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Spatial Frequency Dependence of the Human Visual Cortex Response on Temporal Frequency Modulation Studied by fMRI

Background/Objective: The brain response to temporal frequencies (TF) has been already reported. However, there is no study on different TF with respect to various spatial frequencies (SF).

Materials and Methods: Functional magnetic resonance imaging (fMRI) was done by a 1.5 T General Electric system for 14 volunteers (9 males and 5 females, aged 19-26 years) during square-wave reversal checkerboard visual stimulation with different temporal frequencies of 4, 6, 8 and 10 Hz in 2 states of low SF of 0.4 and high SF of 8 cycles/degree (cpd). All subjects had normal visual acuity of 20/20 based on Snellen's fraction in each eye with good binocular vision and normal visual field based on confrontation test. The mean luminance of the entire checkerboard was 161.4 cd/m2 and the black and white check contrast was 96%. The activation map was created using the data obtained from the block designed fMRI study. Pixels with a Z score above a threshold of 2.3, at a statistical significance level of 0.05, were considered activated. The average percentage blood oxygenation level dependent (BOLD) signal change for all activated pixels within the occipital lobe, multiplied by the total number of activated pixels within the occipital lobe, was used as an index for the magnitude of the fMRI signal at each state of TF&SF.

Results: The magnitude of the fMRI signal in response to different TF's was maximum at 6 Hz for a high SF value of 8 cpd; it was however, maximum at a TF of 8 Hz for a low SF of 0.4 cpd.

Conclusion: The results of this study agree with those of animal invasive neurophysiologic studies showing SF and TF selectivity of neurons in visual cortex. These results can be useful for vision therapy and selecting visual tasks in fMRI studies.

Keywords: functional magnetic resonance imaging, frequency, visual stimulation, fMRI, visual cortex

Introduction

The image formed on the retina is just a pattern of various light intensities and wavelengths which may change from moment to moment. These spatial and temporal variations in the image provide the only information available for visual processing .[1, 2] The information associated with the coarse patterns is reflected by low spatial frequencies (LSF) and finer patterns produce high spatial frequencies (HSF).[3] Most visual scenes present temporal as well as spatial information. Temporal changes can per se be important in edge detection as in the case of stationary flickering lights. Changes in image luminance are translated in temporal frequency (TF). [2]

Although the human brain responses to a wide range of TFs have already been reported, there is no imaging study regarding different TFs with respect to various SFs.[4-6]

Fox et al. studied the stimulus rate dependence of regional cerebral blood flow (rCBF) in human striate cortex by positron emission tomography (PET).

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The results showed that the rCBF response peaked at 7.8 Hz and then declined. Mentis et al. investigated the rCBF response to frequency variation of pattern-flash visual stimulus using PET. They recorded an rCBF response in the striate cortex with its peak at 7 Hz. Kwong et al. investigated the stimulation frequency dependence of visual activation by functional magnetic resonance imaging (fMRI). Their findings agreed with the previous PET observations and showed that the largest MR signal response occurred at 8 Hz. Similar result was found by Thomas et al. [7] They showed that the fMRI signal also peaks at a flicker frequency of 8 Hz. Ozus, et al. studied the rate dependence of human visual cortical responses to brief stimulation.[8] They found that the change in BOLD signal increased up to a stimulus frequency of 6 Hz after which it stays nearly constant.

Neurophysiologic and psychologic studies suggested that there are multiple visual channels tuned to each of the SF bands and that there is a SF and TF selectivity of neurons in visual cortex as well. [9-18] The objective of this study was therefore, to determine the visual cortical activity responses to variations in both TF and SF values and to study their interactions.

Materials and Methods

Subjects

The subjects were 14 (9 male, 5 female) right-handed healthy volunteers. The mean±SD age of participants was 22.4±1.8 (range: 19–26) years. All subjects had normal visual acuity of 20/20 based on Snellen's fraction in each eye with good binocular vision and normal visual field as determined by confrontation. There was no history of visual loss or neurologic problems in subjects. The volunteers were willing to participate in this study and an informed written consent was obtained from each participant.

Visual stimuli

We used a square-wave reversal checkerboard visual stimulation with different temporal frequencies of 4, 6, 8 and 10 Hz in two states of a low SF value of 0.4 and a high SF of 8 cpd. Visual tasks were provided by Presentation Software version 0.60 and projected by a video projector on a screen. The subjects could see the visual stimuli through the non-magnetic mirror in front of their eyes during the image processing. The MRI room was made as dark as possible. Therefore, the visual tasks presented were the only visual stimulation the subject could perceive. The subjects were asked to continue fixation on the center of the screen during rest period without any eye movements. The mean luminance of the entire checkerboard was 161.4 cd/m^2. The black and white check contrast was 96%. The visual angle of the stimulus subtended 11.2° horizontally and 8.3° vertically.

Data acquisition

Experiments were performed with a GE 1.5 T MRI system equipped with echo-planar (EPI) acquisition (TR = 2000 ms, TE = 60 ms, flip angle = 90°, matrix size = 64×64, number of slices =11, FOV = 220 × 220 mm^2, voxel size = 3.44×3.44×4.0 mm^3) sensitive to BOLD contrast. Data were acquired in a steady state trial with a stimulus 'on' for 18 sec and 'off' for 18 sec, *i.e.*, a 36-sec cyclic block design. Each set of SF and TF was presented over 2.5 cycles for a total of 1.5 min per trial. Trial was started on active state, *i.e.*, ran with three stimulus 'on' and two stimulus 'off'. Because there were eight different sets of SF and TF, eight separate run were performed. The functional images were acquired in an axial orientation parallel to the anterior commissure-posterior commissure (AC-PC) line. A functional volume composed of 11 slices with a thickness of 4 mm and spacing of 1 mm, was imaged for 45 times per trial. For each subject, an anatomical whole brain image corresponding to functional image was also acquired with a standard spin-echo pulse sequence (T_1-weighted, TR = 300 ms, TE = 21.4 ms, flip angle = 90°, matrix size = 256×256, number of slices = 11, voxel size = 0.86 × 0.86 × 4.0 mm^3).

Data analyses

Data analyses were carried out using fMRI Expert Analysis Tool (FEAT, version 5.4), and some routines taken from FMRIB's Software Library (FSL, available from www.fmrib.ox.ac.uk/fsl). The following pre-statistics processing was applied: Motion correction using MCFLIRT; non-brain removal using BET; spatial smoothening using a Gaussian kernel of FWHM 5 mm; mean-based intensity normalization of all volumes by the same factor; high-pass temporal filtering

(Gaussian-weighted LSF straight line fitting, with sigma=50.0 s). [19,20] Time-series statistical analysis was carried out using FILM with local autocorrelation correction.[21] Z (Gaussianized T/F) statistic images were thresholded using clusters determined by $Z > 2.3$ and a (corrected) cluster significance threshold of $P=0.05$.[22]

Registration to high resolution (anatomical) and standard images were carried out using FMRIB's Linear Image Registration Tool (FLIRT) .[23] After registration, the activation maps including activated pixels the Z value of which was above a threshold of 2.3, at significance level of $P=0.05$, were superposed on corresponding T_1-weighted anatomical images. To determine a measure for the magnitude of the fMRI signals, an average time course was computed from all activated voxels within the occipital lobe to extract an average signal change, which was then multiplied by the total number of activated voxels, i.e. the average signal change from all activated voxels multiplied by the total number of activated voxels within the occipital lobe, was used as an index indicating the magnitude of the fMRI signal at each set of TF and SF values. This method wasperformed individually in all 14 subjects at each set of TF and SF levels (8 set), hence 112 values were obtained. These

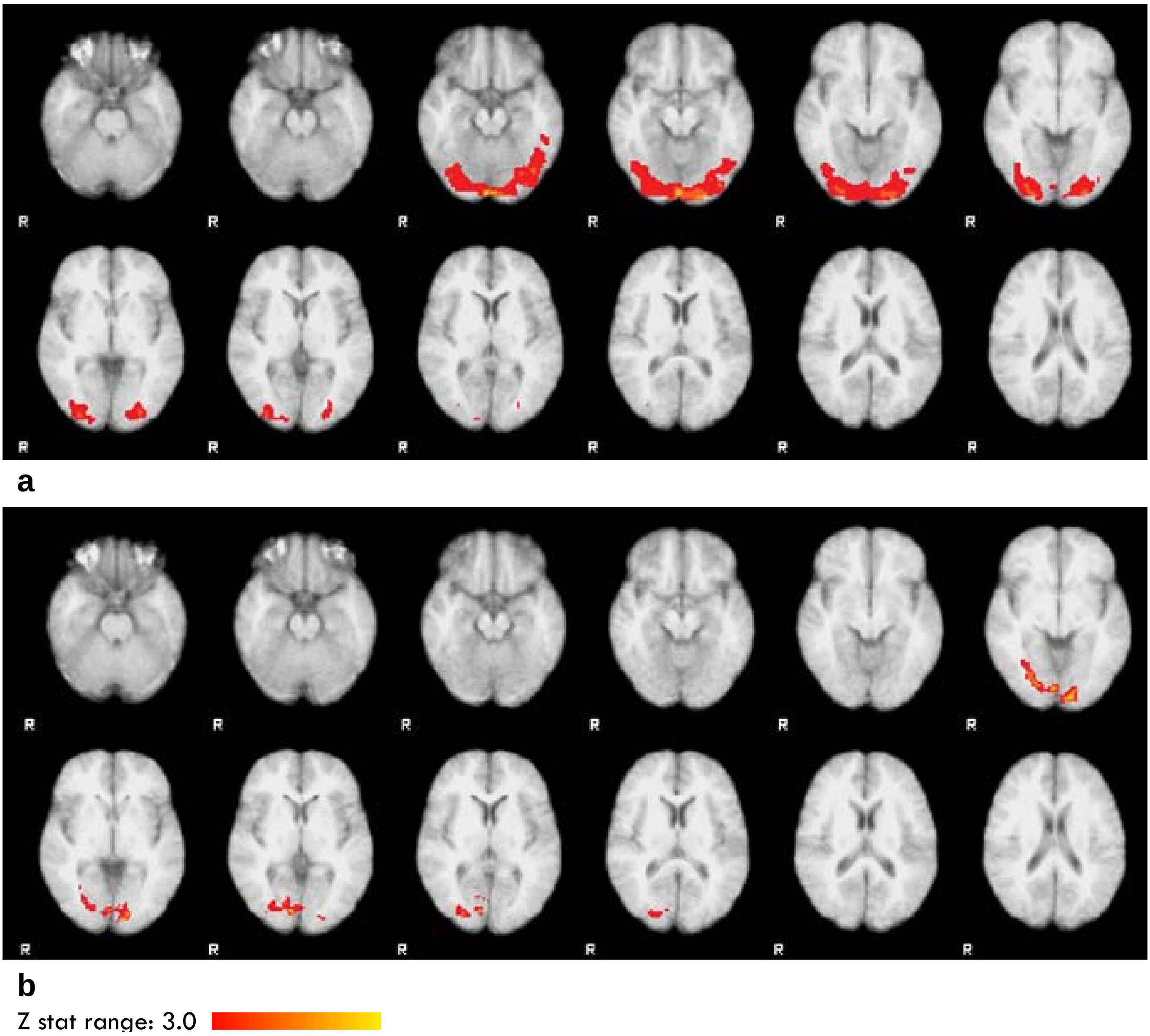

Fig 1. Comparison of activation area with the maximum response at temporal frequency of 8 Hz in LSF of 0.4 cpd (a), and 6 Hz in HSF of 8 cpd (b).

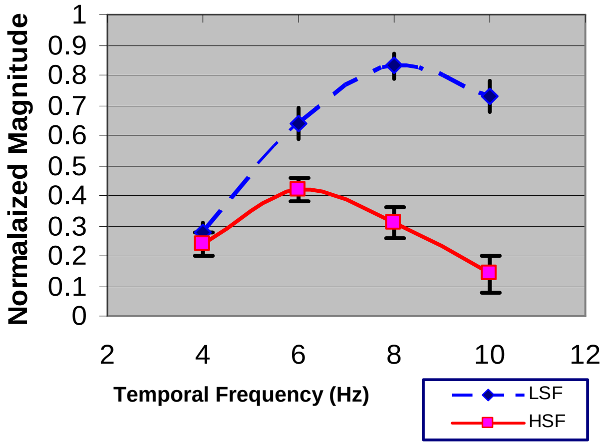

Fig 2. Comparison of the averaged magnitude of fMRI signal (14 subjects) as a function of TF in two states of LSF of 0.4 cpd and HSF of 8 cpd. (The signal has been normalized to its largest value. Error bars represent standard error of mean)

values were then normalized to their largest value. Repeated-measures two-way ANOVA was used for evaluating the effects of two within subjects' factors of SF and TF on the visual cortical responses. We also examined Fisher's least significant difference (LSD) as the post hoc procedure.

Results

The normalized magnitude of fMRI signals as a function of TF and SF averaged between 14 subjects are shown in Table 1. A repeated-measures two-way ANOVA was conducted with two within-factors (SF with 2 and TF with 4 levels). There was a significant interaction between SF and TF ($F_{3,39} = 45.62$, $p<0.001$). This finding illustrates that the magnitude of the fMRI signals changes with variations in either TF or SF of visual stimulation. The maximum magnitude of the fMRI signals happened at a TF of 8 Hz for visual stimuli with a low SF of 0.4 cpd. It also occurred at a TF of 6 Hz for stimuli with a high SF of 8 cpd. For all TF's, except 4 Hz, the magnitude of the fMRI signals at a high SF was significantly lower than that recorded at a low SF (LSD procedure, $p < 0.05$).

Table 1. Normalized magnitude of fMRI signal as a function of TF and SF averaged between 14 subjects.

Temporal Frequency (Hz)	Spatial Frequency (cpd)	Mean Magnitude ± SEM
4	0.4	0.28 ± 0.03
4	8	0.24 ± 0.03
6	0.4	0.64 ± 0.05
6	8	0.42 ± 0.04
8	0.4	0.83 ± 0.03
8	8	0.31 ± 0.04
10	0.4	0.73 ± 0.04

The functional maps due to visual stimulation in maximum BOLD signal to a TF of 8 Hz in LSF state of 0.4 cpd, and to a TF of 6 Hz in HSF state of 8 cpd, were superimposed on the corresponding T_1-weighted anatomical image averaged between 14 subjects (Figure 1).

The averaged magnitude of fMRI signals for 14 subjects, as a function of TF and SF, are illustrated in Figure 2. In the state of LSF, the magnitude of the fMRI increases gradually with the TF, reaching a maximum at a TF of 8 Hz and then declined. In the state of HSF, the signal magnitude however, reached a peak at a TF of 6 Hz and then decreases.

Discussion

The results of our study show that the magnitude of fMRI signals varies as a function of spatio-temporal frequency. We also found that in low SF of 0.4 cpd, the maximum fMRI signal happens at a TF of 8 Hz ($p<0.001$). This finding is consistent with previous reports on light-flash stimulations or reversal checkerboards of low SF. [4-7, 23]

On the other hand, our findings indicate that the magnitude of fMRI signals in response to variation in TF is different for various SF ($p<0.01$). In this regard, the amplitude of fMRI signals at different TF's is significantly dependent on the SF components of the image being presented (e.g., checkerboard). Therefore, the SF characteristics of the viewing checkerboard may alter the TF of responses recorded from the functional activity areas in the brain cortex.

The results of this study are in good agreement with those performed on animal models that provided evidence for selectivity of visual cortex neurons for SF and TF. [9-12]

In this study, at a high SF of 8 cpd, the maximum BOLD signal was produced at a TF <8 Hz, i.e. in 6 Hz ($p<0.001$); this could be explained on the basis of the concepts of P channel (parvocellular pathway: higher SF's associated with lower TFs) and M channel (magnocellular pathway: lower SF's associated with higher TF's).[24]

The fact that the higher the velocity (or TF), the lower the SF to which the cortical visual cell is tuned, justifies the finding of the present study, i.e. with increasing TF from 6 to 8 Hz, those cells responding to SF of 8 cpd showed a pronounced reduction in response to that SF that resulted in a decrease in BOLD signal.[25]

In regard to the psychophysics and psychologic studies, it has been suggested that visual perception is mainly based on SF (Fourier analysis of the image).[14-18] This analysis starts with processing low SFs, followed by processing HSF's. Therefore, SF may be an important index in evaluation of responses of the brain to other physical and psychophysical aspects of vision such as TF.

The results of this study may be useful in planning of "vision therapy" such as treatment of amblyopia, by choosing the optimum SF appropriate for TF. Visual tasks planed in fMRI studies can also benefit the advantage of these physical effects in brain cortical responses.

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