REPRODUCIBLE IMAGING OF RAT CORTICOTHALAMIC PATHWAY BY USING LONGITUDINAL MANGANESE-ENHANCED MRI (L-MEMRI)

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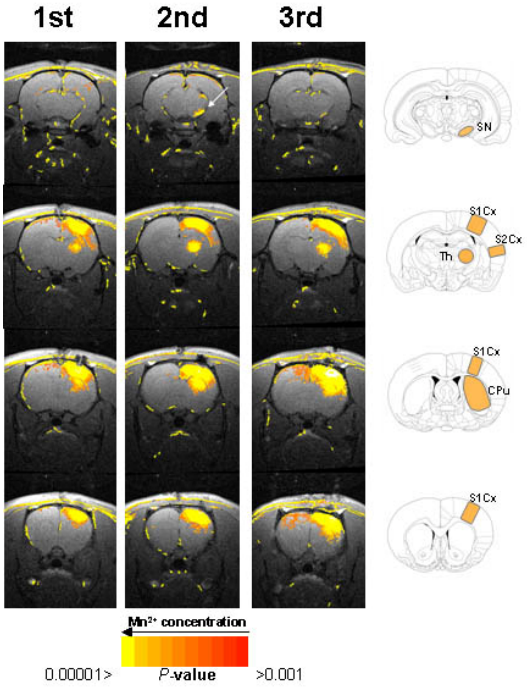
Introduction: Manganese-Enhanced MRI (MEMRI) has been described as a powerful tool to depict architecture of neuronal circuits. The aim of this study was to optimize the experimental conditions of MEMRI to study the somatosensory pathway in a longitudinal way, and to provide functional information on rat corticothalamic connectivity. Preliminary data from our laboratory showed that in an animal model of stroke, ischemic animals with minimal damage in the thalamocortical or/and corticothalamic pathway, spontaneously recovered activation on the S1 somatosensory cortex (S1Cx) (initially disturbed for this experimental model of stroke), as assessed by functional MRI[1]. The aim of the present study was to establish a reliable method that allows us to perform longitudinal MEMRI experiments to observe the integrity of the rat corticothalamic pathway in a repetitive assessment, which can be performed in parallel with functional MRI (fMRI). Therefore, it is of great interest to study, in longitudinally, the dynamic changes occurring in these corticothalamic connections after stroke.

Methods: A plastic guiding screw was implanted in the skull over the S1Cx to allow repetitive injections at the same stereotactic coordinates. $MnCl_2$ (200nL 0.3M) was injected 1.5 mm below the dura by using a calibrated microcapillary. Animals received $MnCl_2$ injections 3 times at 15 days intervals. fMRI experiments were conducted in a separated group of animals also injected with $MnCl_2$ (same conditions as above). The MRI experiments were conducted on a 7 T BioSpec animal scanner (Bruker BioSpin, Ettlingen, Germany). For MEMRI studies, T1 weighted coronal images were acquired by using a conventional multi-slice multi-echo sequence. Scan parameters were: TR = 700ms, TE= 11.5ms, number of repetitions= 10, slice thickness= 1mm, FOV= 2.56x2.56x1.43 cm^3, matrix= 256x256x13 pixels. For fMRI studies, coronal multislice spin-echo (SE) EPI images were acquired using the parameters described before[2]. Both MEMRI and BOLD were analysed by statistical activation maps constructed with the software STIMULATE using a paired Student's t test ($p < 0.01$). Animals were perfused and fixated and brains were cryoprotected for histological analysis.



Results and Discussion: Spatiotemporal patterns showed a significant hyperintensity induced by manganese transport in structures related to the somatosensory pathway, such as globus pallidus, caudate putamen, thalamus and substantia nigra. 7 days after $MnCl_2$ injection hyperintensity was only evident at some points surrounding the injection site. Wash-out of manganese was observed after 15 days from the injection. As shown in figure 1, a strong reproducibility was observed between sessions. fMRI experiments were performed under the same conditions, 24 h after $MnCl_2$ injection. Activation of S1Cx was observed showing that fMRI studies and longitudinal MEMRI can be performed in parallel in the same animals.

Conclusion: This work shows, for the first time, a reliable and reproducible technique to perform longitudinal MEMRI experiments and to study the time-course changes of the corticothalamic connections following stroke in the rat.

Figure 1. Repetitive $MnCl_2$ injections. Probability maps of significant manganese-induced intensity enhancement in T1 weighted images were calculated by comparing images acquired at the preceding prescan and images acquired 24 hours after $MnCl_2$ injections. Three different $MnCl_2$ injections were done separated by 15 days each. Last column shows rat brain atlas drawings of the corresponding slices. S1 somatosensory cortex (S1Cx), S2 somatosensory cortex (S2Cx), caudate putamen (CPu), substantia nigra (SN), thalamus (Th).

References

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