Pharmacology Biochemistry & Behavior, Vol. 13, pp. 385–390. Printed in the U.S.A.

n-Pentylamine: Effect on Motor Activity of Mice[1,2]

EWA WIDY-TYSZKIEWICZ[3] AND THEODORE L. SOURKES

Department of Psychiatry, McGill University, 1033 Pine Avenue West, Montreal, Canada

Received 23 April 1980

WIDY-TYSZKIEWICZ, E. AND T. L. SOURKES. n-*Pentylamine: Effect on motor activity of mice.* PHARMAC. BIOCHEM. BEHAV. 13(3) 385–390, 1980.—Motor and autonomic effects of *n*-pentylamine in mice have been evaluated in relation to aminergic mechanisms by combining administration of the amine with drugs having well known effects on such mechanisms. Some evidence has been found to indicate the importance of dopaminergic pathways in the actions of pentylamine; these actions are modifiable by central blockade of muscarinic receptors with atropine. Serotonin-regulated pathways do not seem important for the effects of pentylamine that have been studied.

Pentylamine Dopaminergic mechanisms Cholinergic-dopaminergic balance Motor activity

THE aliphatic monoamine *n*-pentylamine has been used extensively in this laboratory as a model for the investigation of the action of monoamine oxidase (EC 1.4.3.4) in vivo [25, 27–29]. The model is readily justified by the fact that pentylamine is a classical substrate for that enzyme [20,33], and that both pentylamine and its immediate oxidation product valeraldehyde, derived also from *n*-amyl alcohol in metabolism, are rapidly oxidized in vivo [9,29]. Pentylamine is not simply a chemist's artefact, for it has been detected in samples of fresh and preserved vegetables, fruits, fish products, cheese, and coffee [18]. Moreover, like a number of other aliphatic amines, it has been identified as a normal constituent of mammalian, including human, urine [31].

The literature contains little information on the pharmacology of pentylamine. Barger and Dale [3], who introduced the term "sympathomimetic", tested aliphatic amines on the vascular system and found increasing pressor response with increasing straight-chain length up to C_6. Similarly, structure-activity relationships in regard to cardiac stimulation have been investigated. Maximal activity in the aliphatic amine series was found with *n*-hexyl and *n*-heptylamines. In this group of substances the stimulating effect of pentylamine on the cat papillary muscle preparation was comparable to those of dopamine and tyramine [4]. Our current interest, however, has centered on the effects of *n*-pentylamine on spontaneous locomotor activity in mice. Observations are also presented on the autonomic effects elicited by pentylamine. The aim of this work has been to evaluate the various effects of this aliphatic amine, and their modification, by prior administration of drugs that influence the synthesis of monoamines and their pharmacologic actions.

METHOD

Animals

Swiss male albino mice weighing between 25 and 28 g were used in these experiments. They were purchased from Canadian Breeding Laboratory and Farms, St. Constant, P.Q. Animals were allowed free acess to food and water until the time of pentylamine injection and a 12 hr light (6 a.m. to 6 p.m.)-dark cycle was maintained.

Procedures

Locomotor activity was measured quantitatively by means of an electronic activity monitor (Stoelting). Counts of activity were accumulated at 5-min intervals.

Catabolism of pentylamine in mice in vivo was estimated according to Madras and Sourkes [12]. After intraperitoneal injection with ^{14}C-pentylamine (California Bionuclear Corp., Sun Valley, CA), 4μCi kg^{-1} body weight in a volume of 10 ml kg^{-1} body weight; animals were kept in glass metabolic cages, and their expired gases were trapped by a solution of ethylene glycol monomethylether-ethanolamine (2:1). Samples of the solution were removed periodically and the amount of radioactive CO_2 was counted in a Beckman SL-250 liquid scintillation counter.

Drugs and Injections

The following substances were used: atropine methyl bromide and DL-α-methyl-*p*-tyrosine methyl ester hydrochloride (Sigma, St. Louis, MO); atropine sulphate monohydrate (J. T. Baker Co., Phillipsburg, NJ); disulfiram

[1]This research was supported by a grant of the Medical Research Council (Canada) to T.L.S.

[2]Send reprint requests to: Professor T. L. Sourkes, Department of Psychiatry, McGill University, 1033 Pine Avenue West, Montreal, Quebec, Canada, H3A 1A1.

[3]Visiting Scientists, on leave from the Institute of Physiological Sciences, Warsaw Academy of Medicine, Przedmiescie 26/28, Warsaw, Poland, during the course of the research reported here.

(Ayerst Research Laboratories, St. Laurent, P.Q.); haloperidol and pimozide (McNeil Laboratories, Don Mills, Ont.); thioridazine, (Sandoz, Dorval, P.Q.); *p*-chlorophenylalanine methyl ester hydrochloride (Calbiochem, San Diego, CA); *n*-pentylamine (Matheson, Coleman and Bell, Norwood, OH); phenoxybenzamine hydrochloride (Smith Kline and French, St. Laurent, P.Q.); and reserpine (Ciba Co., Ltd., Dorval, P.Q.).

Soluble drugs were prepared in 0.9% NaCl. Haloperidol was dissolved with a few drops of glacial acetic acid. Disulfiram and pimozide were suspended in a one percent solution of methylcellulose in 0.9% NaCl. The pH of all solutions to be injected was adjusted to 6.5–7.0. Controls received the vehicle alone. Volume of injection was 10 ml kg^{-1} body weight. All injections were by the intraperitoneal route, except for disulfiram. The treatment sequence is described in the legends to the figure and table.

RESULTS

Rate of Metabolism of Pentylamine

Adult mice were given labeled pentylamine, admixed with the unlabeled amine to provide a total dose of 100 mg kg^{-1}. During the first two hours expiration of labeled $^{14}CO_2$ occurred at a fairly constant rate. The cumulative two-hour recovery of radioactivity was 63% ± 1.6 (mean ± SE) for 8 mice.

Effects of Pentylamine Alone

Pentylamine produced a dose-dependent differential pattern of locomotor activity (Fig. 1), along with autonomic symptoms. A low dose, 3 mg kg^{-1}, induced a significant increase in motor activity which lasted for more than two hours. Larger amounts of the amine, 30 and 100 mg kg^{-1}, resulted in decreased locomotor activity. With 30 mg kg^{-1} the decrease occurred immediately after the injection, but it was not statistically significant and did not persist. However, with 100 mg kg^{-1}, locomotion was below control levels throughout the experiment (Fig. 1), although significantly so only in the earliest time periods. These doses led to the gradual appearance of tremor and autonomic symptoms, such as salivation, piloerection, urination, exophthalmos and tail-raising (Straub test). The most pronounced effects were noted at 30–50 min after injection. At that time animals which received 30 or 100 mg kg^{-1} of pentylamine also showed irritability during handling, spontaneous fighting, vocalization and jumping. In the subsequent work only two doses of pentylamine were used: 3 and 100 mg kg^{-1}. These doses provided differential responses in motor activity.

Effects of Reserpine and α-Methyltyrosine

Administration of a single dose of reserpine, 1.0 mg kg^{-1} body weight, caused a profound decrease of motor activity, the mice being essentially inactive for many hours. This effect persisted 48 hr after the injection and longer, as shown by the data in Table 1 (see footnote). α-Methyltyrosine 200 mg kg^{-1}, given just 4 hr before the beginning of activity measurements, also reduced spontaneous activity significantly. When pentylamine was given to mice previously injected with these drugs their quietening effect persisted. Thus, reserpine given as long as 48 hr beforehand eliminated the motor-stimulating effect of the low dose of pentylamine. In a similar experiment reserpine had no additional effect on

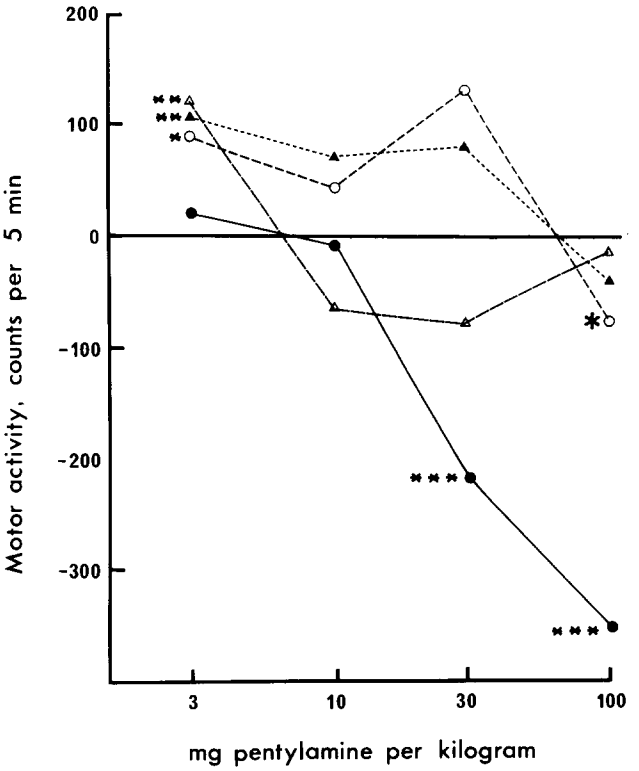

FIG. 1. Dose-dependent effects of *n*-pentylamine on locomotor activity of mice. Ordinate: activity, as movements counted per 5 min, as the difference from the activity of saline-injected controls (indicated by the line at zero level). Abscissa: dose of pentylamine in mg/kg body weight (logarithmic scale). Times of observation: ●——● 5 min: ○——○ 40 min: ▲——▲ 80 min: △——△ 120 min after intraperitoneal administration of pentylamine. The plotted points are the mean cumulative counts per 5 min time interval. Standard errors for points corresponding to 3 and 100 mg kg^{-1} of pentylamine are given in Table 1. Number of animals as follows (dose and number): 3, 30; 10,13; 30,6; 100, 91. $*p<0.05$ $**p<0.01$ $***p<0.001$, as differences from the saline-injected controls.

the depression of activity caused by the high dose of the amine (Table 1). Pentylamine further depressed the activity of α-methyltyrosine-injected mice but only in the period immediately after its injection; this action was statistically significant ($p<0.05$) at 5, but no longer at 40 min, after amine administration.

In other experiments it was found that reserpine given 6 hr before pentylamine not only reduced motor activity but also prevented the appearance of tremor and autonomic phenomena resulting from pentylamine administration. Moreover, ptosis was not observed.

Effects of Other Neuroleptics

The effects of other neuroleptics besides reserpine were tested. Haloperidol, 1.0 mg kg^{-1}, and thioridazine, 20 mg kg^{-1}, decreased the basal level of locomotor activity in control mice by about 75% (Table 2), but pimozide in the dose used, 2.0 mg kg^{-1}, had no significant effect. All three neuroleptics blocked the effect of pentylamine on motor activity: the increase usually seen after 3 mg kg^{-1} of the amine, and the decrease in activity at the higher dose, were

TABLE 1

EFFECT OF DRUGS ON MOTOR ACTIVITY OF MICE

Drugs	Dose mg/kg	No. of mice	Time after drug injection (min) 5	40	80	120
None (saline)		41	458 ± 15	375 ± 25	303 ± 21	262 ± 21
Reserpine	1	8	313 ± 44‡	272 ± 31	200 ± 32*	144 ± 39*
Pentylamine	3	30	468 ± 20	449 ± 22*	400 ± 26†	354 ± 30*
Reserpine	1					
+ Pentylamine	3	8	400 ± 36	339 ± 35§	198 ± 37#	125 ± 60¶
Pentylamine	100	39	112 ± 17‡	289 ± 25*	261 ± 25	245 ± 21
Reserpine	1					
+ Pentylamine	100	8	118 ± 25	375 ± 38	199 ± 33	205 ± 71
α-Methyltyrosine	200	6	278 ± 45‡¶	181 ± 44‡	97 ± 56‡	52 ± 15‡
α-Methyltyrosine	200					
+ Pentylamine	100	6	63 ± 17	141 ± 40	154 ± 43	113 ± 26

Time of injection of pentylamine (or saline) was considered 'zero time'. Reserpine was given 48 hr, α-methyltyrosine 4 hr before motor activity measurements were begun. Mean numbers of counts/min (±SE) are shown.

Superscripts indicate a significant difference of the designated mean from saline controls with the following probabilities: *$p<0.05$,†$p<0.01$, ‡$p<0.001$. Significant differences from the corresponding pentylamine-treated groups are designated as follows: §$p<0.05$, ¶$p<0.01$, #$p<0.001$.

abolished (Table 2). In all circumstances but one the autonomic and behavioral signs did not appear. The exception was in mice receiving pimozide and pentylamine (100 mg kg^{-1}), in which pentylamine-induced salivation persisted.

p-*Chlorophenylalanine*

Because of its ability to inhibit the synthesis of serotonin [10], *p*-chlorophenylalanine was tested. Its administration in a dose of 300 mg kg^{-1} did not affect significantly the activity of the control (saline-treated) mice nor the reduced activity caused by pentylamine in the larger dose used, but it did eliminate the increased activity with the low dose of the amine (Table 2).

p-Chlorophenylalanine did not prevent the appearance of tremor, salivation, tail-raising, vocalization or irritability during handling.

Disulfiram

The action of the neuroleptic drugs suggested that a catecholamine mechanism is at least partially responsible for the effects of pentylamine. Hence, disulfiram, which blocks the conversion of dopamine to norepinephrine was tested in the attempt to differentiate between the roles of these two transmitters. A dose of 300 mg kg^{-1} given intragastrically decreased the basal level of activity of control animals, and also decreased it significantly after mice received pentylamine, 3 mg kg^{-1} (Table 2). However, disulfiram did not block tremor or the autonomic effects. The drug was also tested for a possible inhibitory action on pentylamine metabolism, but it did not significantly influence catabolism of the amine in mice. The percentage of recovery of injected ^{14}C as labeled carbon dioxide in the expired gases at the end of the second hour, determined as described above, for the group receiving disulfiram as well as the amine was 54% ± 6.9, for 5 animals. This was not significantly different from the recovery noted with controls receiving only the amine.

Phenoxybenzamine

This α-adrenergic blocking agent in a dose of 10 mg kg^{-1} decreased motor activity in the control mice by about 65%. It altered activity significantly after pentylamine, by comparison with mice receiving the amine alone. Thus, there was a decrease after pentylamine, 3 mg kg^{-1} ($p<0.01$), and an increase after 100 mg kg^{-1} ($p=0.001$), relative to animals receiving the amine alone. The result of these alterations was that pentylamine causes a dose-dependent increase in motor activity of phenoxybenzamine treated mice. This is in contrast to the biphasic effect of pentylamine alone on motor activity (Fig. 1 and Table 2). Animals did not show any tremor or Straub effect with phenoxybenzamine, but salivation was not completely blocked and the mice were irritable during handling, especially after the large dose of pentylamine.

Atropine

Atropine, 5 mg kg^{-1}, caused an increase of locomotor activity in control mice as well as in those given either dose of pentylamine (Table 2). On the contrary, methylatropine did not have these effects. All mice receiving methylatropine showed essentially the same activity regardless of receiving pentylamine. Both anticholinergic drugs abolished salivation caused by the high dose of pentylamine, but did not prevent the appearance of tremor or the Straub effect.

DISCUSSION

Pentylamine had divergent effects when given at high and low doses, respectively, to mice. Thus, it had stimulating effects in a dose of 3 mg kg^{-1}, and motor-depressing action at

TABLE 2

EFFECTS OF PENTYLAMINE ON MOTOR ACTIVITY OF MICE: INTERACTION OF DRUGS

Drug	Dose (mg kg^{-1})	Time of injection of drugs (hours)	Saline	Pentylamine (3 mg kg^{-1})	Pentylamine (100 mg kg^{-1})
Saline		0	375 ± 25 (41)	449 ± 22* (30)	289 ± 25* (39)
Haloperidol	1	−0.5	123 ± 27¶ (6)	49 ± 13*¶ (6)	99 ± 24§ (6)
Thioridazine	20	−4	85 ± 33¶ (6)	104 ± 51¶ (6)	62 ± 29§ (6)
Pimozide	2	−4	374 ± 31 (8)	295 ± 56¶ (8)	283 ± 63 (7)
p-Chlorophenylalanine	300	−24	386 ± 48 (10)	349 ± 35‡ (6)	285 ± 90 (6)
Disulfiram	300	−4	231 ± 52¶ (10)	284 ± 63§ (10)	201 ± 69 (9)
Phenoxybenzamine	10	−0.5	123 ± 32¶ (10)	325 ± 38†§ (10)	472 ± 32†¶ (10)
Methylatropine	5	−0.5	347 ± 76 (6)	332 ± 91 (6)	316 ± 44 (5)
Atropine	5	−0.5	518 ± 57§ (18)	551 ± 62 (12)	449 ± 66‡ (6)

Motor activity of mice injected with pentylamine (3 or 100 mg kg^{-1}) at zero time, as affected by various drugs given in the doses tabulated, and at the indicated prior times. Controls received saline injections. The mean number of counts during a 5-min interval counted 40 min after the administration of pentylamine (or saline, as in the case of the controls) ± standard error of the mean is shown, with the number of mice given in brackets. The significance of differences owing to pentylamine treatments as compared with saline-injected controls (horizontal comparisons in the table) is indicated by superscripts as follows: *$p<0.05$; †$p<0.001$. For comparisons of the values for the respective pharmacological agents with the control values in the first line of the table, the superscripts indicate probabilities as follows: ‡$p<0.05$; §$p<0.01$; ¶$p<0.001$.

100 mg kg^{-1}. The fact that both effects were blocked by neuroleptics and by the α-adrenergic antagonist phenoxybenzamine suggests that the actions of pentylamine may depend upon stimulation of catecholamine receptors, either directly or indirectly. Of course, the differential effects of the two dose levels of pentylamine could be interpreted as stimulation of the receptor by the lower one and blockade by the higher.

The administration of reserpine produces a marked depletion of the level of catecholamines, serotinon [26] and histamine [8] in the central nervous system, by inhibition of storage mechanisms. Hence it is not possible to ascribe a given effect of the drug to loss of a particular neurotransmitter without other more specific experiments. Reserpine itself has a sedative effect and leads to the reduction of spontaneous motor activity. Normal locomotion can be restored temporarily with large doses of L-dopa [5,7], an effect that is mediated centrally [6]. The low-dose of pentylamine, which has a motor-stimulating effect in otherwise untreated mice, no longer exerts its action in reserpinized animals, even when the reserpine has been given 48 hr earlier. Inhibition of catecholamine synthesis by α-methyltyrosine, an inhibitor of tyrosine hydroxylase, also leads to a decrease of locomotor activity; this effect probably stems from the reduction of brain catecholamines [22], and it is potentiated by the higher dose of pentylamine used here (Table 1, 5 min).

Both cholinergic and catecholaminergic activities seem to be involved in the control of spontaneous locomotion [23]. Recently, Mason and Fibiger [13] have demonstrated the noradrenergic component in this coupling. In the present work an attempt was made to reduce specifically the norepinephrine level in the tissues. The dopamine β-hydroxylase inhibitor disulfiram was given intragastrically, a route of administration chosen to avoid peritoneal irritation which might have independent behavioral effects [30]. The drug caused a decrease of motor activity (Table 2), and this was not affected by pentylamine in either the low or the high dose. The action of disulfiram in interfering with the motor effects of pentylamine is consistent with the view that the amine exerts its action on motor behavior through a noradrenergic mechanism.

In regard to the cholinergic component in regulation of locomotor activity, the stimulating effects of pentylamine were potentiated by atropine, so that cholinergic fibers

presumably play a role in the action of the aliphatic amine as in other motor mechanisms [2,21]. The weak monoamine oxidase-inhibitory action of atropine [15] could also contribute to this potentiation. It is noteworthy that methylatropine did not influence the motor effects of pentylamine. This antimuscarinic alkaloid acts predominantly in the periphery, having very limited sites of action in the brain [32]. Its lack of effect confirms the deduction that the action of atropine in this case is central.

Aliphatic amines cause the release of serotonin from its storage sites, as demonstrated with platelets isolated from rabbit blood [14]. This effect, if occurring also in brain, could lead to behavioral and motor effects. To test this possibility experiments were performed with *p*-chlorophenylalanine, a powerful inhibitor of tryptophan hydroxylase [10], especially at the terminals of serotonin-containing neurons [1], and capable of reducing brain serotonin to low concentrations. As seen in the data of Table 2, this drug does not influence the locomotor activity of mice. Such a result makes it difficult to consider the possibility of a serotonergic mechanism playing an important role in the action on locomotion of an aliphatic amonoamine like pentylamine. However, the inhibitor abolished the motor-stimulating action of pentylamine at low dose (Table 2); this might represent interference with a catecholaminergic mechanism.

Finally, it should be mentioned that the administration of pentylamine can cause the release of histamine, for example, from a guinea pig preparation [17]. Although this action is weak [16,17], there is the possibility that at least some of the effects of a large dose of pentylamine are effected by histamine liberated from the tissues [17].

The appearance, following the injection of pentylamine, of strong salivation, tremor, and spontaneous fighting is remarkably similar to the effects of L-dopa given in combination with an inhibitor of monoamine oxidase [24]. These results suggest that pentylamine is producing its autonomic effects by the release of catecholamines. This is in accord with the view of Palm and Holtz [19] that aliphatic amines provoke sympathomimetic activity (monitored as changes in blood pressure of cat and rat preparations) by an indirect mechanism. In regard to the action of pentylamine in eliciting Straub tail-raising, this phenomenon has been regarded as probably mediated by a dopaminergic mechanism, a view that has been strengthened by a study of the effect of neuroleptic drugs upon it [11]. Although the mechanism of action of disulfiram is not entirely clear, the fact is that the autonomic signs evoked by pentylamine persist in the presence of this drug. If the autonomic effects of this amine are actually mediated by a catecholamine, then the present results with disulfiram place in doubt the likelihood that norepinephrine is the mediator.

REFERENCES

1. Aghajanian, G. K., M. J. Kuhar and R. H. Roth. Serotonin-containing neuronal perikarya and terminals: differential effects of *p*-chlorophenylalanine. *Brain Res.* **54:** 85–101, 1973.
2. Andén, N. E. and P. Bédard. Influences of cholinergic mechanisms on the function and turnover of brain dopamine. *J. Pharm. Pharmac.* **23:** 460–462, 1971.
3. Barger, G. and H. H. Dale. Chemical structure and sympathomimetic action of amines. *J. Physiol., Lond.* **41:** 19–59, 1910.
4. Baum, T. and D. R. Bennett. Structure-activity relationship of aliphatic amines and cardiac stimulation. *Archs int. Pharmacodyn. Thér.* **146:** 280–284, 1963.
5. Blaschko, H. and T. L. Chrusciel. The decarboxylation of amino acids related to tyrosine and their awakening action in reserpine-treated mice. *J. Physiol., Lond.* **151:** 272–284, 1960.
6. Butcher, L. L. and J. Engel. Peripheral factors in the mediation of the effects of L-dopa and locomotor activity. *J. Pharm. Pharmac.* **21:** 614–616, 1969.
7. Carlsson, A., M. Lindqvist and T. Magnusson. 3,4-Dihydroxyphenylalanine and 5-hydroxytryptophan as reserpine antagonists. *Nature, Lond.* **180:** 1200, 1957.
8. Green, J. P., C. L. Johnson and H. Weinstein. In: *Psychopharmacology: a Generation of Progress*, edited by M. A. Lipton, A. DiMascio and K. F. Killam. New York: Raven Press, 1978.
9. Haggard, H. W., D. P. Miller and L. A. Greenberg. Amyl alcohols and their ketones; their metabolic fates and comparative toxicities. *J. ind. Hyg. Toxicol.* **27:** 1–14, 1945.
10. Koe, B. K. and A. Weissman. *p*-Chlorophenylalanine: a specific depletor of brain serotonin. *J. Pharmac. exp. Ther.* **154:** 499–516, 1966.
11. Lee, H. K., C. Y. Chai, M. J. Wayner, P. M. Chung and C. M. Hsu. Effects of neuroleptics on morphine-induced tail erection in mice. *Pharmac. Biochem. Behav.* **7:** 153–157, 1977.
12. Madras, B. and T. L. Sourkes. Formation of respiratory $^{14}CO_2$ from variously labeled forms of tryptophan-^{14}C in intact and adrenalectomized rats. *Archs Biochem. Biophys.* **125:** 829–836, 1968.
13. Mason, S. T. and H. C. Fibiger. Interaction between noradrenergic and cholinergic systems in the rat brain: behavioral function in locomotor activity. *Neuroscience* **4:** 517–525, 1979.
14. May, B., I. Menkens and E. Westermann. Differential release of serotonin and histamine from blood platelets of the rabbit by aliphatic and aromatic amines. *Life Sci.* **6:** 2079–2085, 1967.
15. Mohammed, Y. S. and M. M. Mahfouz. Inhibition of rat brain and heart monoamine oxidase by atropine. *Biochem. Pharmac.* **26:** 871–874, 1977.
16. Mongar, J. L. Effect of chain length of aliphatic amines on histamine potentiation and release. *Br. J. Pharmac.* **12:** 140–148, 1957.
17. Mongar, J. L. and M. O. Schild. Quantitative measurement of the histamine-releasing activity of a series of mono-alkylamines using minced guinea pig lung. *Br. J. Pharmac.* **8:** 103–109, 1953.
18. Neurath, G. B., M. Dinger, F. G. Pein, D. Ambrosius and O. Schreiber. Primary and secondary amines in the human environment. *Food Cosmet. Toxicol.* **15:** 275–282, 1977.
19. Palm, D. and P. Holtz. Über indirekte Wirkungen aliphatischer Amine. *Naunyn-Schmiedebergs Arch. exp. Path. Pharmak.* **251:** 166–167, 1965.
20. Pugh, C. E. M. and H. H. Quastel. Oxidation of alphatic amines by brain and other tissues. *Biochem. J.* **31:** 286–291, 1937.
21. Racagni, G., D. L. Cheney, M. Trabucchi and E. Costa. *In vivo* actions of clozapine and haloperidol on the turnover rate of acetylcholine in rat striatum. *J. Pharmac. exp. Ther.* **196:** 323–332, 1976.
22. Rech, R. H., H. K. Borys and K. E. Moore. Alterations in behavior and brain catecholamine levels in rats treated with α-methyltyrosine. *J. Pharmac. exp. Ther.* **153:** 412–419, 1966.
23. Lloyd, K. G. Neurotransmitter interactions related to central dopamine neurons. *Essays Neurochem. Neuropharmac.* **3:** 129–207, 1978.
24. Sourkes, T. L. Formation of dopamine *in vivo:* relation to the function of the basal ganglia. *Rev. Canad. Biol.* **20:** 187–196, 1961.
25. Sourkes, T. L. Influence of specific nutrients on catecholamine synthesis and metabolism. *Pharmac. Rev.* **24:** 349–359, 1972.
26. Sourkes, T. L. Psychopharmacology and biochemical theories of mental disorders. In: *Basic Neurochemistry, Second Edition*, edited by G. J. Siegel, R. W. Albers, R. Katzman and B. W. Agranoff. Boston: Little Brown, 1976. pp. 705–736.

27. Sourkes, T. L. and K. Missala. Nutritional requirements for amine metabolism in vivo. In: *Monoamine Oxidase and its Inhibition*, edited by G. E. W. Wolstenholme and J. Knight. Ciba Foundation Symposium 39 (new series). Amsterdam: Excerpta Medica North-Holland/Elsevier, 1976, pp. 83–96.
28. Sourkes, T. L. and K. Missala. Action of inhibitors on monoamine and diamine metabolism in the rat. *Can. J. Biochem.* **55:** 56–59, 1977.
29. Symes, A. L., K. Missala and T. L. Sourkes. Iron- and riboflavin-dependent metabolism of a monoamine in the rat in vivo. *Science* **174**: 153–155, 1971.
30. Thornburg, J. E. and K. E. Moore. Stress-related effects of various inhibitors of catecholamine synthesis in the mouse. *Archs int. Pharmacodyn. Thér.* **194:** 158–167, 1971.
31. Williams, R. T. *Detoxication Mechanisms*. New York, Wiley, 1959.
32. Witter, A., J. L. Slangen and G. K. Terpstra. Distribution of ^{3}H-methylatropine in rat brain. *Neuropharmacology* **12:** 835–841, 1973.
33. Zeller, E. A. Oxidation of amines. In: *The Enzymes, Volume 2, Part 1*, edited by J. B. Sumner and K. Myrbäck. New York: Academic Press, 1951, pp. 536–558.