editorial

Reversing the Allostatic Load

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Chronic stress triggers a series of allostatic mechanisms and possibly leads to disease in humans and mammals. The molecular basis of the reaction to chronic stress is the adrenal cortex hormones, as human hydrocortisone. Epinephrine and norepinephrine are protagonists for survival in acute stress. In psychosocial stress, condition with variability, the expected damage is hippocambal remodeling, with subsequent negative effects in learning and memory. The hippocambal alterations seem to be caused by chronic exposure to hypercortisolism, caused by chronic or repeated stress. The reduction of hippocambal volume is a common result of chronic stress conditions and is also present in depressive disorders. The socioeconomic status is an unchanged risk factor and bad prognostic factor for almost every kind of disease arising in conditions of chronic stress. Chronic diseases, psychosomatic diseases and cancer are more often and more difficult to treat in poor people and the same phenomenon appears for mental health disorders. Depression, suicidal or risk -taking behavior and criminality have acquired an epidemic character and in practice indicate a society's picture of sickness. What is more disappointing; the trans-parental transfer of sick genes makes the hope for rehabilitation less probable for the expanding reality of sick populations.

Allostatic load refers to both the body and the psychic sphere. It includes every negative load we withstand before birth (endometrial environment) until today. The theory of *transgenerational transmission* of stress makes this load even "heavier".

Brain gut syndromes are allostatic syndromes

Brain-gut syndromes or functional gastrointestinal syndromes represent a group of disorders with a common pathogenetic basis which is the dysfunction of brain-gut axis. This dysfunction is one characteristic symptom of allostasis. The main brain-gut syndrome is the irritable bowel syndrome and other included disorders are the inflammatory bowel diseases, peptic ulcer, functional dyspepsia, gastro-esophageal reflux, chronic abdominal pain in childhood, and chronic chest pain in adults, related to visceral pain. Brain and gut communicate via the autonomous neural system and gastrointestinal hormones, secreted by the neuroendocrine cells of the diffuse neuro-endocrine system of the gastrointestinal tract. The detection of the neuropeptides of CRF family (Corticotropin Releasing Factor) and selective receptors in the gastrointestinal tract has made clearer the role of HPA (Hypothalamus-Pituitary-Adrenals) axis in brain-gut syndromes. The molecular cross-talk of HPA axis and brain-gut axis and the new discoveries made possible the neuroendocrine mapping of the gastrointestinal tract and enhanced the perspectives for novel molecular therapeutic interventions targeting the brain-gut axis. Thus, we see that the new pharmaceutical approaches seem to be following an "anti-allostatic" direction because they are based on the faults of the physiology that were created by allostasis.

Hypothalamus - Pituitaty - Adrenal (HPA) is the main (anti?) - allostatic sensory organ

Hypothalamus- Pituitaty- Adrenal (HPA) axis is stimulated in bacterial and viral infections resulting in hypercortisolism. Recent evidence indicates that adrenocortical insufficiency may be more common in septic shock, and low-dose hydrocortisone regimens have shown promising results in patients with sepsis. The hyperactivity of HPA axis is corrected during a clinically effective therapy with antidepressant drugs, increasing the number and sensitivity of glucocorticoids receptors (GRs). Novel agents as CRF (Corticotrophin Releasing Factor) antagonists can reduce the high levels of CRF in blood in anxiety disorders, depression, anorexia nervosa and post-traumatic or post-ischemic neuropsychiatric disorders. Agents that interact with CRF- Binding Protein raise the levels of urocortin (neuropeptide, CRF family member) and other free peptides in brain tissue, with neuro-protective effects. Endocrine withdrawal syndromes and drugs-withdrawal syndromes cause changes in the HPA axis that depend on the degree of tolerance and dependence. HPA axis is hyperactive in cocaine-addicted persons, and CRF increase is responsible for neuropsychiatric disorders and the relapse to cocaine use after therapy. CRF antagonists target to the hyperactivity of HPA axis and represent the suggested strategy for cocaine-addicted persons. The change in the HPA axis after long term chemical exposure to relatively high levels of specific environmental agents triggers multiple chemical sensitivity (MCS), a controversial disorder with a pathophysiologic involvement of the brain and the immune system.

The anti-allostatic pattern of life

Until today, we believed that the allostatic load increases only through life and never decreases; just like radiation. The cause for this pessimism was that allostasis was presented like a dynamic negative metamorphosis due to constant adaptations for tolerating environmental and endogenous stressful stimuli. The damage seemed to be permanent. However, recent studies seem to count the allostatic load with biochemical and anosological methods (cynourenin, T-lymphocytes) and show that the allostatic load not only can be counted but also be reduced! If every day of our lives we "kill" with slow and systematic way all the negative loads which come from the environment or from inside (psychiatric disease or mood disorders), we may manage not only to protect ourselves from negative "transformation" but also may manage to rejuvenate ourselves by reversing our existing allostatic load.