Anti-Nogo-A treatment enhanced sprouting of corticospinal axons but did not prevent cell body shrinkage in the motor cortex in adult monkeys subjected to cervical cord lesion.

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Introduction

In adult monkeys, following an unilateral cervical cord injury, corticospinal (CS) axons exhibited regenerative sprouting rostally and caudally to the lesion when Nogo-A (growth inhibitor protein) was neutralised via an antibody. In addition, anti-Nogo-A treatment promoted functional recovery. In a recent study (Wannier et al., 2005), we found that, in primary motor cortex (M1) of monkeys that received a control antibody, the soma of the CS neurons survived to the axotomy but shrank.

Does the anti-Nogo-A treatment prevent such soma shrinkage in M1 ?

Methods

Type of study : Quantitative and qualitative anatomical comparaison across three groups of adult animals :
1) Intact monkeys (n=3)
2) Monkeys subjected to the cervical cord lesion and treated with a control antibody (n=4)
3) Monkeys with the cervical lesion and treated with an antibody neutralizing Nogo-A (n=3)

Cells studied: Pyramidal neurons located in layer V of M1 and labelled with SMI-32.

Conclusions

The anti-Nogo-A treatment did not preserve the axotomized CS cells from soma shrinkage.

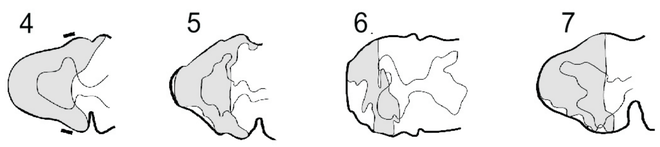
SMI-32 stained axotomized cells were less marked as compared to the cells in the ipsilesional hemisphere; **anti-Nogo-A treatment did not reduce the lesion-induced phenotype modifications of the soma of CS neurons. In conclusion, anti-Nogo-A treatment acts at the level of the axon close to the lesion but not at distance at the level of the soma.**

Results

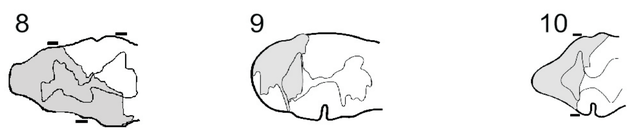
① Localisation of the cervical lesion

The extent of the lesion determines the proportion of transected corticospinals fibers.

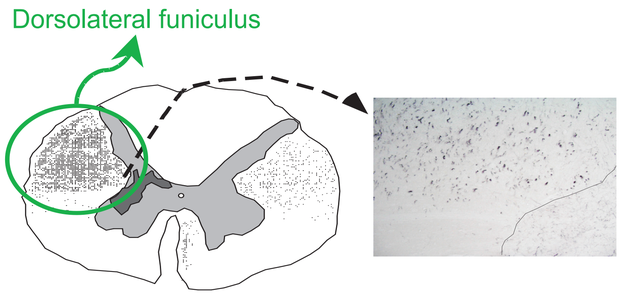
Lesioned, control antibody treated



Lesioned, anti-nogo-A antibody treated



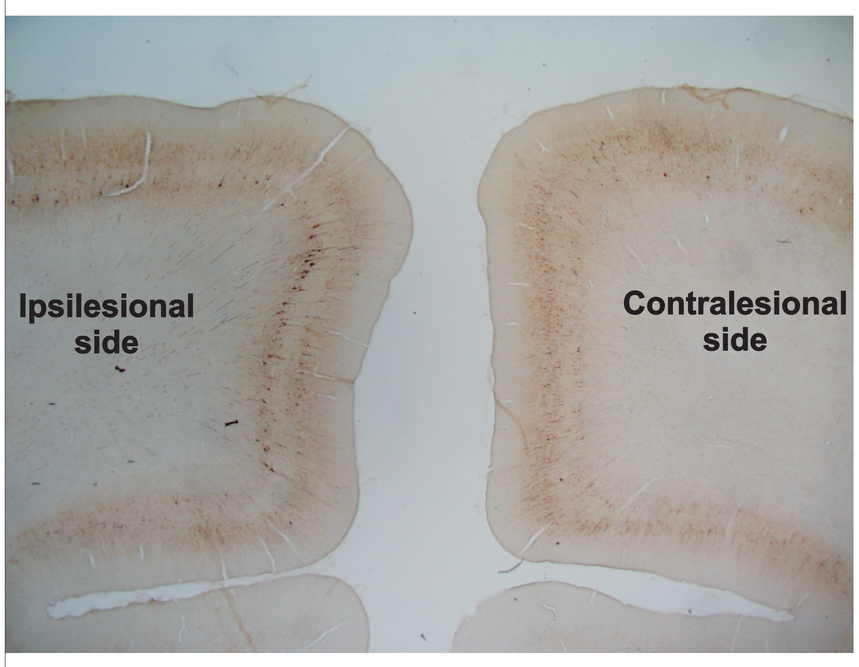
The dorso-lateral funiculus is completely or nearly completely sectioned by the lesion.

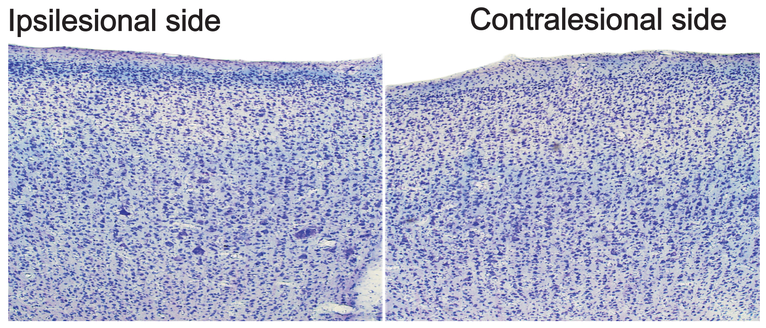


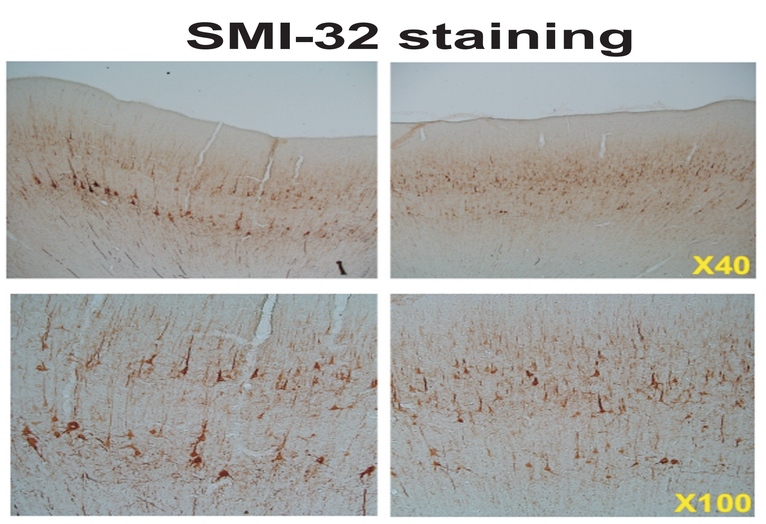
Position of CS fibers labelled after an injection of BDA in M1

② Primary motor cortex stained with Nissl and SMI-32

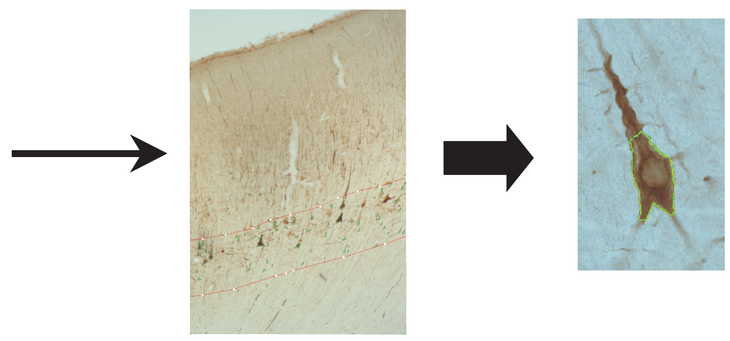
SMI-32 staining highlights the pyramidal cells of layers III and V according to the presence of neurofilaments expressed.



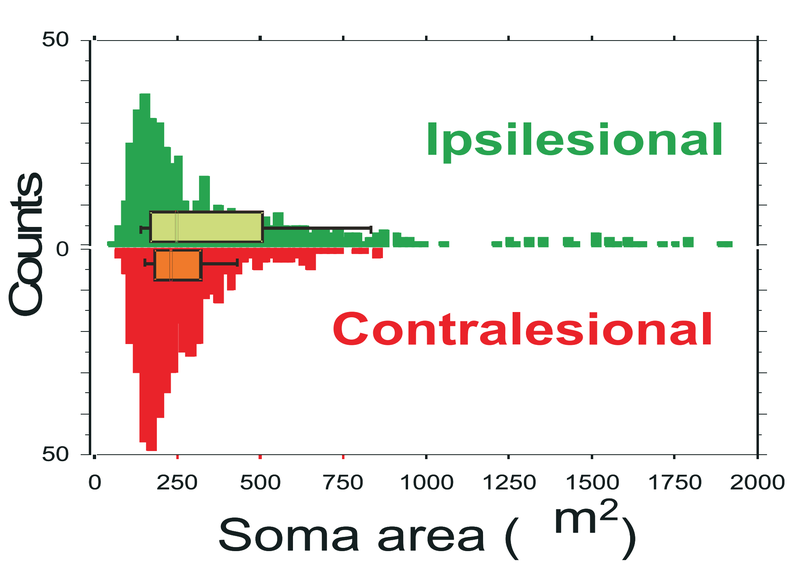




Anatomical assessment
Perimeter of the layer V in M1 in orange
Count the number of SMI-32 positive neurons with the nucleus visible
Contour of the pyramidal cells positive for the SMI-32 marker in green (measurement of the silhouette somatic area)

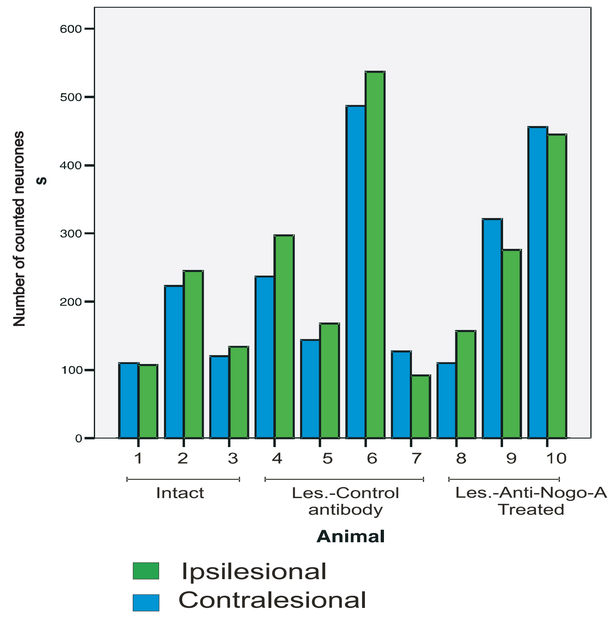


③ Representative cell surface distribution in ipsi- and contra-lesional hemispheres for an injured, anti-Nogo-A treated monkey



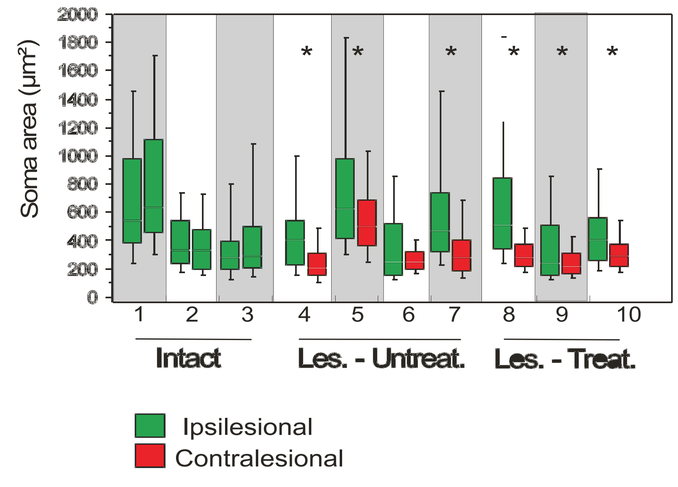
In both hemispheres, small neurons are more numerous than large neurons.
The large neurons are almost completely absent in the contralesional hemisphere.

④ Number of SMI-32 stained neurons per animal and hemisphere



The number of neurons is comparable in both hemispheres suggesting that there is no cell death.

⑤ Distribution in each monkey of the soma area of SMI-32 positive cells in layer V according to the hemispheres



For the lesioned animals, the size of soma is not comparable between the two hermispheres; a soma shrinkage was observed in the contralesional side.

Soma shrinkage was comparable in both groups of lesioned monkeys, irrespective of the treatment.