In vivo monitoring of local inflammation after acute infarction by $^{1}H/^{19}F$ MRI

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Introduction

The noninvasive visualization of inflammatory processes by MRI succeeded up to now only by use of superparamagnetic iron oxide particles (SPIOs) taking advantage of the high affinity of these species for the monocyte-macrophage system[1,2]. Since SPIOs lead to a depletion of the MR signal, in some cases the acquired ^{1}H data sets are difficult to interpret. In the present study we examined the feasibility to image inflammation with a positive ^{19}F contrast. For this purpose we used emulsified perfluorocarbons (PFCs) as contrast agent, which are biochemically inert and are phagocytized similar to SPIOs by the reticuloendothelial system[3,4].

Methods

Experiments were performed at a vertical Bruker DRX Wide Bore NMR spectrometer operating at frequencies of 400.1 MHz for ^{1}H and 376.5 MHz for ^{19}F measurements using a Bruker Microimaging unit (Mini 0.5) equipped with an actively shielded 57-mm gradient set (200 mT/m maximum gradient strength, 110 µs rise time at 100% gradient switching) and a $^{1}H/^{19}F$ 30-mm birdcage resonator. For induction of acute inflammation the left anterior descending coronary artery (LAD) was ligated to provoke myocardial infarction. In another set of experiments focal cerebral ischemia was induced by photothrombosis. After surgery 200-500 µl of a perfluoro crown ether (15C5) emulsion (10%, particle size 130 nm) was injected into the tail vene of the mice. In order to monitor the time course of PFC accumulation in the infarcted areas anatomically corresponding ^{1}H and ^{19}F MR images were acquired with the following parameters: Cardiac imaging; FOV 3x3 cm^2, ^{1}H: ECG- and respiratory-triggered cine FLASH, slice thickness 1 mm, matrix 256x256, acquisition time 2 min, ^{19}F: RARE (RARE factor 64), slice thickness 2 mm, matrix 128x128, acquisition time 20 min. ^{1}H and ^{19}F MR images of the brain were aquired from a FOV of 2x2 cm^2 using a RARE factor of 16 for ^{1}H images but with otherwise identical parameters as given above.

Results and Discussion

One day after induction of myocardial infarction a transient ^{19}F signal was observed over the entire lung. Concomitantly, a beginning infiltration of PFCs into the infarcted area of the heart could be detected, which reached its maximum 6-7 days after ligation of the LAD (Fig. 1A). ^{19}F signal was also found within the surgical wound and the lymph nodes. Similar results as obtained for the heart were observed for the brain after inducing cerebral ischemia by photothrombosis. However, in this case there was no lung activation found and infiltration of PFCs into the border zone of the infarct was detected not until 6-7 days after surgery (Fig. 1B), which is consistent with the delayed time course of macrophage permeation in this model. ^{19}F signal was also observed supracranial at the location of surgery. Figure 1B-E clearly shows a movement of the PFCs with the rim of the infarct over time. The results of the present study show that intravenous application of emulsified PFCs after both experimental stroke and myocardial infarction results in an accumulation of these particles in the infarcted area, most likely after phagocytosis by the monocyte-macrophage system. Therefore, PFCs can serve as "positive" contrast agent for inflammatory processes, which is characterized by a high degree of specificity due to the lack of any ^{19}F background. Since PFCs are not toxic, this approach may also be suitable for human applications.

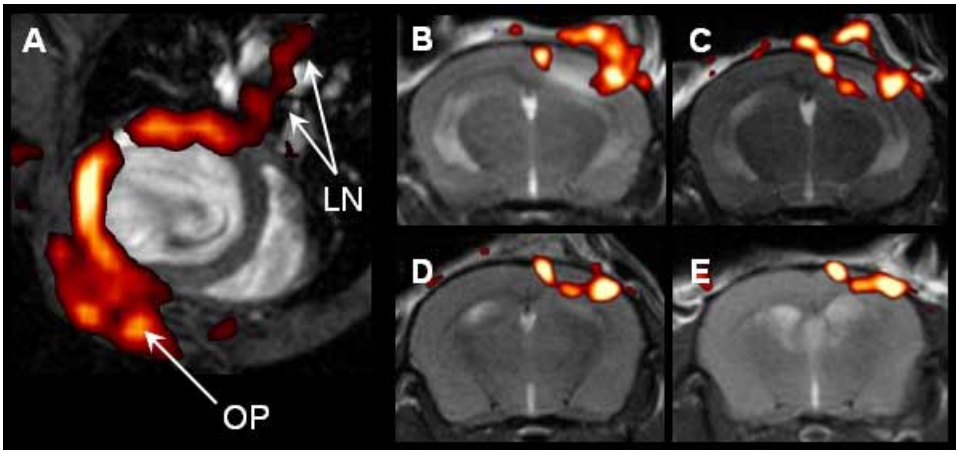

Figure 1: Sections of ^{1}H MR images from mouse heart (A) and brain (B-E) superimposed with the corresponding ^{19}F MR images (red). **A:** Images acquired 7 days after ligation of the LAD showing ^{19}F signal near the infarcted region and also at the location of surgery (OP) as well as within the lymph nodes (LN). **B-E:** Temporal development of the ^{19}F signal after induction of focal cerebral ischemia by photothrombosis. Images were obtained 7 (B), 9 (C), 12 (D), and 19 (E) days after surgery.

References

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