Balloon Modeling of BOLD Responses in Children with Sickle Cell Anemia (SCA)

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Introduction

Functional magnetic resonance imaging (fMRI) methods may help to identify the causes of cognitive impairment in SCA patients. However, **elevated** resting cerebral blood flow in patients with SCA may decrease, or even prevent, the detection with fMRI of stimulus-induced activation in the primary visual cortex (V1)[1]. We used fMRI during simple visual stimulation to characterize the hemodynamic responses to changing neural activity in children with SCA. The BOLD response and CBF response to visual stimulation were evaluated and analyzed via the Balloon Model[2] in relation to hematologic and rheologic variables.

Methods

*Subject*s: The study was approved by the IRB, and informed consent was obtained from each participate. Twenty three pediatric patients with SCA (age 12.4 ± 0.7) with diagnosis of Hb SS were enrolled. Twenty-five age-matched patients (age 11 ± 0.9 years) with posterior fossa brain tumor (BT) comprised the CONTROL group for BOLD fMRI results. *FMRI*: The visual stimulus was a black and white checkerboard with color reversal at 8 Hz. Two sets of functional images were acquired on a 1.5T Siemens Symphony scanner. 1) A single shot T2*-weighted EPI (TR = 2.06 sec, TE = 50 msec, FOV =192 mm, matrix =64x64, slice thickness = 5 mm, 23 slices, and bandwidth = 1954 Hz/pixel) was used in both SCA and BT patients with 4 blocks of 2/28-sec on/off and 3 blocks of 16/24-sec on/off stimulation. 2) A pulsed ASL Q2TIPS sequence (TR = 2200 ms, TE = 26 ms, TI1 = 700 ms, TI1s = 1200 ms, TI2 = 1400 ms, bandwidth = 2170 Hz/Pixel, matrix = 64 x 64, FoV = 192 mm, slice thickness = 7.5 mm, 4 slices, and flip angle = 90°) was used in SCA patients with 8 blocks of 20/20-sec on/off stimulation. *Image Analysis*: SPM2 software (http://www.fil.ion.ucl.ac.uk/spm/) was used in analyzing both sets of functional images and MarsBar (http://marsbar.sourceforge.net/) toolbox was used in retrieving time-course of raw data from activated V1 regions. For each SCA patient, the raw ASL time-course from overlapping V1 regions of both CBF and BOLD activation was retrieved to reconstruct the BOLD and CBF time-courses and to quantify the CBF changes. The balloon model[2] was used to fit the group average BOLD response to visual stimulation for SCA and CONTROL patients.

Results and Discussion

Seventeen of 23 SCA patients (74%) and 22 of the 25 CONTROL patients (88%) showed BOLD activation in the primary visual cortex (V1). The amplitude of the BOLD signal in V1 during visual stimulation was lower in SCA patients than in CONTROL patients. The group average BOLD responses to the 2-sec (not shown) and 16-sec stimulation (Fig. 1) had typical BOLD signal characteristics for both groups. Repeated measures ANOVA revealed significant group and time effects in BOLD signal for both the 2-sec stimulation ($p = 0.0006$) and the 16-sec stimulation ($p = 0.0001$). With ASL fMRI, V1 activation was detected in 16 with BOLD (average activation volume 86 ± 20 voxels (or 5.81 ± 1.35 cm3)) and in 19 with CBF (average activation volume 65 ± 13 voxels (or 4.39 ± 0.878 cm3)). The occipital lobe had average CBF of 94.4 ± 5.1 mL/min/100g for gray matter and 51.5 ± 3.1 mL/min/100g for white matter. CBF increased by 58% from 76 ± 6.8 mL/min/100g to 120 ± 7.4 ml/min/100g in activated cortex (Fig. 1). Modeling showed that differences in the BOLD response between SCA and CONTROL patients may be accounted for by differences in CBF response, change in oxygen extraction fraction during stimulation, CBV, and mechanical characteristics of the cerebral vasculature (Table 1). These findings suggest that the balloon model is useful to relate altered BOLD response to important clinical and physiological parameters in patients with SCA.
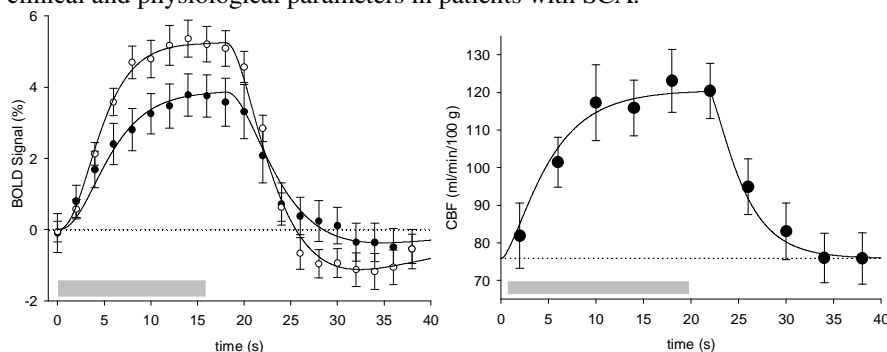

Fig. 1. Average BOLD and CBF responses to visual stimulations for SCA (black circles) and CONTROL (white circles) patients. The solid curves show balloon model fits to the BOLD responses for each group and filtered trapezoidal approximation of the CBF response.

	SCA	CONT.
CBF change (Δf)	0.5	0.8
Baseline O_2 extraction fraction (E_0)	0.43	0.42
Active O_2 extraction fraction (ΔE)	0.12	0.17
Transit time (τ_{MTT})	3.5	2.5
Baseline blood volume (V_0)	0.06	0.04
Flow-volume relation (α)	0.45	0.45
Viscoelatic time const.- inflation (τ_+)	10	10
Viscoelatic time const.- deflation (τ_-)	30	30
Rel. Hemoglobin Concentration (Hb)	0.8	1

References

1. Zou P, Helton KJ, Ogg RJ, Proc. HBM, 2007.
2. Buxton RB, et al. Neuroimage 23, 2004.