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PHYSIOLOGICAL AND MOLECULAR BASIS OF STRESS

„Stress is a result of civilization which man himself no longer can withstand" wrote Hans Selye, the author of modern concept of stress.

ABSTRACT: Stress causes changes in numerous physiological, molecular, biochemical and behavioral events, as a reaction of all living organisms to any homeostasis disturbance, by translating extracellular signals into a specific cellular response *via* the process of signal transduction. This paper briefly summarizes the data from a number of laboratories, including our own, providing results on important physiological and molecular activities of living organisms under different stress conditions.

The aim of this paper is to send the message that stress as a syndrome disturbs all vital functions of living organisms, leading to a broad spectrum of diseases and disturbances. Stress is the silent killer.

KEY WORDS: stress, HPA axis, glucocorticoid receptor, Hsps proteins, signal transduction

AND WHAT IS STRESS?

There is still no clear-cut definition for stress in the medical pathology textbooks, but current literature defines it as „the set of all organic reactions to physical, chemical, environmental, psychological (emotional), infectious, or other aggressions, which are capable of disturbing the homeostasis". Stress is a common phenomenon which is attracting increasing attention. The term „stress", although having a very broad meaning, generally describes a state of disturbed homeostasis, harmony and equilibrium. The disturbing forces, or inputs, are considered „stressors", while the counter-acting forces, or outcomes, are called the adaptation.

It is important to understand that stress always corresponds to a relation between the environment and the individual. It means that an aggression and a

response have occurred and that an interaction took place, as it has been proposed by the Canadian physician Hans Selye, the creator of the modern concept of stress (S e l y e , 1946). In the face of danger, the organism changes its inner balance and priorities into a high physiological arousal, to enable these two functions. The fight-or-flight response (termed by Cannon and Selye in the 1930s) is a pattern of physiological responses that prepare the organism for emergency. When the external balance is disrupted, the body changes its internal balance accordingly. According to Cannon/Selye, the so-called physiological stress is a normal adaptation syndrome. When the response is pathological such as in an ill-adapted individual, or in a situation where the stress stimulus persists for a long time, an organic malfunction takes place, which may lead to transitory disturbances or to severe manifestations of disease. Activation of the stress system results in changes that allow the organism to adapt. S e e m a n et al. (1997) recently suggested to use *allostasis* to describe the process of adaptation to stress and developed a measure of allostatic load based on parameters reflecting levels of physiologic activity across a range of important regulatory systems. The allostatic load is the sum of a number of parameters, and this concept seems a more comprehensive assessment of major risks in the aging process.

It seems that stress will be the syndrome of the century, having in mind a broad spectrum of disturbances in all levels of organization of living organisms.

WHAT ARE THE FUNCTIONAL BASIS OF STRESS?

The scientist who has described for the first time the phenomenon of stress, Hans Selye, has described a generalized physiological response to stress. The hypothalamic-pituitary-adrenal (HPA) axis is the biological interface for neuronal and humoral communication between CNS and peripheral glands, organs responsible for mobilizing the stress response resulting in specific behavioral adaptation.

The perception of an imminent or traumatic event is made by the cortex, a part of the brain structure. This perception is mediated by an enormous network of neurons which comprise large parts of the brain, including the memory circuits.

Once the importance of the stimulus is determined, the cortex activates a subcortical brain circuit in one of its parts, the limbic system, by means of the neural structures which control emotion, as well the autonomous nervous system, responsible for the control of function of the so-called visceral systems (heart, blood vessels, eye pupils, stomach, intestines, glands, etc). These structures are mainly the amygdaloid bodies and the hypothalamus. Their activation will lead to many bodily changes as well as an increase in the secretion of the hormones adrenaline and noradrenaline by the medullar part of the adrenal glands.

We now know that vital chemicals carry messages between brain cells. In essence, they allow brain cells to „talk" to one another. On a typical day in

the brain, trillions of messages are sent and received. Most nerve centers receive input from different types of messengers, and the most important are serotonin, noradrenalin and dopamine. As long as this input is balanced, everything runs along on an even keel. Stress causes problems with brain messengers and the whole brain becomes distressed. Serotonin must work properly in order to maintain normal sleep and mood patterns. Inside of our brain there is a very precise „clock". The body clock is located deep in the center of the brain, in the pineal gland, which is a store of serotonin, the chemical „mainspring" of the clock. Each day, serotonin is chemically converted to melatonin, a related compound, and then melatonin is converted right back to serotonin.

Noradrenalin has many important functions in the body's nervous system. The one that most concerns us here, however, is the role of noradrenalin in setting energy levels. And finally, dopamine seems to be concentrated in areas of the brain immediately adjacent to where the major endorphin-releasing mechanisms lie. Endorphins are responsible for regulating our moment-to-moment awareness of pain. When too much stress causes failure of dopamine function, it causes loss of body's natural „pain killer".

At the same time, the hypothalamus activates the pituitary. Under stressing stimuli, the main hormone produced by this gland is ACTH, also known as the „stress hormone". Carried by blood, ACTH increases the secretion of other hormones, called corticosteroids. These hormones have many actions over the body tissues, by altering its metabolism, the synthesis of proteins, the resistance to invaders of our organism by the immune system, inflammations provoked by infections, or damage of the tissues, etc. The degree of activation of this brain-pituitary-adrenocortical axis can be evaluated by measuring the level of cortisol, one of our inner corticosteroids. Cortisol is the main stress--fighting hormone. When cortisol secretion is high, the body shifts to a „war footing".

The double discharge of hormones which are intensively bioactive, adrenaline and the corticoids has lead scientists to believe that the pituitary and the adrenals are the main mediators of stress.

Stress is associated with activation of the HPA axis. Stress first increases levels of corticotropin-releasing hormone (CRH) and other secretogogues in the hypothalamus. Release of CRH leads to subsequent stimulation of ACTH release from the anterior lobe of the pituitary, that, in turn, stimulates the release of glucocorticoids from the adrenal cortex. Similar effects are noted in aging, where there is a tendency for increased HPA activity and circulating glucocorticoids implicated in the occurrence of hippocampal pathology and memory deficits. The increased glucocorticoid levels have traditionally been ascribed to their physiological function of enhancing an organism's resistance to stress. Glucocorticoids exhibit immunosuppressive activity and are critically involved in adaptation to stress and in the control of metabolism. However, contrary to the traditional view, it has become increasingly clear that glucocorticoids at moderate to high levels also suppress defense mechanisms, such as the anti-inflammatory and anti-allergic activities.

Munck and colleagues (M u n c k and N a r a y - F e j e s - T o t h, 1992) clarified the permissive and suppressive effects of glucocorticoids as follows.

Permissive effects, which are usually stimulatory, are those by which glucocorticoids at basal levels „permit", or normalize responses to stress. In contrast, suppressive actions represent physiological function of glucocorticoids to protect the body against damage from its own activated defense mechanisms, preventing overshoot. Among many examples are the inhibition by glucocorticoids of the production of numerous mediators of defense reactions, including hormones such as antidiuretic hormone and insulin, as well as the immune cytokines and gamma-interferon, all of which are dangerous when in excess. Glucocorticoids suppress production of mediator and induce its receptors simultaneously in two opposing ways and mediator activity as a function of cortisol concentration can be described by a biphasic or bell-shaped curve. Based on these findings, it was suggested that the permissive and suppressive effects, which in juxtaposition appear paradoxical, can be viewed as complementary functions through which defense mechanisms are regulated by glucocorticoids over the full range of their basal and stress-induced concentrations, thereby preventing those reactions from overshooting to threaten homeostasis. Cortisol, as a main representative of glucocorticoid hormones, plays a major role in the intracellular communication and its importance for the survival upon a stress has been well documented long ago. The molecular basis of its action is well presented in Matić's review (Matić, 1995) and a better insight in the complexity of molecular events occurring in a cell during adaptation to unfavorable conditions are explained in many articles.

The events at the physiological level have the basis at the molecular level including activation of complete cellular machinery, including different signal transduction pathways within and between cells. Binding of signal molecule to receptor triggers subsequent intracellular signaling networks. Through a series of steps, the message from that signal gets transmitted and amplified within the receiving cell or molecule, often leading to activation or deactivation of specific transcription factors in the nucleus. Among the corticosteroids, the glucocorticoids are especially attractive because of a current list of their effects might include disparate items. The special roles of glucocorticoids in stress (Matić et al., 1998), their relationship with shock proteins (Čvoro et al., 1998a; Butorović et al., 1994; Čvoro et al., 1998b), acute phase reactants (Poznanović et al., 1997), oncogenes, cancer, endocrine diseases, etc., make a spectrum of responses which can be elicited depending on the cell type, or environmental stimuli (Stanković et al., 1986; Trajković et al., 1981; Trajković et al., 1992; Dunđerski et al., 1996; Dunđerski, 1997).

A vast majority of diverse and widespread physiological effects of glucocorticoid hormones are mediated through the glucocorticoid receptor (GR) protein (Trajković, 1989), a transcription factor directly involved in the regulation of gene expression in glucocorticoid target tissues. *In vivo*, the hormone binding capacity of the receptor, the rate of its transformation to DNA-binding state, the affinity of the GR-GRE interaction and the efficiency of the receptor in transcriptional regulation are all subject to regulation enabling the final cellular response to glucocorticoid hormones to be turned in accordance with

changing physiological and environmental conditions and instantaneous cellular demands (M u n c k et al., 1972; V i d o v i ć et al., 1996)

Steroid-free GR is assumed to be localized in the cytoplasm of target cells, where its two forms: active (i.e., capable of ligand binding) and inactive are maintained in equilibrium. The ligand binding to the receptor promotes its transformation from a weak to a tight DNA-binding form. The transformation process is accompanied by dissociation of the untransformed GR heterocomplexes, comprising some Hsps, an immunophiline and other proteins, and by conformational alteration of its steroid-binding domain and is followed by the nuclear import of the receptor occurring through nuclear pore complexes. Glucocorticoids and other steroid hormone receptors, when present in intact cells in non-activated, non-DNA-binding form, are associated with the dimmers of HSP90. These complexes contain also other heat shock proteins (Hsp70, Hsp56) and some others proteins. Although the Hsps were shown to chaperone the receptor, playing a role in its folding, stabilization and intracellular shuttling, the functional significance of the receptor-Hsps association is still under consideration. After the transformation, the receptor's ligand binding domain remains in a conformation incapable of steroid binding While the ligand binding provokes the GR transformation and nuclear import, the dissociation of the hormone from the receptor contrarily results in its efflux from the nucleus and reappearance within the cytoplasm.

The physical environment of organisms causing stress, damage or even death. Even minor environmental changes may hamper the physiological capacity of organisms to grow, reproduce, or interact socially. Not surprisingly, organisms have developed a variety of adjustments such as behavior, acclimation and heat stress responses, acute-phase responses, etc., that help buffering the physiological impact of environmental change. These adjustments, which can have a profound effect on evolutionary fitness, have been studied from diverse aspects, one of them being the molecular one. Molecular biological interest in the heat shock response was kindled by Ritossa's report (R i t o s s a , 1962) that brief heat treatment of *Drosophila* larvae induced dramatic alterations in gene activity as judged by the changes in puffing patterns observed in the salivary gland polytene chromosomes. Soon thereafter it become clear that all living organisms, from bacteria to man, respond at the cellular level to unfavorable conditions such as heat shock, or other stressful conditions of many different origins, by a rapid, vigorous and transient acceleration in the rate of expression of a small number of specific genes, termed heat shock genes. The products of these genes, commonly referred to as heat shock proteins (Hsps) or stress proteins, most of which are also present under normal circumstances but in lower concentrations, increase and accumulate in cells to reach, in some instances, fairly high levels. A great deal of circumstantial evidence supports the belief that the heat shock response is a rapid, but transient reprogramming of cellular activities aimed to induce or increase the synthesis of the Hsps which would ensure survival during the stress period, protection of essential cell components against heat damage and a rapid resumption of normal cellular activities during the recovery period. Some Hsps, including Hsp90 and Hsp70, serve fundamental cellular roles, chaperoning proteins during folding,

functioning and intracellular trafficking and are found *in vivo* in complexes with a number of transcription factors and protein kinases.

CAUSES AND CONSEQUENCES OF STRESS

In general, acute or chronic stress can be attributed to the biggest problems we encounter in the course of our life. Several researchers have noted that any kind of change in our daily lives, either good or bad, is among the most effective causes of stress. The intensity of stress will depend on the nature and the degree of change, which can go from major ones to relatively trivial life changes.

Certain events in our lives are so severe in terms of psychological stress that they are characterized as a trauma (lesion or damage). Recently, the mental health sciences have recognized the existence of a new syndrome called Post-Traumatic Stress Disorder (PTSD), a real disease, classified in the area of the major anxieties. The syndrome started to be studied in the USA, after return of veterans of the Vietnam war.

This does not apply to war veterans only. It is enough to see what happens to victims to the increasing levels of urban violence. Bombings, automobile accidents or aircraft crashes, earthquakes and floods, kidnapping, rape, child or spousal abuse, etc. are often the cause of post-traumatic stress disorder.

Physicians have recognized that chronic stress has three distinct phases, which occur sequentially one after the other in the case the stressing agents are not suspended:

The acute phase: The phase when the stressful stimuli start to act. Our brain and hormones respond quickly and we usually perceive the effects, but we are unable to see the silent working of repeated stress in this phase.

The resistance phase: The phase when the first mental, emotional and physical consequences of chronic stress start to appear. Loss of concentration, emotional instability or depression, heart palpitations, cold sweating, muscular pains or headaches are the usual telltale signs, but most of the persons do not relate them to stress, and the syndrome may progress to the last and most dangerous phase.

The exhaustion phase: This is the phase when the organism capitulates to stress, when organic and psychological diseases begin.

Since it is not possible in such a brief survey to list, let alone describe the entire array of the disturbances developing during stress situations, we will mention here only some of them:

Stress and aging: The researchers hypothesized that old age results from the accumulated stress experienced during an organism's life span (P l a t n e r , 1961).

Selye and colleagues have proposed and characterized aging as a systematic loss of adaptation (S e l y e , 1976). Aging organisms show an elevation of basal corticosterone level, a major glucocorticoid that plays a key role in the neuropathological effects of stress, and an impaired capacity to adapt to and

recover from stress, suggesting that there is an age-related loss of sensitivity of the brain and pituitary to the negative feedback of high circulating levels of corticosterone. Glucocorticoids sensitize hippocampal structures, making hippocampal neurons less likely to survive coincident neurological insults, perhaps by inhibition of glucose transport leading to energy production decreases within cells (Lupien and Meaney, 1998).

In the 1960s, Harman (1960), based on his findings that aging and ionizing radiation have similar effects on mutagenesis, cancer and cellular damage, proposed „free radical theory of aging". This theory proposes that free radicals are produced in aerobic metabolism and damage they inflict to biomolecules is a major contributor to aging. Oxidative damage to biomolecules produced by oxidants, including free radicals, has been postulated to be a type of endogenous damage, contributing not only to aging but also to a variety of diseases, especially the age-related degenerative diseases.

Stress, cancer and immune system: Stress may be related to the development and progression of cancer, in part due to suppression of immunity (Keller et al., 1981). Stress reduction has been considered as a factor in reducing the mortality rate of cancer patients, and it has been hypothesized that relief or prevention of chronic stress by cognitive therapy may be a promising method for cancer prevention (Cholst, 1996).

Psychological stress adversely affects the immune systems, or affects many features of cellular immune function, including cytokine production (Cooper, 1984). Cellular immunity has an important role in the regulation of wound repair. Pro-inflammatory cytokines, such as IL-1, IL-6, IL-8 and tumor necrosis factor (TNF), help to protect against infection, prepare injured tissue for repair and enhance phagocyte recruitment and activation. Psychological stress is important in the onset and course of major depressive disorders. Patients with major depression show immunosuppression as consequence of hypercorticolism. However, glucocorticoids are not always immunosuppressive, but may enhance certain components of the immune response.

Nutrition and stress: Nutritional status and stress are closely related. Nutrient deficiencies are stressful to the organism. Long-term protein undernourishment, especially if the individual is subject to stress or injury, can be detrimental. Previously outlined immune system malfunctioning in undernourished subjects, especially when protein intake is insufficient, is likely a secondary effect of the HPA overstimulation (Klebanov et al., 1995; Hjaijej et al., 1998; Flynn and Wu, 1997). Chronic food restriction leads predictably to hypercorticosteronemia, hypoglycemia and enhanced adrenal glucocorticoid content. Glucocorticoids follow a diurnal pattern that is more pronounced in animals under the chronic food restriction regimen. The peak elevation can be observed after one month of food restriction. The elevation in blood and adrenal corticosterone levels is a consequence of the fasting-induced adrenal hypertrophy in animals and a cause for reduced responsiveness to acute stress. The influence of chronic food restriction on basal neuroendocrine, immune and adipocyte functions, and the acute-phase response to endotoxic shock were also established.

Protein calorie malnutrition can result in a significant macrophage dysfunction (Curtis et al., 1995). It is believed that this malfunction is more likely to be a consequence of elevated glucocorticoids, rather than of the primary nutrient deficit. In a mouse study comparing standard 24% protein diet with a protein free diet, it has been observed that protein malnutrition after 7 days impaired the macrophage functioning (IL-6 levels were measured), and elevated serum glucocorticoid levels. Administration of the glucocorticoid receptor antagonist, RU486, prevented the impairment of the macrophage functioning. Under the same dietary conditions, exogenous glucocorticoid addition (subcutaneous pellets) reproduced the macrophage impairment.

In the end it can be concluded that stress and the consequent disorders, however extensively discussed as a general and unspecific syndrome, represent in fact the disturbances affecting all functions of an organism that could provoke development of most severe diseases.

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REFERENCES

Butorović, B., Matić, G., Kipić, J., Dunđerski, J., & Trajković, D. (1994): *Synthesis and phosphorylation of hepatic proteins in rats exposed to hypothermic shock*, Arch. Biol. Sci., 6, 65—72ž

Cholst, S. (1996): *Cancer and stress*, Med. Hypoth., 46, 101—106.

Cooper, E. L. (1984): *Stress, Immunity and Aging*, Marcel Dekker, Inc., New York.

Curtis, G. E., McAtear, C. A., Formela, L. & Walsh, A. (1995): *The effect of Nutritional Status on the Cytokine and Acute Phase Protein Responses to Elective Surgery*, Cytokine, 7, 380—388.

Čvoro, A., Dunđerski, J., Trajković, D., & Matić, G. (1998a): *Association of Rat Liver Glucocorticoid Receptor with Hsp90 and Hsp70 Upon Whole Body Hyperthermic Stress*, J. Steroid Biochem. Molec Biol., 67, 319—325.

Čvoro, A., Dunđerski, J., Trajković, D. & Matić, G. (1998b): *Heat stress affects the glucocorticoid receptor interaction with heat shock protein Hsp70 in the rat liver*, Biochem. Mol. Biol. Internat., 46, 63—70.

Dunđerski, J. & Matić, G. (1997): *Metallothioneins: Small proteins serving numerous important functions*, Jugoslav. Med. Biochem. 16: 1—14.

Dunđerski, J., Butorović, B., Kipić, J., Trajković, D., & Matić, G. (1996): *Cadmium affects the activity of rat liver tyrosine aminotrasferase and its induction by dexamethasone*, Arch Toxicol. 70, 390—395.

Flynn, N.E., Wu, G. (1997): *Glucocorticoids Play and Important Role in Mediating the Enhanced Metabolism of Arginine and Glutamine in Enterocytes of Postweaning Pigs*, J. Nutr. 127, 732—732.

Harman, D. (1960): *The free radical theory of aging: The effect of age on serum mercaptan levels*, J. Gerontol., 15, 38—40.

Hjaijej, L., el Feki, A., el Fazaa, S., Gharbi, N., & Kamoun, A. (1998): *Adrenal Cortex Activity in the Malnourished Newborn Rat*, Arch. Physiol. Biochem., 105, 342—346.

Ingenbleek, Y., & Bernstein, L. (1999): *The Stressful Condition as a Nutritionally Dependent Adaptive Dichotomy*, Nutrition, 15, 305—20.

Keller, S. E., Weiss, J. M., Schleifer, S. J., Miller, N. E. & Stein, M. (1981): *Suppression of immunity by stress: Effect of a graded series of stressors on lymphocyte stimulation in the rat*, Science, 213, 1397—1400.

Klebanov, S., Diais, S., Stavinoha, W. B., Suh, Y., Nelson, J. F. (1995): *Hyperadrenocorticism, Attenuated Inflammation, and the Life-Prolonging Action of Food Restriction in Mice*, J. Geerontol. and Biol. Sci. Med. Sci., 50, B79—82.

Lupien, S. J. & Meaney, M. J. (1998): *Stress, glucocorticoids, and hippocampal aging in rat and human.* In: E. Wang and D. S. Snyder (Eds.) *Handbook of the Aging Brain*, Academic Press, San Diego, 19—50.

Matić, G. (1995): *A cross-talk between glucocorticoid receptor-mediated signal transduction pathway and heat shock response*, Yugoslav. Med Biochem. 14, 89—102.

Matić, G., Dunđerski, J. & Čvoro, A. (1998): *Mutually dependent functions of glucocorticoid receptor and heat shock proteins*, Current Topics in Steroid Research, 1, 1—17.

Munck, A., Wira, C., Young, D. A., Mosher, K. M., Hallahan, C. & Bell, P. A. (1972): *Glucocorticoid-receptor complexes and the earliest steps in the action of glucocorticoids on thymus cells*. J. Steroid Biochem. 3, 567—578.

Munck, A., & Naray-Fejes-Toth, A. (1992): *The ups and downs of glucocorticoid physiology. Permissive and suppressive effects revisited.* Mol. Cell Endocrinol., 90, C1-4.

Platner, W. S. (1961): *The effect of stress on the aging process.* Missouri Med, 58, 373—376.

Poznanović, G., Petrović, M. & Magić, Z. (1997): *Reestablishment of homeostasis and the acute-phase proteins*, Panminerva Medica, 39, 291—298.

Ritossa, F. M. (1962): *A new puffing pattern induced by a temperature shock and DNP in Drosophila*, Experientia, 18, 571573.

Seeman, T. E., Singer, B. H., Rowe, J. W., Horowitz, R. I. & Mc Ewen, B. S. (1997): *Price of adaptation-allostatic load and its health consequences. MacArthur studies of successful aging*, Arch. Intern. Med. 157, 2259—2268.

Selye, H. (1946): *The general adaptation syndrome and the diseases of adaptation*, J. Clin. Endocrinol. Metab., 6, 117—?.

Selye, H. 1976: *Forty years of stress research: principal remaining problems and misconcepsions*, Can. Med. Assoc. J., 115, 53—56.

Stanković, J., Dunđerski, Z. & Trajković, D. (1986): *In vitro and in vivo effects of zinc and lead on delta-aminolevulinic acid dexydratase activity in Mus musculus liver and erythrocytes*, Arch. Biol Sci. 38: 1—8.

Stoney, C. M., Bausserman, L., Niaura, R., Marcus, B. & Flynn, M. (1999): *Lipid Reactivity to Stress: Biological and Behavioural Influences*, Health Psychol., 18, 251—61.
Tappy, L., Berger, M. M., & Chiolero, R. L. (2000): *Nutrition and Stress*, Ann. Med. Interne 151, 584—593.
Tataranni, P. A., Cizza, G., Snitker, S., Gucciardo, F., Lotsikas, A., Croousos, G. P., & Ravussin, E. (1999): *Hypothalamic-Pituitary-Adrenal Axis and Sympathetic Nervous System Activities in Pima Indians and Caucasians*, Metabolism, 48, 395—399.
Trajković, D., Radojčić, M., & Petrović, J. (1992): *Delovanje paraquat-a na interakciju testosterona sa specifičnim citoplazmatičnim receptorima testisa pacova.* Arch. Biol. Sci. 34: 9P—10P.
Trajković, D., Matić, G., Radojčić, M., & Petrović, J. (1981): *Effects of trichlorphone and parathion on steroid hormones binding to cytosol receptors of different target tissues of rats*, Acta Biol. Med. Exptl. 6, 71—75.
Trajković, D. (1989): *Steroid hormones and their receptors: I. Structure and function of steroid receptors*, Arch. Biol. Sci., 41: 103—128.
Vidović, S., Čvoro, A., Dunđerski, J., Trajković, D., & Matić, G. (1996): *Hyperthermic stress affects glucocorticoid receptor-mediated transcription in rat liver*, Cell Biol. International, 20, 553—5.

ФИЗИОЛОШКА И МОЛЕКУЛАРНА ОСНОВА СТРЕСА

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Резиме

Стрес изазива многобројне промене физиолошких, молекулских и биохемијских догађаја, укључујући и промене у понашању код виших организама, превођењем екстрађелијског сигнала у специфични одговор ћелије процесом трансдукције сигнала, као реакција сваког живог организма на поремећај хомеостазе. У овом раду учињен је покушај да се кратко сумирају резултати многобројних лабораторија, укључујући и нашу, који пружају доказе о важним физиолошким и молекулским активностима живих организама под различитим стресним условима.

Циљ овог рада је да се пошаље порука да је стрес синдром који ремети све витални функције у живим организмима, доводећи до широког спектра обољења и поремећаја. Стрес је тихи убица.