Formation and storage of dopamine in hamster mast cells following the administration of dopa

SIR,—Using the histochemical fluorescence method of Falck and Hillarp, a large proportion of the mast-cells in rabbit, cat and hamster skin have been shown to be capable of taking up L-3,4-dihydroxyphenylalanine (dopa), to contain dopa-decarboxylase activity and to have an amine storage mechanism sensitive to reserpine (Adams-Ray, Dahlström, Fuxe & Hillarp, 1964). Furthermore, the uptake and decarboxylation of dopa have been found to be specific, as practically no or very little 5-hydroxytryptophan (5-HTP) is taken up by the mast-cells (Adams-Ray, Dahlström & Sachs to be published). Since the amine content of mast-cells in the species mentioned above was much lower in untreated animals than after treatment with dopa, our working hypothesis was that the low concentrations of primary catecholamines found in the mast-cells of normal animals represented only intermediates and that the final product normally stored in the cells was a catecholamine which does not give a fluorescent product after reaction with formaldehyde. Biochemical determinations have now been made to see what primary catecholamine is present before and after the administration of dopa and to test the hypothesis.

The catecholamines were extracted from tissues and separated on ion-exchange columns as previously described (Bertler, Carlsson & Rosengren, 1958, Häggendal, 1962). Dopamine was determined fluorimetrically by the method of Carlsson & Waldeck (1958) as modified by Carlsson & Lindqvist (1962), and noradrenaline by Häggendal's method (1963). The determinations were made in the ear, heart and brain of untreated hamsters, and in hamsters treated with dopa (100 mg/kg subcutaneously) $\frac{1}{2}$, 2 and 24 hr before killing. Each determination was made on pools of tissue extracts from 5 to 7 animals. The time-course experiments were made on normal hamsters and on hamsters that had been bilaterally sympathectomised 10 to 21 days before killing. In all experiments made on the two groups of animals, the hamster ear tissue showed a unique capacity to form and store large amounts of dopamine for more than 24 hr (0·76 μg/g) with a maximum level after 2 hr (1·3 μg/g). The heart and brain tissues, on the other hand, showed a peak of dopamine as early as after 30 min (1·6 and 1·8 μg/g respectively), after which the content rapidly decreased and by 24 hr had reached normal levels (very low amounts in heart and 0·25 μg/g in brain). No significant changes were observed in the noradrenaline contents of the tissues studied after the administration of dopamine. Practically the entire noradrenaline content of the ear is in all probability stored in the adrenergic nerve terminals, since a 90% decrease in noradrenaline content was observed after bilateral sympathectomy (0·013 μg/g).

Since very few or practically no mast-cells belonging to the "monoamine" category are found in the brain or the heart and since this type of mast-cell is found in very large numbers in the ear, the marked differences observed between these tissues in the time course of the dopamine increase in ear tissue after administration of dopa, are in all probability due to the presence of abundant numbers of such mast-cells in the ear. These are able to store high concentrations of dopamine for a much longer time than the adrenergic nerve terminals after the administration of dopa. This is in complete agreement with the histochemical observations, since a marked increase in fluorescence intensity is still observed in the mast-cells 24 hr after injection of dopa. From histochemical observations in normal animals these mast-cells are known to contain low concentrations of primary catecholamines. The present biochemical data suggest that the primary catecholamine stored in the normal hamster ear is

dopamine. The results indicate furthermore that no or very low β-hydroxylase activity is present in these mast-cells, since no increase in noradrenaline content was observed. Preliminary attempts to detect tertiary catecholamines have so far proved unsuccessful.

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Drugs affecting the behaviour and spontaneous bioelectrical activity of the central nervous system in the ant, *Formica rufa*

SIR,—Recently several reports on the influence of neuro- and psychotropic drugs on various species of invertebrates have been published (Witt, Brettschneider & Boris, 1961; Fange, 1962; Katona & Woleman, 1964; Mirolli & Welsh, 1964). The ant seems to be a suitable subject for such investigation because of the relatively high degree of development of the central nervous system and its well developed social behaviour.

We have investigated the effects of certain psychotropic drugs and neurohormones on behaviour and spontaneous bioelectrical activity recorded from the lobi optici of the ant, *Formica rufa*. The ants were kept in a plastic formicarium and were given the drugs orally in honey, or injected into the abdominal cavity, or applied locally to the exposed brain. The investigations included, observations of general behaviour, phototropic reaction and records of spontaneous bioelectrical activity of the lobi optici by tungsten wire electrodes, connected to a conventional EEG apparatus. The characteristic EEG pattern of the lobi optici of the ant, obtained in conditions of normal brightness consisted of 2-5 waves/sec and of amplitude from 5–50μ V. Of the drugs investigated the most marked in their effects were reserpine, chlorpromazine and strychnine.

Reserpine, 0·1–0·5 μg of body weight, given either orally or injected into the abdominal cavity, markedly inhibited the locomotor activity of the ant without causing ataxia or disturbances of co-ordination. Simultaneous outbursts of aggressiveness of a bizarre character were observed, ants from the same population after slight stimuli or even spontaneously attacking each other, a phenomenon never observed in the controls. The EEG pattern was slightly changed with transient slowing of frequency and increase of amplitude. The phototropic reaction was significantly suppressed (Fig. 1).