MORPHOLOGICAL CHANGES IN THE PREFRONTAL CORTEX IN METABOLIC SYNDROME AND SLEEP DEPRECATION

Sherzod Burkhoniddinovich Shamsiddinov
Independent researcher at the Central Asian Medical University
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ABSTRACT

Morphological changes in the prefrontal cortex in metabolic syndrome and sleep deprivation include reduced dendritic spines, decreased gray matter volume, decreased neuroplasticity, and chronic neuroinflammation. These impairments, compounded by each other, lead to significant cognitive deficits (particularly working memory and self-control) and emotional dysregulation.

Relevance. In recent decades, the prevalence of metabolic syndrome has steadily increased worldwide. Concurrently, there has been an increase in the number of people suffering from chronic sleep deprivation due to urbanization, high workload, and lifestyle changes. Both factors have been shown to negatively impact central nervous system function and increase the risk of cognitive impairment.

The prefrontal cortex is one of the most vulnerable brain structures to metabolic and hypoxic damage. Chronic sleep deprivation is accompanied by impaired neuroplasticity, increased lipid peroxidation, and inflammatory responses, which contribute to neuronal damage. In metabolic syndrome, insulin resistance, hyperglycemia, and endothelial dysfunction also contribute.

In recent years, melatonin has received particular attention as a substance with antioxidant, anti-inflammatory, and neuroprotective properties. However, the morphological aspects of its influence on the prefrontal cortex during the combined effects of metabolic syndrome and chronic sleep deprivation remain poorly understood.

Purpose of the study. To study morphological changes in the prefrontal cortex of the brain in metabolic syndrome and chronic sleep deprivation, and to evaluate the effectiveness of melatonin in their correction.

Materials and methods. The experimental study was performed on 60 male Wistar laboratory rats weighing 220–260 g.

The animals were divided into four groups:

Group I (control) — 15 animals;

Group II — metabolic syndrome model (15 animals);

Group III — metabolic syndrome and chronic sleep deprivation (15 animals);

Group IV — metabolic syndrome, sleep deprivation, and melatonin therapy (15 animals).

Metabolic syndrome was modeled by a high-calorie diet for 12 weeks. Chronic sleep deprivation was simulated by restricting sleep to 4 hours per night for 30 days.

Animals in Group IV were given melatonin daily at a dose of 10 mg/kg body weight. After completion of the experiment, a morphological examination of the prefrontal cortex was performed using light microscopy and morphometric analysis.

Statistical processing of the data was performed with the calculation of mean values (M±m), Pearson correlation coefficient (r) and the level of statistical significance of differences ($p<0.05$).

Results. Morphological analysis showed that animals with metabolic syndrome had a decrease in the density of neurons in the prefrontal cortex to 84.3±2.1 cells per visual field compared to the control group (102.7±2.4; $p<0.001$).

With a combination of metabolic syndrome and chronic sleep deprivation, the changes were more pronounced. Neuronal density decreased to 71.8±2.6 cells per visual field, and the number of degeneratively altered neurons increased almost 2.3 times relative to controls ($p<0.001$).

In animals receiving melatonin, the density of neurons increased to 91.5±2.3 cells per visual field, which was significantly higher than the values in the uncorrected group ($p<0.01$).

The average thickness of the prefrontal cortex was: control group - 1.84±0.05 mm; metabolic syndrome - 1.67±0.04 mm; metabolic syndrome + sleep deprivation - 1.51±0.03 mm; metabolic syndrome + sleep deprivation + melatonin - 1.73±0.04 mm.

A strong negative correlation was found between the duration of sleep deprivation and the density of neurons in the prefrontal cortex ($r=-0.78$; $p<0.001$). A negative correlation was also established between blood glucose levels and the thickness of the cerebral cortex ($r=-0.69$; $p<0.01$).

The data obtained indicate that the combination of metabolic syndrome and chronic sleep deprivation has a pronounced damaging effect on the prefrontal cortex. The observed morphological changes were characterized by a decrease in neuronal density, disruption of cortical architecture, and an increase in the number of degeneratively altered nerve cells.

The increased damage caused by the combined effects of these two factors may be associated with the activation of oxidative stress, neuroinflammation, and disruption of energy metabolism in nervous tissue. The findings are consistent with current understanding of the role of metabolic and circadian disturbances in the development of cognitive dysfunction.

Melatonin administration was associated with a pronounced neuroprotective effect, manifested by improved morphometric parameters and a reduction in signs of neuronal damage. The protective effect of the drug is likely due to its antioxidant and membrane-stabilizing properties.

Further research is needed to clarify the mechanisms of the protective effect of melatonin and to develop new methods for the prevention of cognitive impairment in metabolic syndrome.

Conclusions:

1. Metabolic syndrome causes significant morphological changes in the prefrontal cortex, accompanied by a decrease in neuronal density and disruption of cortical architecture;

2. Chronic sleep deprivation significantly increases structural damage to neural tissue in metabolic syndrome;

3. A strong negative correlation was found between the duration of sleep deprivation and the degree of neuronal damage ($r=-0.78$; $p<0.001$);

4. Melatonin supplementation promotes partial restoration of prefrontal cortex morphological parameters and reduces signs of neurodegeneration;

5. The obtained results confirm the potential of melatonin as a neuroprotective agent for patients with a combination of metabolic and circadian disorders..