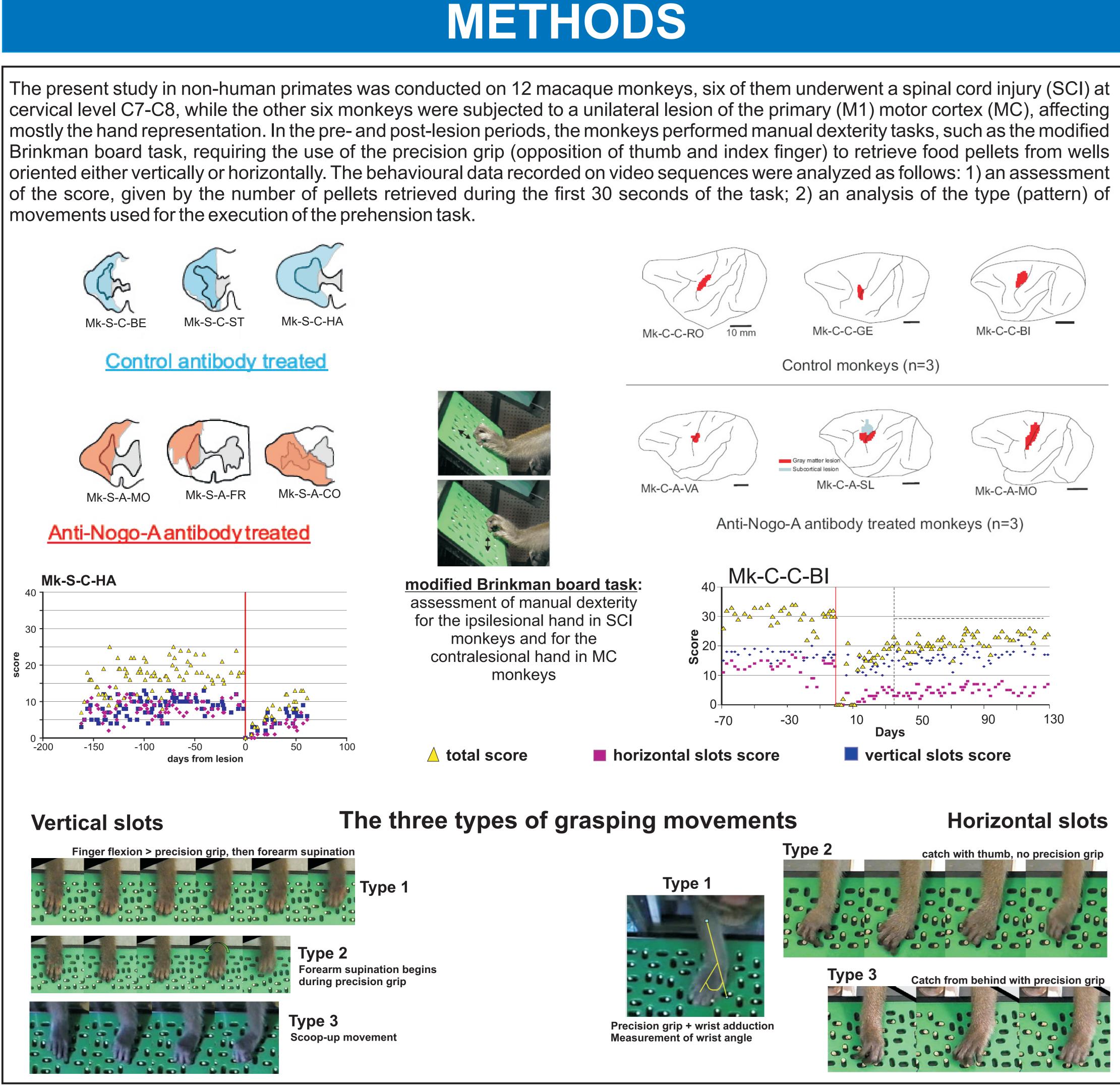
Comparison of mechanisms of functional recovery from spinal cord or motor cortex lesion in adult macaque monkeys and influence of anti-Nogo-A antibody treatment. F. Hoogewoud, A. Belhaj-Saïf, E.M. Rouiller

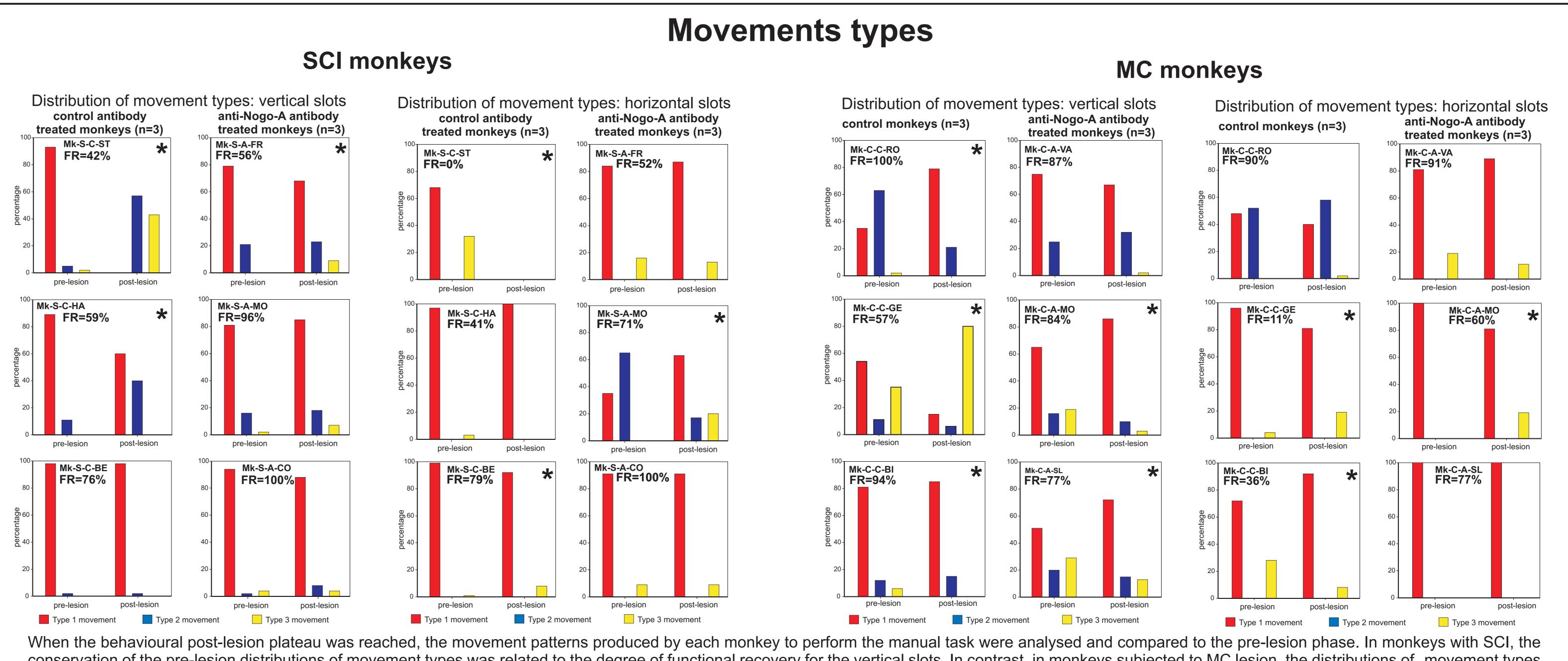


INTRODUCTION

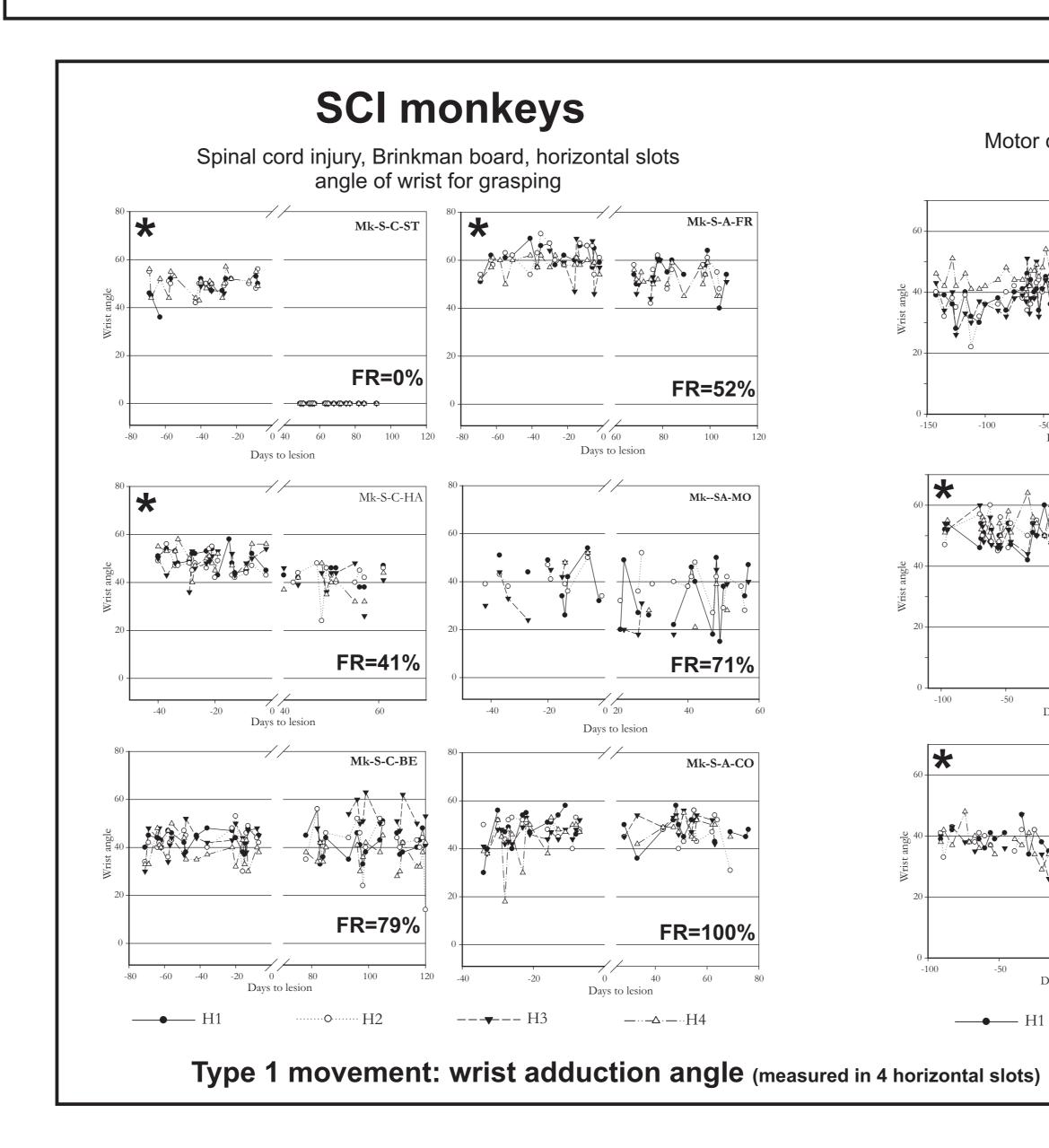
This study investigated in non-human primates the behavioral aspects of functional recovery after spinal cord injury (SCI) or (primary) motor cortex lesion (MC) and therapy with anti-NogoA-antibody. By analyzing movement patterns, we aimed at distinguishing two types of recoveries: 1) "true" functional recovery where the movement patterns are conserved (re-established) in the post-lesion period, so that the same effector muscles are used to accomplish the task as before the lesion; 2) functional compensation, when the strategy to execute the task changed in the post-lesion period, using other effector muscles, as compared to pre-lesion.



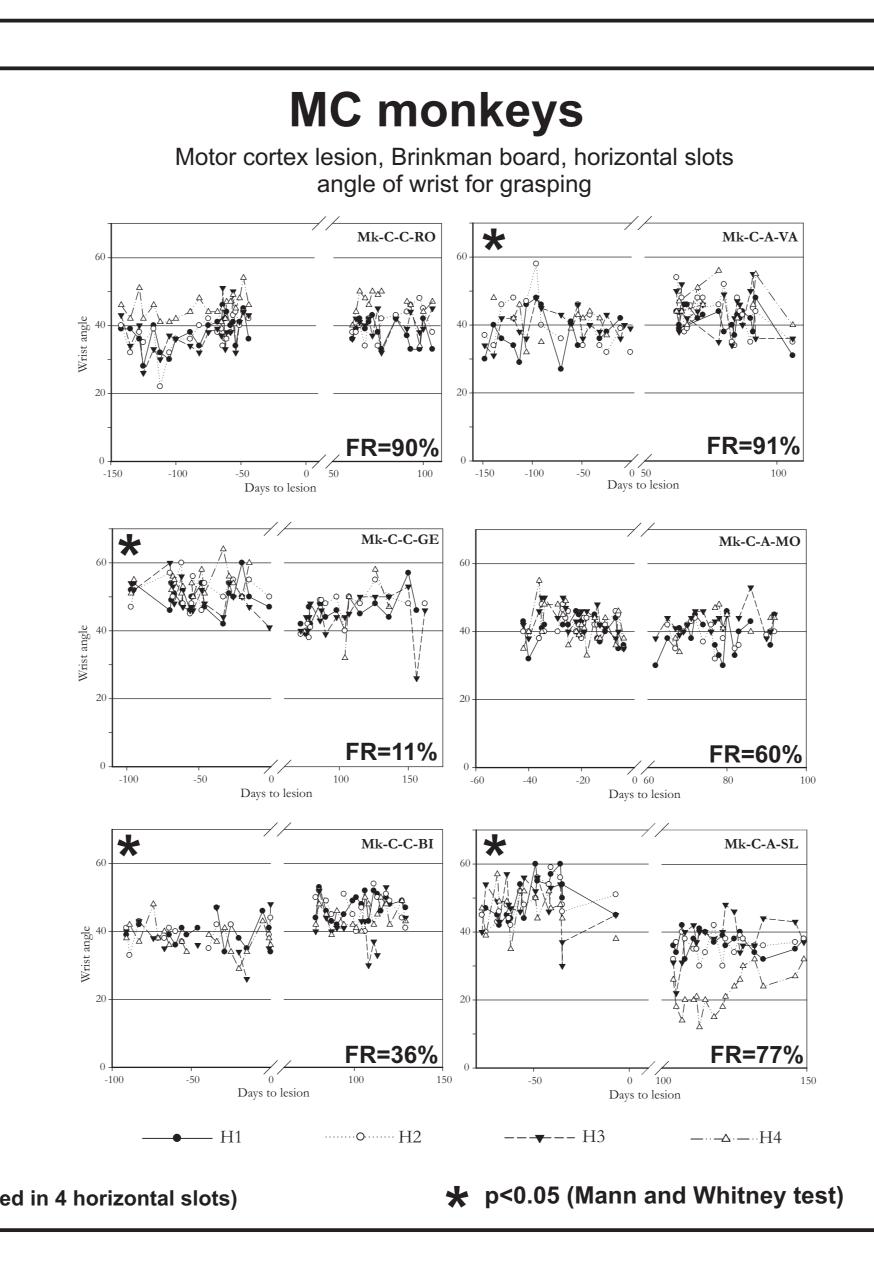
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conservation of the pre-lesion distributions of movement types was related to the degree of functional recovery for the vertical slots. In contrast, in monkeys subjected to MC lesion, the distributions of movement types observed for the vertical slots were modified in most cases, although some monkeys exhibited a substantial functional recovery. In the MC monkeys, for the horizontal slots, there was a relation between better functional FR=extent of functional recovery (score post-lesion/score pre-lesion*100). *p<0.05 (chi-square test) recovery and preservation of the pre-lesion distributions of movement types.



RESULTS



Survey of data

The score data show that, for both types of lesion, there was a dramatic loss of manual dexterity following the injury (score dropped to zero) during a couple of weeks, followed by a progressive functional recovery, reaching after a few weeks a post-lesion plateau, generally lower than the pre-lesion score, indicative of an incomplete functional restitution of manual dexterity.

As reported in previous studies, there is evidence for improved functional recovery in the group of monkeys treated with anti-Nogo-A antibody after SCI (see e.g. Freund et al., 2009 EJN 29: 983-996). For MC lesion, there is also preliminary evidence for enhanced functional recovery in anti-Nogo-A antibody treated monkeys (not yet published).

In the present study, an original aspect of analysis of the behavioural data was introduced for the group of monkeys with MC lesion: as the properties (location, extent) of the MC lesion is very variable among monkeys, we normalized the lesion size (volume in mm³) by dividing it by the surface of hand representation in M1. With such an additional normalization step, the benefits of the therapy appeared more pronounced for the horizontal slots, representing a more challenging prehension task than for the vertical slots.

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Mk-C-C-BI Mk-C-C-C Mk-C-A-VA 80 Mk-C-A-SL Mk-C-C-RO Mk-C-C-GE 0.0 0.2 0.4 0.6 0.8 1.0 1.2 1.4 1.6 1.8 2.0 total slots Mk-C-C-RC Mk-C-A-VA Mk-C-A-SL Mk-C-C-BI Mk-C-C-GE 0.0 0.2 0.4 0.6 0.8 1.0 1.2 1.4 1.6 1.8 2.0 normalized lesion size

In the 6 monkeys subjected to motor cortex lesion and considered for the present analysis, after nomalization of the lesion size, there is preliminary evidence for an enhancement of the recovery of manual dexterity possibly due to the anti-Nogo-A antibody treatment, observable for the horizontal slots only (task more challenging than for the vertical slots).

CONCLUSION

The results show that, after SCI, the anti-Nogo-A antibody treatment improved the functional outcome and favored true recovery reflected by the conservation of movement patterns (for the vertical slots). After MC injury, the distribution of movements types was often different as compared to prelesion (for the vertical slots). In this case, anti-Nogo-A antibody improved functional outcome, with however differences in the distribution of movements types. Still after MC injury, for the horizontal slots, original distributions of movement types were associated to better functional recovery. In clinical practice, those results could have an impact on rehabilitation protocols designed for human subjects to improve functional recovery after SCI or MC injury.



