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BRIEF COMMUNICATION

An Investigation of the Role Played by the Superior Colliculus and Ventromedial Thalamus in Self-Injurious Behavior Produced by Intranigral Microinjection of Muscimol[1]

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BAUMEISTER, A. A., G. D. FRYE AND L. L. MOORE. *An investigation of the role played by the superior colliculus and ventromedial thalamus in self-injurious behavior produced by intranigral microinjection of muscimol.* PHARMACOL BIOCHEM BEHAV **26**(1) 187–189, 1987.—Bilateral injection of muscimol (30 or 60 ng) into the substantia nigra (pars reticulata) of rats produced a variety of stereotyped acts, self-injurious behavior (SIB), and antinociception. Bilateral electrolytic lesions of the superior colliculus strongly suppressed SIB without reducing the antinociceptive effects of intranigral muscimol. Electrolytic lesions of the ventromedial thalamus had no effect on behavioral responses to intranigral muscimol. These studies suggest that the SIB produced by intranigral muscimol is mediated by neuronal pathways that terminate in or pass through the superior colliculus. The ventromedial thalamus does not appear to play a role in mediating behavioral responses to intranigral muscimol.

Stereotyped behavior Self-injurious behavior Muscimol Substantia nigra Superior colliculus Ventromedial thalamus

BILATERAL injection of the GABA agonist muscimol into the substantia nigra of rats produces a behavioral syndrome characterized by stereotyped acts, self-injurious behavior (SIB), and antinociception [1, 2, 7]. Among the nigral efferent pathways that may mediate these effects are projections to the superior colliculus, the pedunculopontine nucleus, and the ventromedial thalamus [3,6]. Current evidence suggests that much of the stereotyped behavior produced by bilateral intranigral injection of muscimol may be mediated by the nigrotectal [10] and nigrotegmental [4] pathways. Nigral efferents to the ventromedial thalamus have been implicated in postural asymmetry and rotational behavior produced by unilateral injections of muscimol into the substantia nigra [5,8]. However, little is known about the involvement of the ventromedial thalamus in stereotyped behavior. Moreover, the pathways that mediate the SIB produced by intranigral muscimol have yet to be defined. The following studies were conducted to evaluate the role played by the superior colliculus and ventromedial thalamus in mediating the effects of intranigral muscimol on spontaneous behavior.

METHOD

Male Sprague Dawley Rats (125–150 g) were anesthetized with sodium pentobarbital (50 mg/kg, IP), and a stainless steel electrode (0.2 mm diameter) insulated except at the tip was placed stereotaxically in the superior colliculus (A 1.75, L ±1.5, V 5) or ventromedial thalamus (A 5.5, L ±1.25, V 7.25). A 2 mA anodal current was then passed through the electrode for 5 seconds. Sham operated controls received identical treatment except that no current was passed through the electrode. Two weeks later these animals, along

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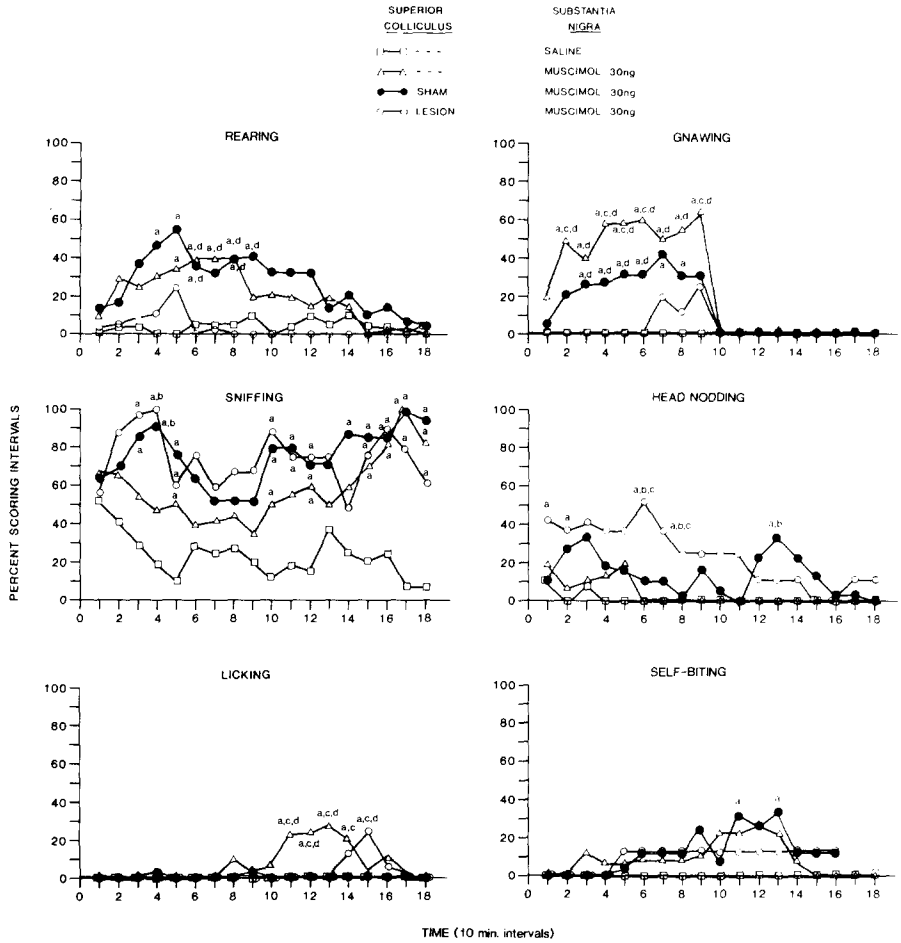

FIG. 1. Effects of lesions of the superior colliculus on stereotyped behavior produced by intranigral muscimol. Mean percent scoring intervals for selected behaviors following intranigral microinjection of muscimol (30 ng) or saline. a: $p<0.05$ compared to unoperated controls receiving intranigral saline; b: $p<0.05$ compared to unoperated controls receiving intranigral muscimol; c: $p<0.05$ compared to sham operated controls receiving intranigral muscimol; d: $p<0.05$ compared to lesioned animals receiving intranigral muscimol.

TABLE 1

EFFECTS OF LESIONS OF THE SUPERIOR COLLICULUS (SC) OR VENTROMEDIAL THALAMUS (VMT) ON THE OCCURRENCE OF SIB*

SC or VMT Treatment	Intranigral Injection	Occurrence of SIB
—	Saline	0/15
—	Muscimol (30 ng)	5/10
—	Muscimol (60 ng)	7/9
SC sham	Muscimol (30 ng)	5/9
SC lesion	Muscimol (30 ng)	1/20†
VMT sham	Muscimol (60 ng)	7/10
VMT lesion	Muscimol (60 ng)	9/11

*Values in the table are the number of animals that exhibited SIB over the total number of animals in the group.

†$p<0.05$ compared to the sham operated control group.

with a group of unoperated controls, received bilateral intranigral injections of muscimol (30 or 60 ng) as previously described [2]. Another group of unoperated controls received intranigral injections of saline. For three hours following intranigral injections, behavior was assessed once every 10 minutes during one minute observation periods. Each one minute observation period was divided into four 15 second scoring intervals. At the end of each scoring interval, a trained observer recorded all behaviors that had occurred during that interval. An animal was scored as exhibiting SIB when self-biting produced an abrasion of the skin. For each observation period, the proportion of scoring intervals in which a particular behavior occurred was calculated for each animal. These data were then subjected to analysis of variance procedures as previously described [9]. Differences between groups with respect to the proportion of animals that exhibited SIB were evaluated using a two-tailed z-test.

RESULTS

Stereotyped rearing and sniffing were observed following

intranigral injection of 30 and 60 ng of muscimol. In addition, intranigral injection of 30 ng of muscimol produced stereotyped licking and gnawing (Fig. 1), whereas 60 ng of muscimol produced stereotyped head nodding and self-biting (data not shown). Although the percent of scoring intervals during which self-biting was observed following intranigral injection of 30 ng of muscimol in unoperated controls was not significantly increased, this behavior occurred with sufficient frequency and intensity to result in self-induced tissue damage in 50% of the animals (Table 1). Seventy-eight percent of the unoperated controls that received 60 ng of muscimol exhibited SIB. Neither dose of muscimol produced sustained increases in locomotion in unoperated controls (data not shown).

As can be seen from Table 1, lesions of the superior colliculus dramatically reduced the occurrence of SIB following intranigral muscimol. In addition, lesions of the superior liculus suppressed muscimol-induced gnawing and rearing (Fig. 1). In contrast, head nodding and locomotion (data not shown) were significantly increased following intranigral muscimol in animals with lesions of the superior colliculus. No effects on spontaneous behavior attributable to lesions of the ventromedial thalamus were observed following intranigral muscimol (data not shown).

Antinociception was assessed in animals with lesions or sham electrode placement in the superior colliculus using the hot-plate and tail-flick tests, as previously described [1,7]. The percentage of animals exhibiting the paw-lick and tail-flick responses following intranigral muscimol was significantly reduced in both groups compared to saline-injected controls. (Percent exhibiting paw-lick and tail-flick responses, respectively, at 90 minutes after intranigral injection of muscimol (30 ng) was 0 and 38% in lesioned animals and 0 and 44% in sham operated controls; 100% of saline-injected controls exhibited the paw-lick and tail-flick responses.) The antinociceptive effects of muscimol in lesioned animals and sham operated controls did not differ.

Histological analyses revealed that the central necrotic zone of lesions of the superior colliculus involved all layers of this structure, but did not extend into the underlying reticular formation. The ventromedial thalamus was completely destroyed by the lesioning procedure.

DISCUSSION

Bilateral injection of muscimol into the substantia nigra of rats produces a complex behavioral syndrome characterized by numerous stereotyped acts, SIB, and antinociception. The present studies have shown that the SIB as well as certain forms of muscimol-induced stereotypy (i.e., gnawing and rearing) are strongly suppressed by lesions of the superior colliculus, suggesting that the nigrotectal pathway may mediate these effects. The nigrothalamic pathway does not appear to play a role in mediating the SIB and stereotyped behavior produced by intranigral muscimol since these behaviors were not altered by lesions of the ventromedial thalamus.

It has been proposed that self-injurious behavior produced by intranigral muscimol is stereotyped gnawing that is directed toward the animal's own body [1,7]. According to this hypothesis, analgesia permits the occurrence of self-directed gnawing, which would otherwise be punished by its pain-inducing consequences. If this hypothesis is correct, manipulations that selectively suppress either the antinociceptive effect of intranigral muscimol or muscimol-induced gnawing should also suppress self-injurious behavior. In a previous investigation [1], we have shown that lesions of the reticular formation, which reduced the effect of intranigral muscimol on the tail-flick test without suppressing stereotyped behavior, completely blocked muscimol-induced self-injurious behavior. The present study shows that it is also possible to block self-injurious behavior by manipulations that suppress stereotyped gnawing without reducing the antinociceptive effect of intranigral muscimol.

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