Diaphragmatic stimulation in the anesthetized rat: a new model of dynamic respiratory pacing

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Background: Respiratory cycle is divided into expiration and inspiration which is controlled by the central nervous system. Normal respiratory rate is around 12-15cpm and the amplitude and frequency of respiratory movements are dependent on subjects' activity, example is increased during physical exercise and decreased upon sleep. The central control is made mainly by carotid chemoreceptors located at the bifurcation of common carotid artery. These receptors sensor the decrease of O_2 and increase of CO_2 and pH. Sensory information is, then, conveyed to the nucleus tractus solitarius, the primary relay station of autonomic integration located at the brainstem, through the nerve of Hering. After being integrated at NTS level, information is headed to pre-Botzinger complex, nucleus ambiguus and rostroventrolateral medulla modifying respiration and cardiovascular activity.

Objectives: This project is included in the construction of a dynamic and physiologic pacing system, implantable on the diaphragm. The main objective of the present work is to record, in an animal model, the variations of phrenic nerve activity, depending on the respiratory frequency that is mechanically induced. These results and the ones to gather by varying the partial pressure of CO_2, O_2 within Helium will be used to build a neuronal network system that would mimic the carotid chemoreflex.

Methods: Wistar rats (n=5), anesthetized, (pentobarbital of sodium, 60mg/Kg), under neuromuscular blockade (Norcuron, 4mg/Kg/h), with mechanical ventilation with room air enriched with O_2. Arterial pressure, ECG, heart rate, respiratory frequency and phrenic's activity were registered. Chemoreceptor stimulation was performed by varying the ventilatory frequency but maintaining a constant inspiratory volume. Phrenic nerve bursts/min were analyzed for each interval of respiratory frequencies and compared to changes of arterial pressure and heart rate.

Results: In 5 animals, was observed that to a ventilatory frequency [30-40[cpm, an average depolarisation of the phrenic nerve of 26,4123 bursts/min (bpm) was recorded. At a frequency of [40-50[cpm, an average of 31,9659 bpm; between [50-60[cpm, an average of 36,0004 bpm. It was also observed that there phrenic activity was absent in the rat1 above 62cpm and the rat2 had a phrenic arrhythmia with a progressive loss of activity above 85cpm.

Conclusions: We conclude that there is an increased phrenic activity in hypoxic conditions, whereas the same activity can be inhibited by hyperoxia as was expected. These results will join others obtain at different experimental conditions in order to build a neural network circuit which will mimic a dynamic and physiological pacing system.

Key-words: Autonomic Nervous System, Respiratory Pacing, Respiratory dynamic