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Achromatic temporal-frequency responses of human lateral geniculate nucleus and primary visual cortex

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ABSTRACT

The sensitivity of the sensory systems to temporal changes of the environment constitutes one of the critical issues in perception. In the present study, we investigated the human early visual system's dependency on the temporal frequency of visual input using fMRI. Blood oxygen level-dependent (BOLD) responses of the lateral geniculate nucleus (LGN) and primary visual cortex (V1) were investigated in a wide frequency range (6–46 Hz) with fine frequency sampling (13 frequencies). Subject-specific functional-anatomic ROIs were derived from the combination of the anatomic template masks and the functional maps derived from multi-session fMRI analyses across all 13 stimulation conditions. Using functional-anatomic ROIs, average responses of LGN and V1 were calculated for each frequency. The V1 surface area was further parsed into 7 eccentricity sectors to detail central and peripheral responses. LGN's response revealed fluctuations on a background of non-significant decrease of the BOLD response with increasing stimulation frequency, while V1 response displayed similar fluctuations with a global maximum in the range of 8–12 Hz, but a rapid and significant decrease with increasing stimulation frequency especially above 14 Hz. This behavior of V1 response valid for both central and peripheral vision emphasizes that the profound low-pass effect of the visual system to visual input emerges in V1, presumably generated by the intra-cortical circuitry of V1 or projections from extra-striate areas. Besides, the high correlation between LGN and V1 BOLD responses across all visual stimulation frequencies supports the oscillatory tuning in thalamo-cortical interactions as previously claimed in electrophysiological studies.

1. Introduction

Visual stimuli at various temporal frequencies have been used as a convenient tool to investigate the frequency response of the visual system (Herrmann, 2001; Rager & Singer, 1998; Regan, 1989). As thalamo-cortical loops are one major source of oscillatory neuronal activities in the brain, determination of the frequency characteristics of the lateral geniculate nucleus (LGN) and the primary visual cortex (V1) is essential in order to evaluate the temporal frequency response of the visual system (Başar, 1980). Functional magnetic resonance imaging (fMRI) provides a non-invasive way of measuring the responses of both structures with a high spatial accuracy. Although the LGN has relatively small volume, its activities can still be measured using fMRI (Büchel, Turner, & Friston, 1997; Chen et al., 1998; Fujita et al., 2001).

The LGN is the main source of visual information for V1, and the main target nucleus of the optic tract, which receives almost 90% of retinal outputs (Gazzaniga, Ivry, & Mangun, 2002). On the other hand, the proportion of retinal inputs with respect to total synapses in the LGN of primates is about 30–40% (Casagrande, Sáry, Royal, & Ruiz, 2005), which implies that the majority of inputs are extra-retinal and have a modulatory effect on rather than being the driver of visual inputs (Sherman & Guillery, 1998). V1 is the source of the largest number of synapses in the LGN, which carry feedback signals from the cortex to the thalamus (Casagrande et al., 2005). Therefore, the LGN is an important site for the modulatory effects of V1 on visual input and can play an important role in the temporal frequency tuning of the visual system.

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A number of positron-emission tomography (PET) and fMRI studies reported activity changes in the visual cortex depending on the temporal frequency of the stimuli (Emir, Bayraktaroglu, Ozturk, Ademoglu, & Demiralp, 2008; Fox & Raichle, 1985; Kastner, Schneider, & Wunderlich, 2006; Kastner et al., 2004; Mullen, Thompson, & Hess, 2010; Muthukumaraswamy & Singh, 2008; Parkes, Fries, Kerskens, & Norris, 2004; Rosa, Kilner, Blankenburg, Josephs, & Penny, 2010; Singh, Kim, & Kim, 2003; Wan et al., 2006). However, these results did not lead to a consensus for several reasons.

First of all, a common problem with the studies that used retinotopic mapping for identifying the V1 region (Kastner et al., 2004; Mullen et al., 2010; Singh, Smith, & Greenlee, 2000) is the variability of responses due to different spatial properties of the visual stimuli. As Mirzajani, Riyahi-Alam, Oghabian, Saberi, and Firouznia (2007) demonstrated, interaction among temporal and spatial frequency effects need to be taken into consideration when investigating the response characteristics of the visual system.

With the exception of the studies by Emir et al. (2008) and Singh et al. (2003) another disadvantage of these studies is the logarithmic sampling of temporal frequencies because of the raster screens used, which allow to vary the temporal frequency only by integer multiples of the refresh rate. As a result, these studies described the temporal frequency-response of V1 by investigating BOLD responses at only three or four frequencies, which resulted in limited correspondence among the studies.

Finally, ambiguity in results might also stem from different ways of defining the region of interest (ROI) in fMRI analyses. Studies that defined the ROI as a limited number of the most active voxels in V1 (Emir et al., 2008; Muthukumaraswamy & Singh, 2008; Parkes et al., 2004; Wan et al., 2006) reported increased BOLD responses with higher temporal frequency, which peaked and plateaued at around 6–10 Hz. Contrarily, studies that defined the ROI by thresholding the BOLD responses more liberally lead to a broader area covering V1 and extra-striatal areas and reported a band-pass response with a peak at approximately 8 Hz (Rosa et al., 2010; Singh et al., 2003).

In the present study, we aimed to study the fMRI frequency-response characteristics of the LGN and V1 in a robust and unequivocal manner. For this, we used diffuse light stimuli to avoid confounding effects of spatial visual patterns on the BOLD response. In addition, light-emitting diodes (LED) were used as light sources, which allowed us to sample the temporal frequencies with a finer resolution compared with raster screens. Finally, we used the intersection area of the functional and anatomic maps for ROI definition. Consequently, the frequency characteristics of the LGN and V1 BOLD responses revealed a clear low-pass effect in V1 but not in LGN. Despite this overall difference between the general frequency responses of both structures, their highly correlated BOLD fluctuations across visual stimulation frequencies supports the existence of oscillatory tuning in thalamo-cortical networks.

2. Materials and methods

2.1. Subjects

Thirty-five healthy volunteers (20 women, 15 men, mean age: 25.60 ± 3.87 years) were recruited for this study after receiving their informed consent. All subjects had normal or corrected-to-normal vision acuity and had no history of sensory system-related pathology or neuro-psychiatric disorder. Ethical approval was obtained from the local ethics committee of Istanbul University, Istanbul Faculty of Medicine, in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) prior to commencing the study.

2.2. Visual stimuli and experimental protocol

The stimuli were reflected on a white surface by a flickering light at temporal frequencies of 6, 8, 10, 12, 14, 18, 22, 26, 30, 34, 38, 42, and 46 Hz. The square-wave stimuli were "on" for the half of a period, thus the energy was constant across all frequencies. Although the edges of the square waves may produce high frequency harmonics, their effect on mean intensity is the same for all stimulation frequencies and far beyond the time constant of the BOLD response.

The mean luminance of the visual stimuli was 100 cd/m^2. The light source was a shielded set of LEDs driven by a digital I/O card (NI DAQCard-6062E) located one meter away from the rear side of the magnet. The screen was a rear-facing 45°-inclined diffuser surface (field of view 54.8°) attached to the top of the head coil of the MRI system and used for diffuse reflection of the exposed light. The subjects' task was to maintain focus on and passively view the fixation cross drawn on the center of the reflection surface.

Each experimental run, during which the fMRI response to one of the 13 flicker frequencies was measured, started with a rest period of 10 dynamic scans, which was followed by 3 alternating blocks of stimulation and rest periods (Fig. 1). Each stimulation and rest block lasted for 15 dynamic scans yielding a total of 100 dynamic scans for each run. Flickers were synchronized to the fMRI volumes by using the synchronization output of the MR scanner. The order of the runs was randomized among the subjects to avoid any systematic effect of time on BOLD responses.

2.3. MRI data acquisition and analysis

Magnetic resonance imaging was performed using a 1.5T Philips Achieva MRI system equipped with SENSE-Head-8 coil at NPISTANBUL Neuropsychiatry Hospital, Istanbul. At the beginning of each experiment, routine cranial MRI examination was performed to detect possible abnormalities in healthy subjects. Additionally, whole-brain high-resolution structural scans were acquired using a T1-weighted MPRAGE sequence with voxel size of 1.25 × 1.25 × 1.2 mm (130 sagital slices, TR/TE = 8.6/4.0 ms, acquisition matrix 192 × 192, duration 369.8 s). Thirteen experimental runs were acquired using T2*-weighted gradient echo (GE), echo planar imaging (EPI) with identical scan parameters (100 dynamic scans, 32 axial slices, slice thickness = 4 mm (without gap),

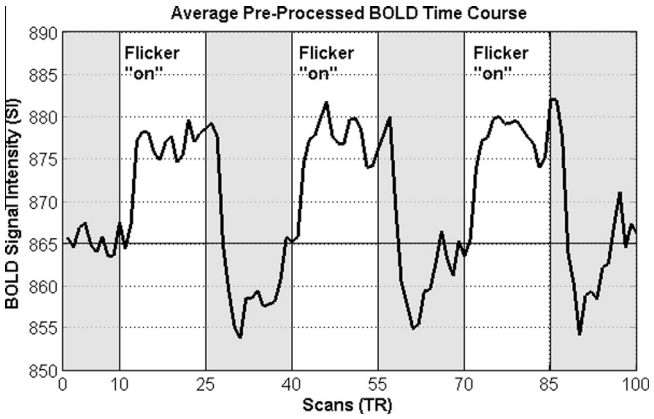

Fig. 1. Experimental protocol and average pre-processed BOLD response of one subject. Each experimental run for one of the 13 flicker frequencies started with a rest period of 10 dynamic scans, which was followed by 3 alternating blocks of stimulation and rest periods of 15 dynamic scans each.