Dependence of CBV-weighted fMRI Signals on dose of Contrast Agents

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ABSTRACT

Signal change in CBV-weighted fMRI signal is dependent on absolute CBV change, dose of contrast agents, and baseline signal intensity. Thus, dose-dependent CBV-weighted fMRI signals were examined in the cat visual cortex at 5, 10, and 15 mg/kg MION conditions. Dependence of baseline R_2* changes on MION dose was also determined. Baseline R2* change induced by MION is the highest at the surface of the cortex, while functional percent-signal changes are the highest at the middle of the cortex, irrespective to the dose of MION.

INTRODUCTION

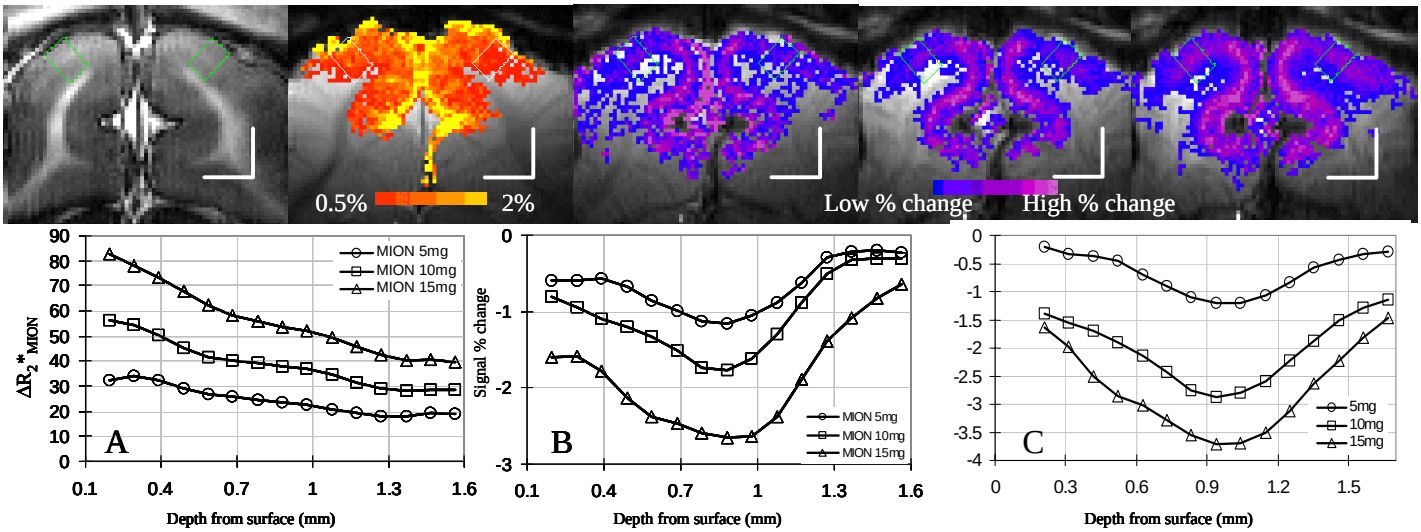
Iron oxides contrast agents such as MION have been used for CBV-weighted fMRI studies (1-3). Signal change in CBV-weighted fMRI is dependent on absolute CBV change, dose of contrast agents, and baseline signal intensity (1). Signal intensity of CBV-weighted fMRI can be maximized by setting TE of 1/ R_2* after the injection of MION. However, a peak of activation can be shifted as a function of MION dose due to a change in the baseline signal intensity. Thus, it is important to determine dose-dependent MION-induced R_2* changes and CBV-weighted fMRI. For this, a well-established cat visual stimulation model can be used. During visual stimulation, the highest neural activity will be occurred at layer IV in the primary visual cortex, while large surface vessels will generate a field gradient from the surface of vessel to cortical tissue. Based on the vascular filter function (1), an activation peak may shift from the surface of the cortex into white matter when a higher MION dose is used. We examined dose-dependent CBV-weighted signal changes in the cat visual cortex.

METHODS

Cats (n = 9) were intubated and ventilated under ~1.3% isoflurane. End-tidal CO_2 (3.0-3.8%) and temperature were maintained under a normal condition. For visual stimulation, drifting square-wave gratings (0.15 cycle/degree, 2 cycles/s) were used. All MRI measurements were performed on a 9.4T/31cm MRI system (Varian) with a 1.6-cm diameter surface coil. Coronal images with 128x128 matrix size and FOV of 2x2 cm^2 were obtained using the 4-segmented EPI technique with navigator echo. Baseline R_2* maps were obtained before and after repeated injections of MION. In 5 animals, 2 mg/kg dose was injected until a total dose reached to 10 mg/kg for determining the relationship between baseline R_2* change and MION dose. In fMRI studies (n = 4 animals), three injections of a 5 mg/kg dose were used (e.g., accumulatively 5, 10 and 15 mg/kg). After every injection, fMRI was obtained. For MR parameters, TE = 10 ms, TR = 0.5 s, and effective TR = 2.0 s. The same threshold was used for all fMRI studies. For cortical depth-specific signal analysis, rectangular sections within the cortex were selected, and pixels along lines perpendicular to the dorsal surface were determined. To average signals at the same depth, pixels were spatially interpolated, then averaged signal profiles across cortical layers were plotted as a function of distance from the surface of the cortex.

RESULTS

Relation between the MION dose and ΔR_2* of gray matter at 9.4T (n = 5) was ΔR_2* (s^{-1}) = 5.49xD (R_2 = 0.98), where D is the MION dose as a unit of mg Fe/kg body weight. Dose-dependent ΔR_2* is consistent with previous results measured at 4.7T, ΔR_2* = 5.80xD (3). This shows that the magnetization of MION is saturated at high fields. A five-image panel shows one animal fMRI studies, consisting of T_1-weighted anatomical image, percent-change maps of BOLD and CBV-weighted fMRI with 5, 10 and 15 mg/kg MION doses of the cat visual cortex (from left to right). Scale bars are 2-mm. Two ROIs overlaid on images were used for further profile analyses. The highest BOLD signal change (yellow color) is occurred at the surface of the cortex. Color bar for 5 mg/kg MION study ranges -0.5 - -2%; 10 mg/kg MION, -0.5 - -3%; and 15 mg/kg MION, -0.5 - -4%. Contrary to the BOLD map, the large signal change (purple) in CBV-weighted fMRI is mostly located in the middle of the cortex, irrespectively of doses. The bottom profiles show MION-induced ΔR_2* w/o stimulation (A) and stimulation-induced % change (B) as a function of distance from the surface of cortex to white matter within ROIs. Data with three MION doses were plotted together. To show consistency, profiles of average % signal change of all four animals were also plotted as a function of depth. The surface of cortex is at 0.0 mm. MION-induced baseline ΔR_2* (A), related with basal CBV and the MION dose, monotonically decreases from the surface to the white matter. However, the maximum signal change induced by visual stimulation is located at ~0.8-1.1mm from the surface of the cortex, independent on the MION dose. Our data suggest that a peak position of CBV-weighted fMRI percent-signal changes is dependent on CBV changes, rather than the dose of contrast agents.



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