of the 5-HT epsp. L-3-4-Dihydroxyphenylalanine increased the initial and final heights of the ipsp and the ILD. 5-Hydroxytryptophan increased the number of stimuli required to reach the final 5-HT height.

This work presents further evidence for the identity of chemical transmitters in the snail brain.

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Actions of phenelzine on the interactions of the metabolism of tryptophan and dopamine in brain

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The acid metabolites 5-hydroxyindole-3-ylacetic acid (5-HIAA) and homovanillic acid (HVA) in cerebrospinal fluid (CSF) have been shown to be derived only from the metabolism of their parent amines, 5-HT and dopamine, occurring in brain. Recently (Moir, 1969) it was shown in dogs that an intravenous injection (50 mg/kg) followed by an intravenous infusion [(20 mg/kg)/h for 4 h] of L-tryptophan led to steady-state levels of the 5-hydroxyindoles in brain in which the concentrations of the 5-hydroxyindoles in various regions were all raised to between 2 and 3 times their normal control values. The concentrations of 5-HIAA in CSF from the cisterna magna during the 3–4 h period after the start of the tryptophan infusion were also three times control values. Surprisingly, concentrations of HVA in these same samples of CSF showed an even greater rise, being 14 times the normal control values; however, normal concentrations of dopamine and its main metabolites were found in the caudate nucleus. In the present experiments, dogs were pre-treated for 10 days with phenelzine (2 mg/kg subcutaneously) and then given, as previously described (Moir, 1969), an intravenous injection—infusion of L-tryptophan or an equivalent volume of saline.

The pattern of concentration changes of the amino-acids tryptophan and tyrosine in erythrocytes, CSF and brain following tryptophan or saline infusion were not affected by phenelzine. In saline-infused dogs phenelzine pre-treatment caused a fall in 5-HIAA concentration in CSF from the lateral ventricle, but not the cisterna magna, while in brain concentrations of 5-HT rose to 400% and 5-HIAA to 150% of normal.

In the phenelzine pre-treated animals a subsequent infusion of tryptophan did not increase brain 5-HT concentrations any further, and while brain concentrations of 5-HIAA showed a slight increase, its concentrations in CSF during the tryptophan infusion behaved exactly as during the saline infusion. These and earlier (Ashcroft, Crawford, Dow & Moir, 1969) results show that phenelzine inhibits the cerebral 5-hydroxyindole pathway at four separate points; tryptophan 5-hydroxylase, monoamine oxidase, 5-HIAA efflux from brain and 5-HIAA efflux from CSF.

The caudate nuclei of dogs treated with phenelzine alone showed high concentrations of dopamine and 3-methoxydopamine and low concentrations of 3,4-dihydroxyphenylacetic acid and HVA. The HVA was also in very low concentrations in CSF from the lateral ventricle and cisterna magna. In the dogs given subsequent

tryptophan infusion the concentration of HVA in CSF at both sampling sites rose markedly during the infusion period. The caudate nuclei of these dogs compared with their phenelzine pre-treated controls had lower dopamine concentrations and raised levels of the three metabolites.

The evidence for an interaction between the two metabolic pathways can be revealed by CSF analyses. Brain analyses can also demonstrate the interaction; however, it is then necessary to reduce the turnover of dopamine and, possibly, also compensatory feedback mechanisms.

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Acute hypothermic response of the rat to intraventricular injection of 6-hydroxydopamine

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Intraventricular injections of 6-hydroxydopamine (6-OHDA) cause a long-lasting depletion of both noradrenaline and dopamine from the brains of rats. The depletion is dose-dependent, the loss of noradrenaline being detectable at lower doses of 6-OHDA than those required to deplete dopamine (Uretsky & Iversen, 1970). These effects have been attributed to the degeneration of catecholamine-containing neurones in the brain.

In the present studies, the intraventricular injection of 6-OHDA into rats at room temperature was followed by a fall in body temperature of up to 4·5° C which lasted for 4 to 5 h. The degree of hypothermia increased with increasing dose in the range 5 to 250 μg 6-OHDA. Depletion of brain noradrenaline content to 20·7$\pm$6·2% (mean $\pm$ S.E.M., n=4) of the control and brain dopamine to 34·6$\pm$6·4% (n=4) of the control by pretreatment with two intraventricular doses of 250 μg 6-OHDA abolished the hypothermic response to a subsequent dose of 250 μg 6-OHDA. It appeared, therefore, that 6-OHDA was causing hypothermia by an interaction with catecholamine-containing neurones. In order to distinguish whether neurones containing noradrenaline or dopamine were necessary for the response, rats were pretreated with three intraventricular doses of 25 μg 6-OHDA. This procedure depleted noradrenaline to 25·0$\pm$2·9% (n=4) of the control while dopamine was unaffected at 89·5$\pm$9·1% (n=4) of the control. Rats pretreated in this way responded to a subsequent dose of 250 μg 6-OHDA with a hypothermia which was no smaller than that following the same dose of 6-OHDA in control rats. Thus, it appeared that neurones containing dopamine rather than noradrenaline were involved in the hypothermic response to 6-OHDA. This interpretation was further supported by the finding that protriptyline HCl (15 mg/kg intraperitoneally) did not reduce the hypothermic response to a dose of 150 μg 6-OHDA injected 120 min later. The simultaneous depletion of noradrenaline by 6-OHDA was significantly reduced by protriptyline under these conditions while the depletion of dopamine was not impaired (Evetts & Iversen, 1970).