Reorganisation of callosal connectivity of the motor cortical areas following unilateral lesion of primary motor cortex (M1) in monkeys: influence of anti-Nogo-A antibody treatment

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Introduction

The motor cortex of macaques is divided into four main regions: the primary motor cortex (M1), the premotor cortex (PM), the supplementary motor area (SMA) and the cingulate motor area (CMA). The callosal connectivity of the motor cortical areas is well established (Jenny 1989; Rouiller et al, 1994; Boussaoud et al, 1999; Marconi et al, 2003).

It was shown that PM plays a crucial role in the spontaneous (incomplete) functional recovery after M1 lesion (Liu and Rouiller, 1999). Furthermore, after M1 lesion, the homolateral projections of PM originally aimed to M1 were re-directed onto the somatosensory cortex (Dancause et al, 2005).

The aim of this study was to investigate whether the pattern of callosal connectivity of PM is modified as a result of unilateral lesion of M1, and whether such changes may be influenced by anti-Nogo-A antibody treatment post-lesion.

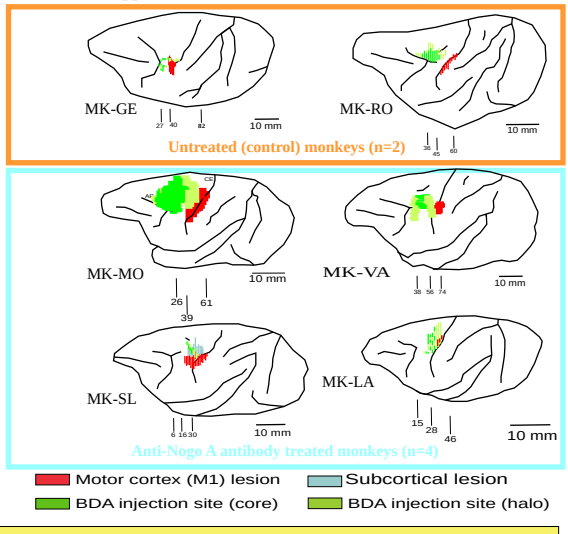
Materials and Methods

Six adult monkeys were involved in this study: four monkeys were treated with the anti-Nogo-A antibody and two were control monkeys. All monkeys were subjected to a unilateral cortical lesion by microinfusion of ibotenic acid in the hand area of M1. The anti-Nogo-A antibody treatment was delivered immediately after the lesion during 4 weeks. The tracer BDA was injected in PM on the lesioned hemisphere. The distribution of BDA-labelled neurons was established on the opposite hemisphere using Neurolucida software. To account for variability due to BDA injection site size and uptake, the data were normalized based on the number of labelled corticospinal axons present in the pyramids.

Photomicrograph of BDA injection site

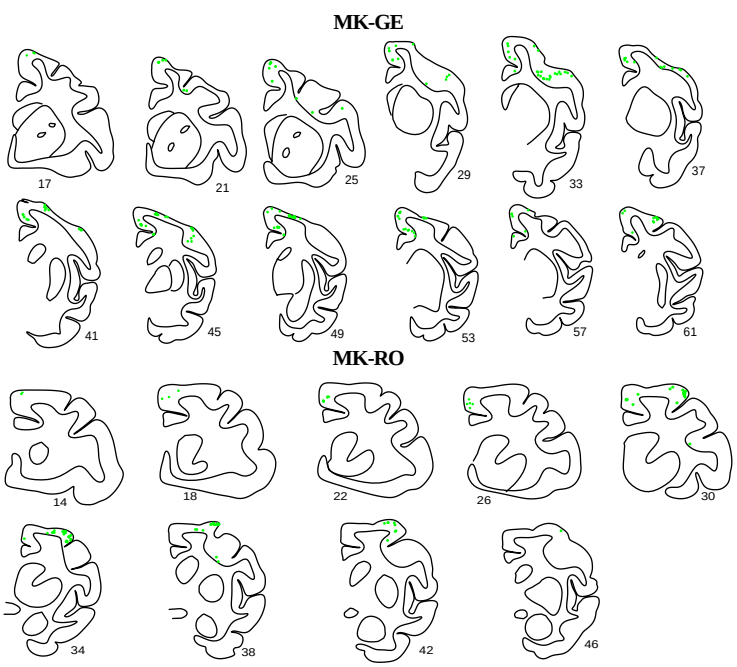
Photomicrograph of BDA labelled cells

Location and approximate extent of lesion and BDA injection sites



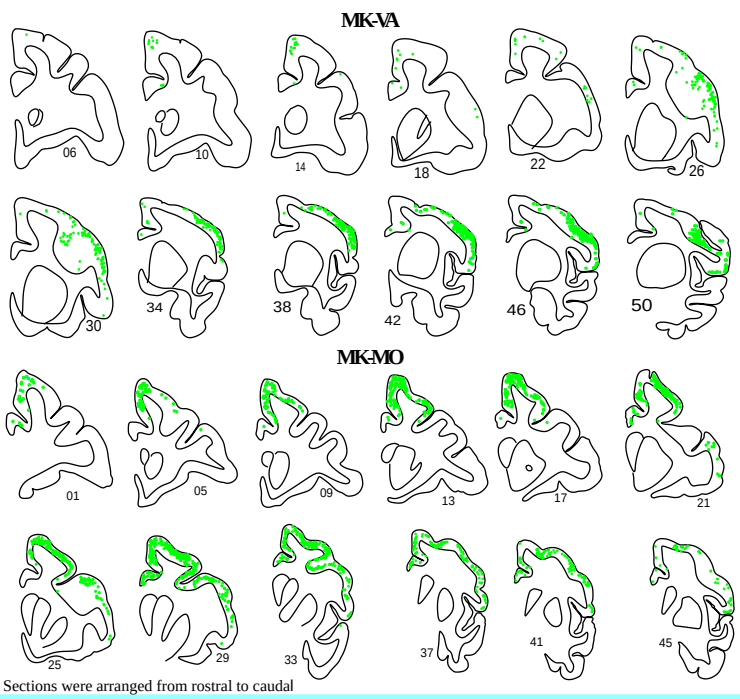
Results

Distribution of BDA-labelled cells in the contralesional hemisphere in control monkeys

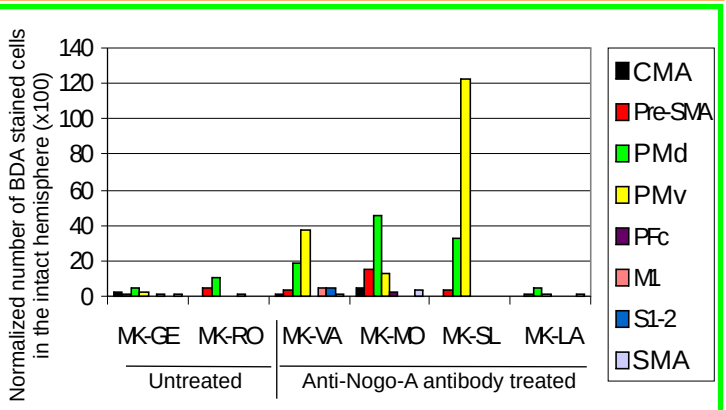


Sections were arranged from rostral to caudal

Distribution of BDA-labelled cells in the contralesional hemisphere in treated monkeys



Sections were arranged from rostral to caudal



The distribution of BDA-labelled cells in the intact hemisphere was more prominent in the group of anti-Nogo-A antibody treated monkeys as compared to the untreated monkeys.

In the anti-Nogo-A antibody treated monkeys, the increased number of BDA-labelled cells was mostly confined to PMd and PMv. There was no increase of labeling in MK-LA, possibly due to a very small lesion in M1 (and no behavioral deficit).

Conclusion

- In line with a significant role of PM in the functional recovery after lesion of M1, we found an enhancement of the callosal connectivity of PM in anti-Nogo-A antibody treated monkeys.
- The re-organization of the callosal connectivity of PM may be related to a trend towards an enhancement of functional recovery in the anti-Nogo-A antibody treated monkeys.

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