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## **Autonomic dysregulation**

Autonomic dysregulation refers to dysfunction or impairment of the autonomic nervous system (ANS), which is responsible for regulating many involuntary bodily functions, such as heart rate, blood pressure, digestion, respiratory rate, and body temperature. The autonomic nervous system has two main components:

Sympathetic Nervous System (SNS): The sympathetic nervous system is often referred to as the "fight or flight" system. It prepares the body for action in response to stress or perceived threats. It increases heart rate, dilates the pupils, constricts blood vessels, and redirects blood flow to muscles to prepare the body for a rapid response.

Parasympathetic Nervous System (PNS): The parasympathetic nervous system is often called the "rest and digest" system. It works to counterbalance the sympathetic system, promoting relaxation and recovery. It slows heart rate, constricts the pupils, stimulates digestion, and promotes relaxation.

Autonomic dysregulation can occur when there is a disruption in the balance between the sympathetic and parasympathetic systems or when either system is overactive or underactive. This can result in a wide range of symptoms and health issues, including:

Orthostatic Intolerance: This condition involves difficulty maintaining blood pressure and heart rate when transitioning from lying down to standing up. It can lead to dizziness, lightheadedness, and fainting (syncope).

Cardiovascular Symptoms: Dysregulation of the autonomic nervous system can lead to fluctuations in blood pressure and heart rate, causing symptoms such as palpitations, rapid heart rate (tachycardia), and fluctuations in blood pressure.

Gastrointestinal Issues: Autonomic dysregulation can affect digestion, leading to symptoms like constipation, diarrhea, or difficulty swallowing.

Temperature Regulation: Dysregulation can impact the body's ability to regulate temperature, causing symptoms such as excessive sweating (hyperhidrosis) or an inability to tolerate temperature changes.

Respiratory Problems: Autonomic dysfunction can affect breathing patterns, leading to rapid or shallow breathing, especially during periods of stress.

Urinary Symptoms: It may result in difficulty controlling urination, urinary retention, or frequent urination.

Sleep Disturbances: Autonomic dysregulation can disrupt sleep patterns, leading to insomnia or poorquality sleep.

Pupillary Abnormalities: Dysregulation can also lead to changes in pupil size and reactivity.

The causes of autonomic dysregulation can vary and may include neurological conditions, autoimmune disorders, certain medications, and genetic factors. Diagnosing and managing autonomic dysregulation can be complex, often requiring specialized testing and the involvement of neurologists or other healthcare specialists.

Treatment options for autonomic dysregulation aim to alleviate symptoms and improve overall quality of life. These may include lifestyle modifications, medications to stabilize blood pressure or heart rate, physical therapy, and specific interventions to address underlying causes. Management often requires an individualized approach tailored to the patient's specific symptoms and needs.

Mitigation of cardiac autonomic dysregulation by neuromodulation technologies is emerging as a new therapeutic modality of heart failure (HF). This progress has necessitated the identification of a biomarker for the quantification of sympathovagal balance, the potential target of 'neuromodulation' strategies. The currently available autonomic nervous system assessment parameters do not truly reflect the sympathovagal balance of the ventricle. Protein kinase A (PKA) is an intracellular enzyme that plays a major role in the pathophysiology of functional and structural ventricular remodeling in HF. Interestingly, sympathetic and parasympathetic activations exert reciprocal influence on the activity of PKA <sup>1)</sup>.

1

Chakraborty P, Po SS, Yabluchanskiy A, Dasari TW. Protein kinase A: A potential marker of sympathovagal imbalance in heart failure. Life Sci. 2023 Sep 2:122069. doi: 10.1016/j.lfs.2023.122069. Epub ahead of print. PMID: 37666387.

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