Biphasic changes in motor behaviour following morphine injection into the nucleus accumbens

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Morphine and morphine-like agents are able to initiate changes in motor behaviour which are characteristic both of dopamine antagonism (catalepsy) and dopamine stimulation (stereotyped behaviour and hyperactivity). Extensive electrolesion studies have given some indication of the dopamine-containing areas involved with mediating catalepsy (the amygdala) and stereotypy (the striatum) (Costall & Naylor, 1973), but the involvement of the different areas with the hyperactivity response to morphine-like agents has not been widely investigated. One area which would appear a suitable substrate for this response is the nucleus accumbens. Dopamine and related agents injected directly into the nucleus accumbens cause hyperactivity which may be modulated by 5-hydroxytryptamine (Costall, Marsden, Naylor & Pycock, 1976). The ability of morphine to increase dopamine function, at least as indicated by stereotypy experiments, is also modulated by 5-hydroxytryptamine (Costall & Naylor, 1975).

Therefore, we investigated the effect of morphine on motor behaviour after bilateral injection into the nucleus accumbens of rats. The technique for intracerebral injection was as described by Costall & Naylor (1975).

Initial studies showed that morphine (1–100 μg) administered bilaterally into the nucleus accumbens, in the absence of any pretreatment, caused biphasic changes in motor activity: a period of catalepsy (catatonia), followed by the development of hyperactivity and stereotyped biting. Hyperactivity was measured in perspex observation cages fitted with photocells, whilst, in separate experiments, catalepsy was measured as the time an animal would maintain an abnormal imposed position with both front limbs extended over a 10 cm. high bar. For example, for morphine (50 μg) the phase of immobility developed within 7 min, persisted for 220 min, immediately followed by hyperactivity, which lasted for a further 200 minutes.

The phase of catalepsy (morphine, 12.5 μg) was inhibited in a dose-dependent manner by nalorphine (2.5–10.0 mg/kg s.c.) and cyproheptadine (0.625–5.0 mg/kg i.p.). Piperoxan (10 mg/kg i.p.) and atropine (2.5 mg/kg i.p.) were ineffective, whilst cataleptic doses of haloperidol enhanced the morphine-induced catalepsy.

Nalorphine (10–40 mg/kg s.c.), aceperone (1.25–20.0 mg/kg i.p.) and piperoxan (20 mg/kg i.p.) reduced the intensity of the hyperactivity/biting phase (50 μg morphine) in a dose-dependent manner, however, cyproheptadine (5 mg/kg i.p.) and fluphenazine (1.25 mg/kg i.p.) were only effective in doses causing motor depression in normal animals. Atropine (5 mg/kg i.p.) and propranolol (10 mg/kg i.p.) failed to attenuate the hyperactivity.

It is concluded that the integrity of the nucleus accumbens is important for the actions of morphine, both to cause immobility and to increase activity. However, whilst dopamine and 5-hydroxytryptamine function would appear important for the production of catalepsy, noradrenergic mechanisms may be more important for the expression of hyperactivity.

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