Neuromuscular electrical stimulation training to minimize cancer- and sepsis-induced cachexia

Disciplines: Cell biology & Skeletal muscle physiology.  
Laboratory: Institut NeuroMyoGène (Director: Pr Laurent Schaeffer), Team CHAZAUD (Stem Cell Environment and Skeletal Muscle Homeostasis)  
Doctoral school: Interdisciplinary Doctoral program in health-sciences (EDISS) - ED 205

Description
Scientific background and rationale:
Cachexia is a common consequence of many chronic diseases including sepsis and cancer1,2. This devastating muscle-wasting syndrome is characterized by a severe loss of skeletal muscle tissue (i.e., atrophy) that results in muscle weakness (i.e., reduced force production). The development of countermeasures to attenuate both skeletal muscle atrophy and weakness is of utmost importance in both diseases.

Neuromuscular electrical stimulation (NMES), which consists of generating visible muscle contractions with portable devices connected to surface electrodes, has been largely used for increasing muscle strength and mass in healthy humans3. So far, the effectiveness of NMES for preventing/attenuating muscle atrophy in cachectic patients remains equivocal4,5. Indeed, the potential benefits of NMES in cachectic patients require an optimization of the stimulation parameters via a careful control of the force produced in response to stimulation which is the major determinant of NMES effectiveness6.

Aim: The aim of the thesis is to investigate whether and to what extent NMES is a promising therapy for increasing force production and skeletal muscle mass in preclinical models of cachexia. The PhD program aims at establishing rigorous protocols to exploit the benefit of NMES on skeletal muscle function. Efforts will be made to understand the influence of NMES on the number and behavior of myogenic precursor cells1 as well as immune, endothelial and interstitial cells that all regulate skeletal muscle homeostasis.

Description of the project methodology: Experiments will be performed in several mouse models of cancer and sepsis. NMES will be delivered by using a strictly non-invasive preclinical ergometer recently developed in the laboratory. Primary outcomes will be in vivo measurements of hindlimb force production and muscle fiber cross-sectional area. A variety of methodologies (immunolabeling, flow cytometry, co-culture) will help to evaluate the specific interactions between environmental cells7,8 and myogenic precursor cells1 that sustain the benefit of NMES in the cachectic context.

Expected results and perspectives: This project may lead to the validation of the mechanisms of action of NMES as an innovative non-pharmacological intervention, which could then be transposed to daily clinical practice.

Required skills: Cell culture, immunostaining, histology.


Key-words: muscle weakness, atrophy, force, muscle stem cells, microenvironment.

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