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Prolactin Induces Grooming in the Rat: Possible Involvement of Nigrostriatal Dopaminergic System

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DRAGO, F., B. BOHUS, P. L. CANONICO AND U. SCAPAGNINI. *Prolactin induces grooming in the rat: Possible involvement of nigrostriatal dopaminergic system.* PHARMAC. BIOCHEM. BEHAV. 15(1) 61–63, 1981.—The possibility that Prolactin-induced grooming involves the nigrostriatal dopaminergic system was studied. Intracerebroventricular injection of rat Prolactin (PRL) in an amount of 10 μg induced grooming in male rats, and neostriatal injection of haloperidol (1 μg/1 μl) markedly suppressed this effect. Local administration of 6-OHDA in the substantia nigra also abolished the influence of intracerebroventricularly administered PRL. Bilateral injections of PRL (10 μg/1 μl) in the neostriatum failed to induce grooming, whereas bilateral injections of peptide into the substantia nigra (1 μg/0.5 μl) elicited the behavioral response. It is probable that PRL induces grooming in the rat by interacting with the nigrostriatal dopaminergic transmission through an action on the cell bodies rather than in presynaptic terminals or at the postsynaptic level of this system.

Prolactin Grooming behavior Nigrostriatal system Haloperidol 6-OHDA

PROLACTIN (PRL) is known to influence several types of behaviors in mammals [10], including grooming [4]. It was found that endogenous hyperprolactinaemia, induced by pituitary homografts under the kidney capsule, is followed by an increased grooming behavior in a novel environment [4]. Since intracerebroventricular injection of rat PRL also induces grooming [4], it is likely that PRL affects grooming behavior through a central action. PRL is able to enhance activity of the dopaminergic system in some brain areas, including the nigrostriatal system [8,11]. Consonant with these findings it was observed that the dopamine antagonist haloperidol blocks grooming behavior of endogenous hyperprolactinaemic rats and of rats which received rat PRL into a cerebral ventricle [4].

The present experiments were aimed to investigate where and how PRL interacts with the dopaminergic system in inducing grooming behavior in the rat.

METHOD

Male rats, weighing 150–160 g, of Wistar strain (Charles-River, Como, Italy) were used. Seven days prior to observation session, rats received a plastic cannula implanted into the brain ventricular system (foramen interventriculare, König and Klippel, A6360), and bilateral stainless steel cannulas into either the neostriatum (König and Klippel coordinates: A=9.4; H=1.0; L=2.0) or the substantia nigra (König and Klippel coordinates: A=2.4; H=2.6; L=1.4). Rat PRL (NIAMDD, U.S.A.), haloperidol (Merck, U.S.A.), and 6-hydroxydopamine (6-OHDA, Serva, West Germany) were dissolved and diluted in saline. Thirty min prior to the observation rats were injected successively with rat PRL (10 μg/1 μl) in the ventricles, and haloperidol or 6-OHDA either in the neostriatum or in the substantia nigra. Another group of animals received rat PRL injections bilaterally either in the neostriatum or in the substantia nigra, and saline injection (in an amount of 1 μl) into the ventricular system. Animals injected with saline both in the ventricles and in the neostriatum or in the substantia nigra served as control. Grooming behavior was analysed as described by Gispen *et al.* [6]. Briefly, 30 min after intraventricular and intracerebral injections, the rats were placed individually into glass boxes (24×12×14 cm) in a low noise room. After 1 min of adaptation, the occurrence of grooming was observed every 15 sec. In a 30 min observation period a maximum of 120 positive scores can be obtained. Results were expressed as mean number of positive grooming scores per treatment group and a difference between groups was assigned to be significant for p values ≤ 0.05 (Dunnett's test or Student's t-test, two tailed).

RESULTS

In accordance with previous observations, intraventricular injection of rat PRL (10 μg/μl) resulted in a significant

TABLE 1

EFFECT OF INTRANEOSTRIATAL INJECTION OF DRUGS INHIBITING DOPAMINERGIC TRANSMISSION ON PRL-INDUCED GROOMING

	Intraneostriatal injection	Intracerebroventricular injection	n	Grooming score*
1	Saline	PRL†	6	72.8±6.1§
2	Haloperidol	PRL†	5	24.2±2.0
3	6-OHDA‡	PRL†	5	44.9±4.2¶#
4	PRL†	Saline	5	21.3±3.0
5	Saline	Saline	6	26.2±4.1

*Data for grooming score are mean±SE.
†In an amount of 10 μg/1 μl.
‡In an amount of 1 μg/1 μl.
§Significantly higher than group 5 ($p<0.01$ with the Dunnett's test).
¶Significantly higher than group 5 ($p<0.05$ with the Dunnett's test).
#Significantly lower than group 1 ($p<0.05$ with the Student's t-test).

TABLE 2

EFFECT OF INTRANIGRAL INJECTION OF DRUGS INHIBITING DOPAMINERGIC TRANSMISSION ON PRL-INDUCED GROOMING

	Intranigral injection	Intracerebroventricular injection	n	Grooming score*
1	Saline	PRL†	7	68.9±8.2§
2	Haloperidol	PRL†	6	66.8±6.1§
3	6-OHDA‡	PRL†	6	19.2±6.0
4	PRL‡	Saline	5	84.7±5.0§
5	Saline	Saline	6	21.1±2.2

*Data for grooming score are mean±SE.
†In an amount of 10 μg/1 μl.
‡In an amount of 1 μg/0.5 μl.
§Significantly higher than group 5 ($p<0.01$ with the Dunnett's test).

increase of grooming during the 30-min test (Table 1). Intraneostriatal injection of haloperidol (1 μg/1 μl) markedly suppressed grooming behavior induced by intraventricularly injected PRL. Moreover, intraneostriatal injected 6-OHDA did not prevent the PRL-induced behavioral effect, but it significantly reduced it. Bilateral injections of PRL (10 μg/1 μl) in the neostriatum failed to induce grooming.

Bilateral injections of haloperidol (1 μg/0.5 μl) into the substantia nigra were uneffective in suppressing PRL-induced grooming (Table 2). However, 6-OHDA (1 μg/0.5 μl) in the substantia nigra abolished the influence of intracerebroventricularly injected PRL on grooming behavior. Moreover, if PRL was injected into the substantia nigra bilaterally as little as 1 μg/0.5 μl per injection was sufficient to elicit the behavioral response (Table 2).

DISCUSSION

Peptides related to ACTH, MSH and LPH are known to induce excessive grooming in the rat when administered intracerebroventricularly [5, 6, 7, 14, 15], and the mechanism of this effect seems to involve the dopaminergic systems projecting from the substantia nigra into the neostriatum and nucleus accumbens. In fact, pharmacological manipulations of dopaminergic terminals in the neostriatum or nucleus accumbens inhibit the behavioral response [3]. Also morphine may induce excessive grooming [1,5], and the dopaminergic terminals in the neostriatum are indispensable for this effect. Moreover, it has been shown that the activity of mesencephalic and diencephalic dopaminergic systems in the rat is influenced by α-MSH, which is equipotent to $ACTH_{1-24}$ in inducing grooming [14], and by morphine [9], as well. Furthermore, several morphine-like endogenous peptides are able to induce excessive grooming in the rat [7].

In cats, the morphine-induced excessive grooming is blocked by bilateral injections of haloperidol into the nucleus caudatus [2]. Haloperidol suppresses excessive grooming induced by ACTH [3,15], as well. In the present study haloperidol appeared to suppress PRL-induced grooming only when administered in the neostriatum. This effect of the drug is most probably a postsynaptic action, since a presynaptic autoreceptor inhibition would be expected to facilitate grooming. In fact, it was found that dopamine agonist such as apomorphine attenuate rather than facilitate ACTH-induced grooming [3]. The full effect of 6-OHDA in suppressing PRL-induced grooming, instead, appeared only after injection of the drug into the substantia nigra. When it has been injected in the neostriatum, a partial inhibition of the PRL-induced behavioral response appeared, which may be related to the initial action of 6-OHDA as false neurotransmitter by displacing dopamine from the nerve terminals [13].

Since PRL injection was uneffective in the neostriatum but effective in the substantia nigra, it is tempting to speculate that the hormone may enhance grooming behavior in the rat by interacting with the nigrostriatal dopaminergic transmission through an action on the cell bodies rather than in presynaptic terminals or at the postsynaptic level of this system. PRL can stimulate the release of dopamine in the nigrostriatal system [8,11], by a presynaptic modulation [11]. Moreover, also ACTH-induced grooming seems to depend on an action at the presynaptic level rather than at the dopaminergic terminals of the nigrostriatal system [3,15].

All of the peptides known to elicit grooming can interact with opiate receptors in the brain [14]. The opiate antagonists naloxone and naltrexone suppress ACTH-induced excessive grooming in the rat [15]. Moreover, opiate receptors sites are discretely localized in the substantia nigra [12]. Thus, it is possible that PRL, such as ACTH, interacts with the opiate receptors in enhancing grooming behavior. Studies are in progress for determining the involvement of opiate receptors in PRL-enhanced grooming.

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