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Functional mapping of the magnocellular and parvocellular subdivisions of human LGN

Rachel N. Denison [a,*], An T. Vu [c], Essa Yacoub [c], David A. Feinberg [a,d], Michael A. Silver [a,b,e]

[a] Helen Wills Neuroscience Institute, University of California, Berkeley, Berkeley, CA 94720, USA
[b] School of Optometry, University of California, Berkeley, Berkeley, CA 94720, USA
[c] Center for Magnetic Resonance Research, Department of Radiology, University of Minnesota Medical School, Minneapolis, MN 55455, USA
[d] Advanced MRI Technologies, Sebastopol, CA 95472, USA
[e] Vision Science Graduate Group, University of California, Berkeley, Berkeley, CA 94720, USA

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ABSTRACT

The magnocellular (M) and parvocellular (P) subdivisions of primate LGN are known to process complementary types of visual stimulus information, but a method for noninvasively defining these subdivisions in humans has proven elusive. As a result, the functional roles of these subdivisions in humans have not been investigated physiologically. To functionally map the M and P subdivisions of human LGN, we used high-resolution fMRI at high field (7 T and 3 T) together with a combination of spatial, temporal, luminance, and chromatic stimulus manipulations. We found that stimulus factors that differentially drive magnocellular and parvocellular neurons in primate LGN also elicit differential BOLD fMRI responses in human LGN and that these responses exhibit a spatial organization consistent with the known anatomical organization of the M and P subdivisions. In test–retest studies, the relative responses of individual voxels to M-type and P-type stimuli were reliable across scanning sessions on separate days and across sessions at different field strengths. The ability to functionally identify magnocellular and parvocellular regions of human LGN with fMRI opens possibilities for investigating the functions of these subdivisions in human visual perception, in patient populations with suspected abnormalities in one of these subdivisions, and in visual cortical processing streams arising from parallel thalamocortical pathways.

Introduction

Parallel processing, the simultaneous analysis of different sensory features in different brain areas, enables the efficient representation of a huge variety of sensory properties (Nassi and Callaway, 2009). An important early site of parallel processing in the mammalian visual system is the lateral geniculate nucleus (LGN) of the thalamus, the primary thalamic relay between the retina and visual cortex (Sherman and Guillery, 2006). In primates, the LGN is composed of magnocellular (M), parvocellular (P), and koniocellular (K) layers. Monkey electrophysiological studies have demonstrated that M and P neurons, which dominate primate vision (Nassi and Callaway, 2009; Schiller et al., 1990), have distinct and complementary spatial, temporal, luminance, and chromatic stimulus preferences (Derrington and Lennie, 1984; Hicks et al., 1983; Hubel and Livingstone, 1990; Kaplan and Shapley, 1982; Reid and Shapley, 2002; Schiller and Malpeli, 1978; Shapley, 1990) as well as response dynamics (Maunsell et al., 1999; Schiller and Malpeli, 1978). As a result, M neurons are well suited for the detection of motion and other rapid visual changes occurring at large spatial scales, while P neurons are well suited for detailed form and color processing.

Although the functions of the M and P subdivisions have been well characterized in the macaque monkey LGN, their study in the human LGN has proven challenging. In particular, the LGN's small size and location deep within the brain have made it difficult to measure distinct signals from the M and P subdivisions using noninvasive techniques. However, there are strong motivations to study these subdivisions in humans, including: understanding their roles in human visual perception, attention, and awareness (Denison and Silver, 2012; Livingstone and Hubel, 1988; Yeshurun and Levy, 2003); characterizing their interactions with large-scale cortical networks; and evaluating their involvement in human disorders such as dyslexia (Stein and Walsh, 1997) and schizophrenia (Butler and Javitt, 2005). Moreover, given the lack of functional data from human M and P subdivisions, the degree to which their functional properties have been conserved across humans and other primates remains an open question. While conservation is expected based on similarities in both visual system anatomy and visual perception between monkeys and humans (de Courten and Garey, 1982; De Valois et al., 1974a, 1974b; Livingstone and Hubel, 1987; Livingstone and Hubel, 1988; Merigan, 1989), perfect homology between the species cannot be assumed (Hickey and Guillery, 1979).

* Corresponding author at: Department of Psychology and Center for Neural Science, 6 Washington Place, New York, NY 10003, USA.
E-mail address: rachel.denison@nyu.edu (R.N. Denison).

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Here we report the first robust demonstration of functional maps of the M and P subdivisions of human LGN using fMRI at 7 T and 3 T, employing stimuli based on the response properties of monkey M and P neurons. Maps with anatomically correct spatial organization were observed in nearly all hemispheres, and individual subjects' maps were reliable across separate scanning sessions.

Material and methods

Subjects

Six adult subjects (25–27 years of age; 1 male, 5 females) participated in the study. Three subjects were scanned in multiple sessions, and two of the subjects were authors. All subjects provided written informed consent, and all experimental protocols were approved by the Committee for the Protection of Human Subjects at the University of California, Berkeley, or the Institutional Review Board for human subjects research at the University of Minnesota, as appropriate. Subjects had normal or corrected-to-normal visual acuity.

Visual display

The stimuli were generated on Macintosh computers using MATLAB (The MathWorks Inc., Natick, MA), Psychophysics Toolbox (Brainard, 1997; Pelli, 1997), and Python with Vision Egg (Straw, 2008) and displayed using gamma-corrected projection systems. In Minnesota, stimuli were projected from a NEC NP4000 (NEC Display Solutions, Tokyo) liquid crystal display projector located outside the scanner room and reflected via a mirror onto a translucent screen positioned over the subject's chest. The screen was viewed via a mirror mounted over the subject's eyes, with a total viewing distance of 23–31 cm. The screen height subtended 20–29° of visual angle, and the screen width subtended 47–70° of visual angle, with variability across subjects arising from differences in screen positioning. In Berkeley, stimuli were projected from an Avotec SV-6011 (Avotec, Inc., Stuart, FL) liquid crystal display projector onto a translucent screen located at the end of the scanner bore behind the subject's head. The screen was viewed via a mirror mounted over the subject's eyes, with a total viewing distance of 29 cm. The screen height subtended 34–37° of visual angle, and the screen width subtended 44–48° of visual angle.

Visual stimulus

An alternating hemifield stimulus (Fig. 1A) was used to localize the LGN (Fig. 1B). This stimulus consisted of a 100% contrast flickering checkerboard pattern that reversed contrast polarity at a frequency of 4 Hz (for the full flicker cycle). This checkerboard had a radial check pattern with a check size of 15° polar angle and an eccentricity that was scaled according to the formula, $s = 0.05 \times r^{0.8}$, where s is the check size and r is the distance from fixation in degrees of visual angle. The checkerboard pattern covered half of the screen except for the central 0.6° of visual angle, which contained background gray luminance (50% contrast, luminance 105 cd/m^2 (3 T) or 1019 cd/m^2 (7 T)). The other half of the screen also contained the gray background. A white fixation point subtending 0.2° of visual angle appeared at the center of the screen throughout the run, and subjects were instructed to maintain fixation while passively viewing the stimuli. For each run, the checkerboard pattern alternated between the left and right halves of the screen, 16 s (7 T) or 13.5 s (3 T) per side, and was presented for 8 (7 T) or 11 (3 T) left-right cycles.

An M/P localizer stimulus (Fig. 1C) was designed to elicit differential responses from voxels with greater M-layer representation and voxels with greater P-layer representation, based on findings from monkey electrophysiology (see Kleinschmidt et al., 1996; Liu et al., 2006 for related approaches). The M/P localizer consisted of 16-s (7 T) or 18-s (3 T) blocks of "M stimuli", "P stimuli", and blank (fixation point only) stimuli. The M and P stimuli were both full-field sinusoidal gratings

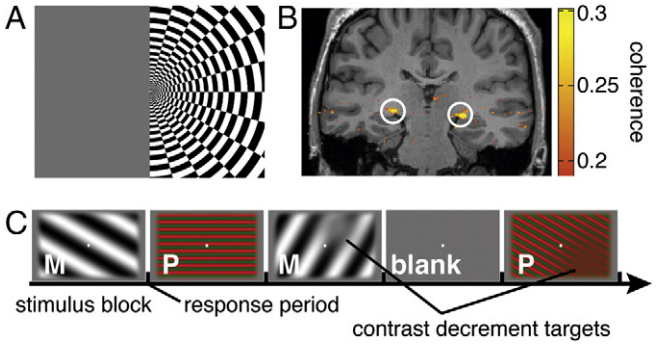

Fig. 1. LGN M/P localization methods. (A) A flickering checkerboard stimulus that alternated between the left and right visual hemifields was used to localize the LGN. (B) LGN definition was based on voxels that responded selectively to contralateral visual field stimulation. Coherence threshold = 0.19 in this example (see Material and methods section). LGN regions are indicated by white circles. (C) M-type (monochrome, low spatial frequency, high temporal frequency, high luminance contrast) and P-type (high color contrast, high spatial frequency, low temporal frequency, low luminance contrast) grating stimuli were designed to elicit differential BOLD responses from the M and P subdivisions of human LGN. Subjects maintained fixation at the center of the screen while viewing blocks of full-field M and P stimuli that were interleaved with blocks of blank stimuli. Concurrently, subjects performed a contrast decrement detection task during the M- and P-stimulus blocks, counting the number of luminance contrast (M blocks) or color contrast (P blocks) targets that appeared in each block.

with sinusoidal counterphase flicker. The outer borders of the stimulus faded into gray to avoid sharp visual edges at the stimulus boundaries. The gratings were presented at one of 6 orientations (0°, 30°, 60°, 90°, 120°, or 150°) and changed to a new random orientation every 3 s, in order to drive different populations of LGN neurons with different spatial receptive fields throughout the block.

The M stimulus was a 100% luminance contrast, black-white grating with a spatial frequency of 0.5 cpd and a flicker frequency of 15 Hz. The P stimulus was a low luminance contrast, high color contrast red–green grating with a spatial frequency of 2 cpd and a flicker frequency of 5 Hz. A spatial frequency of 2 cpd was selected for the P stimulus because contrast sensitivity for isoluminant stimuli is attenuated at high spatial frequencies (De Valois and De Valois, 2000). The blank stimulus was a gray screen of mean luminance.

The red and green levels of the P stimulus were set to be near-isoluminant by performing heterochromatic flicker photometry outside the scanner. Specifically, subjects adjusted the luminance of a green disk to match a red disk of maximum luminance on a neutral gray background by minimizing the perception of flicker as the two disks alternated at a frequency of 7.5 Hz. Two subjects (S2 and S3) performed flicker photometry, and the average value (39% of maximum green luminance) from these subjects was used for all scanning sessions.

Although we did not perform flicker photometry in the scanner for all subjects (due to time constraints as well as a concern about adapting subjects to the red and green stimuli before the M/P localizer scans), we verified that the green luminance value obtained outside the scanner was reasonable for both scanner displays by obtaining flicker photometry data from two subjects on the 7 T display (mean of 41% green) and one subject on the 3 T display (49% green). Since the values needed to achieve isoluminance vary across subjects and across the visual field, our main objective was to create a standard low luminance contrast stimulus that would preferentially activate the P subdivision of the LGN.

On each run, 15 blocks (6 M, 6 P, and 3 blank) were presented in pseudorandom order, with the constraint that the same stimulus type could not appear in adjacent blocks in order to minimize adaptation to the M or P stimuli. A white fixation point subtending 0.2° visual angle appeared at the center of the screen throughout the stimulus blocks, and subjects were instructed to maintain fixation throughout the run.

Subjects performed a target detection task during the M and P stimulus blocks to encourage them to attend to the visual stimuli throughout the run (Fig. 1C). Targets were 2-dimensional Gaussian contrast