

23 February 2018, Friday 3pm – 4pm MD10 Anatomy Museum, Level 2, Seminar Room

## DEPARTMENT OF ANATOMY SEMINAR SERIES

# Sub-Cortical Pathways at the Origin of Long-Term Cardiorespiratory Alterations Induced by Stress

Stress induces brain neuroplasticity, in order to help the organism to react appropriately. In particular, rapid cardiorespiratory adaptations to threatening stimuli occur. However, the central neuronal pathway involved in these adaptations remain poorly understood. In addition, long-term autonomic alterations linked to the appearance of anxiety or depressive state are scarcely studied, and the need for biomarkers is essential. The autonomic nervous system is at the origin of the control of the heart and arterial blood pressure, through activation of neurons in the medulla oblongata. Vagal neurons are at the origin of a slowdown in heart rate, while activation of the sympathetic arm induces vasoconstriction. These neurones are in close connections to neurones generating the respiration.

We found in *in vivo* experiments in rats using pharmacological and electrophysiological techniques that, during acute stress, a hypothalamo-ponto-medullary (HPM) facilitation of the sympathetic activity and hyperventilation occurs, while the involvement of a hypothalamo-mesencephalo-medullary (HMM) circuit is at the origin of the blockade of the vagal cardiac neurones through the activation of serotonin 3 receptors. After chronic stress induced by social defeat and using telemetric recordings, sympathetic activation and vagal inhibition persisted in “sensitive” animals with lower blood levels of the brain derived neurotrophic factor (a sign of vulnerability to depression), but not in “resilient” rats. In addition, medullary serotonin 3 receptors are activated at long-term in “sensitive” animals only to produce a hypoventilation. A better knowledge of the pathways involved in physiopathological situations like chronic or intense stress can help to find new targets in other diseases at the origin of dysautonomia and alteration of the respiration, like stroke and central hypoventilatory syndromes.

### ABOUT THE SPEAKER

From my recruitment in 2000 at INSERM (governmental institution in Medical Research), I have been working on the key role of serotonin in cardiorespiratory alterations induced by stress. First I worked in a team dedicated to explore the role of 5-HT<sub>2</sub> and 5-HT<sub>3</sub> receptors in the brainstem in the modulation of the autonomic nervous system. We found out that, in the nucleus tractus solitarius (NTS), activation of 5-HT<sub>2</sub> receptors facilitate and stimulation of 5-HT<sub>3</sub> receptors inhibit the parasympathetic tone. Then after 2005, with my team we evidenced in *in vivo* experiments on rodents that the modulation of the autonomic nervous system by these receptors took place during acute stress. We finally used telemetric techniques to record biopotentials in conscious animals and we submitted animals to a new model of chronic stress: social defeat based on anticipation.

We found by pharmacological manipulations that two different sub-cortical pathways were at the origin of long-term cardiorespiratory alterations induced by stress. A hypothalamo-ponto-medullary pathway is at the origin of acute hyperventilation, while a hypothalamo-midbrain-medullary pathway (involving NTS 5-HT<sub>3</sub> receptors) acts to induce an increase in sympathetic activity and a blockade of the parasympathetic tone, as well as a long-term bradypnea. The discovery of these central neuronal circuits may help to find new targets to preserve cardiorespiratory functions in pathophysiological situations, in particular during stress.



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All are welcome.