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Nonlinear population receptive field changes in human area V5/MT+ of healthy subjects with simulated visual field scotomas

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ABSTRACT

There is extensive controversy over whether the adult visual cortex is able to reorganize following visual field loss (scotoma) as a result of retinal or cortical lesions. Functional magnetic resonance imaging (fMRI) methods provide a useful tool to study the aggregate receptive field properties and assess the capacity of the human visual cortex to reorganize following injury. However, these methods are prone to biases near the boundaries of the scotoma. Retinotopic changes resembling reorganization have been observed in the early visual cortex of normal subjects when the visual stimulus is masked to simulate retinal or cortical scotomas. It is not known how the receptive fields of higher visual areas, like hV5/MT+, are affected by partial stimulus deprivation. We measured population receptive field (pRF) responses in human area V5/MT+ of 5 healthy participants under full stimulation and compared them with responses obtained from the same area while masking the left superior quadrant of the visual field ("artificial scotoma" or AS). We found that pRF estimations in area hV5/MT+ are nonlinearly affected by the AS. Specifically, pRF centers shift towards the AS, while the pRF amplitude increases and the pRF size decreases near the AS border. The observed pRF changes do not reflect reorganization but reveal important properties of normal visual processing under different test-stimulus conditions.

Introduction

An important question is whether the adult visual cortex is able to reorganize in subjects with visual field defects (scotomas) as a result of retinal or cortical lesions. Studies in subjects suffering from macular degeneration or retinal lesions produced controversial results (Kaas et al., 1990; Heinen and Skavenski, 1991; Chino et al., 1992, 1995; Gilbert and Wiesel, 1992; DeAngelis et al., 1995; Schmid et al., 1996; Murakami et al., 1997; Horton and Hocking, 1998; Calford et al., 1999; Sunness et al., 2004; Baker et al., 2005, 2008; Smirnakis et al., 2005; Giannikopoulos and Eysel, 2006; Masuda et al., 2008; Schumacher et al., 2008; Dilks et al., 2009; Wandell and Smirnakis, 2009; Baseler et al., 2011). Similarly, studies on subjects with lesions of the primary visual cortex or the optic radiation remain inconclusive (Eysel and Schmidt-Kastner, 1991; Eysel and Schweigart, 1999; Eysel et al., 1999; Rumpel et al., 2000; Mittmann and Eysel, 2001; Barmashenko et al., 2003; Zepeda et al., 2003; Dilks et al., 2007; Yan et al., 2012; Imbrosci et al., 2013; Papanikolaou et al., 2014).

Interestingly, changes in the retinotopic maps of the early visual cortex have been observed even in normal subjects after masking the visual stimulus to simulate retinal or cortical scotomas. In particular, when the stimulus was masked to simulate a foveal scotoma, population receptive fields (pRFs) representing the scotoma shifted in locations outside the scotoma border and increased in size (Baseler et al., 2011; Haak et al., 2012a). It was suggested that these pRF changes were due to a combination of the position and size scatter of individual receptive fields within a voxel influenced by modulatory feedback signals from extrastriate visual areas (Haak et al., 2012a). However, a recent study suggests that the observed pRF changes are an artifact of the analysis method and that pRF biases can be eliminated if the masked stimulus is incorporated in the model when estimating the pRF (Binda

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et al., 2013). It is important to characterize these biases in order to ensure that changes in the retinotopic organization observed in patients are not simply an artifact of model estimation in the context of incomplete stimulus presentation (artificial scotoma).

In addition, presenting a truncated visual stimulus, as is typically done in the artificial scotoma, can have nonlinear effects that can modify receptive field location and size estimates in individual neurons. This is expected to be especially prominent for receptive fields in higher areas, which cover a large portion of the visual field. Area V5/MT+ is of particular interest as it has been shown to be modulated by visual stimuli presented inside the scotoma following lesions of the primary visual cortex (V1) (Bruce et al., 1986; Rodman et al., 1989, 1990; Maunsell et al., 1990; Girard et al., 1992; Barbur et al., 1993; ffytche et al., 1996; Rosa et al., 2000; Schoenfeld et al., 2002; Morland et al., 2004; Bridge et al., 2010; Schmid et al., 2010) and has been associated with the phenomenon of subconscious visual perception, called "blindsight" (Poppel et al., 1973; Weiskrantz et al., 1974). Visual field maps and population receptive field sizes have been recently characterized for the human hV5/MT+ complex in normals (Amano et al., 2009). However, it is not known how these are affected by partial stimulus presentation.

Here we used a new method, which estimates the population receptive field (pRF) topography in the visual cortex with minimal bias (Lee et al., 2013) to measure pRF changes that occur in area hV5/MT+ of five healthy subjects after masking the stimulus in the left upper quadrant of the visual field ("artificial scotoma" or AS). This simulates a homonymous quadrantanopic scotoma that occurs often as result of partial V1 or optic radiation lesions. We compared responses obtained under the AS condition with simulations obtained from a linear AS model (or LAS model). The LAS model simulates the pRFs under the AS condition based on the actual pRFs derived under the full stimulus condition (pRF_{FF}) assuming that the only effect of the AS is that it does not stimulate the corresponding part of the pRF. This provides a prediction of the expected position and shape of the residual pRFs under the AS. In other words, the LAS model provides an estimation of the pRF changes expected to occur as a result of the truncated stimulus assuming that the pRF linearly integrates the AS (pRF_{LAS}). We found pRF changes in hV5/MT+ under the AS condition (pRF_{AS}) that are significantly different than those obtained with the LAS model suggesting that the pRFs are nonlinearly affected by the truncated stimulus presented. In particular, pRF_{AS} centers shift towards the border of the AS, the pRF_{AS} amplitude increases and the pRF_{AS} size decreases near the border of the AS. In addition, we found significant errors in pRF estimation which extend inside the AS when estimating the pRF topography using the full stimulus instead of the masked stimulus. These erroneous estimates are not due simply to a methodological artifact, but are the result a significant BOLD spread that occurs inside the AS during the presentation of the truncated stimulus. It is important to understand the changes that occur in order to be able to separate them from true reorganization. We undertake this task below.

Materials and methods

Subjects

Five healthy subjects (S1-S5, 22–65 years old, 1 female) were recruited. All subjects had normal or corrected-to-normal visual acuity. The experiments were approved by the Ethical Committee of the Medical Faculty of the University of Tuebingen.

Data acquisition and preprocessing

Functional and structural MRI experiments were performed at the Max Planck Institute for Biological Cybernetics, Tuebingen, Germany using a 3.0 Tesla high-speed echo-planar imaging device (Trio, Siemens Ltd., Erlargen, Germany) with a quadrature head coil. At least two T1-weighted anatomical volumes were acquired for each subject with a three-dimensional magnetization prepared rapid acquisition gradient echo (T1 MPRAGE scan) and averaged following alignment to increase signal to noise ratio (matrix size = 256 × 256, voxel size = 1 × 1 × 1 mm^3, 176 partitions, flip angle = 9°, repetition time [TR] = 1900 ms, echo time [TE] = 2.26 ms, TI = 900 ms). Blood oxygen level dependent (BOLD) image volumes were acquired using gradient echo sequences of 28 contiguous 3 mm-thick slices covering the entire brain (repetition time [TR] = 2000 ms, echo time [TE] = 40 ms, matrix size = 64 × 64, voxel size = 3 × 3 × 3 mm^3, flip angle = 90°).

At least 5 functional scans were acquired for each subject, consisting of 195 image volumes, the first 3 of which were discarded. The functional images were corrected for motion in between and within scans (Nestares and Heeger, 2000). The functional images were aligned to the high-resolution anatomical volume using a mutual information method (Maes et al., 1997) where the resampled time series values in the volume are spatially interpolated relative to the nearest functional voxels. All subsequent analysis was performed in the interpolated data. However, we took care that this does not affect the retinotopic maps obtained and the statistical comparisons that are performed, because the interpolation method we used does not distort the generated time series and the comparisons we made were between different groups of subjects rather than between different numbers of voxels. Preprocessing steps were performed in MATLAB using the mrVista toolbox (http://white.stanford.edu/software/).

Stimuli

Full field stimulus

Subjects were presented with moving square-checkerboard bars (100% contrast) through MRI compatible digital goggles (VisuaStim, Resonance Technology Company, Inc., Northridge, CA, USA; 30° horizontal and 22.5° vertical field of view, 800×600 resolution, min luminance = 0.3 cd/m^2 and max luminance = 12.2 cd/m^2). The stimulus was presented within a circular aperture with a radius of 11.25° around the fixation point. The bar width was 1.875° and travelled sequentially in 8 different directions, moving by a step half of its size (0.9375°) every image volume acquisition (TR = 2 seconds). Stimuli were generated using Psychtoolbox (Brainard, 1997) and an open toolbox (VISTADISP) in MATLAB (The Mathworks, Inc.). The subjects' task was to fixate a small dot in the center of the screen (radius: 0.0375°; 2 pixels) and respond to the color change by pressing a button. The color was changing randomly with a frequency of one every 6.25 seconds. An infrared eye tracker was used to record eye movements inside the scanner (iView XTM, SensoMotoric Instruments GmbH) (Fig. S4). For two of the subjects (S4-S5) the eye movements under the full field stimulus presentation were not recorded due to technical problems. However, they performed a challenging detection task at fixation and their performance was always >95% correct.

AS-stimulus

Subjects were asked to participate for a second session during which an isoluminant mask was placed in the left superior quadrant of the visual field, simulating a left upper quadrantanopia ("artificial scotoma" or AS). All other stimulus' parameters stayed the same. Eye movements were recorded for all subjects under the AS stimulus presentation (Fig. S4B).

Population receptive field topography

We used a recent method developed by Lee and colleagues which estimates the population receptive field (pRF) topography in the visual cortex (Lee et al., 2013). The pRF structure p_i at voxel i is represented by a set of weights which predicts the BOLD signal $d_i(t)$ at voxel i and time t, using the stimulus protocol $s(t)$ and the hemodynamic response