Title: Cervical High injury and respiratory diaphragm rehabilitation using post-traumatic nerve bridging: a clinical application for ventilatory dependant spinal cord injured patients?.

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Cervical spinal cord injury still has a devastating impact on the respiratory system, leading to acute and chronic respiratory insufficiency which mainly results from diaphragm paralysis due to interruption of the descending respiratory pathways commanding the phrenic motoneurons or to direct injury of those motoneurons whose axons constitute the phrenic nerve (PN) commanding the diaphragm. Respiratory complications are frequent after cervical SCI and contribute significantly to associated morbidity, mortality and economic burden. Although electrical stimulation of the phrenic nerve or the diaphragm remains the current treatment for ventilator dependent patients, this method is still associated with side effects and high costs and does not allow optimum physiological control of respiration. In this context, repair strategies that may result in respiratory functional recovery or improvement after high spinal cord injury are therefore still required.

A potential tissular therapy for reinnervating the diaphragm consists in nerve bridging between laryngeal recurrent nerve (LRN) and phrenic nerve. The LRN expresses a spontaneous respiratory activity in phase with the phrenic nerve but doesn't emerge from the spinal cord, thus making it safe after spinal cord injury. The rationale is thus to reinnervate one hemidiaphragm by laryngeal respiratory fibers. Recurrent-phrenic nerve anastomosis has already been proven to work in healthy animals or after acute SCI (Gauthier et al., 2006) but was never tested in a post-traumatic circumstance. Hence, the original feature of this report concerns the efficiency of the repairing strategy after chronic high spinal cord injury in the rat. A preliminary Hospital Clinical Research Program (PHRC) using this procedure has been recently accepted by the French ethical committee and started in France during 2010.

Short Biography

Dr Patrick Gauthier is involved in studying the post-lesional plasticity and the capacity of « repair strategies » (nerve bridging, cell transplantation) to reduce respiratory deficit induced by high cervical injury. This problem is studied in the adult rat using spinal cord transection and contusion/compression close to clinical situations.

Dr Gauthier was among the first to study axon regeneration in the respiratory motor system following SCI (originally developed in a post-doc stay in the Aguayo's lab, in Montreal, Canada). Using nerve grafting strategies within the medullary respiratory centers and the spinal cord, it has been established that the adult spinal respiratory pathways have the capacity 1) to regenerate; 2) to transmit normal physiological messages after regrowth and 3) to re-establish functional connections. The interest and the efficiency of the nerve graft strategy under post-traumatic conditions in cases of chronic spinal cord injury was also confirmed.

Dr Gauthier has developed a cervical spinal cord contusion model relevant to the clinical situations of respiratory deficit after SCI. This model induces a persistent, reproducible and quantifiable diaphragm respiratory deficit in rats, due to injury of the respiratory cervical pathways. The organization of these pathways has been recently shown to be conserved within vertebrate (Kastner and Gauthier, 2008). Thus, injury of the respiratory spinal tract in rodents appears attractive to validate the effectiveness of repaired strategies in view of clinical trials. The current research activity also consists in evaluating respiratory recovery after transplantation of Olfactory

Ensheathing Cell after chronic cervical contusion. This strategy induces interesting post-traumatic phrenic recovery and diaphragm rehabilitation (Stamegna et al., 2010).