

## Early detection of brain function recovery following stroke. A longitudinal fMRI study of the rat.

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### Introduction

Stem-cell based regenerative therapies are expected to play an important role in the recovery of brain functional losses following stroke. Nevertheless, it is challenging to determine the conditions under which such therapies should be applied, considering that brain function is sometimes restored spontaneously. Using a recently developed longitudinal fMRI protocol for the rat (1), in combination with electrophysiological measurements, we are in the situation to predict the functional outcome of the animals shortly after stroke, making it possible to distinguish animals that qualify for regenerative therapies from those improving without further intervention.

### Methods

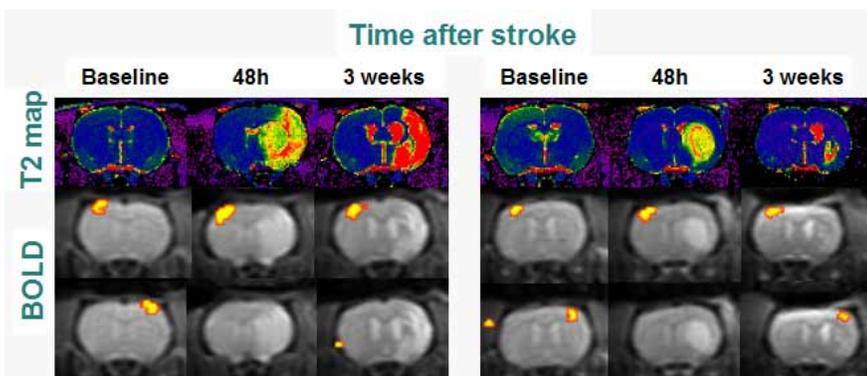
Wistar rats (n=22) were submitted to transient (60 min) occlusion of the middle cerebral artery (MCAO). Under medetomidine anesthesia, a sequence of T2, CBF and BOLD-fMRI longitudinal studies were performed for each animal one week before, and 2 days, 1, 2, 3, 4 and 7 weeks after MCAO. All experiments were conducted at 7T using custom-built coils (12 cm Helmholtz coil for transmission, 3 cm surface coil for reception). Functional BOLD imaging was achieved acquiring multislice SE-EPI images during electrical forepaw stimulation. Both forepaws were alternatively stimulated (2 mA constant current pulses) with a block paradigm (5x[45s rest + 15s stimulation] periods). Somatosensory evoked potentials (SSEPs) were recorded in the same experimental sessions, placing subcutaneous electrodes over both S1 cortical areas of the brain (1mm caudal and  $\pm 3.5$  mm lateral from Bregma). Images were analyzed using Image J and STIMULATE software.

### Results

Before MCAO, normal BOLD and SSEP recordings were obtained during forepaw stimulation for all animals. Following the ischemic insult, three different situations were observed: 1) a group of animals showed unaltered BOLD and SSEP signals. 2) A second group showed normal recordings in the healthy brain hemisphere but presented a transient loss of BOLD signal in the affected hemisphere, accompanied by a distortion (amplitude and latency) of the SSEPs. In this group normal activity (as determined by both BOLD and SSEP) was regained in the affected hemisphere 2 to 3 weeks after MCAO. 3) A third group suffered a total and permanent loss of both BOLD and SSEP signals in the affected hemisphere.

### Conclusions

In our 7 weeks longitudinal study, only function recovery but no signs of reorganization (i.e. shift of functional representation fields) was observed. The observation of abnormal electrical activity in S1, together with a lack of BOLD, one to two weeks after stroke, provides an early indication of late functional recovery following focal cerebral ischemia in the rat.



**Figure 1.** T2 maps and BOLD maps for two animals showing a case of permanent (left) and transient (right) loss of function in the ischemic hemisphere (third row).

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1) R. Weber et al. Neuroimage epub YNIMAG-03439