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SEPTAL POLYDIPSIA IN RATS IS A PRIMARY POLYDIPSIA NOT MEDIATED BY DOPAMINE

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Abstract : Bilateral lesions of nucleus septal lateralis resulted in a sustained and significant increase in water intake, without any change in food intake. Intracerebral injection of dopamine (DA) or of spiperone (a central D_2-receptor antagonist) did not elicit any change in water or food intake. The polydipsia resulting from septal lesions is thus a primary polydipsia, which is independent of food intake, and is not mediated by neurotransmitter dopamine.

Key words : dopamine septal lesion food intake spiperone water intake

INTRODUCTION

In 1965 Harvey and Hunt reported that lesions of septal nuclei in rats cause a sustained increase in daily water intake (1). It was later suggested by Luber et al that this polydipsia due to septal lesions, is probably due to lack of secretion of ADH, with the posterior septal area controlling the activity of supraopticohypophyseal system (2). However, later studies demonstrated that this septal polydipsia is not secondary to polyuria caused by ADH deficiency (3). Mc Cleary suggested that this polydipsia is due to loss of motor inhibition, rather than an increase in thirst drive (4), which results in increased drinking and feeding. Blass and Hanson suggested that this hyperdipsia may be attributable to removal of inhibition, to which hypovolemic controls of drinking are normally subject (5). Bilateral destruction of septal regions in rats has also been reported to cause increased intake of 1.5% saline, when both saline and water was offered to drink at the same time (6). It has also been observed that septal lesions increase the consumption of palatable solutions like sodium saccharine, or sucrose (7, 8).

Thus the mechanisms underlying septal lesion polydipsia are still not very clear. In our earlier studies (unpublished observations), it was observed that the neurotransmitter dopamine (DA) increases food and water intake significantly, when injected into nucleus accumbens and caudatus which are among the central dopaminergic systems. DA has also long been implicated in feeding and drinking in animal models (9-13). Septum is also among the dopaminergic mesolimbic system. This study was therefore designed to assess the role of DA on septal nuclei in relation to feeding and drinking behaviour.

METHODS

Adult male albino rats (Wistar strain) weighing 250-400 g were used for this study. Each animal was kept in a separate cage under constant condition of room temperature 30 ± 3°C. Tap water and standard rodent chow were provided *ad lib.* Daily water and food intake were recorded for consecutive seven days to determine 24 h mean water and food intake.

Cannulae (stainless steel) of desired length and electrodes (stainless steel) were implanted in the septal nuclei by means of stereotaxy using coordinates of Konig and Klippel (14). Cannulations (unilateral) and electrode placements (bilateral) were done under nembutal anesthesia, 40 mg/kg, b.w., IP (Abbot Lab). After surgery animals were allowed 10 days for full recovery after which following experiments were performed.

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Experiment 1 : Seven doses of DA (0.001 μg, 0.01 μg, 0.1 μg, 1.0 μg, 2.0 μg, 4.0 μg and 8.0 μg) were administered into septal nucleus through the cannulae, everyday at 14 hours, following which 24 h food and water intake were recorded. Each dose was administered randomly to a group of 10 animals and was repeated five times for five days.

Experiment 2 : Spiperone (Janssen Pharmaceutical Co, Piscataway, NJ), (SP), a central D_2 receptor antagonist was injected into septal nuclei in five doses (0.5 μg, 1 μg, 2 μg, 4 μg and 8 μg) to five different groups of animals and food and water intakes measured.

Experiment 3 : Bilateral electrolytic lesions of septal nuclei were produced by allowing anodal current (1-2 mA) from a lesion-maker (INCO) to pass through the implanted electrode for 15-20 seconds. 24 h food and water intake were measured for 10 consecutive days following recovery period.

Following completion of experiments all animals were sacrificed and their brains fixed with 10% formalin. Sections of the brains of 5 μ thickness were cut with the help of microtome (ERMA, Japan) and were stained with hematoxylin and eosin. Stained sections were fixed on the slides and the sites of cannulations and lesions were confirmed by taking enlarged microphotograph of the sections. Fig. 1 is the illustrated diagram of the microphotographs.

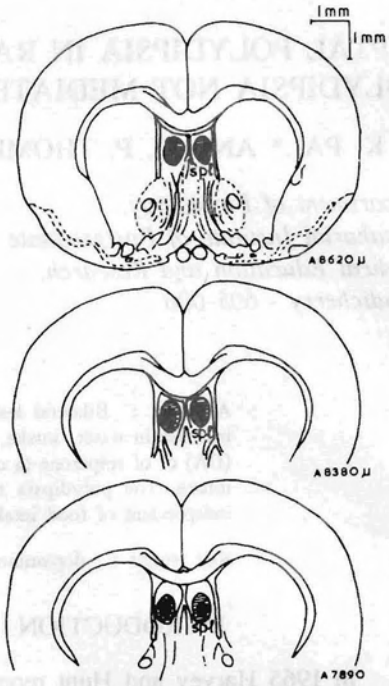

Fig. 1 : Reconstruction diagram of minimum (darkened) and maximum (striped) extent of bilateral lesions of nucleus septal lateralis. Tips of the cannulae were present in the striped area. (spl - nucleus septal lateralis)

RESULTS AND DISCUSSION

There were no significant changes in food or water intake following injections of different doses of DA (expt. 1) or SP (expt. 2) into septal nuclei (Table I). However, after bilateral lesions of nucleus

TABLE I : Effect of (a) administration of DA, (b) SP into septal nuclei on 24 h food and water intake (Mean ± SE).

	(a)			(b)	
	Water intake (ml)	*Food intake (g)*		*Water intake (ml)*	*Food intake (g)*
Basal intake	21.11 ± 0.38	13.38 ± 0.2	Basal intake	21.0 ± 0.80	13.7 ± 0.3
Normal saline	21.31 ± 0.38	13.32 ± 0.1	Normal saline	21.3 ± 0.97	13.4 ± 0.2
DA doses (μg)			SP doses (μg)		
0.001	20.93 ± 0.35	13.19 ± 0.2	0.5	21.5 ± 0.99	13.4± 0.2
0.01	20.76 ± 0.36	13.05 ± 02	1.0	21.5 ± 0.83	13.2 ± 0.2
0.1	20.59 ± 0.42	13.05 ± 0.1	2.0	21.8 ± 0.82	13.1 ± 0.2
1.0	21.48 ± 0.48	13.32 ± 0.2	4.0	22.0 ± 0.82	13.0 ± 0.2
2.0	21.90 ± 0.57	13.10 ± 0.1	8.0	21.4 ± 0.79	13.1 ± 0.3
4.0	21.54 ± 0.42	13.48 ± 0.2			
8.0	21.48 ± 0.52	13.39 ± 0.2			

septal lateralis, there was a sustained and significant rise in water intake, with food intake remaining unchanged (Fig. 2).

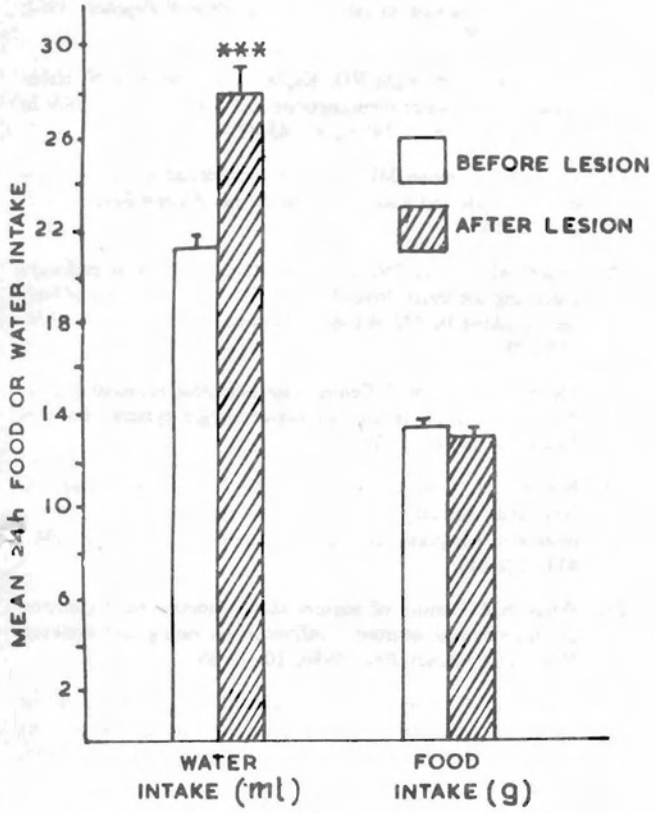

Fig. 2 : 24 h water and food intake (Mean ± SE) before and after lesions of septal nuclei. (***denotes P<0.001).

Enhanced dipsogenesis (increased thirst drive), following septal lesions, indicates that normally septum has an inhibitory influence on the thirst regulating mechanisms. This observation is consistent with the observations of other workers (1, 2, 3, 5). However, there was no change observed in food intake after septal lesions, which is in contrast to the findings of other workers (15), who had suggested that increased water intake may be secondary to increased food intake, or due to increased motor activity.

One of the major efferent connections of the septum is to the habenula. The habenular lesions did not cause increased water consumption (16). Another major efferent projection of the septal region is to the amygdala and hippocampus. However, amygdalar lesions decrease water intake (17) and hippocampal lesions do not affect the reactivity to the taste of fluids (18). Rather hippocampus is believed to contain a facilitatory system for drinking, as injection of carbachol into these regions causes water replete animals to drink (7). So the probable thirst inhibitory output from septum is septo-hypothalamic pathway, which most likely reduces the thirst drive. This pathway contains dopaminergic fibers and the septum itself also contains dopamine receptors (19). But no changes either in food or water intake were observed following DA and SP injections into this system, indicating that dopamine is not the neurotransmitter involved in inhibiting dipsogenesis through septal nuclei, although DA mediates dipsogenesis through other areas in the brain (20-22). The increased water intake after septal lesions was also independent of food intake. It had been earlier observed that this increased water intake is not secondary to polyuria (3). The exact mechanism of septal inhibition of water intake needs further exploration of role of other septal neurotransmitters in relation to water intake.

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