Project 1.14. Can transfer of genes encoding DREADD receptors to selected motoneurons in the transected spinal cord restore motor function? Synaptic and receptor changes in motoneurons caused by chemogenetic activation.

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Background: Research serves to better understand the ability of the motor neurons (MN) in the spinal cord and their neuromuscular connections to plastic changes. These changes, properly modulated, can serve to improve function after spinal cord injury. Groups of MNs stimulating the contraction of functionally different hind limb muscles managing locomotion are impaired to varying degrees after injury. Therefore, selected cell groups will be modified. The studies will be conducted on adult rats. We will use intramuscular gene transfer encoding hM3Dq mutated muscarinic receptors (DREADD), using AAV vectors. The receptors will be selectively activated with clozapine N-oxide (CNO) or DREADD agonists. An activation pattern will be established that is optimal for triggering functional changes, which will be assessed on the basis of gait kinematics and electromyography (EMG) analysis. To obtain material from MN for gene expression analysis, we will use laser microdissection followed byqRT-PCR. The distribution pattern and structure of synaptic endings and membrane receptors will be studied using immunofluorescence, confocal and electron microscopy.

Aim: The solution to the problem that occurs in experimental therapies undertaken after spinal cord injury and results from uncontrolled stimulation of the system of preserved neurons. Paradigms of activation lead to a moderate improvement in motor function, however, they do not restore functional balance between different MNs. The goal is to show whether enrichment of selected α-MN groups controlling hind limb muscles will increase their receptivity, improve locomotion after spinal cord injury.