Hormones and its effects on health during chronic stress exposure

Abstract

Stress is a concept widely used today. Many people live with stress and are continually subjected to the demands of the environment. This concept not only has negative connotations, it also has a positive value, provided it is moderate and punctual.

Alterations in the activity of the hypothalamic-pituitary-adrenal axis (HPA) are related to numerous diseases and psychological disorders. Glucocorticoids have an important anti-inflammatory and immunosuppressive function, however, situations of chronic stress have devastating effects on the immune system, such as the development of infectious, inflammatory and/or neoplastic diseases (cancer) as a result of a decrement in Natural Killer cell activity.

Keywords: stress, immune system, hypothalamic-pituitary-adrenal axis, glucocorticoids, cortisol.

We all know that the mind and the body are strongly connected which means that if the mind suffers an alteration, our body suffers too in one way or another, in other words, what affects one affects another. Several studies have shown that there is a real relationship between stress and the immune system.

Stress could be defined, as the set of processes and neuroendocrine, immunological, emotional and behavioral responses to situations that mean a demand for adaptation greater than the usual for the organism, and/or perceived by the individual as a threat or danger, either for their biological or

psychological integrity. The threat can therefore be objective or subjective; acute or chronic. (Soliemanifar, O., et al., 2018)

In the presence of a moderate or moderate/acute stressor, the body reacts by an increase in the activity of the Sympathetic Nervous System (SNS; increased heart rate, blood pressure, increased breathing, etc.), as well as an increase in the release of certain neurotransmitters (catecholamines, serotonin, neuropeptides, etc.). This response that is triggered in the organism is necessary for the survival of the individual and, therefore, is an adaptive response, which we commonly refer to as allostasis.

This activation of the SNS acts as an alarm signal in response to a stimulus that can threaten the balance of the organism. The concept of allostasis is related to the concept of eustress, a term used to refer to positive, healthy and challenging stress which is well tolerated by the body, used to overcome the state of lethargy. The eustress is therefore beneficial to those who experience it. However, an over-activation of the SNS, and an overproduction and release of neurotransmitters (NT), can have serious consequences in the organism, and this can end up developing certain diseases and disorders, which is known as allostatic load. This term is related to the term distress, which denotes an experience with a negative emotional content that causes confusion, low concentration and anxiety in the body, thus being harmful to the person.

When stress persists over time and becomes chronic, the susceptibility of the individual to develop certain diseases increases, and in addition, may also affect the immune system, which protects us from any disease or infectious

agent, thereby endangering the health of individuals exposed to situations of chronic stress.

One of the mechanisms involved in the physiological response of stress, apart from the SNS, is the hypothalamic-pituitary-adrenal (HPA) axis. The activity of this axis begins in the paraventricular nucleus (PVN) of the hypothalamus and results in the release of glucocorticoids (GCs) and catecholamines (adrenaline and noradrenaline), which are the main stress hormones, and act both peripherally and at the level of the Central Nervous System (CNS).

When experiencing chronic stress, the mind interprets certain external stimuli as something dangerous and harmful, which generates stress. Then the hypothalamus, which is the brain structure responsible for coordinating behaviors that are intended for survival, sends electrical signals to the pituitary gland, and it sends the adrenocorticotropic hormone (ACTH) to the adrenal glands, where cortisol and adrenaline are released.

Cortisol, also known as hydrocortisone, is a glucocorticoid. It is produced on top of the kidneys, in an area known as the adrenal cortex, in response to stress (physical or emotional), and its synthesis and release is controlled by the ACTH and its circadian rhythm. In the morning, the amount of cortisol rises to its peak around 8: 00 am (taking into account a normalized sleep schedule), due to the need to generate energy sources after a long night. In the afternoon it also increases to keep us active, but then it descends progressively. (Dumbell, R., et al., 2016)

In the face of a stressful stimulus, adrenaline gives a quick impulse, increasing energy in case of an escape situation. The breathing, pulse and heart rate are accelerated so that the muscles respond more quickly. The pupils dilate, the blood circulates at a higher speed and this moves away from the digestive system to avoid vomiting. In general, the whole body is prepared to react quickly to certain stimuli.

Adrenaline, is also a neurotransmitter that acts in the brain. In this way, an intense dialogue is established between the nervous system and the rest of the organism, which is very useful when it is necessary to trigger processes that affect many areas of the body in a short time. Once the brain has given the order to increase the amount of production of these two hormones, the first phase of connection between hormones and stress is completed.

The second phase, in which the link between hormones and stress becomes clear, is when the individual reacts to the situation. Taking into account that the situation is interpreted as a threat, the body will react more quickly and more effectively. The adrenaline is the one that will help the individual to react more quickly and the cortisol that will prepare the body to feel stronger.

During the third phase of the connection between hormones and stress, the body will choose an appropriate response. This reaction can consist of the following three options: flee, fight or ‘ paralyze’ (flight, fight or freeze responses to stress). If the individual chooses to flee, hormones and stress will ensure the ability to run faster and farther. If the individual chooses to fight, hormones and stress will ensure a faster and harder reaction to fight. If

the individual chooses to remain paralyzed, and therefore to do nothing, the body will find itself in a state in which the person will have the sensation of being unable to react or do the least.

In situations of stress, the level of cortisol increases. Its main functions are to increase the amount of sugar in the blood, and suppress the immune system to save energy and help the metabolism of fats, proteins and carbohydrates which can be very appropriate for a specific moment, but not when the stressful situation is part of a person’s day to day.

The release of sugar in the blood has the function of maintaining an appropriate level of energy to respond effectively to the stress situation and allowing the individual to be alert. In fact, it is the adrenaline of the brain that sends the signal for glucose to be released into the bloodstream (known as blood sugar), but cortisol contributes to its synthesis. It also contributes to the use of fats and proteins as energy substrates.

Another response of cortisol to a stressful situation is that it inhibits the immune system, because all the energy is necessary to control stress. In addition, this hormone also causes an increase in histamine, which explains why people tend to get sicker or suffer from herpes or allergies when they suffer from this phenomenon. The production of this hormone, either by deficit or excess, can also interfere with the production of thyroid hormones and the conversion of these from T4 to T3.

Cortisol can also disrupt the reproductive system functions, causing infertility or even miscarriage when its levels are too high or chronically elevated. In addition, the chronic increase in cortisol can cause intense hunger and food

cravings due to the metabolic disorder that occurs, and also influences mental blocks and memory problems related to the feeling of “ mind-blanking”.

Glucocorticoids (GCs), have an important anti-inflammatory and immunosuppressive role in the body’s immune system, which is beneficial for the organism since these are able to attenuate the production and release of certain cytokines (macrophages), which induce inflammation in the body. On the other hand, GCs also exert an important anti-inflammatory activity in the SNS. However, when these levels are high, or when stress persists, they stop having this function. (Duque, E., et al., 2016)

Another study on the effects that stress has on the immune system indicates that, among the effects observed, are: a reduced activity of natural killer cells (NK), which are responsible for removing cells infected by certain viruses or cancer, a decrease in antibodies, decrease in lymphocyte proliferation, as well as the reactivation of latent viruses.

As we have seen, a prolonged activation of the HPA axis poses a risk to the health of the individual, since it can lead to the development of certain pathologies, such as: Cushing’s syndrome, chronic stress, panic disorder, diabetes mellitus, hypertension, hyperthyroidism, obsessive compulsive disorder, alcoholism and depression, among others. On the contrary, among the conditions in which a decreased activity of the HPA axis is found are: fibromyalgia, hypothyroidism, rheumatoid arthritis, etc.

As we have previously commented, since a prolonged activation of the HPA axis supposes a risk for the health, with the consequent development of

certain diseases, it is important that there is a control mechanism regulating the activation of the HPA axis. The GCs exert an inhibition on the HPA axis, which takes place at the level of the anterior pituitary gland, the PVN and certain extrahypothalamic structures, such as the hippocampal formation and the medial prefrontal cortex. For this reason, the retro-inhibition exerted by the GCs is essential and necessary to stop the activation of the HPA axis induced by stressful situations and to return to the initial resting situation. (Mariotti, A. 2015)

As explained throughout this paper, not all stress exerts a devastating effect on the organism, since stress, and more specifically moderate stress, turns out to be adaptive for the individual. However, very intense/acute levels and chronic levels of stress do have a detrimental effect on the organism. Therefore, it is necessary to have a series of strategies and techniques that help to manage stress and consequently improve the health of people.

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