ($p = 6.32 \times 10^{-7}$),
54 potassium channel activity ($p = 6.32 \times 10^{-7}$). For **GO biological process**: synaptic
55 signaling ($p = 3.85 \times 10^{-28}$), trans-synaptic signaling ($p = 1.09 \times 10^{-27}$), cell-cell signaling
56 ($p = 1.67 \times 10^{-27}$), anterograde trans-synaptic signaling ($p = 2.24 \times 10^{-27}$), and chemical
57 synaptic transmission ($p = 2.24 \times 10^{-27}$). For **GO cellular component**: synapse ($p = 7.85$
58 $\times 10^{-35}$), neuron projection ($p = 1.90 \times 10^{-31}$), somatodendritic compartment ($p = 2.28 \times$

59 10^{-25}), synaptic membrane ($p = 4.12 \times 10^{-20}$), and dendritic tree ($p = 4.12 \times 10^{-20}$). For
60 **mouse phenotype**: abnormal nervous system physiology ($p = 1.30 \times 10^{-13}$), abnormal
61 CNS synaptic transmission ($p = 1.79 \times 10^{-10}$), abnormal synaptic transmission ($p = 4.67 \times$
62 10^{-10}), abnormal learning/memory/conditioning ($p = 3.39 \times 10^{-9}$), abnormal cognition ($p =$
63 3.39×10^{-9}). For **pathway**: neuroactive ligand-receptor interaction ($p = 1.44 \times 10^{-5}$), spinal
64 cord injury ($p = 3.58 \times 10^{-5}$), ensemble of genes encoding core extracellular matrix
65 including ECM glycoproteins, collagens and proteoglycans ($p = 5.96 \times 10^{-5}$), Myometrial
66 relaxation and contraction pathways ($p = 3.43 \times 10^{-4}$), and calcium regulation in the
67 cardiac cell ($p = 4.47 \times 10^{-4}$). For **disease**: anxiety ($p = 7.79 \times 10^{-13}$), anxiety disorders (p
68 $= 1.30 \times 10^{-12}$), schizophrenia ($p = 8.48 \times 10^{-11}$), mental disorders ($p = 1.61 \times 10^{-9}$),
69 bipolar disorder ($p = 1.61 \times 10^{-9}$).



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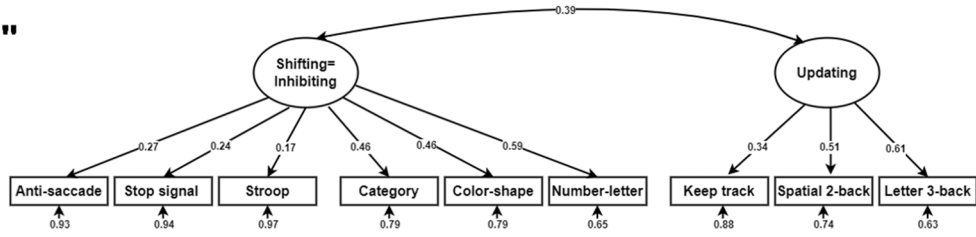
71 **Supplementary Fig. 1. Principal component analysis (PCA) of 2110 subjects.**

72 The PCA is based on ~3 million common SNPs on 1000Genome phase3 data. EAS: East
73 Asian, EUR: European, AFR: African, AMR: Ad Mixed American, SAS: South Asian,
74 StudySample: 2110 subjects used in the current study. Source data are provided as a
75 Source Data file.

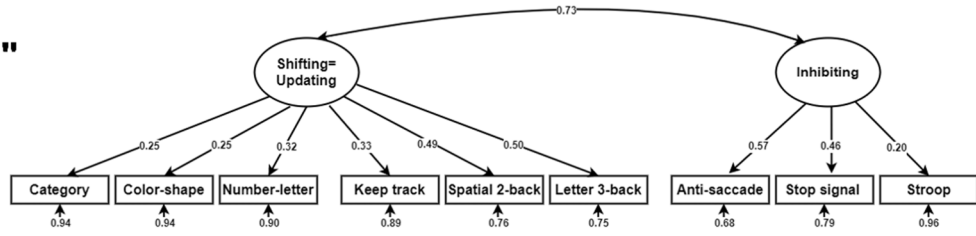
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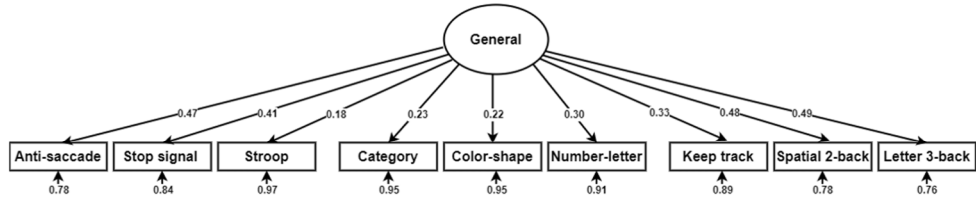
"S/I+U"



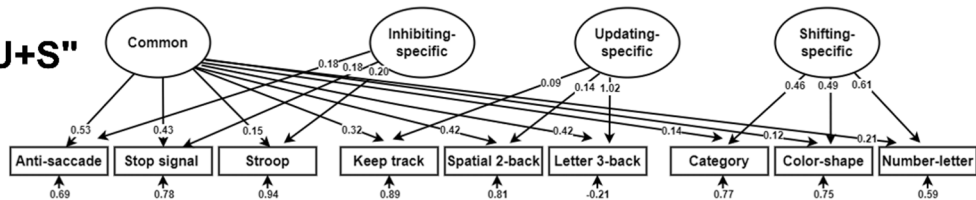
"S/U+I"



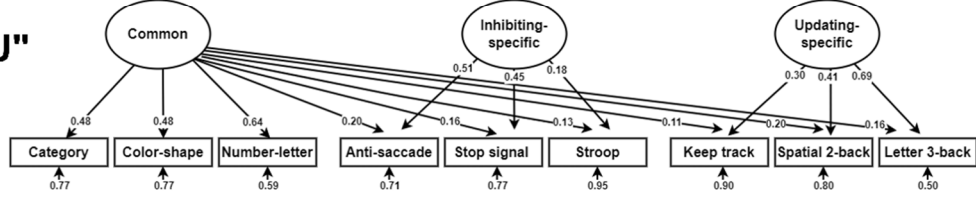
"G"



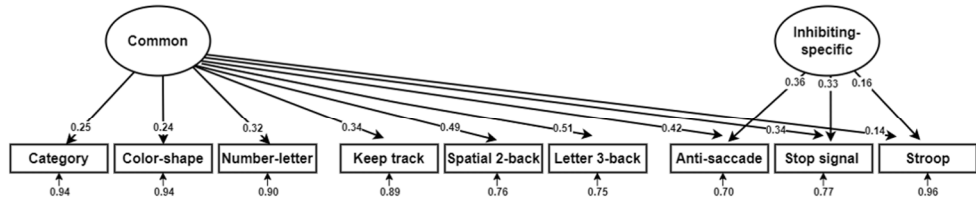
"C+I+U+S"



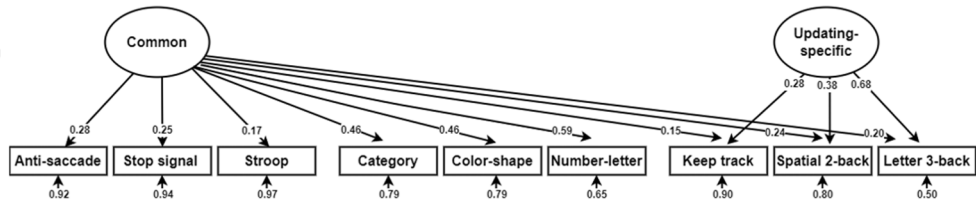
"C+I+U"



"C+I"



"C+U"

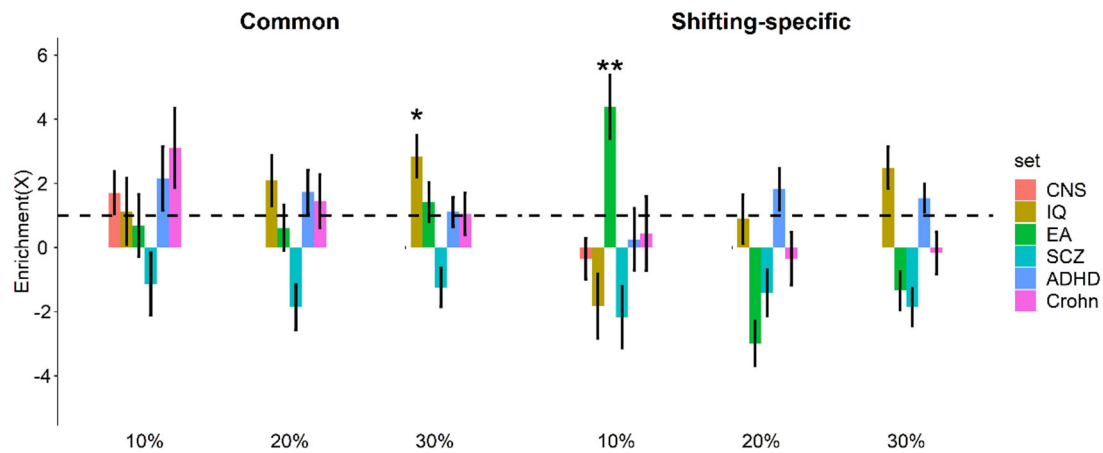


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79 **Supplementary Fig. 2. Latent variable models of EFs (seven other models).** See
 80 Table 1 for fit statistics for these models. Source data are provided as a Source Data file.

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84 **Supplementary Fig. 3. Enrichment heritability pattern of the candidate gene sets**
 85 **for the common EF and shifting-specific components (n = 1454 subjects).** The null
 86 hypothesis of 1.0 enrichment is shown by a dashed dark horizontal line. The *p* values
 87 indicate the significance of the difference from the expectation. Error bars represent the
 88 SE of enrichment folds (= SE(set) / %SNP). Significant results after FDR-BH correction
 89 are marked with asterisks (** represents *p* values < .01, * represents *p* values < .05,
 90 exact *p* values are provided in Source Data file, one-sided test). We selected the top 10%
 91 SNPs of the ranked genome data as trait-associated variants. CNS: genes preferentially
 92 expressed in the central nervous system; IQ: SNPs associated with human intelligence;
 93 EA: SNPs associated with educational attainment; SCZ: schizophrenia-associated SNPs;
 94 ADHD: ADHD-associated SNPs; Crohn: SNPs associated with Crohn's disease. Please
 95 note that the heritability (h^2) is per definition non-negative. However, in some cases,
 96 negative values can be obtained from unbiased estimators. As discussed in Yang et al.⁸
 97 and Elhezzani⁹, a negative estimate could be due to a close-to-zero true value or
 98 substantial uncertainty in estimation. For this reason, negative enrichment was thus not
 99 considered further. Source data are provided as a Source Data file.

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Supplementary Table 1. Descriptive statistics for the nine EF measures

	N	Mean	SD	Min	Max	Skew	Kurtosis	IC
Anti-saccade(d')	2015	.25	.13	.00	.58	.33	-.59	.90
Stop-signal (ms)	1862	215.18	40.89	110.33	320.01	.10	.01	.55 ^a
Stroop (ms)	1990	138.67	82.36	-77.75	347.31	.40	.07	.33
Category (ms)	2042	295.22	138.70	-89.64	667.51	.31	-.08	.51
Color-shape (ms)	1965	326.28	196.78	-181.69	818.83	.57	.10	.70
Number-letter (ms)	1901	300.98	172.15	-153.35	729.32	.62	.04	.79
Keep track (nc)	1980	30.70	3.11	23.00	36.00	-.52	-.27	.67 ^b
Spatial 2-back (d')	1940	2.80	.93	.20	4.65	-.11	-.32	.76
Letter 3-back (d')	1957	1.98	.89	-.07	4.40	.74	-.03	.81

106 SD = standard deviation; Min = minimum; ax = maximum. IC= internal consistency. d' =

107 dprime; ms = millisecond; nc = number of corrected trials.

108 Unless otherwise noted, IC was calculated by adjusting split-half (odd–even) correlations
109 with the Spearman-Brown prophecy formula.110 ^a For the stop-signal task, we used four stair-cases with different starting values, which
111 were randomly mixed together. We therefore calculated the SSRT for the last two blocks.112 The split-half correlation was calculated based on 391 subjects who had at least one
113 inflection point for one of the four stair cases in both blocks were used.114 ^b IC was calculated using Cronbach's alpha across 4 sets of trials at each difficulty level
115 for keep track.

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Supplementary Table 2. Pearson Correlation of the nine EF measures

	1	2	3	4	5	6	7	8	9
1.Anti-saccade	—								
2.Stop-signal	.26***	—							
3.Stroop	.11***	.10***	—						
4.Category	.09***	.06*	.06**	—					
5.Color-shape	.03	.05*	.05*	.24***	—				
6.Number-letter	.10***	.08**	.08***	.31***	.32***	—			
7.Keep track	.16***	.16***	.01	.01	.04	.07**	—		
8.Spatial 2-back	.22***	.16***	.07**	.07**	.06**	.10***	.14***	—	
9.Letter 3-back	.22***	.18***	.05*	.04	.07**	.07**	.22***	.31***	—

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The significant results after FDR-BH correction are noted with asterisks (***) represents p

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values < .001, * represents p values < .05, exact p values are provided in Source Data

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file, two-sided test). Source data are provided as a Source Data file.

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125 **Supplementary Table 3. Model fit statistics of the 12 EF latent variable models (list-**
 126 **wise deletion)**

Model	χ^2	df	CFI	RMSEA	SRMR
Correlated-factors models					
1. I+U+S	44.73	24	.98	.02	.02
2. S/I+U	270.89	26	.73	.08	.07
3. U/I+S	84.44	26	.93	.04	.03
4. S/U+I	347.16	26	.64	.09	.07
5. G	380.25	27	.60	.10	.07
Bifactor models					
6. C+I+U+S	28.91	18	.99	.02	.02
7. C+I+S	46.50	21	.97	.03	.03
8. C+I+U	158.44	21	.85	.07	.06
9. C+U+S	29.44	21	.99	.02	.02
10. C+I	346.93	24	.64	.10	.07
11. C+S	82.45	24	.93	.04	.03
12. C+U	259.38	24	.74	.08	.07

127 The good-fit models are indicated in bold. It is worth noting that although the fit indices of
 128 the bifactor three-factor (C+I+U+S) model were good (CFI= .99, RMSEA = .02,
 129 SRMR= .02), the three tasks' loadings on inhibiting-specific component (anti-saccade: p
 130 = .55, stop-signal: p = .39, Stroop: p = .43) and updating-specific component (keep track:
 131 p = .20, spatial 2-back: p = .20, letter 3-back: p = .10) were not significant.

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Supplementary Table 4. CPM prediction results using two other thresholds

Model	component	$p = .01$		$p = .1$	
		r	$p_{(FDR-BH)}$	r	$p_{(FDR-BH)}$
I+U+S	I	.15	6.5e-4	.18	2.17e-4
	U	.15	5.2e-4	.19	2.17e-4
	S	.07	.10	.06	.09
U/I+S	U/I	.16	4.3e-4	.19	2.17e-4
	S	.07	.10	.06	.09
C+I+S	C	.16	4.3e-4	.19	2.17e-4
	I	.06	.11	.06	.09
	S	.10	.03	.08	.06
C+U+S	C	.16	5.2e-4	.19	2.17e-4
	U	-.01	.57	.07	.19
	S	.09	.04	.08	.06
C+S	C	.16	4.3e-4	.19	2.17e-4
	S	.10	.03	.08	.06

135 I = inhibiting or inhibiting-specific; U=updating or updating-specific; S = shifting or shifting-
 136 specific; U/I = (updating = inhibiting); C = common. Correction for multiple comparisons
 137 was performed with the FDR-BH; one-sided permutation test.

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144 **Supplementary Table 5. The specific brain regions for Common and Shifting-**
 145 **specific components from the CPM results**

Cluster	MNI			N
	X	Y	Z	
Common component				
precentral gyrus	44	-8	57	30
inferior temporal gyrus	-56	-45	-24	29
frontal pole	8	41	-24	27
LOC	-39	-75	44	19
LOC	-41	-75	26	16
frontal pole	6	64	22	16
inferior temporal gyrus	55	-31	-17	15
MFG	48	25	27	15
frontal pole	-39	51	17	15
middle temporal gyrus	56	-46	11	15
Shifting-specific component				
LOC	37	-65	40	20
paracingulate gyrus	6	54	16	19
planum temporale	58	-16	7	16
paracingulate/SMC	7	8	51	15
planum temporale	32	-26	13	14
frontal orbital cortex	27	16	-17	14
LOC	37	-81	1	14
postcentral gyrus	42	-20	55	11
precentral gyrus	2	-28	60	11
central opercular cortex	-55	-9	12	11

146 SMC = supplementary motor cortex, MFG = middle frontal gyrus, LOC= lateral occipital
 147 cortex. N = the number of contributing edges each node had.

148 **Supplementary Table 6. The brain regions for Common and Shifting-specific**
 149 **components from the conjunction of CPM and Neurosynth results**

Components	Neurosynth Cluster	No. of Voxels	COG			Node Atlas
			X	Y	Z	
Common	MFG	50	48	25	27	MFG (86 voxels, MNI= 48,25,27)
Shifting- specific	paracingulate/ SMC	45	6	9	51	Paracingulate (54 voxels,MNI=7,8,51)
	LOC	27	34	-64	40	LOC (72 voxels, MNI=37, -65,40)

150 SMC = supplementary motor cortex, MFG = middle frontal gyrus, LOC= lateral occipital
 151 cortex, COG = center of gravity.

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168 **Supplementary Table 7. Enrichment patterns of the Allen brain expression**

169 **candidate gene sets (using other gene boundaries)**

Components	Gene sets	Gene boundary	<i>P</i> (95%)	<i>P</i> (75%)	EXP#genes (75%)	OBS#genes (75%)	<i>P</i> _(FDR-BH) (75%)	
Common	MFG	25kb	.17	3.0e-4	244	287	3.6e-3	
		50kb	.15	9.4e-3	239	266	5.6e-2	
	SCG	25kb	.38	.10	241	257	.14	
		50kb	.33	.09	237	252	.22	
	LOC	25kb	.37	.09	245	262	.14	
		50kb	.31	.46	240	239	.50	
	BG	25kb	.69	.12	242	256	.14	
		50kb	.11	.09	238	253	.22	
	Updating-specific	MFG	25kb	.14	.08	243	261	.14
			50kb	.57	.16	241	252	.27
SCG		25kb	.16	.11	242	257	.14	
		50kb	.60	.25	238	245	.38	
LOC		25kb	.14	.14	243	256	.15	
		50kb	.74	.11	240	254	.22	
BG		25kb	.04	.43	242	244	.43	
		50kb	.82	.68	239	232	.68	
Shifting-specific		MFG	25kb	.29	.04	145	162	.14
			50kb	.32	.05	143	158	.20
	SCG	25kb	.17	.02	139	161	.12	
		50kb	.64	6.8e-3	138	161	5.6e-2	
	LOC	25kb	.30	.09	150	163	.14	
		50kb	.49	.33	148	152	.44	
	BG	25kb	.96	.12	139	151	.14	
		50kb	.89	.39	138	140	.47	

170 See Table 3 for definition of acronyms. Correction for multiple comparisons was

171 performed with the FDR-BH. One-sided permutation test.

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Supplementary Table 8. High dimensional mediation analyses results

Components	Gene boundary	VIE	VDE	PVM	$p_{\text{permutation}}$	$p_{\text{(FDR-BH)}}$
Common	25kb	.023	.093	.201	4.4e-3	9.4e-3
	35kb	.027	.114	.190	4.7e-3	9.4e-3
	50kb	.034	.142	.193	4.2e-3	9.4e-3
Shifting-specific	25kb	.016	-.096	-.203	.995	.996
	35kb	.016	-.104	-.176	.996	.996
	50kb	.019	-.106	-.220	.996	.996

173 Exposure: genotype of MFG-related genes or SCG-related genes; Mediator: selected
 174 edges in CPM for EF components; Outcome: EF components. VIE = variance indirect
 175 effect, VDE = variance direct effect, PVM = proportion of the variance mediated.
 176 Correction for multiple comparisons was performed with the FDR-BH. One-sided
 177 permutation test.

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