Effets of a spinal cord lesion on corticospinal (CS) and rubrospinal (RS) neurons in adult macaque monkeys treated with an antibody neutralizing *Nogo-A*.

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INTRODUCTION

A unilateral cervical spinal cord lesion performed in adult monkeys affects both CS and RS neurons. In motor cortex (M1), layer V SMI-32 positive neurons, mostly CS neurons, shrink, but their number remains unaffected by the lesion (Wannier et al., J Neurotrauma, 2005). In the magnocellular part of red nucleus (RNm), SMI-32 positive neurons also shrink but in addition to this morphological change, a decrease of the cell number was also observed.

Because the capacity of neurons to recover from an axotomy depends on the availability of trophic factors, and because an anti-Nogo-A antibody treatment indirectly enhances this capacity by increasing the number of uptake sites (i.e. new synapses formed in the process of sprouting and/or regeneration), we asked the following questions:

- After a cervical spinal cord lesion, does an anti-Nogo-A antibody treatment affect the shrinkage of RS and of CS neurons?

- Does this treatment alter the decrease of the number of SMI-32 positive RS neurons?

METHODS

The number and cross-sectional area of the SMI-32 positive pyramidal neurons located in layer V of M1 and of the SMI-32 positive neurons located in the RNm were measured and compared across three groups of animals: intact monkeys, injured monkeys treated with a control antibody and injured monkeys treated with the anti-Nogo-A antibody.

	The CS study	The RS study
Number of Intact animals	5	4
Number of Control animals	4	4
Number of Treated animals	5	7
Total Number of animals	14	15

CONCLUSIONS

1) In the adult macaque monkey, after a unilateral cervical cord lesion, the soma of both the CS and the RS tracts neurons shrink and their level of non-phosphorylated neurofilament expression decreases.

2) In the ipsi- and contralesional M1, the number of SMI-32 positive neurons remains similar. However, in the contralesional RNm, less SMI-32 positive neurons can be detected.

3) Application of an anti-Nogo-A antibody at the lesion site does not prevent the axotomized CS and RS neurons from soma shrinkage and this treatment could not avoid a reduction of the number of RS neurons.

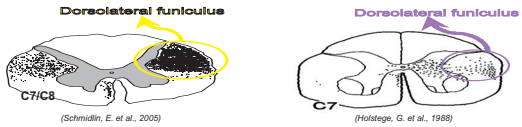
RESULTS: localisation and extent of the cervical spinal cord lesion

Anti-Nogo-A antibody treated animals | **Control antibody treated animals**

Measurements were obtained for both the cortical and RNm SMI-32 positive neurons for thirteen animals. In one animal, only cortex, and in three animals only the RNm were examined

The dorsolateral funiculus was completely damaged by the cervical cord lesion in most animals. For four animals, the lesion was incomplete (open circle).

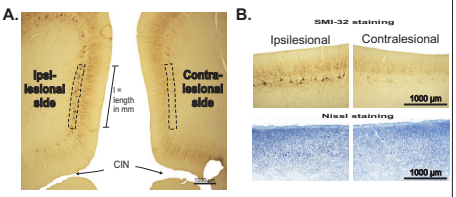
Localisation of the CS and RS fibers in the spinal cord:



CS and RS fibers are mainly located in the dorsolateral funiculus.

RESULTS: motor cortex

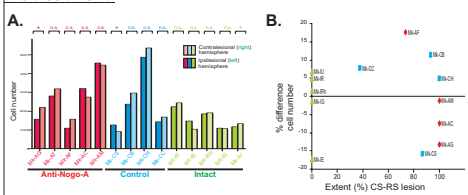
SMI-32 stained the pyramidal neurons of cortical layers III and V. However, an inter-hemispheric difference of staining intensity of the layer V was observed.



A. The two hemispheres of the mesial primary motor cortex (M1) stained with SMI-32.
B. M1 stained with SMI-32 and Nissl.

Compared to the ipsilesional side, the contralesional side of M1 presents more lightly SMI-32 stained pyramidal neurons in layer V. This difference indicates a reduction in non-phosphorylated neurofilaments expression.

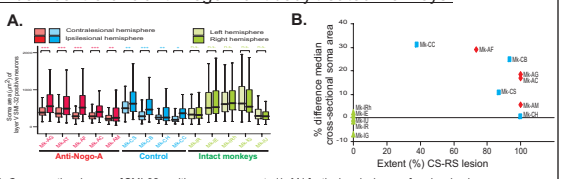
The number of SMI-32 positive neurons counted did not vary between the hemispheres irrespectively of the lesion and/or of the treatment.



A. Mean number per mm of SMI-32 positive neurons counted in M1 on each hemisphere for each animal.
B. Interhemispheric difference in percent of the number of SMI-32 positive neurons counted in M1 as a function of extent of the cervical cord lesion.
(For the monkey Mk-AT, the extent of the lesion could not be determined. In consequence its related value correspond to an horizontal dashed line)

No systematic difference between hemispheres was observed among the three groups of animals, demonstrating that the cervical cord lesion did not generate a sizeable cell loss.

The distribution of the soma cross-sectional areas of SMI-32 positive neurons differed between the two hemispheres of the lesioned animals in both control and anti-Nogo-A antibody treated monkeys.

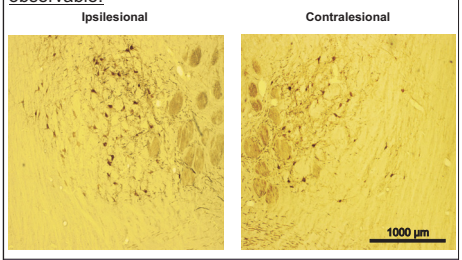


A. Cross-sectional areas of SMI-32 positive neurons counted in M1 for the hemispheres of each animal.
B. Median difference of the cross-section area of the SMI-32 positive neurons counted in M1 in function of the cervical cord lesion.

All lesioned animals have smaller CS soma cross-sectional areas in the contralesional hemisphere, corresponding to a lesion-induced shrinkage of the CS axotomized neurons.
The anti-Nogo-A antibody treatment did not prevent soma shrinkage in the injured animals.

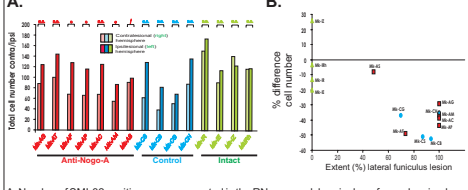
RESULTS: red nucleus

An inter-hemispheric difference of SMI-32 staining between the neurons of the two hemispheric RNm is observable.



In the RNm, the SMI-32 positive neurons appear less numerous and less densely stained on the contralesional side.

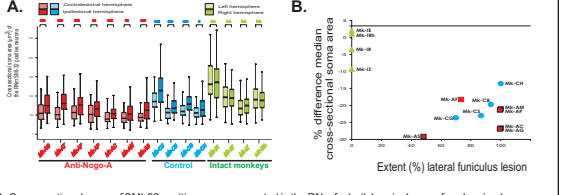
A decrease of the number of SMI-32 positive neurons counted was observed in the contralesional side in absence or presence of the anti-Nogo-A antibody treatment.



A. Number of SMI-32 positive neurons counted in the RNm on each hemisphere for each animal.
B. Interhemispheric difference in percent of the number of SMI-32 positive neurons counted in the ipsilesioned RNm as a function of extent of the cervical cord lesion.

For the lesioned animals, the number of SMI-32 positive neurons counted in the contralesional side of the RNm was inferior to that counted in the ipsilesional side. The anti-Nogo-A antibody treatment did not alter this effect.

In both groups of lesioned monkeys irrespectively of the anti-Nogo-A antibody treatment the distribution of the soma cross-sectional areas of SMI-32 positive neurons varied between the hemispheres.



A. Cross-sectional areas of SMI-32 positive neurons counted in the RNm for both hemispheres of each animal.
B. Median difference of the cross-section area of the SMI-32 positive neurons counted in the RNm in function of the cervical cord lesion.

As observed for the CS neurons, the cervical cord lesion induced cellular soma shrinkage in the contralesional side of the RNm.
The anti-Nogo-A antibody treatment did not reduce the lesion-induced soma shrinkage.

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