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Brain Plasticity and Behavioral and Cognitive Changes in Heart Failure

Parent MB, Ferreira-Neto HC, Kruemmel AR, Althammer F, Patel AA, Keo S, Whitley KE, Cox DN, Stern JE. Heart failure impairs mood and memory in male rats and down-regulates the expression of numerous genes important for synaptic plasticity in related brain regions. **Behav Brain Res. 2021;414:113452. https//:orcid.org/10.1016/j.bbr.2021.113452.**

The association between heart failure comorbidities and cognitive and behavioral disorders has been shown both in humans as in experimental animals. Neurocognitive impairment, including learning and working memory deficits, depression and anxiety, has been correlated with loss of brain grey matter and injury in relevant areas for cognitive functioning, such as the amygdala, hippocampus and prefrontal cortex. However, there is little information on the mechanisms by which heart failure can lead to cognitive and mood impairment.

In this very good work, using a rat model of chronic heart failure with severely reduced ejection fraction, Parent et al. studied changes in the expression of genetic and molecular markers of neuronal plasticity in brain areas critical for cognitive and affective functioning. After four-week anterior descending artery occlusion by ligation, all animals underwent an echocardiogram, and those with ejection fraction below 40% were selected for behavioral studies, carried out between 5 and 10 weeks of evolution. Infarcted rats showed anhedonia, anxiety behavior, learning abnormalities and disruption in spatial and emotional working memory. Brain tissue PCR studies showed that heart failure decreased the regional expression of numerous genes involved in neuronal plasticity. The most significant changes were observed in the prefrontal cortex and the paraventricular nucleus of the hypothalamus, moderate changes in the dorsal hippocampus and central portion of the amygdala, and minimal changes in the ventral and basolateral hippocampus.

There is a well-established relationship between cardiovascular diseases and disturbances in normal brain functioning. Patients with depressive or anxiety disorders are at greater cardiovascular risk and, in turn, those suffering from cardiac diseases have greater prevalence of depression and/or higher cerebral function involvement. This reminds us once again of the close bidirectional interrelationship between the brain and the heart. Different cardiac neuroaxis mechanism disorders have been pointed out as responsible for these conditions, such as autonomous nervous system imbalance, inflammatory stress, hypoxic/ischemic injury and cerebral hypoflow, neurohumoral changes and modifications in afferent nervous impulses that regulate the activity of a hemodynamically altered heart. Other not less important aspects affecting these patients, but more complex to assess in experimental animals, are the subjective components of introspection and consciousness of disease and life finitude in the context of diseases perceived as life-threatening, in addition to the influence of the environment and other psychosocial variables.

Specifically in heart failure, it is relevant to identify the brain structures and the neurobiological mechanisms that underlie behavioral and cognitive disorders in the search for therapeutic options. In this sense, Parent et al. make a significant contribution to the knowledge of neuronal networks that are affected in critical encephalic regions involved in mood and memory disorders in heart failure.

Finding new treatments to prevent or improve the neurological symptoms of patients with heart failure will certainly have a high social and economic impact by improving the prognosis and quality of life of millions of people around the world. Bad life habits and population ageing will increase this impact even more in the next decades.