COX, NMDA, capsaicin, c-fos, substance P, CGRP
COX, NMDA, capsaicin, c-fos, substance P, CGRP

2001 6
2001 年 6 月
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2. L5 (L5) c-fos

3. L5 (L5) SP

4. L5 (L5) SP

5. L5 (L5) CGRP

6. L5 (L5) CGRP

7. L5 (L5) SP

8. L5 (L5) SP

9. L5 (L5) CGRP

10. L5 (L5) CGRP

11. H-E

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1. 5 L5 c-fos

2. 5 L5 SP

3. 5 L5 CGRP

4. 5 L5 SP

5. 5 L5 CGRP
capsaicin, c-fos, substance P, CGRP

MK-801, cyclooxygenase (COX), NMDA

c-fos, substance P (SP), Calcitonin gene-related peptide (CGRP)
MK801, piroxicam, indomethacin, capsaicin. MK801, indomethacin, SP, piroxicam, SP, MK801, capsicin, SP, CGRP. MK801, piroxicam, SP, CGRP. MK801, indomethacin, SP, CGRP. MK801, indomethacin, piroxicam, MK801, capsicin, MK-801, indomethacin, piroxicam.
The page contains text in Chinese and English. The text discusses pain (pain), COX, NMDA receptors, capsaicin, c-fos, substance P, CGRP, prostaglandin, histamine, bradykinin, serotonin, interleukin-1, interleukin-6, and nociceptor (chemical mediators).

Hunt (1987) showed that c-fos mRNA levels in dorsal root ganglion (DRG) increase during inflammatory pain stimulation [20,21]. c-fos expression was also upregulated by morphine [23,27], Besson [6,7,9-18].

Arachidonic acid [arachidonic acid], cyclooxygenase(COX) [cyclooxygenase], prostanoid [prostanoid] [12]. Nonsteroidal antiinflammatory drug (NSAID) [aspirin] [15,19].
COX, prostaglandin, NSAID, spinal intrathecal space, (irritant)
Freund’s complete adjuvant (FCA) mechanical hyperalgesia, (excitatory amino acid receptor) 
N-methyl-D-aspartate (NMDA)-receptor 
prostagladin modulator 
threshold glutamate sensitization 
opioid enantiomers NMDA receptor MK-801 NMDA antagonist (non-competitive NMDA antagonist) MK-801 morphine 
(locomotor-stimulating effects) opioid capsaicin 
(rheumatic arthritis), (osteoarthritis), (diabetic neuropathy), (cluster headache), (postmastectomy pain)
syndrome), (postherpetic neuralgia) (Cordell\Araujo, 1993). COX inhibitor(s) (capsaicin\MK-801 \c-fos, SP, CGRP \COX inhibitor(s) (indomethacin, \piroxicam \MK-801 \c-fos, SP, CGRP \MK-801 \c-fos, SP, CGRP \MK-801 \c-fos, SP, CGRP \MK-801 \c-fos, SP, CGRP \MK-801 \c-fos, SP, CGRP.
II. MATERIALS AND METHODS

1. MATERIALS

200 gm Sprague-Dawley rats were housed in 120 cm cages. (1) indomethacin, (2) piroxicam, (3) NMDA, (4) indomethacin, (5) piroxicam, (6) piroxicam, (7) capsaicin.

2. METHODS

Kaolin was suspended in 0.1 M sodium phosphate buffer, 15 mg/ml, at a concentration of 4%, 0.1 ml/100 g body weight. 2% carrageenan, 0.5 ml/100 g body weight, was injected into the rat hindpaw. The paw oedema was measured at specified intervals.

3. RESULTS

COX inhibitor indomethacin (Sigma chemical co., St. Louis, MO, USA) was administered at 0.5 mg/kg. COX inhibitor piroxicam (Sigma chemical co., St. Louis, MO, USA) was administered at 0.5 mg/kg. NMDA receptor blocker MK-801 (Oclis co., Bristol, UK) was administered at 2 mg/kg. Capsaicin (Sigma chemical co., St. Louis, MO, USA) was administered (10% ethanol, 10% Tween 80, 80% 10% ethanol, 10% Tween 80, 80% ethanol) at 50 mg/kg. The oedema was measured at specified intervals.
4. SUBJECTS

Subjects: indomethacin, piroxicam, MK-801, capsaicin, 24\textdegree C, 12 h, 2\textdegree C, 24 h, 1 h. Sodium pentobarbital, 2% sodium nitrite, 2% heparin, 2% nitric oxide, 2% nitrite, 3% paraformaldehyde, 3% glutaraldehyde, 0.1% picric acid.

For slicing, vibratome is used. The slicing and staining are performed.

5. RESULTS

L5 trige c-fos, SP, CGRP, 1-24, SP, CGRP, SP, CGRP, SP, CGRP.

. c-fos

PBS, 1% sodium borohydride, 3% hydrogen peroxide, 0.02% Triton-X100. Histostain-plus kit (Zymed laboratories Inc., San Francisco, CA, USA), 1:200. Anti-c-fos (Oncogene, La Jolla, CA, USA), 24 h. Diaminobenzidine (DAB, Sigma Chemical Co., St. Louis, MO, U.S.A.).
2. Substances P, CGRP

Substances P, CGRP were analyzed by immunohistochemistry. PBS (0.01 M phosphate buffer, pH 7.4) was used as the washing and staining buffer. For deparaffinization, slides were immersed in xylene and then in a graded series of ethanol for 30 min each. Sections were incubated for 10 min in 3% hydrogen peroxide. Following PBS rinsing, sections were immersed in 1% sodium borohydride for 10 min. Sections were then treated with triton-X100 (0.02%) for 10 min, followed by a 10 min incubation in PBS. Subsequently, sections were incubated for 24 h in Histostain-Plus kit (Zymed Laboratories Inc., San Francisco, CA, USA) at 1:1000 dilution anti-SP antibody (Oncogene, La Jolla CA, U.S.A.), 1:1000 dilution antirat rabbit CGRP antibody (Calbiochem, La Jolla, CA, USA). Sections were then treated in 0.02% diaminobenzidine (DAB, Sigma Chemical Co., St. Louis, MO, U.S.A.) and counterstained with hematoxylin.

6. Discussion

Expression of c-fos, SP and CGRP was examined to determine the effect of administration of SP and CGRP on c-fos expression. SP and CGRP were examined using one-way ANOVA.
III.  

1. II  

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- c-fos  

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- c-fos  

- L5  

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- indomethacin®  MK-801®  c-fos  

- 10 -
...24 h later, c-fos expression was observed in the rats treated with piroxicam, indomethacin, MK-801, L5, and SP. MK-801 treatment induced the highest level of c-fos expression, which was significantly higher than that in the sham group (p < 0.05) (Fig. 1).

At the L5 level, SP stimulation induced a significant increase in c-fos expression compared to the control group (p < 0.05) (Fig. 2). The levels of c-fos expression in the L5 and SP groups were 85694.9 ± 893.0 and 14328.0 ± 364.7 (n=5), respectively. The L5 level of c-fos expression in the L5 and SP groups was significantly higher than that in the sham group (p < 0.05) (Fig. 2). The levels of c-fos expression at the L5 and SP levels were 24 h after the treatment, and the levels of c-fos expression were significantly higher than that in the sham group (p < 0.05) (Fig. 2).

At the L5 level, SP stimulation induced a significant increase in c-fos expression compared to the control group (p < 0.05) (Fig. 2). The levels of c-fos expression in the L5 and SP groups were 85694.9 ± 893.0 and 14328.0 ± 364.7 (n=5), respectively. The L5 level of c-fos expression in the L5 and SP groups was significantly higher than that in the sham group (p < 0.05) (Fig. 2). The levels of c-fos expression at the L5 and SP levels were 24 h after the treatment, and the levels of c-fos expression were significantly higher than that in the sham group (p < 0.05) (Fig. 2).
1. 5°F (L5)  c-fos  MK-801  2°F  c-fos  MK-801  2°F  c-fos  MK-801  2°F  c-fos  MK-801

<table>
<thead>
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<th>2°F</th>
<th>24°F</th>
<th>10°F</th>
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<tbody>
<tr>
<td></td>
<td>0.7±0.58</td>
<td></td>
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</tr>
<tr>
<td>indomethacin</td>
<td>32.0±0.22</td>
<td>17.5±0.23</td>
<td>9.3±0.79*</td>
</tr>
<tr>
<td>piroxicam</td>
<td>8.6±0.16*</td>
<td>6.8±0.17*</td>
<td>4.5±0.35*</td>
</tr>
<tr>
<td>MK-801</td>
<td>1.0±0.16*</td>
<td>6.2±0.17*</td>
<td>12.5±0.51</td>
</tr>
<tr>
<td>capsaicin</td>
<td>1.3±0.15*</td>
<td>5.7±0.56*</td>
<td>0.3±0.52*</td>
</tr>
<tr>
<td></td>
<td>9.6±0.82*</td>
<td>8.0±0.43*</td>
<td>2.0±0.82*</td>
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</table>

* P < 0.05 (one-way ANOVA)
2. In the L5 dorsal horn, the expression of c-fos was significantly increased at 2 hours, 24 hours, and 1 week post-injury compared to the sham group. The expression was further decreased at 24 hours post-injury with the treatment of indomethacin, piroxicam, and MK-801. The expression was also decreased at 1 week post-injury with the treatment of MK-801.

* : P < 0.05 (one way ANOVA)
3. 5(C5) (L5) 555 555 555 555 555 555. 555 555 555 555 555 555 555 555. 555 555 555 555. A. 555; B. 555 555.

<table>
<thead>
<tr>
<th>2. 5(C5) (L5) 555 555 555 555 555 555 555 555</th>
<th>substance P 555 555 555 555 555 555 555 555</th>
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<td>-----------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>A</td>
<td>14328.0±364.7</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>B</td>
<td>85694.9±893.0</td>
</tr>
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<tr>
<td>indomethacin</td>
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<td>-----------------------------------------------</td>
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<tr>
<td>piroxicam</td>
<td>53422.9±901.0</td>
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<tr>
<td>-----------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>MK-801</td>
<td>53424.3±668.7</td>
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<td>-----------------------------------------------</td>
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<tr>
<td>capsaicin</td>
<td>48962.4±642.0</td>
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</table>

- 14 -
P < 0.05 (one way ANOVA)

4. S5 (L5) SP - inflammation, SP - indomethacin, 24hr
SP - piroxicam, 1hr SP - MK-801
2. Substance P

2.1. Substance P

Substance P is a neuropeptide that mediates pain transduction. SP is known to be involved in various physiological processes, including pain sensation. The effects of Substance P on the L5 spinal nerve were investigated (3, 4, 7). The results show that Substance P activates the nociceptors, leading to the perception of pain (3, 7).

Piroxicam, MK-801, and capsaicin were used as controls. The effects of Substance P were compared with the control treatments (3, 3, 6).

382.0 ± 12.5 (n=5)
5. L5 (L5) CGRP in L5 
    indomethacin 
    24 h CGRP in L5

3. L5 (L5) CGRP in L5 

<table>
<thead>
<tr>
<th></th>
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<th>48 h</th>
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<tr>
<td>3.1</td>
<td>38214.0±275.0</td>
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<tr>
<td>3.2</td>
<td>100105.3±587.1</td>
<td>94606.0±635.6</td>
<td>78690.0±922.4</td>
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<tr>
<td>3.3</td>
<td>57853.1±654.9</td>
<td>73983.0±923.9</td>
<td>63606.2±690.6</td>
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<tr>
<td>3.4</td>
<td>74347.7±583.9</td>
<td>68756.4±138.3</td>
<td>60673.2±924.4</td>
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<tr>
<td>3.5</td>
<td>81783.9±759.3</td>
<td>84918.3±435.0</td>
<td>77783.5±651.3</td>
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</tr>
<tr>
<td>3.6</td>
<td>84765.9±706.8</td>
<td>92714.4±621.5</td>
<td>50485.1±711.7</td>
<td></td>
</tr>
</tbody>
</table>

* P < 0.05 (one way ANOVA).
P < 0.05 (one way ANOVA)

6. L5 (L5) CGRP CGRP CGRP CGRP CGRP CGRP CGRP CGRP CGRP CGRP MK-801 CGRP CGRP CGRP CGRP CGRP CGRP CGRP CGRP CGRP
28.6 ± 2.3, 24.8 ± 1.1. Substance P is a potent mediator of pain (4, 8). Substance P levels increased significantly in the substance P group, while substance P levels decreased significantly in the substance P group (4). Substance P levels increased significantly in the substance P group, while substance P levels decreased significantly in the substance P group.

2. CGRP

CGRP is a potent mediator of pain. The levels of CGRP in the CGRP group were significantly higher than in the CGRP group. CGRP levels increased significantly in the CGRP group, while CGRP levels decreased significantly in the CGRP group (4). CGRP levels increased significantly in the CGRP group, while CGRP levels decreased significantly in the CGRP group. CGRP levels increased significantly in the CGRP group, while CGRP levels decreased significantly in the CGRP group.
7. Substance P (SP) and indomethacin. A, 24 h; B, indomethacin.

4. The effect of substance P (SP) on the permeability of capsaicin,
indomethacin, piroxicam, and MK-801. 

<table>
<thead>
<tr>
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<th>24 h</th>
<th>24 h</th>
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<tbody>
<tr>
<td>3</td>
<td>382.0 ± 12.5</td>
<td></td>
<td></td>
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<tr>
<td>7</td>
<td>789.2 ± 2.3</td>
<td>850.4 ± 5.6</td>
<td>758.4 ± 10.2</td>
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<tr>
<td>5</td>
<td>415.0 ± 10.5</td>
<td>402.0 ± 8.6</td>
<td>400.0 ± 6.9</td>
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<tr>
<td>indomethacin</td>
<td>457.6 ± 6.8</td>
<td>513.0 ± 8.6</td>
<td>447.0 ± 10.0</td>
<td></td>
</tr>
<tr>
<td>piroxicam</td>
<td>509.3 ± 7.0</td>
<td>502.0 ± 6.1</td>
<td>498.3 ± 9.6</td>
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<tr>
<td>MK-801</td>
<td>494.6 ± 6.9</td>
<td>514.8 ± 10.5</td>
<td>484.3 ± 8.9</td>
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</table>

*P < 0.05 (one way ANOVA).
Substance P (DRG)

![Bar chart showing Substance P levels at 2hr, 24hr, and 1wk with annotations.

P < 0.05 (one way ANOVA)

8. 5 L5 SP inflamed SP L5 indomethacin SP 2hr 24hr indomethacin SP
3. **Supplemental Experimental Procedures**

   Supplementary experimentation indicates that kaolin and carrageenan promote CGRP displacement. (Figure 5).

   Kaolin and carrageenan are also known to increase COX activity, particularly COX-2, which is inhibited by indomethacin. (Figure 11A). Kaolin and carrageenan further enhance COX activity in a COX-1-dependent manner. (Figure 11B).

   COX activity is significantly reduced by MK-801 capsaiacin, which acts as a scavenger. (Figure 11C, D). NMDA agonists MK-801 and capsaiacin are effective in reducing COX activity. (Figure 11E, F).
5. A. \text{piroxican} ; B. \text{piroxican}.

<table>
<thead>
<tr>
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<th>24 h</th>
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<td>\text{CGRP}</td>
<td>402±11.8</td>
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<tr>
<td>\text{CGRP}</td>
<td>876.3±9.8</td>
<td>873.5±12.5</td>
<td>711.0±10.3</td>
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<tr>
<td>\text{indomethacin}</td>
<td>507.9±8.2*</td>
<td>452.3±5.6*</td>
<td>418.5±8.3*</td>
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<tr>
<td>\text{piroxican}</td>
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<td>409.0±5.9*</td>
<td>451.0±9.5*</td>
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<tr>
<td>\text{MK-801}</td>
<td>579.0±9.6</td>
<td>520.4±7.9*</td>
<td>402.0±13.1*</td>
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<tr>
<td>\text{capsaicin}</td>
<td>650.1±13.5*</td>
<td>601.2±12.6*</td>
<td>579.2±11.1</td>
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</tr>
</tbody>
</table>

* \text{P<0.05 (one way ANOVA).}
* * * * * * *

**P < 0.05 (one way ANOVA)**

* * *
11. A, B, C, indomethacin; D, piroxicam; E, MK-801; F, capsaicin (× 100).
IV.  

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Àý±¸½É¼º¼¶À¯·Î²0%°üÀû¹üÀ§ÀǰüÀý¿îµ¿¿¡¹ÝÀÀ
Çϴ¼¶À¯µé·Î¼­À¯ÇØÇѹüÀ§Àǿ³¹ÝÀÀÀÌÁõ°¡µÈ´Ù
Á¦¥±±ºÀº»ý¸®Àû¹üÀ§ÀǰüÀý¿îµ¿¿¡´Â¹ÝÀÀÇÏÁö¾Ê°íÀ¯ÇØÇÑ
¹üÀ§Àǿ³¹ÝÀÀÇϴ½Ű涣À¯µé·Î³»Ãø¹«¸­°üÀý±¸½É¼º¼¶À¯ÀÇ
33%°üÀû¿îµ¿¹üÀ§¿¡¼­´Â¾àÇѹÝÀÀÀ»º¸ÀÌ´Ù°¡À¯ÇØÇѹüÀ§Àǿ³¹ÝÀÀ
ÀÌÅ©°ÔÁõ°¡µÇ´Â¼¶À¯µé·Î³»Ãø¹«¸­°üÀý±¸½É¼º¼¶À¯
ÀÇ
3 7 . °üÀýÀÇ
¿°Áõ¹ÝÀÀÀÌÀϾ°æ¿ì¿¡´Â°ÅÀÇ´ëºÎºÐÅëÁõÀ̵¿¹ÝµÇ¸ç
prostaglandin, histamine, bradykinin, serotonin, interleukin 1, interleukin 6, SP µî¸¹ÀºÁ¾·ùÀÇÈ­ÇиŰ³¹°Áú
ÀÌ¿°Áõ¼¼Æ÷¿Í¼Õ»óµÉ°æ¿ì¸·ÁöÁú¿¡¼­À¯¸®µÈ
arachidonic acid ·ÎºÎÅÍ COX ¿¡ÀÇÇØÇÕ¼ºµÈ´Ù
À̹ۿ¡µµ°üÀý¿°ÀÇ¿°Áõ¼ºÅëÁõ°ú°ü·ÃÀÌÁ¦±âµÇ°íÀִ¹°Áúµé·Î´Â³ªÅ¸³»´Â°ÍÀ¸·Î¾Ë·ÁÁ®ÀÖ´Ù
40,41 . Prostaglandin¿¡´ëÇØ¼­´ÂÀ߾˷ÁÁ®ÀÖÁö¾Ê´Ù
NGF(Nerve Growth Factor)¿¡µµ°üÀý¿°ÀÇ¿°Áõ¼ºÅëÁõ°ú°ü·ÃÀÌÁ¦±âµÇ°íÀִ¹°Áúµé·Î´Â
interleukin
cytokine NGF trk A NGF trk A SP CGRP NGF trk A 42, 43, 44 NGF trk A NGF trk A (NSAID-COX inhibitor) 42, 43, 44. COX indomethacin piroxicam NMDA receptor antagonist MK-801 capsaicin kaolin carrageenan c-fos mRNA c-fos 2 c-fos 31, 35 c-fos 31, 35 c-fos (globus pallidus) (pontine nucleus) Hunt (1987) Sagar (1988)
Aspirin is a COX inhibitor that decreases prostaglandin production. NSAIDs also inhibit COX and prostaglandin production.

45. c-fos mRNA levels were increased 3-fold in the c-fos knockout mice compared to wild-type controls. This suggests that c-fos may play a role in NSAID-induced analgesia.

46. Buritova and Besson (1998) observed that carrageenan-induced paw edema was reduced by c-fos expression after treatment with indomethacin or piroxicam.

47. Zhang (2000) found that arachidonic acid increased c-fos mRNA levels in COX-2 expressing cells. This suggests that c-fos may be involved in the pro-inflammatory effects of COX-2.

48. AP-1 activity was increased in the COX-2 expressing cells treated with prostaglandin. This suggests that AP-1 may be involved in the pro-inflammatory effects of COX-2.

49. Aspirin, a COX-1 inhibitor, decreased prostaglandin production and inhibited COX activity. This suggests that COX inhibitors may be effective in reducing inflammation and pain.
phospholipase\textsuperscript{A} arachidonic acid cyclooxygenase prostaglandin H2 prostaglandin D2, prostaglandin E2 prostaglandin F2a prostaglandin, prostacyclin thromboxane nonsteroidal antiinflammatory drug (NSAID) COX\textsubscript{1} constitutive COX-1 constitutive, bacterial endotoxin, growth hormone, cytokine inducible form prostaglandin COX\textsubscript{2} constitutive immediate early gene prostaglandin prostaglandin sensitization prostaglandin COX-2 hyperthermia interleukin(IL)-1 pyrogen prostaglandin prostaglandin COX-1 COX-2 indomethacin COX-1 piroxicam piroxicam c-fos


...and, 11 inhibited the C-fiber activity, whereas SP 

55. SP 

B-endorphin 56,57, SP  

56 c-fiber Aδ fibers 57. C-fiber Aβ activity 56,58. C-fiber Aδ activity 59, SP  

intrathecal injection) 60. SP  

nociceptive behavior) 61,62, CGRP  

calcitonin 63,64, CGRP  

63. CGRP  

64,65, CGRP  

63,66-70. CGRP  

67,71,72, CGRP  

67,73, SP  

capsaicin 64, SP  

CGRP  

74. SP  

CGRP  

60,75,77. SP  

CGRP  

68. SP  

CGRP  

78-80, SP  

81. SP  

CGRP  

82. SP  

CGRP  

83. SP  

intrathecal injection) 20. SP  

CGRP  

21. SP  

CGRP  

22.

- 34 -
CGRP and DRG neurons also express COX-2. COX-2 expression is increased by treatment with MK-801, capsaicin, and SP. The expression of the immediate early gene c-fos is induced by MK-801, capsaicin, and SP. COX-2 and NMDA receptor expression is also induced by these treatments. The expression of the immediate early gene c-fos is induced by MK-801, capsaicin, and SP. COX-2 and NMDA receptor expression is also induced by these treatments.
V.  ...

... COX, NMDA, MK-801, capsaicin, NMDA, c-fos, SP, CGRP, SP, CGRP, SP, CGRP, SP, CGRP.

1. c-fos, SP, CGRP, MK801, piroxicam, indomethacin, capsaicin.

2. indomethacin, SP, SP, SP, SP, CGRP, SP, SP, 24h, 1h, SP.

3. piroxicam, SP, SP, CGRP, SP, SP, SP, (1h), SP, SP, CGRP, 1h, SP.

4. MK 801, SP, CGRP, SP, SP, CGRP, MK-801, SP, CGRP, SP.

5. Capsaicin, SP, SP, CGRP, SP, CGRP, SP, CGRP, SP, CGRP.
indomethacin, piroxicam, MK801, capsaicin 对于软骨下骨疼痛的治疗均上调 c-fos 表达。DRG SP, CGRP 在炎症性疼痛中促进 c-fos 表达，这可能与痛觉过敏相关。
IV. ツツツツ


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Abstract

Morphometric study of the effects of various analgesic compound in experimental arthritis model.

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(Directed by Associate Professor Won Taek Lee and Jong Eun Lee)

Arthritis is the most common disease of joint in old age and almost all the old human are suffering from arthritis. Arthritis gives so severe pain hard to endure that it can devastate human. But we still do not know where the arthritic pain comes from and the generation mechanism of it.

For the study of effects of anti-inflammatory drugs on the c-fos immunoreactive neurons, substance P- and CGRP-immunoreactive neurons in dorsal horn and DRG, cyclooxygenase (COX) inhibitors indomethacin (0.5mg/kg), piroxicam (0.5mg/kg), NMDA receptor antagonist MK 801 (2mg/kg), and capsaicin (50mg/kg) were administered to the experimental arthritis model. Male Sprague-Dawley rats were used for this study. Arthritis was induced by injection of 4% kaolin followed by 2% carrageenan into the articular capsule of left knee. Two hours, 24 hours and 7 days after injection, animals were sacrificed and processed for immunohistochemical staining for c-fos in spinal dorsal horn, for substance P (SP) and CGRP in DRG.

The results were as follows; 1. The number of c-fos immunoreactive neurons were significantly decreased at 2h after piroxicam and MK-801 administration and 1 week after indomethacin, MK-801 and capsaicin treatment in the inflamed side of dorsal horn. 2. There were the significant decrease of SP- and CGRP-immunoreactive area 2h after indomethacin administration and 1week after capsaicin treatment in the inflamed side of dorsal horn. 3. The number of SP- and CGRP-immunoreactive neurons in DRG were decreased after drugs administration.
and no difference is in the degree of effectiveness between drugs. Indomethacin and piroxicam which is an inhibitors of COX, significantly reduced the expression of c-fos proteins and desensitized nociceptive primary afferents at the early time, and capsaicin, a pungent algesic substance, decreased the level of c-fos protein, SP and CGRP over a wider time in dorsal horn and DRG.

Key Words : cyclooxygenase inhibitor, NMDA receptor antagonist, capsaicin, c-fos, substance P, CGRP, spinal dorsal horn, dorsal root ganglia, pain, experimental arthritis