17. STRESS AND NEURONAL CELL DEATH: PATHOGENETIC MECHANISMS, MANAGEMENT AND TREATMENT

Author: Postolache Danu

Scientific advisor: Gavriliuc Mihail, PhD, Professor, Head of Neurology Department No. 1, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova

Introduction. The nervous system is the most complex organ in the human body, as structurally – consisting of billions of neurons, as functionally – being responsible for cognition, behavior, and conscience. Therefore, the tiniest modification of nervous system homeostasis can alter its welfare. Psychological and physical stress are the most common causes of neuronal milieu dyshomeostasis, beside aging. Neuroglia, including astrocytes and microglia, is the most important factor in coping with neuronal stress and inflammation, being crucial in events like neuron growth and death.

Aim of study. As the speed and consistency of our everyday life are steadily increasing, psychological stress is becoming a normal part of it. The nervous system is sensible to stress, providing several clinical conditions related to apoptosis and brain atrophy. Our aim was to emphasize the mechanisms of stress-induced neuronal death and the methods of prevention and treatment.

Methods and materials. The current literature review is based on several scientific and medical articles found on PubMed, Google Scholar, Medscape, Elsevier, ResearchGate, Frontiers and medical books.

Results. Severe and prolonged stress, as well as chronic mild stress induce the hyperactivation of hypothalamus-pituitary-adrenal axis, with the consequent release of corticosterone, that collaborates with amine neurotransmitters and proinflammatory cytokines to induce neuronal senescence and cell death by apoptosis. Other means of neuronal damage initiated by chronic stress are the decrease of dopamine and serotonin levels, excitotoxicity, microgliosis, astrogliosis and oxidative stress. All of these are pathological protective reactions directed by endocrine, immune and nervous systems. Paraclinical examinations as PET imaging of TREM1 or caspase-3 activity assay can help setting the diagnosis. Antidepressant drugs, like desipramine, were shown to increase neuronal survival and genesis and to prevent brain tissue atrophy. Adjusting one's daily regimen, physical activity and diet can prevent neuronal apoptosis. Therapy targeting apoptotic genes, proteins and pro-inflammatory cytokines was proven effective.

Conclusion. The modifications seen in stress-affected human brains are similar to those in individuals suffering from neurodegenerative diseases, depression and old age. Synaptic loss and cell senescence lead to severe cognitive decline. Stress-induced damage to the nervous system is focused mainly on the dentate hippocampal gyrus and prefrontal cortex, preventing normal neurogenesis and inducing cell apoptosis. The prophylaxis and treatment of the condition are possible and require further research.