

# CELL STRESS – IMPLICATIONS IN THE ACTIVITY OF SEROTONIN AND DOPAMINE NEURONS

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**Abstract:** *The brain responds to stress in a complex way correlated with the activation and inhibition of the neurons involved in the emotional, cognitive and sensory motor processes. Stress is one of the main activators of the hypothalamic-pituitary-adrenal axis and of the serotonergic and dopaminergic system.*

**Keywords:** *stress, serotonin, dopamine*

**Rezumat:** *Creierul răspunde experiențelor stressante într-o manieră complexă corelată cu activarea și inhibarea neuronilor implicați în procesele emoționale, cognitive, autonome, motorii și senzoriale. Stressul este cunoscut a activa sistemele neurohormonale cum ar fi axa hipotalamo-pituitară-adrenalină și sistemele serotonergice și dopaminergice.*

**Cuvinte cheie:** *stress, serotonina, dopamina*

## INTRODUCTION

The brain responds to stress experiences in a complex way correlated with the activation and inhibition of neurons involved in the emotional, cognitive, autonomous, motor and sensory processes. Chronic stress, which is known to be accompanied by the neurotransmitters' hyperactivity, induces cellular changes that can be regarded as a form of plasticity. Since social stress in animals recalls the symptoms that are similar to those shown by the depressed patients, chronic social stress can serve as an experimental model to investigate the neural processes that may occur during depressive disorders in humans. Recent research revealed a considerable progress in understanding the causes of depression and of cell neural mechanisms that mediate the response to stress.

Stress factors enable the release of mediators, which in turn act on cells, activating the genes and other cellular processes that promote adaptation and survival (allostasis). Thus, the concept of allostasis makes a distinction between systems that are essential for life (“homeostasis”) and the mechanisms that maintain these systems in balance.

Allostasis occurs when the physiological variables exceed the limits of control and are crossing the borders of homeostasis mechanisms.

Allostasis is characterized by an imbalance of the primary mediators that may occur when they are over-used or poorly handled. Allostasis refers to the levels of

activity of the primary mediators, permanently altered, levels that integrate associated behaviours, as a response to the changes/challenges of the environment, such as social interaction, climatic changes, diseases, pollution, various attacks etc.

### Stress and serotonin neurons

Further experiments on mammals confirmed the hypothesis of serotonin shortage (5-HT) in depression.

Serotonin neurons, placed in the dorsal raphe nucleus are projected almost in the entire brain and are involved in many functions including the regulation of the emotional processes. Serotonin neurons of the dorsal raphe nucleus that are projected in the anterior brain are self-active and are released according to a stereotype model that changes during the circadian cycle. Due to their distribution, it was suggested that the serotonergic system is involved in the majority of the brain functions, such as the regulation of the neuron-endocrine secretion, cardiovascular regulation and respiratory activity, sleep, analgesics and motor efficiency.

Low activity serotonin (low brain levels of 5-HT) has negative effects on the emotional status. Stress increases the levels of 5-HT and of metabolites in several brain regions inducing the growth of the turnover rate of the neurotransmitter, although serotonin neurons of the dorsal raphe nucleus are not altered during stress. Stress induces changes in those regions of the brain that are targets of the serotonin neurons, so that repeated exposure of mice to forced swimming increases the concentrations of 5-HT in striatum. Through chronic immobilization in mice, stress may accelerate the 5-HT turnover in the hippocampus and produces low amounts of monoamine (Torres et al.)

More than 14 serotonin receptors are known to mediate the effects of 5-HT (Aghajanian et al.)

The most researched receptor is 5-HT<sub>1A</sub>, which regulates the release of 5-HT. 5-HT<sub>1A</sub> postsynaptic receptors regulate the activity of the neurons in the cortical areas, limbic areas and other areas. For example, they affect the activity of the pyramidal neurons in the hippocampus. 5-HT<sub>1A</sub> receptors like other subtypes are involved in mood and emotional behaviour regulation and there is evidence that these receptors dysfunction is involved in depressive disorders.

Restraint stress decreases the number of 5-HT<sub>1A</sub>

receptor in the hippocampus of mice and this effect was attributed to the stress-induced increase of plasma glucocorticoids, adrenaline hormones that modulate the transcription of several genes (Datson et al.)

Stress-induced decrease in the number of the postsynaptic 5-HT1A receptor in distinct cortical areas and in hippocampus could also be assigned to high levels of glucocorticoids but also to low testosterone.

Social stress in male, regarding the animal studies, decreases testosterone levels and it was observed a return to the normal number of the 5-HT1A-receptor, through testosterone substitution.

### **Stress and dopamine neurons activity**

Dopamine neurons are located in the median brain, hypothalamus and other regions. Mesolimbic-mesocortical dopamine systems, which start in the anterior tegmental area, are involved in the emotional and memory processes. On the other hand, substantia nigra dopamine neurons and the median cerebral tegument are projected towards the telencephalon, including the striatum, forming the nigrostriatal pathway, which initiates the motor responses.

The experiments made on animals revealed that under the strain of a limited space, an increase release of mesolimbic dopamine occurred, followed by a decline, suggesting that such repeated exposure to this kind of stress brought about the inhibition of the dopamine neurons rather than their activation.

Mesocortical dopamine system is obviously more sensitive to stress than the mesolimbic and nigrostriate systems. So far, five distinct dopamine receptors have been inquired, but with no accurate prediction regarding their presynaptic or postsynaptic location. Still, there are indications that show that D1 and D5 receptors are located postsynaptically, while the D2, D3 and D4 receptors are located pre- and postsynaptically, those presynaptic acting as inhibitory auto-receptors. (Vallon et al.)

### **BIBLIOGRAPHY**

21. Aghajanian GK, Sanders-Bush E. Serotonin: In Davis KL, Charney D, Coyle JT, Nemeroff C. eds. Neuropsychopharmacology the Fifth Generation of Progress. Philadelphia, Pa: Lippincott Williams and Wilkins; 2002:15-34.
22. Datson NA, van der Perk J, de Kloet ER, Vreugdenhil E. Identification of corticosteroid responsive genes in rat hippocampus using serial analysis of gene expression. *Eur J Neurosci* 2001;(14):675-689.
23. Duman RS. Neural plasticity: consequences of stress and actions of antidepressant treatment. *Dialogues Clin Neurosci* 2004;(6):157-169.
24. Squire LR, Bloom FE, Mc Connell SK, Roberts JL, Spitzer NC, Zigmond MJ. *Fundamental Neuroscience*. New York, NY: Academic Press; 2003.
25. Sheline YI. Neuroimaging studies of mood disorder effects on the brain. *Biol Psychiat* 2003;(54):338-

352.

26. Torres IL, Gamaro GD, Vasconcellos AP, Silveira R, Dalmaz C. Effects of chronic restraint stress on feeding behaviour and on monoamine levels in different brain structures in rats. *Neurochem Res* 2002;(27):519-525.
27. Vallone D, Picetti R, Borrelli E. Structure and function of dopamine receptors. *Neurosci Biobehav Rev* 2000;(24):125-132.