

Delayed thalamic damage after stroke: discriminator for recovery success from functional loss in the cortex of the rat.

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Introduction

Following occlusion of the middle cerebral artery (MCAO) in the rat, damages affecting thalamocortical projections can cause secondary degeneration of neurons in the ventrobasal thalamus. These delayed secondary damages may explain why, upon electrical stimulation of the forepaw, there is a lack of activity in the (usually spared) S1 somatosensory areas of the cortex. Here we provide experimental data in support of this view, with essential results for the understanding of functional loss and plasticity mechanisms in animal models of stroke.

Methods

Wistar rats (n=18) were submitted to transient (60 min) MCAO. Repetitive MRI experiments were conducted on a 7T scanner, before stroke induction and 2 days, 1, 2, 3, 4 and 7 weeks after MCAO. BOLD-fMRI was done in medetomidine sedated animals, acquiring SE-EPI images (TE=30 ms; TR=3000 ms). Electrical forepaw stimulation was performed using rectangular pulses (2 mA, 3 Hz, 0.3 ms) in a paradigm of 5 blocks of 45 s resting periods and 15 s activation periods. BOLD fMRI was conducted alternately for each hemisphere. Statistical parametric activation maps were constructed with the software STIMULATE. In the same experimental sessions, short latency somatosensory potentials were recorded bilaterally from the primary somatosensory cortices with subcutaneous electrodes (3.5 mm lateral and 1 mm anterior to Bregma). Adhesive tape removal test was used to evaluate sensorimotoric deficits. Healthy animals were trained with daily sessions 3 days before baseline at the day before MCAO. After MCAO, sessions were performed the days before fMRI experiments. After the last fMRI session, brains were cut in coronal 40 μ m thick sections. Hematoxylin-eosin and luxol-cresyl violet, neuronal antibody NeuN and the Vectastain ABC Method (Vector Labs) and 3',3'-diaminobenzidine/NiCl₂ stainings were performed.

Results

Histology of the right ventrobasal thalamus showed no neural damage in animals with no ischemic injury or selective neuronal death in the striatum. Animals with an infarction and either transient loss (1-3 weeks after MCAO) or normal BOLD response in the right S1 area, showed gliosis and neuronal death in the ventral posteromedial (VPM) thalamic nucleus, but normal cytoarchitecture in the ventral posterolateral (VPL) thalamic nucleus. Finally, animals with permanent loss of BOLD response, showed signs of secondary degeneration with a marked atrophy, gliosis and neuronal loss in both the VPM and VPL.

Conclusions

During a lack of functionality on the S1 somatosensory areas of the cortex after stroke, secondary damages to the correspondent thalamic regions can aggravate the functional outcome after stroke with no structural damage in the S1. Recurrence of BOLD response at a few weeks after stroke will depend on the extension of this delayed damage in the thalamus. These results suggest the consideration of specific strategies to protect the corticothalamic connectivity following stroke, in order to preserve/recover normal brain function in cortical areas.

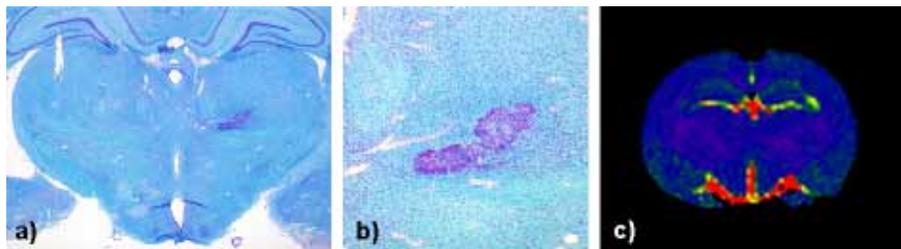


Figure 1. a) Luxol-cresyl violet stained section of a brain from an ischemic animal, showing gliosis in the thalamic region of the affected hemisphere. b) Magnification of a). Gliosis on such small area is not observed in the correspondent T2 map (c).

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