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# BRIEF COMMUNICATION

# Functional Relationship of Lateral Hypothalamus and Amygdala in Control of Eating

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MONTGOMERY, R. B. AND G. SINGER. *Functional relationship of lateral hypothalamus and amygdala in control of eating.* PHARMAC. BIOCHEM. BEHAV. 3(5) 905–907, 1975. – Cannulas were stereotactically implanted in the lateral hypothalamus and the ipsilateral amygdaloid cortical nucleus of 7 male albino rats, Wistar strain. After functional checking of the accuracy of implants by adrenergic elicitation of increased food intake, the animals were injected with combinations of noradrenaline, phenoxybenzamine or tolazoline, or placebo under 6 treatment conditions, while food- and water-satiated. The elicitation of increased food intake in the satiated rat by adrenergic stimulation of the lateral hypothalamus was confirmed, and it was further found that simultaneous adrenergic stimulation of the amygdaloid cortical nucleus augmented this increase. However, simultaneous anti-adrenergic blockade in the amygdaloid cortical nucleus reduced eating to control level. The lack of response of the amygdaloid cortical nucleus to adrenergic stimulation in the satiated rat, under simultaneous stimulation of the lateral hypothalamus with either placebo or an adrenergic blocker, was also demonstrated. It was concluded that the amygdaloid cortical nucleus has a modulatory influence on eating behavior, which is dependent on the level of activity in the lateral hypothalamus, and further that this modulatory influence is necessary to the behavioral output of the hypothalamic system. This is the same relationship between the hypothalamus and amygdala previously demonstrated in regard to drinking behavior and these results are seen as supporting the behavioral generality of the functional relationships reported.

Chemical stimulation of brain  Neurochemical coding of behavior  Lateral hypothalamus  Amygdala
Adrenergic stimulation and antiadrenergic blockade of eating

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ON the basis of studies employing direct chemical stimulation of the brain, a number of functional relationships between central neurobehavioral circuits involved in the regulation of drinking behavior in the rat have been suggested [2, 5, 6]. These are (1) activity in a cholinergically-sensitive amygdaloid circuit is dependent on the level of activity in a cholinergically sensitive hypothalamic-septal circuit; (2) once the amygdaloid circuit is itself activated by direct cholinergic stimulation, it modulates the behavioral output of the hypothalamic-septal circuit; and (3) this modulatory influence is necessary for a behavioral output from the hypothalamic-septal circuit.

These functional relationships were interpreted as suggesting the function of the cholinergically-sensitive amygdaloid circuit was the disinhibition of the hypothalamic-septal circuit by inhibition of a ventromedial hypothalamic system, the role of which is to inhibit the hypothalamic-septal circuit under conditions of water satiation [6].

It has been demonstrated that the cholinergically-sensitive drinking system and adrenergically-sensitive feeding system in the rat are not anatomically identical [2,3] but in close spatial proximity. In one thorough investigation of 184 loci in 20 brain areas, only 15 percent of the loci responded to both adrenergic and cholinergic stimulation with eating and drinking respectively [2] whereas other loci showed either specific cholinergic drinking or adrenergic eating responses. Generally, in those areas studied, the number of adrenergically responsive loci was less than that of cholinergically responsive loci. These findings suggest that, while the cholinergic drinking circuit and adrenergic feeding circuit may be conceptually and anatomically similar, they are not identical, although they are anatomically proximal to each other at a number of points. In the present experiment, the lack of complete congruence between the two drive circuits raised the question as to whether the functional relationship for drinking behavior demonstrated previously between the

hypothalamus and amygdala, two points where the circuits are mutually proximal, would also hold for feeding behavior.

## METHOD

### *Animals*

The animals were 7 male albino rats cannulated with ipsilateral implants into the lateral hypothalamus and the amygdaloid cortical nucleus.

### *Apparatus*

A new cannula, reduced in size, was introduced in this experiment [1]. This new cannula type was considered advantageous since it reduced the amount of tissue damage caused during cannulation, and permitted more accurate localization of the injection. Stimulus solutions were noradrenaline bitartrate ($24 \times 10^{-4}$M), phenoxybenzamine hydrochloride, and tolazoline hydrochloride. Early attempts to use phenoxybenzamine as the adrenergic blocker were frustrated by its limited solubility in water, and it was simply used as a saturated aqueous solution in 0.9 percent saline at room temperature. Is was therefore replaced with tolazoline, which is more soluble, but was only available as an aqueous solution commercially prepared for human application, so that again no choice of concentration was possible. There difficulties with the concentration of the adrenergic blocker were not considered important, since this was not a dose-effect study and only behaviorally effective concentrations were required.

### *Procedure*

The procedure was basically similar to that used previously [5]. Functional tests were conducted to screen out nonresponsive animals; as seems to be generally found, it was difficult to obtain animals which were adrenergically responsive in both loci. In addition because of the demonstration of a cumulative effect from repeated adrenergic stimulation a minimum of two days was allowed between tests [2]. This increased difficulties from chronic infection, and as a result of both these factors complete sets of data were collected on only 7 animals.

To ensure satiation and control palatability effects, animals were given fresh food (Mecon brand rat and mouse cubes) and water, 1 hr before injection. They were then injected with a combination of noradrenaline, and of the adrenergic blockers, or placebo, (1 $\mu$l of one substance into each cannula), according to the conditions in Table 1. After injection, animals were allowed 1 hr further access to the food, which was weighed again, together with any spillage, at the end of the test period. Animals were maintained on ad lib food and water between tests.

The animals were killed at the conclusion of the experiment, under ether anesthesia, and the brains were removed and perfused with Formalin. The tissue samples were then sectioned and stained with Groat's haematoxylin and phloxine. The loci of placements were checked against the De Groot atlas. In each case the two cannula tracks ended in the immediate vicinity of the LH and ACO, respectively. The ranges of De Groot coordinates for the two loci were (i) for the LH, A = + 5.4 ± 0.3, H = -2.6 ± 0.4, L = + 1.8 ± 0.5; (ii) for the ACO, A = + 4.6 ± 0.4, H = -3.7 ± 0.5, L = + 3.8 ± 1.0.

## RESULTS

The results are shown in Table 1. The data were subjected to randomized blocks analysis of variance using the mean square error, $F(5,30) = 4.39$, $\alpha = 0.05$. Rodger's [4], planned contrasts were applied to the data (this technique allows direct comparison of treatments). This showed that Conditions B, E and F were not significantly different from Condition A (double placebo); that Condition C (adrenergic stimulation of the LH) was significantly different from these other 4 conditions; and that Condition D (adrenergic stimulation of the LH and ACO) was significantly different from Condition C.

TABLE 1

MEAN FOOD INTAKE UNDER SIX DIFFERENT TREATMENTS

| | Injected into Lateral Hypothalamus | Injected into Amygdaloid Cortical Nucleus | Mean Food Intake (g) |
|---|---|---|---|
| A | Placebo | Placebo | 1.1 |
| B | Placebo | Noradrenaline | 1.6 |
| C | Noradrenaline | Placebo | 2.2* |
| D | Noradrenaline | Noradrenaline | 3.4† |
| E | Phenoxybenzamine or Tolazoline | Noradrenaline | 1.4 |
| F | Noradrenaline | Phenoxybenzamine or Tolazoline | 1.8 |

*Significantly greater than A, $p<0.05$
†Significantly greater than C, $p<0.05$

This is the same pattern of results as for the previous studies on drinking. The elicitation of increased food intake in the satiated rat by adrenergic stimulation of the lateral hypothalamus was confirmed, and it was further found that simultaneous adrenergic stimulation of the amygdaloid cortical nucleus augmented this increase. However, simultaneous blockade with adrenergic antagonists in the amygdaloid cortical nucleus reduced eating to control level. The lack of response by the amygdaloid cortical nucleus to adrenergic stimulation in the satiated rat, under simultaneous adrenergic blockade of the lateral hypothalamus, was also demonstrated.

## DISCUSSION

The conclusions from the previous two experiments regarding the functional relationships between the initiatory and modulatory circuits in control of drinking are thus extended to eating. The functional relationships of neural circuits proposed earlier [6], are also seen as applicable to eating behavior, and the generality of these relationships, which were originally proposed largely on the basis of findings with cholinergic stimulation and drinking, is supported.

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