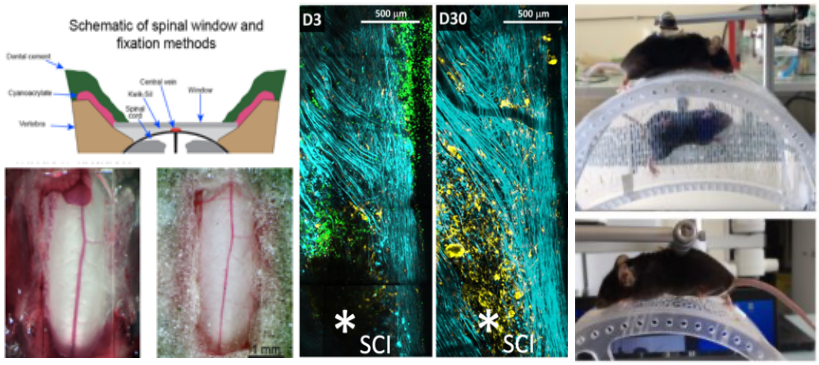

Title:
Intravital imaging study of the neuroimmunomodulatory effect of transcutaneous electrical stimulation combined with physical exercise in spinal cord injury.

Abstract:
While epidural electrical stimulation has been shown to facilitate functional recovery in tetraplegic patients (Kathe et al 2022), transcutaneous electrical stimulation of the spine (TES) is another promising non-invasive approach to help tetra or paraplegic patients recover their sensory-motor abilities even after several years of functional disability (Inanici et al. IEEE Trans Neural Syst Rehabil Eng. 2021, Moritz et. Al Nat. Med. 2024). Although nerve fiber activation and inflammatory responses are among SET's prime targets, their relative contributions to therapeutic effect remain largely unknown. As part of the "NEUROREHABILITATION" interlab project supported by the Carnot Institute and led by INT, we are setting up a mouse model of spinal cord injury, enabling the preclinical development of physical training strategies combined with SET, so that they can then be tested in clinical situations on spinal cord injury patients at the APHM.

The project also includes a fundamental research component, using triple fluorescent transgenic mice equipped with a dorsal glass window for imaging by intravital two-photon microscopy. The cellular mechanisms underlying the therapeutic effect will be characterized by monitoring changes in axon densities, activated microglia and infiltrated monocytes and granulocytes in the spinal cord tissue. By imaging the same animal at regular time intervals for several months after trauma, in the presence or absence of treatment, we aim to identify the most electrosensitive cell populations and see how their electromodulation affects axonal regeneration, as well as functional recovery. Indeed, the locomotor functions of these same animals will be tested regularly during spontaneous or treadmill-trained walking protocols; kinematic analysis of movement will be performed automatically using Deep Lab Cut software.

To facilitate the transfer of preclinical results to clinical practice, blood biomarkers of treatment efficacy will also be sought.

Methods

- Spinal window surgery
- Multi-fluorescent transgenic mice
- Intravital multispectral 2-Photon imaging
- Image analysis by segmentation
- DeepLabcut analysis of locomotor behavior
- Immunohistochemistry
- ELISA assay of blood metabolites

Profile required

For this applicative projet ultimately aiming at improving human patient care, we are looking for an experienced researcher skilled in fine surgery and with a strong interest in intravital imaging and image analysis. Candidate should become able to master all the different steps of the 2 months animal follow up from the day of spinal cord injury to the treatment protocol, imaging and terminal histology. Surgical and imaging procedures are well established and running. Designer level diploma in animal experimentation is mandatory. Motivation, autonomy, rigor and organizational skills are essential. Strong feeling for team work is expected in order to interact daily with two senior researchers, a Phd student and a master student. Taste/skills for image analysis and automation of data analysis chains would be a plus.

Environment:

Within INT's MRS team, this project contributes to the global understanding of locomotor neuronal circuits and their dysregulation in spastic conditions. It is connected to an ongoing thesis project on the effect of infrared light on post-traumatic inflammation. Research activity is moreover supported by INT's technological platforms: INPHIM for intravital microscopy, SurFIN for surgery, BIOMINT for analysis of circulating and tissue biomarkers. Initial funding is for 18 months. Position is available starting 1st January. Earlier start can be discussed.

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https://www.int.univ-amu.fr/recherche/equipes/imapath/
https://www.int.univ-amu.fr/recherche/equipes/pm3/

Team bibliographic references related to the subject:

1. Escarrat V, Perez-Sanchez J, El-Waly B, Collazos-Castro JE, Debarbieux F. Composite Fibrin and Carbon Microfibre Implant to Modulate Postraumatic Inflammation after Spinal Cord Injury. Cells. 2023;12(6):839.

2. Bos R, Drouillas B, Bouhadfane M, Pecchi E, Trouplin V, Korogod SM, Brocard F. Trpm5 channels encode bistability of spinal motoneurons and ensure motor control of hindlimbs in mice. Nat Commun. 2021;12(1):6815. doi: 10.1038/s41467-021-27113-x. PMID: 34819493; PMCID: PMC8613399.

3. Brocard C, Plantier V, Boulenguez P, Liabeuf S, Bouhadfane M, Viallat-Lieutaud A, Vinay L, Brocard F. Cleavage of Na(+) channels by calpain increases persistent Na(+) current and promotes spasticity after spinal cord injury. Nat Med. 2016 ;22(4):404-11.