with buffers of increasing ionic strength, and 4. Elution of the specific enzyme with the free specific inhibitor (same type as bound inhibitor). Affinity separation is only obtained when the 'spacer' has a considerable length. The spacer synthesis is laborious, time-consuming, and very expensive. With pre-synthesis of an inhibitor of sufficient length: 1-(N, N, N-Trimethylammonium)-10-decylamine bromide hydrobromide, and the use of a commercially available diamine (Spermine), first applied by J. Schmidt and M. A. Raftery, Biochem. *12*, 852 (1973) for separation of cholinergic receptor proteins, the synthesis could be simplified in any of the above mentioned ways with no loss in overall yield.

Disposition by Intact Rat Uterus of Oxytocin Analogues Modified in the Cystine Moiety

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[6,1-Cystathionine]oxytocin ['1-carba-oxytocin, *1*; cf. Jošt et al., Coll. Czechoslov. Chem. Commun. *38*, 1073 (1973)] and [1,6-α,α'-diaminosuberic acid]oxytocin (*2*) have been synthesised. The rate of relaxation of the K^+-depolarised rat uterus immersed in oil [Kalsner, Nickerson, Can. J. Physiol. *46*, 719 (1968); Furrer, Rudinger, Experientia *28*, 742 (1972)] after contraction with 1,2,desamino-oxytocin (*3*), its 'l-carba' and 'dicarba' analogues (*4* and *5*), and of [1-hydroxy-2-mercaptopropionic acid]-oxytocin *6* [Hope, Wälti, Biochem. J. *125*, 909 (1971)] has been measured. The overall rate decreases in the order oxytocin $>$ *1* $\sim$ *6* $>$ *2* $>$ *3* $\sim$ *4* $\sim$ *5*. This structural dependence and the clearly multiphasic character of the relaxation curves indicated that one or more processes in addition to enzymic inactivation are involved in the disposition of the hormones.

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Effect of L-Dopa on Endogenous Noradrenaline in Rat Brain

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In the brain of rats, i.p. administration of L-dopa enhanced the disappearance of endogenous noradrenaline (NA) induced by FLA 63, an inhibitor of dopamine-β-hydroxylase. This effect was dose-dependent. In addition, 50 mg/kg L-dopa i.p. significantly increased the cerebral levels of 3-methoxy-4-hydroxy-phenylethylene glycol-sulfate, the main metabolite of brain NA. These findings indicate that L-dopa caused a release of NA, probably due to displacement of the amine by the newly formed dopamine. However, L-dopa administered i.p. alone or in combination with benserazid, an inhibitor of extracerebral decarboxylase, did not modify the content of endogenous cerebral NA.

It is concluded that L-dopa increases the turnover of brain NA whereby the exogenous amino acid is the source of the synthesized amine.

[2-o-Iodotyrosine]oxytocin Inhibits the Response of the Rat Uterus to Oxytocin

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[Tyr(I)^2]-Oxytocin has been prepared by iodination of oxytocin [Thompson, Freychat, Roth, Endocrinology *91*, 1199 (1972)] and by total synthesis using the S-Acm protecting group. The purified and chemically characterised analogue has no uterotonic activity but inhibits the response of the isolated rat uterus to oxytocin in media with or without Mg, with pA_2 ~7.2. Radioiodine-labelled oxytocin should therefore be suitable for studying binding to uterine receptors. The analogue has slight antidiuretic activity but no rat pressor activity in doses up to 250 μg/kg. It inhibits the pressor response to pituitary extract. [2-o-Methyltyrosine]oxytocin has similar properties, showing that the antagonism is due to the steric effect of the o-substituent and not to the change in pK_a of the phenolic hydroxyl caused by the iodine.

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Lack of Correlation between Changes in cAMP and Trans-Synaptic Enzyme Induction

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Treatment of neonatal rats with nerve growth factor antiserum or 6-hydroxydopamine producing an extensive (61–85%) specific destruction of the adrenergic neurons in the rat superior cervical ganglion led to a decrease in the ganglionic cAMP content by 16 to 28% only. This indicates that only a relatively small portion of the total cAMP is localized in the adrenergic neurons. However, administration of 0.4 mg/kg of isoproterenol produced a 12-fold increase in cAMP exclusively in this neuronal pool. Single or repeated injections of isoproterenol did not evoke a TH induction in the superior cervical ganglion. These results, together with observations that experimental conditions leading to a trans-synaptic induction of TH in sympathetic ganglia (swimming stress, treatment with reserpine) did not change cAMP levels do not support the assumption that cAMP plays a key role in trans-synaptic TH induction.
Dissociations between changes in cAMP and subsequent rise in TH also became apparent in the rat adrenal medulla.

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Drug-Induced Rotation in Rats after Unilateral Intracerebral Injection of 5,6-Dihydroxytryptamine (5,6-HT)

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Unilateral stereotaxic injection of 10 μg of 5,6-HT in the medial forebrain bundle (MFB) of rats produces, within 10 days, a marked unilateral decrease of the forebrain levels of serotonin (5-HT) and dopamine (DA) (Saner et

al. 1974), due to unilateral degeneration of serotonergic and dopaminergic non-terminal axons in the MFB (Lorez et al. 1974).

In these 5,6-HT-lesioned rats, apomorphine down to 0.1 mg/kg i.p. induced rotation towards the non-lesioned side, whereas *d*-methamphetamine down to 0.5 mg/kg i.p. evoked ipsilateral rotation. Haloperidol 1 mg/kg i.p. blocked the effect of apomorphine (1 mg/kg i.p.) and *d*-methamphetamine (3 mg/kg i.p.). LSD (100 and 200 μg/kg i.p.) elicited controlateral rotation. Injection of LSD for 5 consecutive days did not result in tolerance. Mescaline, up to 20 mg/kg i.p., proved inactive. Haloperidol 1 mg/kg i.p. was also able to block the rotation induced by LSD. It is tentatively concluded that LSD may exert an apomorphine-like direct stimulation of DA receptors.

Intracellular Uptake and Membrane Binding of Ca in Human Red Cell Ghosts

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The K permeability of resealed human red cell ghosts increases greatly when the intracellular Ca ion concentration (Ca_i) is raised from 10^{-7} to 10^{-6} *M*. This Ca-dependent permeability change was used as a measure of the inward movement of extracellular Ca. Ca-free ghosts were loaded with increasing concentrations of EGTA and incubated in NaCl media containing up to 5 m*M* Ca. Under these conditions the change in Ca_i resulting from uptake of Ca is determined by the intracellular Ca/EGTA concentration ratio and the apparent binding constant of the CaEGTA complex ($\sim 10^7$). The amount of Ca which had penetrated into the cell was calculated from the cellular EGTA concentration which was just insufficient to block the Ca-induced K loss. When the medium contained 5 m*M* Ca the cells took up a total of 0.8 m*M* Ca. The change in Ca_i was only 0.01 m*M*, the rest was probably bound to the membrane. The action of local anesthetics showed that Ca binding and Ca permeability behaved as independent variables: 1 m*M* tetracaine or propranolol decreased Ca binding by 45 and 20% respectively. The Ca membrane transfer was not changed by tetracaine but was increased nearly 5-fold by propranolol.

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5,6-Dihydroxytryptamine: Mode of Administration and Effect on Brain Monoamines

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After intraventricular injection in rats, 5,6-dihydroxytryptamine (5,6-DHT, 50 μg) produced a transient and rather selective depletion of cerebral 5-hydroxytryptamine (5-HT), and a more substantial and permanent reduction of this amine in the spinal cord. On the other hand, unilateral stereotaxic injections of 0.5–10 μg 5,6-DHT in the medial forebrain bundle and the nigrostriatal dopamine (DA) bundle of rats caused a marked dose dependent, and long lasting (> 170 days) decrease of both, 5-HT and DA with only a slight reduction of noradrenaline (NA) in the homolateral telediencephalon. Furthermore, direct application of 5,6-DHT in the dorsal NA bundle did not substantially affect the NA content. In addition, the uptake of 5-HT and DA into brain slices and synaptosomes of the telediencephalic regions homolateral to the stereotaxic injection was reduced. The results suggest that intracerebral in contrast to intraventricular administration of 5,6-DHT causes a destruction not only of 5-hydroxytryptaminergic but also of dopaminergic pathways in the brain, possibly as a result of anterograde degeneration.

Specificity of the Retrograde Axonal Transport of Nerve Growth Factor (NGF)

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NGF promotes growth and differentiation of the peripheral sympathetic nervous system. This protein is taken up into the adrenergic nerve terminals and reaches the cell body by rapid (2.5 mm/h) retrograde axonal transport (RAT) which is blocked by colchicine.

The specificity of RAT was investigated by injecting ^{125}I-labelled NGF and a series of other ^{125}I-labelled proteins with differing (6,000–500,000) molecular weights and isoelectric points (4.5–9.8) into the mouse anterior eye chamber. The preferential accumulation of radioactivity in the superior cervical ganglion of the injected side was taken as a measure for RAT. Of all the proteins NGF and tetanus toxin were the only ones which exhibited a statistically significant ($P < 0.001$) difference (3-fold for NGF, 2-fold for tetanus toxin) between injected and non-injected side. Moreover, small chemical changes of the NGF molecule resulted in a marked reduction of RAT. It is noteworthy that the RAT of NGF is confined to the adrenergic neurons whereas that of tetanus toxin occurs in all the neurons studied, so far. Thus, RAT of tetanus toxin seems to depend on general properties of nerve terminals whereas that of NGF on those specific for adrenergic neurons.

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Does Maprotiline (LUDIOMIL®) Influence Serotonin Uptake and Free Tryptophan Concentration in Human Plasma?

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The influence of maprotiline, a tetracyclic antidepressant, on plasma tryptophan binding, serotonin uptake and content of blood platelets has been studied in healthy volunteers. Plasma total and free tryptophan concentrations were measured after treatment with either maprotiline (100 mg/day) for four days or acetylsalicylate (2 g on the evening prior to and the morning of the experiment) as a known competitor of tryptophan binding to plasma albumin.

No alteration in plasma tryptophan binding was noted after maprotiline treatment in contrast to a marked increase in free tryptophan in the acetylsalicylate group. Neither maprotiline nor acetylsalicylate had an influence on the uptake or content of serotonin in blood platelets from these samples.