Exploring Approaches to Promote Respiratory Motor Plasticity Through Varied and Fixed Interval Intermittent Hypoxia

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Abstracts will be considered for both poster and platform presentations

Neurotrauma (TBI, spinal cord injury, etc.)

In the human population, spinal cord injury (SCI) most commonly occurs at the cervical level. Interruptions of descending pathways here can result in breathing motor deficits through paralysis of the diaphragm, sometimes necessitating mechanical ventilation for survival which greatly decreases patients' quality of life. Fixed interval intermittent hypoxia (FIH) treatment is utilized in rat models to attenuate breathing motor deficits resulting from cervical SCI. FIH consists of the repeated, alternating exposure of a subject to consistent and equal durations of hypoxic and normoxic conditions. Specifically, this treatment induces a prolonged increase in phrenic motor output, a type of respiratory motor plasticity known as phrenic Long Term Facilitation (pLTF). FIH exhibits similarity to the psychological construct of operant conditioning in which the increased incidence and persistence of a desired, spontaneous behavior is trained through reinforcement. As such, each interval of hypoxia can be construed as the period during which the subject responds with heightened respiratory drive and is subsequently reinforced by an interval of normoxia. Provided that FIH procedure is a form of operant conditioning, it can be optimized. Using the fixed or variable duration of the hypoxic interval as our independent variable, we hypothesize that Varied Interval Hypoxia (VIH) treatment will induce a greater, more prolonged increase in phrenic motor output than FIH. To test this hypothesis, we utilized electromyographic recording to assess our dependent variable of diaphragmatic activity. In naïve retired breeder rats (female, Sprague-Dawley) treated by VIH (n=2), episodic spinal cord application of serotonin, previously shown to induce pLTF independently from intermittent hypoxia treatment, depressed breathing motor output, an effect opposite from that observed after FIH (n=2). Preliminary data from C2 hemisected animals (n=3) suggests that exposure to VIH results in an increase in diaphragmatic output achieving 44.89% (stdev.p 15.76%) of maximum induced by nasal occlusion. These data suggest that VIH may paradoxically promote a lower level of respiratory motor plasticity than FIH in naïve models, while potentially inducing significant recovery in post-injury models. Further exploration will focus on post-injury treatment, adjusting the variance of the hypoxic periods for optimum induced recovery, and more robust comparison to control.