

VENTROMEDIAL HYPOTHALAMIC NUCLEI AND FEEDING BEHAVIOR

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ABSTRACT

The role of the ventromedial nuclei of the hypothalamus (VMN) in food behavior was studied in adult male rats, allocated in 3 groups: control, sham and lesioned. Electrolytic lesions were induced stereotaxically (1.2 mA, 15 sec). Results revealed a significant decrease ($p < 0.05$) in body weight (BW) and food intake (FI) in the order of lesioned < sham < control during the first week. However, there were no significant differences in BW and FI between groups in the second week after lesion induction. In the lesioned group, the finikiness syndrome was observed in the second week after lesioning. It was postulated that VMN lesions produce the finikiness syndrome, and this in turn can cause hyperphagia and hypothalamic obesity. Water intake (WI) was significantly lower in the lesioned group in the first and second week after VMN lesion induction. It could be postulated that disturbances in the regulation of WI is part of the VMN lesion syndrome.

Keywords: VMN lesion, food intake, water intake, finikiness.

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INTRODUCTION

Biologically, adaptive regulation of feeding requires continuous evaluation and integration of endogenous humoral signals (e.g., metabolites,¹⁶ hormones,¹⁵ growth factors,⁵ neurotransmitters,²³ etc.), exogenous chemicals² and other sensory information associated with the motivational state of the animal. In general, the ventromedial nucleus of the hypothalamus (VMN) is considered as a neural structure involved in the control of ingestive behavior in rats.⁴ It has been shown that electrical stimulation of VMN inhibits food intake (FI) in the hungry animal¹³ and also causes an increase in lipolysis.^{3,14} Satiation and humoral factors such as glucose, free fatty acids and insulin modify the electrical activity of the individual neurons of VMN.^{15,16,20} However, according to the literature, different conclusions have been made and the exact role

of VMN is not clear yet, since several investigators have reported that VMN lesions induce hyperphagia and an increase in body weight (BW),^{11,19,20,22} while others, using the same techniques, induced hypophagia and growth retardation.^{5,6,13,23} Thus the present study aims at investigating the role of VMN in food behavior and finalizing the discrepancies.

MATERIALS AND METHODS

Studies were performed on 36 adult male Charles River rats, weighing 270 ± 1.87 gr, obtained from breeding laboratories (Shiraz Medical School colony). The animals were kept at room temperature ($22 \pm 2^\circ\text{C}$), 12:12 hr light: dark cycle, and fed on water, rat pellet and carrot *ad libitum*. They were divided into three equal groups: control, sham and lesioned. The last two

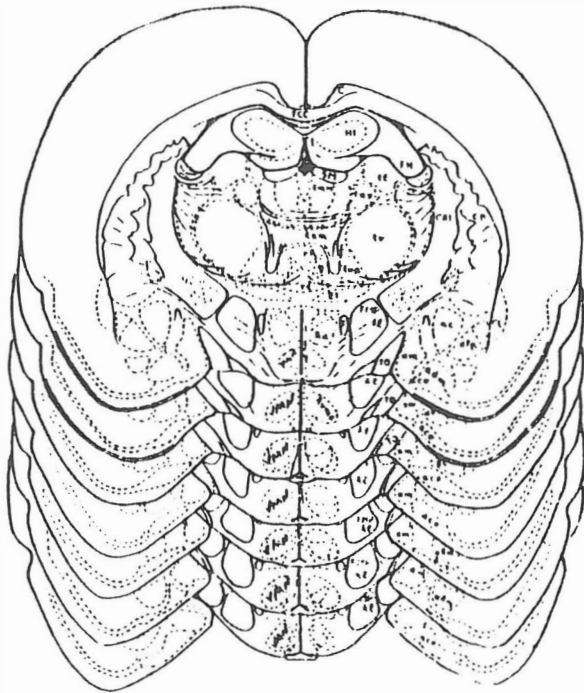


Fig. 1. Schematic representation of VMN on serial stereotaxic plates.

groups were anesthetized with 50mg/kg sodium pentobarbital injected intraperitoneally. In the lesioned group, bilateral lesions of VMN were carried out stereotaxically (1.2 mA, 15 sec) as lateral=±0.8mm, anterior=-0.5mm and vertical=8.4mm from Bregma.^{10,18} In the sham group, the electrode was placed at the same coordinates but no current was given. Thereafter, nutritional behavior was controlled in the lesioned and sham groups for two weeks, from the first day after surgery. At the end of the experiment, deeply anesthetized animals were injected with 10mL of 10% formalin intraventricularly and then immediately decapitated. Brains were examined histologically¹⁸ to locate the exact site of the lesion. Fortnightly recorded data, e.g. percentage changes in BW, FI and water intake (WI) were analyzed. Data were expressed as the mean ± standard error, and statistically significant differences were established by paired t-test, Dunken test and regression test. A value of $p < 0.05$ was considered significant.

RESULTS

The location and extent of the VMN lesion is illustrated in Fig. 1.

Quantitative results

In control and sham groups, there was a linear

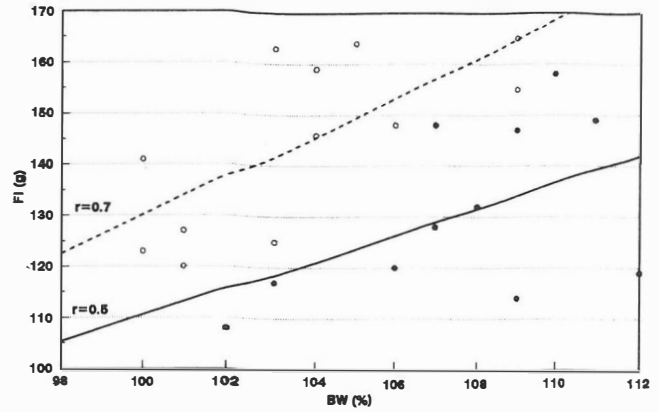


Fig. 2. Correlation between food intake (FI) and body weight (BW) in the first week (○, ---, $p < 0.05$) and the second week (●, —, $p < 0.05$) in the control group.

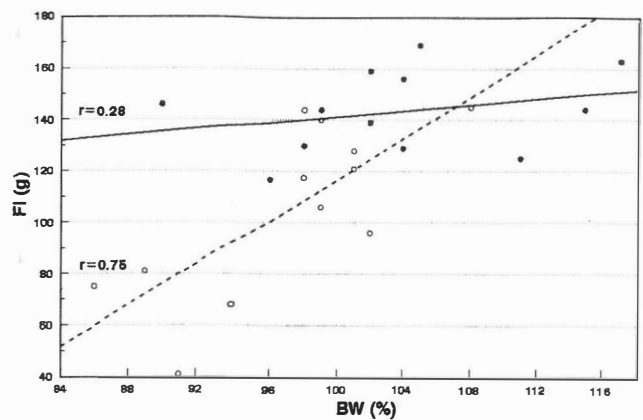


Fig. 3. Correlation between food intake (FI) and body weight (BW) in the first week (○, ---, $p < 0.05$) and the second week (●, —, $p > 0.05$) in the sham group.

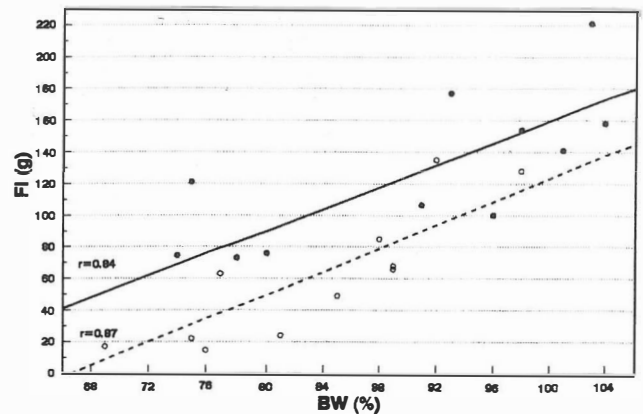


Fig. 4. Correlation between food intake (FI) and body weight (BW) in the first week (○, ---, $p < 0.05$) and the second week (●, —, $p > 0.05$) in the lesioned group.

correlation ($p < 0.05$) between BW and FI only in the first week (Figs. 2,3), while in the lesioned group, there

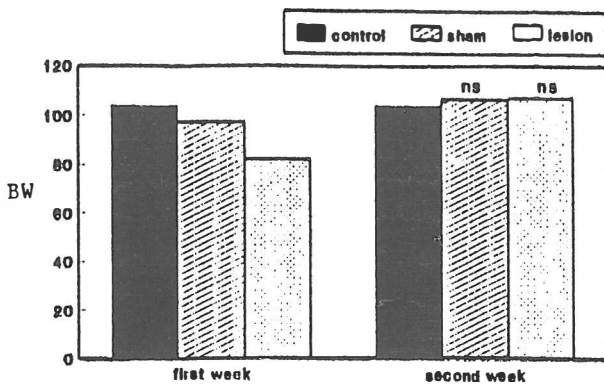


Fig. 5. Comparison of body weight (BW) in control, sham and lesioned groups in the first and second week. *: $p < 0.05$.

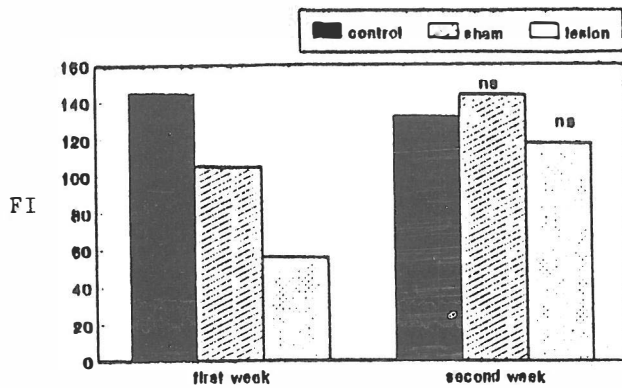


Fig. 6. Comparison of food intake (FI) in control, sham and lesioned groups in the first and second week. *: $p < 0.05$.

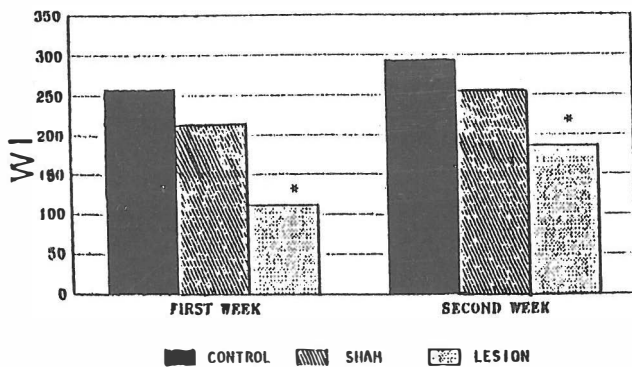


Fig. 7. Comparison of water intake (WI) in control, sham and lesioned groups in the first and second week. *: $p < 0.05$.

was a linear correlation ($p < 0.05$) between BW and FI only in the first week (Fig. 4). According to the data, during the first week, there was a significant decrease ($p < 0.05$) in BW and FI, in the order of lesioned $<$ sham $<$ control, but in the second week, no significant changes were observed in BW and FI between groups (Figs. 5,6).

WI was significantly ($p < 0.05$) lower in the lesioned

group compared to sham and control groups in the first week (Fig. 7). However significant differences existed between control and lesioned rats (lesion $<$ control) only in the second week (Fig. 7).

Qualitative results

In addition to the quantitative results, the animals' appeal for different kinds of foods was altered (finickness syndrome) in the lesioned group. In the preliminary experiments, it was noticed that lesioned animals refused to eat rat pellet up to death, but surprisingly they ate carrot eagerly. This alteration was observed one week after VMN lesioning.

DISCUSSION

In the present study, rats with VMN lesions exhibited a decrease in BW and FI for one week. The differences between lesioned, sham and control groups were significant ($p < 0.05$). These results were similar to the recent observations of King et al.¹¹ They also observed that within 10 days after VMN lesioning, rats became hypoglycemic. Frohman et al.⁵ noticed that hypoglycemia in rats lasted for 5-7 days. They also observed an increase in carcass fat deposition without any increase in BW. Goldman and colleagues⁶ have reported that VMN lesions in weanling rats increased carcass fat deposition and linear growth without any changes in FI and blood glucose. Reynolds¹⁷ has reported that VMN lesioning with radiofrequency did not produce hyperphagia.

The above results are in contradiction with those of other investigators that reported hypothalamic obesity due to hyperphagia after VMN lesioning.^{4,8,9,19}

In the present experiment, one week after (2nd week) VMN lesioning the animals exhibited hyperphagia and as a result became obese (compared to the first week). This finding was in accordance with that of other investigations.^{1,7,12,21}

In the present study, the authors observed that in the VMN lesioned rat, FI influences the rate of increase or decrease of BW. This is in contradiction with the finding of Frohman et al.⁵

However, Egawa and colleagues⁴ observed an increase in diurnal consumption of water and food along with an increase in BW in VMN lesions, which is consistent with our results.

Since there is no report on WI after VMN lesioning, we decided to study this parameter in detail. It was shown that in the lesioned group, WI was significantly lower than sham and control groups in the first and also second weeks after surgery. The question is whether the decrease in WI is due to the lesion of the VMN itself or

a phenomenon secondary to the decrease in FI. Since in the second week when FI was increased, WI still remained low, it could be postulated that the change in WI is part of the VMN lesion syndrome.

During the present experiment, hypersensitivity to external stimuli was observed. For example, pulling the tail of the animal roused a violent reaction. This point was also shown by Yoshida et al.²³ They observed that VMN lesioned animals exhibited an increase in sensitivity similar to denervation hypersensitivity.

One of the defined behavioral characteristics of the VMN lesion syndrome is an over-reactivity to the sensory properties of food, termed finikiness.² In the present experiment, we studied the changes in dietary behavior after VMN lesioning. It was observed that one week after VMN lesioning, the finikiness syndrome appeared and the animal did not eat rat pellet, but instead consumed carrot eagerly. Reynolds¹⁷ observed that using tasteless and bad tasting food in VMN lesioned rats did not lead to hyperphagia and an increase in BW, while using good tasting food resulted in hyperphagia and an increase in BW (finikiness).

In the present experiment, as it was discussed, decreases in BW and FI were observed during the first week after VMN lesioning. However, in the second week the animals exhibited hyperphagia and as a result became obese. This could be formulated and explained as follows:

1- In VMN lesioned rats, surgical procedures produced intense stress, causing hypophagia and as a result a decrease in BW during the first week, but the effect of hypothalamic obesity was showing henceforward.

2- In the present study, a preliminary experiment was carried out to check the finikiness syndrome. It was noticed that lesioned animals refused to eat rat pellet up to death. However, we decided to give them some carrot too and, interestingly, they ate carrot eagerly with hyperphagia. Nevertheless the finikiness syndrome appeared only in the second week after VMN lesioning. The present results are similar to some other results which reported hyperphagia after VMN lesioning.^{4,10,20,22} Although there is no report on food variety in their data, finikiness probably affected FI and BW in their experiments as well.

However, it seems that VMN lesioning would not produce hypothalamic obesity due to hyperphagia if the animal was given the rat pellet, but VMN lesioning would produce the finikiness syndrome, which would cause hyperphagia if the animal was given foods of more palatable taste.

REFERENCES

- Berthoud HR, Renaud J: Acute hyperinsulinemia and its reversal by vagotomy after lesion of the ventromedial hypothalamus in anesthetized rats. *Endocrinology* 105: 146, 1979.
- Black RM, Weingarten HP: A comparison of taste reactivity changes induced by ventromedial hypothalamic lesions and stria terminalis transection. *Physiol Behav* 44: 699-708, 1988.
- Bray A, Nishizawa Y: Ventromedial hypothalamus modulates fat mobilization during fasting. *Nature (Lond)* 274: 900-902, 1978.
- Egawa M, Inoue S, Satoh S, Takamura Y, Nagai K, Nakagawa H: Acute and chronic effects of VMH lesions on circadian rhythm in food intake and metabolites. *Brain Res Bull* 31 (3-4): 293-294, 1993.
- Frohman LA, Bernardis LL: Growth hormone and insulin levels in weanling rats with ventromedial hypothalamic lesions. *Endocrinology* 82: 1125-1132, 1968.
- Goldman JK, Bernardis LL, Mackenzie R, Kodism G, Luboshitzky R: Effect of ventromedial hypothalamic lesion on adipose tissue of weanling male rat. *Diabetologia* 20 (Suppl): 357, 1981.
- Goto Y, Cannenter RG, Berelowitz M, Frohman LL: Effect of ventromedial hypothalamic lesion on the secretion of somatostatin, insulin and glucagon by the perfused rat pancreas. *Metabolism* 29: 986-990, 1980.
- Hustredt BE, Lovo A: Correlation between hyperinsulinemia and hyperphagia in rats with ventromedial hypothalamic lesion. *Acta Physiol Scand* 84: 29-33, 1960.
- Inoue S, Bray GA: The effect of subdiaphragmatic vagotomy in rats with ventromedial hypothalamic obesity. *Endocrinology* 100: 108, 1977.
- Joachim FR, König R, Klippel A: the rat brain, a stereotaxic atlas of the forebrain and lower parts of the brain stem. Nobel Offset Printers, New York, 1967.
- King BM, Diagrepoint PM, Michel RE, Zansler CA, Ahmed JI, Walker A, Frohman LA: Hypothalamus obesity: comparison of radiofrequency and electrolytic lesions in weanling rats. *Physiol Behav* 45: 127-132, 1989.
- Moltz JH, Dobbs RE, McCann SM, Fawcett CP: Preparation and properties of hypothalamic factors capable of altering pancreatic hormone release *in vitro*. *Endocrinology* 105: 1262-68, 1979.
- Mozes S, Kuchar S, Koppel J, Rynikova A, Boda K, Novakova V: RNA content of neurons in the ventromedial nuclei and lateral hypothalamic area relative to feeding status. *Physiol Behav* 43: 287-89, 1988.
- Nishizawa Y, Bray GA: Ventromedial hypothalamic lesion and the mobilization of fatty acids. *J Clin Invest* 61: 714-

- 721, 1978.
15. Oomura Y, Kita H: Insulin acting as a modulator of feeding through the hypothalamus. *Diabetologia* 20 (Suppl): 290-298, 1981.
 16. Partridge WM: Transport of nutrient and hormone through the blood brain barrier. *Diabetologia* 20 (Suppl): 240-254, 1981.
 17. Reynolds RW: Ventromedial hypothalamic lesion without hyperphagia. *Am J Physiol* 204: 60-62, 1963.
 18. Skinner JE: *Neuroscience- A Laboratory Manual*. Philadelphia: W.B. Saunders Company, pp. 221-2, 1971.
 19. Thornton SN, Nicolaidias S, Larue Achagiotis C, Campfield A: Body weight gain after VMH lesions in adult female rats guanethidine-sympathectomized at birth. *Appetite* 17 (1): 47-53, 1991.
 20. Tokunaga K, Fukushima M, Lupien JR, Bray GA, Kemnitz JW, Schemmel R: Effects of food restriction and adrenalectomy in rats with VMH or PVH lesions. *Physiol Behav* 45 (6): 1131-7, 1989.
 21. Van Houten M, Schiffrin EL, Mann JF, Iposner B, Boucher R: Insulin binding sites localized to nerve terminals in rat median eminence and arcuate nucleus. *Science* 207 : 1081-1083, 1980.
 22. Weingarten HP, Change PK, McDonald TJ: Comparison of the metabolic and behavioural disturbances following paraventricular and ventromedial hypothalamic lesion. *Brain Res Bull* 14: 551-560, 1985.
 23. Yoshida T, Bray GA: Catecholamine turnover in rats with ventromedial hypothalamic lesion. *Am J Physiol* 249: R 558- 565, 1983.

