

Chronological Changes in the Rotational Behavior in Response to Apomorphine Administration in 6-Hydroxydopamine Parkinsonian Rat

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Background : Apomorphine-induced rotational behavior of unilateral 6-hydroxydopamine(6-OHDA) lesioned rat is widely used to develop anti-Parkinsonian treatments including drugs, neuroprotective therapy, and neural graft. Time course of changes in rotational behavior after lesioning, however, has not been fully elucidated. The aim of this study was to observe the chronological changes in the rotational response and to find out the optimal period when this model is used for investigation of various therapies. **Methods** : 6-OHDA was stereotactically delivered to the unilateral substantia nigra in 13 rats. Rotational responses to apomorphine administrations were counted in the rotomotor on 2, 4, 8, 12, and 14 weeks after lesioning. **Results** : The total turns for two hours increased continuously up to eight weeks, and then plateaued. **Conclusions** : Apomorphine-induced rotations increase until eight weeks after 6-OHDA lesioning. Therefore, this Parkinsonian model should be used at least eight weeks after lesioning. Even though priming was not excluded as an explanation in the experiment, we reason that progressive degeneration of dopaminergic neurons may explain the chronological changes in rotational behavior.

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Key Words : 6-hydroxydopamine, Rotational behavior, Apomorphine

가
levo-dopa
가
dopamine
가
가
levo-dopa
dopamine
(neuro-
protective therapy)
dopamine
catecholamine
(stereotaxic method)
mine(6-OHDA)
4,5
dopamine
dopamine
dopamine
6
6-OHDA
dopamine
dopamine
D1
D2
phine
dopamine
(denervation supersensitivity)
1-3
(reliability)가
7
apomor-

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dopamine

apomorphine

6-OHDA

apomorphine

6-OHDA

rotation

Ungerstedt

apomorphine

1. 6-OHDA

200-250g Sprague-Dawley

catecholamine dopamine

noradrenaline

desipramine(12.5mg/kg)

pargyline(25mg/kg) 20

pentothal sodium(25mg/kg)

(stereotaxic instrumental device, David-Kopf frame)

2cm 가

Hamilton

syringe 0.2% ascorbic acid 6-OHDA $8\mu\text{g}/4\mu\text{l}$

midbrain Paxinos Watson atlas¹⁰

AP +0.24, L +0.16, DV -2.75mm

6-OHDA가 4

2. 가

hemi-Parkinsonism

2 가 apo-

apomorphine(0.5mg/kg, 가

perplex phine 13

가

rotomotor가

apomor- 1 300

가

3. 2, 4, 8, 12, 14 apomorphine(0.5mg/kg, 5 120 가

4. 2 4 , 4 8 , 8 12 , 12 14 120 mixed model 120 random effect modeling

1. 2, 4, 8, 12, 14 120 가 (p>0.05)(Fig. 1).

2. 120 120 13 2 671±61 , 4 1108±75 , 8 1418±135 , 12 1275±129, 14 1289±124 . 2 4 , 4 8 (p<0.05) 8 12 , 12 14 (p>0.05)(Fig. 2).

apomorphine 2 8 가 , 14 apomorphine 8 . 2 4 . Ungerstedt apomorphine 8 2 가 가 121 (17) 가 , apomorphine 1/2 0.25mg/kg , apomorphine 8 “prim-ing” , apomorphine 가 가 . amphetamine priming 11 amphetamine 12 priming , 5

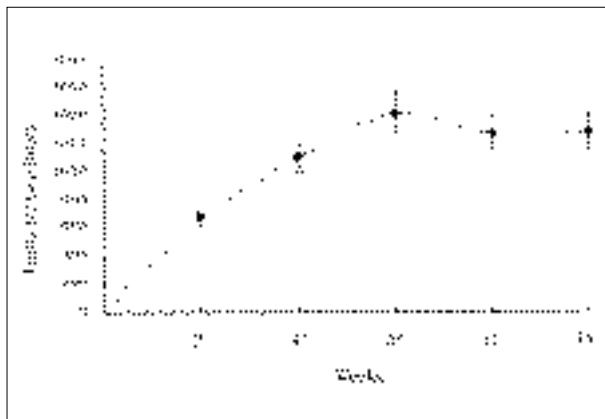
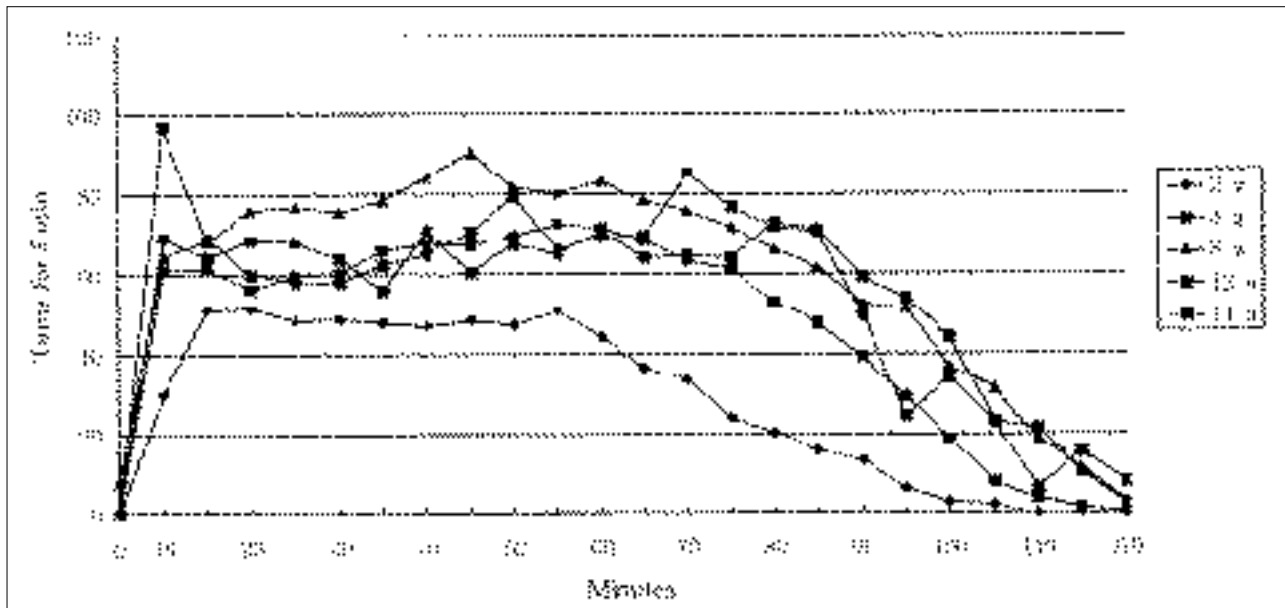


Figure 2. Total turns for 2 hours in response to apomorphine showed significant differences between 2 and 4 week, 4 and 8 week (*: $p < 0.05$), but there were no significant differences between 8 and 12 week, 12 and 14 week ($p > 0.05$). Comparison of means by mixed model was used for test.

6-OHDA

D1 agonist SKF-38393 apomorphine priming

Morelli et al¹²

apomor-

phine priming 3 가

10 priming

apomorphine 12

, 4 가 priming

4 8 가

priming . 8 12

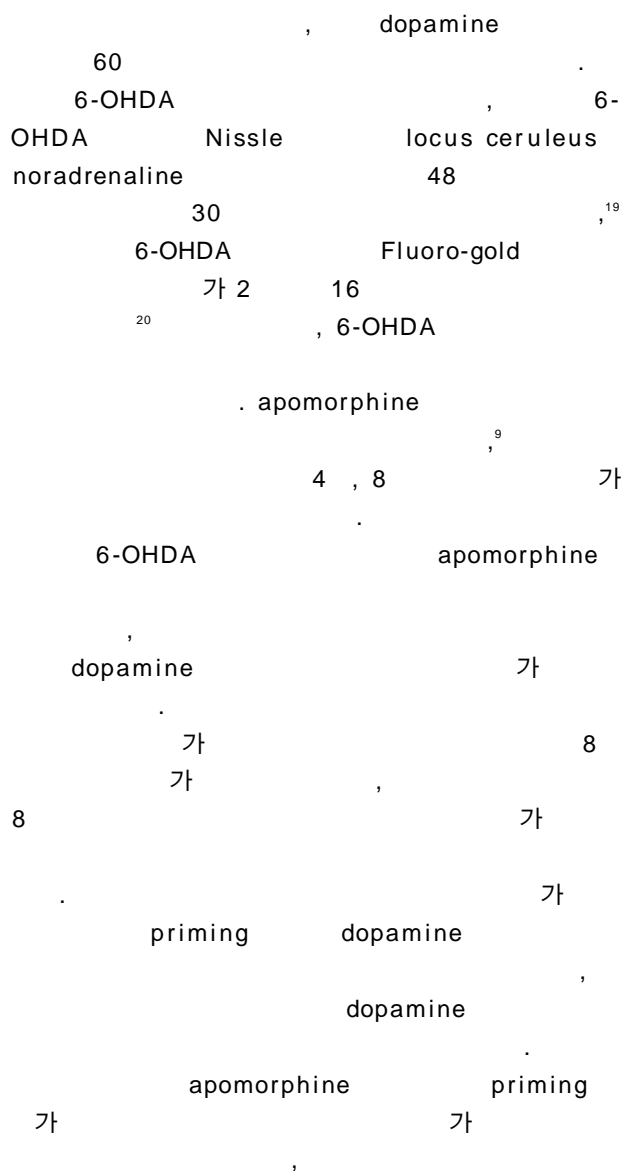
, 12 14 가가

priming

가 .

. 6-

OHDA
dopamine 가
가 dopamine
D2 가(D2 receptor
upregulation) .^{13,14} apomor-
phine 가
가
가 , 가가
가 가 D2
가 D2 2-3 가
가 1
가 ,^{13,15,16} 가가 D2 가
in vitro
dopamine [³H]spiroperidol
4 가 120
¹⁴가 4 8
가 가
6-OHDA
가 . 6-OHDA
2-3 dopamine 96-99%
¹⁶, tyrosine hydroxylase(TH)
1 , 2 TH
가 ,¹⁷ 2
.
dopamine
phenotypic expression
.
가 6-OHDA
silver impregnation
18 60



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