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## The Effect of Chronic Cerebral Hypoperfusion on Middle Cerebral artery Occlusion-induced Cellular Damage in Spontaneous Hypertensive Rats

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**Background:** An ischemic stroke can result from various mechanisms such as atherothrombosis, cardioembolism or hemodynamic compromise. It has been reported that patients with atherothrombotic stroke have less severe neurological deficits and smaller cerebral infarctions than those with cardioembolic strokes. When exposed to a sufficient but sublethal alteration of their environment, most living organisms acquire transient tolerance to subsequent and other lethal environmental changes. **Methods:** We examined the effect of chronic cerebral hypoperfusion on middle cerebral artery occlusion/reperfusion (MCAO/R)-induced cellular damage. Spontaneous hypertensive rats (SHR) that were bred for 4 weeks after bilateral common carotid artery ligation (BCAL) or sham operation were subjected to MCAO/R using a nylon suture model. In paraffin sections obtained from subjects in each group, *in situ* nick translation study were performed and number of dUTP incorporated cells were counted. **Results:** The number of positive cells in the *in situ* nick translation study, which was taken as an indication of cellular injury, was significantly reduced in the chronic cerebral hypoperfusion group ( $166.33 \pm 349.93$ ) when compared with those in the sham operation group ( $1132.08 \pm 1363.64$ ) ( $p < 0.05$ ). **Conclusions:** The findings of this study provide experimental evidence for the hypothesis that chronic sublethal cerebral hypoperfusion is protective for subsequent severe ischemic insults.

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**Key Words:** Middle cerebral artery occlusion, Chronic hypoperfusion

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[1,2,3]. 가 1. 45 250~340 (spontaneous hypertensive rat) 가

[4]. (ischemic tolerance) (22.0 ± 2.0 ), (50 ± 10%), (40~50 phon ), (12 / ) 가

12

[5,6,7,8]. 가 5 5% isoflurane 2% isoflurane heating pad (Harvard Apparatus, Holliston, MA, USA) 37.0 ± 0.5

[7,8]. 가 가 [12,14,15].

(preconditioning) 가 5-0 (sham operation) 4

[9]. / [16,17]. , isoflurane

가 가 가 poly-L-lysine (Sigma, St.Louis, MO, USA) 4-0 (Ethicon, Edinburg, UK) 4

[10,11,12,13,14]. 가 (Sigma, St.Louis, MO, USA) poly-L-lysine (Ethicon, Edinburg, UK) 4-0

Indianapolis, IN, USA) 30  
diaminobenzidine (DAB) (Sigma, St. Louis, MO, USA)

isoflurane

가

2, 3, 5

7.

, 10, 18

Mann-Whitney U

4.

Wilcoxon

ISNT

±

p<0.05

4

/

Longa

5

가

[18]. 4

가

1.

1

(2.57±0.51),

(2.17±0.48)

1,

(p=0.014).

1, 가

1

2. DNA

가 4,

가 0

ISNT

5.

/

urethane peristaltic pump

/

ISNT

가

(Fig. 1)

가

가 (Fig. 2).

rat brain matrix

2 mm

(166.33±349.93)

(1132.08±1363.64)

6. in situ nick translation (ISNT) study

(Fig. 2)(p=0.0457).

DNA

[17]

3 µm

digoxigenin (DIG) dUTP DNA poly-

merase I

가

4

가

DNA

4

[19].

5 pro-

teinase-K

DNA polymerase I

가

(Promega, Madison, WI, USA) 0.1 units/L DIG

DNA labeling mixture (Boeringer Mannheim

Corp., Indianapolis, IN, USA) translation

buffer ([50 mmol/L Tris-HCL] pH7.5, 10mmol/L

14,15,16].

[11,13,

2

MgSO<sub>4</sub> and 50 g/ml BSA) 37 60

30~50%

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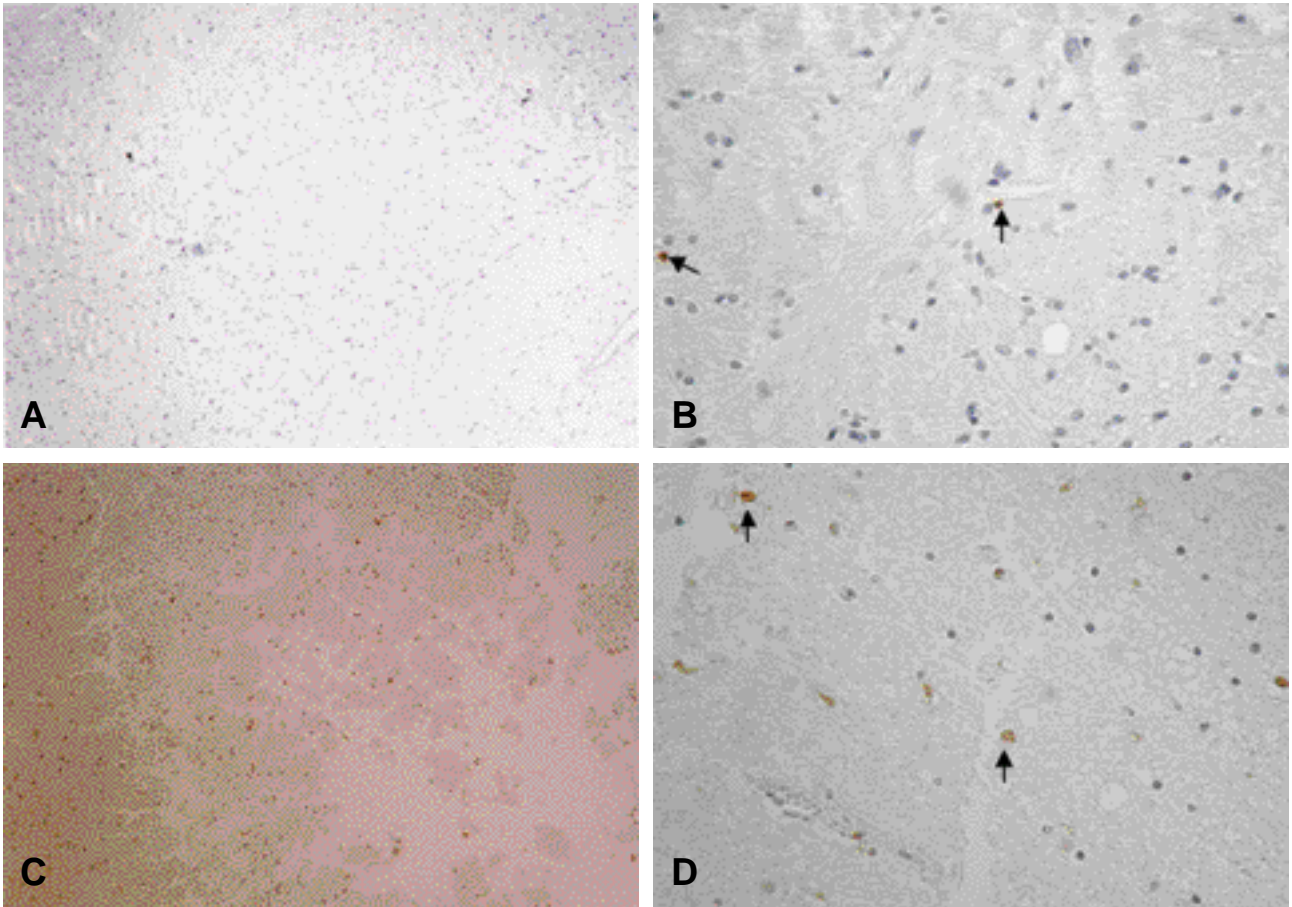
4

. Phosphate buffered saline (PBS)

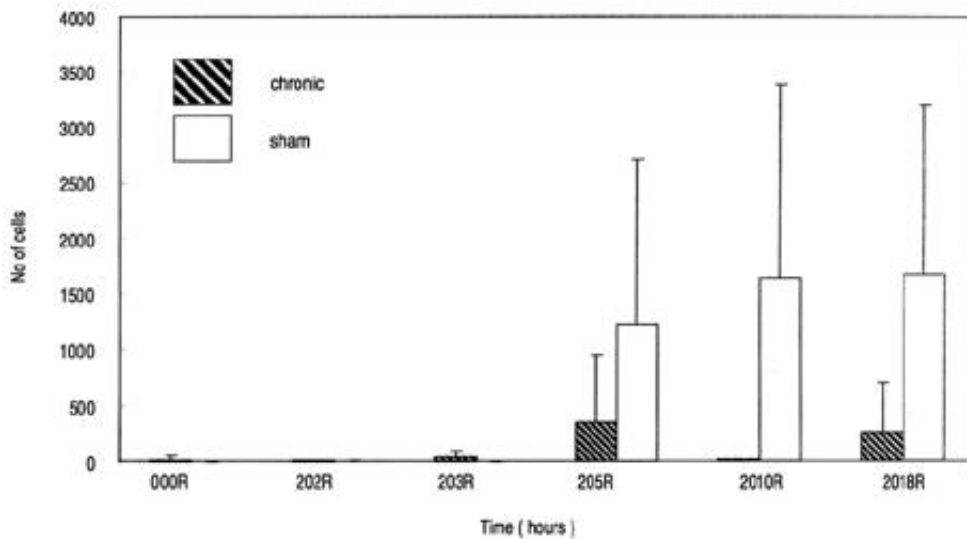
horseradish peroxidase-conjugated

anti-DIG antibody (Boeringer Mannheim Corp.,

[20,21,



**Figure 1.** *In situ* nick translation (ISNT) study in the subjects that underwent middle cerebral artery occlusion for 2 hours/reperfusion for 18 hours (MCAO/R). A, B were pretreated by bilateral common carotid artery ligation (BCAL), and C, D were sham-operated. Many ISNT positive cells were observed in the ischemic core of the sham operated subjects in which focal ischemia was induced by MCAO/R (A, C X100; B, D X400).



**Figure 2.** The number of *in situ* nick translation (ISNT) positive cells at the different time points of reperfusion following middle cerebral artery occlusion for 2 hours. A few ISNT positive cells were observed during the early time point of reperfusion in MCAO subjects that were subjected to bilateral common carotid artery ligation (BCAL). As reperfusion time increased, the number of the positive cells in MCAO subjects that underwent sham operation were markedly increased when compared with those that underwent BCAL (O; occlusion, R; reperfusion).

22,23,24,25,26].

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[11,13,15, 20,24].

[11,13,15,20].

2

가

(ischemic preconditioning) (ischemic tolerance)

가

[4,27,28,29].

가  
(arteriogenesis)  
genesis)

[30,31,32].

(angio

Sparague-Dawley

(3-vessel occlusion)  
(arteriogenesis)  
[31].

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