G37 A unilateral lesion of the hand representation in the primary motor cortex or a partial hemisection of the cervical cord in macaques affects the interhemispheric ratio of SMI-32 stained neurons in premotor cortical areas

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Introduction

The primary motor cortex (M1) of primates is interconnected with premotor areas, in both hemispheres, such as the rostral part of the ventral premotor cortex (PMv-r or F5) and the supplementary motor area (SMA: pre-SMA = F6 and SMA-proper = F3)). The working hypothesis was that after a unilateral lesion of M1, there is a change of the SMI-32 positive cells ipsilesionally in PMv-r and SMA. To assess possible effects of a permanent unilateral lesion of M1 (hand region) or of an hemisection of the spinal cord (C7/C8 level) on PMv-r and SMA, a histological analysis of several macaques' brain was performed by comparing between the 2 hemispheres the neuron density of layers III and V in these premotor areas.

In this study, three subpopulations of adult animals were analyzed: (i) five intact control animals; (ii) seven animals with a unilateral lesion of M1 (two of them were treated with anti-Nogo A antibody); (iii) nine macaques with a unilateral lesion of the spinal cord (three of them were treated with anti-Nogo A antibody).

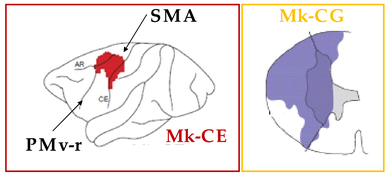

Figure 1. Schematic view of a cortical lesion (red area, left panel) and a spinal lesion (blue area, right panel).

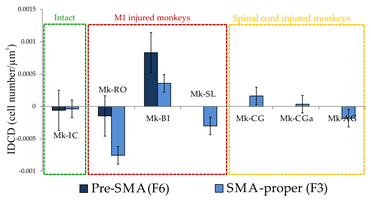

Figure 3. IDCD in layer III of F6 (dark blue) and F3 (light blue), showing a difference in M1 injured monkeys but not in spinal cord injured monkeys. As compared, SCI has no effect on layer III, in contrast to M1 lesion.

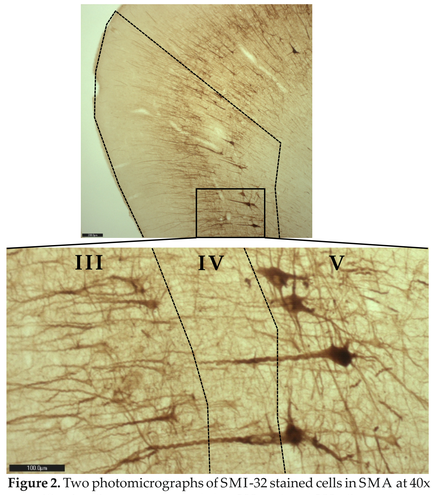

Figure 2. Two photomicrographs of SMI-32 stained cells in SMA at 40x magnification (image above, scale bar 200 µm) and 200x (image below, scale bar 100 µm). The SMA delimitation and the layer's parcellation are shown.

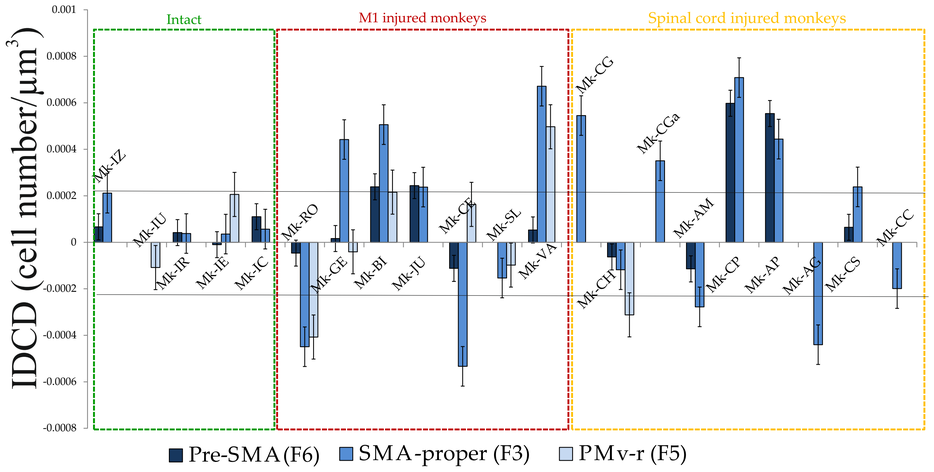

Figure 5. IDCD in layer V of F6 (dark blue), F3 (light blue) and PMvr (sky-blue) in all animals involved in the study.

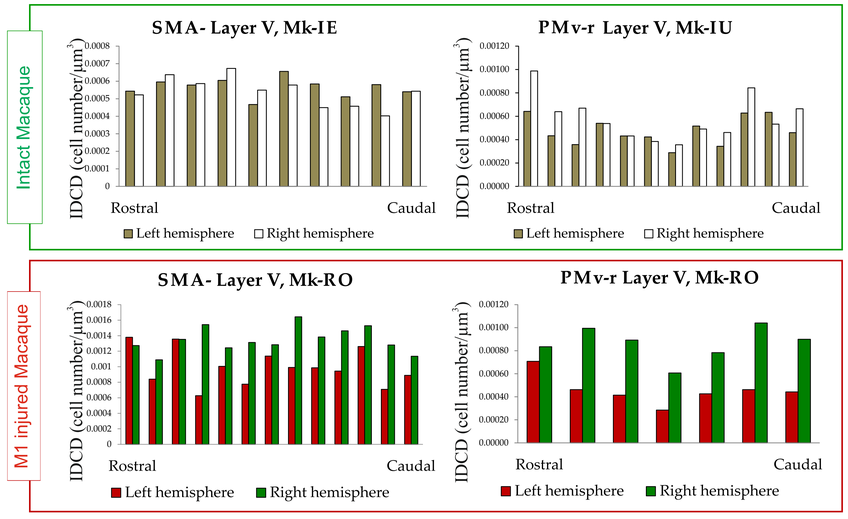

Figure 4. Graphics that show the rostro-caudal gradient of cell density per histological section in layer V. An example for SMA and PMv-r is presented for an intact (above) and an M1 injured (below) animals.

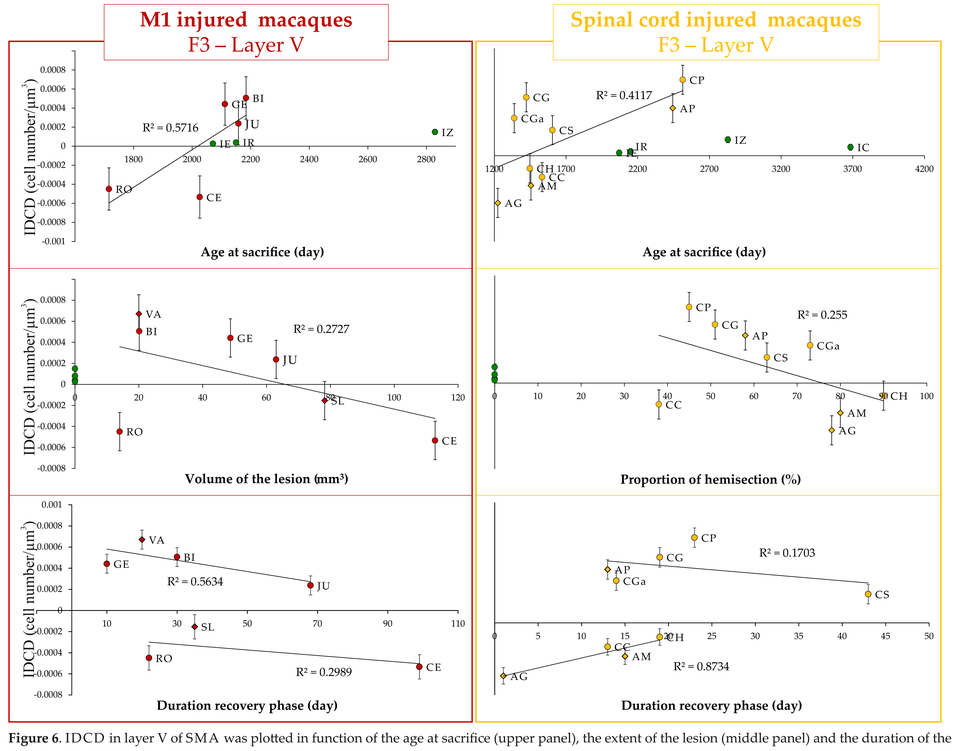

Figure 6. IDCD in layer V of SMA was plotted in function of the age at sacrifice (upper panel), the extent of the lesion (middle panel) and the duration of the recovery phase (lower panel). Intact monkeys in green, M1 injured monkeys in red and spinal cord injured macaques in orange. The diamonds indicate the anti-Nogo-A antibody treated monkeys.

Results

- Intact monkeys have a little interhemispheric difference of cellular distribution in layer III and V of SMA and PMv-r.
- In several injured monkeys, an interhemispheric significant cell density difference was observed (Figures 3 and 5).
- The SMI-32 cell density is more affected in F3 than in F6 (Figure 5), as expected.
- The treatment with anti-Nogo-A antibody does not seem to affect the cell density of the premotor areas.
- Five out of seven M1 injured monkeys and four out of nine spinal cord injured monkeys have a greater layer V SMI-32 cell density in SMA in «intact» hemisphere.
- Age and functional recovery show some correlation with SMI-32 cell›s interhemispheric distribution.

Discussion

After cervical cord lesion (SCI) or M1 lesion, there was a change of SMI-32 expression in layer V of SMA-proper, as expressed by significant positive or negative IDCD in 5 M1 lesion monkeys and 4 SCI monkeys. In contrast, 2 out of seven M1 lesion monkey and 5 out of 9 SCI monkeys did not show a significant IDCD, like intact animals. Largely comparable changes in PMv-r were observed.

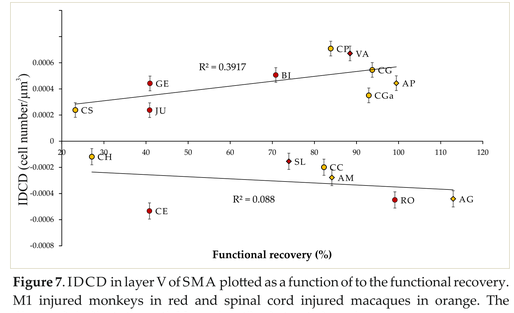

Figure 7. IDCD in layer V of SMA plotted as a function of to the functional recovery. M1 injured monkeys in red and spinal cord injured macaques in orange. The diamonds indicate the anti-Nogo-A antibody treated monkeys.

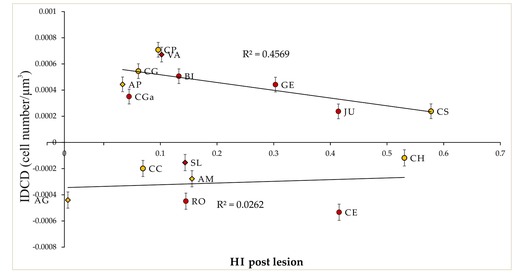

Figure 8. IDCD in layer V of SMA plotted as a function HI post lesion. M1 injured monkeys in red and spinal cord injured macaques in orange. The diamonds indicate the anti-Nogo-A antibody treated monkeys.

Materials and methods

- Cell density = Hemisphere cell number/ Delimited area (µm²) x Sectrion›s thickness (µm)
  Interhemispheric difference of cell density (IDCD) was calculated by subtracting the cell density of the directly affected hemisphere by the cell density of the intact hemisphere.
- Handedness index (HI) post lesion = H-I/H+I from H=score of the healthy hand on the Brinkman board task and I=score of the «affected» hand on the Brinkman board task.
- Positive IDCD means more SMI-32 neurones visible in the lesioned hemisphere. Negative is the reverse.