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Behaviour of *Drosophila melanogaster* is affected by drugs

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Summary. Reserpine, colchicine and Rb⁺ ions exerted specific effects on sexual behaviour and locomotor activity of the fruit fly. Neuroleptics and antidepressants were inactive.

Studies on the action of drugs on *Drosophila* have so far been limited to examination of their toxic and mutagenic properties. The single exception appears to be a recent study on toxicities of neuroleptics to *Drosophila*, in which the effect of the drugs on phototactic movement was also followed². In this communication we present results of an introductory study on the effects of drugs specifically on behaviour of the fruit fly.

Materials and methods. A wild-type strain of *D. melanogaster* N 72 was grown on standard *Drosophila* medium seeded with live yeast at 25 °C in the dark. All experiments were also carried out at 25 °C. Freshly emerged virgin flies were sorted by sex and separately placed into test-tubes with a maintenance medium consisting of 5% glucose and 1% agar. After 3 days were transferred onto a fresh maintenance medium supplemented with the drug to be examined. The drugs were used at concentrations which proved non-toxic or only slightly toxic in preliminary assays. The flies were kept on this drug-supplemented medium for 24 h and then scored for locomotor and sexual activities. The tests were made in a box equipped with artificial dim light from 10.00

to 14.00 h when diurnal fluctuations in behaviour were found to be minimal.

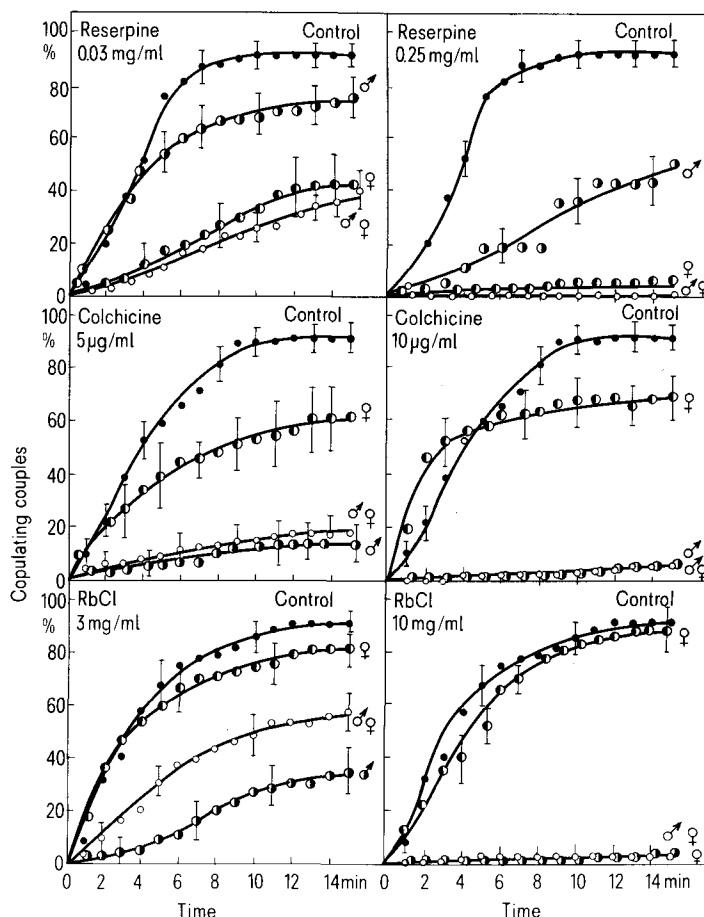
Results and discussion. As shown in the figure, 3 unrelated substances affected sexual behaviour of the flies. The flies fed for 24 h on reserpine exhibited lower mating speed. The decrease in mating speed was essentially due to females: At a low concentration of reserpine, mating speed was almost normal if only males and not females were treated with the drug, and this tendency was apparent at a high concentration of reserpine as well. A reversed situation was observed in the case of flies fed on colchicine or rubidium chloride: Mating speed was almost as high as in the control if only females were treated with the drugs. If the males were treated and brought to copulate with either treated or control females, the mating speed was exceedingly low. Other alkali metal ions, Li⁺ (1 mg/ml), Na⁺ (up to 100 mg/ml), K⁺ (up to 100 mg/ml), Cs⁺ (1 mg/ml) did not affect the sexual behaviour of the flies.

An interdependence between mating speed and locomotor activity in *Drosophila* was repeatedly reported³⁻⁵. In the case studied here, the specific effects of reserpine and

Effect of drugs on locomotor activity of *D. melanogaster*

Drug	Concentration	Sex	Spontaneous activity (% of control)	Jumps (% of control before stimulation)	
				Before stimulation	After stimulation
None (control)		♂	100	100	1857 ± 408
		♀	100	100	1800 ± 810
Reserpine	0.03 mg/ml	♂	149.3 ± 3.0	285.7 ± 94.1	928.6 ± 185.7
		♀	132.0 ± 13.2	245.5 ± 115.3	845.5 ± 397.4
	0.25 mg/ml	♂	168.0 ± 11.8	78.6 ± 70.7	880.6 ± 264.3
		♀	164.5 ± 3.3	129.1 ± 56.8	836.4 ± 368.0
Colchicine	5 µg/ml	♂	85.5 ± 9.3	380.9 ± 38.1	1619.1 ± 161.9
		♀	104.1 ± 2.1	27.2 ± 27.0	1009.1 ± 504.5
	10 µg/ml	♂	65.0 ± 6.5	0	714.3 ± 142.8
		♀	46.3 ± 5.0	0	0
RbCl	3 mg/ml	♂	123.0 ± 10.2	119.1 ± 48.2	10,380.9 ± 2415.2
		♀	20.8 ± 4.1	27.2 ± 4.9	1654.5 ± 185.2

Locomotor activity was assessed by Hay's time-sampling technique⁷. 5 individuals of the same sex were transferred into a Petri dish of 5 cm diameter, left quiet to accommodate for 30 min and then the number of momentarily moving flies were counted at 6-sec intervals for 60 sec. The measurements were repeated 10 times in succession and pooled. Care was observed to avoid the slightest stimulation of the flies either mechanically or optically. To score for stimulated activity, the dish was violently shaken in horizontal position for 6 sec and the number of jumps of all 5 flies within 6-sec intervals were counted for 60 sec. The figures are normalized with respect to controls and expressed with standard mean errors. The sex of males and females is denoted by ♂ and ♀ respectively.



Effect of drugs on mating speed of *D. melanogaster*. Mating speed was measured in a Petri dish of 5 cm diameter divided by a removable membrane into 2 compartments. 20 virgin males and 20 virgin females were placed separately into either compartment and left for 15 min. The membrane was then removed and the number of copulating couples counted for 15 min. ♂, only males were treated by the drug; ♀ only females were treated; ♂♀ both sexes were treated. The vertical bars on the curves indicate standard mean errors.

colchicine on sexual behaviour did not correlate with their effects on locomotor activity. As shown in the table, reserpine slightly raised spontaneous locomotor activity and slightly lowered the stimulated activity both in males and females. Colchicine had an inhibitory effect on locomotion, pronounced at a high concentration, but again its effect was similar in males and in females. The effect of Rb^+ ions on locomotor activity was sex-dependent: Spontaneous activity was inhibited in females but not in males; on stimulation, the males, not the females, became 'irritated' and exhibited a conspicuously high motor activity which persisted for some time. It is feasible that this high 'irritability' of the males may account for their failure to undertake normal courtship and mating.

The following drugs had no effect on either locomotor activity or sexual behaviour. Neuroleptics: perphenazine (5 mg/ml), levopromazine (5 mg/ml), plegomazine (1 mg/ml), fluphenazine (1 mg/ml), trifluoperazine (1 mg/ml) chlorprotixene (3 mg/ml), haloperidol (0.03 mg/ml); antidepressants: imipramine (1 mg/ml), thioridazine (1 mg/ml), amitriptyline (3 mg/ml).

The interpretation of these data depends upon assumptions on the mechanism of action of the drugs employed in this study. A number of recent studies on mammalian nervous system strongly indicate that neuroleptics act rather specifically on dopaminergic paths, blocking the postsynaptic dopamine receptors or affecting the presynaptic side⁶. Reserpine appears to deplete transmitter stores in neurons with less specificity affecting dopaminergic, adrenergic and serotonergic paths⁸. It seems reasonable to assume that the same mechanisms hold in the insect nervous system.

The failure of neuroleptics to affect either locomotion or mating would suggest an insignificant role of dopaminergic paths in shaping *Drosophila* behaviour. The paths in which other biogenic amines are involved may be operative, however, since reserpine did exert a specific action on behaviour of the fly. The effect of colchicine points to a role of microtubules in male sexual behaviour. The specific action of Rb^+ ions, which may be related to their ability to replace K^+ in some neural functions, may be of interest to those studying pharmacology of rubidium salts in view of their prospective use in psychiatry. Because of predominant role of cholinergic and gabaergic paths in the insect nervous system⁹, studies of effects of agonists and antagonists of these paths on *Drosophila* behaviour may be most interesting.

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