THE EFFECT OF SMALL DOSES OF ADRENALIN ON THE BIOLOGICAL ACTIVITY OF THE BLOOD UNDER NORMAL CONDITIONS AND CERTAIN MORBID CONDITIONS OF THE DIENCEPHALIC AREA

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Certain functional tests (cold and hot) are being used in our laboratory to determine the mechanisms of homeostatic reactions. Our previously published communications have shown [2, 6, 7, 10, 12] that certain functional loads cause specific reactions in both healthy subjects and in patients with certain forms of diencephalic pathology. Certain conclusions as to the condition of the autonomic nervous system and its various sections under normal conditions and under conditions of neural pathology can be drawn from the correlation of the biologically active substances of the blood (sympathins and parasympathins). We continued our study of the biological activity of the blood, using an adrenalin test developed in our laboratory.

The main purpose of this investigation was to study the biological activity of the blood (sympathomimetic and parasympathomimetic substances) and to determine true and pseudo-cholinesterase activity.

EXPERIMENTAL

A frog's heart, isolated by Ya. A. Rosin's method [11], was used to determine the level of sympathins and parasympathins in plasma; the level of acetylcholine (AC) was determined in whole blood by Z. V. Belyaeva's modification (1953) of Fyuner's method. Pseudo-cholinesterase activity (PCE) was determined by the method of Zubkova and T. V. Pravdich-Neminskaya [8], and true cholinesterase activity (TCE) was determined by our laboratory's modification of E. A. Matlina's method: after the erythrocytes have been washed out, the activity of the enzyme in the destroyed erythrocytes is titrometrically determined in the presence of a substrate (acetylcholine) and an indicator (phenol red). Blood was taken from an ulnar vein of healthy and sick subjects in the morning, on an empty stomach, before adrenalin was administered and then 10 or 20 minutes after the administration of 0.3-0.5 ml of a 0.1% adrenalin solution. The data obtained were statistically processed.

RESULTS

First Series. Effect of Adrenalin on the Sympathetic Activity and Acetylcholine Content of the Blood. The sympathetic and parasympathetic activity of 19 healthy and 20 sick subjects was investigated before and after the adrenalin test, with the TCE taken into account. Patients with neuroendocrine, neurotrophic and vasculo-autonomic disorders of the diencephalic area (classified according to N. I. Grashchenkov [5]) were divided into groups depending on the character of the clinical autonomic reactions*. The results of the investigation showed that, in both healthy persons and patients with different diencephalic disorders, the administration of adrenalin could cause either no reaction at all or a partial reaction characterized by change in one or two objective indices (arterial pressure, pulse or respiration), sometimes combined with mild sensations of tachycardia, or a pronounced reaction typical of sympathoadrenal or vagoinsular crisis, with change of pressure, pulse and respiration and the development of unpleasant subjective sensations such as tremor, chill and feelings of inner tension [9].

* The clinical examination of the patients was carried out by A. D. Solov'eva.

In seven out of the ten healthy persons who showed no clinical reaction to the administration of adrenalin, the sympathetic and parasympathetic activities of the blood either increased or decreased simultaneously. In three cases, only the parasympathetic activity increased. TCE was reduced in all ten cases, and the original PCE level was maintained in all the subjects.

In the group of persons who showed a partial or pronounced reaction (11 people), nine persons manifested a sympathoadrenal reaction, two, a vagoinsular reaction. The correlation of the biologically active substances depended on the clinical character of the reaction: in five out of the nine people with a sympathetic reaction, the sympathetic activity of the blood increased, and the parasympathetic decreased; in the two persons with a vagoinsular reaction, the AC level in the blood increased, and the sympathetic activity decreased. The clinical reaction and the biological activity of the blood did not correspond in four of the subjects. Analysis of these cases showed, however, that the reaction either had not yet occurred or was already over at the time the blood was taken. The TCE was depressed in all 11 cases.

Six of the 20 patients with neuroendocrine, neurotropic and vasculoautonomic disorders of the diencephalic area whom we examined showed no reaction to the administration of adrenalin. In four of these patients, the sympathetic and parasympathetic activities changed similarly and therefore compensated each other. In patient P., in whom the level of sympathins increased, and in patient T., in whom the AC level increased, homeostatic correlations were maintained by a decrease in the level of adrenalin-like substances (S. V. Ugoleva's investigation [13]). The TCE decreased in three cases and did not change in the three others. The PCE did not change.

There were 14 persons in the group of patients who manifested a clinical reaction (partial or pronounced). The reaction was sympathoadrenal in six of these patients; there was an increase in the level of sympathins the 10th minute, attended by either a decrease in the AC level or an increase in TCE. The clinical indices did not tally with the changes in the biological activity of the blood in the other eight patients. This was probably because the reaction to the administration of adrenalin took place either before or after the time that the blood was taken, due to the pathologic lability or inertia of the nerve processes which is often observed with neuroendocrine disorders of the diencephalic area.

In a few cases, we observed the reaction to have different phases, one succeeding the other at specific intervals. Ten minutes after the adrenalin was administered to patient I., for example, we observed a predominance of parasympathetic activity (an increase in the AC level attended by reduced TCE and a decrease in the level of sympathins) until the 20th minute, when a sympathoadrenal reaction developed (Fig. 1).

The TCE decreased in nine cases, increased in two and did not change in the other three.

Therefore, our data show that ten minutes after the administration of adrenalin, a simultaneous increase in the sympathetic and parasympathetic activities of the blood was observed in the majority of the patients with diencephalic disorders, i.e., a reaction similar to the normal reaction. In a number of cases, however, the increase in the level of parasympathetic substances was not sufficient to compensate the increase in sympathetic activity, i.e., a pronounced sympathoadrenal reaction developed. As comparison of the clinical data with the changes in the biological activity of the blood showed, the administration of adrenalin often caused alternating sympathetic and parasympathetic reactions in healthy people. One must assume, therefore, that the stable, one-sided reactions which could be observed in the patients develop as a result of the pathologic process in the diencephalic region.

Second Series. Effect of Adrenalin on Pseudo- and True Cholinesterase Activity. We determined the activity of pseudo- and true cholinesterase in 18 healthy persons aged 18-28 (7 men and 11 women). In ten cases, the investigation was performed 10 minutes after the administration of 0.3 ml adrenalin, in five cases, it was performed 20 minutes after the administration of the same dose os adrenalin and in three cases, 20 minutes after the injection of 0.5 ml adrenalin. The original PCE varied from 0.6 to 0.8 (in mg of AC, hydrolyzed for 30 minutes). The PCE usually showed no change after the adrenalin injection (although changes within the method's margin of error were observed in a few cases).

In healthy people, the arithmetic mean level of the original TCE constituted 4.34, with a mean deviation of 1.35, i.e.,(the original level normally fluctuated between 3 and 7). The TCE decreased in all 18 subjects after the adrenalin injection. Statistical analysis of the data obtained from the group composed of the most similar subjects (after the injection of 0.3 ml adrenalin) allows the assumption that the decrease we observed in the TCE of healthy persons is the normal reaction (coefficient of significance $-\underline{t} = 5$).

In the same 18 persons, the AC content of the blood increased after the adrenalin injection in 12 cases, decreased in five cases and did not change in one case; on the average, it increased 40% of the original level. Comparison of the changes in the TCE with those in the AC content (Fig. 2, a) shows that, in healthy persons, the consistent depression of TCE caused by the administration of small doses of adrenalin is attended by either a decrease or an increase in the AC level. Our data indicating the different physiological roles of pseudo– and true cholinesterase are confirmed by the literature data [4, 14].

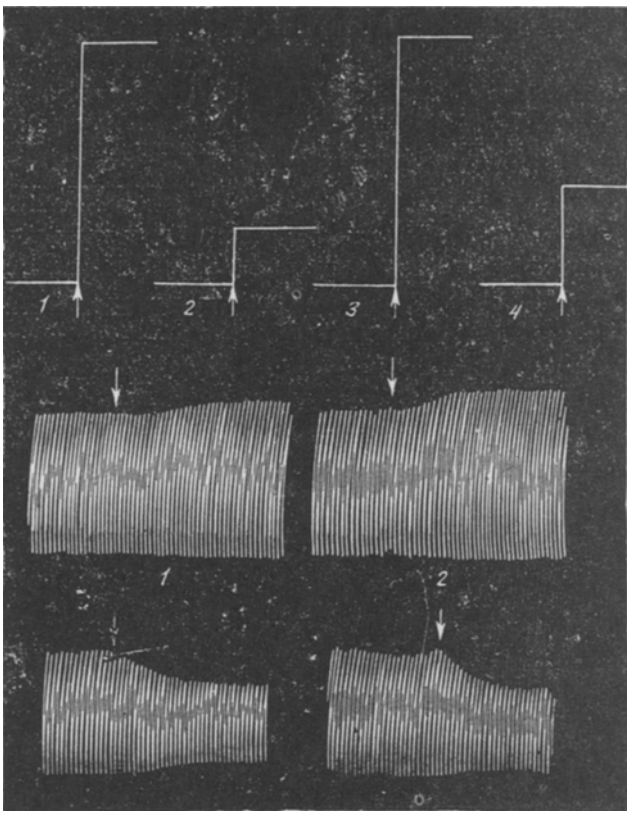

Fig. 1. Biological activity of patient I's blood before and 10 min after adrenalin injection. a) AC level in blood; 1, 3) effect of standard AC solution on leech's muscle; 2) AC level before test; 4) AC level after test; b) effect on frog's isolated heart of serum obtained from patient before test; c) effect on frog's isolated heart of serum obtained from patient after test (b and c: 1 – dilution 1:1500, 2 – dilution 1:15; – beginning of experimental solution's effect).

Twenty-five patients with different forms of diencephalic pathology were examined; two tests were done on eight of these patients (a total of 33 examinations). The administration of adrenalin caused no change in the PCE in any of the 33 cases, but considerable changes were observed in the TCE: it decreased in 19 cases, increased in 5 and did not change in 9 cases.

The literature indicates that the changes in TCE depend on its original level [1, 3]; in our experiments, therefore, in each separate case and before all 33 examinations, we determined the original TCE level. We could not find any relationship between the initial TCE level and the change following the administration of adrenalin. In 11 out of the 14 cases in which the adrenalin did not depress TCE, the original TCE level was within the normal range.

In the 19 cases of diencephalic pathology in which the adrenalin injection caused depression of TCE, the depression was not consistent in nature: the coefficent of significance was $t = 2.2 < 3$, while in the control group, t equalled $5 > 3$ (see Table).

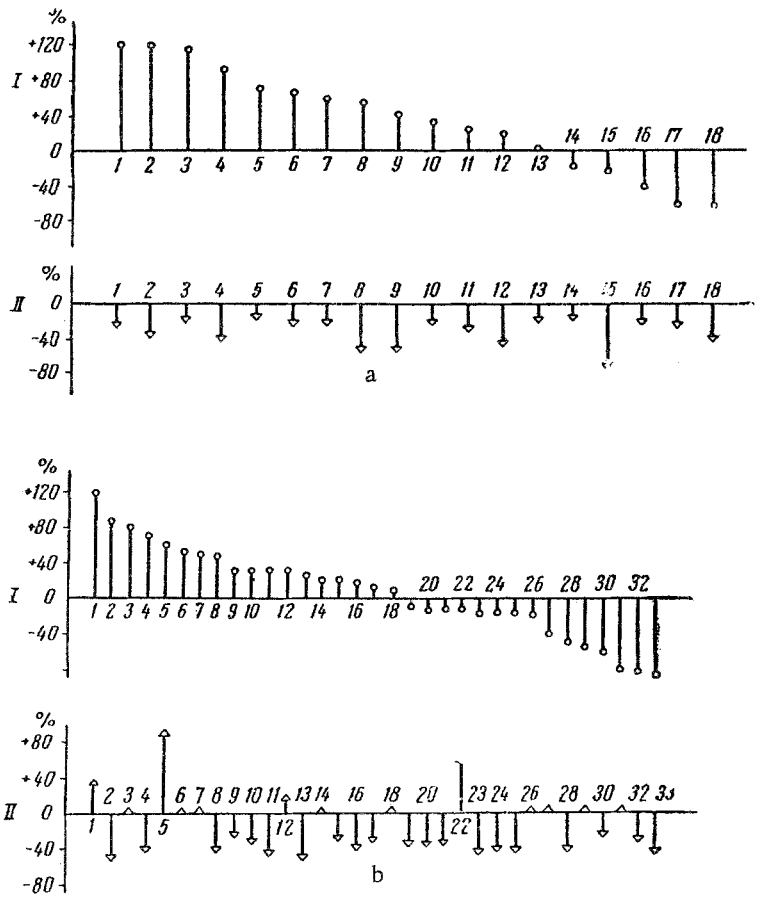

Fig. 2. Change in the AC level (I) and TCE (II) after adrenalin injection (in % of original levels). a) In healthy persons (18 cases); b) in patients with diencephalic disorders (33 cases).

Average Original Level of TCE and TCE Depression following Adrenalin Administration to Healthy Persons and Patients with Diencephalic Disorders

Group of subjects	N	M (in mg)	m	ΔM (in %)	δm (in %)	t
Healthy	10	4.84	± 0.45	27	± 5.4	5
Patients	33	4.9	± 0.28	11	± 5	2.2

Note: N – number of subjects; M – arithmetic mean; m – average error of arithmetic mean; Δ – average TCE depression; t – coefficient of significance. To facilitate comparison of the results obtained under normal and pathologic conditions, the table gives the statistical data obtained from two groups (healthy persons and patients) investigated under identical conditions – in both groups, blood was taken 10 minutes after the injection of 0.3 ml adrenalin.

In nine cases, the AC level and TCE increased or decreased simultaneously. In nine cases, the AC level increased while the TCE decreased, and in one case, the opposite was observed, i.e., opposite changes in the two indices were observed in ten cases. In the other 14 cases, either the AC level or the TCE changed, while the other factor did not (see Fig. 2, b).

Therefore, when the correlation between the AC content and the TCE in healthy people is compared with that in patients with different diencephalic disorders, it is evident that similar and opposite changes are observed equally often in both groups. Consequently, the TCE is only one of the factors regulating the AC content, another factor being the increase in the store of free AC by means of its synthesis and liberation from the protein complex. Change in the TCE, however, is important to parasympathetic activity because increased or decreased TCE can enhance or depress the potential activity of the parasympathetic system even when there is no change in the AC level.

The results we obtained led us to conclude that the administration of adrenalin in small doses enhanced parasympathetic activity in a majority of healthy persons and in a number of the patients with disorders of the diencephalic region. Stable reactions typical of sympathoadrenal crisis developed in some of the patients. Small doses of adrenalin do not affect PCE.

Small doses of adrenalin depressed TCE in all the healthy subjects and in some of the patients with diencephalic disorders. The TCE is not depressed by the administration of adrenalin in some forms of diencephalic pathology; a distorted reaction (increased TCE) is observed in some cases.

SUMMARY

To investigate the limits of homeostasis (adaptive reactions) in healthy individuals and in patients suffering from certain forms of diencephalic affection, the biological activity of the blood (sympathin and parasympathin content and the activity of the false and true cholinesterase) was studied prior to and after the administration of adrenalin in low doses. There was a rise of the blood sympathetic activity in conjunction with a vegetative reaction of the sympathoadrenal type or an increase of the parasympathetic activity in association with the vagoinsular type of reaction. During simultaneous increase or reduction of the sympathetic and parasympathetic activity the clinical vegetative reaction was usually absent. After adrenalin administration the activity of pseudo-cholinesterase remained unchanged. The activity of true cholinesterase decreased in all of the healthy individuals examined but rose in some patients with diencephalic affection.

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