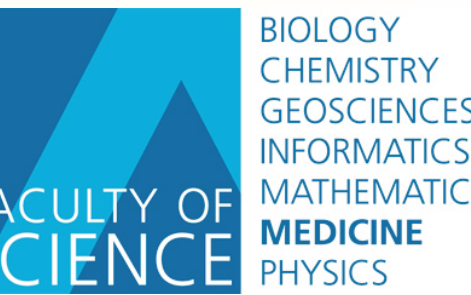


# Regenerative sprouting of corticospinal (CS) fibers following cervical section in adult monkeys is associated with functional recovery and both are enhanced by **anti-Nogo-A** treatment

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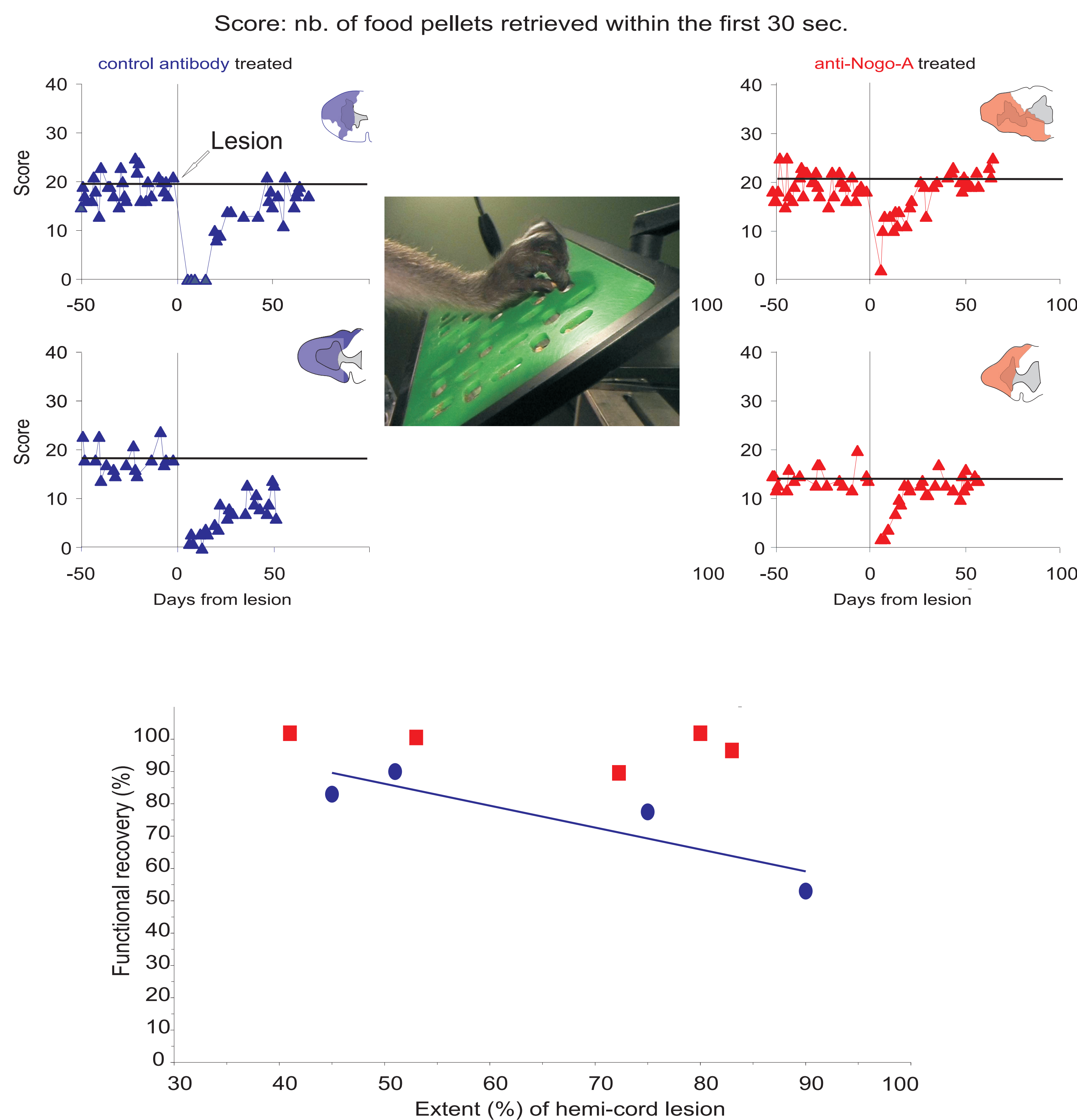
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## Introduction:

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?

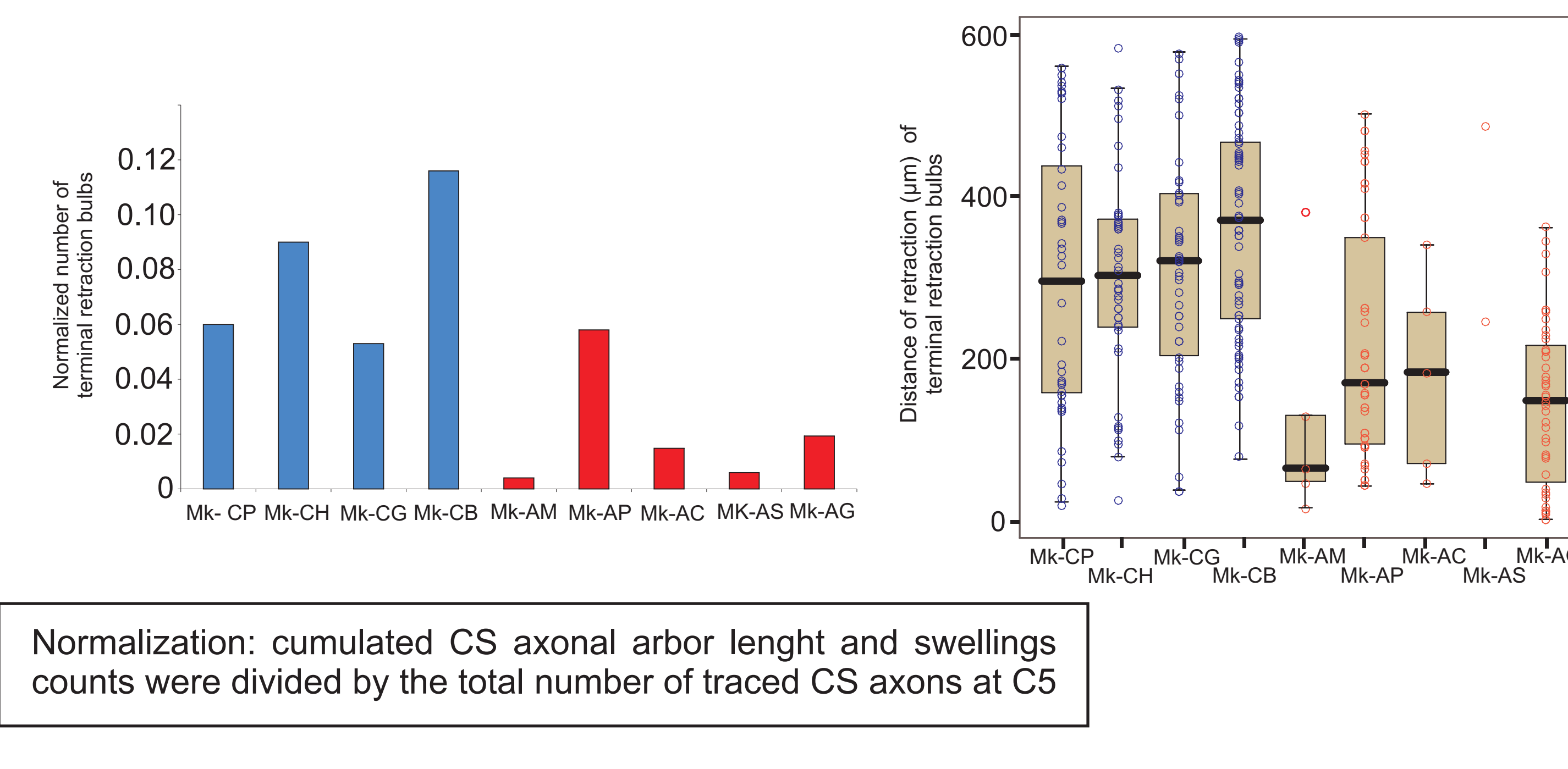
**Fig 1**  
 Typical behavioural data in 4 monkeys  
**Anti-Nogo-A** treated monkeys recovered faster and completely irrespective of the lesion extent for a manual dexterity task requiring the precision grip. In contrast, **control** monkeys showed limited manual dexterity recovery for large cervical lesions.



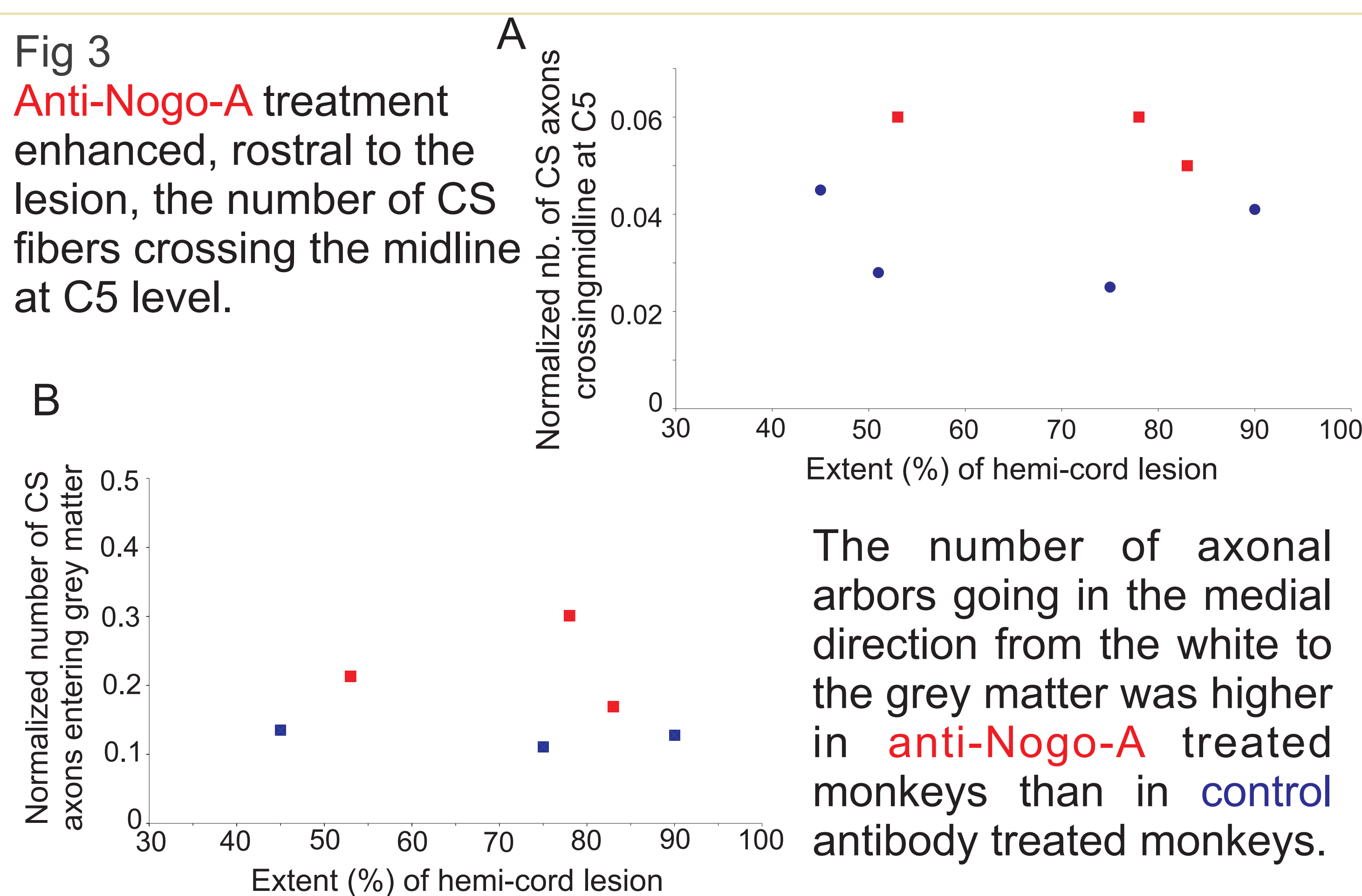
## Materials and Methods:

- ~ 12 young (3-5 years) adult macaque monkeys weighing from 3.5 to 5.5 kg were subjected to an unilateral section of the cervical cord level (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.
- ~ Six monkeys were treated with a 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.

**Fig 2**  
**Anti-Nogo-A** treated monkeys showed rostral to the lesion a significant reduction of retraction bulbs as seen on axotomized CS axons and a decrease of axonal dieback (distance of retraction) as compared to **control** antibody treated monkeys.



**Fig 3**  
**Anti-Nogo-A** treatment enhanced, rostral to the lesion, the number of CS fibers crossing the midline at C5 level.

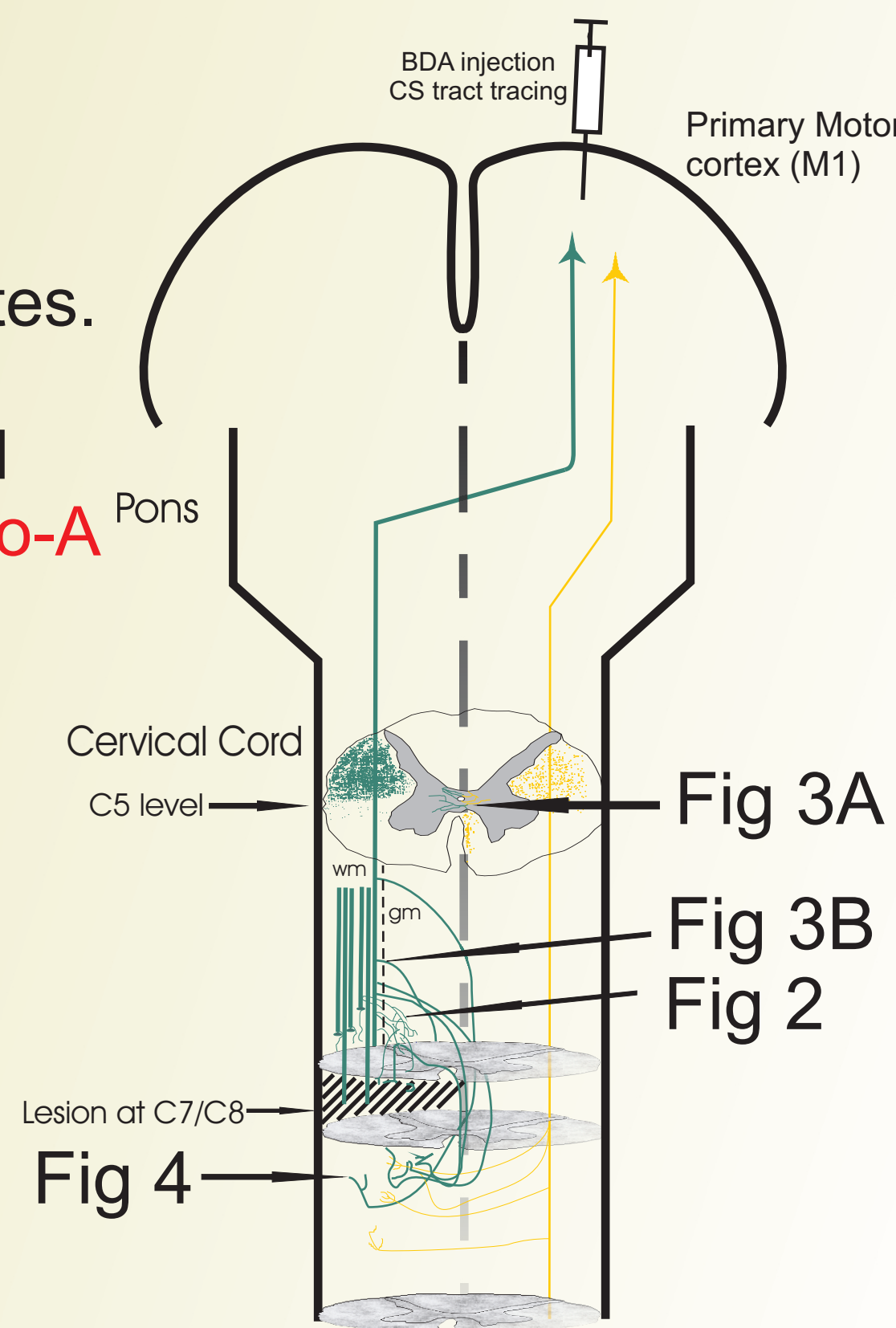


## Conclusion:

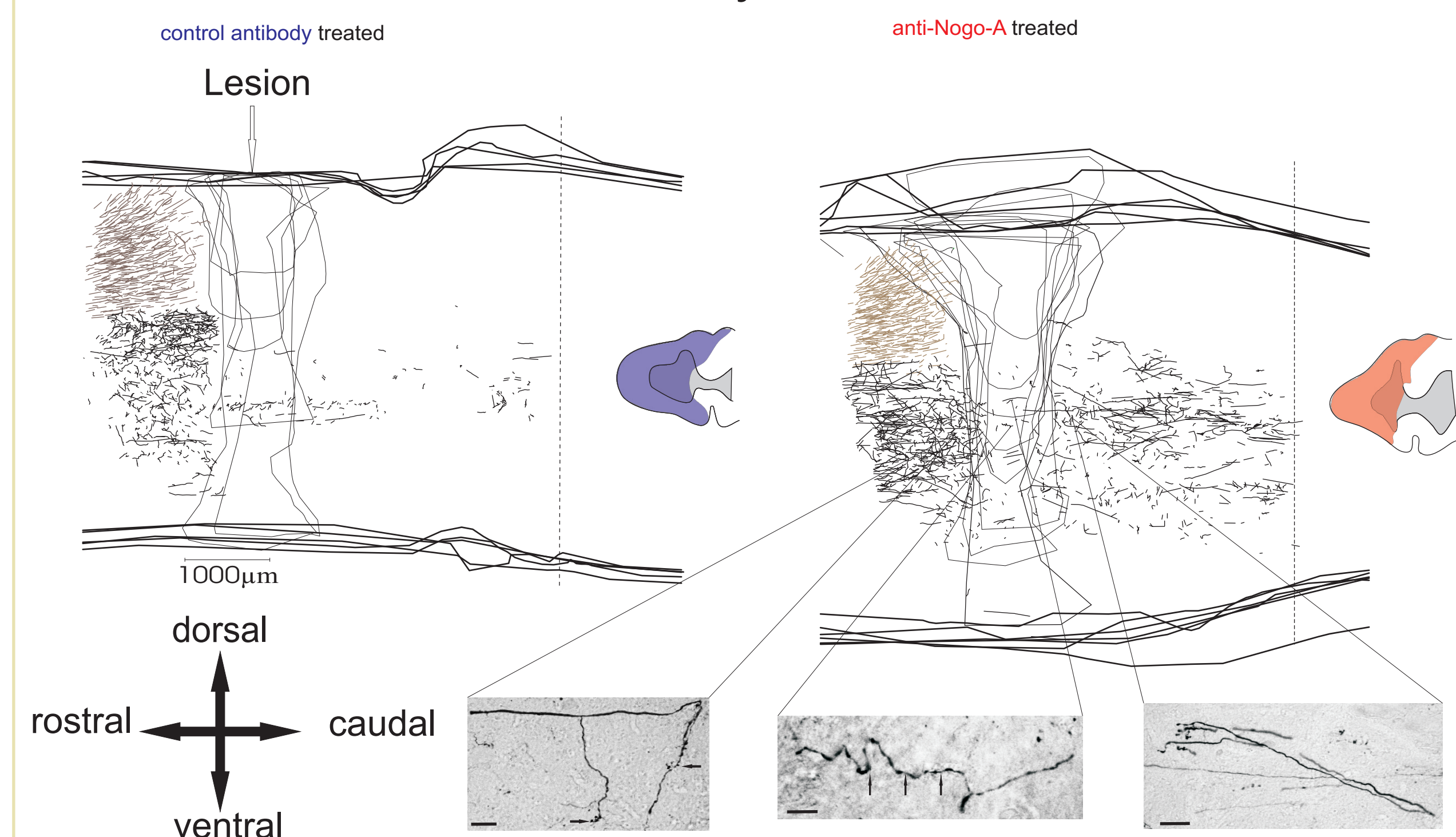
Functional recovery from spinal injury is significantly enhanced by **anti-Nogo-A** treatment in adult primates.

Regenerative sprouting of the injured CS tract is promoted by the **anti-Nogo-A** treatment as reflected by:

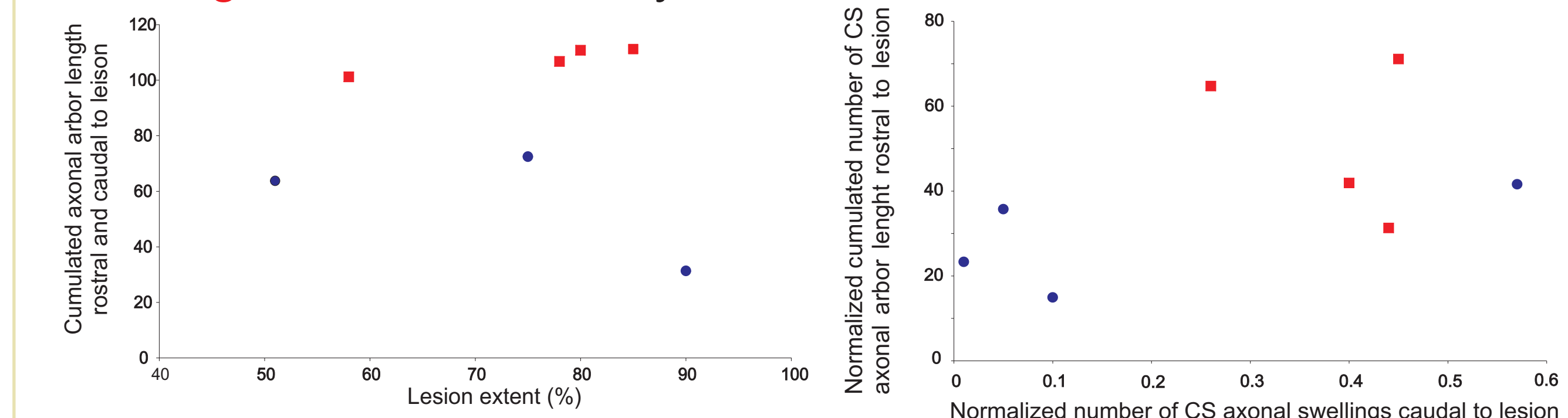
- a reduction of retraction bulbs,
- an attenuation of axonal dieback,
- higher numbers of CS crossing the midline at C5,
- a higher density of axonal arbors around the lesion
- an enhanced numbers of swellings caudal to the lesion, associated to an increased sprouting of CS axons rostral to the lesion.



**Fig 4**  
 Superimposed reconstructions of paralongitudinal sections of the cervical-thoracic cord showing the lesion and the BDA labeled CS fibers in a territory around the lesion.



Photomicrographs showing typical BDA labeled CS axonal arbors and swellings (arrows) rostral, caudal and within the lesion in an **anti-Nogo-A** treated monkey.



As compared to **control** antibody treated monkeys, **Anti-Nogo-A** treated monkeys display a higher density of CS fibers caudal to the lesion, correlating with better functional recovery. The treatment enhanced also the number of swellings caudal to the lesion, associated to an increased sprouting of CS axons rostral to the lesion (Fig 3).