Identification of cortical and subcortical sites involved in the generation of muscle sympathetic nerve activity through MSNA-coupled fMRI

VG Macefield[1,2,3] & LA Henderson[4]
[1]College of Medicine, Mohammed Bin Rashid University of Medicine & Health Sciences, Dubai, UAE; [2]School of Medicine, University of Western Sydney; [3]Neuroscience Research Australia, Sydney; [4]Department of Anatomy & Histology, University of Sydney, Australia

We recently showed that it is possible to use intraneural microelectrodes to record muscle sympathetic nerve activity (MSNA) while performing functional magnetic resonance imaging (fMRI) of the brain; by correlating fluctuations in BOLD (Blood Oxygen Level Dependent) signal intensity within the brainstem with spontaneous fluctuations in MSNA we functionally identified the medullary nuclei involved in the spontaneous baroreflex modulation of MSNA. We have since gone on to identify suprabulbar areas within the brain that may contribute to the generation of spontaneous MSNA at rest. By taking advantage of the neurovascular coupling delay associated with BOLD fMRI, and the delay associated with conduction of a burst of MSNA to the peripheral recording site, we can identify structures in which BOLD signal intensity covaries with MSNA. A positive relationship between MSNA and BOLD signal intensity was found in the mid-insula and dorsomedial hypothalamus on the left side, and in dorsolateral prefrontal cortex, posterior cingulate cortex, precuneus, ventromedial hypothalamus and rostral ventrolateral medulla on both sides. Inverse relationships were observed between MSNA and BOLD signal intensity in the right ventral insula, nucleus tractus solitarius and caudal ventrolateral medulla. We have since applied MSNA-coupled fMRI to identify functional changes in the brain in patients with high levels of MSNA associated with obstructive sleep apnoea, before and after treatment, and to understand why MSNA increases or decreases during muscle pain. These results emphasize the extensive interactions between cortical and subcortical regions in the ongoing regulation of MSNA and hence blood pressure in awake human subjects.

Assessment of cardiac autonomic control by ambulatory electrocardiogram (ECG)

J. Hayano[a], E. Yuda[a], Y. Yoshida[a], E. Watanabe[b]
[a]Nagoya City University Graduate School of Medical Sciences, Japan
[b]Fujita Health University School of Medicine, Japan

R-R intervals of ECG show physiological fluctuations called heart rate variability (HRV). HRV originates in the brain and contains important information on the activity state of the autonomic nervous system that regulates the heart. Decreases in HRV and in its complexity observed in ambulatory ECG are known to be predictors of mortality risk including sudden cardiac death. Although these relationships have been explained by autonomic dysfunction, this explanation has obvious limitation since ambulatory HRV is affected by physical and mental activities and environmental factors. For example, ratio of low-frequency to high-frequency components (LF/HF) that has been used as a marker of sympathetic activity is *decreased* in cardiac patients with increased mortality risk in large-scale prospective studies. This may be explained by the fact that LF/HF in ambulatory ECG reduces with the proportion of time spent in laying position in the day. This limitation of HRV in ambulatory ECG may be overcome by the use of HRV for the assessment of autonomic responses to spontaneous stimuli. One of such approach is heart rate turbulence that assesses the baroreceptor reflex control of R-R interval to transient hypotension caused by spontaneous ventricular ectopic beats. Another one is the amplitude of cyclic variation of heart rate (Acv) that assesses tachycardia occurring at the end of sleep apnea. Reduction in Acv reflects the impairment of vagal reflex function and provides strong predictor of mortality risk in post-myocardial infarction, end-stage renal disease, and chronic heart failure patients.

Methodological Approaches to Assessment of Autonomic Control of Peripheral Circulation

J. K. Shoemaker
School of Kinesiology, Western University, London, ON N6A 3K7, Canada

In 1968, the first reported microneurographic recordings of muscle sympathetic nerve activity (MSNA) in humans revealed the bursty behaviour of efferent sympathetic nerve activity. Understanding the determinants of the efferent nerve activity should give insight into central mechanisms affecting sympathetic neuronal recruitment patterns and strategies and how these are affected by, or perhaps contribute to, disease processes. However, whereas the timing of bursts can be explained by baroreflex physiology, the variability in burst size has been more difficult to understand. This presentation will address the development of thought and techniques related to understanding the patterns of MSNA. Emphasis will be placed on how current activities have been forged by key hypotheses generated in the mid to late 20th century. These ideas proposed three neurophysiologic possibilities of postganglionic sympathetic recruitment: 1) rate-coding variations of active fibres, 2) recruitment of a latent neuronal population comprised of larger, faster conducting axons, and/or 3) synaptic delay modulations within the central nervous system. Using evidence from experimental preparations in anesthetized smaller animals, to recent signal processing approaches with multi-fibre recordings in humans, this lecture will discuss attempts to address these hypotheses. New information supports a variety of recruitment options available within the peripheral sympathetic nervous system that affect MSNA burst size and timing. Possible clinical applications of these concepts will also be addressed.

Approaches to Quantification of Autonomic Control of Cerebral Circulation

C. O. Tan [a,b,c]
[a] Department of Physical Medicine and Rehabilitation, Harvard Medical School, Boston, MA, USA
[b] Cerebrovascular Research Laboratory, Spaulding Rehabilitation Hospital, Boston, MA, USA
[c] Department of Radiology, Massachusetts General Hospital, Boston, MA, USA

The brain requires steady delivery of oxygen and glucose, without which neurodegeneration occurs within minutes. Thus, the ability of the cerebral vasculature to maintain steady blood flow is critical to neural health. Recent availability of blood flow and pressure measurements with high temporal resolution has allowed exploration of the mechanisms underlying this ability. These explorations have been further enhanced by the ability to apply sophisticated analytic approaches that exploit the large amounts of data that can be acquired, and have led to unique insights. Among these is the increasing recognition that the integrity of cerebrovascular function depends, at least in part, on autonomic function. However, most analytical methods rely on linear approaches with inherent limitations (acknowledged in the studies that employed these methods) that can preclude precise description of the role that autonomic effectors play in cerebrovascular control. For example, recent studies have revealed characteristic time scales wherein autoregulation (the ability of cerebral vasculature to buffer against swings in pressure) is most active, as well as specific scales wherein autonomic mechanisms are prepotent. However, given that effective autoregulation results in relatively unchanging flow despite changing pressure, estimating the pressure–flow relationship can be limited by the error inherent in linear models. The main focus of this talk is to provide a critical overview of the current analytical approaches to understand cerebrovascular control, in an attempt to better evaluate the inferences drawn from the data, and to outline analytical approaches to delineate the precise role of autonomic control in cerebrovascular function.