The Effect of Age on the SNR of CBF and BOLD Measures of Functional Activity

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Introduction

Previous studies have shown that the signal-to-noise ratio (SNR) of BOLD fMRI measures appears to decrease with age, most likely reflecting an age-related increase in low frequency noise fluctuations [1,2]. Here we extend the prior work by using arterial spin labeling (ASL) MRI to examine the effect of age on the SNR of cerebral blood flow (CBF) and BOLD responses to a memory encoding task. Physiological noise reduction methods were used to minimize the contributions of cardiac and respiratory fluctuations. We confirm the prior findings that BOLD SNR decreases with age, but find a relatively smaller effect of age on the SNR of CBF measures when physiological noise reduction is used.

Methods

Fifteen healthy young (age range 23-31) and nine healthy elderly (age 66-82 yrs) subjects participated in the study. None had any history of cognitive impairment. Subjects viewed a series of novel and familiar landscape scenes, presented in a block design. Each block consisted of 10 familiar or novel images, with 2s per image and a 0.5s gap between images. A total of 5 blocks of each type were presented per run (250s), with 3 runs per subject. Subjects maintained attention by using a button box to indicate whether images were horizontally or vertically oriented. Imaging was performed on a 3T GE Signa whole body system. Arterial spin labeling data were acquired with a PICORE QUIPSS 2 sequence with dual-echo spiral readout and the following parameters: TR=3s, TI1/TI2=700/1400ms, TE1=2.8ms, TE2=24 ms, flip angle 90, FOV 240mm, 64x64 matrix. Five 6mm slices aligned with the hippocampus were acquired. Cardiac and respiratory fluctuations were recorded using a pulse oximeter and respiratory effort belt, respectively, and used to form physiological noise regressors. For each subject, a hippocampal region of interest (ROI) that included both the hippocampus and para-hippocampal gray matter was defined using a high resolution anatomic T1-weighted image. CBF (TE1 data) and BOLD (TE2 data) responses were analyzed with a general linear model (GLM) as described in [3], with and without the inclusion of physiological noise regressors. For each subject, the number of activated voxels within the anatomical ROI was determined using a threshold of p= 0.01. In statistical comparisons of SNR measures (derived from the GLM), all voxels within the anatomical ROI with a correlation coefficient greater than zero were included in the analysis.

Results

Panel (a) in the figure shows the average number of activated voxels per subject both before (blue) and after (red) physiological noise reduction. The application of noise reduction increased the number of activated CBF voxels by 90% and 200% for young and old subjects, respectively, but resulted in smaller increases in the number of activated BOLD voxels of 35% and 29% for young and old, respectively. After noise reduction, there were considerably more activated voxels in the young subjects as compared to the old, with 75% and 140% more activated CBF and BOLD voxels, respectively. This was in part due to fact that the anatomic ROI was approximately 50% larger in the young subjects as compared to the old, reflecting the effects of age-related atrophy. Panel (b) shows the fraction of activated voxels, defined as the number of activated voxels divided by the number of voxels in the anatomic ROI. Here the fractions of activated voxels in the young are 20% and 60% greater than in the old for the CBF and BOLD voxels, respectively. Panel (c) shows the mean functional SNRs after physiological noise reduction. The SNRs in the older subjects were significantly lower than that of the young subjects for both CBF (8% lower; $p = 0.005$) and BOLD measures (40% lower; $p<10^{-20}$).

Discussion

Physiological noise reduction is clearly critical for improving the sensitivity of CBF measures, especially in older subjects. After noise reduction, the SNR of both CBF and BOLD measures is lower in the older subjects, but the relative difference is smaller for the CBF measures. The decrease in BOLD SNR with age has been attributed to an increase in low frequency noise components [1]. In the CBF responses, these low frequency components are largely attenuated by the filtered subtraction process used to estimate perfusion responses from the ASL data [4]. The relative difference between CBF and BOLD SNRs is relatively small (10%) in the old as compared to a 65% difference in the young, most likely reflecting the greater insensitivity of the CBF measures to any age-related increases in low frequency noise.

References [1] D'Esposito et al, NIMG 10:6, 1999. [2] Huettel et al, NIMG 13:161, 2001. [3] Restom et al, NIMG 31:1104, 2006. [4] Aguirre et al , NIMG 15:488, 2002.