'high-affinity' transport system ($K_T \sim 7\ \mu M$). Further, Curtis, Game & Lodge (1976) have recently obtained electrophysiological evidence for potentiation of iontophoretically-applied GABA in the central nervous system by inhibiting both neuronal and glial carriers. This does not of course imply that carrier-mediated transport affects the action of synaptically-released GABA.

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References

BOWERY, N.G., BROWN, D.A., COLLINS, G.G.S., GALVAN, M., MARSH, S. & YAMINI, G. (1976). Indirect effects of amino acids on sympathetic ganglion cells mediated through release of γ-aminobutyric acid from glial cells. *Br. J. Pharmac.*, **57**, 73–91.

CURTIS, D.R., GAME, C.J.A. & LODGE, D. (1976). The *in vivo* inactivation of GABA and other inhibitory amino acids in the cat nervous system. *Exp. Brain Res.*, **25**, 413–428.

IVERSON, L.L. & KELLY, J.S. (1975). Uptake and metabolism of γ-aminobutyric acid by neurones and glial cells. *Biochem. Pharmacol.*, **24**, 933–938.

KROGSGAARD-LARSEN, P. & JOHNSTON, G.A.R. (1975). Inhibition of GABA uptake in rat brain slices by nipecotic acid, various isoxazoles and related compounds. *J. Neurochem.*, **25**, 797–802.

LEVI, I.G. & RAITERI, M. (1974). Exchange of neurotransmitter amino acid at nerve endings can simulate high affinity uptake. *Nature (Lond.)*, **250**, 735–737.

Inhibition of substance P release from the isolated rat substantia nigra by GABA

T.M. JESSELL (introduced by L.L. IVERSEN)

MRC Neurochemical Pharmacology Unit, Department of Pharmacology, University of Cambridge

The undecapeptide substance P is widely distributed within the rat central nervous system and highest levels are found in the substantia nigra (Kanazawa & Jessell, 1976). In addition biochemical and immunohistochemical studies have indicated the presence of substance P containing fibres in striato-nigral and pallido-nigral pathways in the rat brain (Kanazawa, Emson & Cuello, 1976). Using a sensitive radioimmunoassay we have previously demonstrated the potassium-evoked and calcium-sensitive release of endogenous substance P from superfused slices of rat hypothalamus (Jessell, Iversen & Kanazawa, 1976), and in the present study we have refined this technique to investigate the release of substance P from the isolated rat substantia nigra.

Substantia nigra tissue from two rats (10–12 mg) was dissected from 0.8 mm thick coronal sections of the mesencephalon and chopped at 0.2 mm intervals in two directions. Nigral slices were superfused at 37°C with Krebs bicarbonate containing 0.5% albumin at a rate of 375 μl/min. Superfusate samples were collected at 1 min intervals and substance-P like immunoreactivity in each sample, and in the nigral tissue recovered after superfusion was determined by radioimmunoassay. After 5 min of superfusion the spontaneous efflux of substance P remained constant (8.40 ± 0.31 fmol mg^{-1} min^{-1}, mean ± s.e. mean $n=4$) and represented approximately 0.5% of tissue stores released per minute. Raising the potassium concentration in the superfusing medium to 47 mM for 2 min evoked 39.03 ± 4.04 fmol/mg (mean ± s.e. mean $n=4$) increase in substance P release. Furthermore, the potassium-evoked release of substance P from the rat substantia nigra was calcium-dependent and increased as a function of the Ca^{2+} concentration over the range of 0.1 to 3.0 mM Ca^{2+}.

In addition to the substance P pathway described, there is also strong evidence for a descending GABA mediated projection from the corpus striatum to the substantia nigra, although the synaptic connections of GABA-releasing neurones within the substantia nigra are unknown (Dray & Straughan, 1976). Superfusion of substantia nigra slices with Krebs bicarbonate containing GABA (5×10^{-5} M) inhibited the potassium-evoked release of substance P by $77.6 \pm 12.0\%$ (mean ± s.e. mean $n=8$). The inhibitory effect of GABA could be reversed by the addition to the superfusion medium of picrotoxin (5×10^{-5} M), a GABA receptor antagonist. Superfusion with Krebs bicarbonate containing picrotoxin (5×10^{-5} M) in the absence of GABA did not affect the spontaneous or potassium-evoked release of substance P. It is likely, therefore, that GABA-containing neurones exert an inhibitory effect on substance P terminals within the substantia nigra, although the mechanism of this inhibition remains to be clarified.

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References

DRAY, A. & STRAUGHAN, D.W. (1976). Synaptic mechanisms in the substantia nigra. *J. Pharm. Pharmac.*, **28**, 400–405.

JESSELL, T.M., IVERSEN, L.L. & KANAZAWA, I. (1976). Release and metabolism of substance P in rat hypothalamus. *Nature* (in press).

KANAZAWA, I., EMSON, P. & CUELLO, A.C. (1976). Evidence for the existence of substance P-containing fibres in striato-nigral and pallidol-nigral pathways in rat brain. *Brain Res.* (in press).

KANAZAWA, I. & JESSELL, T.M. (1976). Post-mortem changes and regional distribution of substance P in the rat and mouse nervous system. *Brain Res.*, **117**, 362–367.