The role of vagal function in the risk for cardiovascular disease and mortality

Abstract

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide. The understanding of the risk factors for CVD may yield important insights into the prevention, etiology, course, and treatment of this major public health concern. We review the evidence for the role of vagal function in the risk for cardiovascular disease and mortality. Using a broad range of indicators of vagal function including resting heart rate, heart rate recovery, heart rate variability, and baroreflex sensitivity we show that decreased vagal function is associated with an increased risk for morbidity and mortality. These effects are independent of traditional risk factors. Moreover, we show that decreased vagal function is associated with both traditional and emerging risk factors as well as modifiable and non-modifiable risk factors. Most importantly, we provide evidence to support the notion that decreased vagal function precedes the development of a number of risk factors and that modification of risk profiles in the direction of lower risk is associated with increased vagal function. We close with a brief overview of the neural concomitants of vagal function and suggest that a model of neurovisceral integration may provide a unifying framework within which to investigate the impact of risk factors, including psychosocial factors, on cardiovascular disease.

Keywords

Cardiac vagal control; Cardiac vagal tone; Heart rate variability; Risk factors; Heart disease; Hypertension

Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality, in both men and women. This is particularly true for the developed countries (Murray and Lopez, 1996, Yusuf et al., 2001). A wide range of risk factors for cardiovascular disease have been identified but as yet a unified model that can account for this diversity of risk factors has not been put forward. The important role that the vagus nerve plays in health and disease has been known for some time (Darwin, 1998). However, only relatively recently have researchers and clinicians started to investigate how this knowledge can be incorporated into a greater understanding of the etiology, manifestations, course, outcomes, and treatment of disease.

Here we review some of the evidence linking vagal function to cardiovascular disease and mortality. We show that autonomic imbalance in which vagal inhibitory influences are deficient is associated with increased morbidity and all-cause mortality. Importantly we show that all of the established and emerging risk factors for CVD are associated with decreased vagal function. We then show that this autonomic imbalance may be due to decreased prefrontal inhibitory control over sympathoexcitatory circuits in the brainstem. This model of neurovisceral integration may provide a unified approach to the understanding of the role of vagal function in the risk for cardiovascular disease and all-cause mortality.

Section snippets

Autonomic imbalance and disease

There is growing evidence for the role of the autonomic nervous system (ANS) in a wide range of diseases. The ANS is generally conceived to have two major branches—the sympathetic system, associated with energy mobilization, and the parasympathetic system, associated with vegetative and restorative functions. Normally, the activity of these branches is in dynamic balance. For example, there is a well-documented circadian rhythm such that sympathetic activity is higher during daytime hours and …

Decreased vagal activity and morbidity and mortality

There are multiple measures that can be used to index activity of the vagus nerve. Resting HR, by virtue of being under tonic inhibitory control via the vagus, is a

simple, inexpensive, and non-invasive measure of vagal function. The HR change following cessation of exercise is another measure that has been used to characterize vagal function. The decrease in HR after termination of exercise has been termed HR recovery and standardized methods have been developed for its assessment. Measures of …

Vagal function and the etiology and progression of CVD risk

The evidence for an association between reduced vagal function and mortality appears to be quite strong. Most of these studies examined the association after controlling for other known risk factors such as diabetes and hypertension. However there is also evidence to suggest that reduced vagal function leads to such risk factors. Thus, those studies that control for those known risk factors for which there exists evidence that reduced vagal function might lead to those risk factors may in fact …

Emerging risk factors: inflammation and psychosocial factors

Inflammation is now thought to play a major role in cardiovascular disease (Ridker, 2001). Importantly, evidence linking decreased vagal function with increased inflammation is quickly accumulating. Tracey (2002) has described the cholinergic anti-inflammatory pathway in which acetylcholine and vagal function tonically inhibits release of proinflammatory cytokines. Clinical evidence in humans is just now starting to become available. In a study of 121 women with coronary heart disease, 24h …

Neural correlates of vagal function

It is important to appreciate the role that the brain serves in regulation of the autonomic nervous system. As such, any review of the role of vagal function and morbidity and mortality would be incomplete without some discussion of the neural correlates of autonomic control and vagal function.

A number of researchers have identified functional units within the central nervous system (CNS) that are involved in autonomic regulation. One such functional unit is the central autonomic network (CAN; …

Summary

In this paper, we have tried to provide an overview of the evidence for the role of vagal function in cardiovascular disease risk and mortality. We showed that there is a large body of data to suggest that decreased vagal function is an independent risk factor for all-cause mortality. In addition, we showed that decreased vagal function is a common factor in all of the major risk factors for CVD both modifiable and non-modifiable. Furthermore, we showed that decreased vagal function …

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