

Density of corticospinal (CS) fibers caudal to a cervical hemisection in primates correlates with behavioural recovery and is enhanced by **anti-Nogo-A** treatment

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Introduction:

Axons of the mammalian adult central nervous system demonstrate limited ability to regenerate after injury. In rodents subjected to spinal cord lesion, neutralizing the neurite growth inhibitor protein '**Nogo-A**' promoted regeneration of CS axons and improved significantly functional recovery.

Is this true for primates?

Fig 1 Typical behavioural data in 4 monkeys

Anti-Nogo-A treated monkeys recover faster and completely irrespective of the lesion extent for a manual dexterity task, requiring the precision grip.

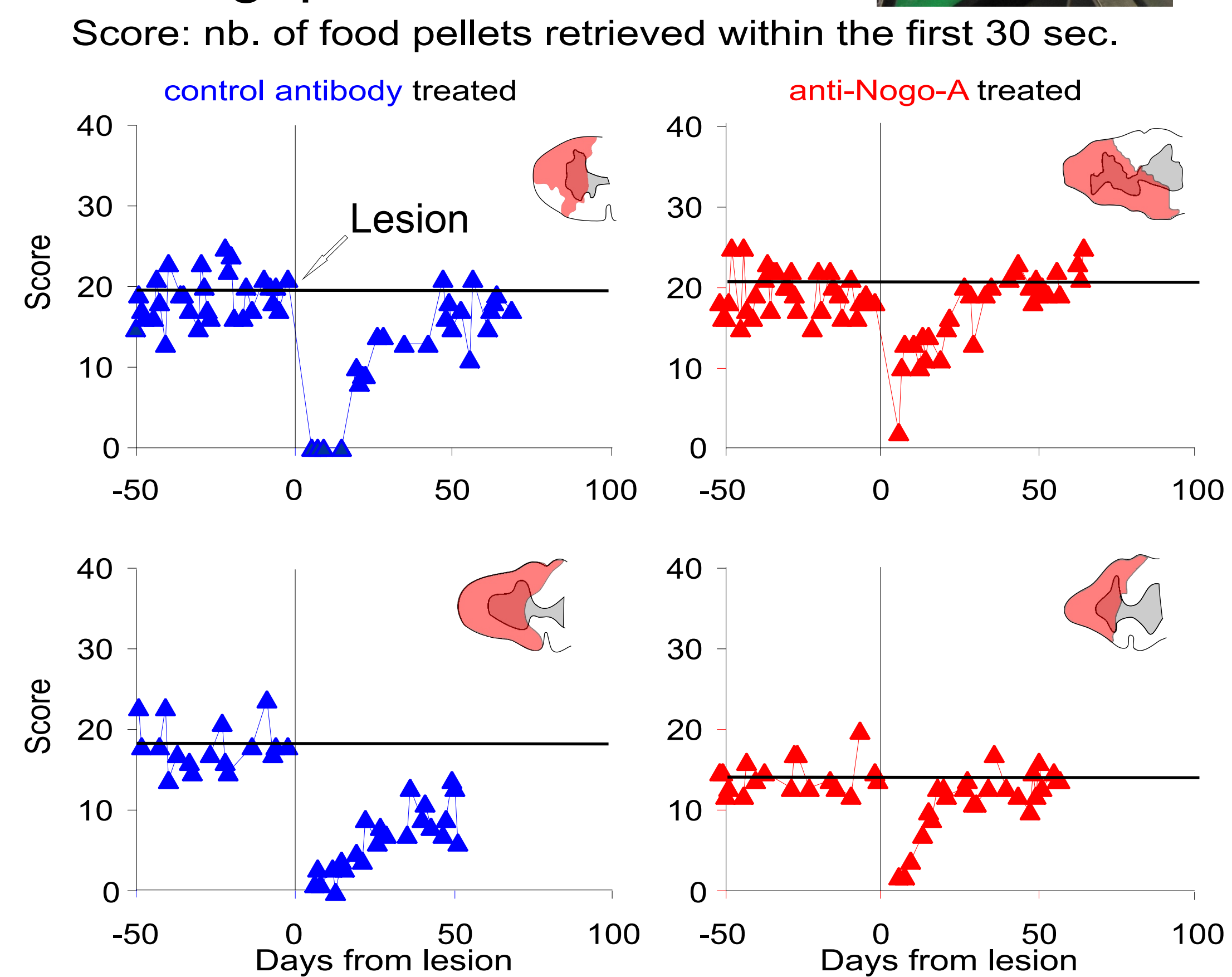
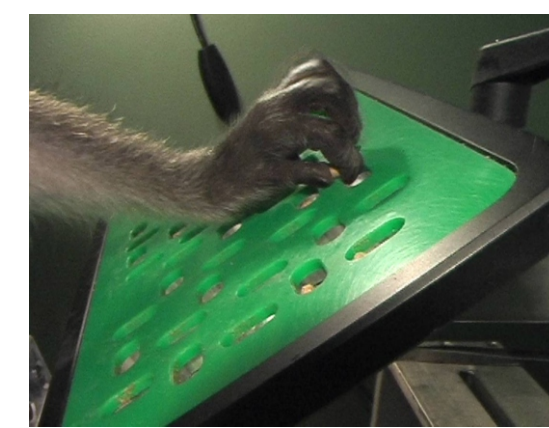
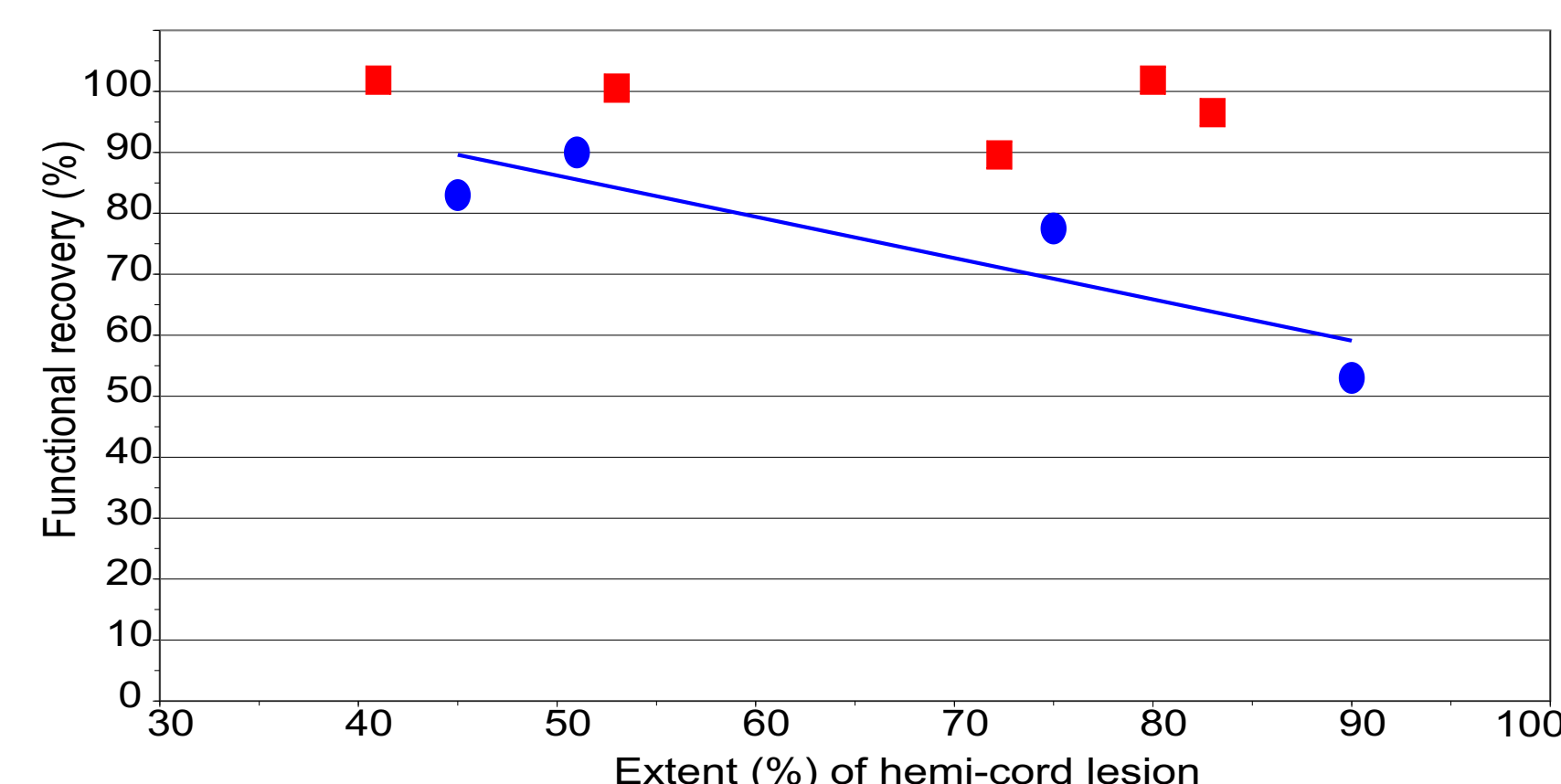


Fig 2

Control monkeys show limited manual dexterity recovery for large hemi-cord lesions, whereas **anti-Nogo-A** treated monkeys, irrespective of the lesion size, demonstrate complete manual dexterity recovery.

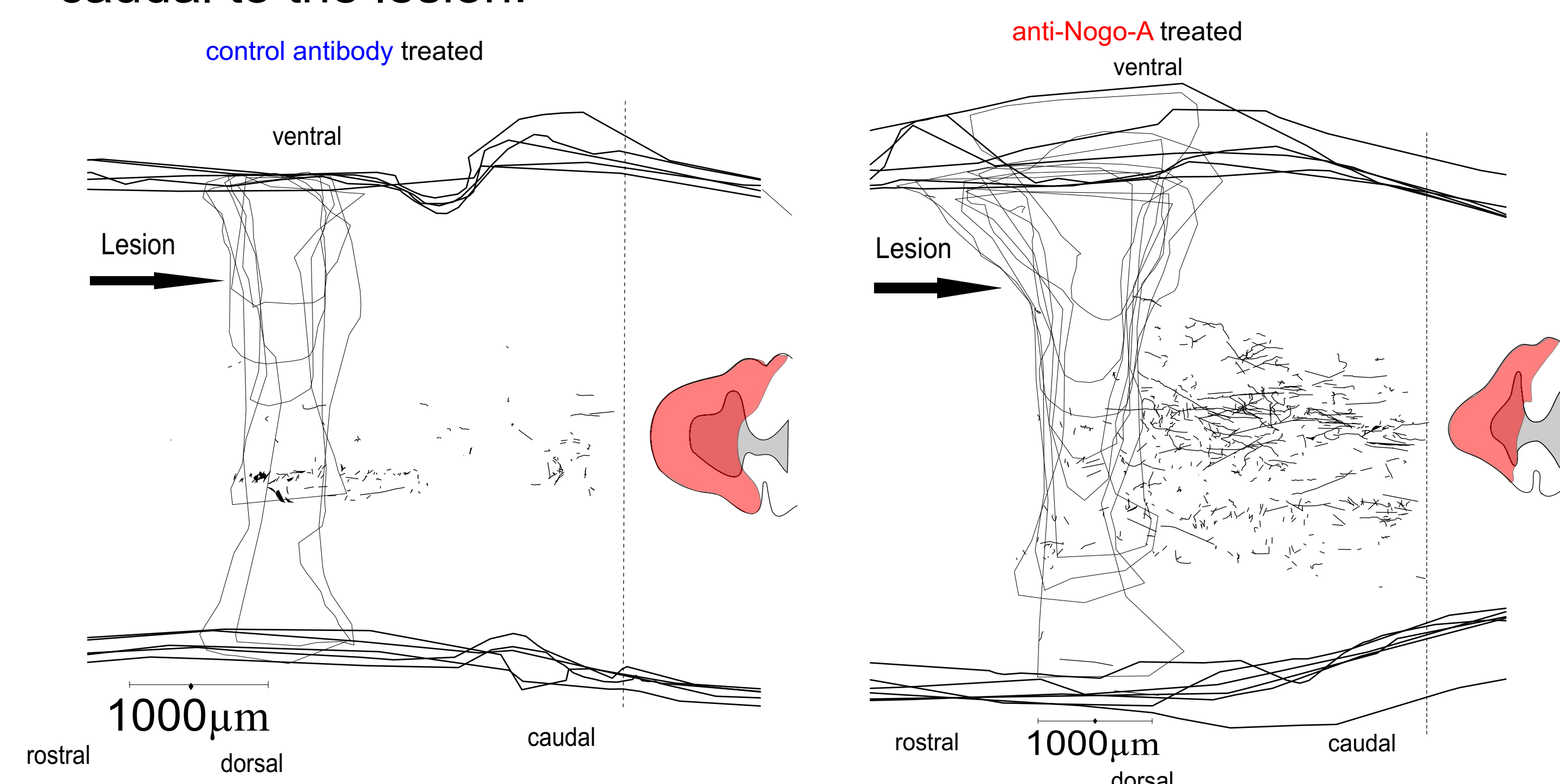


Materials and Methods:

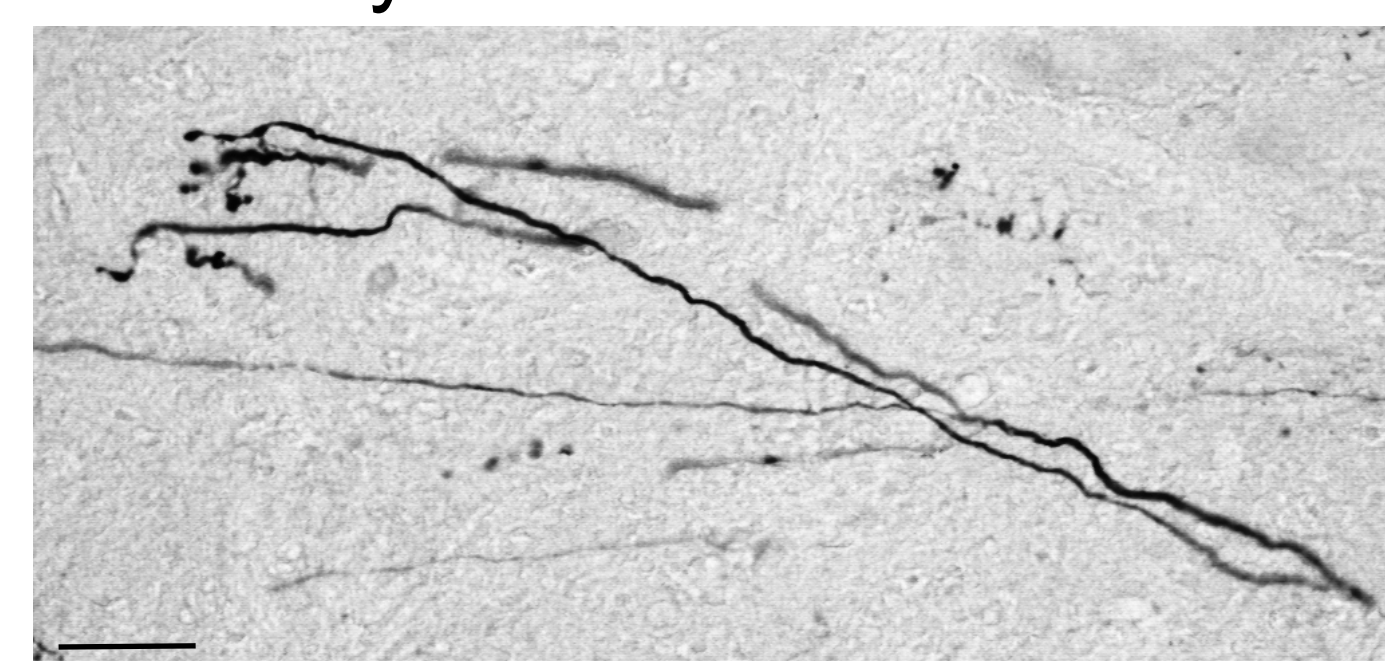
- ~ 12 young (3-5 years) adult macaque monkeys weighing from 3.5-5.5 kg were subjected to an unilateral hemisection of the cervical cord (C7/C8)
- ~ Quantitative assessment of functional recovery pre- and post-lesion: Manual dexterity test requiring the precision grip: opposition of the index finger and thumb to retrieve a food morsel out of a slot.
- ~ Lesion extent: Total surface of the sectioned hemi-cord against the entire hemi-cord.
- ~ 6 monkeys were treated with the monoclonal **anti-Nogo-A** antibody, whereas a control antibody was intrathecally infused in the other six monkeys.
- ~ Anterograde tracer: Biotinylated Dextran Amine (BDA) was injected into the motor cortex (M1) to stain the CS tract within the spinal cord.
- ~ Normalization: cumulated CS axonal arbor length and swelling counts were divided by the total number of CS axons at C5 level.

Fig 3

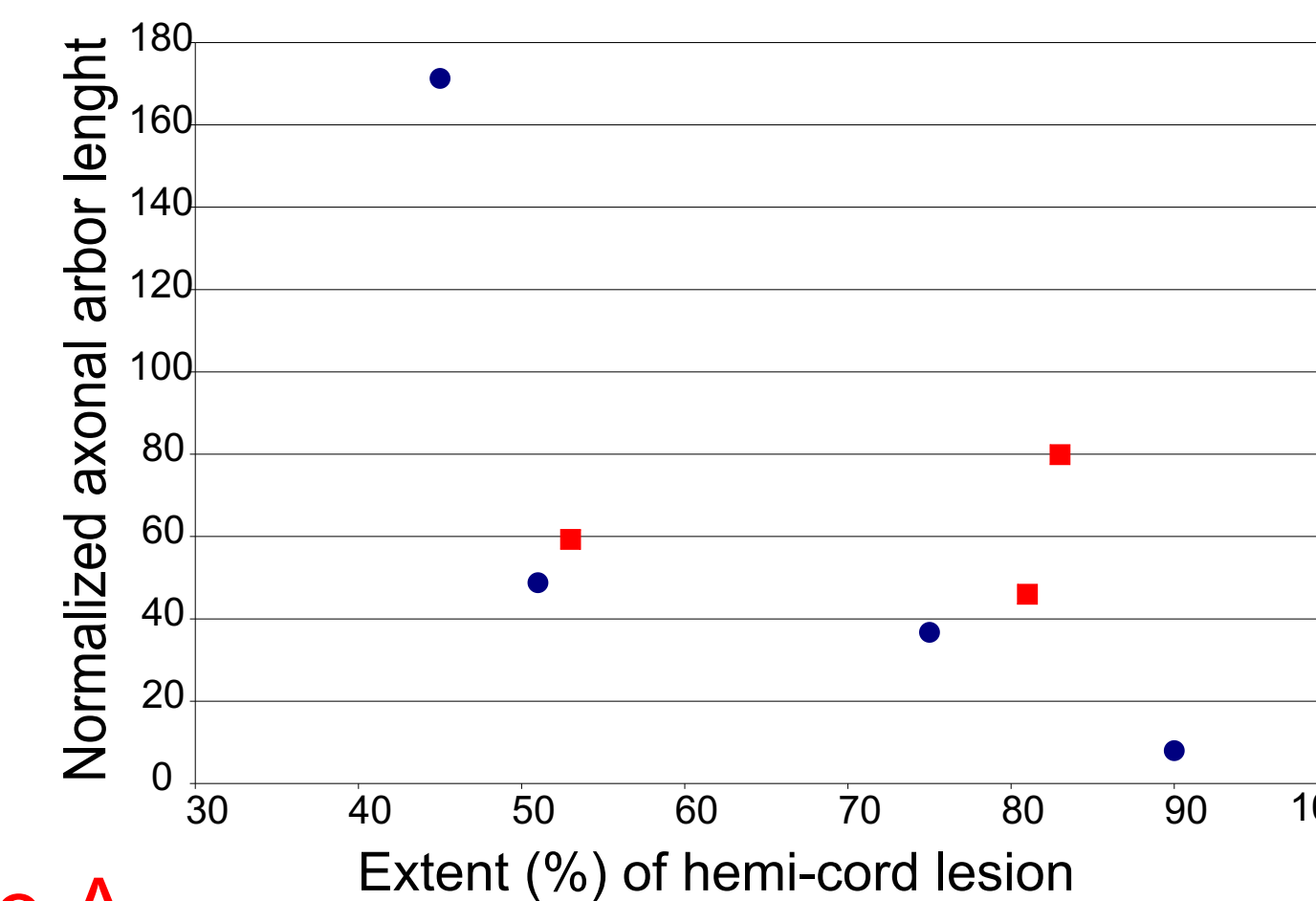
Superimposed reconstructions of paralongitudinal sections of the cervical-thoracic cord showing the lesion and the BDA labeled CS fibers in a territory 3 mm caudal to the lesion.



Anti-Nogo-A treated monkeys display a higher density of CS fibers caudal to the lesion, correlating with functional recovery.



Photomicrograph showing typical BDA labeled CS axonal arbors caudal to the lesion in an **anti-Nogo-A** treated monkey.



Conclusion:

Functional recovery is enhanced by **anti-Nogo-A** treatment in adult primates.

Anatomical reorganization (i.e. reconstruction) of the injured CS tract parallels the functional recovery and is enhanced by **anti-Nogo-A** treatment.

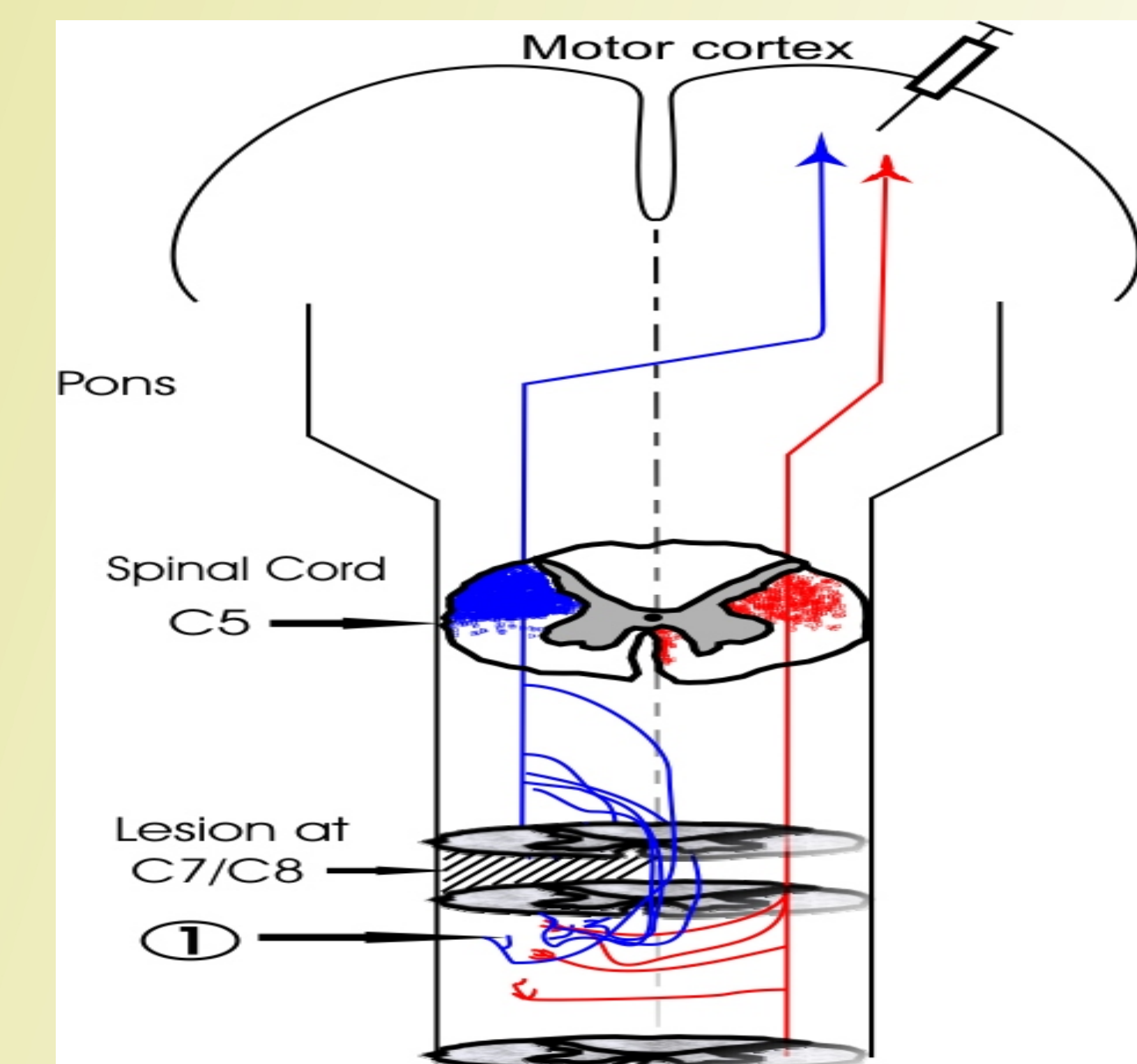
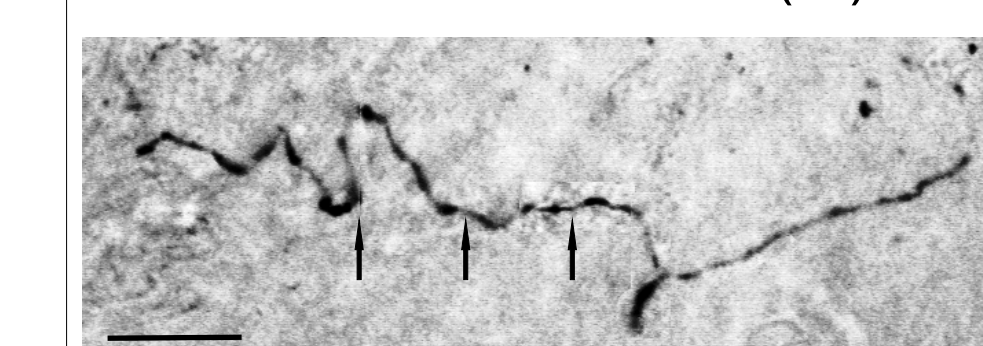
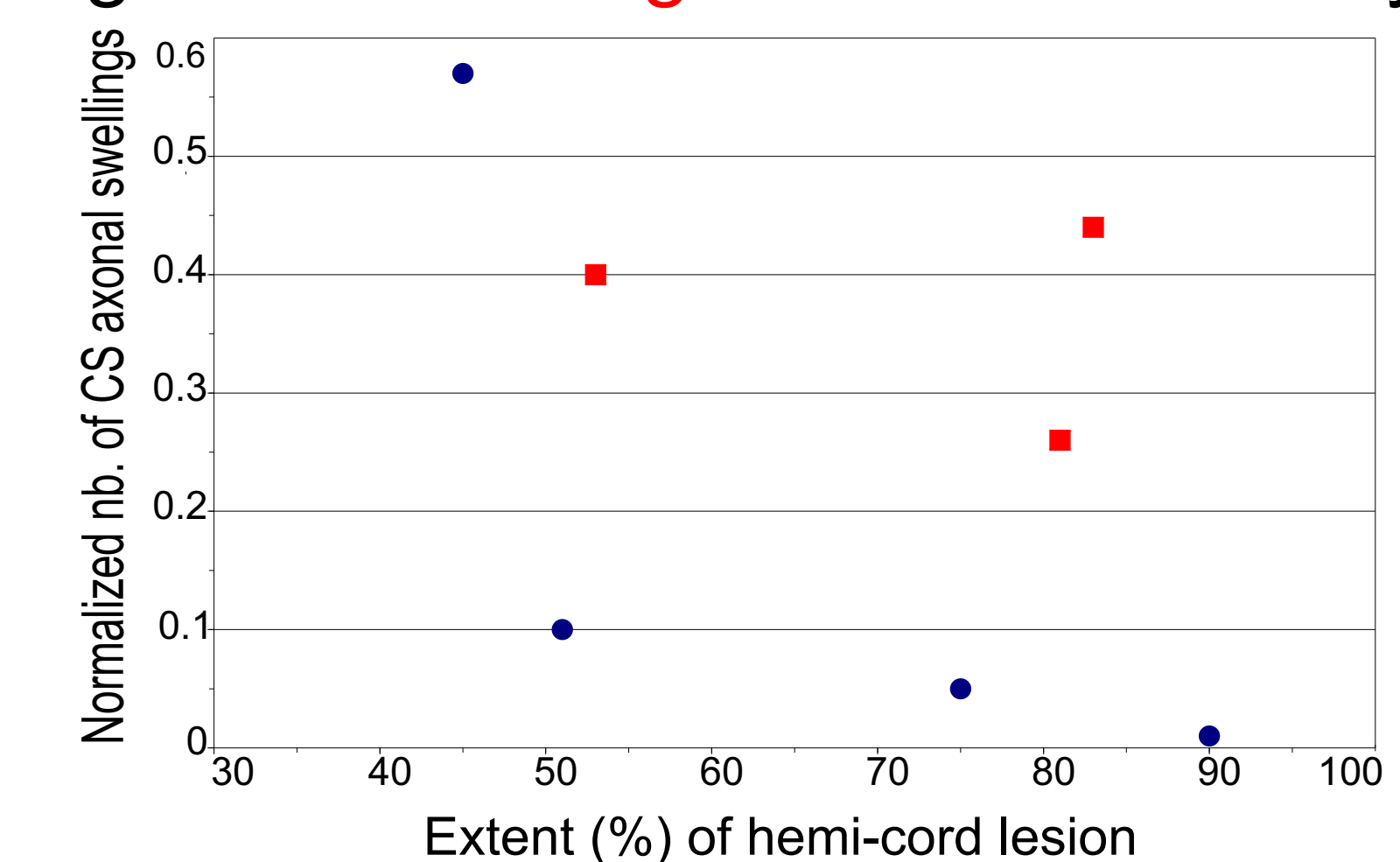


Fig 4

Normalized numbers of axonal swellings extending up to 3 mm caudal to the lesion are higher in **anti-Nogo-A** treated monkeys.



Photomicrograph showing a BDA labeled CS fiber with swellings (arrows) in the lesion.

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Conflict of Interest: Work supported by Novartis Pharma