Monoamines drugs in post-stroke motor recovery

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Until now, tPA thrombolysis within the first hours of the stroke is recognized as the only validated treatment able to improve the spontaneous À and most of the time incomplete À recovery of neurological functions after stroke. However, we have learnt from research over the last decade, in part based on the considerable improvement of neuroimaging techniques, that spontaneous recovery of neurological functions was associated with a large intracerebral reorganization of the damaged human brain. The question of whether lesioned-brain plasticity can be modulated by external factors like pharmacological agents is now addressed with the aim of improving recovery and reducing the final disability of patients. We review in this talk, the preclinical and clinical arguments for a direct action of monoamines in promoting recovery after stroke in humans.

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Non-invasive brain stimulations and post-stroke motor recovery

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The main objective of Innov-in-Stroke project is to develop a generic technology for repairing Central Nervous System (CNS) damages through an implantable prosthesis that combines Micro/Nano-engineering of its surface and graft of neural stem cells. The originality relies on the use of human adult neural stem cells which are naturally present in the brain and can be expanded in vitro and the fact that the material hosting the stem cells will be designed and fabricated by lithography. Through the very precise control of the topography of the polymer constituting the prosthesis, we will induce stem cell adhesion and differentiation and we will be able to guide the regenerated neurons along specific directions. Once equipped with functional stem cells, the lithographically designed prosthesis becomes a bioprosthesis which can be implanted through surgery. The developed technology can be used for various repairing applications in the CNS. In this project, we will mainly focus on brain regeneration after stroke.

We optimize the design of the prosthesis in terms of biocompatible support material, micro/nanopatterning (size, shape and depth of topographical features), specific chemical coating and molecular functionalization. We also investigated the possible benefit or toxicity of Double walled CNT (DWCNT) for stem cells viability, adhesion and differentiation. The project is divided in
three main work packages: the bioprosthesis manufacturing, the bioprosthesis characterization in vitro by histology and electrophysiology, and the functional validation of the bioprosthesis in rodents by in vivo imaging, histology and behavioural assessment. The core of the project will be to replace the corticospinal tract, guide axonal growth to the internal capsule, and induce a functional motor recovery in rats. The immunogenicity of the bioprosthesis, the inflammatory response from the host to the prosthesis and to the biodegradation products released after implant will be also investigated.

This project is highly interdisciplinary, involving on the one hand neurologists, neurosurgeons involved in brain implantation and human adult neural stem cells biopsy, researcher in neuroimaging, biologists involved in cell culture and characterization (Inserm UMR 825; Cerco) and on the other hand chemists involved in nanomaterial (CNTs) synthesis and functionalization (CIRIMAT, LPCMIB), physicists involved in nanotechnology and nanofabrication (LAAS, ITAV).

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