Behavioral/Systems/Cognitive

Differentially Organized Top-Down Modulation of Prepulse Inhibition of Startle

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Prepulse inhibition (PPI) of startle is tha

(M , 2007; M M D , 2007; C K , 2010), PPI (S ., 2001), PPC / (K ., 1999; ., 2002; G ., 2010) (R C , 2009).

Materials and Methods

A . A (A1, LA, PPC) - , (K NA), , L ' - , 86 - S D (, 10 ; , 280 300) / : (1) A1/K NA (= 14), (2) A1/ (= 14), (3) LA/K NA (= 16), (4) LA/ (= 14), (5) PPC/K NA (= 14), (6) PPC/ (= 14).

T K NA , 10 K NA - (S1BF) . T S1BF LA A1 . T (D ., 2009 ,). B , (C317G ; P O) 10% - (400 / , . .) . R , - : (1) A1: , −4.6 ; , ±6.5 ; , −4.2 ; (2) LA: , −3.1 ; , ±5.2 ; , −7.8 ; (3) PPC: , −4.4 ; , ±3.1 ; , −1.6 (F ., 2003); (4) S1BF: , −3.1 ; , ±5 ; , −2.5 .

R 1 24 ± 2 C 12 / , . T G B L A C , P U A H N R S N (2006).

. T PPI - (D ., 2009 , 2010). B , , - , 10 (0 10 H , 100 B SPL) - , , - (N K L M P , P U -) . B , (- 16 H) (500). S

. (2007), F . 2 , , - - (15 20) - (20 25) . T - (. .,) 100 52 , . T , 100 , 50 - - (1.3, 2.6, 3.9 H) - - (2.3, 4.6, 6.9 H) . E MATLAB - (N K L M P , P U) 16 H 16 . S (B & K ; 2230) , , F / P . T - 60 B SPL.

. A 1 , 6 . F 3 , (., 2007), , . F 30 3 , - (60 B SPL), . N . T . O , (BC) . T 5 , 10 - 60 B SPL. T 25 35 (, 30). T - PPI (. ., - -). T - - +1 ( ) −1 ( ) . D (., 1949; L ., 1999; L , 2002), - (L ., 2005; H ., 2011), ( ) (-). I , (0 10 H , 60 B SPL) . T - +1 −1 , . T , : ( ) ( ). N - - - (L ., 2004).

I -

A1 (2.0 μ), LA (1.0 μ), PPC (2.0 μ), S1BF (2.0 μ) ~1 . D , 5.0 μ (, 0.38 ; , 1.09 ; C A , BD B). PPI (AI) 15 . S K NA (L K , 1992; M ., 2003), PPI 2 K NA (AR).

O , , . US, 60 20 30 . F , 80 (60 CS 20 CS) 10 . A , PPI (AE).

D . T PPI : PPI = (−)/( ).

S , - - (- -) - (-), PPI . PPI PPI / - (BC) - / . M - - ANOVA B ' ( ) ( ) SPSS 13.0 . T - 0.05.

. , . L DC (500 μA 10). B 10% 30% , 50 μ (−20 C). S - .

Results

Table 1. Startle amplitudes to the startling stimulus alone

Groups	Amplitude in the device scale unit				
	Before conditioning	After conditioning	After injection	After recovery	After extinction
A1/KYNA ($n = 12$)	1425 ± 281	1640 ± 299	1662 ± 258	1644 ± 296	1400 ± 354
A1/vehicle ($n = 12$)	1486 ± 246	1662 ± 258	1720 ± 251	N/A	1516 ± 187
LA/KYNA ($n = 12$)	1104 ± 466	1336 ± 537	1354 ± 571	1267 ± 535	1055 ± 561
LA/vehicle ($n = 12$)	1207 ± 424	1400 ± 438	1432 ± 423	N/A	1267 ± 456
PPC/KYNA ($n = 12$)	1346 ± 355	1541 ± 379	1598 ± 406	1564 ± 405	1355 ± 460
PPC/vehicle ($n = 12$)	1290 ± 415	1449 ± 413	1479 ± 426	N/A	1268 ± 506
S1BF/KYNA ($n = 10$)	1109 ± 316	1252 ± 433	1286 ± 220	1268 ± 390	997 ± 212

Values represent mean ± SD.

Table 2. Group mean baseline PPI values (under perceived prepulse/masker colocation and before the conditioning/conditioning-control manipulation)

Groups	Lower-frequency prepulse (%)	Higher-frequency prepulse (%)
A1/KYNA ($n = 12$)	31.7 ± 7.1	31.5 ± 8.9
A1/vehicle ($n = 12$)	32.7 ± 9.4	32.8 ± 11.1
LA/KYNA ($n = 12$)	34.6 ± 12.2	34.6 ± 11.9
LA/vehicle ($n = 12$)	36.6 ± 17.4	36.4 ± 15.7
PPC/KYNA ($n = 12$)	31.2 ± 7.5	30.5 ± 7.9
PPC/vehicle ($n = 12$)	34.4 ± 7.0	32.0 ± 7.8
S1BF/KYNA ($n = 10$)	36.0 ± 7.4	36.9 ± 7.8

Values represent mean ± SD.

Effects of KYNA injection on PPI induced by conditioned prepulse

F 2 PPI K NA ( ) L ’ ( ) A1 ( ), LA ( ), PPC ( ), - , . T , K NA (F . 2 , ,). F K NA (A1/ K NA, LA/K NA, PPC/K NA), F 2 BC - PPI. H , , - (AC), PPI , - . T , K NA PPI (AI) . A , 2 (AR). F , (AE), PPI BC. S . F , 5 (: BC, AC, AI, AR, AE) × 2 (, : ,) - - ANOVA ($F_{(4,44)} > 23$; < 0.001). P ( ) ( ) (1) - BC, PPI - ($_{(11)} < 1.7$; > 0.05); (2) PPI AC BC (< 0.01); (3) AC, PPI ($_{(11)} > 7.4$; < 0.001). F K NA - , - -

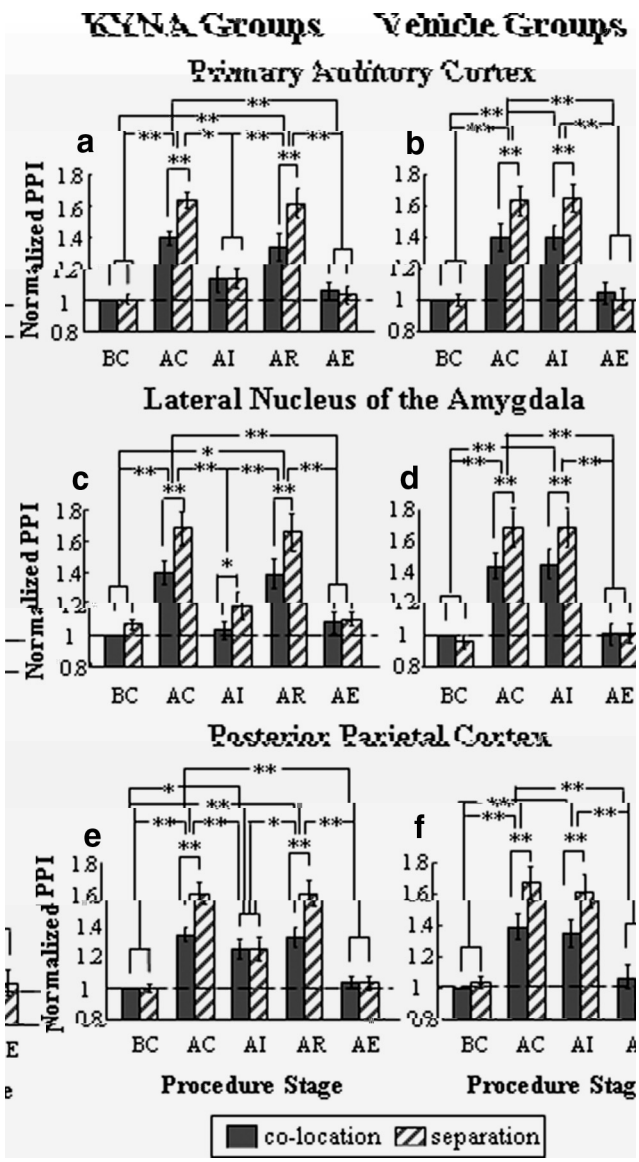

Figure 2. Normalized PPI induced by the conditioned prepulse at different procedure stages in A1/KYNA group ($n = 12$) (***a***), A1/vehicle group ($n = 12$) (***b***), LA/KYNA group ($n = 12$) (***c***), LA/vehicle group ($n = 12$) (***d***), PPC/KYNA group ($n = 12$) (***e***), and PPC/vehicle group ($n = 12$) (***f***). The filled bars represent the conditions when the prepulse was perceptually colocated with the noise masker, while the diagonal bars represent the conditions when the prepulse was perceptually separated with the noise masker. BC, Before conditioning; AC, after conditioning; AI, after injection; AR, after recovery; AE, after extinction. In this and the next figures, all the PPI values were normalized relative to the value at the procedure stage BC and under the prepulse/masker colocation condition. Error bars represent the SEM. $^{**}p < 0.01$ and $^{*}p < 0.05$ (by repeated-measures ANOVA, Bonferroni's pairwise comparisons, and paired *t* tests).

PPI ( ).

Effects of blocking the A1 on PPI induced by conditioned prepulse

F K NA A1 (F . 2 , AI), - PPI - (, $_{(11)} = 0.335$, > 0.05). A , PPI AI - AC (< 0.05), BC (> 0.05). T (AR), PPI

AC (> 0.05)
AI (< 0.01).
M ,
((11) = 8.152; < 0.001). A ,
PPI BC (> 0.05),
((11) = 1.616;
> 0.05). T , A1
- PPI
- PPI .

Effects of blocking the LA on PPI induced by conditioned prepulse

F K NA LA (F . 2 ,
AI), PPI
AC (< 0.01). M ,
26.3%
30.0% , PPI
BC (> 0.05). H ,
PPI ((11) =
2.282; < 0.05). T (
AR), PPI
AI (< 0.01)
AC (> 0.05). A , -
((11) = 7.233; < 0.001). A -
AE, PPI
BC (> 0.05),
((11) = 0.788; > 0.05). T , LA -
- PPI
- PPI .

Effects of blocking the PPC on PPI induced by conditioned prepulse

F K NA PPC (F . 2 ,
AI), PPI

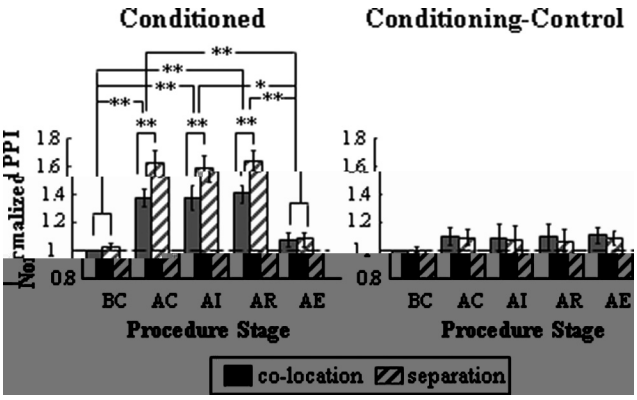

Figure 4. Normalized PPI elicited by the conditioned prepulse (left panel) and conditioning-control prepulse (right panel) at different procedure stages in the S1BF/KYNA group ($n = 10$). See Figure 2 legend for the explanation of symbols and abbreviations. $^{**}p < 0.010$ and $^{*}p < 0.05$ (by repeated-measures ANOVA, Bonferroni's pairwise comparisons, and paired t tests).

($F_{(4,44)} = 3.459$; < 0.05), ($F_{(1,11)} < 0.4$; > 0.05), ($F_{(4,44)} < 1.0$; > 0.05). P PPI AI - AC AR (< 0.05). M , - L , PPI (A1/ , LA/ , PPC/). F , 4 (: BC, AC, AI, AE) × 2 ( ) - ANOVA ($F < 4.4$; > 0.05), ($F < 1.4$; > 0.05).

Effects of blocking the S1BF area on PPI induced by conditioned prepulse

T K NA , PPI 10 K NA S1BF . A F 4 , 2 μ K NA S1BF PPI , PPI - - (> 0.05). T , K NA .

Discussion

Two types of top-down enhancements of PPI

T PPI (C , 1996; I ., 1998; R K , 2006; F ., 2007; H ., 2007; ., 2007; L ., 2008; D ., 2009 , 2010). F , , PPI (H ., 2007; ., 2007; L ., 2008; D ., 2009 , 2010; I ., 2010). A , - (-) PPI (D ., 2009 , 2010). M , , A1, LA, PPC, PPI .

Contributions of the A1

S CNS, K NA (-) (S ., 1990). U K NA ( ): F , - , K NA -NMDA NMDA (S C , 1985; K ., 1989; T ., 1989). T , K NA - , . I , K NA , - . F , K NA (L K , 1992; M ., 2003).

T - PPI - A1 K NA, - - PPI.

I A1 PPC (R - L D , 1993; R ., 1994) (, ., 2008). I A1 - / - PPI - , A1 - - . I , (O'L ., 1997; H ., 2000), (F ., 1998; P I , 2008), - (J ., 1999; K ., 2007), (B -C ., 2007), A1 . P , , A1 ( ) - (D ., 2011). E A1 (P ., 2006; J , 2011), (F ., 2007), (L M , 2011). T , A1 / - , - PPI. M , A1 - PPI, IC (H ., 1991; D ., 1997; C ., 2005; S , 2009), - (PPT), (S M , 2009; S , 2010). T , A1 - PPI PPI . S A1 PPI , A1 PPI - .

Contributions of the LA

I , , - - PPI - LA. I LA (R L D , 1992; P ., 1997), LA (CS) (US). M , - , , (M M D , 2007), LA CS US (B ., 2005; S ., 2005), LA (-). T , LA , - , - . S LA - - PPI , LA / - . B , - PPI : (1) (H ., 1985), PPT (T ., 2007); (2) (M D , 2000), PPI (F ., 2001). U A1, LA PPI - , - PPI . S PPI PPI - , PPI LA , - - LA PPI.

Contributions of the PPC

T PPC - PPI - - PPI - , PPC . I , , PPC (K ., 1999; ., 2002; G ., 2010). I , (R C , 2009), - (F ., 2003), - (K , 2009), (B G , 2010), - (B ., 1998). A , PPC (R ., 1994), (R L D , 1993; M D ., 1996). T , , PPC .

Effects of the conditioning/conditioning-control manipulation on responses to the startling stimulus alone

C (D ., 2010), , / - (AC), (T 1). , - . T , - / - (D ., 2010). N - (., CS) CS (., 3700) CS (K ., 1993; D , 1997). T , - . M , , K NA A1, LA, PPC, S1BF , / - A1, LA, PPC, S1BF. T K . (1993) D (1997) - , , ( ) - -NMDA- 6- -7- -2,3- - (LA) (K ., 1993) AMPA 2,3- -6- -7- - : , (D , 1997).

New animal models for studying mental disorders

I , PPI , , (D ., 2000; B ., 2001; H ., 2007). H , PPI - PPI (S ., 2006). M , - / (ADHD), PPI , ADHD (H ., 2002, 2003). S PPI - PPI, , A1 (J ., 1993; B ., 2005), (A K , 2005; S ., 2007), PPC (D ., 2004; C ., 2009), - PPI . F , , - - PPI . T , PPI , , ,

(F ., 1992; Q ., 1997; M Q , 2002), - PPI - (PTSD) (A , 1997).

Summary: differentially organized top-down modulations of PPI

A PPI (F ., 2001; L , 2002), PPI - (L ., 2009). P - PPI (B G , 1998; M ., 2010). T , , , A1, LA, PPC, - PPI - PPI . PPI : T PPC , LA , A1 . T , - PPI PPI, - . I , - PPI - , , ADHD, PTSD.

References

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A A, K RS (2005) S : ? P N 77:283–298.

B VP, G MA (1998) M - NMDA . J N 18:8394–8401.

B EM, O CC, K JJ, B JK, V MN, K JL (2005) D - / - . A G P 62:1129–1136.

B -C A, F C, B J, A PE, G MH, B O (2007) E . J N 27:9252–9261.

B HT, H VK, V VT, V J, P RR, H AK, L JE, T J (2005) U . J N 25:4198–4205.

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B DJ, H PC, G M (1998) R - . J N 18:8038–8046.

C KS, G MA, B DL (1993) I - . A J P 150:1862–1867.

C S, JF (1996) T : C57BL/6J . H R 99:168–175.

C JM, K EH (2010) M : . C P R 30:203–216.

C DL, S RM, S BR (2005) U . B R 1042:62–72.

C P, P C, D'A E, M R, P A (2009) T - / . E J P N 13:299–304.

D J, S M, M P (2004) A , : . S R 70:241–261.

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D ME, S AM, H EA, N KH, F DL (2000) O . P R 96:187–197.

D R, S J, R G (1997) P . P R 46:215–222.

D , H Q, , G GC, L L (2009) B - . J N 101:1647–1659.

D , L J, , L L (2009) P - - - . C A B N 9:44–58.

D , M T, Q, , L L (2009) T - . E J N 30:1779–1789.

D , , L L (2010) E - - - . B B R 206:192–201.

D , H , R B, B T, , L L, A C (2011) H . C C 21:698–707.

F A, M MJ, D M (1992) E - NMDA . J N 12:854–863.

F M, L L, JS (2001) B . P 156:216–224.

F JA, I JR, T JPJ , S (1989) T : I. E , , , . H F 31:307–318.

F JE (1979) H . P B 23:291–297.

F MT, B MD, B MG (2003) P - . J N 23:676–681.

F JC, M NA, B TD (2007) I - - . P 44:339–342.

F JB, E M, S SA (2007) A - . J N 98:2337–2346.

F N, N T, I M, T T, S H (1998) R - . B R C B R 7:99–109.

G FK (1975) T . P 12:238–248.

G AS, E M, D, S JT, S (2010) C - . J N 30:14330–14339.

H SN, G HJ, G EA, N J (1985) E - , - . J C N 235:322–335.

H L J , R JS, B JS (2002) I - - . P 39:674–677.

H L J , AR, P E J , L TM (2003) T - . P 165:118–127.

H EA, R MJ, H MM, N AS, G KE, N RE, S LJ, B MS (2007) D

. S R 93:288 295.
H H, A A, O J (1991) T . J C N 304:103 122.
H HS, I JR (1980) R : I. S . P R 87:175 189.
H HS, O (1971) P . P S 24:233 235.
H HS, S JL (1965) A . J C P P 60:53 58.
H J, , P J, L , , L L (2007) T , H R 223:1 10.
H , L J, , Q T, , M L, , L L (2011) P . J C N 23:1003 1014.
H K, L I, K S, B K, G A, P OB (2000) E : ^{15}O-PET . H B M 10:87 97.
I D, M D, F , S C, O H, M S, K N, H K, I M, S E (2010) E . P N B P 34:183 188.
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J L, M S, S NJ (1999) A : . N L 266:125 128.
J S, AM (2011) T . N N 14:246 251.
J DC, D P, I, R , V HG J (1993) I - . B P 33:513 519.
K RP (2009) T - . N L M 91:197 206.
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K M, C S, F A, D M (1993) I -NMDA CNQ - . B N B 59:5 8.
K H, G DR, N AC, P TB, L B KS, M MM (1999) T - . N 9:269 277.
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K K, E SB, F GR (2007) F - - . J C N 19:1721 1733.
L C, H A (1939) T . N : F R .
L CC, M JC (2011) A . N N 14:108 114.
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L L, K LM, F BJ, B RJ (1998) P : . P B 65:133 139.
L L, P RP, JS (1998) P . B N 112:1187 1198.
L L, D M, Q JG, S BA (2004) D - ? J E P H P P 30:1077 1091.
L L, Q JG, H , A C, S BA (2005) A - . H R 202:235 247.
L L, D , L N, , (2009) T - . N B R 33:1157 1167.
L N, P J, R, C, , L L (2008) A - - . B N 122:107 118.
L R , C HS, A, G SJ (1999) T . J A S A 106:1633 1654.
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M S (2007) T . S 317:1043 1044.
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P DB, S EE, M MM (2006) P - . J N 26:4970 4982.
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R RL, C JV (2009) P . N L M 91:104 113.
R RL, C HC, K V, C JV (1994) R . E B R 100:67 84.
R LM, L D JE (1992) E . J N - 12:4501 4509.
R LM, L D JE (1993) I - : - . C C 3:515 532.
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S GE, D V, L D JE (2005) T : - . J N 25:10010 10015.
S BR (2009) P VI . N 159:246 258.
S BR (2010) P - . N 166: 231 240.
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J P 52:135 145.
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S NR, G MA, B DL (2001) N -
, - . P 156:194 215.
S NR, L GA, C KS, S J, H MH, B DL (2006)
S : , , , , . A G P 63:1325 1335.
T K, N T, K H, M K, M T, A S, M H,
, N T, T K, K (2007) N
GABA - . B P 62:148 157.
T AM, VE, F DM (1989) G NMDA-
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DL, D M (1997) D
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H, N EB, R MR (1949) T
. A J P 62:315 336.
J, H, L L (2008) T -
. N B 24:173 182.
S, S J, S JT, C RL, S MA, P JJ,
C SM (2002) T
. N N 5:995 1002.
JS, L L, S B , F P (2002) T ,
. N B R 26:1 11.
D, H J, , L L (2007) M 5
- . N 52:476 486.