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PHYSIOLOGY

Pain Sensitivity of Trout and Analgesia Induced by Intranasal Administration of Dermorphine

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Pain is the major sense in vertebrates that performs signaling and protective functions in the case of potential damage to the body. The problem of pain, which is of prime importance for humans, is extensively investigated in higher vertebrates [1], However, only a few works have attempted to study the sense of pain in fish. Verheijen [2] regarded a kind of "cough" observed in carps on damaging their mouth with a sharp hook as a manifestation of pain. Other authors showed that morphine, an exogenous analgesic compound, rose the threshold of pain induced in goldfishes by electrical stimulation [3]. In lampreys, the spinal cord and trigeminal ganglion contain the cells that respond by discharges on pressure applied with a strength that could damage the skin [4]. These studies suggest that fishes, like higher vertebrates, have a system of pain reception.

This work was designed to study dermorphin (Y-dA-F-G-Y-P-S), one of the strongest mammalian endogenous analgesic opioids on pain sensitivity of rainbow trout.

Experiments were performed with a total of 42 rainbow trout *Oncorhynchus mykiss* weighing 200 - 400 g taken from a trout-breeding farm. An originally designed electromechanical system was used to record the strength developed by the caudal trunk in response to painful (mechanical or electrical) stimulation. The fish were semirigidly fixed (by the oral and thoracic fin) in a flow chamber so that the upper part of the head and olfactory organs remained above water. A recording device was fastened to the wall of the chamber, and a movable plexiglas fork held the caudal trunk caudally of the adipose fin. When the fish moved its caudal trunk in response to nociceptive stimulation, the locomotor reaction was recorded in terms of the impulse of the developed force (N·s) using a specially designed electronic integrator with a digital display. The nociceptive stimulus was produced by strongly compressing the fin with scissors; which did not mechanically damage the organ, puncturing skin with a needle; or stimulating the caudal fin with a 0.1-s train of 30 electric pulses of O.5 ms each. The stimulating electrodes were inserted into the caudal fin in order to exclude the direct stimulation of muscle fibers. The amplitude of the stimulus was adjusted individually for each fish. The recording system was synchronized with the nociceptive stimulus. The fish nociceptive sensitivity was measured at 5-min intervals for 1 h before and 1 - 2 h after administration of dermorphin (0.20, 0.30, 0.40, 0.50, 0.60, and 0.75 mg/kg). The drug was dissolved in 20 μl of distilled water and injected simultaneously into both olfactory sacs. Control fish received injections of 20 μl of distilled water. Changes in nociceptive sensitivity were expressed in percentages of the preinjection level. The data were processed using the Wilcoxon-Mann-Whitney test [5].

Our results indicate that trouts reacted to most nociceptive stimuli with a strong movement of the caudal trunk. The reaction was not observed in rare cases (7%). The caudal fin, both dorsal fins, the thoracic fin, the skin around the eyes, and the epithelium of olfactory sacs were the most sensitive nociceptive zones; the skin on the head and trunk was less sensitive. As pointed out earlier, the effects of dermorphin were studied by applying nociceptive stimuli to the region of the caudal fin, because the stimulation of its selected areas evoked reproducible responses. Intranasal administration of dermorphin caused a concentration-dependent decrease in the nociceptive sensitivity by 12 - 55% (Fig. 1). The concentrations of 0.60 and 0.75 mg/kg were the most effective. The analgesic effect was usually observed within minutes after injections and lasted for at least 1 h (up to 2 - 3 h in some fish). Repeated administration of dermorphin after 30 min produced further (approximately by 30%, $p < 0.05$) decreases in pain sensitivity. The most reproducible reactions were observed in 200-g specimens aged 2 years. The specimens weighing 300 - 400 g displayed unstable responses to dermorphin; individual fish even showed an increase in pain sensitivity, probably because of the maturation of sex products. However, gonads were not examined in this study.

Thus, dermorphin, when injected into the olfactory sacs, produced a significant analgesic effect on rainbow trout.

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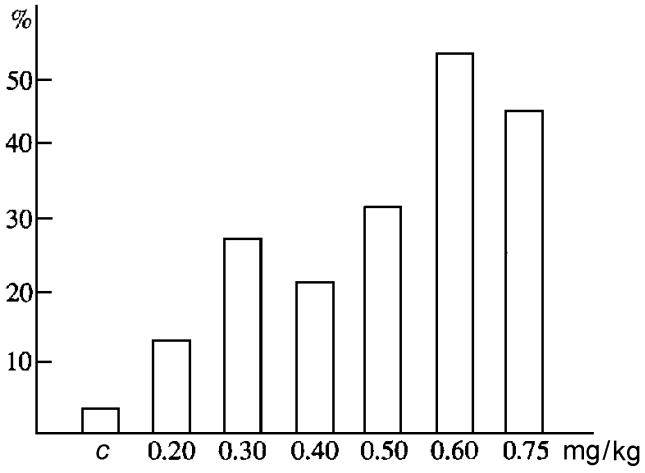

Fig. 1. Changes in pain sensitivity (mean analgesic effect) within 1 h after intranasal administration of dermorphin to rainbow trout. All changes from the control level (*c*) are statistically significant ($p < 0.01$).

In rats, intranasal dermorphin produced much stronger analgesic effects than intraperitoneal injections [6]. The analgesic effect of dermorphin injected into olfactory organs was observed in White Sea cod. The action of this peptide on the central nervous system after intranasal administration is not clear [7]. However, our data suggest that fishes, like higher vertebrates, possess, at least partly, the system of nociception. The method described in this paper permits the functional characterization of this system.

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