guinea-pig ileum (GI).

Injection of the challenging antigen (BGG, 5 mg/ml per animal) into the Krebs solution perfusing the hind quarters caused a contraction of all three tissues. When mepyramine (0.1 μg/ml) was added to the fluid bathing the tissues, there was no response of the GI, while the RSS and RC still contracted. When samples of perfusate were collected and assayed for histamine fluorimetrically according to the method of Shore, Burkhalter & Cohen (1959) and Evans, Lewis & Thompson (1973), it was found that before challenge the perfusate contained 9 ng/ml, while during the 30 min following challenge it contained 48 ng/ml. It was found that the maximum amount of histamine was released during the first 3–5 min after challenge. The samples were extracted for radioimmunoassay for prostaglandin E_2 and prostaglandin $F_2\alpha$ according to the method of Hennam, Johnson, Newton & Collins (1974) and Jose, Niederhauser, Piper, Robinson & Smith (1976). The mean content of the 30 min perfusate collected before challenge was 0.26 ng/ml prostaglandin E_2 and 0.18 ng/ml prostaglandin $F_2\alpha$, while during the 30 min following challenge the values were 1.34 ng/ml prostaglandin E_2 and 0.41 ng/ml prostaglandin $F_2\alpha$. The difference was only significant in the case of prostaglandin E_2. When indomethacin (1 μg/ml) was added to the fluid perfusing the hind quarters, there was no difference in the prostaglandin content of perfusate collected before and after challenge. The maximum release of prostaglandin was during the period 10–30 min after challenge.

When the challenge was repeated, the contractions of the guinea-pig ileum were considerably greater than after the first challenge. This was not the result of an increase in the amount of histamine release as only 2.7 μg was released after the second challenge compared with 4.2 μg after the first. The increased responses were due to sensitization of the tissue by a material apparently released from the hind quarters as the sensitivity to additions of standard histamine also increased. The increased sensitivity varied from five to one hundred fold, and occurred in 9 out of 15 experiments. The concentrations of prostaglandins released after challenge did not cause sensitization of the GI to histamine.

It is concluded that anaphylaxis in the guinea-pig hind quarters causes the release of histamine followed later by release of a prostaglandin, probably E_2. In addition there was in the majority of experiments, release of an unknown material which sensitized the guinea-pig ileum to histamine.

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Evidence from behavioural reactions to fenfluramine, 5-hydroxytryptophan, and 5-methoxy-N,N-dimethyltryptamine for differential effects of short-term and long-term lithium on indoleaminergic mechanisms in rats

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Lithium may impair storage of 5-hydroxytryptamine (5-HT) within nerve terminals, and so interfere with stimulus-release coupling (Collard, 1978), which could explain why its short-term effects on rat behaviour are compatible with reduced physiological availability of 5-HT (Harrison-Read & Steinberg, 1971; Harrison-Read, 1978). After long-term lithium administration (≥2 weeks) however, some of these behavioural effects are no longer apparent, even though indirect measures suggest that the 5-HT storage defect persists (Judd, Parker & Jenner, 1975). Behavioural tolerance may result from 5-HT supersensitivity, which compensates for reduced 5-HT release (Harrison-Read, 1978).

In order to investigate this possibility further, male hooded rats (mean weight 210 g) were pretreated with LiCl 2 mmol/kg i.p. daily for 0 days (saline controls, S), 5 days (short-term lithium, SL), or 21 days (long-term lithium, LL). Nine or 10 rats in each pretreatment group were then given (±)-fenfluramine HCl (10 mg/kg i.p.), (±)-5-hydroxytryptophan (5-HTP, 200 mg/kg i.p., preceded by carbidopa, 25 mg/kg), or 5-methoxy-N,N-dimethyltryptamine (5MeODMT, 1.75 mg/kg i.p.). Fenfluramine releases 5-HT from nerve endings, 5-HTP is the precursor of 5-HT, and 5MeODMT is a putative indoleamine agonist. Rats were examined 8 min after injection of 5MeODMT, and 40 and 120 min after fenfluramine and 5-HTP. Six behavioural features which appear to result specific-

ally from direct or indirect stimulation of indoleamine receptors (Jacobs, 1976), were each rated, on a blind basis, with a score of 0, 1, or 2.

The rated response to fenfluramine was significantly ($P<0.01$) increased in the lithium pretreated rats. By contrast, the response to 5-HTP was only significantly ($P<0.05$) greater than that of controls in LL rats (Figure 1). Although the enhanced response to 5MeODMT in LL rats was not significant, a further study in groups of 9–10 rats, with doses of 0.75–2.00 mg/kg, demonstrated a significantly ($P<0.05$) increased overall response to 5MeODMT in LL rats (Kolmogorov-Smirnov two-sample test, 2-tailed, $D=0.29$, n_1, $n_2=46$).

The greater behavioural response to fenfluramine in SL and LL rats may reflect an increase in the amount of extra-granular 5-HT released by the drug, due to lithium impaired intra-neuronal storage. The enhanced behavioural response to 5-HTP and 5MeODMT in LL, but not SL rats, supports the suggestion that indoleamine receptors become supersensitive as a result of continued reduction of normal 5-HT release by lithium.

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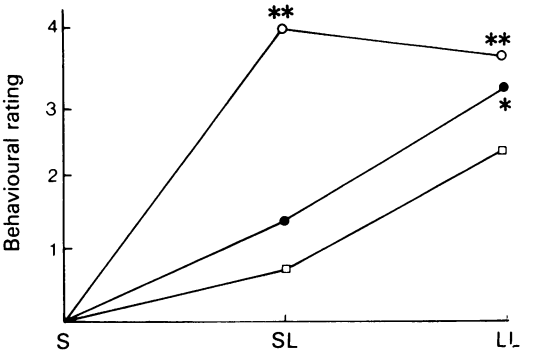

Figure 1 Ratings for postural tremor, fore-paw treading, hind-limb splay, Straub tail, head-weaving, and hypersalivation and/or ejaculation, were summed for each rat. Mean ratings of SL and LL rats are expressed as differences from mean ratings of S rats. There were significant differences between ratings after (○) fenfluramine and (●) 5-HTP, (Kruskall-Wallis one-way analysis of variance, $P<0.01$ and $P<0.05$ respectively). LL rats had higher scores than controls after fenfluramine and 5-HTP, as did SL rats after fenfluramine, (Mann-Whitney U test, 2-tailed, $*P<0.05$; $**P<0.01$). Lithium pretreatment did not significantly affect scores after (□) 5MeODMT, although the trend was similar to that after 5-HTP.

Exploratory behaviour and aversive thresholds in rats following microinjection of morphine into central and medial nuclei of the amygdala

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The amygdaloid complex, an area rich in opiate receptors (Atweh & Kuhar, 1977) and opioid peptides (Watson, Akil, Sullivan & Barchas, 1977), has recently been implicated in morphine-induced alterations in aversive thresholds and open field behaviour (Rodgers, 1977, 1978). In this experiment we extend investigations to the effects of intra-amygdaloid opiate injections on exploratory behaviour.

Male hooded rats were anaesthetized with Equithesin and bilaterally implanted with guide cannulae aimed at the central (A/P: + 6.0, L: ± 3.9, V: 8.5) or medial (A/P: + 5.2, L: ± 3.5, V: 9.5) nucleus of the amygdala. Two weeks post-operative recovery was allowed before testing commenced. Rats were randomly assigned to flinch-jump and holeboard tests and then randomly allocated to vehicle (sterile water), morphine sulphate (10 μg), naloxone hydrochloride (1 μg) or morphine plus naloxone (10 μg + 1 μg) groups. In all cases injections were made bilaterally in a volume of 0.5 μl over 20 s. Cannula placements were verified histologically after trypan blue injection and data from animals with placement errors were excluded.

In the flinch-jump test, electric shock was applied through the grid bars of the test chamber (18 × 15 × 13 cm) as previously described (Rodgers, 1978). Mean jump thresholds were determined for each rat before and after injection. At both sites,