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Body Temperature of Rats After Prostaglandins E_2 and $F_{2\alpha}$ and Their Precursor

JACEK SPŁAWIŃSKI, BARBARA WOJTASZEK AND ZBIGNIEW GÓRKA*

*Pharmacological Laboratory, 11 Szopena Str., 35-055 Rzeszów and *Institute of Pharmacology, 12 Smetna Str., 31-343 Cracow, Poland*

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SPŁAWIŃSKI, J., B. WOJTASZEK AND Z. GÓRKA. *Body temperature of rats after prostaglandins E_2 and $F_{2\alpha}$ and their precursor.* PHARMAC. BIOCHEM. BEHAV. 15(4)657–658, 1981.—Prostaglandins E_2 and $F_{2\alpha}$ and arachidonic acid were injected into various brain structures outside the hypothalamus in rats. The body temperature rise induced by PGE_2, but not by $PGF_{2\alpha}$ or arachidonic acid, was probably due to its diffusion or transport into the hypothalamus. Comparison of the latencies of the hyperthermic responses to PGE_2, $PGF_{2\alpha}$, and arachidonic acid revealed that PGE_2 was the most rapidly acting agent in structures located close to the hypothalamus. In contrast, arachidonic acid acted most rapidly after administration into the nucleus reticularis pontis caudalis.

Hyperthermia Hypothermia Prostaglandin E_2 Prostaglandin $F_{2\alpha}$ Arachidonic acid

PROSTAGLANDINS of the E series probably mediate pyrogen fever in placental mammals (see [4] for review). In support of this theory is the finding that in rats administration of PGE_2 into the anterior hypothalamic preoptic area (AH/PO) induced fever with a much shorter latency than fever induced by *E. coli* endotoxin [6,7]. We decided to study the influence of PGE_2 on the rat body temperature after administration into those sites outside the hypothalamus where sensitivity towards endotoxin had been found previously [6].

METHOD

Cannulae were implanted stereotaxically, using the coordinates of Skinner [5], into the various brain structures of male Wistar rats (280–350 g). The details of the surgical procedure, the injection technique, the verification procedure, and preparation of solutions have been given elsewhere [6,7]. The coordinates of the sites identified post mortem are shown in Table 1.

Esophageal temperature (T_{es}) was measured every 30 min following drug administration, with an additional measurement at 15 min, in restrained rats held in plastic cages. Environmental temperature was 22±1°C. The following parameters were measured. The maximal change of body temperature (ΔT_{es}, °C) from the base-line (the average of the last three measurements before injection) and the time to peak response (min).

Before injection of drugs the sensitivity of rats to control solutions, prepared identically to drug solutions, was tested. The hyperthermic response obtained, if any, was then subtracted from the hyperthermic response to drugs. In each animal PGs were injected first, followed by AA (arachidonic acid). The reason for this sequence was that we previously have found that, unlike with PGs, there was a sensitization to the hyperthermic response to AA with each consecutive injection (unpublished data). At least a one-week interval separated each injection, and each drug was given only once.

RESULTS AND DISCUSSION

With the exception of three locations, i.e. the S. nigra zona reticulata (abbreviations explained in Table 1), crus cerebri (at the level of caudal edge of the commisura posterior), and the N. anterior med. thalami, PGE_2 always produced a monophasic rise in T_{es}. Table 1 summarizes the results obtained.

The body temperature rise of rats following PGE_2 injection into the various hypothalamic nuclei is best explained by diffusion or transport of PGE_2 into the AH/PO [7]. The same explanation may hold for the present results as the time required to reach maximum positive response increased with measured distance of the injection site from the hypothalamus. However, the time required to reach maximum temperature rise following PGE_2 after its injection into the Tractus rubrospinalis was relatively short.

The presence of a secondary control mechanism of thermoregulation in the lower brainstem of rats has been postulated [2]. Our previous results suggested that the lower brainstem of rats is highly sensitive to *E. coli* endotoxin [6]. Time to peak of endotoxin-induced response, 71 and 125 min [6], after its injection into locations within the lower brainstem is comparable to that necessary to bring about a full response to PGE_2 (cf. Table 1). In contrast, comparison of latencies of temperature responses evoked by endotoxin

TABLE 1

EFFECTS OF ADMINISTRATIONS OF PROSTAGLANDIN (PG) E_2 (0.2 μg), $PGF_{2\alpha}$ (1.0 μg), AND ARACHIDONIC ACID (AA) (10.0 μg) IN A VOLUME OF 0.5 μl* INTO VARIOUS BRAIN STRUCTURES ON THE ESOPHAGEAL TEMPERATURE (T_{es})† IN RATS

Location	Coordinates of cannula-guides			PGE_2			$PGF_{2\alpha}$			AA		
	Anterior	Lateral	Horizontal	N‡	Δ T	Time to peak	N	Δ T	Time to peak	N	Δ T	Time to peak
F. med.§ prosencephali	6.75	1.5	1.0	4	1.7	25	1	0.4	30	1	0.8	30
N. anterior med. thalami	5.75	1.0	0.5	2	0	—	2	0	—	0	—	—
Capsula interna	5.25	2.5	−1.0	2	0.6	28	1	0	—	0	—	—
N. ventralis med. thalami	4.75	1.0	−0.5	1	1.0	46	1	0	—	2	1.2	180
F. mamillothalamicus	4.25	1.0	−1.5	1	1.5	45	2	0.8	21	1	1.3	30
N. ventralis med. thalami	3.75	1.0	−0.2	1	0.5	100	1	0	—	0	—	—
Crus cerebri	3.75	2.0	1.5	0	—	—	1	0.1	30	1	0.6	180
S. nigra zona reticulata	3.25	2.0	−1.5	2	0.5	150	2	0.6	72	0	—	—
Crus cerebri	1.25	1.0	3.0	2	−0.5	30	1	0.6	30	0	—	—
	Posterior											
Tractus rubrospinalis	1.75	2.5	−5.0	2	0.4	30	1	0.5	30	2	0	—
N. reticularis pontis c.	2.25	1.0	−4.0	2	0.5	150	1	0.6	30	2	0.6	24

*All compounds were injected only once. For each animal the hyperthermic response, if any, to a prior injection of vehicle was subtracted from the response to the specific compound.

†Mean values of maximal change in T_{es} (Δ T, °C) and mean time to peak response (min) are given.

‡Number of animals.

§Abbreviations: F., fasciculus; med., medialis; N., nucleus; S., substantia; c., caudalis.

and PGE_2 injections into the AH/PO indicate that the latter acted five times faster [7]. Therefore mediation by PGE_2 of response to endotoxin obtained from the lower brainstem seems unlikely. This suggests that the interaction between endotoxin and PGE_2 in rats may be specifically confined to the hypothalamus.

PGE_1 introduced into the medulla oblongata induces a fall in the rat body temperature [3]. We also observed a fall in body temperature of rats when PGE_2 was administered into the S. nigra zona reticulata and crus cerebri behind the commisura posterior (Table 1). $PGF_{2\alpha}$ induced a rise of body temperature when injected into the former location and, similarly to PGE_2, a fall of body temperature when injected into the latter location. The significance of these findings is, at present, unknown.

Our own data suggested that the participation of $PGF_{2\alpha}$ in the hyperthermic response to AA is more likely than the participation of PGE_2 [7]. We therefore studied the influence of AA and $PGF_{2\alpha}$ on the temperature of rats after administration into some of the areas explored with PGE_2.

The time necessary to obtain peak positive temperature response after injection of $PGF_{2\alpha}$ remains, in contrast to PGE_2, relatively constant regardless the site injected (Table 1). Comparison of the magnitudes and the time required to reach the positive peak response indicated that PGE_2 is acting more rapidly and stronger than $PGF_{2\alpha}$ or AA, when these agents were injected into the F. med. prosencephali, a structure near the AH/PO. In contrast, the body temperature response was faster after AA or $PGF_{2\alpha}$ than PGE_2 following their injection into the N. reticularis pontis c. (Table 1). Fast action of the precursor makes it unlikely that its effect is mediated by $PGF_{2\alpha}$ or PGE_2, or both. It could be that this AA-induced rise of the rat body temperature is mediated by other metabolites than $PGF_{2\alpha}$ or PGE_2 [1] or that specific receptor for AA is involved.

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