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ROLE OF NIGRO-NEOSTRIATAL DOPAMINERGIC FIBERS IN COMPULSIVE GNAWING BEHAVIOR IN RATS

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Recently we have shown that implantation of crystalline dopa or apomorphine into the neostriatum of rats results in intense compulsive gnawing behavior during several hours. However, similar implants in the substantia nigra were ineffective[1].

It has been reported that the substantia nigra sends nerve fibers to the corpus striatum and that at their terminals dopamine is released[2, 3, 4].

In this paper data are reported indicating that the dopaminergic nigra-striatal neurons are involved in compulsive gnawing behavior in rats, and that these neurons are activated by cholinergic stimulation.

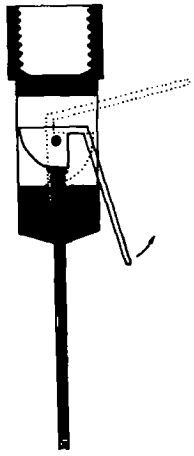

FIG 1
Implantation cannula

Material and Methods

Male albino rats weighing 140-160 g were used. Physostigmine salicylate in crystalline form was implanted stereotaxically with the aid of a stainless steel cannula, delivering about 30 µg of the compound by pushing a stylet down the cannula (Fig. 1). Implantation was performed under light ether anesthesia. The animals were then placed in a metal

cage with a wire-mesh floor, on which rats were able to gnaw[5], and their behavior was observed during several hours.

In some experiments atropine was injected intraperitoneally 15 minutes before implantation, at a dose level of 20 mg/kg.

Results

1. Implantation sites are shown in Fig. 2. Implantation of physostigmine into the substantia nigra in 18 rats resulted in compulsive gnawing behavior during 1-2 hours, starting within 30 minutes after implantation.

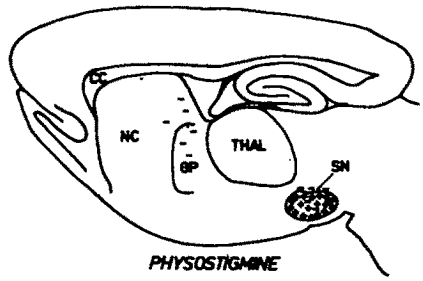

FIG. 2

Implantation sites of physostigmine

\+ evoking gnawing behavior

\- ineffective

In 5 rats nigral implants were ineffective, presumably because in these cases the implant was outside the substantia nigra.

Implantation of physostigmine into the caudate nucleus and globus pallidum was ineffective in all cases (6 rats).

2. Of a group of 18 rats, 9 animals were pretreated with atropine, and the other 9 rats received a saline injection. After subsequent implantation of physostigmine into the substantia nigra, none of the atropine-treated animals showed gnawing

behavior; in 6 out of the 9 saline-treated rats compulsive gnawing was induced by the implant.

Discussion

Evidence is rapidly accumulating that dopaminergic nerve cells lying in the substantia nigra, send their fibers to the neostriatum, where dopamine is released upon stimulation. During preparation of this paper data were published indicating that destruction of the substantia nigra in monkeys results in a depletion of striatal dopamine[6], and that electrical stimulation of the substantia nigra in cats was followed by an increase of dopamine content in the caudate nucleus[7].

The present results from chemical stimulation of the substantia nigra confirm these reports. Implantation of physostigmine, which by cholinesterase blockade was expected to cause a local accumulation of acetylcholine, apparently stimulated the dopaminergic neurons. Hence, it is concluded that cholinergic nerve fibers end synaptically on the dopaminergic nigral cells.

The caudate nucleus is involved in motor functions associated with emotional behavior[8]. A decrease in dopamine content of the caudate nucleus results in parkinsonian akinesia[9], and accumulation of dopamine in the neostriatum causes in rodents compulsive gnawing behavior[1]. Since cholinergic stimulation of the substantia nigra in rats provokes this gnawing syndrome, a functional significance of the nigro-neostriatal dopaminergic fibers has been established.

Summary

Implantation of crystalline physostigmine in the substantia nigra in rats resulted in compulsive gnawing behavior, which

has also been found to result from dopa or apomorphine implantation in the neo-striatum.

Atropine pretreatment prevented the effect of physostigmine implants. It is concluded that dopaminergic nigro-neostriatal fibers play a role in gnawing behavior, and that these fibers are activated by cholinergic transmission.

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