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# EFFECTS OF OPIOID SUBTYPES ON BLADDER OVERACTIVITY IN RATS WITH CEREBRAL INFARCTION

### Aims of Study

To determine the influence of different opioid peptides on bladder hyperactivity after left middle cerebral artery (MCA) occlusion, cystometric recordings were obtained from conscious rats.

## **Methods**

For this study, female Sprague-Dawley rats weighing 200-270 g. were used. A bladder polyethylene catheter was inserted at the apex of the bladder dome and a stainless steel cannula for intracerebroventricular administration was implanted into the right lateral ventricle under halothane anesthesia. After the animals had recovered from the anesthesia, control cvstometrography (CMG) was performed for two hours, using physiological saline at room temperature at a constant rate of 0.04 ml./min. This was followed by occlusion of the left MCA with 4-0 monofilament nylon thread under halothane anesthesia. In sham-operated (SO) rats, the same procedures except for the MCA occlusion were performed. Two hours after the induction of MCA occlusion or sham operation, CMG was again performed while the animals were conscious. DAGO ([D-Ala<sup>2</sup>,Phe<sup>4</sup>,Gly<sup>5</sup>]-enkephalin, mu agonist), DPDPE ([D-Pen<sup>2,5</sup>]enkephalin, delta 1 agonist), deltorpin II (delta 2 agonist), and U-50488 (kappa agonist) were administered intracerebroventricularly (1 µl.) at graded doses (0.1, 1, 10, 100, 1000 ng.). The drug dosage was increased at 60 minute intervals. Bladder capacity, residual volume, micturition threshold pressure, and bladder contraction pressure were determined from each the CMGs. Finally the rat brain was stained by perfusing it with 2% 2,3,5-triphenyletrazolium, and the volume of the infarction was measured.

#### **Results**

Bladder capacity in conscious rats was significantly reduced after the left MCA occlusion. Intracerebroventricular administration of DAGO and DPDPE significantly increased bladder capacity in cerebral infarcted (CI) and SO rats, but differences between the CI and SO rats were mostly small or insignificant (Fig. 1, 2). Deltorpin II at any dose did not produce any change in bladder capacity in both CI and SO rats (Fig. 3). Intracerebroventricular administration of U-50488, on the other hand, significantly increased bladder capacity in CI rats but not in SO rats (Fig. 4). None of the drugs at any dosage affected residual volume, micturition threshold pressure, or bladder contraction pressure. The mean infarcted volumes (DAGO: 202.1 +/- 10.4 mm<sup>3</sup>, DPDPE: 201.9 +/- 15.7 mm<sup>3</sup>, deltorpinII: 207.0 +/- 12.9 mm<sup>3</sup>, U-50488: 203.1 +/- 15.2 mm<sup>3</sup>) were not statistically different from those observed in the vehicle-treated rats (209.6 +/- 13.2 mm<sup>3</sup>).



Figure 1-The effect of DAGO on bladder capacity





\*: p< 0.05

Figure 3-The effect of deltorpin II on bladder capacity







\*: p< 0.05, \*\*: p< 0.001

# **Conclusions**

Intracerebroventricular administration of U-50488 significantly increased bladder capacity in CI rats but not in SO rats. This result indicates that the kappa opioid receptor on the supraspinal central nervous system may play a role and may be a target for medication in bladder hyperactivity after cerebral infarction.