EXTERNAL SEMINAR

INMED Conference Room

Monday, 16th October 2017 - 11 a.m

Dr Simon McMULLAN

Invited by: Clément MENUET
Françoise MUSCATELLI

Group Leader, Neurobiology of Vital SystemsCortical
Faculty of Medicine & Health Sciences
Macquarie University, NSW 2109, Australia

simon.mcmullan@mq.edu.au

Amplified respiratory drive to RVLM C1 neurons underlies the altered respiratory-sympathetic coupling and hypertensive phenotype of the SHR rat

Increased sympathetic nerve activity predicts the development of hypertension in humans and animals, including the spontaneously hypertensive rat (SHR), a widely used polygenetic model of hypertension. Here we consider the role played by adrenergic C1 neurons in the rostral ventrolateral medulla (RVLM) in relaying respiratory-locked sympathoexcitation and its significance to the development of hypertension in the SHR.

We first found that acute pharmacogenetic silencing of RVLM C1 neurons abolished the inspiratory-locked sympathoexcitation characteristic of the juvenile SHR, and that ablation of RVLM C1 neurons in early life prevented the onset of hypertension in adult SHR, indicating that C1 neurons are a critical relay for respiratory-sympathetic coupling and that chronic activation of C1 neurons contributes to the development of hypertension. We then examined putative sources of respiratory drive to C1 neurons using a targeted trans-synaptic retrograde tracer. We identified monosynaptic inputs to RVLM C1 neurons at all levels of the neuraxis, including respiratory subnuclei in the pons and brainstem. The greatest density of inputs came from the ventrolateral medulla itself, and included neurokinin-1 receptor immunoreactive neurons in the PreBötzinger Complex and cholinergic neurons in the region that corresponds to the post-inspiratory complex, putative markers of excitatory respiratory neurons in these regions. In contrast, we did not identify significant inputs from inhibitory Bötzinger neurons.

Our data point to C1 neurons as a critical node for the transmission of respiratory-sympathetic activity, potentially via excitatory modulation from PreBötzinger and post-inspiratory neurons, and suggests a pathogenic role for this mechanism in the establishment of hypertension.

Parc Scientifique de Luminy
163 Avenue de Luminy
13273 MARSEILLE Cedex 09

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