

Dynamic Assessment of the Autonomic Nervous System Activity in Patients with Paroxysmal Atrial Fibrillation

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The long-term goal of this program is to develop quantitative tools for dynamic assessment of autonomic nervous system activity (ANSA), specifically its cardiovascular effects. Although various indices of heart rate variability (HRV) have long been used for general assessment of ANSA, methods for dynamic analysis are lacking. At present, no method has been developed for tracking instabilities or extreme fluctuations of ANSA that may lead to life-threatening cardiac arrhythmias and sudden death. The project will focus on the validation of recently developed quantitative technique for tracking the changes in ANSA, referred to as Modified Karhunen-Loeve transform (MKLT). Using MKLT, the PI and colleagues showed that multidimensional disturbances of cardiac rhythm (MDCR) predicted spontaneous initiation of ventricular tachyarrhythmias (VTA) and atrial fibrillation (AF). Because ANSA is known to play a major role in the modulation of cardiac rhythm and because changes in ANSA are known to participate in arrhythmogenesis, we hypothesized that MDCR indicates pronounced instabilities of ANSA that predispose to the initiation of spontaneous arrhythmias. As a model of spontaneous arrhythmias, we will focus on paroxysmal AF whose initiation is known to have a strong relationship to the changes in ANSA. We will examine MDCR that arise during pharmacological maneuvers that affect ANSA. These will include stimulation of beta1-adrenergic receptors of the heart with dobutamine, beta-adrenergic blockage with propranolol and parasympathetic blockage with atropine. At the next step, we will compare MDCR that arise during pharmacological tests with spontaneous MDCR that precede initiation of paroxysmal AF in the same patient population. The patients will undergo 72-hour ambulatory (Holter) ECG monitoring in the antiarrhythmic drug-free state. In addition, we will examine the effects of clinical data, including age, sex, LVEF and presence of structural heart disease on the manifestations of MDCR. We will also compare MDCR, as detected by MKLT, with the traditional time and frequency domain HRV-indices. The results will yield a critical examination of the utility of MDCR for signaling pronounced instabilities in ANSA which might predispose to the initiation of spontaneous cardiac arrhythmias.