【Grant-in-Aid for Scientific Research(S)】
Integrated Science and Innovative Science (Comprehensive fields)

Title of Project : Explorations into development of autonomic neuromodulation system to treat refractory heart failure

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Research Area : Comprehensive Fields
Keyword : Neuromodulation, Treatment, Autonomic regulation, Cardiovascular regulation

【Purpose and Background of the Research】

Despite major progresses in latest medicine, cardiovascular diseases remain the number one killer of human. Among them, heart failure (HF), the common final stage of every cardiovascular disease, has unacceptably poor prognosis (5 year survival <50%). There is an urgent need to promote medical science to save those patients.

Thanks to extensive investigations on HF, it has been well established that cardiovascular dysregulation plays a central role in the pathogenesis of HF. HF induced metabolic as well as hemodynamic disturbances excessively activate the regulatory system and worsen HF. Since the most powerful regulatory mechanism is the autonomic nervous system (ANS) and conventional treatments cannot totally control ANS, we developed an intelligent mechanism that electrically controls ANS by feedback regulation of the afferent autonomic nerves. We called such artificial systems integrated with physiological systems as *bionic systems*. The purpose of this investigation is to develop bionic systems to treat refractory HF.

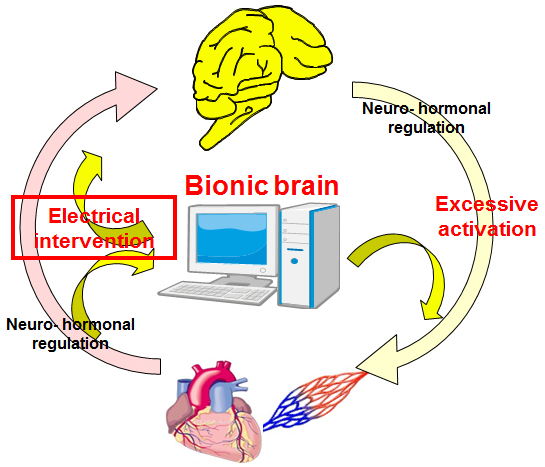

Fig.1 Schematic diagram of bionic system. See text for details.

【Research Methods】

Recent investigation indicated that systolic dysfunction accounts only for 50% of HF. The rest of patients have well preserved systolic function. We will develop bionic systems that are tailored for specific pathophysiology.

1. HF with impaired systolic function: In animal models, we will develop a bionic system that modulates the afferent baroreceptor nerve to deactivate sympathetic tone and activate vagal tone. We will evaluate its impact in terms of cardiac function and survival.
2. HF with preserved systolic function does not have effective treatments. Patients are known to be old, women and hypertensive and intolerant to volume overload. We hypothesized that atherosclerosis induced baroreflex failure plays a significant role in this pathophysiology. We will develop a bionic system to restore normal baroreflex function.

【Expected Research Achievements and Scientific Significance】

Most of the anti-HF agents work by intervening in the regulatory system. Their impact on survival, however, remains limited. In this investigation, we will electrically stimulate the afferent ANS to optimally regulate the systemic ANS. Electrical regulation of ANS could immediately adapt to incessantly changing physiological conditions. Therefore, it would have more powerful therapeutic impacts on HF than conventional treatments.

【Publications Relevant to the Project】

Sugimachi M, Sunagawa K. Bionic cardiology: exploration into a wealth of controllable body parts in the cardiovascular system. IEEE Rev Biomed Eng. 2: 172-186, 2009.

Li M, Zheng C, Sato T, Kawada T, Sugimachi M, Sunagawa K. Vagal nerve stimulation markedly improves long-term survival after chronic heart failure in rats. Circulation. 2004;109(1):120-4.

【Term of Project】 FY2011-2015

【Budget Allocation】 165,200 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.med.kyushu-u.ac.jp/cardiol/research_units/baio/index.html