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GROOMING ELICITED BY INTRACEREBROVENTRICULAR BOMBESIN AND ELEDOISIN IN THE MOUSE

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Summary

The behavioral effects of centrally administered bombesin and eledoisin were investigated in the mouse. Both peptides produced syndromes of compulsive stereotyped grooming. Manipulations known to affect other forms of grooming were ineffective in modifying the above syndromes. The findings argue for novel subtypes of peptide mediated grooming.

Introduction

Bombesin and eledoisin are both biologically active peptides derived from amphibian skin. They have been established to affect a variety of centrally mediated physiological processes in mammals (e.g. DeCaro, Micossi, Venturi, Brancati and Scarnati, 1974; Rivier and Brown, 1978), and may therefore be similar to or identical with endogenous mammalian neuropeptides. One prominent class of peptide mediated effects in mammals is compulsive grooming, and peptides as diverse as opioid peptides, ACTH derived peptides and substance P derived peptides have previoisly been shown to elicit this behavior (Dunn, Green and Isaacson, 1979; Fog, 1970; Gispen, Reith, Schotman, Weigant, Zwiers and DeWeid, 1977; Katz, 1979). Other treatments known to increase grooming include systemic morphine, under selected conditions (e.g. Fog, 1970) and stress (Katz and Roth, 1979). Bombesin and eledoisin are distinct from the above and heretofore they have not been systematically examined for their ability to affect grooming. The present report therefore examined both compounds' effects upon this behavior.

Materials and Methods

Subjects: Adult male Swiss Webster derived albino mice, 25-35 g each were individually maintained with food (Teklad 4.0% fat rodent diet S-0836) and tap water continuously available, and normal 12h/12h lighting cycles (lights on 0700 - 1900 h). Room temperature was maintained at 22°C.

Surgery: Mice were injected intraperitoneally with 80 mg/kg of sodium pentobarbital (Nembutal). Chronic stainless steel ventricular cannulae were fashioned from 26 2-hypodermic needles and stereotactically implanted using coordinates from Slotnick and Leonard (1975) for the lateral cerebral ventricle. The cannula was attached to the skull using three stainless steel screws and acrylic dental cement. Further details of surgery are available in previous papers (Katz, Carroll and Baldrighi, 1978). Seven days were allowed for recovery from surgery.

Drugs: Doses of bombesin and eledoisin (#7113, 7101: Peninsula Labs, San Carlos, California) were injected in a constant volume of 5 ul Ringer-Locke vehicle solution, using a Hamilton microsyringe and an infusion time of less than 30 sec. Naloxone HCl and morphine sulphate were injected 1 ml/.1 kg intraperitoneally 5-10 minutes prior to central injection of standard doses of .1 ug Bombesin and 1.0 ug Eledoisin. All drugs were prepared immediately prior to use.

Behavioral Procedure: Mice were extensively (72h) habituated to handling and placement in the apparatus (transparent 28 x 18 x 13 cm plexiglas observation chambers) prior to testing. This involved a minimum of 12 exposures, each of six hours duration. Four hours additional habituation preceded actual drug testing. The test period was the twenty minute interval immediately after peptide or vehicle injection. Subjects were placed in the boxes with a bedding material of fresh pine chips. Seconds of grooming per session were recorded. Facial grooming, flank grooming, anogenital grooming and tail preening were considered as grooming behaviors.

Results: Both drugs produced substantial grooming. Unlike grooming syndromes described for ACTH related peptides, yawning and stretching neither preceded nor accompanied the grooming behavior. The behaviors which did occur consisted exclusively of facial grooming (greater than 90% of recorded grooming for all subjects was directed at the head or face). In addition to normal facial washing, an atypical form of grooming consisting of extensive scratching of the neck and upper body quadrant with the hindpaws was also present. Pharmacological manipulations were not effective in modifying the amount or type of grooming present. A dose response curve for both peptides is included as Table 1. It may be seen that both compounds increased grooming in a monotonic fashion. Based upon the above dose response study and previous reports two additional procedures were utilized in attempting to reduce grooming. It may be seen in the second table that treatment with an opiate receptor agonist and antagonist was ineffective in modifying grooming in the present circumstances.

Table One:

Induction of Excessive Grooming in the mouse by Central Injection of Bombesin and Eledoisin (mean sec/20 min ± s.e.m.)

	Dose µg				
	0.00	.01	.10	1.00	10.00
Bombesin (n=10)	35 ± 15	107 ± 9	476 ± 33	>590	>590
Eledoisin (n=10)	22 ± 8	95 ± 18	154 ± 27	209 ± 39	250 ± 75

[a]P<05 by randomization test in comparison with control.

Table Two:

Pharmacological Antagonism of Bombesin and Eledoisin Elicited Grooming (Percent Control)

Treatment	Dose mg/kg	Bombesin (.1 µg)	eledoisin (1.0 µg)[a]
Control	0	100	100
Naloxone	5.0	108	122
	10.0	117	85
	15.0	95	90
Morphine	2.5	116	98
	5.0	82	113
	10.0	107	95

[a]All scores as % control; n=6 mice/cell in all cases p>.05 by randomization test.

Discussion

The present findings suggest the existence of a novel non-opioid form of neuropeptide mediated grooming behavior. Whether both peptides are acting on a common substrate, or simply elicit phenotypically similar behaviors is not resolved. Since relatively few behavioral effects are established for these peptides, the present results are of interest in characterizing their neurobiological roles. It must be noted that one previous report did not find eledoisin induced grooming behavior (DeCaro et al., 1974). A number of differences of procedure as well as species differences may explain this discrepancy. In comparison with the present findings, the previous report examined different doses of peptide in the rat in an open field test.

It is not clear what properties the various compounds which elicit grooming share. Clearly peptides which are related to endorphins and ACTH are derived from a single parent compound (e.g. Mains, Eipper, and Ling 1977; Guillemin, Vargo, Roissier, Minick, Ling, Rivier, Vale, Bloom 1978; Watson, Akil, Richard, Barchas 1978). The grooming behaviors elicited by opiates, endorphins, ACTH derived fragments, and stress are similar, consisting of yawning and stretching followed by head to tail licking. They are, in addition, all naloxone reversible. Thus they may represent one major subcategory of grooming effects.

What of the remaining peptides? These may represent one or possibly more additional and distinctive classes of effect. The grooming elicited by bombesin and eledoisin, and also the grooming elicited by substance P is not accompanied by yawning, not directed at the whole body in an organized fashion, nor is it reversible through opiate blockade. Thus it may be distinctive, although the question of homogenelty within the category remains an empirical issue. One final issue is the selectivity of the present effects. The absence of pharmacological reversal precludes strong statements regarding the selectivity and specificity of the effect at this time, and emphasizes the need to find specific antagonists of the above peptides. While the significance of peptide induced grooming is not yet fully understood, the present results suggest possible novel behavioral functions for the peptides in question.

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