Antagonistic Effects of Tryptamine and β-Phenylethylamine on the Behaviour of Rodents

ACCORDING to Brodie and Shore, the behaviour of higher animals depends on neurohumoral agents produced in the diencephalon. Catecholamines such as noradrenaline and dopamine are said to act as ergotropic agents, whereas serotonin is their antagonistic trophotropic factor[1,2]. The essential validity of these concepts has been confirmed many times[3,4]. There are, however, some discrepancies concerning the supposed stimulating (ergotropic) effects of catecholamines; some results confirm their alerting action, but others point to a depressing effect[5,6]. We found[7–11] that not only catecholamines, but also their amino-acid precursor L-dopa, suppress exploratory behaviour in mice, whereas amphetamine derivatives, as well as β-phenylethylamine and its amino-acid precursor phenylalanine, enhance it; there is a mutual antagonism between the two groups of substances. Serotonin too suppresses exploratory activity in mice and produces a Parkinson-like state in rats, similar to that produced by reserpine. β-Phenylethylamine antagonizes these effects of serotonin[12]. We concluded that β-phenylethylamine rather than catecholamines should be considered the ergotropic agent, while serotonin, as proposed by Brodie and Shore, is its antagonistic trophotropic factor. It seems to us that catecholamines may function differently in particular systems, but they do not seem to stimulate motor activity. Amphetamine and its derivatives may act by liberating β-phenylethylamine.

Table 1. EFFECT OF β-PHENYLETHYLAMINE DERIVATIVES ON RESERPINE AND TRYPTAMINE PARKINSON-LIKE SYMPTOMS IN THE RAT

Drug	Dose (mg/kg)	No. of animals	Animals with Parkinson-like symptoms: Catatonia	Akinesia	Tremor	Rigidity
Reserpine	5	20	18 (90%)	19 (95%)	19 (95%)	18 (90%)
Reserpine + β-phenylethylamine	5 50	20	1* (5%)	1* (5%)	20 (100%)	2* (10%)
Reserpine + methylamphetamine	5 2	20	1* (5%)	1* (5%)	20 (100%)	1* (5%)
Tryptamine	80	20	10 (50%)	19 (95%)	19 (95%)	0
Tryptamine + β-phenylethylamine	80 50	20	2* (10%)	2* (10%)	20 (100%)	0
Tryptamine + methylamphetamine	80 2	20	1* (5%)	1* (5%)	20 (100%)	0

* Values statistically significant ($P < 0.01 > 0.001$).

Dewhurst reached similar conclusions[13–15], except that he included tryptamine among the stimulating agents, maintaining that phenolic amines such as catecholamines and serotonin are depressing, whereas non-phenolic amines such as β-phenylethylamine and tryptamine are stimulating. Nevertheless, according to our results, tryptamine affects the behaviour of mice and rats in a manner very similar to that of serotonin. β-Phenylethylamine is an antagonizing rather than a synergizing agent to the effects of tryptamine. We have measured effects on exploratory activity in mice, using an actophotometer[16], and we have produced a Parkinson-like state in rats. Twenty female hooded rats (180–280 g body weight) received each of the doses indicated in Table 1. Drugs were dissolved in distilled water and injected intraperitoneally, 1 ml./100 g body weight. β-Phenylethylamine derivatives were administered 2 h after reserpine and 30 min after tryptamine. Results were evaluated by an "all or none" reaction as follows. Catatonia was considered to be present when the rats, put on a table with their forelimbs placed on a platform 6 cm high, remained still for at least 1 min. Akinesia was found when the rats made no exploratory movements for 2 min at least. Rigidity was present when the rats allowed themselves to be dragged by the tail without making escape movements. Absence or presence of tremor was assessed visually. Because tryptamine does not produce rigidity, this was not tested in assays with this substance.

The degree of phenylethylamine antagonism was expressed as the percentage of rats which still had Parkinson-like symptoms. Statistical significance was assayed according to Bancroft[17].

In our other investigations groups of six male white mice (18–30 g) were put in individual cages, and injected intraperitoneally 30 and 15 min before locomotor activity was measured for 10 min in the actophotometer. Reserpine was always administered 24 h before test. Results are shown in Table 2.

Table 2. EFFECTS OF RESERPINE, TRYPTAMINE, AND β-PHENYLETHYLAMINE DERIVATIVES ON THE EXPLORATORY BEHAVIOUR OF MICE

First injection	(mg/kg)	Second injection	(mg/kg)	Actophotometer reading (mean ± S.E.)
Distilled water		Distilled water		65 ± 5
Tryptamine	80	Distilled water		8 ± 4*
Reserpine	2	Distilled water		7 ± 2*
Distilled water		Methylamphetamine	2	101 ± 8*
Distilled water		β-Phenylethylamine	80	90 ± 9
Tryptamine	80	Methylamphetamine	2	101 ± 14*
Tryptamine	80	β-Phenylethylamine	80	91 ± 14*
Reserpine	2	Methylamphetamine	2	174 ± 14*
Reserpine	2	β-Phenylethylamine	80	48 ± 8*

* Results statistically significant ($P < 0.01 > 0.001$).

Tables 1 and 2 show that reserpine as well as tryptamine produces hypokinesia in mice. The reserpine syndrome in rats consists of catatonia, akinesia, tremor and rigidity, whereas tryptamine only produces catatonia, akinesia and slight tremor. These symptons, with the exception of tremor, which is enhanced, are antagonized by β-phenylethylamine and methylamphetamine. It seems that tryptamine produces not stimulation, but depression-like phenomena, and that β-phenylethylamine acts as its antagonist. Tryptamine as well as β-phenylethylamine passes the blood–brain barrier[13,18] and so there can be no objection on this count. We cannot explain the differences between our results and those of Dewhurst; maybe they have resulted because we used different animal species (rodents rather than newly hatched chickens) or because of some other experimental details.

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