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

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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) and introduce other behavioural tests of manual dexterity 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:

~ 12 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:

(i) **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

(ii) **Rotating Brinkman board** task, testing the ability of the monkey to anticipate and control a prehension movement aimed towards moving pellets placed in wells on a rotating panel

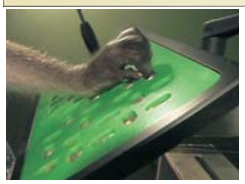
(iii) **Hidden Brinkman board** task, testing the ability to perform a motor exploration of a board consisting of 20 wells with pellets in absence of visual control

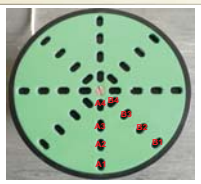
~ Lesion extent: Total surface of the sectioned hemi-cord against the entire hemi-cord.

~ 6 monkeys were treated with an anti-Nogo-A specific antibody, whereas a control antibody was intrathecally infused in the other six monkeys.

Conclusion:

In line with our previous report (Freund et al. 2006), anti-Nogo-A antibody treated monkeys recover better than control antibody treated monkey for the parameter contact time. Furthermore the two newly introduced tests show that recovery occurs for more challenging performances such as a precison grip in a dynamic situation and during motor exploration without visual feed-back. The anti-Nogo-A antibody treated monkey tested recovered better then two control antibody treated monkeys.





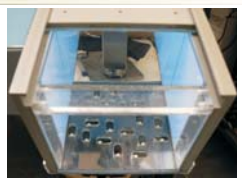
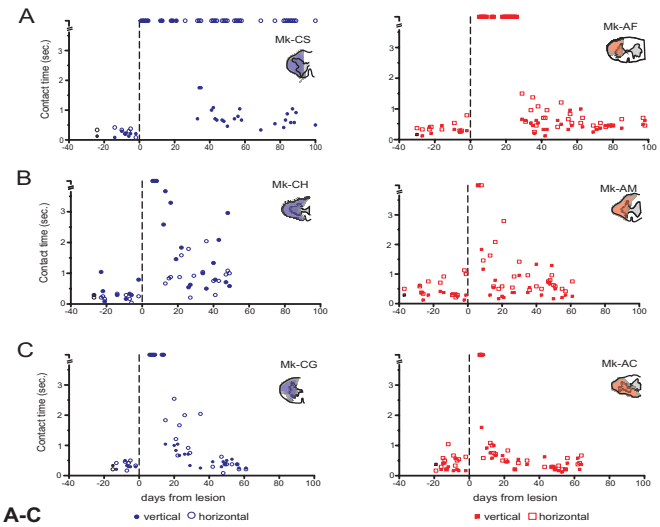


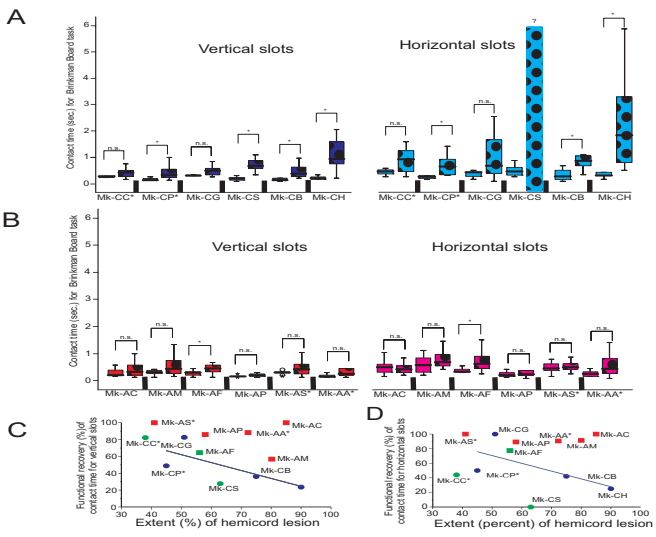
Fig 1 "Modified Brinkman board" (contact time for first pellet)



Panel A-C

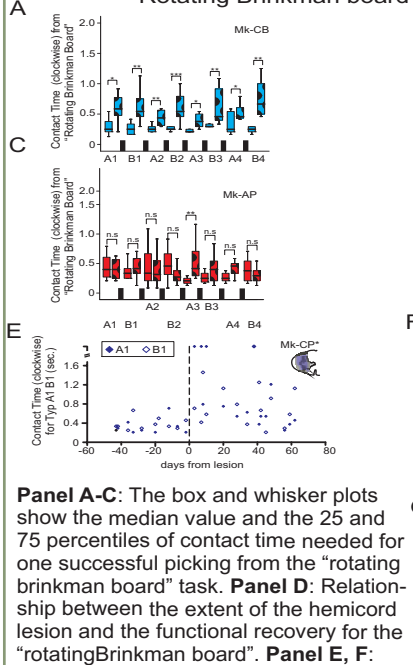
Analysis of the contact time, i.e. time needed for a successful picking as achieved through the opposition of index and thumb in a pad to pad fashion. Data is shown for control antibody and anti-Nogo-A antibody treated monkeys pre- and post-lesion.

Fig 2 "Modified Brinkman board" (contact time for first pellet)



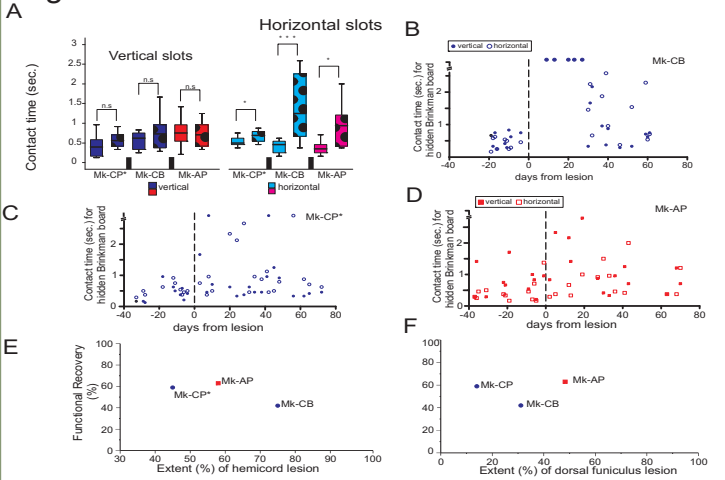
Panel A, B: The box and whisker plots show the median value and the 25 and 75 percentiles of contact time needed for the first successful picking pre-lesion (first column) and the last ten post-lesion performance for the "modified Brinkman board" task. **Panel C, D**: Relationship between the extent of the hemi-cord lesion and the functional recovery of contact time for successful picking for vertical (C) and horizontal (D) oriented slots.

Fig 3 "Rotating Brinkman board" (clockwise; contact time)



Panel A-C: The box and whisker plots show the median value and the 25 and 75 percentiles of contact time needed for one successful picking from the "rotating brinkman board" task. **Panel D**: Relationship between the extent of the hemicord lesion and the functional recovery for the "rotatingBrinkman board". **Panel E, F**: Time course of functional recovery of contact time.

Fig 4 "Hidden Brinkman board" (contact time for first pellet)



Panel A: The box and whisker plots show the median value and the 25 and 75 percentiles of contact time pre- and post-lesion. **Panel B-D**: Time course of recovery of contact time. **Panel E-F**: Relationship between the functional recovery observed for the "Hidden Brinkman Board " and the extent of the hemi-cord and of the dorsal funiculus lesion extent, respectively.