Diazepam facilitates the potassium-stimulated release of [^{3}H]-dopamine from rat striatal tissue

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There is considerable pharmacological and electrophysiological data which suggests that the benzodiazepines facilitate GABAergic transmission in the mammalian CNS (Costa, Guidotti & Mao, 1975; Haefely, Kulcsar, Möhler, Pieri, Polc & Schaffner, 1975). There is evidence to support two alternative, though not mutally exclusive, mechanisms for this facilitation: Guidotti, Toffano & Costa (1978) have suggested that the benzodiazepines increase the affinity of the GABA receptor for its neurotransmitter, while Mitchell & Martin (1978) have shown that a number of benzodiazepines can increase the K^+-induced release of GABA from frontal cortex tissue *in vitro*. We report here the results of some experiments which demonstrate that diazepam facilitates the K^+-induced release of dopamine (DA) from rat striatal tissue, an effect which does not appear to involve GABA.

The method used was essentially that of Raiteri, Angelini & Levi (1974). Briefly, rat striatal tissue was chopped into prisms 0.1 × 0.1 × 2 mm and suspended in a physiological medium. Following pre-incubation at 37°C, the tissue was allowed to take up [^{3}H]-neurotransmitter and then placed onto filters in thermostatically-maintained chambers. The tissue beds were continuously superfused with medium and 1 min (0.5 ml) fractions collected; for stimulus-induced experiments, normal medium was replaced by medium containing 15 mMK^+.

Diazepam (10^{-5}M) caused a significant 47.5 ± 12.5% (n = 8) increase in the release of [^{3}H]-DA caused by 15 mM K^+, but exhibited no effect on the basal (unstimulated) release. Starr (1977) has reported that GABA causes a similar facilitation of K^+-induced DA release from striatal tissue, though this is contrary to the finding of Stoof & Mulder (1977). In view of our demonstration that a number of benzodiazepines can facilitate GABA release from frontal cortex tissue, the possibility that the facilitated DA release observed here was secondary to an effect on GABA release was investigated. In these experiments, we were unable to demonstrate any facilitation of basal or 15 mM K^+-induced release of [^{3}H]-GABA from striatal tissue by 10^{-5} M diazepam. Furthermore, we could find no evidence from our experiments that exogenous GABA (10^{-5} M to 10^{-3} M) was able to facilitate basal or K^+-induced release of [^{3}H]-DA from this tissue. It would therefore appear that the facilitation of K^+-induced DA release by diazepam does not involve GABA, but may be due to a direct pre-synaptic control of DA release, presumably via benzodiazepine receptors.

However, in another series of experiments it was found that the facilitation of K^+-induced [^{3}H]-DA release by 10^{-5} M diazepam (39.3 ± 10.2% increase over K^+ alone) was significantly reduced in the presence of 10^{-5} M bicuculline (16.9 ± 7.9% increase over K^+ alone), (n = 5), a similar reduction being observed with bicuculline methiodide; though using picrotoxin (10^{-5} M) we were unable to affect the facilitation of DA release caused by diazepam.

The experiments reported here describe an enhancement of K^+-stimulated release of [^{3}H]-DA from striatal tissue by diazepam, which does not appear to be mediated by GABA. The effect is not secondary to GABA release nor is it mimicked by exogenous GABA, although it is inhibited by bicuculline (generally considered to be a specific GABA antagonist) whilst being unaffected by picrotoxin.

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