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Autonomic rhythms in health and disease

Alexander V Gourine & Susan A Deuchars

This issue of *Experimental Physiology* contains symposium reports that were presented on the 3rd August 2017 at the 38th World Congress of the International Union of Physiological Sciences in Rio De Janeiro.

Maintenance of physiological autonomic variability is strongly associated with health and preservation of organ function. The brainstem harbours vital neural circuits which control breathing and the activities of the sympathetic and parasympathetic arms of the autonomic nervous system, ultimately maintaining key physiological rhythms. Impaired autonomic activity (autonomic dysfunction) associated with aging and various disease states is accompanied by loss of physiological variability and may contribute to disease progression, decline in exercise capacity and reduction in quality of life (Machhada et al., 2017). The symposium reviewed the latest breakthroughs in our understanding of the functional organisation of the central nervous mechanisms which generate autonomic rhythms. The symposium also discussed the application of novel autonomic neuromodulation techniques designed to restore sympathetic/parasympathetic balance and limit pathophysiological consequences of autonomic dysfunction.

Deuchars et al. (2018) gave an overview of factors such as gap junctions (Lall et al., 2017) which contribute to the control of the sympathetic activity in health and disease. She then presented new data on how autonomic balance can be modulated in humans. Recent advances in device-based neuromodulation have made it possible to alter autonomic balance in humans by delivering low-level electrical stimulation to the regions on the outer ear (Clancy et al., 2014). The authors demonstrated that non-invasive electrical stimulation of the tragus of the ear shifts autonomic balance towards parasympathetic (vagal) dominance and discussed pathways that may be involved in this effect. This novel neuromodulation technique may prove to be highly effective in treatment of disparate disease states associated with autonomic dysfunction.

Stornetta and Guyenet (2018) focused on a particular group of brainstem neurones which constitutes the C1 cell population of catecholaminergic and glutamatergic neurons located in the rostral ventrolateral medulla. Interestingly, these neurons appear to innervate both sympathetic and parasympathetic preganglionic neurons and, therefore, can potentially modulate the activities of both arms of the autonomic nervous system. The role of C1 neurones in central nervous mechanisms of cardiovascular control becomes especially important in conditions of physiological and/or environmental stress, when increases in sympathetic activity are critical to maintain homeostasis. Activity of these cells also appears to be critically important for the operation of intrinsic neural mechanisms which protect peripheral tissues against ischaemia/reperfusion injury (Abe et al., 2017). These mechanisms were previously shown to recruit parasympathetic (vagal) pathways (Basalay et al., 2016; Mastitskaya et al., 2016).

Song Yao (Setiadi et al., 2018) addressed the importance of the blood-brain barrier integrity for maintenance of cardiovascular homeostasis. The blood-brain barrier appears to be disrupted in cardiovascular disease, associated with increased sympathetic nerve activity, including hypertension and heart failure. Circulating humoral factors such as angiotensin II and pro-inflammatory cytokines may contribute to this disruption by down-regulating the expression of endothelial tight junction proteins that are critical components of the blood-brain barrier. The authors suggested that treatments which preserve or restore the integrity of the blood-brain barrier may prove to be effective in the treatment of autonomic disease.

The last presentation of the symposium focused on modulation of vital brainstem respiratory and autonomic circuits by neighbouring astroglial cells. The authors discussed anatomical and functional features of astrocytes that allow them to detect and respond to changes in the brain parenchymal levels of metabolic substrates (oxygen and glucose) (Angelova et al., 2015), and metabolic waste products (carbon dioxide) (Turovsky et al., 2016). The evidence was presented suggesting that altered astroglial function may contribute to the pathogenesis of disparate neurological, respiratory and cardiovascular disorders such as Rett syndrome (Turovsky et al., 2015) and systemic arterial hypertension (Marina et al., 2015).

The symposium reports published in this issue of *Experimental Physiology* might be of interest to a wide range of physiologists interested in fundamental neuroscience, functional organization of neural circuits, autonomic rhythms, neuroglial interactions, cardiovascular and respiratory physiology.

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