learning were restricted to the CA1 field. The CA1 region has extensive cortical and subcortical connections that do not depend on indirect pathways through other hippocampal cell fields, and activation of CRE-dependent transcription in CA1 accompanies contextual conditioning[6], suggesting that this area may be important in associative contextual conditioning. Given that hippocampal *BDNF* expression accompanies learning and that hippocampal *BDNF* expression declines with age[15], decreased availability of *BDNF* may represent an important component of age-related memory impairments.

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An oblique effect in human primary visual cortex

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Visual perception critically depends on orientation-specific signals that arise early in visual processing. Humans show greater behavioral sensitivity to gratings with horizontal or vertical (0°/90°; 'cardinal') orientations than to other, 'oblique' orientations. Here we used functional magnetic resonance imaging (*f*MRI) to measure an asymmetry in the responses of human primary visual cortex (V1) to oriented stimuli. We found that neural responses in V1 were larger for cardinal stimuli than for oblique (45°/135°) stimuli. Thus the *f*MRI pattern in V1 closely resembled subjects' behavioral judgments; responses in V1 were greater for those orientations that yielded better perceptual performance.

Behavioral measurements reveal that the human visual system is more sensitive to horizontal and vertical stimuli than to stimuli at other orientations[1–3]. Evidence from single-neuron electrophysiology[4,5] and evoked-potential studies[6] sup-

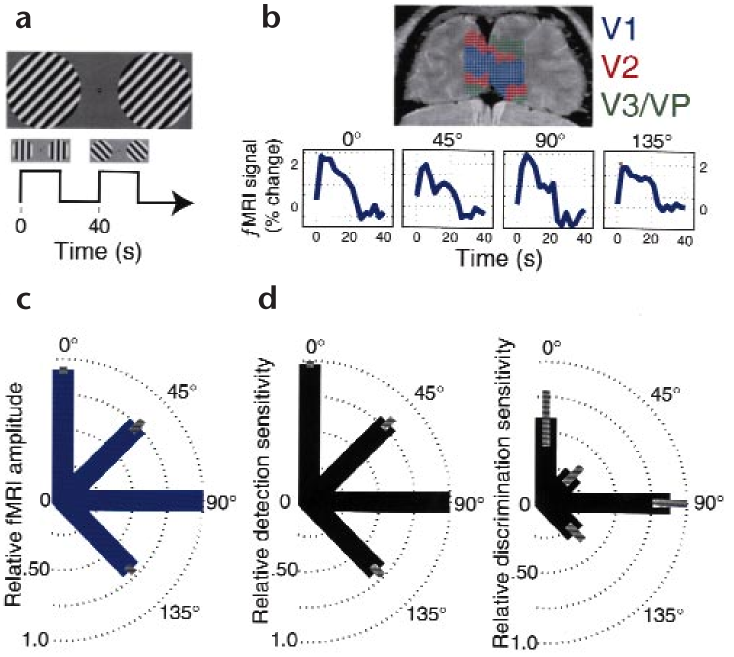

Fig. 1. *f*MRI and behavioral measurements of an oblique effect in human striate cortex. (**a**) Stimuli were suprathreshold (75% contrast) 3 cpd gratings displayed as 2 patches (3°, centered 4.5° from fixation). Gratings of the same orientation and random phase were presented in 20-s blocks at 1 image per s. (**b**) Blue, red and green pixels shown in an occipital slice (perpendicular to calcarine sulcus) represent visual areas (V1, V2 and V3) defined using *f*MRI retinotopic-mapping techniques[13–15]. Active pixels (3.125 × 3.125 × 5 mm) in each visual area were selected from a separate scan using radial checkerboard patches of the same spatial configuration as the stimulus. An oblique effect is evident in the raw *f*MRI time courses averaged across all subjects. (**c**) Bars represent mean *f*MRI response amplitudes in V1 plotted as a function of orientation (averaged across all three subjects). For each block, *f*MRI amplitudes were estimated as the sinusoid best fits to the data. Estimated amplitudes were then averaged by orientation across subjects. The mean peak response was 2.09%. Here average amplitudes are shown relative to the maximum response for each subject; however, all statistics were calculated from raw amplitudes. Cardinal amplitudes were reliably larger than oblique amplitudes ($F_{2,1} = 32.43$, $p < 0.05$; subject was a random factor). Similar results were obtained in a second experiment ($F_{3,1} = 33.99$, $p < 0.01$). This effect was robust, as 6 of 7 subjects showed a within-subject effect ($t_{22} > 2.012$, $p < 0.05$), and the seventh subject showed a strong trend ($p = 0.08$). Differences were not artifacts of the display device, as absolute cardinal orientations still produced the largest responses in V1 when the display was tilted 45°. In each plot, error bars depict s.e. (**d**) Bars represent normalized sensitivity as a function of orientation. Measurements were made for both contrast detection and orientation discrimination using the same stimulus configuration and subjects described above. Thresholds were determined by fitting a Weibull function to the data from a spatial two-alternative, forced-choice task using a staircase procedure, and were then converted to sensitivity scores (1/threshold).

ports an early cortical locus for this effect, but the neural basis underlying this perceptual asymmetry remains controversial[7–9]. Therefore, we asked whether the responsiveness of human visual cortex could account for differences in the perception of oriented stimuli.

We collected *f*MRI data (3 T BOLD, 8 slices, T*R* = 2.5 s) from 3 subjects who viewed parafoveal sinusoidal gratings at oblique (45°/135°) and cardinal (0°/90°) orientations (**Fig. 1a**). We also measured psychophysical thresholds for contrast detection and orientation discrimination for each subject using the same stimuli.

We found that *f*MRI responses in V1 were reliably greater for cardinally oriented gratings than for oblique gratings. Analysis of both the averaged *f*MRI time series (**Fig. 1b**) and the estimated response amplitudes (**Fig. 1c**) revealed a neural oblique effect in human V1. In contrast with V1, extrastriate visual areas analyzed (V2, V3, VP) did not show a reliable oblique effect. To confirm that the spatial arrangement of the stimuli did not amplify the oblique effect, a second *f*MRI experiment used gratings that were confined to a single annular region. The results from four subjects replicated our original findings; subjects showed a robust oblique effect only in V1.

The patterns of neural activity measured in V1 closely matched subjects' perceptual sensitivity (**Fig. 1d**). V1 response amplitudes were well correlated with both behavioral measures, although the correlation was greater for contrast detection ($r = 0.89$) than for orientation discrimination ($r = 0.71$). This suggests that contrast detection relies more heavily on the responses of V1 neurons than does orientation discrimination[10].

Our *f*MRI measurements were consistent with theories positing that the oblique effect results from asymmetries between populations of V1 neurons. Differences in either the neural activity (due to increased gain) or the relative number (due to increased density) of cardinal neurons could account for the oblique effect. Our findings are in agreement with single-neuron electrophysiology[4,5] and optical imaging studies[11] that find more V1 neurons tuned to cardinal orientations than to oblique orientations.

Outside of V1, we failed to find a reliable oblique effect. Because response amplitudes in extrastriate cortex tended to be much smaller than corresponding responses in V1, it is possible that the reduced amplitudes obscured small differences in *f*MRI responses for cardinal and oblique stimuli. However, it is also possible that a neural oblique effect is simply absent from regions outside of V1. The uniform responses we found in extrastriate visual areas were consistent with reports from single-neuron recordings in macaque V2 that find no reliable difference between the relative numbers of cardinal and oblique neurons[12].

Our results demonstrate that V1 produces a larger response to cardinal stimuli than to oblique stimuli. Further, the striking correlation we found between neural activity and behavior strongly suggests that this neural asymmetry in human V1 underlies the perceptual oblique effect. These measurements represent a new direction in human neuroimaging by demonstrating that distinct populations of neurons within a cortical area can be isolated and functionally linked to perception.

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