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BRIEF COMMUNICATION

Norepinephrine Concentrations in Brains and Hearts of Hyperreactive Septally Lesioned Rats

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MONTGOMERY, R. L. AND E. L. CHRISTIAN. *Norepinephrine concentrations in brains and hearts of hyperreactive septally lesioned rats.* PHARMAC. BIOCHEM. BEHAV. 1 (4) 491–492, 1973.–It was observed that hyperreactive septally lesioned rats have no significant alterations in concentrations of brain norepinephrine. Heart norepinephrine concentrations of septally lesioned animals showed a significant decrease ($p<0.005$).

Brain Heart Norepinephrine Septal lesions

THE POSTOPERATIVE behavior of septally lesioned rats is characterized by violent and explosive reactions in response to previously neutral stimuli. The septal animals appear to be frightened, highly aggressive and somewhat unpredictable to various types of stimuli. This hyperreactivity in septally lesioned rats is probably related to autonomic functions.

The slowing of heart rate following septal stimulation has been reported by several investigators [1, 2, 3, 4, 7, 8, 10, 11, 12, 13, 14]. It is not clear, however, whether the decreased heart rate associated with septal stimulation is due to inhibition of sympathetic activity, parasympathetic excitation, or a combination of the two effects.

Several investigators have explained the decreased heart rate following septal stimulation in terms of inhibition of sympathetic activity. Manning *et al.* [13] found that bilateral vagotomy and cholinergic blocking agents did not influence heart rate decreases that occurred following stimulation of the septum in anesthetized cats. Holdstock [8] noted a lack of galvanic skin responsiveness following septal stimulation and assumed an inhibition of sympathetic activity.

Holdstock [9] found that septal lesions interfered with autonomic hyperreactivity. He observed that septally lesioned animals when compared with controls exhibited smaller initial heart rate acceleration to shock. A smaller galvanic skin response was likewise reported for septally lesioned animals when compared with controls. It appeared that animals with septal lesions were less responsive autonomically.

Catecholamine substances such as norepinephrine and epinephrine that are synthesized in the brain and in sympathetic nerve tissues are important in the coordination of neural and glandular activity, influencing both the blood vessels and the heart. It is therefore the purpose of this experiment to determine if certain aspects of the behavioral hyperreactivity in septally lesioned rats may be related to the concentration of heart and brain norepinephrine.

METHOD

Animals

Sixteen adult male rats of the Sprague-Dawley strain weighing approximately 250–300 g were employed in this experiment. Experimental animals were anesthetized with ethyl ether. The skull was exposed and small bilateral holes drilled into the skull 1.0 mm anterior and 0.5 mm lateral to bregma. Electrolytic lesions were produced by means of a lesion-producing apparatus using bregma as a reference point. The septal lesions were produced by passing 2 mA of current for 15 sec through stainless steel electrodes, which were 0.24 mm in dia. and insulated except for 0.5 mm at the tip. An ear cathode completed the circuit. Sham-operated control animals were subjected to similar operational techniques, with the exception of no induced current.

Preoperative evalutions of behavior studies included the following: (a) resistance to capture; (b) vocalization; (c) response to a stationary visual stimulus; (d) response to touch; (e) response to a moving object; (f) catatonic behavior; (g) response to a puff of air. Postoperative evaluations of behavior were obtained in the same manner as the preoperative scores. This enabled us to ascertain the effectiveness of the septal lesions. Septally lesioned rats were hyperre-

sponsive to all types of stimuli when compared with the sham-operated animals.

All animals were sacrificed by decapitaiton between 11 and 12 o'clock on the sixth day following surgery (a peak period in hyperreactivity of septally lesioned animals). After decapitation the brains and hearts were rapidly removed, weighed and placed in containers surrounded by dry ice. The whole brain with cerebellum was used for catecholamine determinations.

Norepinephrine concentrations were estimated in both the hearts and brains by means of spectrophotofluorometric techniques similar to those used by Welch and Welch [16].

RESULTS

Brain norepinephrine of rats with septal lesions was not significantly decreased when compared with the sham-operated control animals (Table 1). Heart norepinephrine was decreased at a significant level ($p<0.005$).

TABLE 1

BRAIN AND HEART NOREPINEPHRINE CONCENTRATIONS OF SEPTALLY LESIONED RATS

Treatment	Tissue	Number	Concentration ngs/g of Tissue	±SE
Sham-operated	Brain	8	396	±82
	Heart	8	415	±80
Septal	Brain	8	297	±41
	Heart	8	268	±38

DISCUSSION

Tranquilizers such as reserpine [15] and chlorpromazine counteract septal hyperreactivity at doses that do not cause sedation in normal rats. It is assumed that chlorpromazine suppresses central sympathetic outflow by modulating the concentraiton or action of norepinephrine in the brain. Heller *et al.* [5,6] reported that septal lesions appeared to have no significant influence on brain norepinephrine concentration. Our data likewise indicated that septal lesioning caused no significant decreases in brain concentration of norepinephrine. The concentration of heart norepinephrine was decreased at a significant level of confidence ($p<0.005$). The decreased levels of norepinephrine in hyperreactive rats is difficult to interpret and evaluate since it could be related to an increased uptake or decreased production of norepinephrine. Decreased heart rates, absence of galvanic skin responsiveness, and hypersensitivity to tranquilizers (chlorpromazine) in septally lesioned rats makes it tempting to relate each of the above to decreased levels of brain and heart norepinephrine; however, our data only partially verify this hypothesis.

In summary, our data may have some bearing on Holdstock's hypothesis [9] that the behavioral hyperreactivity of septal rats is not entirely mirrored by autonomic hyperreactivity. This data may also add to the concept of independent representation of autonomic functions.

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