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Effect of prostaglandin $F_{2\alpha}$ on brain and stomach 5-hydroxytryptamine

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$PGF_{2\alpha}$ initially inhibits the rate of 5-HT synthesis in both rat brain and stomach and subsequently stimulates it. The results suggest that PGs of E and F series modulate tryptaminergic neuronal activity which in its turn variously affects 5-HT mediated responses.

We have reported that of the three prostaglandins PGE_1, PGE_2 and $PGF_{2\alpha}$, only PGE_1 potentiated morphine antinociception (Bhattacharya et al 1975) and itself possessed an antinociceptive effect in rats (Sanyal et al 1977, 1979). Morphine- and PGE_1-induced antinociception was antagonized by $PGF_{2\alpha}$ (Sanyal et al 1977). Juan & Lembeck (1977) reported that $PGF_{2\alpha}$ reduced the algesic effect of bradykinin by antagonizing the pain-enhancing action of endogenously released PGE. Similar antagonism between the central and peripheral actions of PGE_1 and $PGF_{2\alpha}$ have been reported (Crunkhorn & Willis 1969; Bhattacharya et al 1978). Again, $PGF_{2\alpha}$, in opposition to the well documented inhibitory effect of PGE_1 on gastric secretion, which appears to be a 5-HT mediated effect in rats (Goel et al 1983), stimulated basal and pentagastrin-stimulated gastric secretion in conscious and anaesthetized rats (Guha et al 1979; Goel & Sanyal 1982). PGE_1 has further been reported to increase 5-HT turnover of both rat brain and stomach but not of intestine (Haubrich et al 1973; Debnath et al 1978). We set out to determine whether the antagonism between the pharmacological effects of PGE_1 and $PGF_{2\alpha}$ is due to their different effects on 5-HT metabolism in rat brain and stomach.

Methods

The effect of graded doses of $PGF_{2\alpha}$ (Upjohn) on brain 5-HT content, estimated spectrophotofluorometrically (Snyder et al 1965), was studied using albino rats decapitated 15 min after administration of $PGF_{2\alpha}$ or 30 mM NaCl.

The rates of 5-HT accumulation (Neff & Tozer 1968) were studied in both saline and $PGF_{2\alpha}$ (2 mg kg^{-1} i.p.) treated rats given tranylcypromine sulphate (10 mg kg^{-1} i.p.) and killed at different times (0, 15, 30, 45, 60 and 90 min). The rate of 5-HT accumulation (i.e. synthesis) was calculated by first determining separately the differences between '0' min brain 5-HT level and values at the chosen times. Each difference is then appropriately multiplied to obtain the computed change in 60 min, the mean of all the computed values being expressed as the rate of accumulation h^{-1}.

* Correspondence.

Results and discussion

The brain content of 5-HT was significantly less after 1 and 2 mg kg^{-1} i.p. $PGF_{2\alpha}$ (Table 1) than in controls. The results of the rate of accumulation studies are illustrated in Figs 1, 2. The differences in the time-matched 5-HT contents, both in brain and stomach, indicate that $PGF_{2\alpha}$ initially decreased the rate of accumulation or synthesis of 5-HT and then, after 45 min in brain and 60 min in stomach, increased it. The rate of accumulation has therefore, been calculated for brain taking into consideration the values separately between 0 and 45 min and those between 45 and 90 min.

Table 1. Effect of $PGF_{2\alpha}$ in Wistar albino rats on the brain 5-HT content.

Treatment mg kg^{-1} i.p.	n	5-HT (mg g^{-1} wet tissue) Mean	s.e.m.	*P* value
1. Control (saline treated)	5	531	20	
2. $PGF_{2\alpha}$				
0·5	5	495	18	NS
1·0	5	456	16	<0·05
2·0	5	382	19	<0·001

Table 2. Morphine (7·5 mg kg^{-1} i.p.) antinociception at 15 and 75 min after administration of $PGF_{2\alpha}$ (2·0 mg kg^{-1} i.p.).

Drug treatment	n	Increase in tail-flick latency† (sec) Mean	s.e.m.
Morphine (M)	9	12·8	0·49
$PGF_{2\alpha}$ + M at 15 min	5	8·5***	0·62
$PGF_{2\alpha}$ + M at 75 min	5	19·2**	1·62

† Indicates responses at 15 min after morphine administration.

** and *** indicate level of significance at $P < 0·01$ and $< 0·001$ respectively (Student *t*-test) compared to morphine group.

In the case of stomach however, the rate of accumulation of 5-HT has been calculated taking into consideration the data between 0–60 min only. The data agree

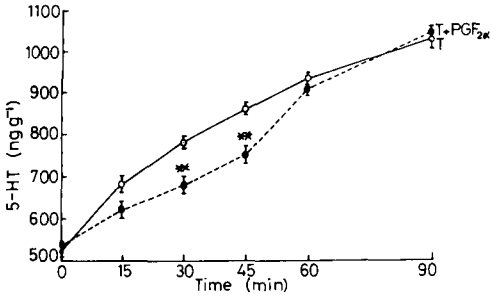

FIG. 1. Effect of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$, 2·0 mg kg^{-1} i.p.) on brain 5-HT at different time intervals after tranylcypromine sulphate administration (10 mg kg^{-1} i.p.) 5-HT value at each point of time for each group represents mean ± s.e.m. of 5 rats. * and ** indicate P values at <0·05 and <0·01 respectively compared to the respective controls at similar time intervals. Rate of accumulation of 5-HT has been separately calculated from 0–45 min and from 45–90 min and expressed in terms of ng g^{-1} of wet tissue h^{-1} for both the groups of rats. The values from 0–45 min 528 ± 54 and 321 ± 21 for the control and $PGF_{2\alpha}$ treated groups respectively—the difference is statistically significant at $P < 0·05$. The values from 45–90 min being 244 and 601 for the control and $PGF_{2\alpha}$ treated groups respectively. T-control group treated with tranylcypromine only. T + $PGF_{2\alpha}$-group treated with tranylcypromine and $PGF_{2\alpha}$.

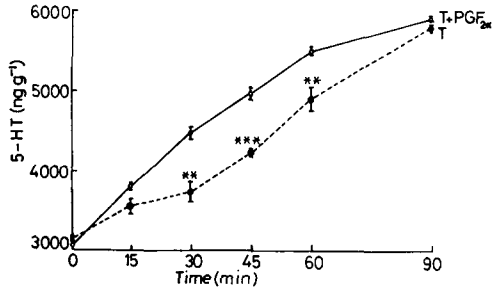

FIG. 2. Effect of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$, 2·0 mg kg^{-1} i.p.) on stomach 5-HT at different time intervals after tranylcypromine sulphate administration (10 mg kg^{-1} i.p.). 5-HT value at each point of time for each group represents mean ± s.e.m. of 5 rats. *, ** And *** indicate P values at <0·05, <0·01 and <0·001 respectively compared to respective controls at similar time intervals. Rate of accumulation of 5-HT has been calculated from 0–60 min for both the groups of rats. The values being 2677·8 ± 151·6 and 1590·0 ± 135·6 for the control and $PGF_{2\alpha}$ treated groups respectively—the difference is statistically significant at $P < 0·01$.

with those of Bhattacharya (1982) who studied the effect of $PGF_{2\alpha}$ on brain 5-HT up to 60 min but did not report any biphasic response.

We previously discovered that morphine- and PGE_1-induced antinociception are 5-HT-mediated because brain tryptaminergic neuron degeneration by 5,6-dihydroxytryptamine, and receptor blockade by methysergide, blocked the antinociceptive effect of both the agents (Sanyal et al 1977, 1979). As morphine antinociception is dependent on tryptaminergic neuronal activity, the antinociceptive effect of morphine (7·5 mg kg^{-1} i.p.) was studied by the radiant-heat method in rats, at 15 min and 75 min after $PGF_{2\alpha}$ (2 mg kg^{-1} i.p.) (Table 2). As expected, morphine antinociception was significantly inhibited and potentiated respectively at 15 and 75 min after $PGF_{2\alpha}$, which is in support of the biphasic and time-dependent effect of $PGF_{2\alpha}$ on the rate of synthesis of brain 5-HT.

It is thus concluded that PGs of the E and F series modulate tryptaminergic neuronal activity which in its turn variously affects 5-HT mediated responses.

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