Differential BOLD Hemodynamics in Young and Elderly: Emphasis on Post-Stimulus Undershoot

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Introduction

Studies on age-related changes in the BOLD hemodynamic response (HDR) have focused on the amplitude and time-to-peak (TTP) of the BOLD HDR [1,2]. Changes with age in cerebral blood flow (CBF), cerebral blood volume (CBV), cerebral metabolic rate of oxygen ($CMRO_2$) and oxygen extraction fraction (OEF) have been reported [3,4], all of which influence different features of the BOLD HDR including the post-stimulus undershoot [5]. In this study, differences in the magnitude of the BOLD response post-stimulus undershoot were examined between young adults and seniors, using a semantic picture naming task.

Methods

Twenty (10 male, 10 female) neurologically normal young adults (age 20-34 years) and twenty (10 male, 10 female) neurologically normal older adults (age 68-84 years) participated. Written informed consent was obtained for all the subjects. The picture naming task involved overtly naming objects from a library of 120 gray-scale photographs of animals, tools and vehicles (shown individually for 3.4 sec each) alternated with pseudo-random inter-stimulus intervals (ISIs ranging between 13.6, 15.3, 17.0 and 18.7 sec) of passive abstract pattern viewing in an event-related design. There were 15 trials in each of eight 323 sec functional runs. FMRI scanning parameters: 3T Siemens Allegra scanner with quadrature head coil; 1-shot gradient echo EPI scan, TR/TE/Flip Angle = 1700 msec/30 msec/70°; 240 mm FOV, 64 x 64 matrix, 3.75 mm x 3.75 mm in-plane resolution; whole brain coverage with 28 contiguous 4.0 mm slices.

The observed FMRI voxel time-series was modeled as the convolution of the experimental visual cue stimulus vector and the estimated best-fit twelve-lag impulse response (IR). Voxelwise maps of IR positive BOLD and undershoot amplitudes (as a percentage of the estimated time-series baseline) were constructed. These functional activation maps were warped to Talairach space, resampled at a $1mm^3$ resolution, and subsequently spatially smoothed with a gaussian kernel (FWHM = 3 mm). Between-group t-tests were performed to assess the significance of differences in positive BOLD and undershoot amplitudes between younger and older adults. The undershoot differences were assessed only in the voxels which exhibited significant positive BOLD activation ($|t_{39}| > 4.3$; uncorrected $p < 0.0001$), in both young adults and elderly taken as one group. The t-maps of undershoot differences were further clustered ($|t_{38}| > 2.0$; cluster volume threshold 100 µl; cluster-level $p < 0.0008$), and ROI cum group averaged BOLD HDRs were obtained for all significant clusters. Between-group differences in TTP, full width at half maximum (FWHM), and amplitude were tested among these cluster ROI and group averaged HDRs, to examine if there was a relation between the differences in undershoot and those in other parameters of the BOLD HDR.

Results and Discussion

Figure 1 (a-f) shows regions of significant differences in undershoot between elderly and young adults ($|t_{38}| > 2.0$; $p < 0.05$; cluster threshold 100 µl; cluster-level $p < 0.0008$) for the naming task. Voxels in red and blue represent areas where the elderly subjects and young adults exhibited greater post-stimulus undershoot, respectively. Young adults exhibited larger post-stimulus undershoot compared to elderly subjects in a number of areas bilaterally during the semantic picture naming task, including lateral occipital cortex, fusiform gyrus, medial frontal gyrus, anterior cingulate gyrus, superior temporal gyrus, and precentral gyrus. In the 23 such clusters, the young adults exhibited greater positive BOLD amplitude (paired $t_{22} > 7$; $p < 10^{-7}$), smaller FWHMs (paired $t_{22} < -4$; $p < 0.0001$) and slightly shorter TTPs (paired $t_{22} < -3$; $p < 0.005$). Figure 2 shows HDRs for the two groups in two representative areas of the brain. Possible explanations of the above observations include impairment of vasoreactivity [6] or decreased oxygen metabolism [7] among the elderly, or a combination of both events.

Older adults exhibited greater undershoot in fewer areas, including left and right thalamus, cerebellum and middle temporal gyrus. However, no significant differences in FWHMs or TTPs were observed between groups in the 8 such clusters, whereas the amplitudes were only slightly higher among the elderly (paired $t_7 > 2$; $p < 0.08$), indicating the phenomenon of greater undershoot among the elderly may have different physiological underpinnings.

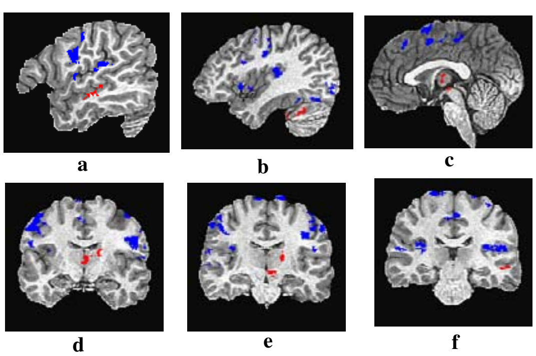

Figure.1 Sagittal: R54 (a), R40 (b), L0 (c) and coronal (d,e,f) slices of the between-group t-test maps showing regions of larger undershoot in elderly (red) and young adults (blue).

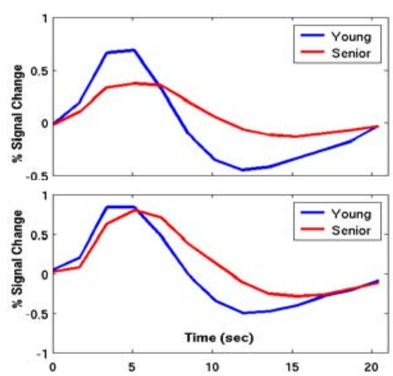

Figure.2 Representative group averaged HDR in the right precentral gyrus (top) and left medial frontal gyrus (bottom) of elderly (red) and young adults (blue).

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