SPATIOTEMPORAL ORGANIZATION OF MEMBRANE HYDROLYSIS AND TRANSPORT SYSTEMS IN THE RAT SMALL INTESTINE

G. I. Loginov

UDC 612.332.72

Glucose transport along the concentration gradient during incubation for 90 min in 0.2% solutions of glucose and soluble starch was studied by the "everted sac" method in five segments of the small intestine in Wistar rats. The serous fluid was replaced with a fresh portion of Ringer's solution every 15 or 30 min. Substrate loading was shown to synchronize the enterocyte population and to stabilize the transport system. During both continuous and interrupted substrate loading, the dynamics of glucose absorption over a period of about 1 h differed in the five segments. The differences were due to the properties of autoregulation of the transport systems and the level of reactivity of the given enterocyte population. Alternation of segments with unequal reactivity was found along the intestine. The transport of starch glucose between 8 and 16 h (the rats were killed every 2 h) fell sharply in the proximal and, to a lesser degree, in the middle segments. Conversely, absorption in the distal segments between 8 and 12 h was considerably intensified. The dynamics of transport of starch glucose during each hour varied unequally along the intestine. The results are discussed with allowance for the possible role of oscillatory processes in an individual population of enterocytes and in the small intestine as an integral system.

KEY WORDS: glucose transport; small intestine; spatiotemporal organization.

The concept of structural-functional temporal discreteness has acquired the status of a universal biological law. It has been shown, in particular, that all levels of organization – from macromolecules to the organism as a whole – are characterized by their own biorhythms and by interchanging activity of their functional elements [1-3]. Meanwhile, in the literature, there are only isolated data on the temporal dynamics of digestive and transport activity of the enterocytes [7, 8].

The dynamics of hydrolysis and transport of carbohydrates in the small intestine was investigated in vitro under different experimental conditions.

EXPERIMENTAL METHOD

Wistar rats kept on an ordinary diet but deprived of food for 18-20 h before the experiments were used. The rats were decapitated and the small intestine (without the duodenum) was divided into five equal segments. In the experiments of series I the mucoserous transport of glucose was investigated by means of a modified "everted sac" technique [9]. Segments of intestine about 10 cm long were everted with the mucous membrane on the outside, filled with 1 ml Ringer's solution, and incubated for 90 min at 37°C in 50 ml of oxygenated 0.2% glucose saline, pH 7.4. Every 15 min the serous fluid was completely removed, the concentration of glucose in it was determined [11], and the cavity of the segment was refilled with a fresh portion of Ringer's solution. In this way the dynamics of absorption was studied against the background of continuous substrate loading and with periodic stepwise changes in the concentration gradient between the mucous and serous surfaces of the intestinal segment. To reveal the pattern of autoregulation of the transport systems, in the experiments of series II the dynamics of absorption was studied during interrupted substrate loading.

M. I. Kalinin Andizhan State Medical Institute. (Presented by Academician G. M. Frank.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 83, No. 5, pp. 556-558, May, 1977. Original article submitted January 30, 1976.

TABLE 1. Mucoserous Glucose Transport (in mg %) in Various Segments of Rat Small Intestine during Continuous Substrate Loading

Incubation medium	Incubation period, min	Segment of small intestine				
		1st	2nd	3rd	4th	5th
Glucose	0–15	100	77	160	100	47
"	15–30	255	255	390	250	100
"	30–45	245	240	370	275	108
"	45–60	245	205	345	256	90
"	60–75	230	205	345	205	93
"	75–90	158	206	303	190	63

In the experiments of series III the rhythms of membrane hydrolysis and transport of carbohydrates over periods of several hours were studied. The rats were decapitated every 2 h in the period between 8 and 16 h. The mucoserous transport of glucose was investigated during incubation of the everted segments for 90 min in a 0.2% solution of soluble starch. The serous fluid was completely replaced every 30 min.

EXPERIMENTAL RESULTS

The dynamics of glucose absorption along the intestine was varied. A difference in the duration of the periods of saturation and a constant level of transport and also in the dynamics of the subsequent slowing of absorption was observed between the segments (Table 1).

The properties of the transport systems were evaluated with respect to three parameters. The first characterized the activity of the given segment of intestine as a percentage of the total activity of five segments; the second the activity during each period of incubation as a percentage of the total activity of the segment in an experiment lasting 90 min; and the third the activity during each period of incubation as a percentage of the level of absorption in the course of incubation for 0-15 min.

The changes in the first parameter in the course of incubation and in the second between one segment and another did not exceed 5%. Consequently, substrate loading synchronizes the erythrocyte population and stabilizes the transport system. The difference between the dynamics of absorption over a period of about 1 h observed under these conditions can be explained by the reactive properties of the enterocytes [10] and variations in autoregulation of the transport systems in enterocyte populations whose energy metabolism properties vary at different points along the intestine.

The increase in absorption in the course of incubation (from the level after 0-15 min of incubation) was particularly marked in the second and fourth segments. The relative transport activity in the late periods of incubation was higher in these segments of the intestine than in neighboring segments. These results confirm the existence of a gradient of reactive properties in the small intestine [10], and the gradient itself coincides with that described earlier for membrane hydrolysis systems of certain carbohydrates and peptides [6]. This suggests that alternation of segments with unequal reactive properties along the length of the small intestine is a characteristic feature of its spatial organization as an integral organ [6].

The effect of removal of the substrate load twice (Table 2) differed along the intestine. The functional activity of the transport systems was considerably reduced in the first and second segments, and reduced still more in the fourth segment. Particularly sharp inhibition was observed in the third and fifth segments, where transport was virtually absent through both the luminal and the basal membrane between the 60th and 90th minutes of incubation. Since absorption at these times of incubation was relatively effective in the previous series of experiments, the phenomenon described above cannot be explained by fatigue of the transport systems. It likewise cannot be explained in the light of views on substrate regulation.

It follows from data in the literature [2, 4, 5, 12] that the high degree of heterogeneity and compartmentalization of the enterocytes must determine the existence of several periodic components for mucoserous transport. Under natural conditions summation of several different fluctuations takes place, with greater or lesser synchronization depending on variation in the degree of correlation [13]. External stimulation (graded in strength and duration) can change the character and phase of the fluctuations or even suppress them completely [15].

TABLE 2. Mucoserous Glucose Transport (in mg %) in Different Segments of Rat Small Intestine during Interrupted Substrate Loading

Incubation medium	Incubation period, min	Segment of small intestine				
		1st	2nd	3rd	4th	5th
Glucose	0—15	67	57	88	59	27
Glucose	15—30	156	156	172	138	57
Ringer's solution	30—45	95	108	123	98	33
Glucose	45—60	118	135	115	78	12
Ringer's solution	60—75	98	100	0	58	0
Glucose	75—90	130	108	0	39	0

However, whereas the system of the small intestine as a whole is characterized by fluctuations, the phase shifts along its length may be of real importance, for they determine differences in the response of different segments of the intestine to the same stimulus.

Between 8 and 16 h, the transport of starch glucose changed unequally along the intestine. Absorption fell sharply in the proximal segments of the intestine (by more than two-thirds) and the degree of decrease was significantly lower in the middle segments. In the distal segments of the intestine, on the other hand, between 8 and 12 h the transport of starch glucose was almost doubled. Investigation of the hourly dynamics (0-30, 30-60, and 60-90 min of incubation) under these conditions shows that against the background of fluctuations with a period of several hours, the functional properties of the enterocytes did not remain constant but varied unequally in the proximal and distal segments.

The results of these experiments confirm the existence of fluctuations with a period of several hours in the systems of membrane hydrolysis of carbohydrates [14]. The differences discovered in the responses of the various segments suggest the possible existence of fluctuations along the length of the intestine.

LITERATURE CITED

1. S. É. Shnol' (editor), Biological Clocks [in Russian], Moscow (1964).
2. B. Chance et al. (editors), Biological and Biochemical Oscillators, Academic Press, New York (1973).
3. Biological Rhythms in Mechanisms of Compensation of Disturbed Functions (Abstracts of Proceedings of an All-Union Symposium) [in Russian], Moscow (1973).
4. A. M. Zhabotinskii, Concentration Autooscillations [in Russian], Moscow (1974).
5. G. A. Kostenko, L. L. Litinskaya, A. M. Veksler, et al., Dokl. Akad. Nauk SSSR, 211, 714 (1973).
6. G. I. Loginov, M. I. Tadzhibaeva, and S. F. Kuz'mina, in: Collection of Scientific-Research Reports from the Central Scientific-Research Laboratories of Higher Medical Establishments in Uzbekistan [in Russian], Vol. 2, Samarkand (1974), p. 39.
7. G. I. Loginov and A. M. Ugolev, in: Proceedings of the Fourth Inter-Institute Scientific Conference of Physiologists and Morphologists of Pedagogic Institutes [in Russian], Yaroslavl' (1970), pp. 231-233.
8. E. E. Nurks, "Some characteristics of digestive and transport functions of the intestinal epithelium (on the example of carbohydrates) depending on different diets," Author's Abstract of Candidate's Dissertation, Riga (1972).
9. L. F. Smirnova and A. M. Ugolev, Dokl. Akad. Nauk SSSR, 215, 231 (1974).
10. A. M. Ugolev, Membrane Digestion. Polysubstrate Processes, Their Organization and Regulation [in Russian], Leningrad (1972), p. 154.
11. A. M. Ugolev, N. N. Iezuitova, et al., Investigation of the Digestive Apparatus in Man [in Russian], Leningrad (1969), pp. 192-196.
12. L. Kh. Éidus and L. L. Litinskaya, Dokl. Akad. Nauk SSSR, 222, 1456 (1975).
13. M. Hoopten, in: Identification and Systemic Parameter Estimation, Part 2 (Proceedings of the Third IFAC Symposium), Amsterdam (1973), pp. 599-606.
14. M. Saito, Biochim. Biophys. Acta, 286, 212 (1972).
15. A. Winfree, Physiol. Today, 28, 34 (1975).