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

G ,[1,2] J L ,[3,4] G [5] J [6] F [7,8] H ,[7,8] L ,[1,7,9] [1,2,9,10,11]

[1]C B C [2] C , , B 100871, C , [3]C C E [4] C B F , G 518060, C , [5]K L B B C (E), , 710069, C , [6] I E , C , G 510631, C , [7] C L , [8] L [9] K -IDG/ G I B , [10]K L (E), [11]B K L B H , , B 100871, C

G J L .
C C , , 5 , B 100871,
C . E : 104@ . .

Abstract

(SLC6A4) (COMT) , 26 1317 C H . C SLC6A4 COMT (DDC) , -L- ,

Key words: ; DDC; COMT; SLC6A4; G A

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© A (2017). A C C A -C L (:// . / - /4.0/), - , , , . F - , . @ .

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Introduction

, 2004; K et al., 2008; A ,
2008). C

(et al., 2010;
et al., 2014)

(A , 2008; H et al.,
2011 ,).

Materials and methods

Participants

(G 2013)
C , C , -

C H (80.1% ,)
18.66 ± 0.90)
15 . A 100

(
behavioral test; D et al., 2006; G et al., 2016). I 1582
, 5

A 1317

(
). A
(. . <50, $= 30.58$,
D = 5.35)
(1971; et al., 1999)
(. . <50, $= 33.3$, D = 6.31)
D (1965;
et al., 1999),
(51, 51, 53, 53, 53, 54, 54, 55 59,)

(51, 51 56,)
. G
12

D H
E C
C ,

The behavioral test

G et al. (2016),
D et al (2006)
(et al., 2009; et al., 2013). A

(. .)
,
(. .)

(K 20
50') (L 30 50'),

. F
,
. F ,

(K 80 100' vs K
100 40%').

. E 48 (16 , 16
16),
D et al. (2006).

A (500:1)
. G et al. (2016)

($<75\%$, =57.9% ± 17.6%; 1317 , = 90.5% ± 6.5%)

(4.44% ± 1.75%)
1317 (14.51% ± 0.34%), $t_{(1580)} = 9.16$, P < 0.001.
F ,
( ).

(= 1591 , D = 551)
(= 1601 , D = 544)
(= 1776 , D = 353 ; -
= 1872 , D = 376), $t_{(1580)} = 6.639$, P < 0.001
$t_{(1580)} = 9.375$, P < 0.001

Genotyping

D A
G -610L A I
I H
H -8 1 C I

Gene selection and preprocessing

K
E G G (KEGG; ://
/).
( ) (TH),
-L- (DDC),
(VMAT2) , ( )
(DRD1–5), ( )
(DAT1,

A
Tyrosine
TH
L-DOPA
DDC
DA
VMAT
DA
DA
DAT
Presynaptic
Neuron
B
Tryptophan
TPH
5-HTP
DDC
5-HT
VMAT
5-HIAA
HTR1B
5-HT
MAOA
5-HT
SLC6A4
DA
Synaptic
cleft
DA
DA
DAT
COMT
3MT
MAO
DA
HVA
MAO
DOPAC
COMT
DRD2
DRD3
DRD4
D2-Like
DRD1
DRD5
D1-Like
Astrocyte
5-HT
Synaptic
cleft
5-HT
5-HT
SLC6A4
HTR2A
Gq
HTR1
A/B/D/E/F
HTR2
A/B/C
HTR3
A/B/C
HTR
4/6/7
HTR5
Astrocyte
Postsynapic
Neuron
opamine pathway genes
Serotonin pathway genes
D

Fig. 1. D . D (A) (B) -), ( ), ( ) ( ). C - , - , . A K E G G (KEGG; :// . /); , et al., 2014.

SLC6A3), -O- (COMT), - A (MAOA) B (MAOB) (, et al., 2011; et al., 2014) ( ) 5- - (TPH 1 TPH2) , ( ) 5- (HTR1A/B/D/E/F, HTR2A/B/C, HTR3A/B/C/D/E, HTR4, HTR5A/B, HTR6-7, HTRA1-4) , ( ) - - (SLC6A4) (B et al., 2016) (F 1). HTR3D HTR3E (et al., 2003; B : G E E , :// . . /). DRD4, DRD5, HTR1A/B/D/F, HTR5B, HTRA2 HTRA4 . G A LI K (et al., 2007; et al., 2014): ( ) H E 10^{-4} (AF) 0.1 0.05; ( ) 0.05 ( ) . - , G A (D) - LI K (et al., 2006; et al., 2007) . LI K (et al., 2007) (et al., 2006). F , 19 .

Principle component analysis

A . (C :// . - .). LD , , G A (CA) - LD (A , 2008). , , (C) 90% (A , 2008; et al., 2014). (LD), C - . C LD (D et al., 2001; et al., 2001; G et al., 2002), (1). F , 6 90.2% DDC 47 G A .

Gene-behavior association analysis

- -F (. .) (A , 2008; H et al., 2011 ,). -F . F

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Table 1.

	F	G	C	%_	R²		A	R²		Partial-F	p_{unc}	p_{perm}	p_{emp}
D		TH	2	2	100	0.001		<0.001		0.712	0.491	0.484	0.485
		DDC	47	6	90	0.010		0.006		2.329	0.031*	0.031*	0.038*
		VMAT2	17	9	90	0.003		<0.001		0.501	0.875	0.878	0.862
	/	DAT1	16	6	91	0.005		<0.001		1.027	0.406	0.408	0.466
	C	COMT	18	6	91	0.012		0.009		2.648	0.015*	0.014*	0.027*
		MAOA	6	3	90	0.003		<0.001		1.143	0.331	0.325	0.346
		MAOB	37	5	92	0.005		0.002		1.367	0.234	0.232	0.293
		DRD1	1	1	100	0.000		<0.001		0.097	0.756	0.756	0.780
		DRD2	16	8	90	0.004		<0.001		0.721	0.673	0.680	0.770
		DRD3	41	12	92	0.014		0.006		1.617	0.081	0.081	0.099
		TPH1	2	2	100	0.001		<0.001		0.719	0.487	0.476	0.477
		TPH2	6	4	93	0.002		<0.001		0.519	0.721	0.718	0.753
		SLC6A4	8	3	90	0.006		0.004		2.795	0.039*	0.038*	0.037*
		HTR1E	16	6	91	0.007		0.003		1.545	0.160	0.158	0.199
		HTR2A	44	12	90	0.013		0.005		1.492	0.120	0.121	0.123
		HTR2B	3	2	100	0.001		<0.001		0.596	0.551	0.551	0.519
		HTR2C	22	8	90	0.006		<0.001		0.920	0.499	0.499	0.517
		HTR3A	4	4	100	0.001		<0.001		0.364	0.834	0.831	0.833
		HTR3B	22	6	90	0.001		<0.001		0.228	0.968	0.967	0.970
		HTR3C	2	1	99	0.000		<0.001		0.124	0.725	0.724	0.677
		HTR4	46	14	91	0.015		0.005		1.422	0.135	0.136	0.075
		HTR5A	7	4	92	0.006		0.003		1.866	0.114	0.114	0.118
		HTR6	2	1	100	0.000		<0.001		0.000	0.990	0.992	0.982
		HTR7	22	6	93	0.006		0.002		1.316	0.247	0.242	0.301
		HTRA1	34	9	91	0.007		<0.001		0.974	0.460	0.456	0.441
		HTRA3	19	5	92	0.004		0.001		1.133	0.341	0.356	0.370

C , ; %_ , C ; p_{unc}, P F- ; p_{perm}, P ;
p_{emp}, P .
* P < 0.05.

$$F_{k, df(full)} = \frac{RSS(reduced) - RSS(full)}{df(reduced) - df(full)} \Big/ \frac{RSS(full)}{df(full)} \qquad (1)$$

Principle component analysis

(1) (H et al., 2011). k

A A/B

2003), = 0.62% ± 0.08%

Gene-behavior association results (COMT, SLC6A, DDC MAOB;).

(COMT: P = 0.028, SLC6A4: P = 0.038, DDC: P = 0.070 , MAOB: P = 0.029),

Permutation tests

(H et al., 2011 ; et al., 2014).

(B , 2001; , 2004; C et al., 2008; G et al., 2014),

P).

(C , 2001).

Empirical tests

, P -F
G A
(et al., 2014). E p
( )
( )
. A
,
(2).

Protein–protein interactions

K ,
H I G 10 (
I G /) (://
et al., 2015)

, ( ) (
) ,
, - , -
, (H et al.,
1999; G , 2003). I
(B et al., 2004). ,
. C '
I G 10, CL
(= 4),
(:// /, B
- H , 2006), F 1).

SNP–SNP interactions

,
CA
- . F
, , CA ,
- ,
- ,
.
90%
(
3).

Results

Behavioral results

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

: 59.75%±0.47% (E) vs 45.23% ± 0.46%
, $t_{(1316)}$ = 42.08, $P < 0.0001$.
(.)
, . I
(F , 1990; H
2010), 2 (: F vs) × 2 (: vs
) (A _ A)
, $F_{(1, 1315)}$ = 15.587, $P < 0.001$, $F_{(1, 1314)}$ = 14.701, $P < 0.001$,
. I ,
, ,
β = -0.052, t = -1.903, $P = 0.057$.
(, 2009;
et al., 2011).

-

Gene-behavior association results

C
COMT (G
et al., 2016),
, ,
COMT 0.9% R^2
= 0.009, -F = 2.648, $P = 0.015$. ,
et al. (2009) 5-H L
, ,
SLC6A4 0.4%
R^2 = 0.004, -F = 2.795, $P = 0.039$. I ,
DDC ,
, R^2 = 0.006, -F = 2.329, $P = 0.031$,
0.6% .
, (1).
,
. A C
10 000),
(1), COMT: $P = 0.014$,
SLC6A4: $P = 0.038$, DDC: $P = 0.031$.
G
, .
,
B (FD)
(D).

, ,
G A ,
. D ,
(1), ,
(1), COMT: $P = 0.027$, SLC6A4:
$P = 0.037$, DDC: $P = 0.038$.
B MAOA/B - ,

DDC   MAOB

FC-

B   , K.L.,   , D. . (2010). I   -
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B   , A., K   , G., C   , ., et al. (2003).   -
-                  D   A   -
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C   , J., G   , ., E   , G., et al. (2010). A
              44
                                -                         . *Journal of Psychiatric Research*, **44**(11), 717 24.

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