indices to catecholamines has often been observed [6, 7]. The mean frequency of manifestation of the effects in individual subjects was 86 ± 2.4%. Naturally, by increasing the dose of AM, 100% of effects could be achieved, but this could have led to the development of side effects. In this investigation the AM were tolerated well in all cases.

Definite differences were found in the indices for adults and children. Responses of the cardiovascular system and oxygen consumption were more clearly manifested in children, changes in the fatty acids and lactate levels more clearly in adults. On average for the groups, however, no significant differences were found: The ratio for adults/children was 1.07 for all indices, 0.9 for α-effects, 1.02 for β_1-effects and 1.18 for β_2-effects. Moreover, there was highly significant and close correlation ($r_s = +0.85$ $P < 0.001$) between the mean shifts of the indices in adults and children.

LITERATURE CITED

1. V. P. Baluda, V. N. Malyarovskii, and I. A. Oivin, Laboratory Methods of Investigation of the Blood Clotting System [in Russian], Moscow (1962), pp. 47 and 143.
2. T. T. Berezov (ed.), Manual of Laboratory Exercises in Biochemistry [in Russian], Moscow (1976), p. 166.
3. I. V. Komissarov, Drug Regulation of Adrenergic Processes [in Russian], Kiev (1976).
4. B. A. Kudryashovand L. A. Lyapina, Fiziol. Zh. SSSR, No. 4, 550 (1972).
5. V. I. Kulinovskii, Probl. Endokrinol., NO. 6, 94 (1967).
6. V. I. Kulinskii, Probl. Endokrinol., No. 5, 67 (1970).
7. V. I. Kulinskii and L. I. Zolochevskaya, Probl. Endokrinol., No. 5, 61 (1974).
8. A. Arnold and G. P. McAuliff, J. Pharm. Pharmacol., 21, 624 (1969).
9. R. F. Furchgott, Ann. N. Y. Acad. Sci., 139, 953 (1967).
10. D. G. Gibson, Drugs, 7, 8 (1974).
11. B. A. Kudryashov (A. B. Kudrjashov), L. A. Lyapina (L. A. Ljapina), and T. N. Kovaleva, Folia Haematol. (Leipzig), 99, 76 (1973).
12. Kuo-Shu-Hul, T. K. Kamaka, and K. Lum Bert, J. Pharmacol. Exp. Ther., 202, 301 (1977).
13. A. M. Lands and A. Arnold, Nature, 214, 597 (1967)

RELATIONS BETWEEN BLOOD SUPPLY AND MOTOR-SECRETORY RESPONSES OF THE SMALL INTESTINE TO INTEROCEPTIVE STIMULATION BY ACETYLCHOLINE

V. A. Pastukhov

UDC 612.33-06:612.822.2

KEY WORDS: small intestine; blood supply; motor activity; secretion; acetylcholine.

Much attention has recently been paid to the study of central and peripheral cholinergic mechanisms in the regulation of activity of the visceral systems under normal conditions and during emotional stress [1, 2, 6, 9, 11]. The methods used for this purpose include both determination of the endogenous concentrations of acetylcholine (ACh) and of the enzymes cholinacetylase and cholinesterase, connected with its metabolism, in the tissues and bloodstream, and the study of the effect of exogenous ACh on functions of the body. Investigation of the principles and mechanisms of action of ACh on the functions of the digestive organs and the character of their interaction is an urgent task.

The object of this investigation was to study relations between blood supply and specific functions (motor and secretory) of the small intestine during irrigation of an isolated segment of the intestine with ACh solution.

Laboratory of Cortico-Visceral Physiology, I. P. Pavlov Institute of Physiology, Academy of Sciences of the USSR, Leningrad.

(Presented by Academician of the Academy of Medical Sciences of the USSR V. N. Chernigovskii.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 90, No. 10, pp. 397-400, October, 1980. Original article submitted April 30, 1979.

0007-4888/80/9010-1331$07.50

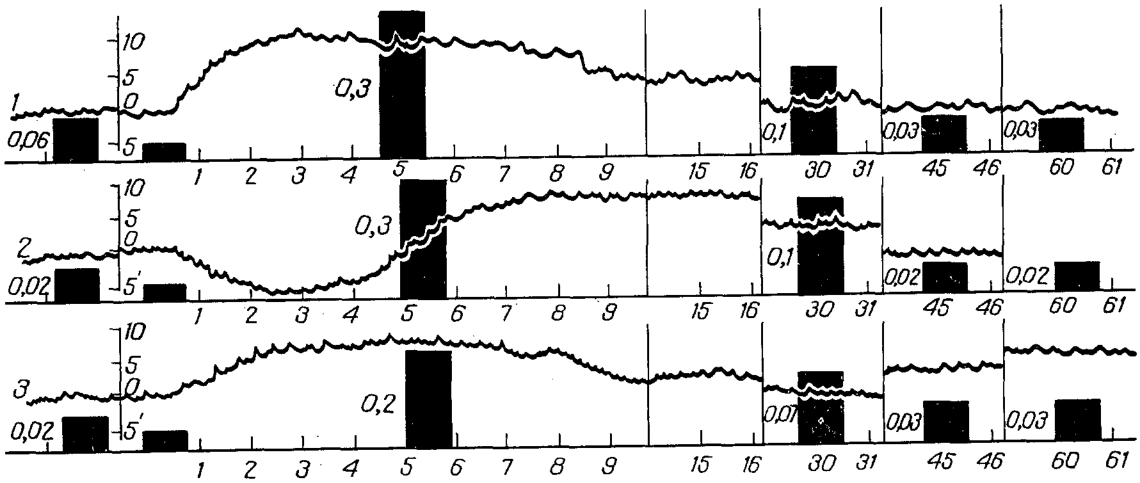

Fig. 1. Variance of mutual relations of VVBF in superior mesenteric artery (1, 2, 3) and intensity of secretion (in ml/min) of isolated segment of small intestine (columns with numbers on left) before and after irrigation (bold lines along abscissa) with ACh solution ($5 \cdot 10^{-5}$ g/ml), 20 ml, in the course of 30-35 sec. Abscissa, time (in min); ordinate, VVBF (in conventional units). Vertical lines on right hand side of figure indicate gaps in record of VVBF.

TABLE 1. Latent Periods (in sec) of Changes in VVBF and Motor Responses of Small Intestine in Dogs After Irrigation with ACh Solution (M ± m)

Animal No.	VVBF	Motor activity	P
1	9±4	48±12	<0,01
2	21±7	57±18	<0,01
3	28±11	48±14	<0,01
4	14±6	53±13	<0,05
5	11±5	49±19	<0,01

EXPERIMENTAL METHOD

Chronic experiments were carried out on five dogs weighing 18-23 kg. Thiry—Vella fistulas were formed in the small intestine of the animals, for which purpose the proximal segment of jejunum 25-30 cm long was used. Simultaneously thermoelectric probes for recording the blood supply or volume velocity of the blood flow (VVBF) were implanted on the superior mesenteric artery or its large branch supplying blood to the segment of intestine forming the fistula. VVBF was recorded on a mirror galvanometer. The intestinal juice was collected from both openings of the fistula. Motor activity was recorded by a balloon-manometric method. A balloon of special design (fixed on two sides to a perforated tube), 20 cm^3 in volume (pressure 25-30 mm Hg), was introduced through the proximal opening of the fistula to a depth of 8 cm. The balloon did not prevent the passage of irrigating solution, the volume of which was measured after irrigation, along the fistula. Full details of the technique were described previously [5].

Experiments were carried out during the morning, 18-20 h after the last meal. For 30-45 min the initial level of VVBF, motor activity, and secretion of the intestine was recorded. Next, 20 ml of ACh solution in a concentration of $5 \cdot 10^{-5}$ g/ml was injected through the proximal opening of the fistula in the course of 30-35 sec. Recording of VVBF and the motor-secretory response of the small intestine continued until they had returned to their initial levels. In control experiments these functions were recorded for 1-1.5 h during mechanical stimulation of the isolated segment of intestine (the balloon and tube used for recording motor activity) and to injection of physiological saline (20 ml in the course of 30 sec). The temperature of all solutions was 37°C. Statistical analysis of the results, using the method of analysis of variance, was carried out by means of Student's tables [7].

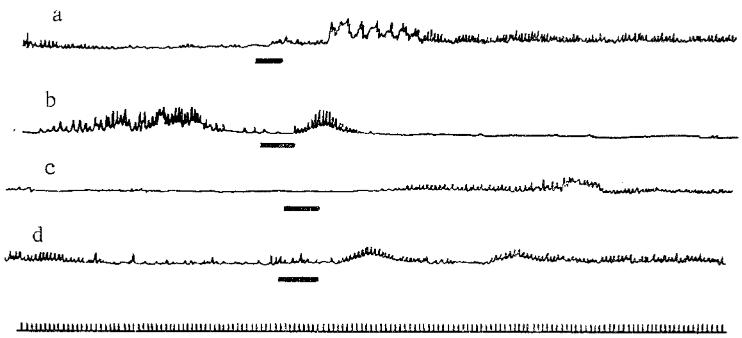

Fig. 2. Motor activity of isolated segment of small intestine before (d) and after irrigation with solutions of ACh (a), procaine (b), and with ACh solution 2-4 min after irrigation with procaine solution (c). Bold lines are stimulation markers. Time marker 5 sec.

TABLE 2. Effect of Irrigation of Isolated Segment of Small Intestine with ACh Solution on Its Secretory Activity in Dogs (M ± m)

Animal No.	Volume of juice in 30 min, ml		P
	in response to mechanical stimulation	after irrigation with ACh solution	
1	2,1±0,7	12,0±3,4	<0,001
2	1,0±0,4	9,5±3,5	<0,001
3	3,7±0,9	16,2±4,8	<0,001
4	2,5±1,0	13,3±2,7	<0,001
5	2,5±1,3	14,0±5,1	<0,001

EXPERIMENTAL RESULTS

Irrigation of the isolated loop of small intestine with ACh solution caused changes in VVBF in the mesenteric arteries and in the motor-secretory responses of this segment of intestine. The changes in VVBF occurred sooner than those in motor activity and secretion (Table 1).

Three types of changes in VVBF were distinguished (Fig. 1); 1) In 47% of cases, after the latent periods shwon in Table 1, an increase in VVBF was observed. Its highest level occurred during the first 7-9 min, and it returned to its initial level after 30-35 min; 2) in 18% of experiments VVBF fell initially, after 3-5 min it regained its initial level, and thereafter it increased for 30 min or more; 3) in 24% of cases the initial changes were the same as in the first variant. After 40-45 min a second increase in VVBF was observed for 10-15 min.

The motor activity of the intestine after irrigation with ACh solution became peristaltic in character, with well-marked segmentation contractions later (Fig. 2a), and it remained increased for 15-20 min.

The secretory activity of the isolated segment of intestine after irrigation with ACh solution was sharply increased in all experiments for 15-20 min also (Table 2, Fig. 1). The greatest secretory activity was observed in the first 8-12 min. In cases when there was an initial fall in VVBF (for 1-2 min) no weakening of secretory activity was observed at that time. Evidently such a very small decrease in the blood supply to the small intestine had no significant effect on its secretory activity. When the increase in blood supply was repeated, secretion was not increased.

Dissociation between blood supply and secretory activity of the small intestine for a few minutes was observed previously in the course of their investigation in experiments using a food stimulus (600 ml of milk) [5].

In response to mechanical stimulation changes in VVBF were very small, the intestinal contractions were peristaltic and segmentational in character, and the intensity of secretion was 0.02-0.06 ml/min. Irrigation of the segment of intestine with 20 ml phhsiological saline for 30 sec caused no significant changes in the functions of the small intestine studied. Preliminary irrigation of the isolated segment of intestine with 0.5% procaine solution (the volume of solution, its temperature, and the duration of irrigation were the same as for irrigation with ACh solution) either completely prevented the acetylcholine effect on the blood supply and motor and secretory response of the intestine or reduced the observed effects significantly (Fig. 2, b-d). This suggests that the action of ACh on these intestinal functions is reflex in character, in agreement with the results of numerous investigations which demonstrated reflex influences from different zones of the gastrointestinal tract not only on blood vessels of the small intestine, but also on the heart, systemic arterial pressure, and peripheral vascular tone [4, 5, 8]. Cholinergic agents evidently act through the ganglia of the intestinal nervous system [3, 12].

The direct effect of ACh on smooth-muscle elements of arteries and arterioles, and also on capillary endothelial cells, also must be ruled out in these experiments. The last effect mentioned, on capillary endothelial cells, was demonstrated in experiments with intravital microscopy of capillaries in many organs [5].

Exchange processes between muscular, secretory, and other cells of the small intestine, as in other organs, and the vascular system take place chiefly at the capillary level. Morphological investigations have shown that capillaries have no efferent vasomotor innervation or, more exactly, no such innervation has yet been found. It is therefore only on vessels in whose walls smooth muscles are present (arteries, arterioles, venules, and veins) that a reflex effect of ACh can be confidently accepted. Dilatation of small arteries and arterioles in response to stimulation by ACh causes an inflow of blood and an increase in the intracapillary pressure. Dilatation of the capillaries of the organ takes place as a result of this, i.e., indirectly. It has been shown by intravital microscopy that this dilatation takes place mainly through flattening of the endothelial cells. Conversely, the blood flow in the muscular coat and mucous membrane of the small intestine may be reduced by constriction of arterioles and of venules connected with them [10].

Irrigation of an isolated segment of small intestine with ACh solution against the background of mechanical stimulation thus causes changes initially in the blood supply and later in the motor and secretory responses of the small intestine. The primary changes in VVBF may be both positive and negative (temporarily) and they do not always coincide with changes in the specific functions of this organ. In most experiments the above-mentioned parameters returned to their initial level simultaneously. However, in some experiments a second increase in blood supply to the intestine was observed at a time when its motor and secretory functions had returned to the background level. It can be tentatively suggested that the initial changes in blood supply took place on account of active dilatation of the small arteries and arterioles of the intestine. Later, changes due to general hemodynamic shifts (cardiac output, systemic blood pressure, etc.) may have been superposed on these initial changes.

LITERATURE CITED

1. M. G. Airapet'yants, Zh. Vyssh. Nerv. Deyat., No. 2, 379 (1977).
2. M. G. Airapet'yants and K. Hecht, in: Physiology and Pathology of Cortico-Visceral Interrelations [in Russian], Leningrad (1978), pp. 26-35.
3. Yu. P. Kachalov, A. D. Nozdrachev, and A.G. Pogorelov, Fiziol. Zh. SSSR, No. 1, 1530 (1978).
4. V. A. Lebedev, Mechanisms of Chemoreception [in Russian], Moscow—Leningrad (1965).
5. V. A. Pastukhov, "Blood supply of certain organs in connection with their activity and the general hemodynamics under normal conditions and in functional pathology of higher levels of the brain," Doctoral Dissertation, Leningrad (1970).
6. V. A. Pastukhov, in: Abstracts of Proceedings of the 5th Conference on Tissue—Blood Barriers [in Russian], Moscow (1978), pp. 332-333.
7. P. F. Rokitskii, Biological Statistics [in Russian], Minsk (1973).
8. V. N. Chernigovskii, Interoreceptors [in Russian], Moscow (1960).

9. J.W. Bean and M. M. Sidky, Am. J. Physiol., 194, 512 (1958).
10. H. G. Bohlen, H. Henrich, K. W. Gore, et al., Am. J. Physiol., 235, H40 (1978).
11. A. Karlin, Life Sci., 14, 1385 (1974).
12. D. M. Jacobowitz, J. Invest. Dermatol., 69, 106 (1977).