EFFECT OF GLUCOSE ON THE ACTIVITY OF FEEDING CENTRES BEFORE AND AFTER PARASAGITTAL CUTS BETWEEN MEDIAL AND LATERAL HYPOTHALAMUS

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Summary: Intracarotid administration of isotonic glucose (0.5 *ml* of 5.4%) in the starving albino rats produced an increase in the multiunit activity (MUA) of ventromedial hypothalamus (satiety centre) and a decrease in the MUA of the lateral hypothalamic area (feeding centre). Intracarotid infusion of normal saline did not change the MUA of any of these centres. Parasagittal knife cuts placed in between the satiety and feeding centres did not affect the responsiveness of these centres to glucose administration as indicated by the recorded multiunit activity.

Key words: multiunit activity feeding centre rat parasagittal cut satiety centre effect of glucose

INTRODUCTION

The role of hypothalamus in the regulation of food intake is well recognised (1,4). Electrophysiological studies on the satiety (ventromedial hypothalamus) and feeding centres (lateral hypothalamic area) have demonstrated that the satiety centre is activated while the feeding centre is inhibited on increase in glucose utilisation, and vice-versa (2,3,5,8,). It has been suggetsed that the control on hunger is exercised by the modulation of the activity of satiety centre which provides inhibitory pathways to the feeding centre meaning that activation of satiety centre on glucose infusion would inhibit the feeding centre activity through these inhibitory pathways (2,3,6,12,15,16). Recently, it has been demonstrated that the neurones which increase or decrease their firing rate on direct application of glucose by inotophoretic technique are present both in the satiety and feeding centres (16). There is thus a possibility of the existence of two more or less independent glucostatic mechanisms, one in the ventromedial hypothalamus, and the other in the lateral hypothalamic area. This paper reports experiments performed to test such a possibility by observing the effect of glucose administration on the activities of these centres before and after breaking the inter-centre connections with the help of parasagittal knife cuts.

MATERIALS AND METHODS

Experiments were conducted in albino rats of either sex.

Operative procedures : The animals were not fed on the morning of the experiment. The rats were anaesthetised with intraperitoneal urethane in dosage of 175 *mg*/100 *g* body weight. Carotid artery was cannulated by introducing a polyethylene catheter. The head was then fixed in the stereotaxic instrument and a small trephine hole was made in the skull according to the stereotaxic coordinates (11).

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After recording the multiunit activity of hypothalamic regions and studying the effects of glucose infusion on this, parasagittal cuts were made between the medial and lateral hypothalamus with the help of a specially designed micro-knife made up of stainless steel (15 mm x 2.5 mm) mounted on a straight tungsten wire. The knife fixed in the stereotaxic instrument was lowered to the hypothalamic region and moved to produce the desired cuts. Multiunit activity was again recorded and glucose infusion repeated.

Recording of multiunit activity : This was recorded with the help of stereotaxically guided micromacro-electrodes of tip diameter 10-20 μ. The potentials picked up were fed through a Tektronix plug-in low level AC differential preamplifier to a Tektronix 502A oscilloscope and photographed by a Grass C4 camera. At th end of the experiment the site of recording was marked by passing a DC current of 3 m.amp. for 15 sec and then perfusing the brain with ferrocyanide formalin solution for producing Prussian blue reaction at the site of iron deposit.

Glucose administration : After obtaining a stable discharge pattern of the hypothalamic units, 0.5 ml of 5.4 percent (isotonic) glucose solution was injected through the carotid artery. Before this a similar volume of isotonic saline (0.9 percent) was injected to serve as control. Subsequently, after making parasagittal knife cuts and obtaining a stable multiunit discharge, glucose injection was repeated and its effects were again observed. Since after glucose infusion the time interval for return of multiunit activity to pre-injection level varied from 20-60 min, the interval between the injections of glucose before and after parasagittal cut was kept at more than 2 hours.

RESULTS

Ninety rats of either sex were used in the present study. The steady units could be obtained from 25 rats and the results of these are presented. As reported earlier (2) the hypothalamic units are of lower frequency and smaller amplitude and so the failure rate of recording stable units for longer periods was quite high.

The quantitative analysis of the results was done by counting the number of spikes per unit time. As it is difficult to do such a count from records of multiunit activity (recorded from more than one unit) an integrator was also used to give the average responses. It was observed that the integrated multiunit activity analysis matched well with the spike counts.

General characteristics of hypothalamic Unit Activity : It was observed that as the animals were starving for about 18 hours, the frequency of multiunit discharge from lateral hypothalamic area (LHA-feeding centre neurones) was higher as compared to that from the region of ventromedial nucleus (VMN-satiety centre neurones). The rate of discharge from VMN varied from 2-9/sec, while from LHA it ranged from 15-42/sec. The activity from other hypothalamic areas ranged from 2-24/sec being lower in the dorsomedial region

In majority of the animals after the parasagittal knife cuts, the frequency of firing was slightly elevated both from VMN and LHA. The records of other areas did not show significant changes.

Effect of glucose : Glucose infusion (0.5 *ml* of 5.4%) produced an increase in the activity of satiety centre neurones and a decrease in the multiunit acitivity of feeding centre neorones. Activities recorded from other hypothalamic regions did not show much change. Infusion of 0.9% saline did not produce any changes in the activities of various hypothalamic regions.

Satiety Centre (VMN) : In 12 rats electrodes were guided to and histologically confirmed to be in the ventromedial nuclei. Fig. 1 illustrates a typical multiunit record from the satiety centre before and after parasagittal cut while Fig 2 summarises these changes in the multiunit firing rates. A significant increase in the multiunit activity was observed after

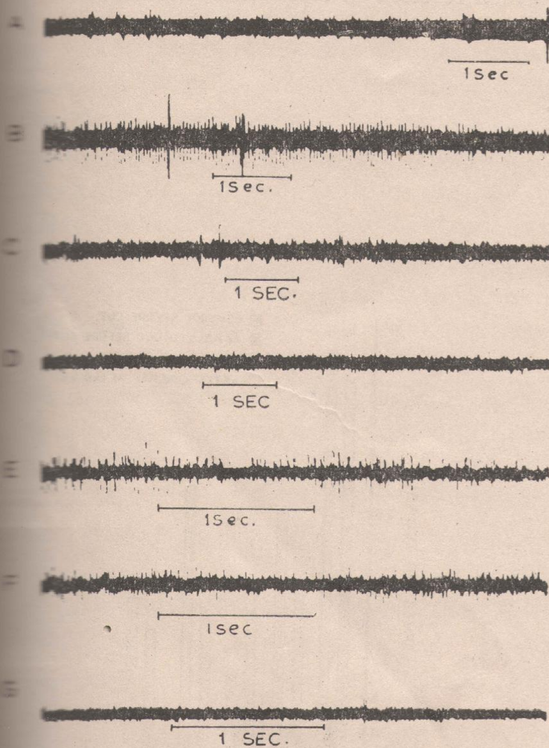

Fig. 1: Multiunit activity of the 'satiety centre' of a rat before glucose administration (A), 10 and 30 min after glucose infusion (B & C), after parasagittal cut between VMN and LHA(D) and retesting with glucose infusion 10, 30 & 50 min after (E, F & G). The increase in MUA activity of the satiety centre after glucose infusion is evident. The increase lasted longer after the parasagittal knife cut.

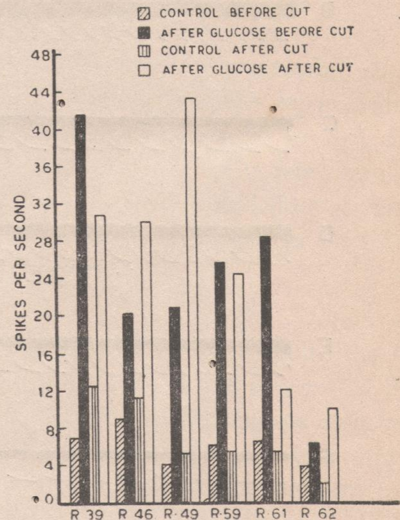

Fig. 2: Mean frequencies of multiunit discharges from satiety centre in 6 rats before and after glucose infusion in normal state and after parasagittal knife cut.

glucose infusion both before and after parasagittal knife cuts. The effect of glucose starte within 2 minutes of its infusion but it took about 10 minutes for the peak increase in activit to occur, while its effect persisted for about 50 minutes.

Feeding Centre (LHA) : In 7 rats the electrodes were confirmed to be in the latera most portion of the lateral hypothalamus at the same rostro caudal plane as that of VM (satiety centre). Fig. 3 illustrates typical multiunit record from the feeding centre before an after parasagittal cut while Fig. 4 summarises these changed in the firing rates of feedin neurones. The multiunit activity of these neurones was significantly decreased after gluco infusion both before and after parasagittal cuts. The responses of the feeding centre neuron occurred almost instantaneouslv after glucose infusion and lasted for about 15-20 minute In some animals the unit activity could be recorded for longer periods and it was possible give second or third glucose injections, each of which resulted in reproducible results.

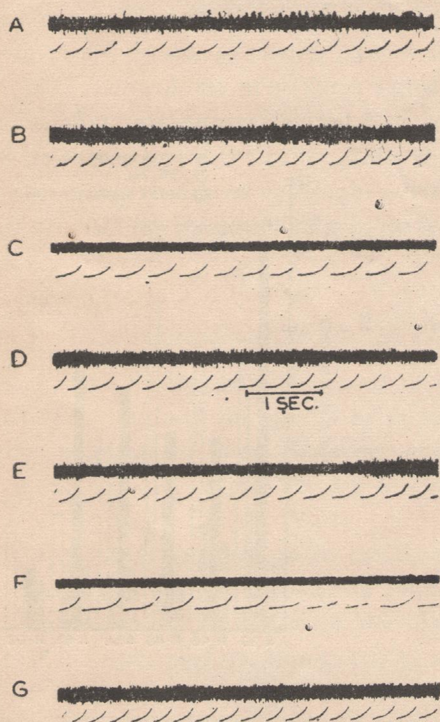

Fig. 3: Multiunit activity of the 'feeding centre' of a rat before glucose administration (A), 5 min after normal saline (B), and 15 min after glucose infusion (C & D), effect of parasagittal knife cut (E), and retesting with glucose infusion at 2 and 15 min after glucose infusion (F & G). Marked decrease in the MUA on glucose infusion is quite evident.

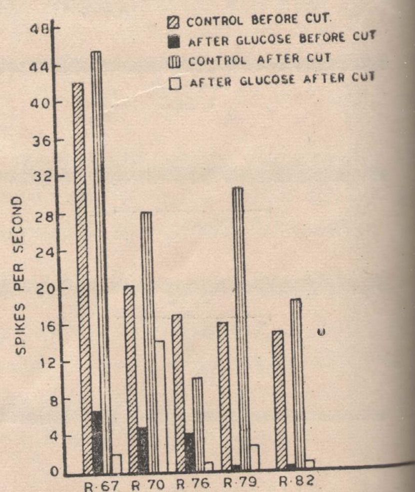

Fig. 4: Mean frequencies of multiunit discharges f feeding centre in 5 rats before and after glu infusion in normal state and after parasag knife cut.

Other hypothalamic regions : In 8 other rats the electrodes were confirmed to be in some other areas of hypothalmus (arcuate nucleus, fornix, medial forebrain bundle, dorsomedial nucleus etc.). The activity of these neurones did not show any significant change on glucose infusion either before or after parasagittal knife cut.

It is, therefore, clearly brought out from these experimental observations that, not only glucose infusion selectively and inversely changes the electrical activity of the satiety and the feeding centre neurones, these changes occur even after the midline neuronal connections between these two centres are severed. Thus the effect of glucose is possibly directly produced on the neuronic population of these two centres.

DISCUSSION

The results of the present study are consistent with the observations of other workers (2,3,8,9,19), who have shown a reciprocal relationship of the electrical activity between the hypothalmic feeding centres in response to glucose. The morphological basis of the reciprocal relation between the feeding and satiety centres is not yet settled. Arees and Mayer (6) have shown internal connections from ventromedial nucleus (VMN) to lateral hypothalmic area (LHA), while Dreifuss *et al.* (10) have proposed the presence of indirect connections from LHA to VMN via amygdala. The observations are suggestive that the direct connections between the VMN and LHA are not specifically responsible for inhibiting the LHA on excitation of VMN with increased glucose utilization, as proposed previously (2,8,9,13). In the present study even after severing the connections between VMN and LHA the units from both these regions still responded to glucose infusion in a reciprocal manner. It would thus appear that the neurones of feeding centre may also be independently sensing the changes in the level of glucose or glucose utilization in the body.

Booth(7) has shown inhibition of feeding on microinjection of glucose into the LHA, and Oomura *et al.*(16) have produced evidence indicating that even in the absence of VMN, the lateral hypothalamic area can produce postprandial inhibition of feeding via information received from the stomach receptors. Our results are consistent with the observations of these workers suggesting that the feeding centre neurones also have an independent role to play in bringing about satiation. These results, however, do not rule out any additional effects through inhibition of feeding centre on the activation of satiety centre. Considering the nature of cells in the feeding and satiety regions, it is possible that the whole neurone population may not have the same sensitivity to glucose. There may be low threshold or high threshold neurones(14), there may be slowly adapting and quickly adapting neurones, and there may even be neurones responsive only to changes in the level of glucose and not the actual level at any time. This may explain the variability in the duration of change in the activity of these neurones as well as the variable time taken for the initiation of these changes.

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