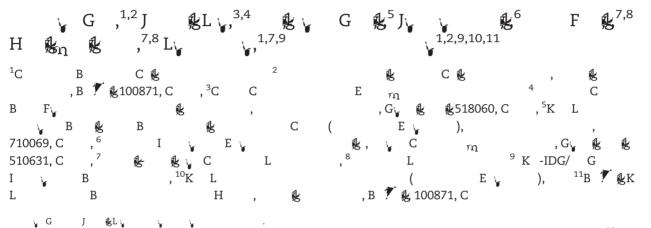
Social Cognitive and Affective Neuroscience, 2017, 1534 1544

doi: 10.1093/scan/nsx062 A A ↓ D : 19 A 2017 ≰

Identifying new susceptibility genes on dopaminergic and serotonergic pathways for the framing effect in decision-making



Abstract 影 m i m m m (SLC6A4) (COMT) 1 m m m 彤 m m 彤 m m 彤 m m m 化 化 C 26 🏨 1317 C Η m m 彤 SLC6A4 🕵 COMT 🎎 -L- m 彤 m m m m (DDC) m 4 彤 彤 1 ŝ, ١. m m & DDC; COMT; SLC6A4; G A Key words: m 弘 m

Received: 1 A 2016; Revised: 18 J 2017; Accepted: 17 A 2017

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Introduction

D 1 £. m m) ١. m 彤 (. . m), m ' (, 1981; K Κ 1 m m m , 1984; K et al., 1999). (K m 1979; , 1997), m 贴 et al., 1982; D 🍟 👖 , 2004). V 、影 \r m 1 m m 彤 m m m ١. m m (H et al., 2004; D et al., 2008). m m m ¥ 1 m m (🔒 m 🕏) m 影 m m et al., 2009; 🖕 et al., 2013; G (D et al., 2006; et al.. 2016). m , D_m , 2008), (D 🍟 👘 贴 m ' 1 ¥ , 2011). 兆(🔓 С m ٧. 彤 m m 1 (K V m 1979; , 1997; D et al., 2006; et al.. 2009; G et al., 2016), m (m , 2011; C et al., 2012; C 彤 Ł 彤 1 . A m 弘 m m 账 影 m et al., 2009; Ki , 2009; (C et al., 2009; D C et al., 2012; H et al., 2010; F _{rn} et al., 2011; H V et al., 2014), et al., 2013; 贴 1 Ł m (C et al., 2009, = 36;1 m 4 et al., 2009, = 30) 5-H L 影 m m 1 m (SLC6A4), 龜 I m 5-H L () m m 4 m m (= 98) 影 **₽**() m COMT COMT _ 158 彤 影 m m 4 & C m / 4 m m 彤 影 m m , m (G et al., 2016). H ,账 m m 6 (2009; ≰ et al., 2010), m m m € H m

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m et al., 2010: 影. 1, 2010; (-L et al., 2010; G et al., 2014). F m COMT 🎎 Ł Ł

m m (& m &) m et al., 2003; G et al., 2006; K -K 🐇 et al., 1998; E et al., 2003; et al., 2004; m et al., 2005; D m et al., et al., 2007; et al., 2007; **∦**et al., 2008;

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, 2006). n 2010; Η ,張 m 🐁 (MAOA m m MAOB) 彤 m (D 🙀 et al., 2009) m m sm (K **∦**et al., 2007; et al., 2009).

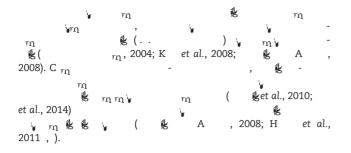
₩. G Ł m -L 1, 2010; Ł (m, 2011; F et al., 2013; et al., 2010; B G 6 , 2014). J L m 5-H L 8 V (/), () 彤 m 🕏 Ł m m (H et al., 2002; C et al., 2005; H et al., 2005) 彤 _ (et al., 2014); 1 4 (B et al., 1998; L G , 2004; L - 🔓 et al., 2005; 2010), 北北 影 m m 5-H L 5-H L 彤 LE et al., 2009). (١. m -L- m 彤 m

(DDC), 彤 (C et al., 2010) (B \$ m et al., 2003). С

m m 彤 m 兆 I m m , 2008; (C А et al., 2011 ,) ₿et al., Н (2007; **∦**et al., 2010) (G A) 影 m 彤 NB. ٧. , 26 🏂 m m 影 m m А m m KEGG 1 £€/), (:// .<u>R</u> m m 1 m et al., 2011; (兆 m

et al., 2014; B 💡 et al., 2016). G 4 () 彤 G А m m ١ m (LD) 影 m m , 2008) 彤 m et al., 2010). С 彤 V mm 1 貼 4 m-

(C) m 🖌 m m m m, 2004; А , 2008). (



Materials and methods

Participants

(G 2013) 影 m m С С 彤 影 . . Y m m m 1 С (80.1% Η 1 m , m 18.66 ± 0.90) 15 100 . A V, m m 彤 m m m , m m À 1 m m m 彤 影 R m 悲悲 behav-(1582 ioral test; D et al., 2006; G et al., 2016). I , 5 彤 Ņ ¥ . N, m 1317 А m 彤 彤 1 m V m). A m m 彤 (. <50, = 30.58, m m m D = 5.35) ₿ A 1 Υ. (🍾 🏂 1971; **张**et al., 1999) 彤 m <50, _m = 33.3, D=6.31) (. m m 🏂 1965; € D (🍾 彤 V. & et al., 1999), 贴 (51, 51, 53, 53, 53, 54, 54, 55 59,) 彤 m m m 彤 (51, 51 56,) 彤 G m m . m ١ 12 彤 V V 彤 m m m 4 D Η m Е C mm 彤 C 🏚 彤

The behavioral test

¥	m	G et al. (2016),
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彤 (. .) V m ١ m, 12 m). (. m m m m m)(.4 K 20 (. m 50') m m m 4 (. m)(.&L 30 50'), ₿m m 彤 . F 1 m m m ١, . F 18 m m (.<u>R</u> Κ 80 100'vs K 100 40%'). V m ٧ <u>影</u> 影 m . E 48 (16 彤 , 16 16), 1 m m D et al. (2006). m 彤 m m 彤 LB. m . A m m m (500:1) m m G et al. (2016) m m Y m (<75%, m ١. 1317 =57.9%±17.6%; $=90.5\%\pm6.5\%$) ٧. (4.44%±1.75%) 影 m m m m 1317 🔒 (14.51% \pm 0.34%), $t_{(1580)} =$ 9.16, P < 0.001. m F 彤 m m m m (彤 m 🍾 m) 彤 $= 1591_{rm}$, $D = 551_{rm}$) m m $= 1601_{rn}$, $D = 544_{rn}$) rnm m $= 1776_{rn}$, $D = 353_{rn}$; r_n fn

Genotyping

t₍₁₅₈₀₎ = 9.375, P < 0.001

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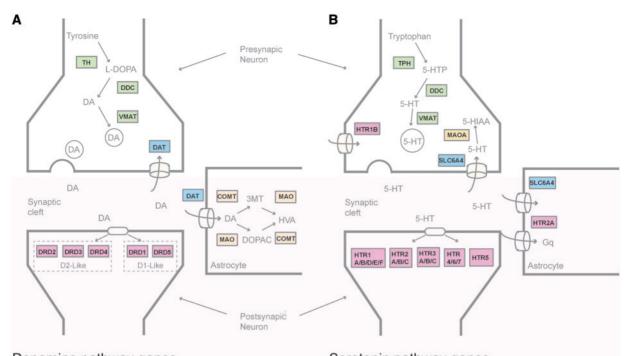
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Gene selection and preprocessing

 $=\!1872_{\tau \eta}$, $D\!=\!376_{\tau \eta}$), $t_{(1580)}\!=\!6.639,\,P\!<\!0.001$

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		(DRD1–5),	()	m			
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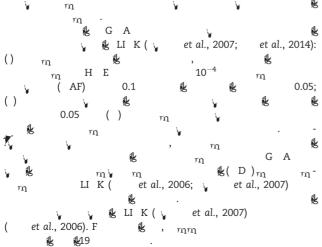
 Dopamine pathway genes
 Serotonin pathway genes

 Fig. 1. D
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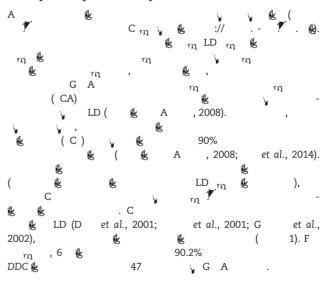
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(COMT), m SLC6A3), -0-₇₁ A (MAOA) B (MAOB) (m et al., 2011; et al., 2014) m () (TPH 1 TPH2),() 1 5-(HTR1A/B/D/E/F, HTR2A/B/C, m HTR3A/B/C/D/E, HTR4, HTR5A/B, HTR6-7, HTRA1-4), () m 🖕 et al., 2016) (F 🎉 (SLC6A4) (В 1). HTR3D HTR3E 🕵 4 m et al., 2003; (

B≰ : G E E , :// ≰ .. . /). DRD4, DRD5, HTR1A/B/D/F, HTR5B, HTRA2 HTRA4



Principle component analysis

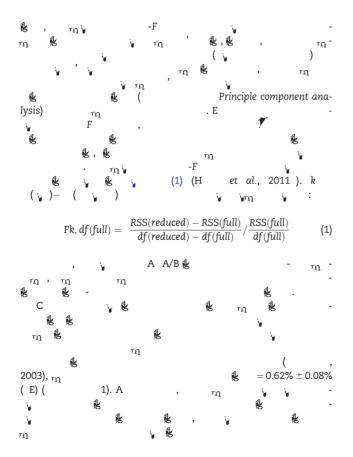


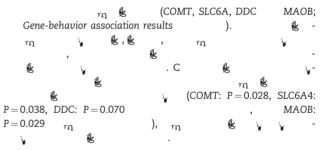
Gene-behavior association analysis



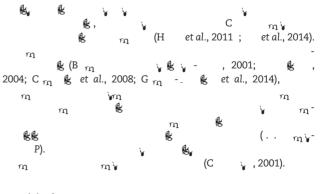
Tabl	e 1. 🍟	າກາກ	m		ĸ		ĸ									
		F		G		С	%_	R ²	彤	А 🏌	R ²	彤	Partial-F	p _{unc}	p_{perm}	p_{emp}
D m	ກ			TH	2	2	100	0.00)1		<0.001		0.712	0.491	0.484	0.485
				DDC	47	6	90	0.01	.0		0.006		2.329	0.031*	0.031*	0.038
				VMAT2	17	9	90	0.00)3		<0.001		0.501	0.875	0.878	0.862
			/	DAT1	16	6	91	0.00)5		<0.001		1.027	0.406	0.408	0.466
		С		COMT	18	6	91	0.01	.2		0.009		2.648	0.015*	0.014*	0.027
				MAOA	6	3	90	0.00)3		<0.001		1.143	0.331	0.325	0.346
				MAOB	37	5	92	0.00)5		0.002		1.367	0.234	0.232	0.293
				DRD1	1	1	100	0.00	00		< 0.001		0.097	0.756	0.756	0.780
				DRD2	16	8	90	0.00)4		<0.001		0.721	0.673	0.680	0.770
				DRD3	41	12	92	0.01	.4		0.006		1.617	0.081	0.081	0.099
				TPH1	2	2	100	0.00)1		< 0.001		0.719	0.487	0.476	0.472
				TPH2	6	4	93	0.00)2		<0.001		0.519	0.721	0.718	0.753
				SLC6A4	8	3	90	0.00)6		0.004		2.795	0.039*	0.038*	0.032
				HTR1E	16	6	91	0.00)7		0.003		1.545	0.160	0.158	0.199
				HTR2A	44	12	90	0.01	.3		0.005		1.492	0.120	0.121	0.123
				HTR2B	3	2	100	0.00)1		< 0.001		0.596	0.551	0.551	0.519
				HTR2C	22	8	90	0.00)6		< 0.001		0.920	0.499	0.499	0.51
				HTR3A	4	4	100	0.00)1		<0.001		0.364	0.834	0.831	0.833
				HTR3B	22	6	90	0.00)1		< 0.001		0.228	0.968	0.967	0.970
				HTR3C	2	1	99	0.00	00		< 0.001		0.124	0.725	0.724	0.672
				HTR4	46	14	91	0.01	.5		0.005		1.422	0.135	0.136	0.07
				HTR5A	7	4	92	0.00)6		0.003		1.866	0.114	0.114	0.118
				HTR6	2	1	100	0.00	00		< 0.001		0.000	0.990	0.992	0.982
				HTR7	22	6	93	0.00)6		0.002		1.316	0.247	0.242	0.303
				HTRA1	34	9	91	0.00)7		<0.001		0.974	0.460	0.456	0.442
				HTRA3	19	5	92	0.00)4		0.001		1.133	0.341	0.356	0.370

С, m ;%_ C ; p_{unc}, P Brni F-; p_{perm}, mb Р ү; m Р р_{етр}, _{тп} Р * Р<0.05. \mathbf{V} -



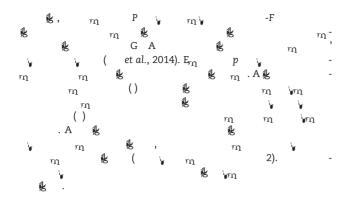


Permutation tests

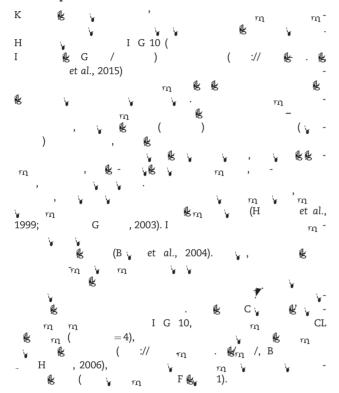


Empirical tests

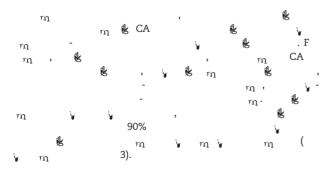
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Protein-protein interactions



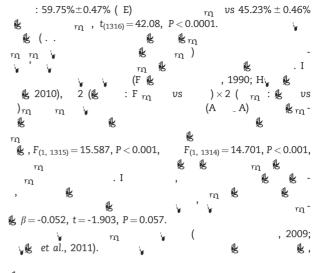
SNP-SNP interactions



Results

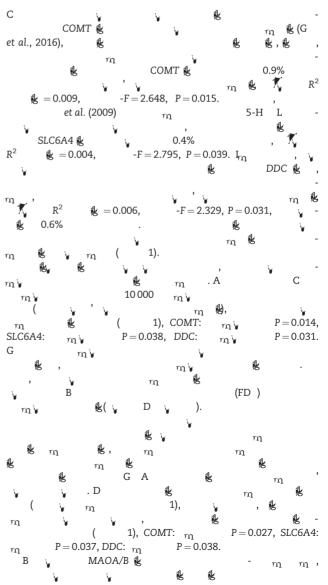
Behavioral results

C (D et al., 2006; et al., 2009; et al., 2013; G et al., 2016), g m g g g g



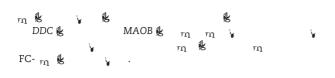


Gene-behavior association results



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k m m MAOB k m m ¥ m 🕏 m 2.8% 6 ×, R² **₺** = 0.028, -F = 2.499, P = 0.031.m m (P = 0.038)(P = 0.043).m m m MAOA 🏂 CA Ł 彤 m . H 影 彤 6 m DDC 🎄 m SLC6A4 🕵 彤 Ł 彤 m COMT 🎉 MAOB 🎉 6 影 彤 m 3). (m ΙG 彤 彤 彤 m N 4 (COMT, SLC6A4, DDC MAOB) 彤 ¥ m 🕏 ¥ mmik (G CA F 🎉 1). m 6 m (H , 1975), m k 彤 m 彤 m & COMT & , m & F 🎉 2 (🍟). F 4680 m K B LD 彤 - V ,



- B & , K.L., 髮 , D. . (2010). In 影 影影 ¥-. Neuroimage, **53**(3), 804 9.
- B Birn, A., K , G., C , ., et al. (2003). B D A . . American Journal of Medical Genetics Part
- B: Neuropsychiatric Genetics, **117**(1), 18 22.
- B , ., _ H , J. (2006). E 🍟 ま 影 -V . BMC _ m Bioinformatics, 7(1), 1.
- B 🖕 , C., H 🚓 , C., G 🖕 , A. (2004). C 🖕 彤 ¥ rn . BMC Bioinformatics, 5(1), 1. C m ዿ, A., A γ ℓ, F., ዿH.,
- ≰ H. (2008). m 🦕 -. Source Code for m 🖌 Biology and Medicine, **3**, 15.
- C, ., m, K., H, B. ., F 🎉 , A., C , . ., L , K. . (2005). B :
- 6 & & -6 . Proceedings of the National Academy of Sciences of the United States of America, **102**(34), 12224 9.
- C , D., J , , , , , K., , B. (2012). m · Management Science, 58(1), 21 34.
- C , J. . (2001). A m **87**(1), 52 8.
- C , , , , A.C., , . . (2008). 彤 .
- Trends in Cognitive Sciences, **12**(1), 31 40.
- C , J., G , ., E r_{11} , G., et al. (2010). A 44 g_{11} r_{11} r_{12} r_{13} r_{14} r_{15} r_{15} r
- C , H., & , .(2012). Th Claremont McKenna College Robert Day School of Economics and Finance Research Paper (2012-01).
- C , L.G., , ., ., ., et al. (2009). G **`**-R
- τŋ 🏂 Social Cognitive and Affective m Neuroscience, **4**(4), 399 408.

- n n 's 's & & 'm . Cognitive, Affective, & Behavioral Neuroscience, **12**(4), 678–91.
- H , D. ., K , , , , J.L., C & .-C., , , . . (2011). Frontiers in Genetics, **2**, 73.
- H , D. ., , J.L., K m_1 , ., et al. (2011). $g = (G A): m_1$, Neuroimage, 56(4), 1875 91.
- H, E., B, ., F, . (2004). B : g g m J Autism and Developmental
- Disorders, **34**(2), 229 35. H, g, g L. (2010). rn g rn . Personality and Individual Differences, **48**(5), 649 53.
- I_{n_1} , K., K_{n_1} , K., r_{n_1} , A., et al. (1999). $r_n = r_n$
- Neuroscience Letters, **269**(1), 37 40. J , ., L , . (2014).
- , ., ..., , . (2017). τη τη (5-Η L). τη ⁶ε τη τη γ . Neurobiology. Progress in Neurobiology, **117**, 41 53.
- Society, 205 91. K r_{r_1} , D., , A. (1984). C , , , r_{r_1} . American Psychologist, **39**(4), 341.
- K & J., , .K., L , .J., et al. (2006). F m -A A A B m m . Movement Disorders, **21**(12), 2175 80.
- K , . ., C , ., C , L.G., et al. (2002). G rn & rn rn B 13 & , . Neurotoxicology
- 23(4), 515 9.
- K & A., K , K., H $_{rn}$, J., et al. (2007). A A -A $_{rn}$ & $_{rn}$. Neuropsychobiology, **56**(56), 191 6.
- K -K & B. ., G , J., & & . . (2007). C , H 1B, , American Journal of Medical Genetics Part B: Neuropsychiatric Genetics

, C.A., B , G.B., A , J., et al. (2007). C (158) 5H L

: 🍾 m A H C 🔓 . Genes, Brain and Behavior, **6**(7), 647 52.

τη, Ε. ., Κ , ., Α_{τη} , Α. (2010). D 8 n n n 彤 یں۔ ہیں۔ K Progress in Neurobiology, **92**(2), 112–33.

, A.L., , J., & , ., , .E., , .А., , D. (2006). _{тд}

₿m-🖕 . Nature Genetics, **38**(8), 904 9.

, ., , B., -B , K., et al. (2007). LI K: -18 m V -Ł . The American Journal of Human Genetics, 81(3),

559 75. , D.E., C 🤹 , ., B , ., et al. (2001). L 🍕

6 m m k m .Nature, 411(6834), 199 204. C. (2013). m & m & m & m & Frontiers in Human Neuroscience, 7, 242.

, A. ., G , . (2003). 🙀 🏨

. Proceedings of the National Academy of Sciences, 100(3), 1128 33.

, B., , G.C., et al. (2009).A 🍇 , J. .,

rn n k n k . Journal of Neuroscience, **29**(18), 5985–91.

, J., D , C.J., H , E., G , K.D. (2009). rn rn - A & rn -rn ADHD , rn in ADHD , rn in . Journal of Autism & Developmental Disorders, **39**(1), 67 74. А m

g = 0, D = 0, B = 0, C = 0,. Clinical Neuropharmacology, **28**(5), 228–37.

, Е.Е. (2009). Гарта . Nature, **461**(7261), 218 23. , D.J. (2004). Е **К**

. Genetic Epidemiology, **27**(4), 348 64.

الله المعالي . Neuroimage, **53**(3), 810 21. المعالي , H. ., J، لا جاري , ., , A.I., H המושר, A. . (2003). R

8 6 -Em . Psychological Science, **14**(1), 7–13.

, E., , I., 🔥, L., et al. (2014). D

\$ m & & $m \not \otimes m$. Proceedings of the National Academy of Sciences, 111(26), 9615 20.