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MR molecular imaging of early endothelial activation in focal ischemia.

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Focal ischemia followed by reperfusion initiates a harmful P- and E-selectin-mediated recruitment of leukocytes in brain microvasculature. In this study, we tested whether a novel magnetic resonance (MR) contrast agent (Gd-DTPA-sLe (x) A), which is designed to bind to activated endothelium could be detected by MR imaging (MRI) in a focal stroke mouse model. MRIs (9.4T) of the brain were acquired 24 hours after transient middle cerebral artery occlusion. T1 maps were acquired repeatedly before and up to 1.5 hours after the intravenous injection of either Gd-DTPA or Gd-DTPA-sLe(x) A. Analysis of images included a pixel-by-pixel subtraction of T1 maps from the precontrast T1 maps and quantification of T1 within the ischemic area. After injection of Gd-DTPA-sLe(x) A, T1 decreased compared with precontrast levels, and an interhemispheric difference between the pre-post contrast T1 developed within the stroke lesion at a mean time of 52 minutes after injection ($p < 0.05$). Animals injected with Gd-DTPA did not exhibit changes in T1 signal intensity between regions of the ipsilateral and contralateral hemispheres, indicating that the reductions in T1 observed with Gd-DTPA-sLe(x) A were unrelated to blood-brain barrier breakdown. Fluorescent-labeled sLe(x) A administered intravenously was observed to bind to the endothelium of injured but not control brain. The study suggests that the contrast agent Gd-DTPA-sLe(x) A can be used to visualize early endothelial activation after transient focal ischemia in vivo with MRI. Ann Neurol 2004;56:116-120

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