Behavioral/Systems/Cognitive

Differentially Organized Top-Down Modulation of Prepulse Inhibition of Startle

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D a P , S a H a R a C , K La a Ma P (M E a), P U ,
B 100871, C a

(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).

CS

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

	Amplitude in the device scale unit				
Groups	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 - , - -

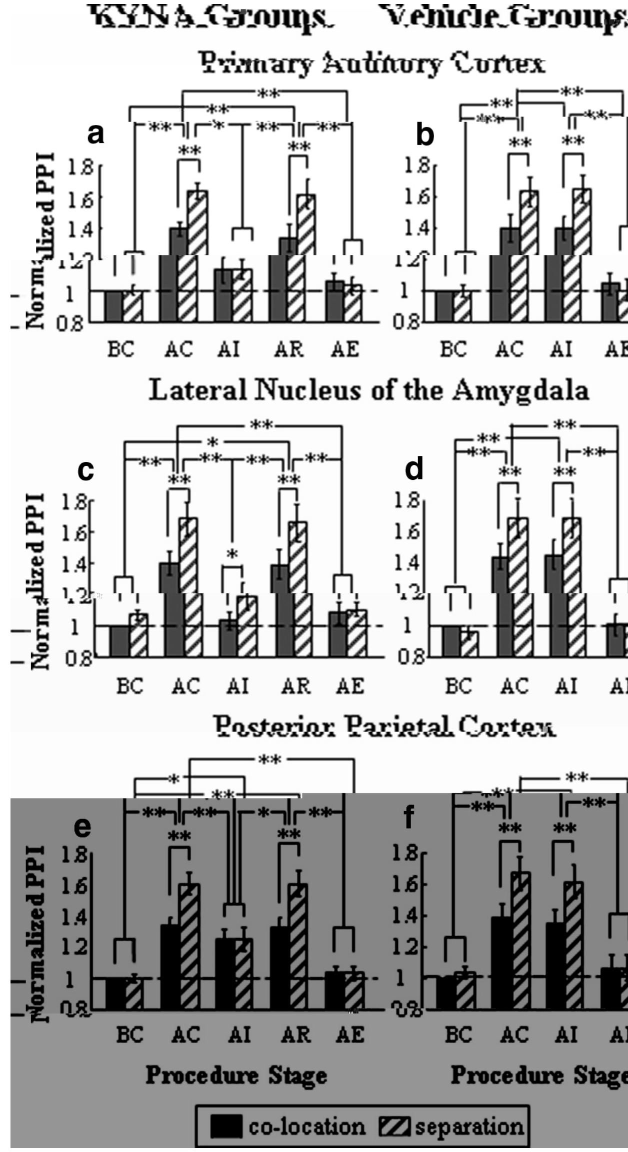

Figure 2. Normalized PPI induced by the conditioned prepulse at different procedure stages in A1/KYNA group ($n = 12$) (***a***), A1/vehicle group ($n = 12$) (***b***), LA/KYNA group ($n = 12$) (***c***), LA/vehicle group ($n = 12$) (***d***), PPC/KYNA group ($n = 12$) (***e***), and PPC/vehicle group ($n = 12$) (***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 ($p > 0.05$)
AI ($p < 0.01$).
M ,
($t_{(11)} = 8.152$; $p < 0.001$). A ,
PPI BC ($p > 0.05$),
($t_{(11)} = 1.616$;
$p > 0.05$). T , A1
- PPI
- PPI .

Effects of blocking the LA on PPI induced by conditioned prepulse

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

Effects of blocking the PPC on PPI induced by conditioned prepulse

F K NA PPC (F . 2 ,
AI), PPI
AC 1TD ( )-20 8.2( ) 57140TD4 (A83()T /F41T 1.10010473 (0.01))-267,.3(1TD 4.3(
AR), PPI
AI ($p < 0.01$)
AC ($p > 0.05$). A , -

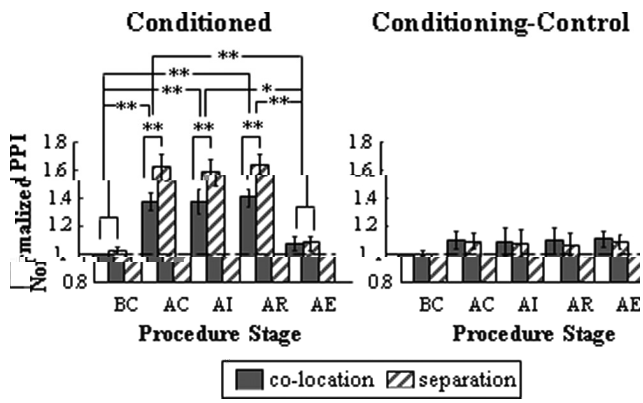

Figure 4. Normalized PPI elicited by the conditioned prepulse (left panel) and conditioning-control prepulse (right panel) at different procedure stages in the S1BF/KYNA group ($n = 10$). See Figure 2 legend for the explanation of symbols and abbreviations. $^{**}p < 0.010$ and $^{*}p < 0.05$ (by repeated-measures 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

A R (1997) T . N B R 21:755 765.
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.
B DL, G MA (1990) S : . A G P 47:181 188.
B DL, G MA, S NR (2001) H , , . P (B) 156:234 258.
B JI, G B (2010) L . N - L M 94:191 198.
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.
D M, G PM (1977) P . J C P P 91:549 563.
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 JP J, 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 : 15O-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.
I JR, A P, P J, V J (1998) C : J A S A 104:1696 1704.
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 (1999) T . P N 59:107 128.
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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, Q (2002) A . H R 168:113 124.
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.
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L R , C HS, A, G SJ (1999) T . J A S A 106:1633 1654.
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Q GJ, A JL, L D JE (1997) F . N 19:613 624.
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.
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R S, K M (2006) E . I J P 60:10 14.
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.
S T , C JH (1985) Q
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S NR, L GA, C KS, S J, H MH, B DL (2006)
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T K, N T, K H, M K, M T, A S, M H,
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GABA -
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H, N EB, R MR (1949) T
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JS, L L, S B , F P (2002) T ,
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26:1 11.
D, H J, , L L (2007) M 5
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. N 52:476 486.