Amino acid-induced stimulation of [^{3}H]-dopamine release from rat striatum *in vitro*

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It is apparent that the factors regulating the release of dopamine (DA) from nerve terminals of the nigrostriatal pathway are complex. Not only is there an involvement of presynaptic DA receptors (Westfall, Besson, Giorguieff & Glowinski, 1976), but the finding that both acetylcholine (Giorguieff, Le Floc'h, Glowinski & Besson, 1976; de Belleroche & Bradford, 1978) and GABA (Giorguieff, Kemel, Glowinski & Besson, 1978) enhance the release of DA newly-synthesized from [^{3}H]-tyrosine, suggests additional control mechanisms. We have investigated the effects of a number of amino acids upon the release of DA from rat striatal slices, with particular emphasis on the actions of glutamic acid, since this substance is probably the excitatory transmitter of the cortico-striatal pathway.

Striatal slices (1 mm thickness) were prelabelled with [^{3}H]-DA (50 nM) by incubation in Krebs-bicarbonate medium containing nialamide (10 μM) and ascorbic acid (1 mg/ml) for 20 min under 95% O_2–5% CO_2. Slices were then blotted and transferred individually through a series of flasks containing 5 ml buffer. The effect of test compounds on the release of radioactivity was studied by their inclusion in the medium during the sixth 5 min incubation period. L-glutamate (20–100 μM) produced a dose-related increase in the release of [^{3}H]-DA and this exhibited an absolute requirement for Ca^{2+}. The effect could be mimicked by a number of related excitatory amino acids including D-glutamate, L-aspartate (but not the D-isomer), cysteate, kainate and ibotenate. The conformationally-restricted excitatory analogue of glutamate, *cis*-1-amino-1,3-dicarboxycyclopentane (McLennan & Wheal, 1978) was found to be a potent releaser of [^{3}H]-DA, where the *trans*-isomer, which on theoretical grounds should have only a weak action at glutamate excitatory receptors, was inactive. The compounds L-glutamine, β-aminoglutarate, leucine and arginine were also inactive, thus indicating an involvement of specific receptors. The addition of two proposed glutamate antagonists, glutamate diethylester and 2-amino-4-phosphonobutyric acid (100 μM) resulted in a marked diminution in the release of DA evoked by L-glutamate. The addition of procaine (1 mM) or tetrodotoxin (0.5 μM) did not reduce the stimulated release, suggesting that the glutamate receptors are localized on the dopaminergic terminals themselves.

Preliminary experiments have also been performed with the putative neurotransmitter amino acids GABA, glycine and proline. When tested at a concentration of 100 μM, each substance produced a significant stimulation of [^{3}H]-DA release. The effects of GABA were reduced in the presence of bicuculline (50 μM), whilst the actions of both glycine and proline were potently inhibited by the addition of strychnine (1 μM). It thus seems possible that glycine and perhaps also proline, may have roles in synaptic function in the rat striatum. Although there is little evidence for a transmitter role for glycine in supra-spinal regions, it is of interest that application of glycine to nigral neurones results in inhibition of striatal DA release (Cheramy, Nieoullon & Glowinski, 1978).

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