Chapter 9
Autonomic Cardiovascular Regulation in the Newborn

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ABSTRACT

This paper reviews the baroreflex mediated heart rate response in human infants with a focus on data acquisition, signal processing and autonomic cardiovascular modeling. Baroreflex mediated heart rate response is frequently used as an estimate of autonomic cardiovascular regulation. Baroreflex mediated heart rate response may be viewed in terms of a negative-feedback system. To study fluctuations in this feedback system, continuous registration of ECG and blood pressure waveforms are required. From these waveforms, time series of R-R interval and blood pressure values are derived. This paper focus on spontaneous baroreflex sensitivity (e.g., R-R interval change per unit of arterial blood pressure change, ms/mmHg) calculated from cross-spectral analysis of spontaneous occurring changes in R-R interval and blood pressure. Despite different methodology (sequence method; transfer function analysis; head-up tilt) there is fairly good agreement of spontaneous baroreflex sensitivity values during homeostasis. Preterm infants and term newborns have values of 2-4 and 10-15 ms/mmHg, respectively. These values are much lower than found in adults, approximately 25 ms/mmHg. The clinical relevance of a limited baroreflex function may be that acute perturbations of the cardiovascular system are poorly counteracted and may result in poor cerebral perfusion.

INTRODUCTION

Preterm infants face an increased risk of mental or motor disabilities, which are related to cerebral hemorrhage or ischemia. Approximately 20-25% of preterm infants below 32 weeks of gestation have cerebral hemorrhage (McCrea & Ment, 2008). The etiology of cerebral hemorrhage is complex. Although numerous perinatal factors (gestational age; maternal infection; antenatal administration of steroids; respiratory distress syndrome etc.; severity of illness) are associated with brain lesions, cerebral hemorrhage has generally been attributed to alterations in cerebral blood flow

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to the immature germinal matrix microvasculature (Inder & Volpe, 2004). Adequate cerebrovascular autoregulation is found in clinically stable preterm infants and a pressure-passive cerebral perfusion is present in sick preterm infants who develop subsequently intraventricular hemorrhage (Pryds & Edwards, 1996). Significant fluctuations in cerebral blood flow appear important in the pathogenesis of cerebral hemorrhage and may be related to an impaired blood pressure control mechanism (Liem & Greisen, 2010; Borch, Lou, & Greisen, 2010).

The baroreflex buffers sudden changes in systemic blood pressure by adapting heart rate, vascular resistance and myocardial contraction. This control of blood pressure is achieved by regulatory adjustments initiated by a change in the pressure load at specialized pressure sensors located at the aortic arch and the carotid sinuses. Heart rate responses are mediated by both parasympathetic and sympathetic efferent nerve activity, whereas vascular resistance and myocardial contraction are adapted by sympathetic nerves primarily.

The importance of the baroreflex is to stabilize perfusion pressure in the face of disturbances of circulatory homeostasis. In preterm infants, the disturbances of circulatory homeostasis may be due to perinatal transition (*e.g.,* changes in circulatory volume), illness (*e.g.,* sepsis) or intensive care management (*e.g.,* artificial ventilation). Because vascular resistance and myocardial contraction are difficult to measure in human infants, autonomic changes related to baroreflex control are usually studied by evaluating heart rate and blood pressure fluctuations only (Stauss, 2002). Spectral analysis offers the opportunity to decompose spontaneously occurring fluctuations in blood pressure and heart rate into a power spectrum, and to relate the character of the fluctuations to physiological processes. Low frequency cardiovascular fluctuations of approximately 0.1 Hz in human adults are ascribed to the baroreflex activity and presumed to be under sympathetic and parasympathetic control, whereas high frequent fluctuations are associated with respiratory activity (respiratory sinus arrhythmia) and are under parasympathetic control only (Task Force, 1996).

This paper reviews the baroreflex mediated heart rate response in human preterm infants with a focus on medical signal processing and autonomic cardiovascular modeling. Consecutively the following topics are discussed: background of autonomic cardiovascular reflex control of blood pressure; baroreflex as a closed loop control system; spectral analysis of baroreflex mediated heart rate control; methods exploring baroreflex mediated heart rate control and clinical data in infants.

BACKGROUND

The importance of cardiovascular reflex control is to supply appropriately oxygenated blood to the different tissues in the face of disturbances of circulatory homeostasis (Timmers, Wieling, Karemaker, & Lenders, 2003). The sensory monitoring for the circulatory homeostasis entails (1) mechanical information about pressure in the arterial system and (2) chemical information about the level of oxygen and carbon dioxide in the blood. After integration in the brainstem efferent information is conveyed through the parasympathetic system and sympathetic system to the different effectors. Figure 1 shows a diagram of these neuronal pathways that are involved in autonomic cardiovascular regulation.

Baroreceptors are distension-activated mechanoreceptors which are located in the aorta and the carotid arteries. The nerve endings in the baroreceptors are activated as the elastic elements of the vessel wall expand or contract. The chemoreceptors are located in the carotid bodies at the bifurcation of the common carotid arteries and respond to the partial pressure of oxygen and carbon dioxide in the blood. In this chapter only baroreflex regulation will be discussed.

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