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Prostaglandin E_1 Fever in the Crayfish *Cambarus bartoni*

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CASTERLIN, M. E. AND W. W. REYNOLDS. *Prostaglandin E_1 fever in the crayfish* Cambarus bartoni. PHARMAC. BIOCHEM. BEHAV. 9(5) 593–595, 1978.—Groups of 10 crayfish were injected with prostaglandin E_1, at 1 of 3 pharmacological doses (0.5, 0.1 or 0.05 mg), into the haemocoel, and individually allowed to thermoregulate in electronic shuttleboxes for 24 hr. The mean preferred temperature of each group was then compared with their mean preferred temperature for 24 hr prior to injection, and with the mean preferred temperature of 10 crayfish injected with pyrogen-free saline. Dosage-dependent increases in preferred temperature were observed in the crayfish injected with PGE_1, ranging from 1°C at the lowest dosage to 3.4°C at the highest dosage, above the normal thermal preferendum for this species of 22.1°C.

Fever Prostaglandin E_1 Thermoregulation Thermoregulatory behavior Preferred temperature Crayfish *Cambarus bartoni*

PROSTAGLANDINS of the E series have been shown to induce fever in a number of vertebrate animals [1, 5, 9, 22], although the precise nature of their role in thermoregulation and fever has been a subject of considerable controversy [7]. PGE fever has been shown to be mediated behaviorally [9,14] as well as physiologically. Febrile responses can be induced by various pyrogens in ectothermic organisms, in which fever is mediated entirely by behavioral means [2–4, 6, 12, 14, 16–19]. Lower vertebrates are capable of quite precise behavioral thermoregulation [2–4, 6, 12, 15–20], and neuroamines which have postulated thermoregulatory roles in the CNS control of body temperature in mammals also affect the preferred temperatures of fishes [10,11]. There is an experimental advantage in studying behavioral thermoregulatory responses, in that they are overt and easily observed and quantified [6, 11, 14–20].

The ability to thermoregulate behaviorally has also been demonstrated in invertebrate animals, including crayfish [4, 8, 13]. Although very little is known of the central neural mechanisms controlling thermoregulation in decapod crustaceans [4], it has been demonstrated that they, like vertebrates, exhibit a behavioral fever when injected with bacterial pyrogens [4]. Fever has been shown to have adaptive value in enhancing survival from infection in lizards [2,12] and in fish [6]. The phylogenetically widespread distribution of fever suggests that it plays some significant role in host defense responses to infection [2, 6, 12]. The purpose of the present investigation was to determine whether prostaglandin E_1 would induce fever when injected into the crayfish *Cambarus bartoni* (Arthropoda: Crustacea: Decapoda).

METHOD

Forty crayfish (*Cambarus bartoni*), weighing approximately 8 g each, were tested individually in electronic shuttleboxes, described elsewhere [15,20]. This device (Ichthyotron) permits an animal to control, by its movements, water temperature (and, thereby, its own temperature). Each animal was allowed an initial 24 hr to attain its final thermal preferendum [21]—negating any effects of prior acclimation temperature, which are expressed only in acute preferenda—and then was tested for an additional 24 hr to obtain baseline preferendum data. Then each animal was injected with 0.1 ml of saline containing 0.05, 0.1 or 0.5 mg of PGE_1 (groups of 10), or with saline alone (N=10), or handled but not injected; after which each animal was tested for an additional 24 hr period for comparison with the pretreatment baseline (Fig. 1). Twenty-four hr periods were used to control for circadian-rhythm effects [4–6, 8, 15–19, 21]. Massive pharmacological doses of PGE_1 were used to induce a response of sufficient magnitude and duration to produce a significant 24-hr increase over the control period, and also because of uncertainty concerning how much PGE_1 injected into the haemocoel might reach the active thermoregulatory site (presumably in the CNS, but the location in crayfish is unknown).

RESULTS

The control groups, either injected with pyrogen-free saline, or handled but not injected, exhibited no significant difference (t-test, 0.05) in preferred temperature from the 22.1°C mean characteristic of all animals during the initial 24-hr test period prior to treatment. Animals injected with PGE_1 exhibited a dose-dependent febrile response (Fig. 1) of 1 to 3.4°C above the normal 22.1°C baseline ($\Delta T=0$ in the figure). These increases were statistically significant (t-test, 0.05).

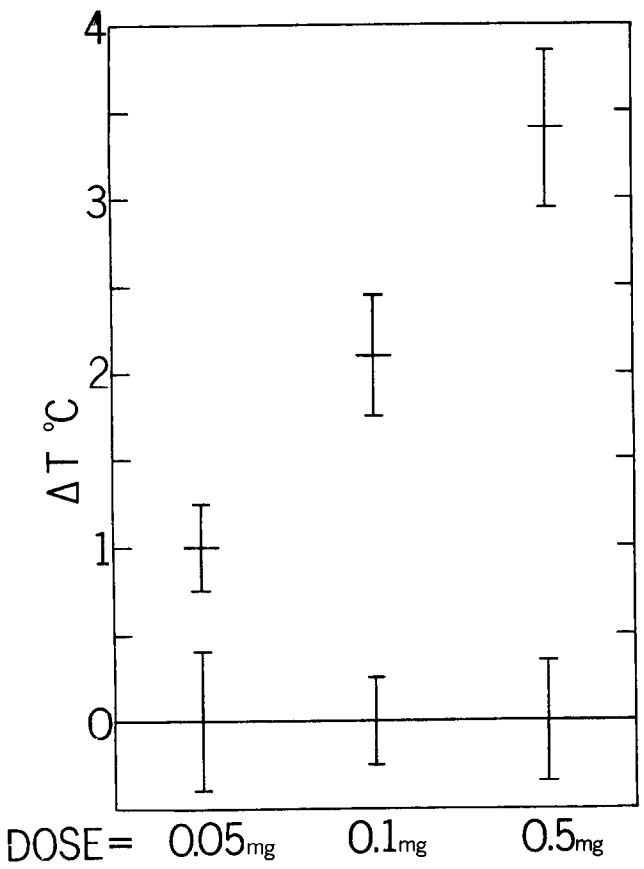

FIG. 1. Prostaglandin E_1 fever in the crayfish *Cambarus bartoni*. The $\Delta T=0$ baseline represents the normal 22.1°C final thermal preferendum (afebrile) for this species (vertical bars represent ± 1 standard error of the mean). Not shown are controls which showed no significant increase in thermal preferendum following handling or saline injection. Crayfish injected with PGE_1 showed dose-dependent significant increases (ΔT) above the afebrile baseline during the 24 hr after injection (mean $\pm$ 1 SEM).

DISCUSSION

It is apparent from the results (Fig. 1) that injection of pharmacological doses of PGE_1 into the haemocoel of crayfish induces a behavioral fever (increase in preferred temperature), presumably by raising the thermoregulatory "set-point" [12]. It is not currently known where the site of thermoregulatory control is located in the crayfish, but it is presumably in the central nervous system. It is not certain how much (if any) PGE_1 may have actually reached this site by crossing whatever blood-brain barrier may exist in decapod crustaceans; nor is it known whether or to what extent PGE_1 may be present in the crayfish CNS, or take part in normal thermoregulatory processes, or how rapidly it is catabolized in the haemolymph or other tissues. The duration of the observed febrile effect, relative to that observed for PGE_1 in vertebrates, suggests that the injected PGE_1 may initiate some sort of "chain-reaction" process in the crayfish with effects that outlast the PGE_1 itself. If this be the case, the PGE_1 itself need not actually reach the thermoregulatory site. Once the thermoregulatory control site is located, the presence or absence of PGE_1, its normal physiological concentrations in the CNS (if present), and variations in its concentrations during febrile and afebrile states can be determined.

We have demonstrated that crayfish exhibit a febrile response to PGE_1 at pharmacological doses, as well as to bacterial pyrogens [4]. The role of behavioral fever in enhancing defense responses of crayfish to infection remains to be demonstrated, but it seems not unlikely that fever in crustaceans may play a role similar to that in vertebrates [2, 6, 12].

PGE_1 fever has been demonstrated in amphibians [14] as well as in mammals [1, 9, 22] among the vertebrates. However, it has not yet been reported in reptiles (M. J. Kluger, personal communication [12]), nor in fishes (unpublished data). We injected several fish (*Micropterus salmoides*) intraperitoneally with PGE_1 with no apparent thermoregulatory response; however, because of the route of administration it is uncertain whether any PGE_1 actually reached the thermoregulatory center in the PO/AH area of the hypothalamus. The essential role of PGE_1 in mammalian fever has recently come into question [7], so the actual physiological relevance of PGE_1 with respect to febrile mechanisms is uncertain. However, the finding that PGE_1 will induce fever in organisms as phylogenetically distant as crayfish and mammals suggests that there is some general effect of prostaglandins on thermoregulatory neurons, or some role that they play in signalling the presence of infection or trauma. Eventual elucidation of this mechanism may greatly enhance our understanding of basic thermoregulatory control systems in animals, and/or of fever in response to infection.

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