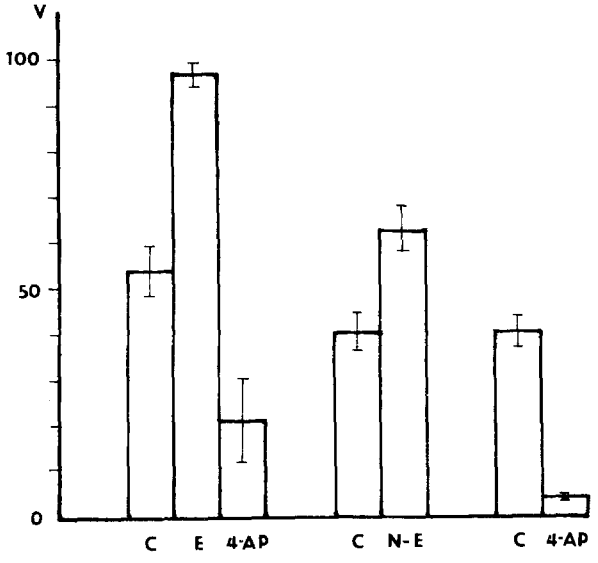

Figure 2. Changes of the average SD threshold (ordinate) elicited by DAME (E), 4-aminopyridine (4-AP) and naloxone (N). C: untreated cortex. E: 30–60 min after local application of DAME. 4-AP: 30 min after application of 4-aminopyridine to the DAME treated cortex. N–E: 30–60 min after application of DAME to naloxone (1 mg/kg) pretreated rats. 4-AP: 30–60 min after 10-min treatment of intact cortex with 4-aminopyridine.

that the 4-aminopyridine counteracts the DAME induced inhibition.

The specificity of the DAME effect, is confirmed by its attenuation in the naloxone-treated rats. Partial suppression of the DAME elicited cortical SD by naloxone was reported by Sprick et al.[7] but the reduction of the DAME induced increase of SD threshold seems to be a more consistent manifestation of the DAME-naloxone antagonism.

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0014-4754/85/050625-03$1.50 + 0.20/0
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Naloxone prevents the analgesic action of α-MSH in mice

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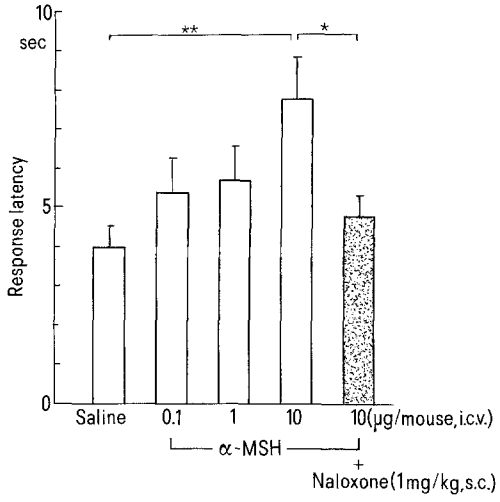
Summary. α-MSH (0.1, 1, 10 μg) was administered intracerebroventricularly and its action on pain sensitivity was investigated by the hot-plate method in mice. α-MSH produced dose-dependent analgesia and this analgesic effect was prevented by naloxone (1 mg/kg, s.c.). It is possible that α-MSH may play a role in the mechanism of pain through endogeneous opioid systems.
Key words. α-MSH; analgesia; naloxone.

α-MSH, one of the neuropeptides, is released, stored by the intermediate lobe of the pituitary[1] and widely distributed in the central nervous system[2]. Various studies concerning the effects of MSH on learning and memory processes have been reported[3,4]. On the other hand several interactions between opiates and MSH have been reported[5,6]. Morphine and β-endorphin induce an increase of plasma α-MSH levels[7]. Furthermore, it is reported that α-MSH elicits excessive grooming[8] and that the peptide-induced behavior could perhaps reflect the agonistic properties on the opiate recepter[9]. The present study was carried out to examine the involvement of α-MSH in the development of analgesia.

Male ddY strain mice weighing 20–22 g were used after acclimatization in a breeding room for one week. To test the analgesic action of α-MSH, the hot-plate method as described by Woolfe and Macdonald[10] was used. Mice were placed on the hot-plate (55 ± 0.5 °C) and the latency to the response (licking the feet, jumping or rapidly stamping the feet) was recorded. α-MSH dissolved in 0.9% NaCl solution was injected intracerebroventricularly (i.c.v.) in a volume of 5 μl. I.c.v. injection was made at the coordinates described by Haley and McCormick[11]. A microsyringe equipped with a 27 gauge needle was used. 5 min after the i.c.v. injection of MSH, pain sensitivity was measured. In order to study the interaction of MSH analgesia with opioid peptides, naloxone was administered s.c. 5 min before the MSH injection.

As can be seen in the accompanying figure, central administration of α-MSH had a dose-related analgesic action. It is proposed that α-MSH acts either directly or indirectly to activate the release of endogeneous agents which produce analgesia. Since α-MSH analgesia is prevented by naloxone, this released endogeneous substance probably interacts with opioid receptors. It is reported that MSH is metabolized very rapidly, i.e. in approximately 2 min[12]. So, in the present study, experi-

ments were carried out 5 min after i.c.v. injection of MSH. Only the 10 μg dose of α-MSH produced analgesia during 20 min period. Sandman and Kastin report that intraventricular administration of MSH induces hyperalgesia in rats. Our present data contrast strikingly with their findings and may suggest the existence of some species differences in the capacity of rats and mice to activate the opioidergic system in response to MSH. There is an evidence that an analog of $ACTH_{4-9}$ produces significant analgesia, and it is reported that physiologically β-endorphin and ACTH may have effects that are functionally similar in nature[13]. ACTH, α-MSH and β-endorphin coexist within the arcuate nucleus and pituitary cells[14,15]. And it is also reported that α-MSH induces excessive grooming similar to that seen with ACTH and β-endorphin[8] and that the grooming activity correlates well with the intrinsic analgesic activity of these LPH fragments[9]. We also observed that α-MSH elicited grooming in concurrence with analgesic action and these were reversed together by naloxone. These suggest that MSH may have a functional role in the analgesic mechanism similar to those of ACTH and β-endorphin.



The control group received saline i.c.v. and s.c. Each histogram represents the mean ± SE of 12 animals. * $p < 0.05$. ** $p < 0.01$.

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0014-4754/85/050627-02$1.50 + 0.20/0
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Magnesium enhances human pancreatic elastase digestion of ^{125}I-labeled elastin

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Summary. The effect of some divalent cations, especially Mg^{++}, on elastinolysis by porcine or human pancreatic elastase has been determined using ^{125}Iodine-labeled elastin as substrate. Elastin degradation was significantly increased in the presence of 10^{-3} M Mg^{++}. If elastin was pre-incubated with 0.5 (w/v) Triton, there was a further increase in elastinolysis to 2.6 times the original rate.
Key words. Porcine and human pancreatic elastase; elastin; Triton-Mg^{++}.

Previous attempts to establish the effects of cations and or anions as well as other modifying agents on pancreatic elastase digestion of insoluble elastin have yielded ambiguous results[1-3]. Although it is known that an increase in extracellular Mg^{++} concentrations induces relaxation and vasodilation, and hypomagnesia can potentiate contractile activity, the role of Mg^{++} in the genesis of vascular diseases[4] and the relationship between Mg^{++} levels and atherosclerosis is poorly understood. Even less is known with regard to connective tissue metabolism. Bernier et al.[5] reported that Mg^{++} increased the initial velocity of elastinolysis two-fold at 10^{-2} M concentration. This activation is of great potential interest especially as it may enhance the activity of human pancreatic elastase II which when purified according to Largman et al.[6] or Rabaud et al.[7] exhibits only 30% of the activity of the same amount of porcine pancreatic elastase. In the present study we have explored the effect of Mg^{++} on the elastinolysis of ^{125}I-labeled elastin as well as the role of some other factors in the modulation of the activity of porcine and human pancreatic elastases on insoluble labeled elastin.

Materials and methods. Porcine pancreatic elastase purified by the method of Shotton[8] was obtained from Choay (Paris). Its elastinolytic activity was determined in our laboratory by comparison with known standards of elastase from Elastin Prod-