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 the growth inhibitor protein Nogo-A was neutralised via an antibody. In addition, the anti-Nogo-A treatment enhances 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 of the CS neurons survived to the axotomy but their soma shrank.
Does an anti-Nogo-A treatment prevent such soma shrinkage in M1 ?

Methods :

Type of study : Quantitative and qualitative anatomical comparison across three groups of adult animals :
1) Intact monkeys (n=5)
2) Monkeys subjected to a cervical cord lesion and treated with a control antibody (n=4)
3) Monkeys with a cervical lesion and treated with an antibody neutralizing Nogo-A (n=5)

Cells studied: Pyramidal neurons located in layer V of M1 stained with the SMI-32 antibody.

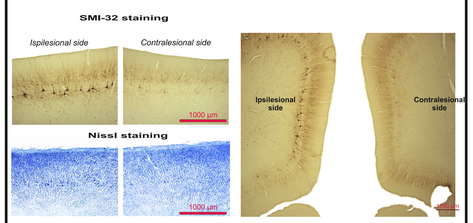
Conclusion :

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 ipsilesioned hemisphere;
anti-Nogo-A treatment did not reduce the lesion-induced phenotype modifications of the soma of CS neurones.

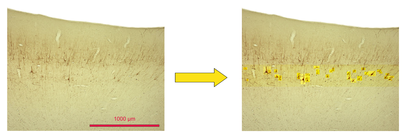
Results

1) Primary motor cortex stained with SMI-32 and Nissl



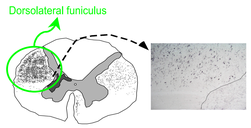
SMI-32 staining highlights the pyramidal cells of layers III and V according to the presence of neurofilaments expressed

In the contralesional side less neurons are observed. Is this situation due to cell death or to a lower expression of neurofilaments proteins ?



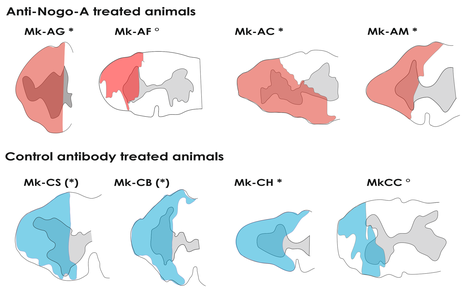
Underlining lightly stained neurons suggests a decrease in neurofilaments expression

2) Localisation of the cervical lesion



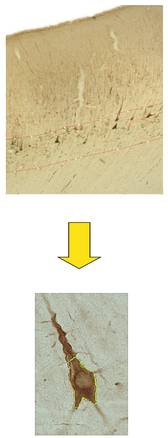
Position of CS fibers labelled after an injection of BDA in M1

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



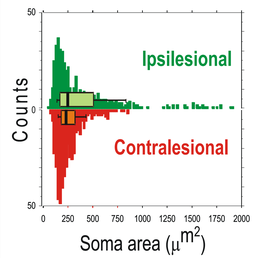
The dorso-lateral funiculus is completely or nearly completely sectioned by the lesion.

3) Anatomical assessement



➔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)

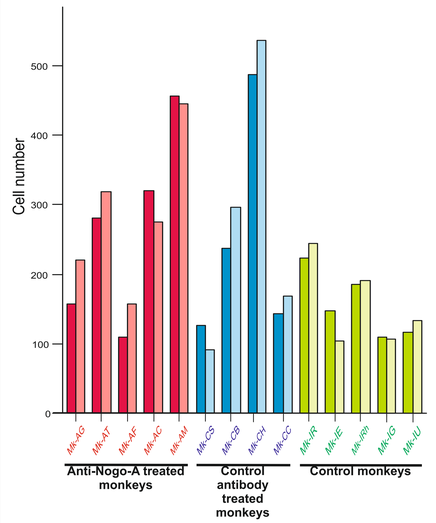
4) Representative cell surface distribution in ipsi.- and contralesional hemispheres for a Anti-Nogo-A treated animal



➔ In both hemispheres, small neurons are more numerous than large neurons

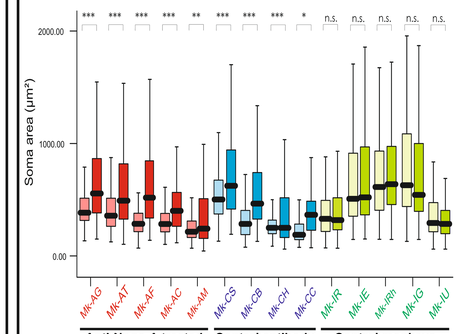
➔ The large neurons are almost completely absent in the contralesional hemisphere

5) Number of SMI-32 stained neurons per animal and hemisphere



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

6) 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 the soma is not comparable between the two hemispheres; a soma shrinkage was observed in the contralesional side

➔ Soma shrinkage was comparable in both groups of lesioned monkeys, irrespective of the treament