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The growth stimulating factor in parabiotic rats

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Littermate Wistar rats were parabiosed at 30 days and daily individual food intake and individual weight gain of fifteen parabiotic pairs were recorded as control parabiotic pairs. Another fifteen pairs were used for the experiment in which one partner of parabiotic pair was completely fasted for 4 days and then refed ad libitum till body weight returned to the prefasting level and throughout the experiment, individual body weight changes and individual food intake of both partners of test parabiotic pairs were recorded. During fasting period, daily food intake and weight gain of non-fasted partner of test parabiotic pair increased significantly over that of the individual rat in control parabiotic pair. Moreover, weight loss of fasted partner is same as that of individual fasted rat. The above findings indicated the presence of factor/factors in plasma of fasted partner stimulating food intake and growth of non-fasted partner of the test parabiotic pair. The present study also reveals that there is greater body weight increase per. g. food consumed (food conversion efficiency) of fasted partner during refeeding period whereas that of non-fasted partner decreased significantly during that period. Food intake and factors controlling it have been extensively studied by Physiologists and Nutritionists interested in growth and its regulation. Various external and endogenous stimuli initiate and terminate feeding. Of the endogenous stimuli humoral factors and their mode of action are the subjects of several recent studies (1,3,4,6). The present study is undertaken in order to further clarify and assess the role of humoral factor in the regulation of food intake and growth.

MATERIALS AND METHODS

Parabiotic procedure

Littermate Wister rats were Parabiosed at 30 days. The operative procedure was essentially that described by Bunster and Meyer (2).

Determination of individual food intake and individual weight changes

10 days after operation, parabiotic pairs were fully active and feeding normally. There were no signs of skin rejection between partners and the existence of

plasma exchange was demonstrated in some of the pairs by using radio-iodinated serum albumin.

The parabionts were trained to consume their entire daily ration of food in a 6:00 hour period. Subsequently, the pairs were conditioned to eat in the specially designed partitioned cages, which permitted some freedom of movement but prevented access to food or water in the partner's compartment. The diet was that of the Department of Medical Research, Burma, Rat chow with an energy value of 3.25 Kcal/g. Water from individual bottle was available at all times. Environmental temperature was maintained between 22° and 25° C and was recorded daily.

An adjustable stage was specially designed and used in conjunction with a balance in order to weigh the individual partner of the parabiotic pair under light anaesthesia seperately. The balance used was Top-Pan, Top E.500 balance with the accuracy of 0.01 g. This method of seperate weighing of the individual partner of the parabiotic pair was demonstrated to be accurate within ± 0.05 g.

Design of experiment

Control parabiotic pairs:Fifteen parabiotic pairs were kept as controls and their daily individual food intake and weight gain were recorded.

Test parabiotic pairs: Fifteen pairs of rats were used for the experiment in which one partner of parabiotic pair was completely fasted for four days and then refed ad libitum till body weight returned to the prefasting level. Individdual body weight changes and individual food intakes of each partner (fasted partner as well as non-fasted partners) were recorded throughout the prefasting, fasting, and refeeding periods.

RESULTS

The mean daily individual food intake of each partner of control parabiotic pairs was determined and shown in Fig. 1. The average daily food intake of each partner of control parabiotic pair for the entire period of experiment was found to be 11.41 ± S.D. 0.15 g.

The average food intake of non-fasted partner of the test parabiotic pairs during prefasting period, fasting period and refeeding period are shown in Figure 1. During the fasting period the food intake of non-fasted partner increased significantly (5% probability level) over that of the individual rat of the control parabiotic pair. It was highest on the first day then gradually decreased till it reached the prefasting level during refeeding period.

As shown in Figure 1, the daily food intake of the fasted partner during refeeding period was highest on the first day of refeeding and then it declined slowly and reached the perfasting level on twelveth day after refeeding.

The mean individual weight gains of each partner of the control parabiotic pairs were shown in Figure 2. The average daily individual weight gain in control parabiotic pair is

1.54 ± S.D 0.91 g.

The effect of complete fasting and refeeding of one partner on the weight of each partner of the test parabiotic pairs was shown in Figure 2. During the fasting period the mean body weight of the non-fasted partner increased significantly over that of individual rat in control parabiotic pairs.On refeeding, weight of fasted partner increased abruptly on the first day and prefasting weight is gained on twelveth day after refeeding.It is surprising to see that there was marked weight increase of the non-fasted partner on the first day of refeeding period. The weight of the non-fasted partner then fell gradually and reached the prefasting level on the sixth day of the refeeding period. As expected, the weight of the fasted partner fell rapidly the during fasting period and on refeeding increased rapidly to prefasting level within twelve days.

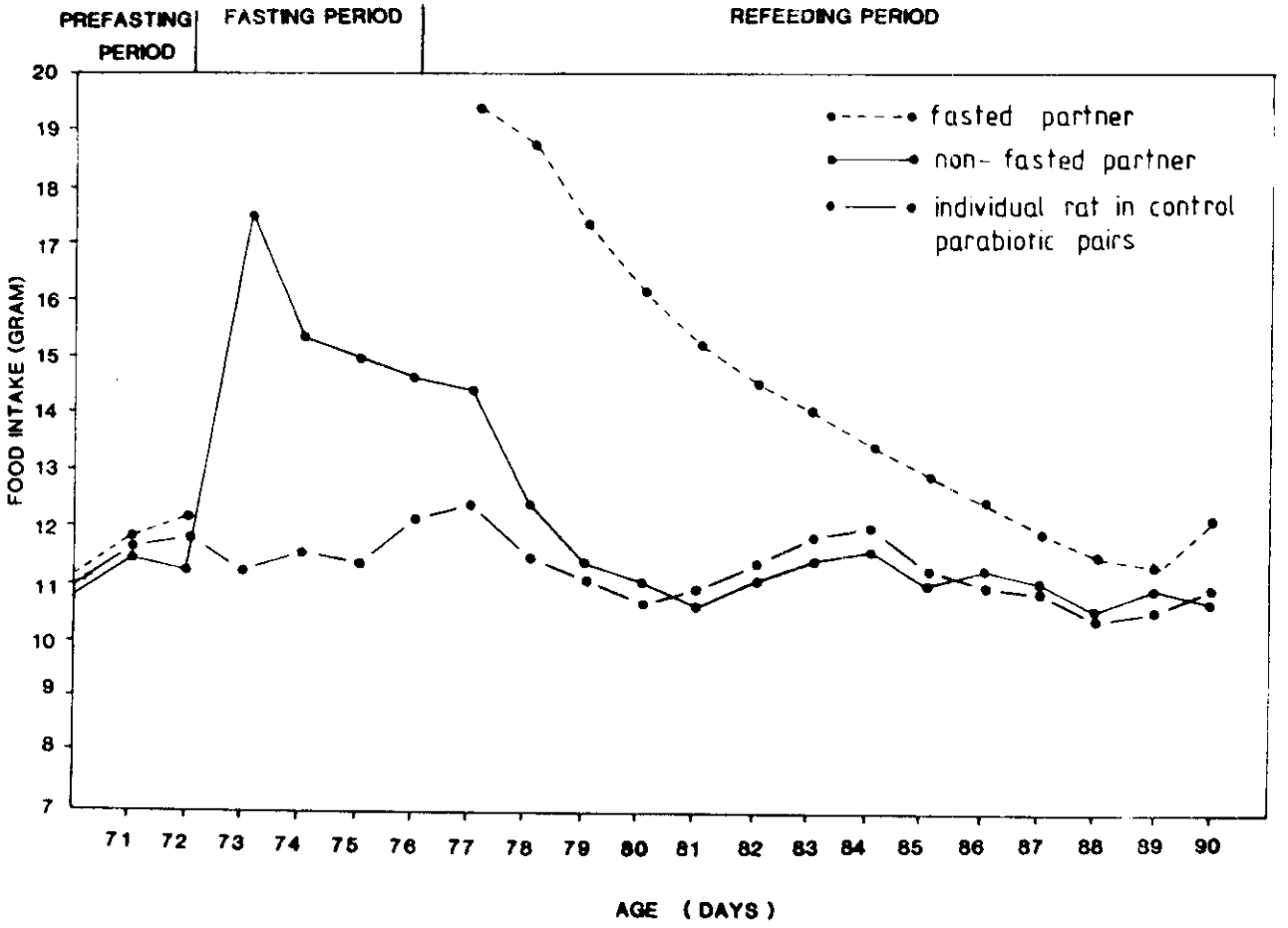

Figure.1- The effect of complete fasting and refeeding of one partner on changes in food intake of other partner in test parabiotic pairs.

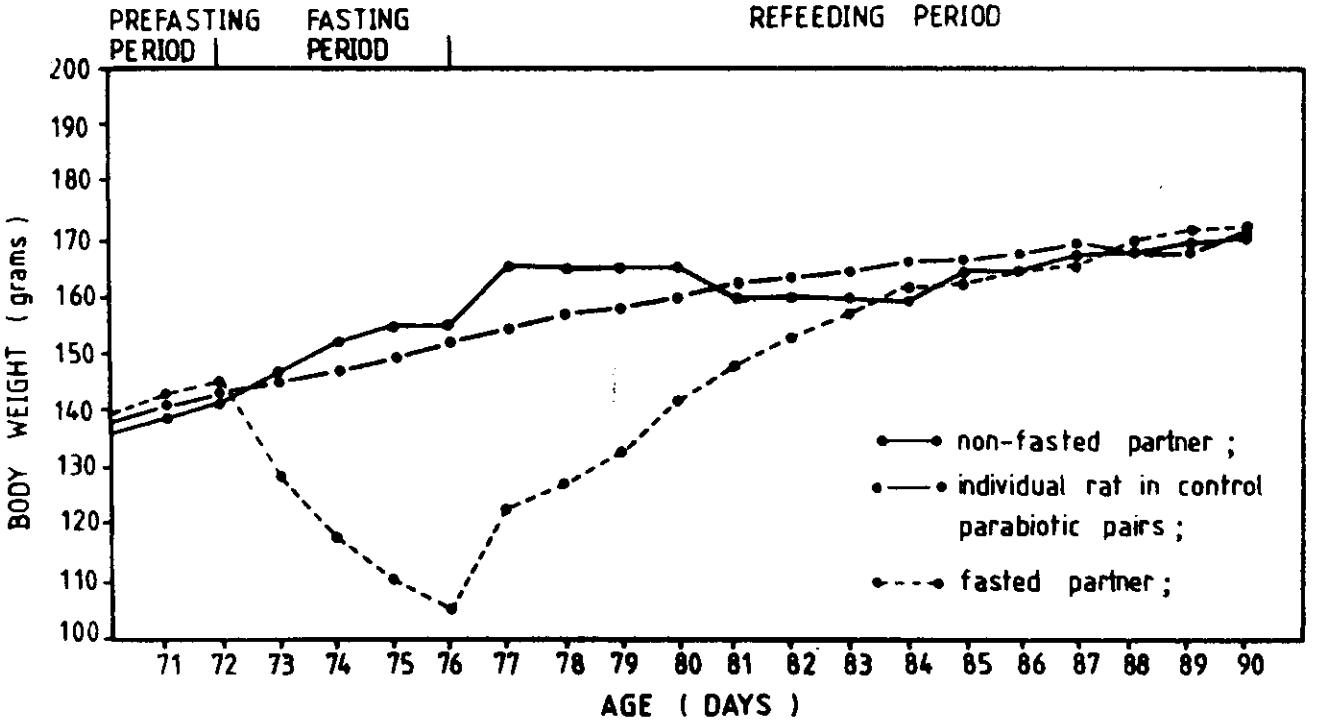

Figure.2- The effect of fasting and refeeding of one partner on changes in growth(weight) of both partners in test parabiotic pairs.

Food conversion efficiency (i.e., body weight increase per g. of food consumed) was calculated for different periods of experiment in both fasting and non-fasting partner and shown in Table 1. The table portrayed that the food conversion efficiency of fasted and non-fasted partner did not differ significantly from one another during prefasting period. There was no difference in food conversion efficiency of non-fasted partner between the prefasting and fasting period. However, the food conversion efficiency of fasted partner was significantly increased during refeeding period whereas that of non-fasted partner decreased significantly (significant at 5% probability level).

Table 1. Food conversion efficiency (percent) of fasted and non-fasted partner of test parabiotic pairs

Parabiotic Rats	Prefasting period	Fasting period	Refeeding period
Fasted partner	20.42	-	32.79
Non-fasted partner	21.39	20.95	9.23

DISCUSSION

The marked increase in food intake of the non-fasted partner of the test pair during the fasting period idicates that the fasting state has generated some factor/factors in the fasted partner which was transmitted through plasma to

the non-fasted partner and has stimulated the latter to increase its food intake.

It appears that this factor can be generated and act rapidly. Its stimulatory effect is highest on the first day and then gradually declines but continues to be active throughout the fasting period. On resumption of feeding the stimulatory effect decreases rapidly to prefastion level indicating that the generation and transmission of the humoral factor has rapidly declined. The mechanism of action of this humoral factor may be either through inhibition of satisty centre or stimulation of feeding centre.

The observation of a gradual decline in stimulatory effect of the humoral factor even during the fasting period may be explained as due to decreased generation and transmission of the humoral factor or due to decrease in response of the satiety or feeding centre. Parameswaren et al.(5) described the existence and circulation of humoral factor inhibiting food intake in parabiotic rats where one partner was electrically stimulated in the hypothalamus . Our two studies therefore complement and reinforce each other.

As expected, the increase food intake of the non-fasted partner of the test pair was accompanied by a greater weight gain when compared with that of the individual rat of control parabiotic pair. Moreover, this increased weight gain continued into the refeeding period up to five days even though food intake had declined to prefasting levels.

The great increase in food intake and rapid weight gain in the fasted partner when refeeding commences is noteworthy. It is probable that the humoral factor in the circulation at the beginning of the refeeding period may have stimulated this urgent increase in food intake and rapid weight gain. With the commencement of refeeding the generation of the humoral factor probably gradually declined with consequent decline in food intake and in rate of weight gain.

A consideration of the changes in food conversion efficiency shows that this may also play a role in the weight changes observed. The greater food conversion efficiency in the fasted partner during refeeding may have contributed toward the rapid regain of body weights to prefasting levels. Also the lowered food conversion efficiency in the non-fasted partner during refeeding may also have contributed toward the shedding of excess weight gained during fasting period and the return to prefasting level. This observation complement those of Perbjorntrop, Edstrom, Kral, Lundholm, Presta, Walk and Yang (6) who observed that greater food efficiency is responsible for inability of the obese subjects to loose weight to a level commensurate with decrease in food intake. These changes in food conversion efficiency during refeeding in fasted and non-fasted partners suggest that the humoral factor

may not only influence the satiety/feeding centre but may also influence on metabolism in some manner which is still not clearly understood.

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