Anti-Nogo-A antibody treatment promotes functional recovery in adult primates after unilateral cervical lesion: behavioral data

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Supported by NCCR-Neuro

Introduction:

In adult macaque monkeys, after lesion of the cervical cord, neutralization of the neurite outgrowth inhibitor protein Nogo-A leads to significant sprouting of corticospinal axons and to behavioral improvements. The data reflecting enhanced functional recovery were based on a global quantitative evaluation of manual dexterity as well as on a couple of semi-quantitative test (Freund et al. 2006). The present investigation aims at refining the analysis of the standard behavioral assessment of manual dexterity ("modified Brinkman board" task) with the goal to better assess the impact of a lesion at cervical level as well as the time course and extent of recovery, comparing control antibody and anti-Nogo-A antibody treated monkeys.

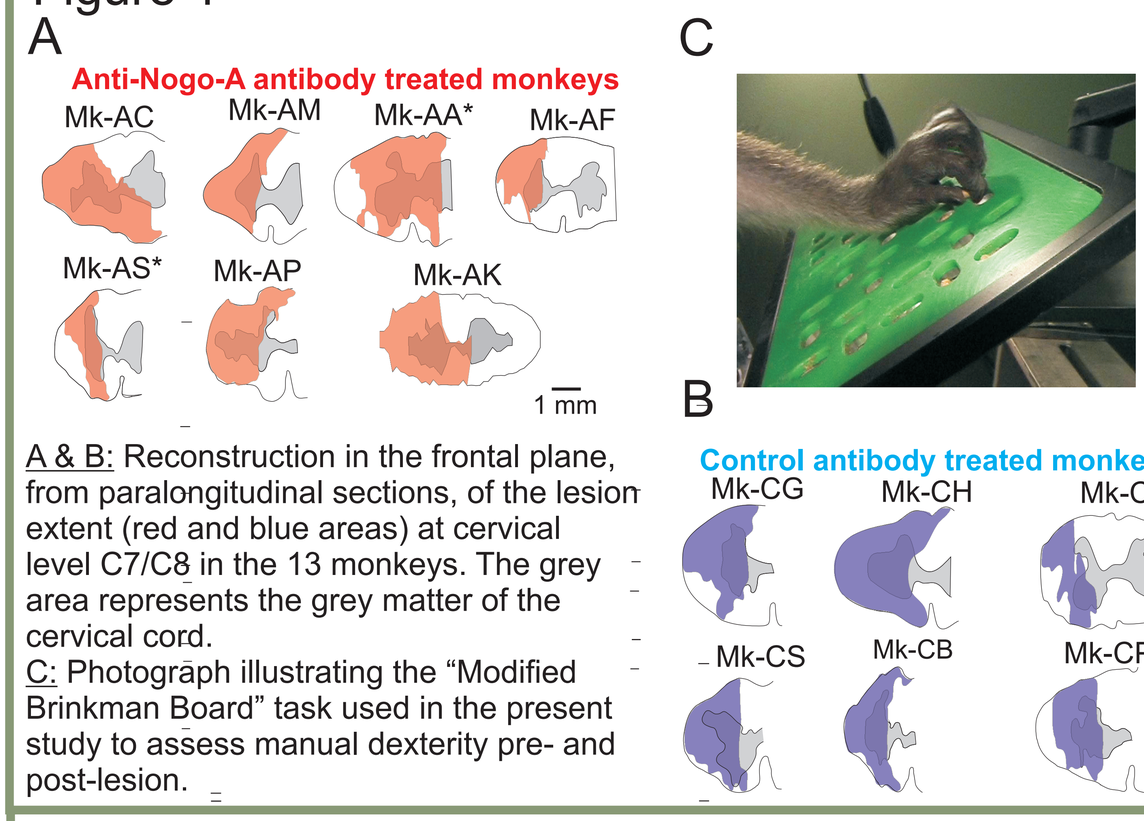
Materials and Methods:

- 13 young (3-5 years) adult macaque monkeys weighing from 3.5-5.5 kg were subjected to an unilateral section of the cervial cord (C7/C8 border)
- Quantitative assessment of manual dexterity pre- and post-lesion: **Modified Brinkman board** task, the time required to manipulate and extract the first pellet aimed for by the animal was analyzed and the total number of pellets retrieved within the first 30s from vertically and horizontally slots was counted.
- Lesion extent: Total surface of the sectioned hemi-cord against the entire hemi-cord.
- **7** monkeys were treated with an anti-Nogo-A specific antibody, whereas a control antibody was intrathecally infused in the other six monkeys.
- A new statistical test was introduced to assess the overlap/segregation between two groups of data (Figures 2E,F; 4C,D), taking into account two parameters, namely the extent of the lesion and the percent of functional recovery. We use Fisher's linear discriminant function providing maximal separation between the two groups.

Conclusion:

We conclude, based on a newly introduced readout of the behavioural assessment of the manual dexterity (contact time in the "modified Brinkman board" task) and a more appropriate statistical analysis, that anti-Nogo-A antibody treatment promotes significant improvement of functional recovery from cervical cord hemi-section in adult macaque monkeys. Moreover, no negative side effects, such as allodynia, were observed during the entire administration of the anti-Nogo-A antibody treatment.

Figure 1

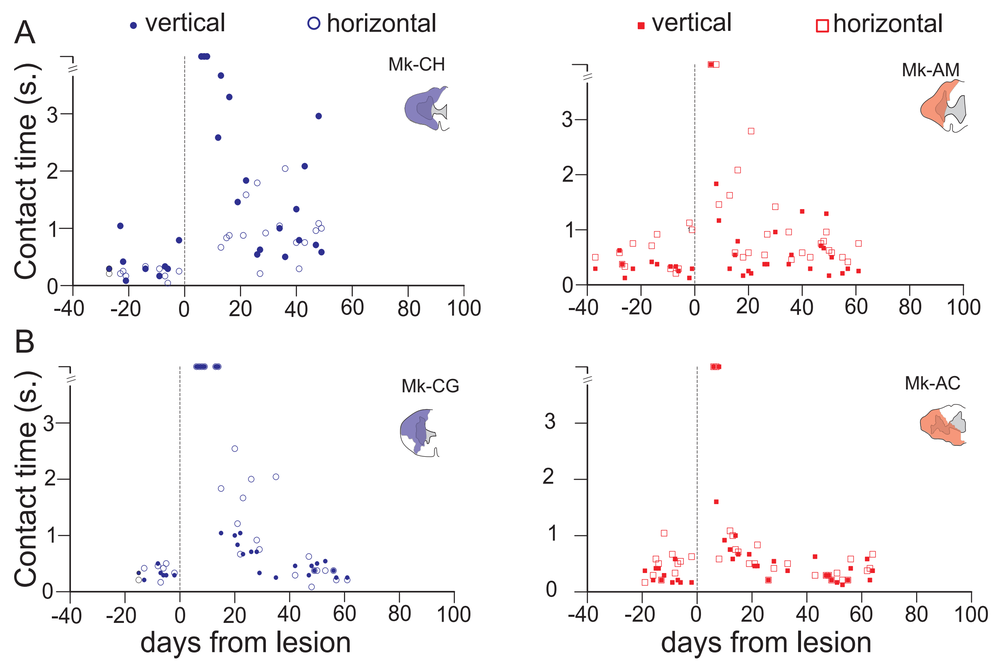


A & B: Reconstruction in the frontal plane, from paralongitudinal sections, of the lesion extent (red and blue areas) at cervical level C7/C8 in the 13 monkeys. The grey area represents the grey matter of the cervical cord.

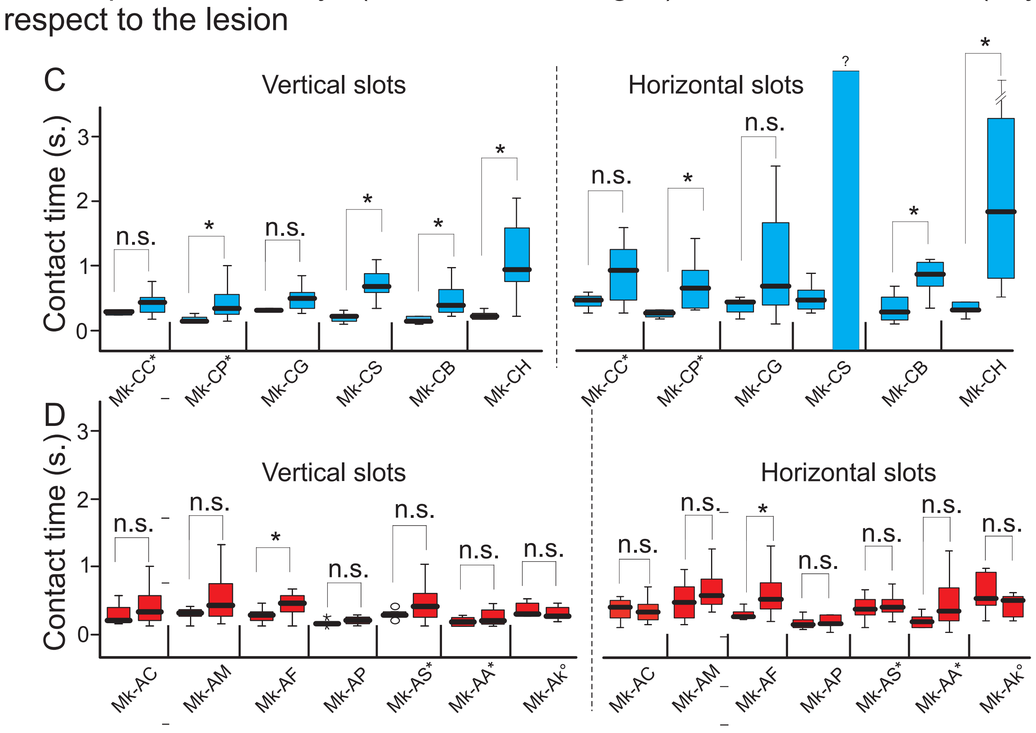
C: Photograph illustrating the "Modified Brinkman Board" task used in the present study to assess manual dexterity pre- and post-lesion.

Figure 3

"Modified Brinkman board" (contact time first pellet)



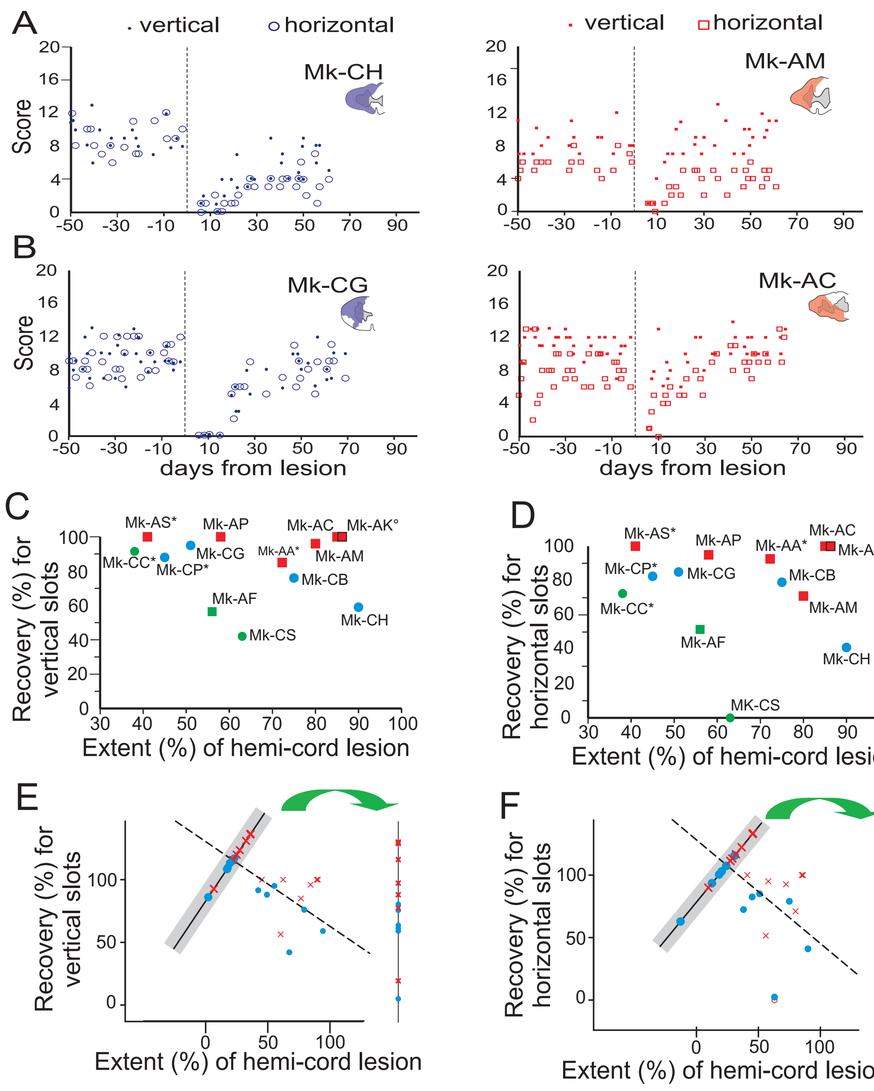
A & B: The contact time (in seconds), i.e. the time needed for a successful picking using the opposition of index finger and thumb in a pad to pad fashion, was plotted for two pairs of monkeys (the same as in Fig. 2) as a function of time (days) with respect to the lesion



C & D: The contact times, measured before lesion and within the last 10 post-lesion sessions in the plateau reflecting the recovery, are distributed in the form of box and whisker plots. For each monkey, the left bar is for pre-lesion data whereas the right bar is for the post-lesion data.

Figure 2

"Modified Brinkman board" (nb. of pellets in 30 seconds)

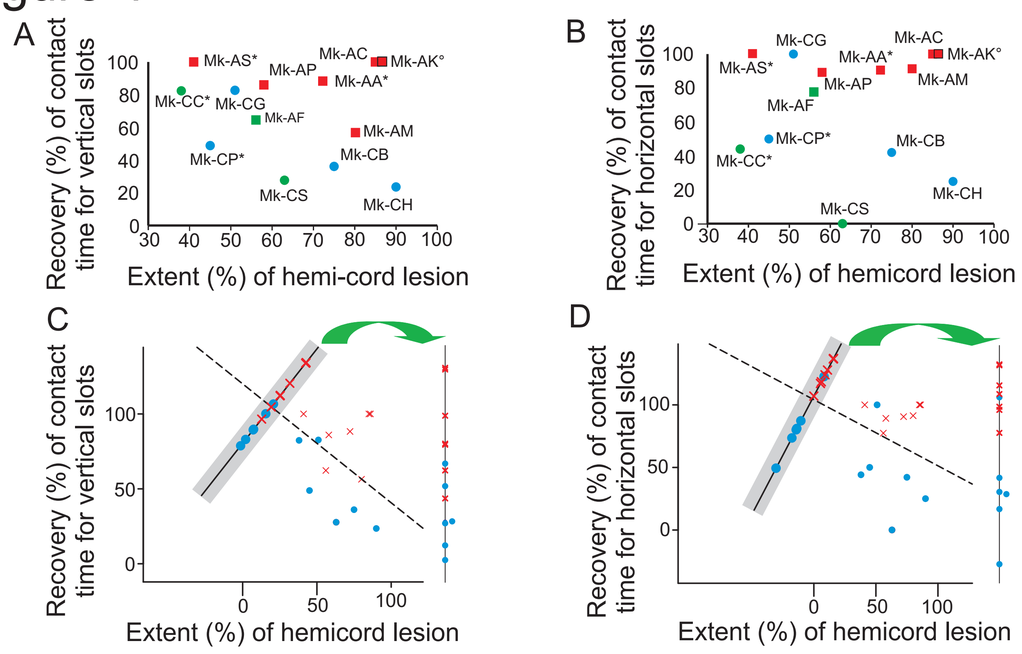


A & B:Quantitative assessment of manual dexterity based on scores for two "pairs" of monkeys.The scores were plotted separately for the vertical (dots) and horizontal (open symbols) slots.

C & D: Relationship between the extent of the hemi-cord lesion in % and the degree of functional recovery in % for the "Modified Brinkman board" test for vertically (C) and horizontally (D) oriented slots.

E & F: Illustration of the statistical analysis conducted on the data presented in panels C and D, respectively.

Figure 4



A & B: Relationship between the extent of the hemi-cord lesion and the functional recovery for the contact time needed for the first successful picking. Same conventions as in Figure 2C,D.

C & D: Graphic illustration of the statistical analysis conducted on the contact times for the vertical (C) and horizontal (D) slots (n=6 for control antibody treated monkeys and n=7 for anti-Nogo-A antibody treated monkeys). Same conventions as in Figure 2E,F.