

# Effect of septal lesions on food intake, and body weight regulation in male and female albino rats

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## Abstract

**Background and Aim:** Presently, obesity is among the major health problems, which is, in general, more common in females than males. As the exact mechanism of gender difference in the neural regulation of obesity has not been fully elucidated, the effective control of this problem remains unanswered. Therefore, this study was an attempt to assess the gender difference in food intake (FI), water intake (WI), and body weight (BW) gain by the mesolimbic centers that profoundly influence the behavioral aspects of feeding in albino Wistar rats.

**Methods:** Twenty-four albino Wistar rats were divided equally into medial septal and lateral septal groups with 6 male and 6 female rats in each. Bilateral electrolytic lesion of the respective nuclei was performed by stereotaxy and postlesion parameters were recorded.

**Results:** Following lesion of medial septal nuclei, FI increased significantly in both male ( $P < 0.05$ ) and female ( $P < 0.001$ ) rats, but the percentage increase was more in females than in males. Similarly, BW also increased significantly in both male ( $P < 0.05$ ) and female ( $P < 0.001$ ) rats, but the percentage increase was significantly more in females ( $P < 0.001$ ). Following lesion of lateral septal nuclei, WI increased significantly in both male ( $P < 0.001$ ) and female rats ( $P < 0.05$ ), but the percentage increase was significantly more in male rats.

**Conclusion:** The above-mentioned findings suggest that medial septal nucleus strongly inhibits feeding and adiposity behaviors in female rats, and lateral septal nucleus strongly inhibits the drinking behavior in male rats.

**Key words:** Body weight, food intake, lateral septal nucleus, medial septal nucleus, water intake

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## INTRODUCTION

Regulation of body weight (BW) and adiposity is influenced by various factors such as nutritional, hereditary, social, and environmental factors.<sup>[1]</sup> Hypothalamic and extrahypothalamic areas (limbic system) in the brain are known to influence the behavioral aspects of feeding and adiposity.<sup>[2,3]</sup> Nucleus septum, being an important component of limbic system, has been proposed to be involved in the regulation of adiposity and BW gain through its close association with the hypothalamic feeding centers.<sup>[4]</sup> Previous studies have shown that lateral septal nucleus is involved in feeding and drinking behavior in rats.<sup>[5,6]</sup> Dev *et al.* have reported that nucleus

septal medialis does not play a greater role in the regulation of food intake (FI) and BW in rats and it is not directly linked to energy homeostasis in rats.<sup>[7]</sup> However, until date, no work is available to confirm the role of both lateral and medial septal nuclei in the control of feeding and drinking behavior and adiposity in animal models and the difference between these two nuclei on this behavioral regulation. There exists a difference in the regulation of feeding behavior between males and females, and

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in general, obesity is more common in females than in males.<sup>[8]</sup> Therefore, in this study, we have attempted to assess the gender difference between lateral and medial septal nuclei in the control of feeding behavior and adiposity in male and female rats.

## MATERIALS AND METHODS

### Animals

After the approval of the research council and animal ethics committee of Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), a total of 24 (12 males and 12 females) institute-bred healthy adult albino rats of Wistar strain weighing between 150 and 250 g were obtained for the study. The rats were housed in individual plastic cages with wire lids in the Animal Research Laboratory of Physiology department, JIPMER. A layer of husk was spread on the floor of the cages. 12 h light–dark cycle was maintained. Standard rodent chow and fresh tap water was available *ad libitum*. Rats were allowed to habituate in individual cages for 10 days before basal measurements were taken.

### Basal food intake and body weight recordings

After 10 days of habituation, 40 g of standard rodent chow and 100 ml of fresh tap water *ad libitum* was provided every day. Daily FI, water intake (WI), and BW were measured for 1 week to determine the mean 24 h basal recordings.

### Groups

Animals were divided randomly into two following groups:

- Medial septal group (bilateral lesion made in the medial septal nuclei; 6 males and 6 females)
- Lateral septal group (bilateral lesion made in the lateral septal nuclei; 6 males and 6 females).

### Procedures

#### Anesthesia

Different anesthetic agents were used because the depth of anesthesia required for different procedures differed. For blood collection, we require only light anesthesia, hence ether was used as the anesthetic agent for blood collection. Injection ketamine (0.25 ml/250 g BW) was injected intraperitoneally for making lesion and for sacrificing the animal; double the dose of ketamine was injected intraperitoneally as described by Dev *et al.*<sup>[9]</sup>

#### Electrolytic nuclear lesion

The stereotaxic procedure was performed as described by Pal *et al.*<sup>[10]</sup> for making the brain lesions. Bilateral electrolytic lesions of nucleus septal medialis and

nucleus septal lateralis were made by introducing electrodes into the respective nuclei on both sides according to the coordinates obtained from the stereotaxic atlas of rat brain by König and Klippel,<sup>[11]</sup> and allowing the anodal current of 0.5 mA to pass through the electrode.

### Parameters

- BW: It was measured in grams everyday with an electronic weighing machine for a period of 1 week
- FI: FI was measured in grams daily with an electronic weighing machine for a period of 1 week
- WI (ml): WI was measured in milliliters daily for a period of 1 week.

After the lesion procedure, the animals were allowed to recover from the stress of the intervention for a period of 7 days during which FI, WI, and BW were not measured.

### Sacrifice of animals

After recording 1 week of postinterventional readings, all animals were sacrificed following the standard procedure as described by earlier.<sup>[10]</sup>

### Statistical analysis of data

For data analysis, all values were expressed as mean  $\pm$  standard error. The differences among the means were evaluated by one-way analysis of variance using GraphPad InStat (Version 3, USA) software. *Post hoc* test was performed by Tukey-Kramer multiple comparison test. The difference was considered statistically significant if probability of chance was less than 0.05 ( $P < 0.05$ ).

## RESULTS

### Medial septal group

Table 1 shows the effect of lesion of medial septal nuclei on FI, BW, and WI in both male and female rats. Though the FI, BW, and WI in the prelesion state were more in male rats than female rats, the difference was not statistically significant. Following lesion of medial septal nuclei, FI increased significantly in both male ( $P < 0.05$ ) and female ( $P < 0.001$ ) rats [Table 1] compared to their prelesion values. When the postlesion value was compared, the increase in FI was significantly more in female rats ( $P < 0.001$ ) compared to male rats. Furthermore, the percentage increase in FI was significantly more in female rats ( $P < 0.001$ ) than in male rats [Table 2]. Similarly, BW also increased significantly in both male ( $P < 0.05$ ) and female ( $P < 0.001$ ) rats [Table 1], but the postlesion values were not significantly different between male and female rats. However, the percentage increase in BW was significantly more in female rats ( $P < 0.001$ ) than in male rats [Table 2]. There was no

**Table 1:** Comparison of food intake, water intake, and body weight following lesion of medial septal nuclei in both male ( $n=6$ ) and female ( $n=6$ ) rats

Parameters	Prelesion		Postlesion		P
	Male	Female	Male	Female	
FI (g/day)	13.02±0.48	12.6±0.42	15.8±0.65*	18.8±0.60***,ff	<0.0001
WI (ml)	22.24±0.80	21.8±0.56	23.05±0.74	22.80±0.70	0.6016
BW (g)	220.50±4.20	206.40±4.12	238.60±4.40*	248.80±4.82***	<0.0001

Data expressed are mean±SE. \*Comparison with the respective prelesion value, <sup>f</sup>Comparison between postlesion male and female rats. Analysis of data was done by one-way ANOVA and *post hoc* by Tukey-Kramer test. \* $P<0.05$ , \*\*\* $P<0.001$ , <sup>ff</sup> $P<0.001$ . Lesion means the lesion making needle electrode was introduced into the medial septal nuclei and current was passed.  $P<0.05$  was considered significant. BW: Body weight, FI: Food intake, WI: Water intake, SE: Standard error

**Table 2:** Comparison of mean percentage increase (from their pre-lesion values) in food intake, water intake and body weight of post-lesion male and female rats of both medial and lateral septal groups

Parameters	Medial septal group		Lateral septal group		P value
	Male	Female	Male	Female	
FI (g/day)	19.8±0.50	49.2±0.42***	5.07±0.12###	8.52±0.13***###	<0.0001
WI (ml)	3.64±0.12	4.58±0.15*	26.80±0.30###	17.75±0.24***###	<0.0001
BW (g)	8.20±0.15	20.54±0.24***	3.02±0.10###	6.04±0.18***###	<0.0001

Data expressed are mean±SE. The (\*) represents comparison between male and female rats within the group, (##) represents comparison between males of both the groups and females of both the group. Analysis of data was done by one-way ANOVA and *post hoc* by Tukey-Kramer test. \* $P<0.05$ ; \*\* $P<0.01$ ; \*\*\* $P<0.001$ ; # $P<0.05$ ; ## $P<0.01$ ; ### $P<0.001$ . BW: Body weight, FI: Food intake, WI: Water intake

**Table 3:** Comparison of food intake, water intake, and body weight following lesion of lateral septal nuclei in both male ( $n=6$ ) and female ( $n=6$ ) rats

Parameters	Prelesion		Postlesion		P
	Male	Female	Male	Female	
FI (g/day)	13.8±0.50	12.2±0.46	14.50±0.52	13.24±0.60	0.359
WI (ml)	22.68±0.70	21.4±0.82	28.76±0.86***	25.20±0.74* <sup>f</sup>	<0.0001
BW (g)	221.50±4.50	210.10±4.12	238.60±4.20	228.20±4.30	0.0556

Data expressed are mean±SE. \*Comparison with the respective prelesion value, <sup>f</sup>Comparison between postlesion male and female rats. Analysis of data was done by one-way ANOVA and *post hoc* by Tukey-Kramer test. \* $P<0.05$ , \*\*\* $P<0.001$ , <sup>f</sup> $P<0.05$ . Lesion means the lesion making needle electrode was introduced into the lateral septal nuclei and current was passed.  $P<0.05$  was considered significant. BW: Body weight, FI: Food intake, WI: Water intake, SE: Standard error

significant change in WI following lesion of medial septal nuclei in both sexes, but the percentage increase in WI was significantly more in female rats ( $P < 0.05$ ) than in male rats [Table 2].

### Lateral septal group

Table 3 shows the effect of lesion of lateral septal nuclei on FI, BW, and WI in both sexes. There was no significant change in FI and BW following lesion of lateral septal nuclei in both sexes. However, WI increased significantly in both male ( $P < 0.001$ ) and female rats ( $P < 0.05$ ). When the postlesion value were compared, the increase in WI was significantly more in male rats ( $P < 0.05$ ) compared with female rats. Furthermore, the percentage increase in WI was significantly more in male rats ( $P < 0.001$ ) compared with female rats [Table 2].

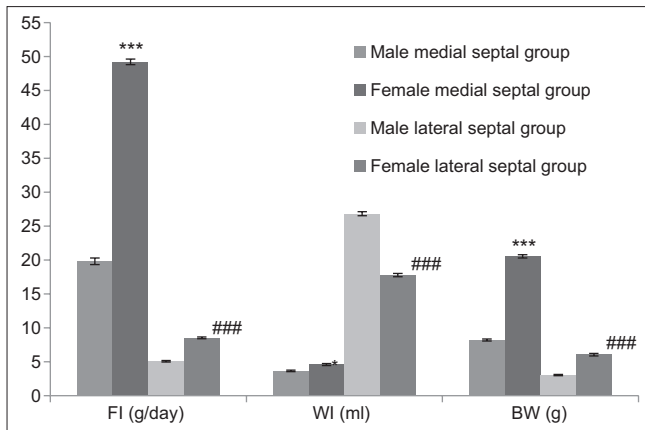
### Medial septal versus lateral septal group

Figures 1 and 2 show a comparison of the effects of lesion of medial septal and lateral septal nuclei on FI, BW, and WI in both male and female rats in terms of

mean percentage changes. Following lesion in male rats, the mean percentage changes in FI and BW was significantly high in medial septal group ( $P < 0.001$ ) compared with lateral septal group, whereas the mean percentage changes in WI was significantly high in lateral septal group ( $P < 0.001$ ) [Figure 1]. Following lesion in female rats, the mean percentage changes in FI and BW was significantly high in medial septal group ( $P < 0.001$ ) compared with lateral septal group, whereas the mean percentage changes in WI was significantly high in lateral septal group ( $P < 0.001$ ) [Figure 2].

## DISCUSSION

Following lesion of medial septal nuclei, there was a significant increase in FI and BW in both male and female rats. This indicates that normally medial septal nuclei inhibit feeding behavior and adiposity. The increase in both FI and BW was greater in female rats ( $P < 0.001$ ) compared with the increase in male rats ( $P < 0.05$ ) [Table 1]. This shows the presence of gender difference in the septal



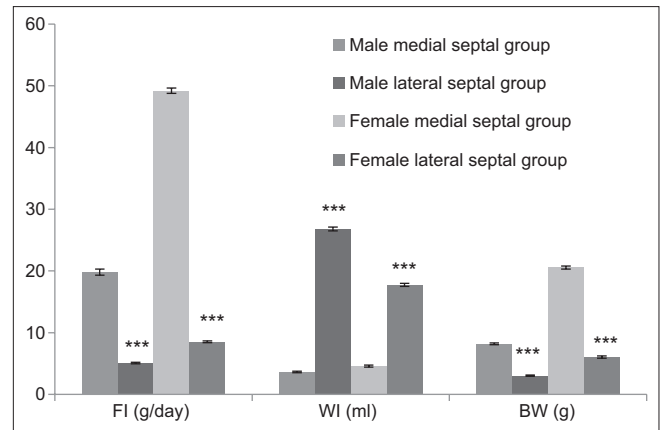
**Figure 1:** Male - female difference of mean percentage change (from their pre-lesion values) in food intake, water intake, and body weight of postlesion male and female rats of both medial and lateral septal groups. BW: Body weight, FI: Food intake, WI: Water intake. The (\*) represents comparison between male and female rats of medial septal group, (#) represents comparison between male and female rats of lateral septal group. \*\*\* $P < 0.001$ ; ### $P < 0.01$ ; #### $P < 0.001$

regulation of these functions. This corroborates with the report of Pankey *et al.*, in which, the influence of medial septal nucleus was reported to be more in female rats.<sup>[6]</sup> These findings clearly depict that adiposity is directly linked to FI, as FI and BW gain was almost parallel. One could argue that increase in BW may also be due to increase in WI leading to water retention. However, in this study, in medial septal group, the WI was not appreciably increased with the significant increase in FI and BW gain, which excludes the possibility of fluid retention contributing to the increase in BW. This behavioral pattern of feeding and weight gain is different in females from males, depicting that obesity is more prevalent in females of any age group compared to their male counterparts. Hence, the observations of this study clearly establishes medial septal nucleus among the brain centers in the control of obesity, especially in females.

Following lesion of lateral septal nucleus, the increase in FI and BW was not significant in both male and female rats. However, the increase in WI was significant in both sexes, males drinking more than females [Table 3]. This clearly indicates that lateral septal nucleus mainly controls the drinking behavior, and this drinking behavior is independent of feeding behavior. This is in confirmation with our previous report<sup>[5]</sup> that depicts septal polydipsia following lesion of lateral septal nucleus. Hence, the report of this study explains that increase in WI following lateral septal lesion is a primary polydipsia independent of FI.

## CONCLUSION

The report of this study reveals maximum gain in FI and BW in female rats following medial septal lesion and



**Figure 2:** Male - female difference of mean percentage change (from their pre-lesion values) in food intake, water intake, and body weight of post-lesion male and female rats of both medial and lateral septal groups. BW: Body weight, FI: Food intake, WI: Water intake. The (\*) represents a comparison between males of both the groups and females of both the group. \*\*\* $P < 0.001$

maximum gain in WI following lateral septal lesion. These findings indicate a stronger role of the medial septal nucleus in the control of adiposity in female rats, revealing the possibility of intervention of this nucleus in the future management of obesity, especially in females. The lateral septal nucleus plays a significant role in drinking behavior, especially in male rats.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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