Pyridoxine deficiency produces a marked depression in GABA levels (Table 1, "Saline only" groups). This finding is in accord with earlier reports in which pyridoxal binding agents or B_6 anti vitamins caused lowering of GABA in brain, and in which glutamate decarboxylase activity was shown to be substantially depressed in B_6-deficient animals.[4] The lowered level in the B_6-deficient group was not further depressed by the administration of ethanol, however. Thus the "GABA shunt" appears to have little quantitative significance under conditions of B_6-deficiency and therefore the depressant effect of ethanol on this pathway is not manifest. In this regard it is noteworthy that both glutamate decarboxylase and GABA transaminase require pyridoxal phosphate as coenzyme.

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REFERENCES

1. R. A. FERRARI and A. ARNOLD, *Biochim. Biophys. Acta* **52**, 361 (1961).
2. H. M. HÄKKINEN and E. KULONEN, *Nature, Lond.* **184**, 726 (1959).
3. E. ROBERTS and S. FRANKEL, *J. Biol. Chem.* **187**, 55 (1950).
4. C. F. BAXTER and E. ROBERTS, in *The Neurochemistry of Nucleotides and Amino Acids p.* 127, edited by R. O. Brady and D. B. Tower. Wiley & Sons, New York (1960).

Inhibition of monoamine oxidase activity in sympathetic ganglia of the cat

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IN CATS, the administration of certain drugs that inhibit monoamine oxidase (MAO) is followed by a transient blockade of transmission of electrical impulses through the superior cervical ganglion (1–4). In order to determine whether there is any relationship between ganglionic blockade and inhibition of MAO, the present experiments were designed to characterize this inhibition in the sympathetic ganglia after treatment with two drugs: iproniazid* and N-benzyl-N-methyl-2 propynylamine hydrochloride (MO-911).*

From cats anesthetized with α-chloralose the superior cervical and stellate ganglia were removed before and after intravenous injections of MO-911 and iproniazid, and assayed for MAO activity by a method described previously.[5] The MAO-activity of ganglia removed prior to the administration of a MAO-inhibiting drug ranged from 2·8 to 12·4 (expressed as μmoles indoleacetic acid formed from tryptamine/g tissue per hr of incubation). In each of 10 individual animals, however, the MAO activities of the four ganglia differed by no greater than 15%, and no significant difference between stellate and superior cervical ganglia was detected. It was therefore possible to study inhibition of MAO by using the enzymic activity of one ganglion as a control to compare with that of other ganglia from the same cat. The control ganglion was removed prior to the injection of an MAO-inhibiting drug and was designated as having 100% MAO activity. The levels of MAO in ganglia removed later from the same cat were expressed as the percentage of activity with respect to the control ganglion.

The results of these experiments are presented in Table 1. MO-911, in doses of 10 mg/kg or greater, produced significant inhibition of MAO activity within 10 min and maximal inhibition within 30–60

* MO-911 (pargyline) was kindly supplied by Abbott Laboratories and iproniazid by Hoffmann-LaRoche, Inc.

min. Complete inhibition could be achieved with doses of 20 mg/kg or greater. After the administration of iproniazid, in doses of 25 mg/kg or greater, the onset of MAO inhibition was observed later, at 30 min; maximal inhibition occurred within 120 min. Complete inhibition of MAO activity was not achieved, even with doses as high as 400 mg/kg. No significant recovery of MAO activity was detected within 24 hr after the administration of either drug.

TABLE 1. MAO ACTIVITY* IN GANGLIA OF THE CAT AT VARIOUS INTERVALS AFTER INTRAVENOUS INJECTIONS OF MO-911 AND IPRONIAZID

Dose† (mg/kg)	No. of cats	10 min	30 min	60 min	120 min	24 hr‡
MO-911						
5	2	89 ± 11	94 ± 8	87 ± 4		
10	3	27 ± 11	18 ± 14	5 ± 3·3		
20	2	19 ± 5	0·5 ± 0·5	1 ± 0·5		
40	4	13 ± 7·5	1 ± 0·5	0 ± 0	0·5 ± 0·5	1·5 ± 1·5
Iproniazid						
12·5	2		98 ± 4	101 ± 1	104 ± 9·5	
25	3		98 ± 0	86 ± 9·3	75 ± 1·3	
50	3		93 ± 4·3	76 ± 2·7	56 ± 4	
100	5		56 ± 4·2	35 ± 8·8	29 ± 2·2	34 ± 5
200	4	100 ± 2·5	57 ± 5·5	25 ± 6·2	19 ± 6	18 ± 7
400	2	98 ± 5·5	45 ± 8	33 ± 0·5	20 ± 5	

* Expressed as percentage of MAO activity remaining as compared with activity of control ganglion (mean ± mean deviation).

† Expressed as mg of drug base.

‡ Each 24-hr figure represents values obtained in 2 cats.

A comparison of these findings with those of Goldberg and DaCosta (2–4) reveals a rough correlation between the time of onset of ganglionic blockade and the time of onset of MAO inhibition with both drugs. However, a dose of 50 mg/kg of iproniazid, which results in ganglionic blockade, will produce only 45% inhibition of MAO, while a dose of 20 mg/kg of MO-911, which is followed by 100% MAO inhibition, will not block ganglionic transmission. Furthermore, complete recovery of ganglionic transmission occurs within 30 min after a dose of MO-911 sufficient to produce complete inhibition of MAO activity lasting at least 24 hr. After recovery of transmission, the administration of another dose of MO-911 results in another short interval of depressed ganglionic transmission. Obviously, the second dose could not have increased inhibition of MAO, since the enzyme was already completely inhibited. It is concluded that MO-911 and iproniazid depress ganglionic transmission in the cat by some mechanism other than the inhibition of MAO activity.

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REFERENCES

1. S. B. GERTNER, *Nature Lond.*, **183**, 750 (1959).
2. L. I. GOLDBERG and F. M. DACOSTA, *Proc. Soc. Exp. Biol. N.Y.*, **105**, 223 (1960).
3. F. M. DACOSTA and L. I. GOLDBERG, *Fed. Proc.* **20**, 318 (1961).
4. F. M. DACOSTA and L. I. GOLDBERG. To be published.
5. W. LOVENBERG, R. J. LEVINE and A. SJOERDSMA, *J. Pharmacol. Exp. Ther.* **135**, 7 (1962).