Microcirculatory Disturbances in Rat Brain upon Neurosis

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In vivo study of the microcirculation in the basin of the midbrain artery of neurotized rats by means of biomicroscopy demonstrated changes in arteriole form and interruption of blood flow in venules. Bilateral occlusion of the common carotid arteries led to the dilation of all observed arterioles in control rats. The response to occlusion in neurotized animals was found to be as follows: 54% of arterioles showed dilation, 21% showed constriction, and 25% did not change in diameter. Constriction was observed in 59% of studied venules, while 41% of venules did not change in diameter. Interruption of blood flow in venules was observed in some cases.

Key Words: *microcirculation; rat brain; neurosis*

According to existing notions, cerebral circulatory hypoxia mediated by dystonia of vessels plays an important role in the pathogenesis of induced neuroses [1]. However, until now a direct study of the tonus of cerebral vessels under the conditions of this particular pathology has not been performed. Photorecording of the cerebral microvessel response to ligation of the carotid arteries is one method of studying their reactivity [3]. The purpose of the present work was to study the response of the cortical pial vessels of neurotized rats to bilateral occlusion of the common carotid arteries (CCA).

MATERIALS AND METHODS

Eighteen male Wistar rats with a body weight of 180-220 g were used in the experiments (9 control and 9 experimental animals). Neurotization was induced by "white" noise applied for 3 weeks (at a frequency of 350-3500 Hz, 60-70 dB above the threshold of human audibility for six hours daily) and probability (0.5) reinforcement of light flashes (at a frequency of 2 Hz) using a special scheme of electrodermal stimulation of limbs by an alternating current whose strength slightly exceeded the threshold of vocalization. We studied the pial vascular net of the right hemisphere and observed 102 arterioles with an initial diameter of 20-80 μ and 97 venules with an initial diameter of 20-220 μ. The animals were kept under anesthesia (chloral hydrate, 60 mg/100 g intraperitoneally). The *in vivo* study of the microcirculation in the basin of the midbrain artery was performed by means of biomicroscopy via a contact objective [3]. The inner diameter of vessels was determined by photos with a graduated grid. Statistical significance was determined by Student's test.

RESULTS

In all control rats arterioles between branches initially exhibited a cylindrical form, which is considered to be one of the signs of normal vascular tonus [3]. Venules were found to be filled with blood.

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In two cases we observed "a bottlelike" shape of arterioles in experimental rats, indicating a failure of autoregulatory properties [5], and in one case we observed interrupted blood flow in a venule with a diameter of 70 μ.

The CCA test revealed more marked changes in arteriole tonus of neurotized animals.

Control animals responded to the CCA test by dilation of all arterioles studied (n=39) on average by 132.6±2.8%. Four percent of the studied venules (n=47) slightly increased their lumen, and 52% of venules diminished in diameter (up to 83.4±1.47% of the initial value). The other venules did not change their diameter upon neurosis (the two latter groups of venules were observed in each experiment). Stasis did not occur in any type of vessels.

The arteriole response to the CCA test in neurotized rats (n=63) was different. Fifty-four percent of the vessels responded by an increase in diameter (on average by 141.7±5.03%), while 21% responded by constriction (73.3±2.72% of the initial value). Both groups of arterioles were observed in four experiments and in two experiments no dilation was observed at all. Twenty-five percent of the vessels did not change their diameter.

Fifty-nine percent of the examined venules (n=50) responded by a diminished diameter (on average up to 82.9±1.41%), and 41% of the vessels showed no change in diameter, which virtually did not differ from the control. Interruption of blood flow in venules with diameters of 30 and 90 μ occurred in 2 experiments, and in one experiment a venule with a diameter of 20 μ and a length of 500 μ "disappeared" altogether as a result of decreased blood filling.

Since the dilation index in neurotized rats proved to be a little higher than in the control, the experimental rats were divided into two groups for an analysis of this tendency: a group of animals showing dilation only (four rats) and a group with mixed arteriole response (five rats). The dilation index in the first group proved to be higher than in the control (151.4±6.24%, p<0.01), and in the second group it was lower than the control (121.8± ±3.08%, p<0.01). Thus, although some kind of microcirculatory disorders occurred in almost all experiments on neurotized rats, the picture of changes in the pial arteriole response was not uniform.

The findings demonstrated a decrease and distortion of the dilation response of pial arterioles to ischemia in some neurotized animals (56%). Earlier studies of morphologists on neurotized rabbits reported that besides dystonic vascular disturbances in the sensorimotor cortex, there occurred hypoxic changes of capillaries and neurons [4]. Later studies showed a decrease in the rate of the local blood flow [7] and activation of lipid peroxidation [6] in the basin of the midbrain artery of neurotized rats. On the basis of these findings it was speculated that tonus disturbances of cerebral vessels were the cause of ischemic damage, since they can lead to an imbalance between the tissue demand for oxygen and its supply by blood vessels [2]. By virtue of the fact that the CCA test can be considered as verification of the reserve capacities of the cerebral vascular system, our results demonstrating their decrease in the case neuroses speak in favor of the proposed hypothesis.

Of special note is the fact that dilation in response to the CCA test even exceeded the control in some animals subjected to neurotization (44%). This may be associated with the individual sensitivity of rats to the effects of stress [8] and needs to be experimentally verified.

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