for the biochemical studies. Thirty days after denervation (CP DA depleted by 84%) striatal DA receptor density, as assessed using [^{3}H]-haloperidol binding, was elevated by 34% (range 26–28%, $P < 0.001$); the activity of DA stimulated adenylate cyclase in striatal homogenates was unchanged. A 17% increase in ACB DA receptor density was recorded but this did not achieve significance ($P > 0.05$); no changes were observed in the TUO or FC. The LH lesions caused 77–86% depletions in ACB and TUO DA.

One or three days of treatment with intrastriatal DA (100 μg daily) failed to alter the number of haloperidol binding sites in the CP, TUO, ACB or FC. However, 7 days of treatment caused a 47% decrease (38–58%, $P < 0.001$) in haloperidol binding in CP tissue. Whilst there was also a tendency for the number of haloperidol binding sites to be reduced in both the ACB and TUO after 7 days of intrastriatal DA, this never achieved significance (range 11–31%, $P > 0.05$). The number of binding sites in the FC remained unchanged.

The data indicates a differential response of the receptor population in the striatal and mesolimbic areas to denervation: the number of haloperidol binding sites were significantly increased in the CP but not in the ACB or TUO. Also, the data provides the first evidence that chronic stimulation of DA receptors in the CP by DA can reduce the number of DA receptor sites in this area independent of significant changes in receptor numbers, as indicated by haloperidol binding, in mesolimbic or cortical areas.

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Effects of benzodiazepines and barbiturates in a GABA-dependent animal model: interactions with muscimol in the globus pallidus

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Benzodiazepines can interact with γ-aminobutyric acid (GABA)-mediated neurotransmission (Costa, Guidotti, Mao & Suria, 1975; Haefely, Kulcsar, Moehler, Pieri, Polc & Schaffner, 1975). Their ability to potentiate GABA at postsynaptic receptor sites might underlie some of their pharmacological actions (Haefely, 1977; MacDonald & Barker, 1978). We have investigated the effects of benzodiazepines and barbiturates on GABA-mediated neurotransmission in the globus pallidus (GP) using an *in vivo* animal model (Crossman, Lee & Slater, 1977).

Female Sprague-Dawley rats (180–200 g) were fitted with a chronically-implanted electrode for stimulating the neostriatum and a cannula for microinjection into the ipsilateral GP. Electrical stimulation of the neostriatum causes a contralateral head-turn. The time taken for a 90° head-turn is measured. GABA antagonists shorten the response time but the GABA agonist muscimol increases it (Crossman *et al.*, 1977).

Benzodiazepines (administered either i.p. or in GP) resembled GABA agonists and caused slowing of the head-turn. The doses required (i.p.) to increase the response time by 50% (ED_{50}) were: chlordiazepoxide 10.8 mg/kg; diazepam 3.7 mg/kg; lorazepam 1.5 mg/kg and clonazepam 0.6 mg/kg. Diazepam no longer slowed the head-turn after twice daily injections of 3 mg/kg for 4 days. The sedation also disappeared after a few days.

Table 1 The interaction of benzodiazepines and barbiturates with muscimol in the head-turning model

Drug	*Dose (mg/kg i.p.)*	*Mean % slowing*	*Muscimol* *Dose in GP*	*Mean % slowing*	*Drug and muscimol together: mean % slowing*
Chlordiazepoxide	10	84*	1 ng	16*	375*
Chlordiazepoxide	10	84*	25 ng	101*	395*
Diazepam	3	54*	1 ng	16*	32*
Diazepam	3	54*	25 ng	60*	1317**
Phenobarbitone	4	8	1 ng	10	19
Phenobarbitone	4	8	25 ng	157**	108*
Pentobarbitone	4	42*	1 ng	13	57*
Pentobarbitone	4	42*	25 ng	354*	529**

Each result is the mean from 6 animals. Significance of differences (before v. post drug) was determined by the paired Student's t test. * $P < 0.05$; ** $P < 0.01$.

Rats were treated simultaneously with chlordiazepoxide (10 mg/kg i.p.) and muscimol (1–25 ng in GP). Mutual potentiation of their individual effects upon head-turning was observed (Table 1). A similar synergism occurred between diazepam (3 mg/kg) and the larger doses of muscimol (10–25 ng). These findings could be explained by muscimol increasing the affinity of benzodiazepines for their specific receptor and thus potentiating their effects. A similar interaction has been demonstrated *in vitro* (Tallman, Thomas & Gallager, 1978).

The anticonvulsant barbiturate phenobarbitone (2–16 mg/kg i.p.) had no significant effect on head-turning after 1 h. Phenobarbitone did not potentiate the effect of muscimol in GP. The sedative barbiturate pentobarbitone (2–16 mg/kg) caused a dose-dependent slowing of the head-turn (ED_{50} 5.9 mg/kg) and potentiated the effect of muscimol (10–25 ng) in GP. Smaller doses of muscimol were not potentiated. Sedative barbiturates such as pentobarbitone may interact with the GABA receptor-ionophore system (Ticku & Olsen, 1978). Anticonvulsant barbiturates have a much weaker effect at this site.

These results demonstrate that benzodiazepines and sedative barbiturates possess GABA-like properties when tested in the head-turning model.

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