Autonomic Nerve System and Immune Functions in Cardiovascular Disease

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ABBREVIATIONS

ANS: Autonomic Nerve System (ANS); DAMPs: Damage Associated Molecular Patterns; IL-1β: Interleukine 1β; IR: Ischemia Reperfusion; MI: Myocardial Infarction; PAMPs: Pathogen Associated Molecular Patterns; ROS: Reactive Oxygen Species; TNFα: Tumor Necrosis Factor alpha; VNS: Vagus Nerve Stimulation

INTRODUCTION

In daily life, immune functions keep the body healthy by protecting it from potential injury caused by threats from outside, physical forces or exhaustion. Therefore, it is involved in recognizing and fighting pathogen associated molecular patterns (PAMPs) from the external environment and damage associated molecular patterns (DAMPs) from injured tissue inside the body [1]. But it is also involved in repairing damaged tissue and restoring organ function [2,3]. In a healthy physical situation, immune functions are necessarily well balanced. Too high activity can lead to unnecessary inflammatory harm while under performance may open the way for illness caused by the presence of malfunctioning cells [4,5]. Health as such, is dependent on a well-regulated immune system. Today, the autonomic nerve system (ANS) is emerging as the major regulator of immune function [5-7]. In the ANS, the sympathetic branch is associated with pro-inflammatory activity while the parasympathetic part is considered anti-inflammatory. In the last two decades, research yielded a serious amount of proof that electrical stimulation of the vagus nerve (VNS) causes attenuation of inflammatory responsiveness. Today VNS is, in some cases still experimentally, used as a treatment for inflammation associated ailments like rheumatoid arthritis, inflammatory bowel disease and heart failure [8-10].

In literature, the connection of autonomic innervations with inflammatory processes in atherosclerosis and chronic heart disease was already made some time ago [11]. However, merely the same inflammatory cytokines like IL-1β, IL6 and TNFα, are involved in cardiovascular disease as well as in the VNS treated ailments and, in some VNS studies, in experimentally induced sepsis. Recent studies report attenuation of inflammatory cytokine release and therefore better outcome after experimental myocardial ischemia-reperfusion in rat and pig models [12-15]. Still, relevant data in humans and mice are scarce.

CONCLUSIONS AND DISCUSSION

Inflammatory response is activated upon an initial injury in the arterial wall caused by factors such as reactive oxygen species (ROS), hypertension or an external force. Although a possible causality is still unclear, our hypothesis is that inflammatory activity stimulates nerve growth towards the affected area to support the ongoing process. Normally when tissue homeostasis is restored, inflammatory activity as well as local innervation will return to healthy levels but in some cases collateral damage and production of debris will stimulate the continuation of this complex process, leading to unnecessary tissue damage and, eventually, to disease.

The use of an implantable stimulator will help to assess the effects of long term stress-free vagal stimulation in a laboratory animal model. We hypothesize that development of tissue damage, caused by persistent excessive inflammation, will be far less in vagus stimulated, and therefore inflammatory attenuated, animals. Obviously, a number of steps are still to be examined.

Since two decades, the interaction between the autonomic nerve system and inflammatory processes is gaining increasing interest worldwide. More studies on this topic will expand our understanding of the processes involved. It may eventually provide new means for clinical intervention in inflammation related disease.

REFERENCES


