DYNAMICS OF EVOKED BRAIN POTENTIALS AND OF BIOLOGICALLY ACTIVE SUBSTANCES IN THE BLOOD OF CHILDREN EXPOSED TO COLD

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A state of stress [23, 24] in a healthy child is accompanied by changes in the body functions. If powerful factors act or if the organism is in an enfeebled state, stressors evoke pathological changes, whereas in ordinary circumstances physiological changes develop, leading to the creation of a "state of nonspecifically increased resistance" [10, 11]. This increased resistance to the action of stressors is of very great prophylactic importance in maintaining the child's health. According to Selye, this resistance is nonspecifically increased during the resistant stage of stress, in relation not only to the acting stimulus, but also to other factors. Such phenomena have been observed in hypoxia [2, 12], during the action of dibazol (2-benzylbenzimidazole HCl), radix ginsengi, vitamin B_{12} [5, 10, 11], and after muscular exercise [6-8]. However, the effect of brief exposure to a stressor agent such as a cold stimulus proved especially interesting. This has long been used for the prevention of common colds in children and for "hardening" them. In the modern view, this stimulus causes a reflex stimulation of the activity of the adrenal medulla, as a result of which the concentration of adrenalin circulating in the blood stream is increased. The increased adrenalin concentration activates the reticular formation, both through the chemoreceptors of the reflexogenic zones of the aorta and carotid arteries and also directly. All the stimuli are relayed to the reticular formation and hypothalamus, and from thence to the pituitary, also via collaterals of the afferent tracts [1, 17-22]. This accounts for the role of the reticular formation of the brain stem as an important structural component of the adaptation reaction during "hardening."

The reflex secretion of adrenalin and acetylcholine is of great importance in the mechanism of activation of the reticular formation by afferent stimulation from the periphery and by corticofugal impulses from the cerebral cortex. Under the influence of cold stimulation of the skin receptors of the hands, the concentration of adrenalin itself in the blood of healthy persons rises while the acetylcholine concentration falls; clinically this is manifested by an increase in the tone of the parasympathetic division of the nervous system [4, 9]. The results obtained indicated that the cold test could be used to determine the limits of the homeostatic reactions of the adult person.

After the brief action of a cold stimulus on the receptors of the trigeminal nerve of children fatigued as a result of study, their fatigue was observed to disappear, their normal higher nervous activity was restored, and their depressed autonomic components (psychogalvanic, vascular, respiratory) of their conditioned reactions were strengthened [15].

The object of the present investigation was to study the dynamics of the electrical reactivity of the brain and of the biologically active substances of the blood in clinically healthy children aged 13-15 years, in response to the reflex action of a cold agent on the skin receptors for a period of 1 min.

EXPERIMENTAL METHOD

The method of evoked brain potentials was used, and the coefficient of synchronization and combined energy

Content of Catecholamines and Acetylcholine in Blood of Healthy Children and Adults

Biologically active substances	Children		Adults	
	variations in level (in μ g%)	arithmetical mean	variations in level (in μ g%)	arithmetical mean
Adrenalin-like substances	2.20-18	8.50	4-12	7.50
DALS	0-4.40	0.94	0.2-3.50	0.44
K_{sp}	0.65-1.30	0.97	0.2-1.36	0.98
Acetylcholine	0.25-1.20	0.90	0.3-0.50	0.45

of the potentials were determined by the method of Lowell and Dossett [13]. The concentration of adrenalin-like substances and of their reversibly oxidized dehydro forms (DALS) was determined by Shaw's method as modified by A. M. Utevskii and M. L. But [16]. The relative content of unoxidized adrenalin was assessed from the coefficient of specificity (K_{sp}). When $K_{sp} \leq 1$ no free adrenalin was present in the blood and unidentified adrenalin-like substances (chromogens) appeared; when $2 > K_{sp} > 1$, both adrenalin and chromogens were present in the blood, while if $K_{sp} \geq 2$ only free adrenalin was present. The blood acetylcholine level was determined by Fühner's biological method, as modified by Belyaeva, using the dorsal muscle of a leech [3].

Altogether 10 children were investigated. The spectrum of the evoked brain potentials of the child was investigated in the morning before breakfast. The pulse rate and arterial pressure were then taken and 7 ml of blood was withdrawn from a vein. A cold agent (10°) was then applied to the skin receptors for 1 min, and the pulse rate and arterial pressure were again determined, blood was again taken from the vein, and the spectrum of the evoked potentials was investigated.

EXPERIMENTAL RESULTS

The main tendency of the dynamics of the evoked potentials of the electroencephalogram (EEG) after exposure to cold was a slight fall of the coefficient of synchronization (K_{syn}) and a more marked fall in their energy in different parts of the spectrum (ΣA_{syn}). The opposite tendency was observed during mental fatigue [13] and after blocking the adrenergic and cholinergic structures of the synapses of the reticular formation of the brain stem in children [15], when both parameters of the evoked potentials showed a tendency to increase. In 6 of the 10 children studied a tendency for the values of K_{syn} and ΣA_{syn} to rise was observed, in 2 children these indices remained essentially unchanged, and in 2 children an actual increase in K_{syn} and ΣA_{syn} was observed.

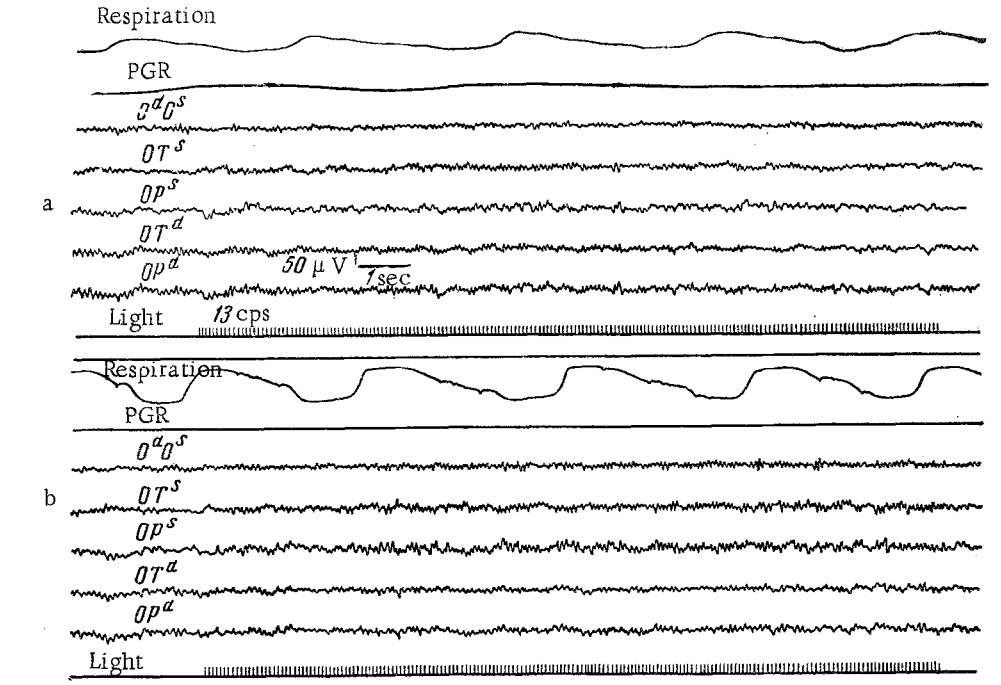
The following remarks must be made concerning the accompanying table. In 3 of 10 children and in half the adults no DALS were present in the blood. The value of K_{sp} suggested that the fraction of adrenalin-like substances in the blood consisted largely of chromogens. Comparison of the original values of the blood concentrations of adrenalin-like substances and of DALS, and of K_{sp}, shown in the table indicates that there was no great difference between these indices in children and adults. At the same time, the greater stability of the first 2 indices in children than in adults is worth noting.

Analysis of the blood acetylcholine concentration before cold stimulation (initial background) showed that this index was much higher in children than in adults (0.9 μ g% compared with 0.3-0.5 μ g%). After exposure to the cold stimulus the concentration of adrenalin-like substances in the blood varied from 2.9 to 12.7 μ g%, with a mean value of 7.4 μ g%. It should be emphasized that the increase in this index characteristically found in adults in response to the cold stimulus was seen in only about half the cases in children. The DALS level varied between 0.6 and 3.3 μ g% after cold stimulation, with a mean value of 0.9 μ g%.

Analysis of these results demonstrates that the concentration of adrenalin-like substances and DALS, and also the value of K_{sp}, corresponded roughly to the values established in adults. K_{sp} and the concentration of adrenalin-like substances rose in 5 cases, fell in 4 and remained unchanged in 1 case. From the values of K_{sp} it may be supposed that the fractions of adrenalin-like substances after cold stimulation consisted predominantly of chromogens.

Whereas in adults, in response to cold stimulation the acetylcholine concentration in the blood fell, in children, in the same conditions, it rose in 8 of 10 cases, varying from 0.4 to 1.42 μ g% (mean value 1.08 μ g%).

The changes in the pulse rate after application of the cold stimulus were similar to the changes in the level of adrenalin-like substances and K_{sp}: in 5 children the rate increased, in 4 it decreased, and in 1 it remained unchanged. The arterial pressure rose in 7 cases, fell in 1, and remained unchanged in 2 cases.



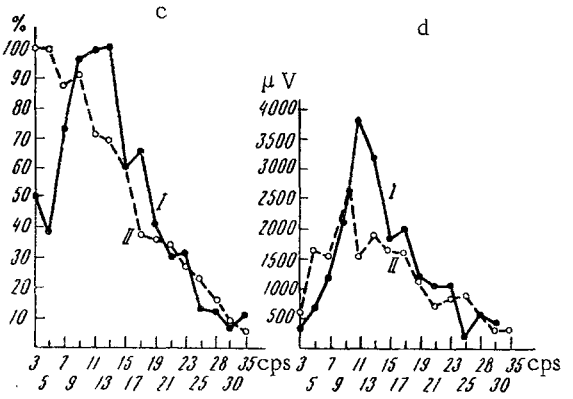
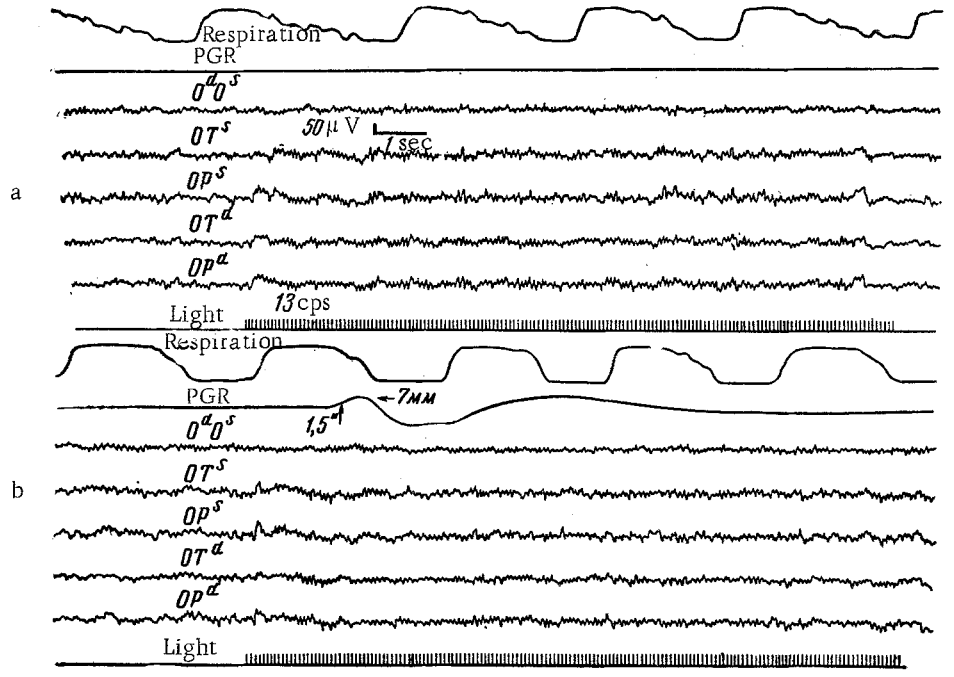


Fig. 1. Results of investigation of evoked brain potentials of subject L., aged 13 years (December 23, 1960). a) EEG before action of cold agent; b) 10 min after action of cold agent; c) graph of coefficient of synchronization (K_{syn}) of evoked potentials; d) graph of combined energy (ΣA_{syn}) of evoked potentials for each frequency of stimulus. PGR) psychogalvanic reflex. On graphs: I) before cold stimulus; II) after cold stimulus.

The EEG of one of the subjects (Fig. 1a) shows the recording of evoked potentials with a frequency of 13 cps before the action of the cold stimulus in 5 occipital leads. Cold stimulation interfered with the assimilation of the light flashes in the middle part of the spectrum of photic stimulation (Fig. 1b). As is clear from the graphs shown in Fig. 1c and d, the value of K_{syn} for a frequency of 13 cps fell from 100 to 69%, while the combined energy A_{syn} fell correspondingly from 3200 to 1900 μV. The reaction of the child to the cold stimulus was parasympathetic in character: the pulse rate fell from 82-72/min and the arterial pressure from 105/68 to 98/80 mm. The concentration of adrenalin-like substances in the blood fell from 10.6 to 5.3 μg%, and K_{sp} rose from 0.65 to 0.73; the blood level of DALS was not determined. The acetylcholine concentration in the blood rose correspondingly from 1.03 to 1.13 μg%.

The results of the investigation of another subject during the action of the cold stimulus are given in Fig. 2. The synchronization of the evoked potentials on the EEG changed only very slightly, in the direction of weakening. The clinical reaction of this child to the cold stimulus differed somewhat from that of the first: the pulse rate fell from 84 to 80/min, while the arterial pressure rose from 105/60 to 125/75 mm. The concentration of adrenalin-like substances fell from 7.9 to 5.5 μg%, while the level of DALS rose from 0.5 to 3.3 μg%, and K_{sp} rose from 1.2 to 1.4. The concentration of acetylcholine in the blood rose from 0.82 to 1 μg%.

Comparison of the changes in the EEG parameters, the level of biologically active substances in the blood, and the clinical changes shows that as a result of the action of a cold stimulus the tone of the subcortical formations (the



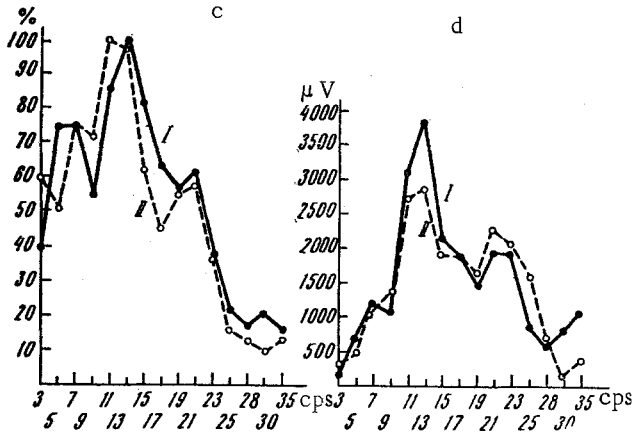


Fig. 2. Results of investigation of the evoked brain potentials of subject Shch., aged 15 years (February 17, 1961). Legend the same as in Fig. 1.

ascending activating system of the reticular formation of the brain stem) and of the cerebral cortex was increased. The changes in the concentration of adrenalin-like substances in the blood and the increase in K_{sp} arising immediately after the action of the cold stimulus demonstrate the reflex participation of the adrenals in this reaction. In turn, this inevitably had a secondary influence on the subcortical formations of the brain and the cerebral cortex. Evidently the increase in the acetylcholine concentration in the blood played a part in raising the tone of the reticular formation in response to the action of cold. The mechanism of this effect, whether reflex or humoral, will be investigated later. The factors listed above bring about an increase in the diffuse afferent system (the number of points of excitation) of the child's cerebral cortex. The latter evidently leads to the creation of conditions less favorable to the synchronization of the evoked potentials, and, consequently, raises the level of the synaptic transmissions of the cerebral cortex and subcortical formations. In Fig. 2b for instance, a psychogalvanic orienting reflex with an amplitude of 7 mm and a latent period of 1.5 sec can be seen to appear, demonstrating an increase in the tone of the reticular formation of the child's brain stem. Before the action of cold, this reflex to interrupted light was not present Fig. 2a).

It is worth noting that the indices of the level of adrenalin-like substances in the blood were less stable in children than in adults. The high blood concentration of acetylcholine observed in children before and after cold stimulation was much higher than the corresponding value obtained in adults.

SUMMARY

A study was made of apparently healthy children aged 13-15 years. A method of potentials modified by Lowell and Dosset was used to determine the energy characteristics of evoked potentials for each frequency of the stimulus (A_S) and synchronization coefficient (K_S) of all the frequencies of light stimuli before and after cold stimulation (+10°C). Simultaneous determinations were made of adrenalin-like substances (ALS) in the venous blood, their dehydro forms (DALS), the specificity coefficient after Shaw's method (modified by Utevsky and But), as well as of acetylcholine (AC) by Funer's method (modified by V. S. Belyaeva). As a result of cold stimulation there was a reduction of K_S and a more pronounced fall in ΣA. As compared to adults a considerable instability of the ALS level was noted in children; higher (as compared to adults) AC values were revealed in children, the values increasing under the effect of cold; in adults they were found to drop.

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