ARRHYTHMOGENIC ROLE OF THE AUTONOMIC NERVOUS SYSTEM

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Annotation: This thesis explores the role of the autonomic nervous system in cardiac arrhythmias, highlighting classical and novel mechanisms, neuro-cardiac modulation, and the dualistic nature of the neuro-cardiac axis in arrhythmogenesis**.**

Keywords: Autonomic nervous system, cardiac arrhythmias, neuro-cardiac axis, sympathetic activation, parasympathetic tone, arrhythmogenesis, ventricular fibrillation, atrial fibrillation, intrinsic cardiac nervous system.

Excessive sympathetic activation has been linked to ventricular arrhythmias and sudden cardiac death, while heightened parasympathetic activity has been implicated in atrial fibrillation (AT) [1,2]. Despite the traditional view that the ANS serves as a protective and adaptive system, new facts able to suggest that the neuro-cardiac axis may cause more negative effects than be friendly in certain pathological conditions [3].

Objective: to explore the relationship between the ANS and cardiac arrhythmias, focusing on the mechanisms of autonomic dysfunction and its role in specific arrhythmias.

A well-balanced sympatho-vagal interaction ensures adaptive responses to physiological stressors. A shift towards sympathetic dominance is associated with increased risk of ventricular arrhythmias and sudden cardiac death. A dominant parasympathetic tone generally exerts a protective effect, reducing the likelihood of malignant arrhythmias [5].

The heart possesses a network of epicardial ganglia and intrinsic cardiac

neurons that modulate local electrophysiological activity, including changes in ganglionic density, receptor expression, and neurotransmitter balance, in response to chronic stress, myocardial infarction, or inflammation. These alterations can create localized areas of autonomic imbalance, increasing arrhythmic susceptibility, particularly in the atria. [3] Following myocardial injury or repeated adrenergic stimulation, autonomic pathways may become sensitized, leading to increased neural firing, enhanced reflex responses, and ectopic activity. This neural plasticity – particularly in sympathetic stellate ganglia and intrinsic cardiac neurons – amplifies arrhythmic potential by promoting triggered activity and shortening refractory periods. [3] Through cytokine release and regulation of neurotransmitter reuptake, autonomic ganglia glial cells may influence ganglionic excitability and contribute to sustained arrhythmic substrates under chronic stress or disease conditions [5, 6]

Pro-inflammatory cytokines such as IL-6 and TNF-α can modulate autonomic tone by altering central and peripheral neuronal excitability. Conversely, vagal activity exerts anti-inflammatory effects via cholinergic signaling. Dysregulation of this axis during systemic inflammation contributes to electrical instability and may trigger both atrial and ventricular arrhythmias. [7]

Besides classical neurotransmitters, additional substances play a role in cardiac rhythm regulation:

- Neuropeptide Y (NPY): Released in sympathetic neurons; enhances sympathetic stimulation and reduces vagal inhibition. High NPY levels correlate with an increased incidence of ventricular arrhythmias and VF during myocardial ischemia.

- Galanin: Regulates cardiac tone by reducing parasympathetic activity. Increases during acute myocardial injury, leading to reduced vagal inhibition and a higher arrhythmic potential.

- Adenosine Triphosphate (ATP): Acts as an agonist for both sympathetic and parasympathetic receptors. Affects calcium channels, which can contribute to arrhythmias [3, 8 ,9].

Vagal overactivity can trigger AF episodes, particularly at night, after eating,

or during relaxation. The shortening of the atrial effective refractory period makes reentry more likely. Vagotonic AF is common in endurance athletes due to chronic high vagal tone [4, 5, 6]. Excessive vagal activation leads to profound bradycardia, sinus pauses, and even transient asystole. Triggers include: prolonged standing, emotional distress, pain, gastrointestinal stimulation [5]. SNS overactivity is strongly associated with ventricular fibrillation (VF), particularly in patients with structural heart disease, myocardial infarction, or heart failure. SNS triggers both automatic and reentrant arrhythmias, leading to electrical instability [1, 5]. Increased SNS activity promotes AF, especially in response to stress, exercise, or acute illness. The mechanism involves shortening of the refractory period, increased automaticity, and enhanced triggered activity [5]. SNS overactivity can induce atrial tachycardia, atrioventricular nodal reentrant tachycardia, and atrioventricular reentrant tachycardia. These tachycardias often appear during exercise, emotional stress, or catecholamine infusion [5]. SNS activation enhances conduction through accessory pathways, increasing the risk of rapid atrial fibrillation degenerating into VF and sudden cardiac death [3, 5]. Long QT Syndrome (LQT)-1 patients are prone to arrhythmias during exercise, while LQT-2 patients experience arrhythmias due to emotional stress or auditory stimuli (e.g., alarm sounds). Catecholaminergic Polymorphic Ventricular Tachycardia is an arrhythmogenic disorder triggered by SNS activation, often occurring in young individuals during physical activity or stress [5]. Acute ischemia exacerbates SNS activation, leading to ventricular tachycardia, VF, and electrical storm. Local norepinephrine release contributes to myocardial damage and increases susceptibility to VF [3, 5].

Conclusion: the autonomic nervous system plays a dual role in cardiac function, acting as both a regulator of normal rhythm and a contributor to arrhythmogenesis when its balance is disrupted. Understanding these mechanisms is crucial for developing effective therapeutic strategies.

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