

# Recovery of a drawer-pulling task in control antibody and combined anti-Nogo-A / BDNF treated adult macaque monkeys subjected to cervical cord lesion

Freund P<sup>1</sup>, Beaud M<sup>1</sup>, Bloch J<sup>3</sup>, Mir A<sup>4</sup>, Schwab ME<sup>2</sup>, Rouiller EM, Wannier T<sup>1,2</sup>

1: Dept of Medicine, Uni Fribourg; 2: Brain Research Inst., Uni Zurich; 3: CHUV, Lausanne; 4: Novartis, Basel

### Introduction:

In adult macaque monkeys, a unilateral section of the cervical cord leads to persistent motor deficits which recover over time in a fashion depending on lesion size. Neutralizing the neurite outgrowth inhibitor protein Nogo-A leads to significant sprouting of the corticospinal tract and to enhanced recovery in a task requiring fine control of finger movements (Freund et al 2006, 2007). The present investigation aims at exploring whether a drawer pulling task enables to obtain additional guantitative information on the process of recovery, in particular by investigating the characteristics the grip and load forces exerted in order to open the drawer.

#### Methods:

Currently, four adult macaque monkeys (3-5 years old; 3.5-5.5 kg) were either treated with a control antibody (N=2) or with a combination of BDNF and a monoclonal antibody neutralizing Nogo-A (N=2). We measured the grip force exerted by the fingers on the drawer knob, the load force exerted to pull the drawer open, the time to pull the drawer open and the time required to pick a food reward out of the drawer. A torque motor could generate a force of chosen constant amplitude to oppose to the pulling force.



Conclusions: All monkeys showed a transient alteration in their capacity to execute the task. They then recovered and their scores returned to near pre-lesioned values. A persistent loss of grip and pulling force was observed in two animals, while the two other animals ended using force parameters very similar to those observed during the pre-lesion period. The relationship between grip and load force remained permanently modified in two animals. These data suggests that the unimanual drawer-pulling task is a useful tool to characterize and follow up recovery after a unilateral spinal cord lesion.

#### Results:



The lesion was set at the C7/C8 border and sectioned all or most of the dorsolateral funiculus on one side. This deprives the spinal cord situated caudally to the lesion of the overwhelming majority of its corticospinal and rubrospinal inputs.



Time used to fully open the drawer and pick a food pellet in function of the day before or after the lesion.

Immediately after the lesion, both for pulling and picking, there is either a strong increase of the time required to perform the task or a transient incapacity. After few days, all animals were able to open the drawer successfully and pick the food reward. Their scores rapidly returned to values similar to those observed during the prelesion period. Note that the time course of recovery for the pulling and picking capacity differed and that the characteristics of this difference depended on the animal.

Each data point depicts the average picking time (±SD) from one daily session (~ 10-20 trials).

## Grip and load force used before and after the lesion, when the behavioral capacity had stabilized.



After recovery, the grip and load force decrease in two animals and returned to pre-lesion values in two other animals. The box and whisker plots indicate the median, the 25 and the 75 percentiles of the grip and load forces exerted by the hand on the side of the lesion and measured in presence of a resistive force of the drawer of 6.5 N. On the scarrer plots, each data point represents a single successful trial, linear regression lines are given.