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PHARMACOETHOLOGIC STUDY OF ANALGESIA INDUCED BY INTRASPECIFIC CONFRONTATION

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Psychological aspects of pain and analgesia, especially under conditions of intraspecific conflict, have so far received little study. One line of research in this field is to study dependence of pain perception and response to pain on experience of victory or defeat in intraspecific conflicts. For a long time the view has been held that in a situation of conflict, confrontation, fighting, or strong emotions, pain sensation is depressed. This phenomenon, in its general form, has been named "stress-induced analgesia," and its experimental principles have been established [15]. However, pharmacoethologic aspects of this phenomonon have not been analyzed in detail.

The aim of this investigation was to study the dynamics of pain thresholds in animals under intraspecific confrontation conditions (fighting), when one animal is the attacker, another is simply the defender, which loses the fight. The aims of the investigation also included a pharmacoethologic analysis of the phenomenon of analgesia induced by intraspecific confrontation.

EXPERIMENTAL METHOD

Experiments were carried out on 49 male CC57BL/6 mice, 35 of which were kept in groups (10 at a time), and 14 mice were kept in isolation in single cases. Only highly aggressive dominant mice were isolated, and only those animals whose latent period of first attack did not exceed 5 sec were used in the experiments. In special tests nonaggressive grouped mice were subjected to "measured" (controlled) attacks from dominant mice on their territory in single cages. Each cycle of attack was limited artificially to 20 bits, which induced submissive and defensive behavior in nonaggressive mice in the form of specific acts and postures [2, 4].

Pain thresholds in dominant and subordinate mice were measured in seconds by the tail flick test, with heating from focused light, by means of a special instrument with automatic recorder. Measurements were made before attacks and 2, 5, 15, 30, 45, and 60 min after 20 attacks. Success of the attacks was monitored by analysis of the behavior of the mice which were defeated — they lay on their side, then stood vertically in a defensive posture, and very rarely, lay supine, with the ventral surface toward the oponent [1-3]. Analgesia was considered to be complete if the mice did not flick their tail in the course of over 14 sec.

For pharmacologic analysis of the phenomenon, naloxone, an antogonist of opiate receptors, in doses of 0.1-1 mg/kg, and the GABA antagonist bicuculline, in doses of 1-2 mg/kg, were used. All drugs were injected intraperitoneally.

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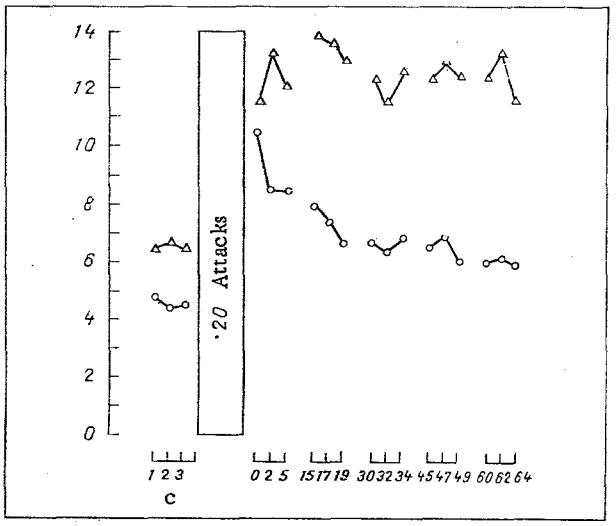

Fig. 1

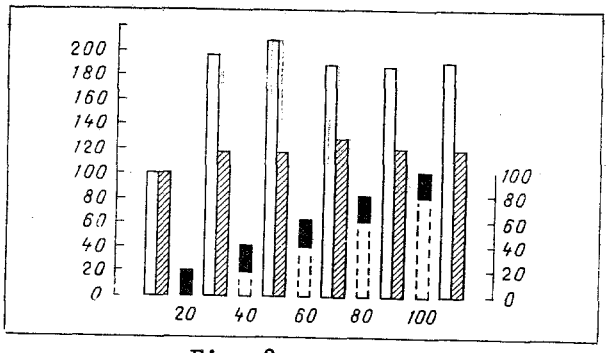

Fig. 2

Fig. 1. Changes in pain threshold in dominant (circles) and submissive (triangles) mice after intraspecific confrontation, including 20 attacks with bites. Horizontally — time (in min); vertically — latent period of tail flick (in sec). C) Control.

Fig. 2. Effect of naloxone on pain thresholds in submissive animals after several series of attacks by dominant mice. Vertically: on left — latent period of tail flick (in % of initial level), on right — cumulative number of attacks. Unshaded column — control, obliquely shaded — naloxone 1 mg/kg, shaded black — number of attacks in one series, broken lines — cumulative number of attacks.

EXPERIMENTAL RESULTS

Pain thresholds in defeated mice, adopting vertical defensive stances, were found to be sharply raised in a situation of intraspecific confrontation 2-5 min after a series of attacks (the rapid component of response) and they remained high for 1 h (delayed component of response). Pain thresholds in attacking mice (victors) after a transient rise 1-5 min after the fight quickly returned to their initial levels, i.e., the delayed component of response was poorly defined in these animals (Fig. 1).

In a separate series of experiments in which the number of attacks on the submissive animal increased in time (from 20 to 100 attacks with bites in five consecutive cycles of attacks) and with testing of pain thresholds after every 20 attacks, it was found that the increase in pain thresholds, i.e., maximal tolerance to pain, occurred after the first two cycles of attacks (Fig. 2), after which (60-100 attacks) there was no strengthening of the analgesia. Stability and low variability of intraspecific behavior of the defeated mice were noted: The behavioral spectrum was drastically narrowed, intraspecific sociability was absent, free movements over the territory was absent, definsive and submissive acts or static sitting predominated.

Analgesia induced by intraspecific confrontation and fighting has a definite opiate-dependent component, for injection of naloxone, 0.1 mg/kg, significantly reduced the delayed component, and an increase in the dose to 1 mg/kg also reduced the rapid component of response. Naloxone in a dose of 1 mg/kg counteracted the developing analgesia induced by prolonged attacks on submissive animals (Fig. 2).

The GABA antagonist bicuculline, in doses of 1 and 2 mg/kg, did not induce changes similar to those of naloxone in pain thresholds but, on the contrary, bicuculline itself significantly raised the initial pain thresholds. Against the background of bicuculline, attacks with bites induced a relatively small (10-15%) rise in the thresholds. Evidently the GABA-ergic component does not play such an important role in the mechanisms of confrontation-induced analgesia as the opiate component.

Under conditions of intraspecific confrontation of animals inhibition of pain sensation thus takes place; its dynamic differs in attacking and defeated animals. The situation of agonistic interaction is a stress situation for animals of both groups, but this stress is manifested to a greater degree and mainly in submissive animals.

Incidentally, analgesia induced by defeat in an intraspecific fight is reversed by naloxone (but not by bicuculline), whereas analgesia induced by electric shocks to the limbs (duration of the period of stimulation under 30 min) is not reversed by naloxone, evidence of differences in the mechanism and specific nature of the action of pain in an intraspecific fight situation [7]. This state of affairs can be conformed by facts indicating that analgesia from cold water is not transmitted by opiate mechanisms [6].

Meanwhile, evidence in support of opiate mechanisms of analgesia induced by defeat in fighting is given by data [7] on cross-tolerance between morphine-analgesia and analgesia induced by defeat in fighting. The relative stability of the rapid component of this analgesia to naloxone may to some extent be explained by the multicomponent nature of the mechanisms of its origin (the role of ACTH and of other neuropeptides and hormones in the formation of this component of the response to pain and stress-intraspecific confrontation is not ruled out).

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