Endogenous stem cell tracking by MRI after local injection of contrast agent

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Introduction:

Magnetic resonance imaging offers a noninvasive method for tracking magnetically labeled cells. During the adult life, there is a constant generation of neuronal progenitors in the subventricular zone (SVZ) of the lateral ventricle (LV) and the subgranular zone (SGZ) of the hippocampus. This proliferation is increased under pathological conditions, such as stroke or neurodegenerative disease.

Our aim was to monitor proliferative cells of the SVZ by MRI after their in situ labeling with iron oxide nanoparticles, and to follow their migration along the rostral migratory stream (RMS) towards the olfactory bulb (OB), as a first step to establish in vivo monitoring of endogenous neurogenesis after stroke.

Methods:

1µL contrast agent (Endorem®, 1µg/µL) was stereotactically injected in the rat brain (intraparenchymal) close to the SVZ.

3-D T2*-weighted images were acquired on a 7T experimental MR scanner (TR:200ms; TE:20ms; 78µm isotropic resolution), immediately after contrast injection, after 2d and 4d, and up to 6 weeks. BrdU was intraperitoneally administered 24h before the contrast injection, and after every scanning session. After the last time point, animals were sacrificed, immunohistochemical stainings for BrdU and iron were performed in sagittal and coronal sections.

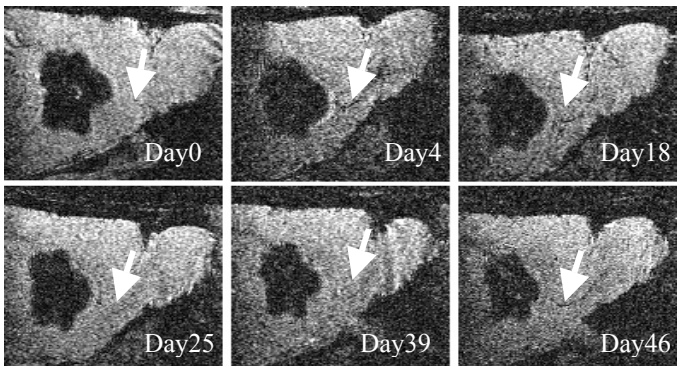

Figure 1: A huge hypointense area was detected after iron nanoparticle injection, but no hypointensity was detectable along the rostral migratory stream immediately after injection. A hypointense line along the rostral migratory stream (arrows) was detected 4 days after contrast agent injection and, after a transient decrease (3-4 weeks), it was strongly hypointense again after 6 weeks.

Results:

At 2 and 4 days after contrast agent injection, T2*-weighted MR images show a line of hypointensity extending from the lateral ventricle to the olfactory bulb, following the RMS and the olfactory ventricle (OV). Cells containing iron particles were observed in the SVZ, while free iron particles were detected in the LV and RMS. BrdU immunoreactive cells were detected along the RMS and in the OB, but cells co-staining for iron and BrdU were only observed in the LV. After 3-4 weeks, a reduction of the contribution of contrast agent was monitored, and a secondary increase was detected after 6-7 weeks.

Conclusions:

Proliferating cells can be labeled in situ with iron particles, and their migrational dynamics can be followed along the RMS and the ventricular space. But caution must be used as the signal of labeled proliferating cells may be masked by the flow of free iron particles in the early period.

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