DIFFERENTIAL EFFECTS ON SELF-STIMULATION AND MOTOR BEHAVIOUR PRODUCED BY MICROINTRACRANIAL INJECTIONS OF A Dopamine-Receptor Blocking Agent

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SUMMARY

Intraperitoneal injections of a dopamine-receptor blocking agent, spiroperidol, equally and severely attenuated self-stimulation in two groups of rats which either performed the motor task of licking a tube or performed the more complex task of pressing a bar in order to obtain stimulation in the lateral hypothalamus. Unilateral microinjections of 9 μg of spiroperidol into the nucleus accumbens attenuated self-stimulation without producing an apparent impairment of motor behaviour. The same injections into the corpus striatum produced an impairment of motor behaviour but self-stimulation was almost unaffected. The effect of spiroperidol on self-stimulation can therefore be dissociated from the effect on motor behaviour. These results suggest that dopamine receptors are involved in self-stimulation independently of their role in motor behaviour.

Pharmacological and behavioural studies suggest that dopamine is involved in brain stimulation reward [2,5,16]. Self-stimulation of the lateral hypothalamus and of other brain areas [11] is attenuated by the injection of pharmacological agents which block dopamine receptors [10,11,13,15]. Since, however, it is known that dopamine plays an important role in motor behaviour [6], the role of motor disturbance in the attenuation of self-stimulation produced by these pharmacological agents is not clear. Therefore, we have studied the effects of injections of a dopamine-receptor blocking agent, spiroperidol [1], on motor behaviour and self-stimulation in rats. In one experiment, the effects of intraperitoneal injections of spiroperidol were compared in two groups of animals which either licked a tube to obtain brain stimulation reward, or pressed a bar in order to obtain brain stimulation reward. It has been shown that injections of spiroperidol attenuate bar-pressing to obtain water without attenuating licking to obtain water [11]. Thus the effect of spiroperidol on drinking depends on the nature of the
response required to obtain water [11]. If spiroperidol has a severe effect on self-stimulation even when the animal has to lick a tube to obtain the stimulation, then it is possible that the spiroperidol is affecting the reward and not just the response required to obtain the stimulation.

In the second experiment intracranial injections of spiroperidol were made on different days into either the corpus striatum or the nucleus accumbens septi, both of which contain dopamine [14]. The effect of these injections both on lateral hypothalamic self-stimulation and on motor behaviour was determined. The plan of this experiment was to determine whether it is possible to dissociate impairments of motor behaviour and self-stimulation by injecting the spiroperidol into brain areas mainly related to motor function [6] or self-stimulation [4,9,11,12].

Eighteen adult male Sprague-Dawley rats, weighing 250—350 g were used in these experiments. All the rats were implanted bilaterally with monopolar electrodes (00 gauge stainless-steel insect pins) in the lateral hypothalamus for self-stimulation. The stimulation parameters, apparatus and general procedure have been described elsewhere [10,11]. The six rats used in the second experiment were implanted with guide cannulae (outer diameter 0.6 mm) in both the corpus striatum and nucleus accumbens using the atlas of König and Klippel [7], as well as with stimulation electrodes. The level-head coordinates were: lateral hypothalamus, 3 mm posterior to bregma, 1.5 mm lateral to the midline and 7.6 mm beneath the dura (−3.0, 1.5, 7.6 mm); nucleus accumbens, +1.6, 1.0, 5.5 mm; and corpus striatum −1.5, 2.5, 5 mm. At the conclusion of the experiments every injection site was verified histologically (see Fig. 1).

The 12 rats used in the first experiment were given, in random order, intraperitoneal injections of 0.016, 0.062, 0.25 and 1.0 mg/kg of spiroperidol dissolved in 1/100 M tartaric acid.

The six rats used in the second experiment were given intracranial injections through a thin flexible polythene tube connected at one end to a 10 µl Hamilton microsyringe and at the other end to an inner cannula (0.3 mm outer diameter). The unilateral injections were of 9 µg of spiroperidol injected

![Diagram of brain regions](image)

Fig. 1. Sites of unilateral injections into the nucleus accumbens and corpus striatum.
ipsilaterally to the self-stimulation site in 2 μl of 1/100 M tartaric acid, and the bilateral injections, 4 or 6 μg each side, also in 2 μl of tartaric acid. Each dose was given to each site in random order once in every animal. Control injections of 1/100 M tartaric acid had no effect on the behaviours measured.

The motor behaviour of the rats in the second experiment was assessed by an observer who did not know which animal had undergone which treatment. The animals were scored for: (1) the time they remained with their front paws over a wooden rod raised six inches from the ground; (2) the time between being dropped from a height of ten inches and their first locomotion; (3) the time the animal could be arranged in bizarre positions (presence of waxy flexibility); (4) the time they took to right themselves when turned on their back; (5) hind leg withdrawal reflex; (6) splaying of back legs and (7) locomotor activity. The last three tests were scored according to a scale ranging from 0 (no impairment) to 3 (major impairment). These seven scores were combined with equal weight to give an overall assessment of motor performance, which was expressed as a percentage of the maximum impairment measured with these scales. The tests were made 5 min after the animals stopped self-stimulating and also at the end of the experiment (i.e., one hour after the injections). The results were analysed with the Mann-Whitney U-test and the Fisher exact probability test.

Fig. 2 shows the results of the first experiment. Self-stimulation was severely attenuated by a dose of 0.062 mg/kg of spiroperidol even when licking was the response required to obtain the stimulation. There was no significant difference at any dose of spiroperidol between the degree of attenuation of self-stimulation and the placebo.
stimulation of the rats which licked and of the rats which bar-pressed to obtain the stimulation.

For Experiment 2 Fig. 3A shows how self-stimulation was affected by unilateral injections into the nucleus accumbens or corpus striatum. Fig. 3B shows the main results of this experiment. After unilateral injections of 9 µg of spiroperidol into the nucleus accumbens there was an attenuation of the self-stimulation rate of 90% and an impairment of motor performance of 10%. After injections of 9 µg into the corpus striatum there was an attenuation of the self-stimulation rate of 18% and an impairment of motor performance of 38%. The impairment of self-stimulation produced by the nucleus accumbens injection was greater than that produced by striatal injection ($P = 0.016$, Mann-Whitney U-test) and the impairment of motor performance produced by striatal injections was greater than that produced by injections into the nucleus accumbens ($P = 0.048$, Mann-Whitney U-test). There was also a significant interaction between the effects of site and type of impairment ($P < 0.025$, Fisher exact probability test). It was not possible

![Fig. 3A](image1)  
![Fig. 3B](image2)

**Fig. 3.** A: effects of unilateral microinjection of 9 µg of spiroperidol into the nucleus accumbens and corpus striatum on self-stimulation of the lateral hypothalamus. Each point represents the mean of 15 one-minute measurements of self-stimulation rate expressed as a percentage of the preinjection self-stimulation rate for the six rats. The significant differences between each point in the two groups are expressed by +, $P < 0.05$; ++, $P < 0.002$; ++++, $P < 0.001$, and were calculated using a $t$-test. The vertical lines indicate the standard error of the mean. B: effects of unilateral and bilateral microintracranial injections of spiroperidol into the nucleus accumbens and corpus striatum on motor and self-stimulation behaviour. The self-stimulation points shown are the mean self-stimulation rates in five one-minute periods at the end of the experiment (one hour after the injection) for the six rats. The impairment of self-stimulation or motor behaviour is shown as a percentage of the maximum impairment measurable for the same six rats (i.e., zero self-stimulation rate, and maximum values on the scales used to measure motor impairment).
with bilateral injections to dissociate the impairment of self-stimulation from the impairment of motor behaviour using the technique of injections into the two different brain sites.

The first experiment confirms the finding that self-stimulation is attenuated in a dose-related manner by intraperitoneal injections of spiroperidol [8,10,11]. The finding that licking to obtain self-stimulation was severely impaired by an i.p. dose of 0.062 mg/kg of spiroperidol, whereas licking to obtain water is relatively unimpaired by the same dose of spiroperidol [11], suggests that spiroperidol affects the self-stimulation itself and not just the motor behaviour required to obtain the stimulation. This finding could be taken to suggest that dopamine receptors are involved in self-stimulation in a way which is not due just to their role in motor behaviour.

The second experiment shows that unilateral injections of the dopamine-receptor blocking agent spiroperidol into the nucleus accumbens can attenuate self-stimulation almost completely without producing a substantial impairment of motor performance. Furthermore, a large impairment of motor performance is produced by injections into the corpus striatum, and the self-stimulation is almost unaffected. Therefore, the attenuation of self-stimulation produced by injections of spiroperidol into the nucleus accumbens does not appear to be due to interference with dopamine receptors in the corpus striatum which are involved in motor behaviour. Attenuation of self-stimulation without apparent motor impairment using intracranial injections of spiroperidol has also been reported in the monkey [8]. These results complement the finding that unilateral injections of amphetamine into the nucleus accumbens, but not into the neostriatum, facilitate self-stimulation [3].

The above results indicate that the blockade of dopamine receptors in the corpus striatum which are involved in motor behaviour does not account for the effects of spiroperidol on self-stimulation. Thus it is possible that dopamine is involved in brain stimulation reward. Nevertheless, the possibility cannot be excluded that a different and subtle type of neurological deficit produced by spiroperidol accounts for its effects on self-stimulation.

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