

EFFECT OF FUNCTIONAL STRAIN OF THE CNS AND ENDOCRINE DISTURBANCES ON DEVELOPMENT OF EXPERIMENTAL ATHEROSCLEROSIS IN DOGS

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Functional strain on the CNS was combined in chronic experiments on seven dogs with other factors changing the hormonal status of the animal – castration and injection of mercazolyl* in doses of 1.5–2.5 mg/kg (group 1). The six control dogs (group 2) underwent castration and injection of mercazolyl only. The animals of group 1 developed persistent hypercholesteremia, atherosclerotic changes in various intramural arteries, especially of the myocardium, and also degenerative changes in the parenchyma of certain organs, which were not found in the animals of group 2. The results of this investigation demonstrate the important role of functional strain on the CNS as a leading "risk" factor responsible for disturbances of the regulation of lipid metabolism and the development of atherosclerotic changes in the vessels.

KEY WORDS: central nervous system; strain (neurosis); castration; mercazolyl.*

Previous experimental investigations [3, 4, 7–15] demonstrated the important role of prolonged functional strain on the CNS in the disturbance of metabolism of endogenous cholesterol, thus providing an approach to the study of some mechanisms of the pathogenesis of atherosclerosis.

In the present investigation the effect of prolonged strain on the CNS was studied on endogenous cholesterol metabolism and on the development of structural changes in the cardiovascular system and organs after modification of the hormonal status.

EXPERIMENTAL METHOD

Experiments (duration six years) were carried out on 13 male dogs, of which seven were experimental (group 1) and six were controls (group 2).

Functional stress and strain on the CNS were induced by the formation of a breath-holding reflex and its subsequent reproduction [8, 9]. Periods of reproduction of the reflex (duration 30–40 or 80 days) alternated with periods of rest of the same duration. Conditioned-reflex activity was assessed by calculating the total percentage of positive responses in the form of a change in the breathing pattern or breath-holding. Altogether seven periods of reproduction of the reflex were carried out, in which the first stress varied in strength and duration and was applied against a normal or abnormal hormonal status. The latter was produced by castration and by moderate inhibition of thyroid function by means of the thyrostatic agent mercazolyl (1.5–2.5 mg/kg).

The control dogs underwent castration only and they received mercazolyl in the same dose as the experimental dogs.

* 1-methyl-2-mercaptoimidazole.

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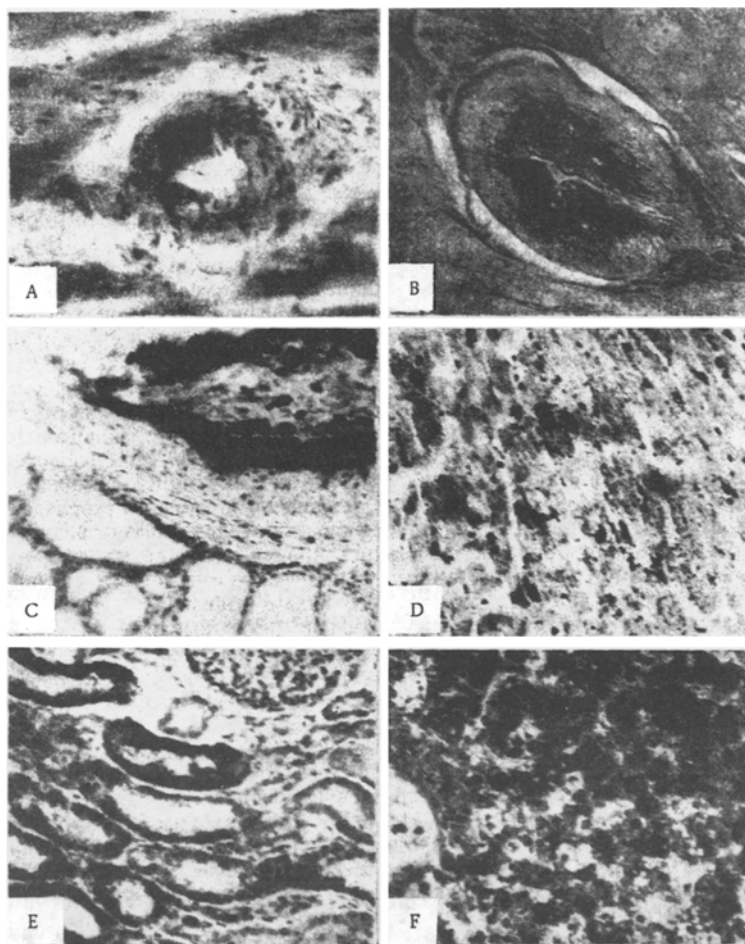


Fig. 1. Structural changes in vessels and organs of dogs with strain of CNS combined with inhibition of endocrine function. A) Dog Rubin; segmental fatty infiltration of wall of small myocardial artery; B) dog Sharik; intramural artery of myocardium: atherosclerotic plaque obliterating lumen of vessel; C) thyroid gland: lipoidosis of wall of large artery; D) dog Sharik; fatty degeneration of myocardial muscle fibers; E) dog Tserber; kidney: fatty infiltration of epithelium of convoluted tubules with enlargement of their lumen; F) dog Sharik; infiltration of liver cells with large fat droplets. A, C, D, E, F) Goldman's stain, 140 \times ; B) Steedman's stain, 140 \times .

The content of total cholesterol and its fractions in the blood serum was determined by the method of Balakhovskii and Balakhovskii [1] in the initial period, the period of strain on the CNS (on the 5th, 10th, 20th, 30th, 40th, 60th, and 80th days), and during the period of rest on the experimental dogs and at corresponding times on the control dogs. After the end of the experiment the animals were killed by electrocution and a morphological study made of the cardiovascular system and internal organs (myocardium, liver, kidneys, spleen, lungs, adrenals, thyroid gland). Atherosclerotic changes in the intramural vessels and in the aorta were detected by the use of Van Gieson and Goldman's methods, and mucopolysaccharides (MPS) of the ground substance of the vessel walls were detected by Steedman's method.

EXPERIMENTAL RESULTS

The initial serum total cholesterol level of the experimental and control dogs was 146.0 ± 1.4 and 150.0 ± 1.9 mg/100 ml, respectively. In the experimental dogs 6 years later the total serum cholesterol was 6-66% (mean 32%) higher than initially, whereas in the control group it was increased in half of the animals by 3-18%, but was below the initial level in the rest (the mean value for the group as a whole was the same as initially).

The high blood-cholesterol level at the end of the experiment is evidence that long periods of rest after strain of the CNS did not restore normal cholesterol metabolism in the experimental animals.

Functional strain on the CNS, in conjunction with modification of the hormonal status, was thus accompanied by marked changes in cholesterol metabolism which developed in this group of experimental dogs sooner than in animals exposed to functional strain on the CNS only [11].

Histological examination of the vessels of the heart from the dogs of group 1, in which the blood cholesterol level was 6-28% higher than initially (the dogs Iris, Rubin, Belyak, and Seryi), revealed changes in the myocardial arteries of medium and small caliber in the form of an accumulation of acid MPS in thickenings of the intima, or of segmental or circular fatty infiltration of the intima and media of the vessels (Fig. 1A).

When the blood cholesterol level was raised much higher than initially (by 34-66%; dogs Tserber, Ryzhik, Sharik), definitive atherosclerotic plaques with a well-marked connective-tissue skeleton and with a ground substance dominated by neutral MPS were found along with lipoidosis in the walls of the myocardial vessels. These plaques almost completely obliterated the lumen of the vessels, as was seen particularly clearly in the dogs Ryzhik and Sharik (Fig. 1B).

Simultaneously with changes in the myocardial arteries, in some dogs lipoidosis was found in the walls of the small and larger arteries of the thyroid glands (Fig. 1C). Widespread lipoidosis of the small follicular and trabecular arteries of the spleen occurred in all the dogs of this group. Foci of thickening of the intima, with predominance of sclerotic changes and with no features of fatty infiltration, were observed in the aorta.

Irrespective of the degree of elevation of the blood cholesterol level, in all the dogs of group 1 degenerative changes were found in various organs. For instance, in five of the seven dogs fatty degeneration of the muscle fibers of the myocardium was present and was particularly marked in the dog Sharik (Fig. 1D). The lumen of the convoluted tubules in the cortex of the kidney was widened and the epithelium showed marked features of fatty degeneration (Fig. 1E). In a few cases droplets of fat were found in the endothelium of the glomerular capillaries.

Fatty infiltration of the cells in the liver cells with large droplets was found in dogs with a considerably elevated blood cholesterol (Fig. 1F). In some (three of seven) dogs the content of lipids in the cells of the zona fasciculata and zona glomerulosa of the adrenals was increased and the boundaries between the various zones were disturbed. In three dogs fatty degeneration of the smooth muscles surrounding the large bronchii was found in the lungs. In most dogs the vessels of the internal organs were dilated and contained lipemic plasma.

No atherosclerotic changes were present in the vessels of the control dogs. A varied degree of fatty degeneration of the parenchyma was found in their internal organs (kidneys, liver, adrenals), but it was much less severe than in the experimental dogs.

Comparison of the results of the biochemical and pathomorphological investigations shows that castration and prolonged administration of mercazolyl are accompanied by transient disturbances of the endogenous blood cholesterol level and by moderate degenerative changes in certain organs participating in the regulation of lipid metabolism. However, under these experimental conditions the animals' cardiovascular system remained intact.

The application of functional strain on the CNS in conjunction with a modified hormonal status gave rise to a lasting increase in the endogenous cholesterol level and to the development of atherosclerotic changes in various intramural arteries, chiefly in the myocardium, and also to the appearance of degenerative changes in the parenchyma of some organs. Changes discovered in the vascular system of the animals of group 1 were similar in character to the structural changes discovered in the blood vessels of dogs receiving an atherogenic diet [2, 5, 6, 16].

The results thus demonstrate the important role of functional strain on the CNS as one of the leading "risk" factors determining a disturbance of the regulation of lipid-cholesterol metabolism and the onset of atherosclerotic changes.

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