SStudy of the effects of repetitive trans-spinal magnetic stimulation on functional and tissue recovery in an experimental model of transverse myelitis in mice

Sujet proposé par

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Biology and Physiopathology of the spinal cord

M2 Research project title

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Keywords

spinal cord injury, non-invasive treatment, transverse myelitis, functional recovery, mouse model, remyelination, oligodendrocytess

Description of the project

The essential role of the spinal cord is to transmit and receive motor, sensory and autonomic information between the brain and the rest of the body. Damage to the spinal cord, known as spinal cord injury (SCI), is often the result of physical trauma or, more rarely, inflammation. Traumatic SCI (TSCI), which is most common, is caused by external physical damage. The mechanisms that are induced following TSCI are better known and begin with a primary lesion characterised by direct physical damage on the spinal cord with tissue and cell destruction. A few minutes later, a secondary lesion develops, characterised in particular by inflammation and destruction of the myelin sheath, leading to neurotoxicity and the death of neurons and oligodendrocytes. To date, no treatment can be offered to patients suffering from TSCI. Although SCI is most often traumatic, there is a rare form of non-traumatic SCI; transverse myelitis (TM), which results from inflammation of the spinal cord. This disease leads to progressive demyelination of axons and neuronal death, resulting in loss of motor and sensory function. Our team has shown in rodent models that repetitive trans-spinal magnetic stimulation (rTSMS) can non-invasively reduce inflammation and induce remyelination and axonal regrowth in TSCI. As these pathophysiological processes are common to both types of SCI, we hypothesise that rTSMS may induce similar effects in non-traumatic SCI such as TM. To do this, we will use a mouse model of TM based on detergent intraspinal injections, and half of these animals will then be treated for a week with rTSMS. The locomotor capacities of these animals will be assessed every week using automated tests, and finally the animals will be sacrificed in order to carry out immunohistochemical and RNA expression analyses. Through this study, we hope to demonstrate the benefits of repetitive trans-spinal magnetic stimulation, a non-invasive treatment, for TM, an inflammatory demyelinating disease.

Methods and techniques

Animal models and experimental groups In this study, 2 experimental paradigms will be tested. The first will measure the effects of rTSMS when the treatment is initiated the day after induction of the myelitis model at the start of the inflammatory phase. The second will measure the effects of this treatment when it is implemented at the peak of demyelination induced by LPC, i.e. 7 days after its injection. Different experimental times to measure the histological and/or functional effects of rTSMS will also be carried out. For each group and each experimental time-point, 20 mice per group (10 males and 10 females) will be used for the in vivo studies (functional and histological studies) and similarly 20 mice per group (10 males and 10 females) will be used for the gene expression analyses

(RNASeq studies), i.e. a total of 260 mice; 160 mice for the in vivo studies and 100 mice for the RNASeq studies. - Measurement of the effects of rTSMS when treatment begins the day after LPC injection. Histological studies : Myelitis group, LPC injection Stim group, LPC injection and rTSMS treatment for 7 days, with treatment starting on D1. For a first batch of experiments, all animals will be fixed at D8 for histological studies. Then, for a second batch of experiments, mice will be fixed at D14 for histological studies. Functional and histological studies : Myelitis group, LPC injection Stim group, LPC injection and rTSMS treatment for 7 days, with treatment starting on D1. All animals will undergo functional tests at D8, D15, D22 and D29, and will be fixed at D29 for histological studies. - Measurement of the effects of rTSMS when treatment begins 7 days after LPC injection. Histological studies : Myelitis group, LPC injection Stim group, LPC injection and rTSMS treatment for 7 days, starting on D8. All animals will be fixed at D15 for histological studies. Functional and histological studies : Myelitis group, LPC injection Stim group, LPC injection and rTSMS treatment for 7 days, with treatment starting on D8. All animals will undergo functional tests at D8, D15, D22 and D29, and will be fixed at D29 for histological studies. - Measuring the effects of rTSMS on gene expression Gene expression analysis by RNASeq : In order to correlate the histological results with the transcript analysis, the same experimental time-points as described above will be used. Myelitis group, LPC injection Stim group, injection of LPC and treatment by rTSMS for 7 days with start of treatment on D1 or D8. For all animals, the spinal cords will be extracted after sacrifice, 8 or 15 days after the injection of LPC, and will be placed in trizol in order to carry out RNASeq studies.

References (at least 3)

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