Cardiac dysfunction caused by brain injury can lead to potentially long-lasting cardiac complications. The main causes of neurogenic stress cardiomyopathy are subarachnoid hemorrhage (SAH), traumatic brain injury (TBI), hemorrhagic and ischemic stroke, central nervous system (CNS) infections, and epilepsy. Stroke is a good model to study neuro-cardiac influences because the location of the lesion can be precisely identified. In this review article, the authors from Switzerland discussed the pathophysiology of neurogenic cardiac injury and cardiac dysfunction in stroke. They described the brain-heart axis and highlighted the main pathophysiological mechanisms of stroke-heart interactions.

Brain-heart interaction

For many decades, animal or clinical studies have shown that the brain influences cardiac structure and function. Data from historical sources, such as the study by Beattie et al. (1930) demonstrated that chloroform-induced ventricular tachyarrhythmia was abolished by the mid-collicular, but not higher, diencephalic section. Later, in 1960 the scientists reported intriguing changes in the electrocardiogram (ECG) after SAH.

The anatomical structures involved in cardiac regulation extend from the spinal cord to the cerebral cortex. The CNS directly affects cardiac function *via* sympathetic and parasympathetic efferents from the brainstem cardio-regulatory centers.

According to neuroimaging and electrophysiological studies, the insula, an anatomical structure in the temporal lobe, plays a cardinal role in autonomic nervous system regulation at the cortical level. The lesions of the CNS, particularly the insular cortex, can change the balance of sympathetic and parasympathetic tone, increase plasma catecholamine concentrations, cause myocardial damage, and increase the incidence of cardiac arrhythmias. The right insula is considered the center of sympathetic autonomic control, while the left insula is considered the center of parasympathetic autonomic control.

The pathophysiology of neurogenic cardiac injury

Acute brain injury can induce cardiac dysfunction in the absence of cardiac disease. Factors that could explain this relationship include hemodynamic disorders and subsequent cerebral hypoperfusion, development of secondary cerebral cardioembolic complications, disturbances of oxygenation, neurohormonal mechanisms, systemic and cerebral inflammation, disruption of the blood-brain barrier (BBB), and activation of glial cells.

The most prevailing theory is that sympathetic hyperstimulation, due to physical or emotional triggers, leads to direct catecholamine toxicity, epicardial and microvascular coronary vasoconstriction, and adrenoreceptor-mediated damage. At the cellular level, the local action of catecholamines leads to changes in calcium homeostasis and β-adrenergic signal transduction, resulting in coronary microcirculation impairment.

In contrast to the acute inflammatory response which develops within hours to a few days after brain injury, a detailed analysis of the chronically compromised systemic immune response is still missing, and the underlying mechanisms are largely unknown. The systemic inflammation and the excessive release of interleukin (IL)-1 seem to play an important role in the development of neurogenic stress cardiomyopathy. A recent study revealed that stroke triggers persistent inflammation in multiple organs by inducing innate immune memory. Specifically, it has been discovered that IL-1β-mediated epigenetic changes in the myeloid compartment play a role in cardiac fibrosis, leading to diastolic dysfunction

following ischemic brain injury. https://doi.org/10.1016/j.cell.2024.06.028

Clinical presentations of neurogenic stress cardiomyopathy

Cardiac manifestations after neurological pathologies are highly variable and associated with electrocardiographic (ECG) and echocardiographic findings. The clinical spectrum of cardiac dysfunction in patients with acute ischemic stroke includes myocardial injury, cardiac troponin elevation, heart failure, arrhythmias, and sudden cardiac death.

Acute ECG changes are more frequently found in cases of intracerebral hemorrhage or SAH than in cases of acute ischemic stroke. The two major categories of ECG changes during neurogenic heart disease are dysrhythmias (e.g., atrial and ventricular tachyarrhythmias, sinus bradycardia, and tachycardia) and repolarization changes mostly found in the anterolateral and inferolateral leads. In patients with neurogenic stress cardiomyopathy, the most frequent ECG findings are prolongation of the QT-interval and T-wave inversion. The most frequent echocardiographic findings are abnormalities in the left ventricular wall motion.

Cardiac systolic impairment is not uncommon after a severe neurologic injury. Previous studies in mice have demonstrated that stroke results in chronic systolic dysfunction lasting up to 8 weeks after the brain injury, leading to a delayed reduction in left ventricular ejection fraction and an increase in left ventricular volume.

In patients with SAH, the incidence of cardiac dysfunction, if ECG criteria are used, is 100%. If echocardiographic criteria are used, 10%–15% of patients develop global systolic dysfunction with a left ventricular ejection fraction lower than 50%, while almost 30% of patients present abnormalities in wall motion. After a stroke, more than 60% of patients experience ECG abnormalities, 25% are diagnosed with serious arrhythmias, and approximately 19% develop at least one significant cardiac adverse event. Cardiac systolic impairment occurs in 13% to 29% of patients with ischemic stroke and 22% of patients with TBI.

The coexistence of "heart and brain failure" following a heart disease

As the brain-heart axis is bidirectional, brain complications may be the consequence of cardiac dysfunction. They are related to cerebral hypoperfusion, oxygenation disturbance, activation of the hypothalamic-pituitary-adrenal axis, and systemic inflammation. The term "cardiogenic dementia" has been used to describe the coexistence of "heart and brain failure" following a heart disease.

Concerning clinical management and therapeutic implications, the authors concluded that therapeutic management of neurogenic cardiac dysfunction is conservative. The emphasis is on cardiac function improvement, adequate oxygenation, prevention of further neuroinflammation, and maintenance of cerebral homeostasis and perfusion pressure.

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