# Habituation of the BOLD response in fMRI of the human auditory and visual cortex

M. A. Elliott[1], L. Bloy[1], J. Hulvershorn[1]
[1]Radiology, University of Pennsylvania, Philadelphia, PA, United States

**Introduction:**

Standard analysis of fMRI data is predicated upon a linear model of the BOLD hemodynamic response function (HRF). However, several studies have demonstrated non-linear behavior of the HRF in response to differences in inter-stimulus interval (ISI)(1,2), or for small stimulus duration(3,4). Additionally, there is considerable, though inconsistent, evidence of habituation of the BOLD response during the course of an experiment. PET studies have shown reduction in thalamic blood flow in response to successive auditory stimuli(5), but no habituation was seen in the auditory cortex. fMRI studies, however, have revealed habituation of the HRF amplitude in the human auditory cortex(6). Temporal measures of the HRF, such as latency or time-to-peak (TTP), have been utilized in fMRI investigation of mental chronometry(7), schizophrenia(8), and vascular dynamics(9). In this study, an event-related fMRI study which activated the primary auditory and visual cortices was examined for trends in habituation of the BOLD response. In both activated regions, the average BOLD TTP decreased significantly with increasing stimulus count. Conversely, the amplitude of the BOLD response in the visual cortex increased significantly, but no signficant change was seen in the auditory cortex.

**Methods:**

Forty-three functional MRI sessions were collected on a Siemens 3T scanner with gradient-echo EPI with the following parameters: TR=2s, TE=30ms, FOV=240mm, voxel size=3.75x3.75x4mm, slices=19, slice gap=0, repetitions=200, experiment time=6:40, axial-oblique slice orientation. The functional paradigm consisted of 44 pseudo-randomized, event-related presentations of simultaneous 2-sec visual and auditory stimuli. The maximum and minimum delays between successive presentations were 30 seconds and 0 seconds, respectively. The mean interval between events was 6.8 seconds. Activated voxels were detected with a design matrix constructed with the canonical HRF plus its first derivative. Voxels exceeding a threshold of $p < 0.001$ ($z = 3.09$) were selected for further analysis. To assess habituation effects, the 44 stimulus onsets were divided into four groups of 11 consecutive stimuli, hereafter referred to as Periods 1 through 4. Voxels found to be activated by the full model analysis were masked by anatomical ROIs for the primary visual and auditory cortices, and then regressed to the 4-condition model using an unbiased deconvolution technique(10). The deconvolution model determined the HRF at 9 time points, modeling the response to 16s post-stimulus onset. The peak HRF amplitude (Contrast) and its TTP were determined for each experimental period at each activated voxel. Within each subject, the average Contrast and TTP across voxels were then linearly fit versus experimental Period, and the slopes of these fits were used as the metric to assess the presence of habituation in Contrast and TTP.

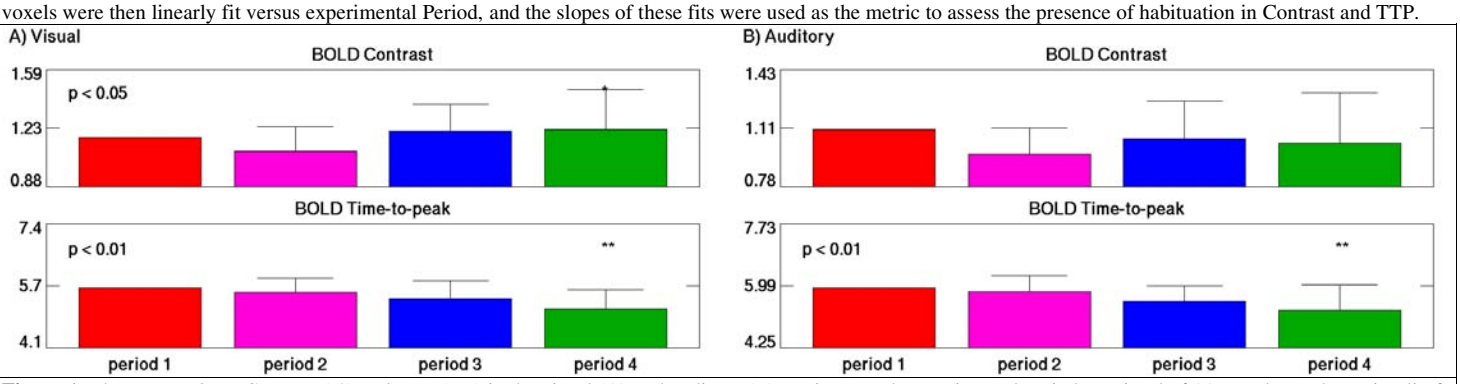


**Figure 1**. The mean BOLD Contrast (%) and TTP (sec) in the visual (A) and auditory (B) cortices. Each experimental period consisted of 11 pseudo-random stimuli of 2-sec duration, and lasted approximately 100 sec. In the visual cortex, the within-subject slopes of Constrast and TTP were significantly different than zero, with Contrast *increasing* ($p<0.05$) and TTP *decreasing* ($p<0.01$) during the experiment. In the auditory cortex, the change in Contrast was not significant, but TTP again *decreased* significantly ($p<0.01$).

**Results:**

All subjects activated robustly and bi-laterally in the visual and auditory cortices. Visual cortex: The average Contrast across all subjects was seen to *increase* in the visual cortex over the course of the experiment, while the average TTP *decreased*. Both effects were statistically significant, with the Contrast increasing from 1.18% to 1.23% ($p<0.05$) between periods 1 and 4, respectively. The average TTP decreased from 5.69s to 5.13s ($p<0.01$). Auditory cortex: No significant change was seen in the BOLD Contrast of the auditory cortex, but a significant *decrease* in TTP was observed, decreasing from 5.94s to 5.31s ($p<0.01$).

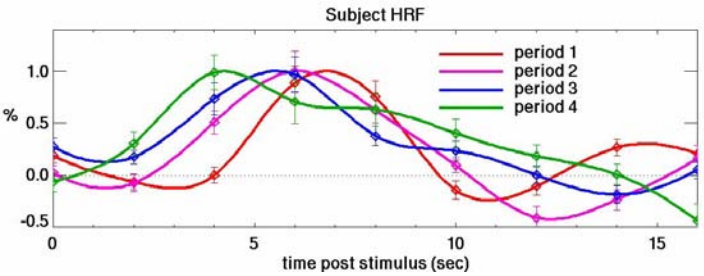


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**Figure 2**. Single subject HRFs from the auditory cortex, showing decreasing time-to-peak with increasing experimental period. The TTPs for periods 1 through 4 were 6.8, 6.1, 5.4, and 4.7 sec, respectively. The HRF amplitudes have been normalized to unity for clarity of the change in TTP.

**Discussion:**

The conventional concept of habituation predicts a reduced, and possibly delayed, response to lengthy stimuli, as demonstrated by Pfleiderer et al(6). However, the results described here indicate that brief auditory and visual stimuli produced an enlarged and faster BOLD response with increasing stimulus count. This is consistent with previous observations of performance priming(11), in which subjects respond faster and more accurately to repeated presentations of the same stimuli. Whether the BOLD response to a particular stimulus is habituated or primed, such non-linear behavior of the HRF is relevant to conventional fMRI analysis methods, which assume linearity of the response. Moreover, group or individual differences in functional activation may reflect actual differences in the baseline primed state, or conversely, differences in the priming or habituative capacity of the neuro-vascular networks involved.