

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 (PMvr or F5) and the supplementary motor area (SMA). The working hypothesis was to observe a decrease of the SMI-32 positive cells ipsilaterally. 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 PMvr and SMA, a histological analysis of several macaques' brain was performed by comparing the neuron density of layers III and V in the premotor areas.

Macaque monkeys

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).

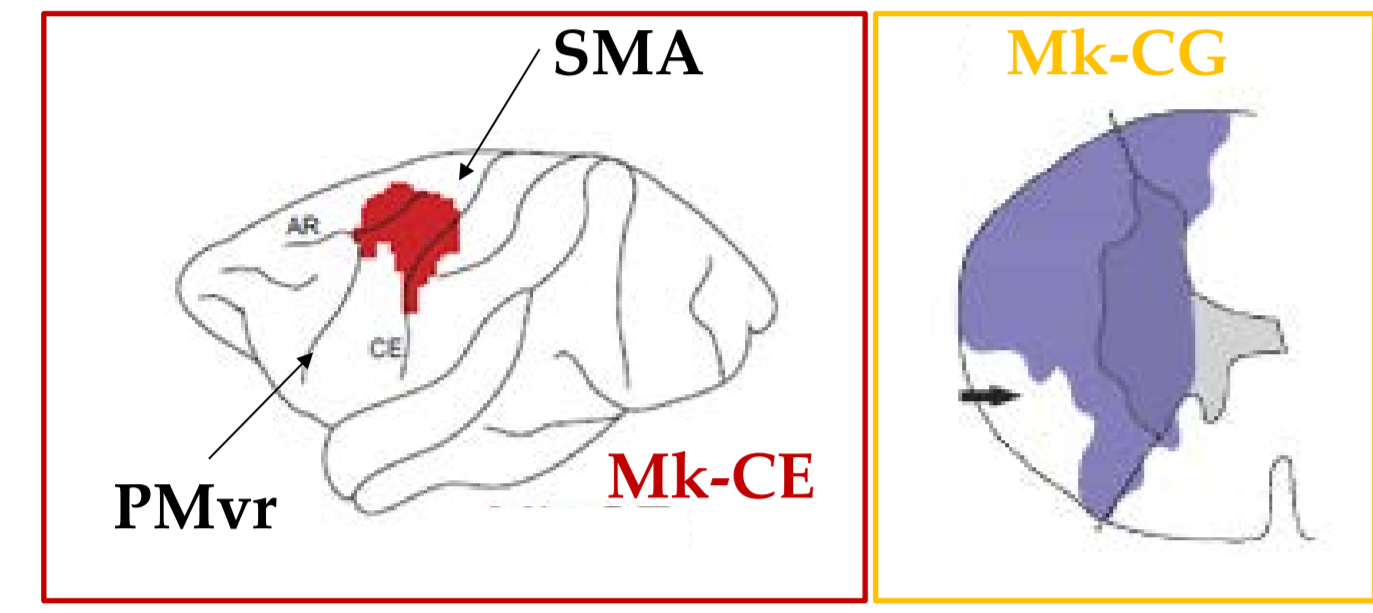
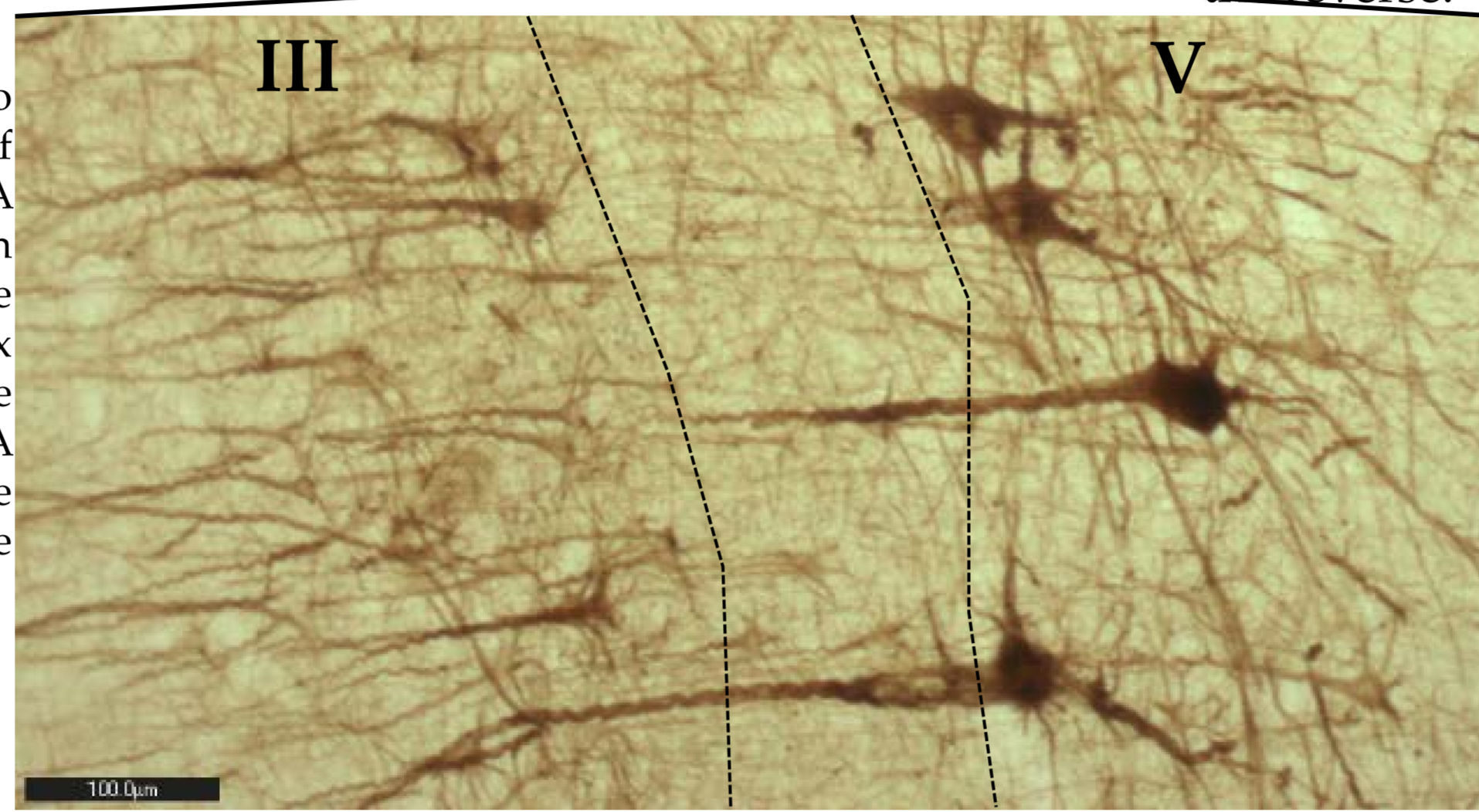
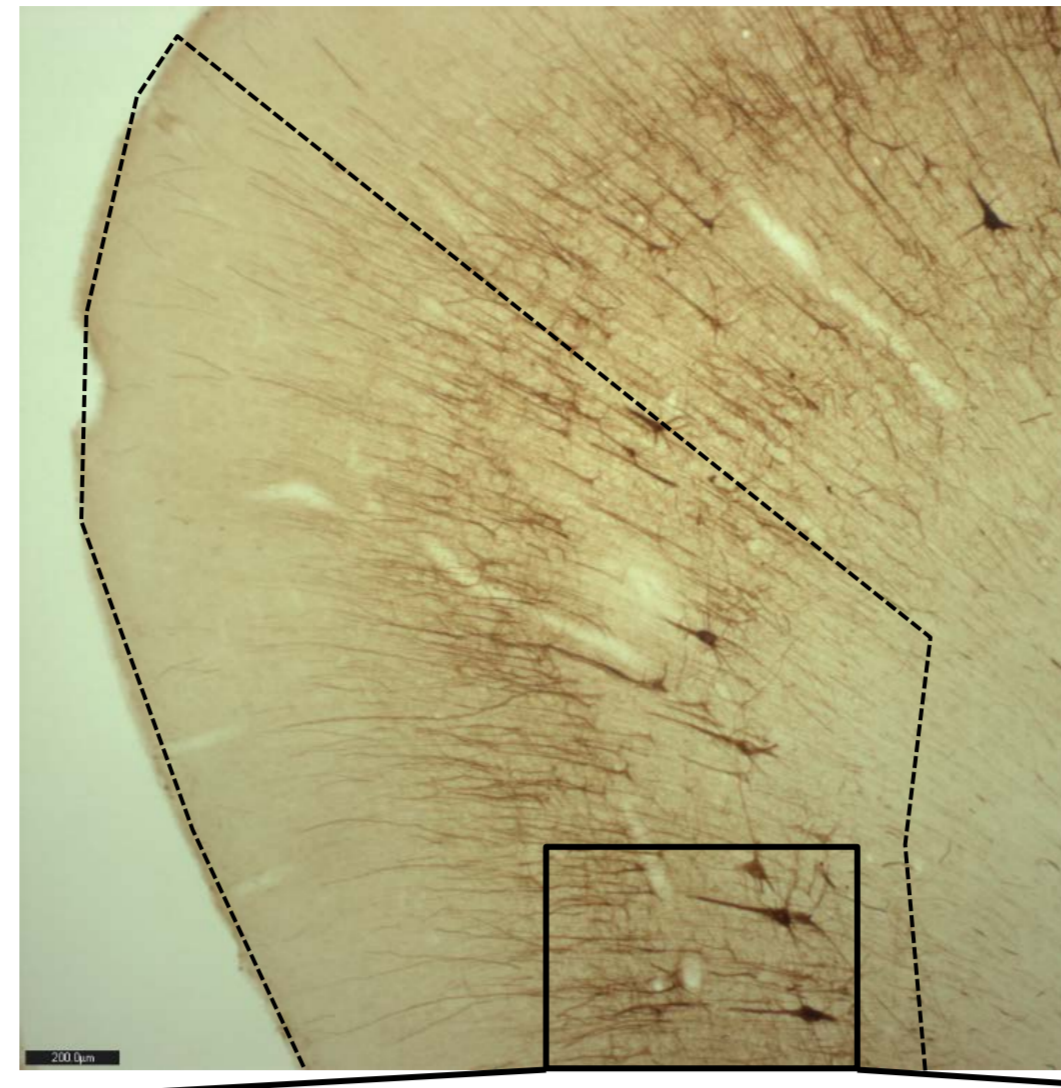


Figure 1. Schematic view of a representative cortical lesion (left) and spinal lesion (right).

Figure 2. Two photomicrographs of SMI-32 stained 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 division are shown.



Materials and methods

- SMA delimitation: rostral: the ventricles, the Sulcus arcuatus superior (Sas) and the Sulcus arcuatus inferior (Sai) had to be visible. Caudal: it was defined when the Sulcus centralis appeared.
- PMvr delimitation: rostral: Sas, Sai and mainly Sulcus principalis had to be present. Caudal: it was identified with the fusion of Sas and Sai and the origin of Arcuate sulcus.
- Cell density = $\frac{\text{Hemisphere cell number}}{\text{Delimited area } [\mu\text{m}^2] \times \text{Section's thickness } [\mu\text{m}]}$
- 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 = $\frac{H-I}{H+I}$, from H=score of the healthy hand on the Brinkman board task and I=score of the injured hand on the Brinkman board task.
- Positive IDCD means more SMI-32 neurones visible in the intact hemisphere. Negative is the reverse.

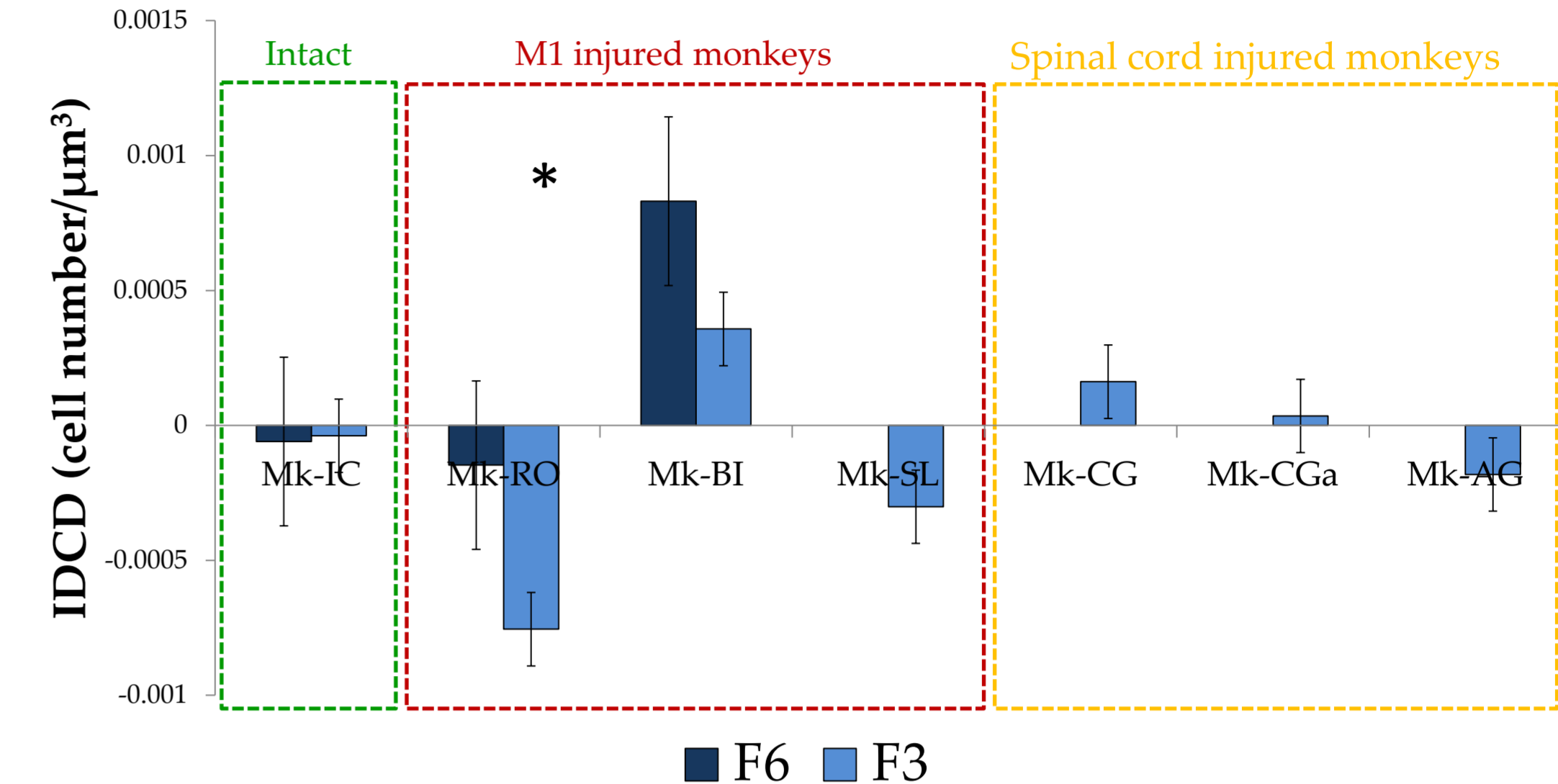


Figure 3. IDCD in layer III of F6 (dark blue) and F3 (light blue), showing a difference in M1 injured monkeys but not in spinal cord injured monkeys.

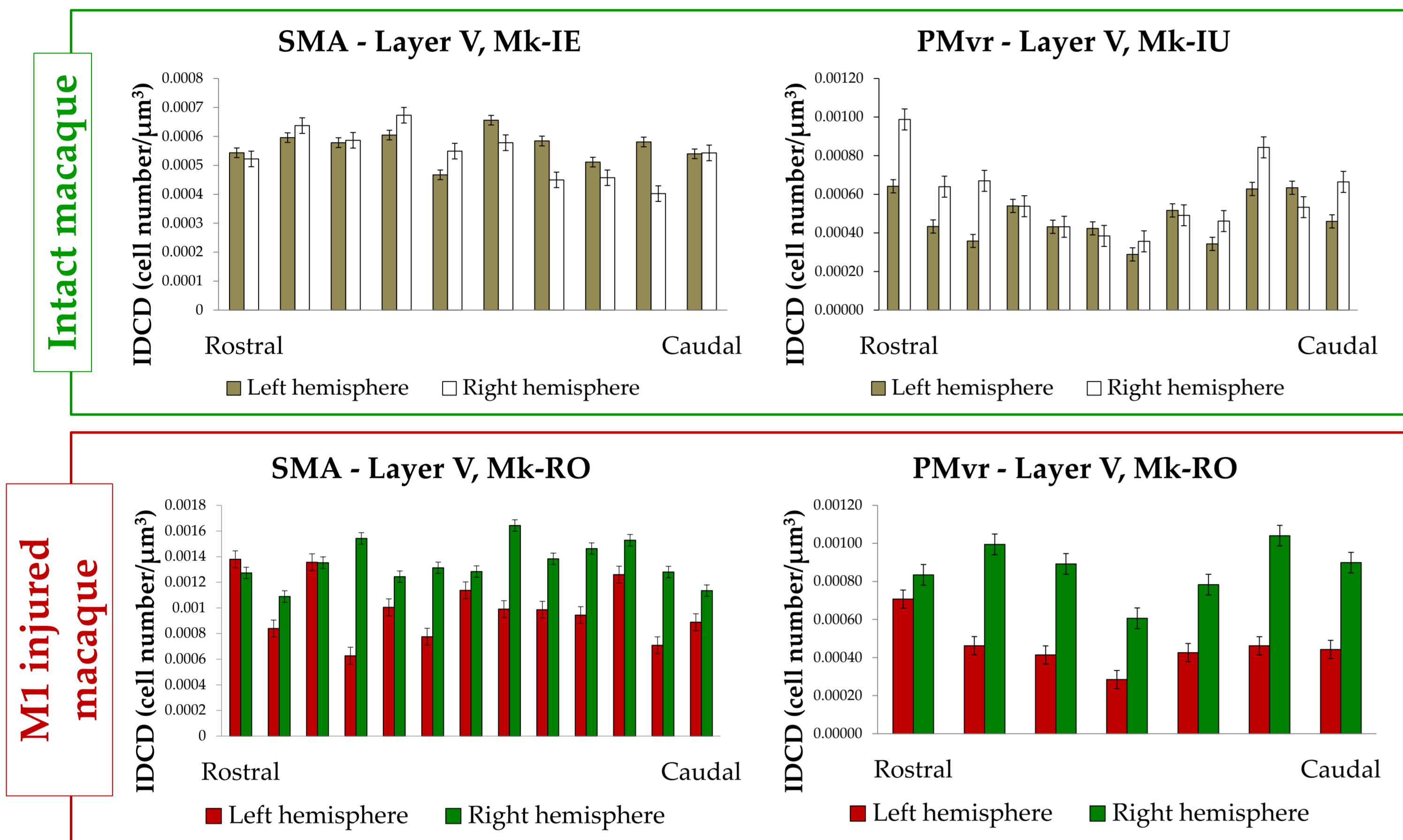


Figure 4. Graphics that show the rostro-caudal gradient of cell density per histological section in layer V. An example for SMA and PMvr is presented for an intact (above) and an M1 injured (below) animals is presented.

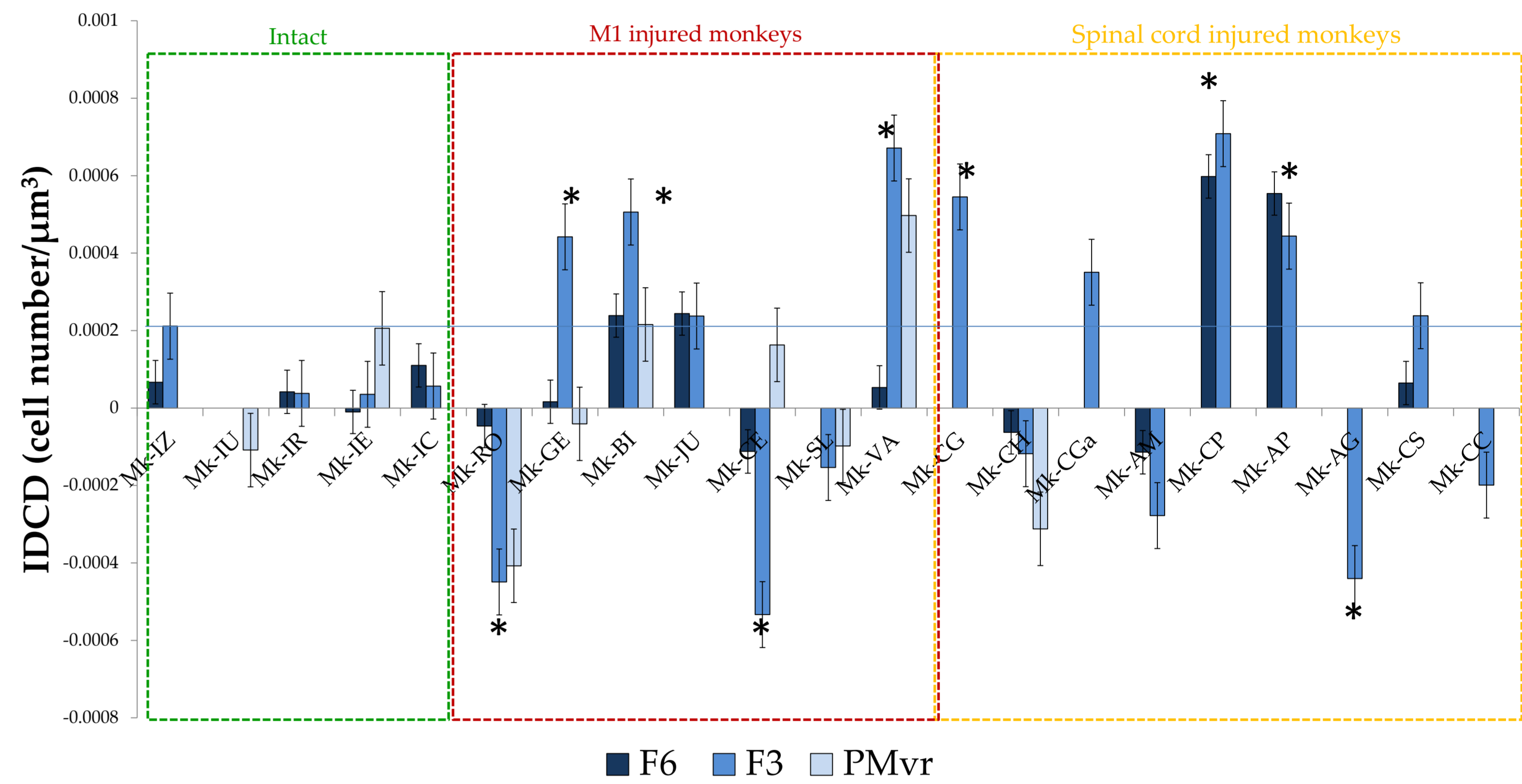


Figure 5. IDCD in layer V of F6 (dark blue), F3 (light blue) and PMvr (sky-blue) in all animals involved in the study.

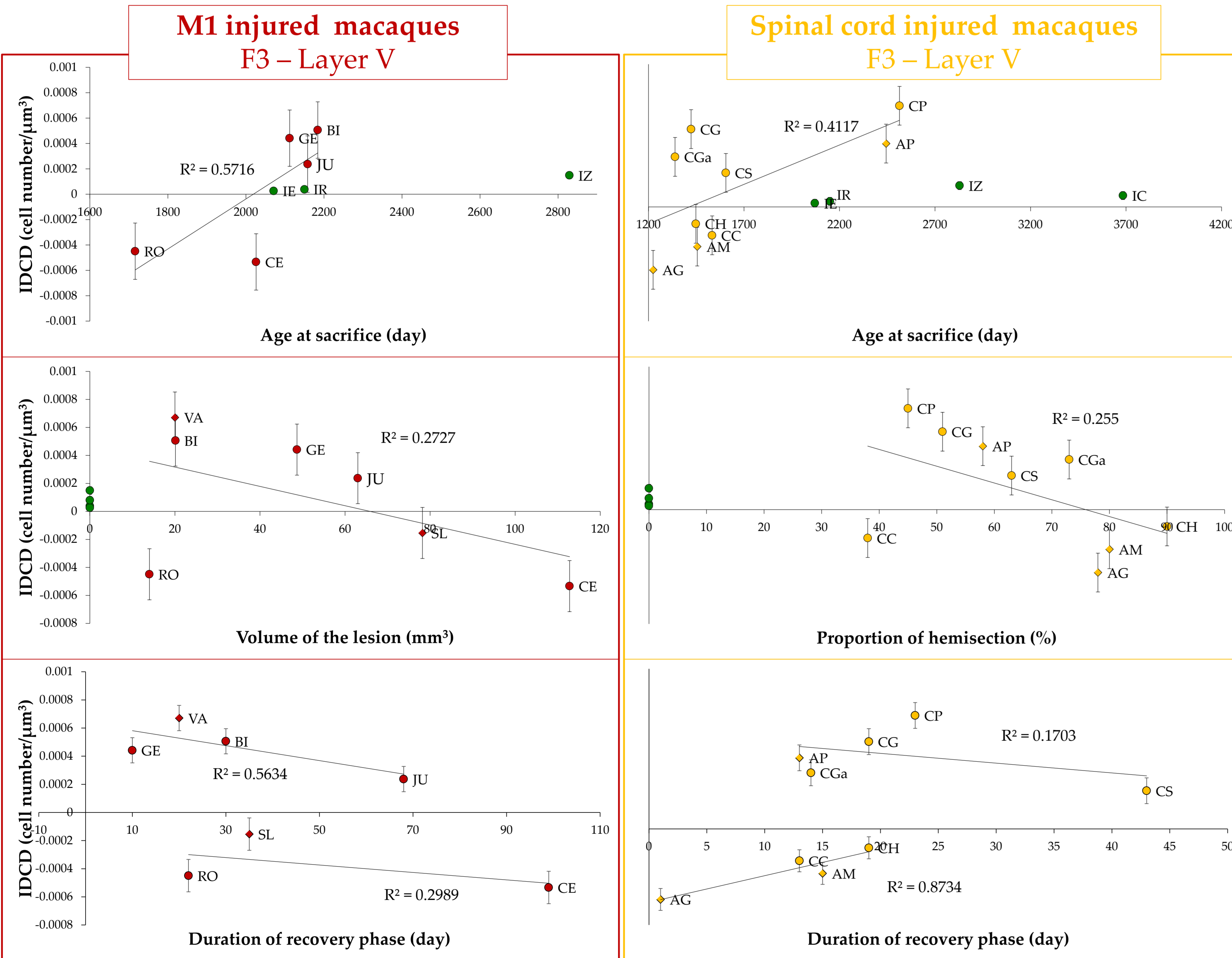


Figure 6. IDCD in layer V of SMA was plotted in function of the age at sacrifice (upper panel), the extent of the lesion (middle panel) and the duration of the recovery phase (lower panel). Intact monkeys in green, M1 injured monkeys in red and spinal cord injured macaques in orange. The diamonds indicate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

Results

- Intact monkeys have a little if significant difference of cellular distribution in layer III and V of SMA and PMvr.
- In several injured monkeys, an interhemispheric cell density difference was observed (Figures 3 and 5).
- The cell density is more affected in F3 than in F6 (Figure 5).
- 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 cell density in SMA in intact hemisphere.
- Age and functional recovery show some correlation with cellular interhemispheric distribution.

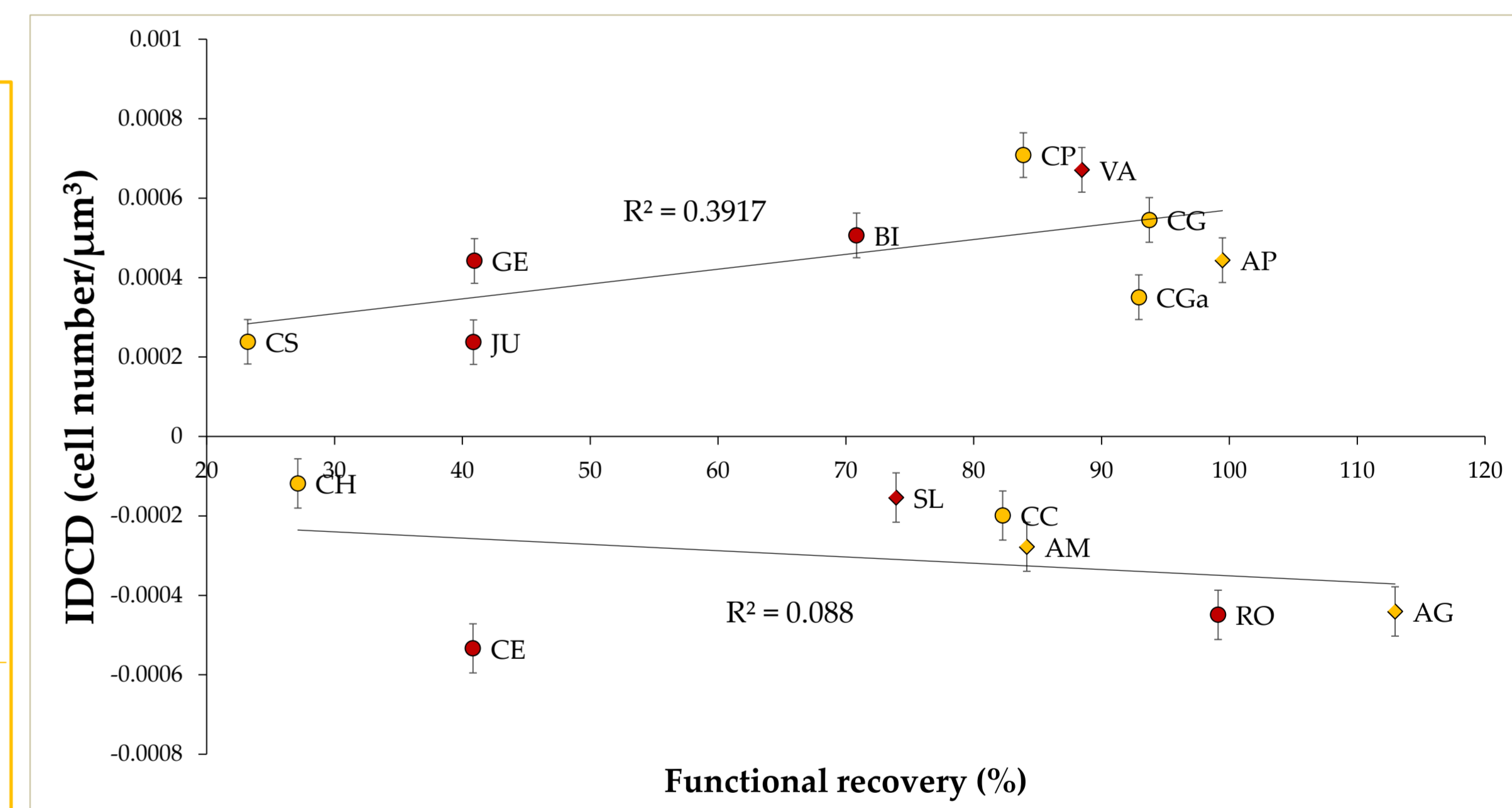


Figure 7. IDCD in layer V of SMA correlated to the functional recovery. M1 injured monkeys in red and spinal cord injured macaques in orange. The diamonds indicate the anti-Nogo-A antibody treated monkeys.

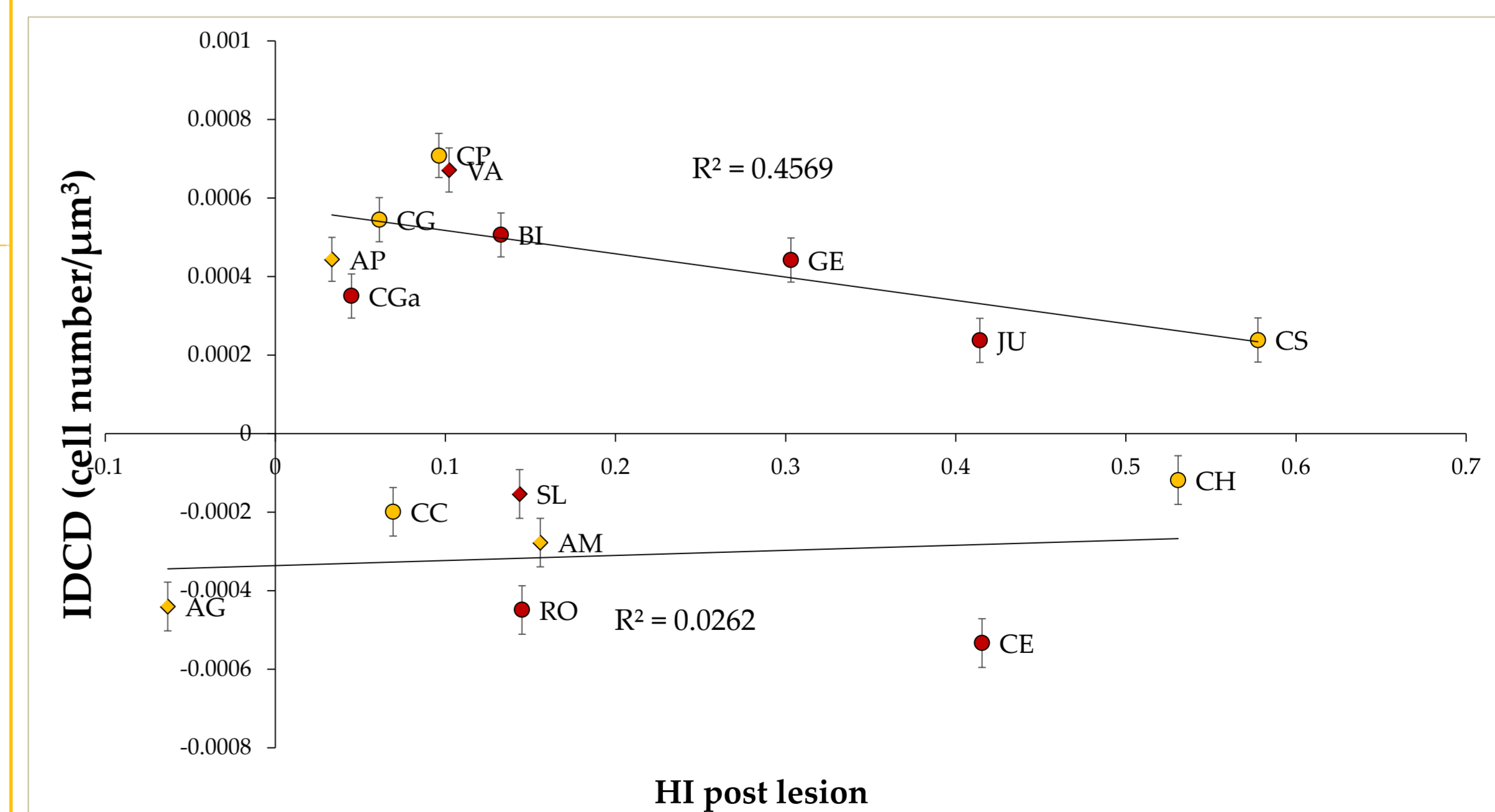


Figure 8. IDCD in layer V of SMA correlated to HI post lesion. M1 injured monkeys in red and spinal cord injured macaques in orange. The diamonds indicate the anti-Nogo-A antibody treated monkeys.

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 four SCI monkeys and 5 M1 lesion monkeys. In contrast, one out of seven M1 lesion monkey and 3 out of 9 SCI monkeys did not show a significant IDCD, like intact animals. Largely comparable changes in PM-vr were observed.