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STUDY OF DIFFERENT TYPES OF ADRENERGIC SYSTEMS IN MAN

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KEY WORDS: adrenergic systems; α-, β_1-, and β_2-adrenoreceptors.

Investigations of sensitivity to hormonal and cyclic nucleotide control are no less important than determination of concentrations of hormones and cyclic nucleotides. This approach is particularly important when studying the biochemistry and physiology of catecholamines under normal and pathological conditions. However, an obstacle to its use is the lack of methods of evaluating the state of adrenergic systems in man.

A change in the response to catecholamines is not necessarily the result of changes in adrenoreactivity. In fact, any response to catecholamines involves the sensory component — the adrenergic system (the adrenoreceptors themselves and subsequent elements) and the effector component, such as the contractile system of blood vessels. Clearly, changes may take place not only in the sensory, but also in the effector component, especially in disease.

Before reliable conclusions can be drawn on the location of changes in the first component, it is essential to study at least two parameters with respect to which the first component is identical but the second differs. If, under these circumstances, changes in the response to adrenomimetics (AM) are identical, it can be concluded that the disturbances are in the adrenergic system. The use of parameters which differ only in the first component, such as the response of the blood pressure to isoprenaline and histamine (or acetylcholine), is noteworthy.

Another feature which distinguishes our approach is that it takes into account the presence of different types of adrenoreceptors, namely α and β, and also the presence of subtypes β_1 and β_2 among the latter [3, 9, 10, 13]. The first type was stimulated by the relatively specific α-AM phenylephrine [9], β_1- and β_2-receptors were stimulated by the specific β-AM isoprenaline [3, 10, 13].

EXPERIMENTAL METHOD

Tests were carried out on 13 healthy adults aged 19-22 years and 22 healthy children aged 10-14 years. Phenylephrine was injected subcutaneously in a dose of 10 mg into the adults and 9 mg into the children, and isoprenaline was given in doses of 7.5 and 6.2 mg (sublingual-

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TABLE 1. Changes in Physiological and Biochemical Parameters in Response to Administration of Adrenomimetics

Subjects	Statistical index	Effect of phenylephrine			Effects of isoprenaline							
		α			β₁			β₂				
		minimal arterial pressure, mm Hg	blood clotting time, sec	fibrinolysis time, min	heart rate, beats/min	oxygen consumption, ml/min	nonesterified fatty acids, μeq/ml	minimal arterial pressure, mm Hg	vital capacity, liters	forced vital capacity, liters	lactate, mg%	glucose mg%
Adults	$M \pm m$, абс.	7,5±2,1	—68±37	—60±18	8,5±0,9	72±18	0,26±0,022	—7,9±1,3	0,23±0,050	0,40±0,030	10,1±2,1	20±2,1
	P	<0,05	<0,1	<0,05	<0,001	<0,05	<0,001	<0,001	<0,05	<0,001	<0,001	<0,001
	$M \pm m$, %	10±2,7	—18±9,5	—21±6,2	12±1,2	26±6,4	50±4,0	—10±1,7	5,8±1,2	13±1,0	102±20	27±2,8
Children	$M \pm m$, абс.	12,1±2,0	—92±18	—33±12	17,3±3,6	79,9±9,9	0,16±0,031	—11,8±1,2	0,25±0,033	0,12±0,033	4,1±0,9	14,3±4,2
	P	<0,001	<0,001	<0,05	<0,05	<0,001	<0,001	<0,001	<0,05	<0,05	<0,001	<0,05
	$M \pm m$, %	21±3,4	—25±4,8	—14±5,1	23±4,9	34±4,2	28±6,1	—21±2,1	4,9±1,3	13±1,2	50±1,1	20±6,0

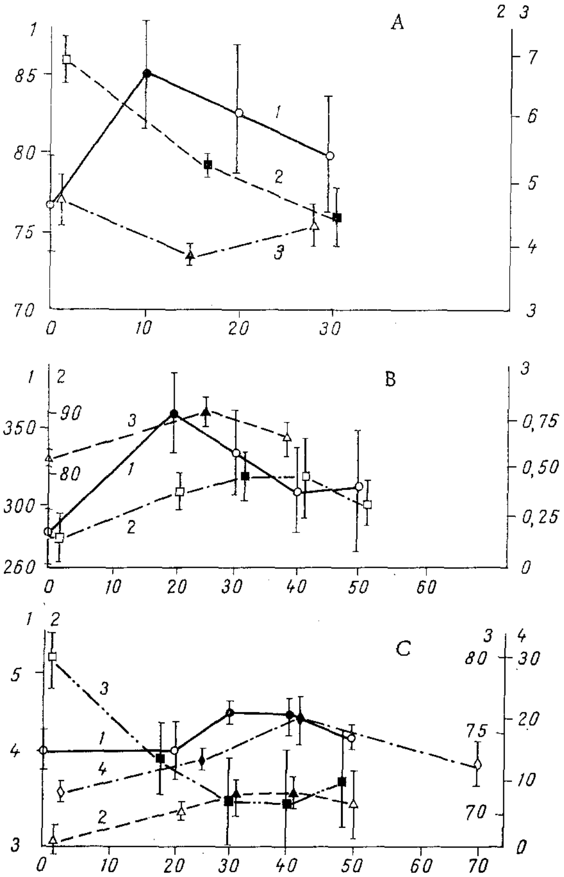

Fig. 1. Dynamics of response of adults to adrenomimetics. A) Response to phenylephrine (α-effects); B, C) responses to isoprenaline: B) β_1-effects, C) β_2-effects. Abscissa, time (in min) after injection of adrenomimetic. Legend and scales for ordinates: A: 1) minimal arterial pressure (in mm Hg), 2) blood clotting time (in min), 3) fibrinolysis time (in h); B: 1) oxygen consumption (in ml/min), 2) pulse rate (beats/min), 3) nonesterified fatty acids (in mM): C: 1) vital capacity (in liters), 2) forced vital capacity after 1 sec (in liters), 3) minimal arterial pressure (in mm Hg), 4) lactate (in mM). Filled symbols indicate significant change in the parameter.

ly, until complete absorption), according to age. The oxygen consumption and vital capacity of the lungs were determined on the Meta-40 spirograph, the blood glucose by the o-toluidine method, blood lactate by the method of Barker and Summerson, serum fatty acids by a colorimetric method [2], and the clotting and fibrinolysis time as in [1].

EXPERIMENTAL RESULTS

Altogether three α-effects of phenylephrine were studied: the minimal pressure, clotting time, and fibrinolysis time of the blood. The fact that the last two effects belong to the α-group [4, 11] was confirmed: phenylephrine led to a fall in these parameters (Table 1), but isoprenaline did not have this effect ($P > 0.2$). Three β_1- and four β_2-effects of isoprenaline also were studied [3, 8, 10, 12, 13]. The type of receptor responsible for catecholamine-induced hyperglycemia is disputed [3, 5, 12].

Investigation of the dynamics of the responses revealed optimal times (Fig. 1). The response of the minimal pressure to phenylephrine was maximal at the 10th minute, that of fibrinolysis and blood clotting at the 15th minute; the responses to isoprenaline developed more slowly: oxygen consumption, blood sugar, and fatty acids after 20-25 min, and the remaining parameters after 30-40 min.

The smallest response to AM was observed in effects connected with muscular contraction (hypotension, tachycardia, parameters reflecting the state of the bronchial muscles), followed by blood clotting and fibrinolysis; metabolic indices showed the most marked effects: oxygen consumption, fatty acids, lactate. Greater sensitivity of biochemical than of physiological 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.

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

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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.

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