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Building surfaces from borders in Areas 17 and 18 of the cat

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Abstract

Several brightness illusions indicate that borders can dramatically affect the perception of adjoining surfaces. In the Craik–O'Brien–Cornsweet illusion, in particular, two equiluminant surfaces can appear different in brightness due to the contrast border between them. Although the psychophysical nature of this phenomenon has been well characterized, the neural circuitry underlying this effect is unexplored. Here, we have asked whether there are cells in visual cortex which respond to edge-induced illusory brightness percepts such as the Cornsweet. Using optical imaging and single unit recordings methods, we have studied responses of the primary (Area 17) and second (Area 18) visual cortical areas of the anesthetized cat to both real luminance change and Cornsweet brightness change. We find that there are indeed cells whose responses are modulated in phase with the modulation of the Cornsweet stimulus. These cells are present in both Area 17 and Area 18, but are more prevalent in Area 18. These responses are generally weak and are found even when receptive fields are distant from the contrast border. Consistent with perception, cells which respond to the Cornsweet border are modulated in antiphase to the Narrow Real (another border-induced illusory brightness stimulus). Remarkably, we also find evidence of edge-induced responses to illusory brightness change using intrinsic signal optical imaging. Both real luminance change and edge-induced brightness change produces a greater imaged response in Area 18 than in Area 17. Thus, in the absence of direct luminance stimulation, cells in visual cortex can respond to modulation of distant border contrasts. We suggest that the perception of surface brightness was encoded in the early visual cortical pathway by both surface luminance contrast signals in Area 17 (Rossi, A. F., Rittenhouse, C. D., & Paradiso, M. A. (1996). The representation of brightness in primary visual cortex. *Science*, *273*, 1104–7) and border-induced contrast signals that predominate in Area 18. © 2001 Published by Elsevier Science Ltd.

Keywords: Cornsweet; Optical imaging; Brightness illusion; Area 18; Cat

1. Introduction

The perception of form arises from a number of visual cues, among them the brightness (perceived luminance) properties of surfaces and how these surfaces are delimited by object boundaries. Most physiological studies have approached the neural representations of surface brightness and boundaries as separate issues (for review see Paradiso, 2000). However, a number of brightness illusions (e.g. Craik–O'Brien–Cornsweet, White's assimilation, Argyle brightness illusions) appear to depend on the pattern of contrast borders, indicating that edge information can have profound effects upon our perception of surface properties (Cornsweet, 1970; Kingdom & Moulden, 1988; Adelson, 1993). Recently, studies using simultaneous contrast stimuli (Rossi, Rittenhouse, & Paradiso, 1996; Rossi & Paradiso, 1999) established that a brightness response to luminance modulation of flanking regions can be observed in Area 17 of the cat. Although this demonstrated that brightness percepts due to surface luminance contrast can be implemented as early as primary visual cortex, it remained unclear whether borders also contribute to this brightness response.

Here, we have studied the neural processing of a border-induced brightness effect, the Craik–O'Brien–Cornsweet illusion. This illusion, also known as the Cornsweet illusion, has been well characterized in a number of psychophysical studies (Burr, 1987; Kingdom & Moulden, 1988; Wachtler & Wehrhahn, 1996; Purves, Shimpi, & Lotto, 1999). It is a stimulus in which two equiluminant surfaces appear to differ in

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brightness because of an intervening border contrast (Fig. 1, compare Cornsweet and Real). Unlike simultaneous contrast stimuli, the Cornsweet is a stimulus that induces a brightness percept purely by virtue of border contrast without accompanying surface luminance contrast. In comparison, in the Narrow Real stimulus (Fig. 1, bottom), the gradual change in luminance at the Cornsweet border is replaced by a stepped luminance contrast. This results in a border-induced brightness illusion which is reversed; that is, perceived surface contrast is opposite to that of the Cornsweet (cf. Kingdom & Moulden, 1988). Using the Cornsweet and Narrow Real stimuli, we sought to isolate the contributions of borders to brightness perception.

There are no studies of distant border-induced brightness response in the visual cortex. In this paper, we report the presence of single cells whose firing rates are modulated by border-induced brightness changes. We also report the presence of optically imaged responses to illusory brightness change. Both our imaging and single-unit recordings show that these border-induced responses are more prevalent in Area 18 than in Area 17.

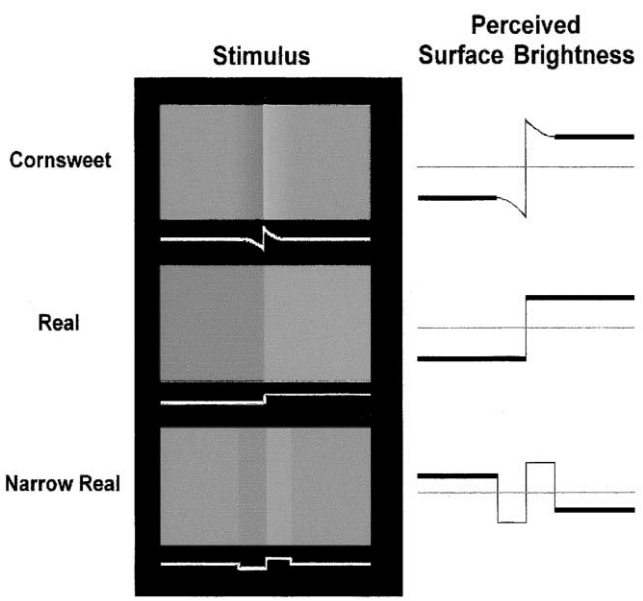

Fig. 1. Real and illusory brightness stimuli with their actual luminance profiles below. On the right, the perceived surface brightness contrast is depicted (bolded lines). Top: Cornsweet stimulus in which the two surfaces are equiluminant but appear similar to the real in brightness. Luminance profile below shows exponential decay of luminance near border. Middle: perceptually equivalent real luminance contrast stimulus in which the right surface is brighter (greater luminance) than the left surface. Bottom: in the Narrow Real stimulus, the two surfaces are also equiluminant but the luminance profile at the contrast border is stepped. This extinguishes the brightness contrast percept seen in the Cornsweet, and, in fact, produces an opposite contrast percept (depicted at right).

2. Materials and methods

2.1. Surgical preparation

Eight adult cats (2.6–3.5 kg) were studied in these experiments (eight hemispheres total). Animals were anesthetized with thiopental sodium (1–2 mg/kg/h i.v.), paralyzed with vercuronium bromide (100 μg/kg/h i.v.), and artificially ventilated according to a protocol approved by the Yale Animal Care and Use Committee. Anesthetic depth was assessed continuously via implanted wire EEG electrodes, end-tidal CO_2, oximetry and heart rate monitoring, and by regular testing for response to toe pinch. Eyes were dilated (atropine sulfate), refracted, and fitted with contact lenses of appropriate curvature (Danker Laboratories Inc, Sarasota, FL) to focus on a computer screen (Barco Calibrator PCD-321, Belgium; Number Nine video board). Proper focusing was determined by an opthalmoscope and confirmed by the physiological recording of cells with small receptive fields (less than 1 deg width in Area 17). Eyes were aligned by converging the receptive fields (RFs) of a binocular Area 17 cell with a Risley prism over one eye. Alignment was checked before and after each recording. Craniotomy and durotomy (centered around Horsley–Clark coordinates A-1, L 3) were performed to expose visual Areas 17 and 18.

2.2. Visual stimuli

Real and illusory brightness stimuli were created using a custom-made computer program and presented on a calibrated monitor. The monitor was tested with a photometer at the range of contrasts used in this study and shown to be linear; i.e. in this range a contrast increment is equivalent to the same contrast decrement. We also determined that modulating one part of the screen does not cause any luminance variation in other parts. All stimuli were presented binocularly. Although edge-induced brightness effects have been reported under both monocular and binocular conditions, the effect is more robust under binocular presentation (Paradiso & Hahn, 1996). Each stimulus was a rectangular field divided into two half fields of uniform brightness by a stationary linear contrast border. In the real luminance stimulus ('Real' condition, Fig. 2A, top), brightness contrast between the two halves was sinusoidally modulated in time (0.5 Hz, 16 frames per modulation cycle, sign reversing around a mean luminance of 32 Cd/m^2, i.e. contrast incremented and then decremented in 16 luminance steps). Increase in luminance of one surface was coupled with a decrease in luminance of the other. Thus, overall luminance remained constant throughout the modulation period. In the illusory brightness stimulus ('Cornsweet' condition, Fig. 2A, middle) only the immediate border contrast was modulated, but it pro-

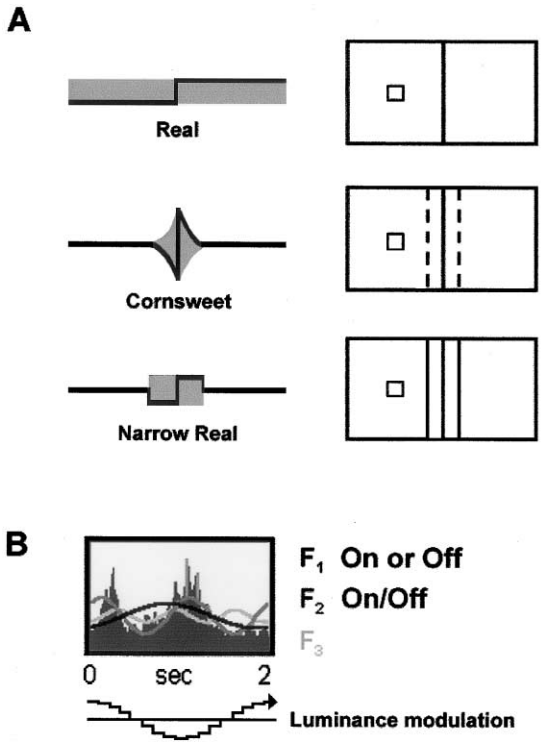

Fig. 2. Methods: (A) Stimulus. Left: luminance profiles of Real, Cornsweet, and Narrow Real stimuli used (same as shown in Fig. 1). In the experiment, each contrast border was sinusoidally modulated, giving appearance of uniformly increasing and decreasing surface brightness (see Section 2). Shaded areas indicate regions of luminance modulation; unshaded areas indicate regions without any luminance modulation. Right: schematic of Real, Cornsweet, and Narrow Real stimuli and extent of Cornsweet (dotted lines) and Narrow Real (solid lines) borders. Contrast borders were placed such that recorded receptive fields (small box) were positioned well away from contrast border, in regions without any actual luminance modulation. Actual stimuli as they appeared on the screen are shown in Fig. 1(B), calculation of modulation index. Sinusoids were fit to each PSTH at one (F1, black line), two (F2, dark gray line), and three (F3, light gray line) times the temporal frequency of the luminance modulation. The F1 and F2 components correspond to On- or Off- and On-and-Off responses, respectively. For each temporal frequency, we calculated a modulation index by determining the contrast ratio (range 0–1) of the fitted sinusoid. Below is shown the stepped (16 contrast steps) sinusoidal modulation of luminance around the mean (32 Cd/m^2).

duced a percept of distant surface brightness modulation very similar to that of the Real stimulus. The Cornsweet luminance profile decayed exponentially on either side of the border with a width (from peak to surface) of 1–2 deg of visual angle (see Cornsweet luminance profile in Fig. 2A, middle). The distance of half decay was one quarter the width of the modulated strip, i.e. 0.25–0.5 deg wide. As with the Real stimulus, the border contrast was modulated sinusoidally over time at 0.5 Hz (sign reversing around a mean luminance of 32 Cd/m^2, 16 frames per modulation cycle).

Real and Cornsweet stimuli were perceptually matched in brightness (Burr, 1987). That is, the peak-to-peak contrasts for Cornsweet stimuli (range 16–30%) were twice that of the paired Real luminance stimuli (range 8–15%). This level of Cornsweet contrast approaches the psychophysically measured peak of the effective contrast range (Burr 1987), and the constantly changing luminance at the border resulted in a strong illusion of changing surface brightness.

To differentiate neuronal response to a distant Cornsweet border from response to the presence of any distant luminance modulation, we devised a 'Narrow Real' stimulus condition (Fig. 2A, bottom). This stimulus has identical width, position, overall luminance, and temporal modulation characteristics as the Cornsweet stimulus (0.5 Hz, sign reversing around a mean luminance of 32 Cd/m^2, peak-to-peak contrast 8–15%, width 1–2 deg). However, in contrast to the Cornsweet stimulus, the luminance profile at the Narrow Real stimulus border is a 'step' rather than exponential decay (see Narrow Real luminance profile in Fig. 2A, bottom). This stimulus evokes an appearance of two narrow bands modulating in brightness; luminance increases in one band as it decreases in the other. The direction of the central border contrast of this stimulus is the same as that of the Cornsweet. However, the Narrow Real stimulus contains two additional borders of the opposite contrast. This results in an illusory surface brightness percept which is in antiphase to the Cornsweet brightness percept (see Fig. 1, cf. Kingdom & Moulden, 1988). This stimulus controls for the presence of distant luminance modulation by evoking single-unit responses in antiphase to that of the Cornsweet. However, we do not expect this difference to be detected in our optical images, since the optical map is obtained by summing over multiple contrast cycles. In addition to Narrow Real, we used a 'Blank' control condition that comprised an unmodulated isoluminant gray field of the same mean luminance (32 Cd/m^2) and size as the other stimuli. This stimulus provided a means to index background or 'spontaneous' cortical activity.

2.3. Optical imaging

In three cats, an optical chamber was adhered to the skull, filled with silicone oil, and sealed with a glass window. Images of reflectance change (intrinsic hemodynamic signals) corresponding to local cortical activity were acquired using an Imager 2000 (Optical Imaging Inc., Germantown, NY) with 630 nm illumination (for details see Grinvald et al., 1988; Bonhoeffer, Kim, Malonek, Shoham, & Grinvald, 1995; Ts'o, Frostig, Lieke, & Grinvald, 1990). Signal to noise ratio was enhanced by trial averaging (50–80 trials per stimulus condition) and by synchronization of acquisition with heart rate and respiration. Animals were positioned on a floating bench (Newport, Irvine, CA) to minimize motion artifacts.

Determination of the 17/18 border was based upon differences between these areas in spatio-temporal frequency response to sinusoidal horizontal and vertical gratings (Bonhoeffer et al., 1995; Shoham, Hubener, Schulze, Grinvald, & Bonhoeffer, 1997). High spatial frequency stimuli (0.58 cycles/deg, 4 deg/s) and low spatial frequency stimuli (0.14 cycles/deg, 14 deg/s) were used to preferentially activate Areas 17 and 18, respectively.

To further support the optically imaged location of the 17/18 border, we electrophysiologically mapped the imaged region. Changes in receptive field size and reversal of receptive field progression (the reflection across the vertical meridian) were used as further indications of the 17/18 border location (Tusa, Palmer, & Rosenquist, 1978; Tusa, Rosenquist, & Palmer, 1979). This optically and electrophysiologically determined border position was then used to guide electrode placement and to demarcate Area 17 and 18 regions in optical images obtained with Real and Cornsweet stimuli. The extent of visual field represented in the craniotomy was also determined by electrophysiological mapping. This information was used to determine the placement of the stimulus contrast borders in the optical imaging portion of experiments.

To examine visual response to real and illusory brightness stimuli, optical images were acquired during the presentation of Real, Cornsweet, Narrow Real, and Blank stimuli (50 trials for each stimulus, 3-seconds duration per stimulus, 10–15 seconds interstimulus interval). Stimuli were presented in random order. Between stimulus presentations, the Blank stimulus (32 Cd/m^2) was displayed. Contrast borders for all stimuli were placed at least 1 deg outside the area being imaged (as determined electrophysiologically). All borders were placed at identical locations and modulated in luminance at 0.5 Hz.

Acquired images were summed and compared. To compare across conditions, Real, Cornsweet, and Narrow Real images were referenced to Blank (Blank-subtracted). We also used reflectance values obtained from imaged skull areas as a reference for image comparison. The relative activations of Areas 17 and 18 were compared by examining their respective pixel distributions with respect to baseline reflectance distributions from skull areas. Imaged areas were subsequently targeted for electrophysiological characterization of single cell response to Real, Cornsweet, Narrow Real, and Blank stimuli.

2.4. Single-unit recording

Subsequent to imaging, the chamber window and silicone oil were removed and the exposed cortex was stabilized with agar. Glass-coated tungsten electrodes (Ainsworth, Northampton, UK) were inserted into superficial layers of Areas 17 and 18. Amplified raw spike activity was output from an audio speaker, and the electrode was advanced until modulation of spike firing could be heard in response to a dim full-field luminance modulation. Response characteristics and receptive fields of single units were determined using a hand-held projection lamp. For some units, a window discriminator (BAK Electronics Inc., USA) was used and spike occurrences were time-stamped at 0.1 ms temporal resolution using Hist (Rockefeller University, New York, NY). For most of the recordings a template-based spike sorting system (Spike2, Cambridge Electronic Design, Cambridge, UK) was used to sample spike activity at 0.02 ms temporal resolution. Because the Cornsweet illusion is perceptually comparable to Real stimuli only for weak contrasts (Burr, 1987), we attempted to isolate units sensitive to low contrasts. We estimate that less than 20% of the cells we encountered were responsive to our full-field luminance stimulation.

Classical receptive fields (CRF) were defined as minimum response fields whose borders were determined by flashing a small patch of light (about 1 deg^2) of approximately the same luminance (32 Cd/m^2) as the test stimuli against a dark background. We mapped the edges of the CRF by moving the patch towards the CRF and determining the position of increased response to the nearer edge of the light patch. For cells with orientation preference we used a small bar of light of the preferred orientation and of optimal length to map the CRF. When the two mapping methods resulted in different receptive field sizes, we always erred on the conservative side and used the larger measured CRF. We then recorded spike activity from these cells in response to Real, Cornsweet, Narrow Real and Blank stimulus conditions. The luminance profiles of these stimuli were identical to those presented during optical imaging. The stimulus was placed such that one surface was centered on the CRF of the isolated unit (see Fig. 2A, diagrams at right). The size of the stimulus was cropped using a non-reflective black paper mask so that the edges of the surface extended several receptive field widths away from the edge of the CRF and the stimulus contrast border bisected the masked region (see Fig. 2A, diagrams at right). During electrophysiological sampling, the Blank stimulus condition comprised an even gray (32 Cd/m^2) luminance level and was used to measure spontaneous activity levels. Due to the low firing rate of recorded cells, spike collection often required an extended period of time and we sometimes lost cells before we could complete the presentation of all stimulus conditions. As a result, the Narrow Real and Blank stimulus conditions were not tested for all cells.

2.5. Data analysis of spike responses

For each stimulus, spike responses were collected for a period of 10 minutes and peri-stimulus time histograms (PSTH) were generated (192 bins, 11 ms bin width). Since the stimulus was modulated at 0.5 Hz, spikes were collected for approximately 300 stimulus modulation cycles per PSTH. Because many PSTH profiles appeared to modulate in response to sinusoidal stimulus changes, we devised a modulation index (MI) to measure the depth of firing rate modulation. For each PSTH, we fitted sinusoids using least squares method at one, two, and three times the temporal frequency of the stimulus (F1, F2, F3, see Fig. 2B). Stimulus-evoked responses had maximal amplitude modulation at one of these frequency components. Transient peaks sometimes occurred in PSTHs in response to steps in luminance change (for example, see Fig. 6A,E,F). Because these transient responses were not so well fitted by sinusoids, we also devised an alternative method of sinusoidal fitting to these transient peaks, using a sliding 'comb-like' filter (in which only every 12th bin is included for the sinusoidal fitting). Modulation indices using this filter were typically 30% larger for the responses exhibiting transient peaks. However, cells that showed strong modulation based on comb filter also tended to show strong modulation using regular sinusoidal fit. Consequently, results of analyses using this method did not differ from that using the full PSTH (not shown). For the data shown in this paper, we have fitted sinusoids to the full PSTH rather than to the comb-filtered PSTHs, as the comb-filtering discards 11 of every 12 PSTH bins, reducing the precision of measurements.

For each of the F1, F2, and F3 frequency components, we calculated an MI from the contrast ratio of response, defined as $(\max - \min)/(\max + \min)$ of the fitted sinusoid. Thus, a modulation index of zero indicates a flat PSTH, whereas an MI of 1.0 indicates full modulation. Because the sinusoid is fitted by least squares method to the PSTH, it is possible, although extremely infrequent, for the min of the fitted sinusoid to be negative, resulting in a MI greater than 1.0. This method of calculating MI's inherently produces a bias towards larger MI's in spike trains with few spikes (e.g. < 800). To correct for this bias, we derived a one-to-one mapping function that allowed reliable comparison of MI's from spike trains of different length (Hung, Ramsden, & Roe, 2001). Cells were classified as either an 'F1 cell', 'F2 cell', or 'F3 cell' based upon the frequency component with the maximum contrast ratio during the Cornsweet stimulus. Perceptually, the F1 and F2 components correspond to the On- or Off- and the On-and-Off responses, respectively. Since the F1 component corresponds to the temporal period of the stimulus modulation, this component of the response is most closely associated with the perceived brightness of the stimulus. For each cell, the modulation index was also calculated for spontaneous activity (recorded during 'Blank' stimulus presentation) to determine the basal level of modulation in the absence of stimulus modulation.

To determine the confidence level of measured response contrast ratios, we used the following randomization method. We generated 100 artificial spike trains from each spike train, by randomizing the arrival order of the interspike intervals (ISIs) for each spike train (thus preserving the overall spike train length and ISI distribution). The modulation indices of the artificial spike trains were ranked and compared against the experimentally recorded modulation index to arrive at a confidence level.

3. Results

3.1. Determination of visual field map and 17/18 border

To determine the position of the 17/18 border, we optically imaged intrinsic cortical signals in three cats in response to different gratings of varying spatial and temporal frequencies. Fig. 3 illustrates a 7.5 mm $\times$ 3 mm area overlying Areas 17 and 18 in the right hemisphere of one cat. An orientation map obtained in response to presentation of high spatial frequency gratings is shown in Fig. 3A and that to low spatial frequencies in Fig. 3B. Although the high spatial frequency grating activated the entire imaged area, the orientation maps were stronger in posterior and medial portions of the image. In contrast, the low spatial frequency gratings produced greater activation in anterolateral portions of the imaged area (bottom right corner of Fig. 3B) and poorly defined orientation maps elsewhere. Consistent with previous reports (Bonhoeffer et al., 1995), the location of the 17/18 border is readily mapped by subtraction of these low spatial (sum of horizontal and vertical conditions) and high spatial (sum of horizontal and vertical conditions) frequency response conditions (Fig. 3C). The 17/18 border suggested by this subtraction is shown by the dashed line in the corresponding blood vessel map (Fig. 3D). Note that, in this case, since we only used horizontal and vertical grating stimuli, the full orientation map may extend slightly beyond the dotted line (in the posteromedial direction) in some locations. Because the imaged signal is poorer near regions of high cortical curvature, we have excluded pixels in the anterolateral corner of these images (determined by thresholding the blood vessel map) and have assigned them an average gray value. The remaining portions of the images are thus obtained from reasonably flat portions of the cortex

and, as evidenced by the orientation maps obtained, are not contaminated by artifact due to cortical curvature.

To corroborate this border location electrophysiologically, we mapped the imaged area with multiple electrode penetrations (indicated by dots in Fig. 3D). Fig. 3E and F illustrate the receptive fields recorded at the cortical locations shown in Fig. 3D; these receptive fields extend from 0 to 5 deg azimuth and −1 to −8 deg elevation. Consistent with the reported visual map in cat Areas 17 and 18 (Tusa et al., 1978; Tusa et al., 1979), the penetrations map with a descending azimuthal progression from posterior to anterior (e.g. penetrations 1–5). These recordings were made in the right hemisphere, and therefore the vertical meridian is to the right of the RFs. As penetrations crossed from Area 17 to Area 18, we observed significant increases in receptive field size and reversals in receptive field progression (e.g. penetrations 4–7 and 8–11). Thus, the electrophysiological data support the location of the 17/18 border suggested by our imaging. We also examined coronally cut cytochrome oxidase and Nissl stained sections (not shown) which exhibited the characteristic change in layer IV thickness at the 17/18 transition zone (Otsuka & Hassler, 1962; Law, Zahs, & Stryker, 1988). The locations of these transition zones are consistent with and support the imaged 17/18 border location. These same imaging and electrophysiological procedures were used to determine the 17/18 border location in two other cats.

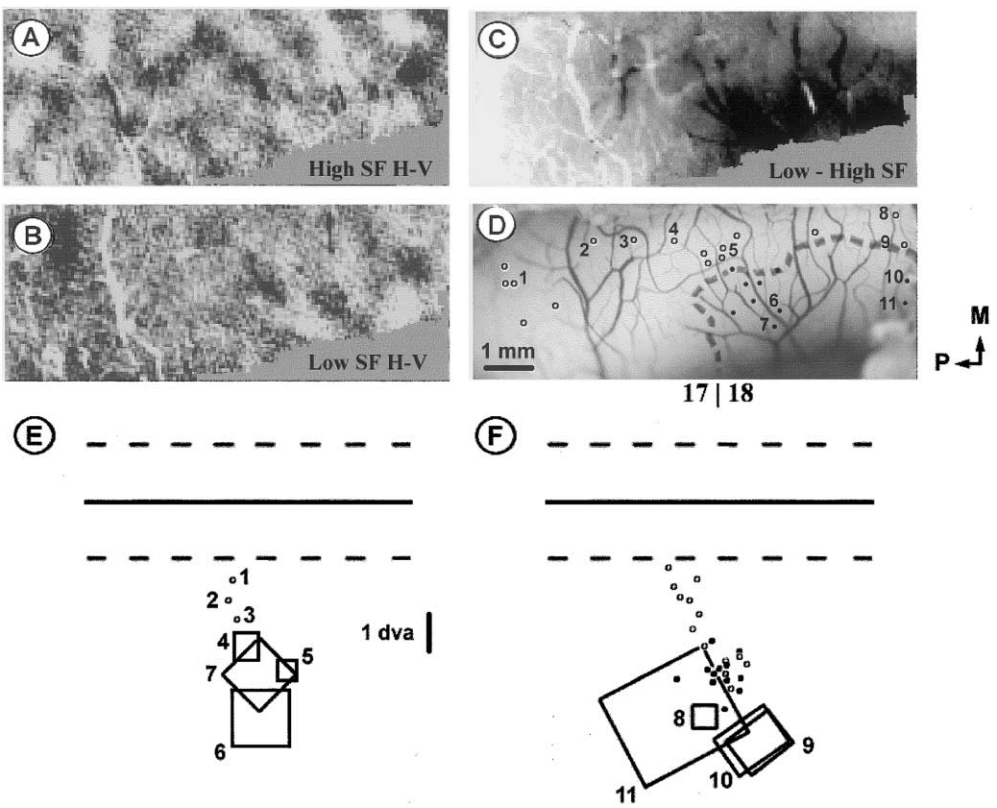

Fig. 3. Mapping the 17/18 border. (A) Orientation map in Areas 17 and 18 obtained in response to high spatial frequency gratings (0.58 cpd drifted at 4 deg/s, sum of 60 trials, right hemisphere). Subtraction of horizontal and vertical grating responses. Dark pixels indicate preferential response to horizontal orientation, lighter pixels indicate preference for vertical orientation. The lower-right corner of each image is masked due to surface curvature and dura artifact in that region (see D). Posterior to left, medial to top for (A–D). Scale ±0.2% change in reflectance; 0% indicated by gray level of mask at lower-right corners. (B) Orientation map in Areas 17 and 18 obtained in response to low spatial frequency gratings (0.14 cpd drifted at 14 deg/s). Subtraction of horizontal and vertical grating responses. Greater responsiveness is seen in Area 18 (lower right region). (C) Low vs. high spatial frequency map. Subtraction of the sum of horizontal and vertical responses in A from the sum of horizontal and vertical responses in B. Dark pixels indicate a preference for low spatial frequency; light pixels indicate a preference for high spatial frequency. This subtraction provides the approximate location of the 17/18 border. (D) Blood vessel map showing electrode penetrations in Areas 17 (○) and 18 (●). Dashed line indicates 17/18 border defined as 75% threshold (of full range) of image shown in C. We have used this as an estimate of the 17/18 border location. (E and F) Electrophysiological mapping of visual field representation within imaged area. The position of the contrast border in the Real condition is indicated by horizontal solid line at top. The center of the Cornsweet contrast border is indicated by the solid line, and the extent of the exponential decay (1.5 deg) by the dashed line. Thus, during Cornsweet stimulation (see Figure 4), almost the entire imaged region is away from the Cornsweet border (only the region near Penetration 1 may experience some stimulation by the edge of the Cornsweet). As recordings were made in the right hemisphere, the vertical meridian is to the right of the receptive fields. Consistent with the location of the 17/18 border, Penetrations 4–7 and 8–11 undergo a reversal of receptive field progression at the vertical meridian as well as an increase in receptive field size. These penetrations help to confirm the location of the 17/18 border suggested by optical imaging and to determine the appropriate placement of the Cornsweet border. Vertical scale bar: 1 dva (degree visual angle).

This method provides a reasonable approximation of the 17/18 border location. It is sufficient for the purposes of placing the real/illusory contrast border position (see below) and sufficient for placing our electrode penetrations confidently either in Area 17 or in Area 18, away from the 17/18 border. Furthermore, it is unlikely given the known stimulus preferences and topography of Areas 17, 18, and 19, that this could be the Area 18/19 border. In cats ($n = 5$) in which we did not determine the 17/18 border location by imaging, we recorded in posteromedial-to-anterolateral sequences of penetrations until a reversal in receptive field position and change in receptive field size was observed. In these cases, cells were subsequently sampled well away ($>$ 500 μm) from this estimated border region.

3.2. Real and illusory brightness imaging reveals greater activation in Area 18 than Area 17

Psychophysically, the Cornsweet stimulus produces a salient percept of surface brightness contrast, one which appears similar to that of a real surface contrast of roughly half the peak-to-peak Cornsweet border contrast (see Fig. 1, cf. Burr, 1987). Our preliminary electrophysiological investigations had indicated that some cells in cat visual cortex do respond as if they 'perceive' the illusory brightness change induced by Cornsweet border modulation (Hung, Ramsden, & Roe, 1998). Since Area 18 has been implicated in the processing of higher order stimuli such as illusory contours (Sheth, Sharma, Rao, & Sur, 1996; Leventhal, Wang, Schmolesky, & Zhou, 1998; Mareschal & Baker, 1998), we wanted to know whether we could detect any areal differences in response to real and illusory brightness by optical imaging methods.

To address this question, we imaged cortical responses to perceptually matched Real and Cornsweet brightness stimuli (Burr, 1987) presented on a computer monitor (see Figs. 1 and 2, Section 2). In the 'Real' stimulus, an increase in luminance of one surface was coupled with a decrease in luminance of the other. In the 'Cornsweet' stimulus, only the local border contrast was modulated, but it produced a percept of distant surface brightness modulation very similar to that of the Real stimulus (Kingdom & Moulden, 1988).

To ensure that imaged responses were not in direct response to border contrast, the contrast border was placed outside the visual field represented in the imaged region (as determined by receptive field mapping at the edges of the imaged region, see Fig. 3D–F). Thus, during Real brightness modulation, the visual field represented within the imaged region (both Areas 17 and 18) was stimulated directly by luminance modulation. During Cornsweet stimulation, no portion of the imaged region 'saw' true luminance change. We therefore reasoned that any activation in the imaged area in response to the Cornsweet stimulus would reflect an illusory (i.e. higher order) perceptual brightness response.

For comparison, we used Blank and Narrow Real stimulus conditions. Blank conditions were images collected during presentation of an even gray screen (stimulus condition without modulation or contrast border, see Methods). Images collected during blank screen presentation represent basal levels of cortical reflectance. The Narrow Real stimulus condition is another edge-induced illusory brightness stimulus (see Fig. 1 bottom, 2A bottom). This Narrow Real stimulus shares the same direction of border luminance contrast as the Cornsweet, but produces an illusory surface brightness percept which is opposite in sign to that of the Cornsweet (cf. Kingdom & Moulden, 1988). Since the optical signal to each stimulus is summed over multiple bright-to-dark and dark-to-bright phases, this difference in sign would not be detectable by optical imaging. As such, we predicted that the Narrow Real and Cornsweet stimuli would produce similar imaging response. The difference in sign would only be detectable by physiological methods (see below). Real, Cornsweet, Narrow Real, and Blank stimuli were randomly interleaved during image collection.

To increase our confidence in comparison across imaged conditions, we also measured variance in bone reflectance signals (measured from nearby skull in the same field of view). This served not only to estimate non-biological noise contributions to our functional maps (e.g. shot noise related to camera sensor), but also provided a reliable, non-fluctuating baseline from which to compare multiple maps. Absolute reflectance values were determined for imaged regions. All pixel values in Areas 17 and 18 were then expressed as percentage change from the Blank condition. These typically produced pixel values ranging from 0 to 0.5% reflectance change.

The blank-subtracted images obtained following Real, Cornsweet, and Narrow Real stimulation are shown in Fig. 4 (images are scaled at $\pm 0.2\%$ reflectance change). At the right of each image is shown its distribution of gray-scale pixel values for the skull, Area 17 and Area 18. The upper value of skull reflectance distribution is indicated by the left dashed line; median value of Area 18 reflectance distribution for Real stimulation is indicated by the right dashed line and downward arrow at top. The location of the 17/18 border, as revealed by imaging spatiotemporal frequency response, is indicated by the dashed line in Fig. 4E. Imaged response to the Real stimulus is shown in Fig. 4A. Activation (dark pixels) in Area 18 is greater than that in Area 17 during Real luminance modulation (99% of Area 18 pixels were above the upper limit of the skull distribution (Fig. 4A, right, dark gray shading), versus 44% of Area 17 pixels (Fig. 4A, right, light

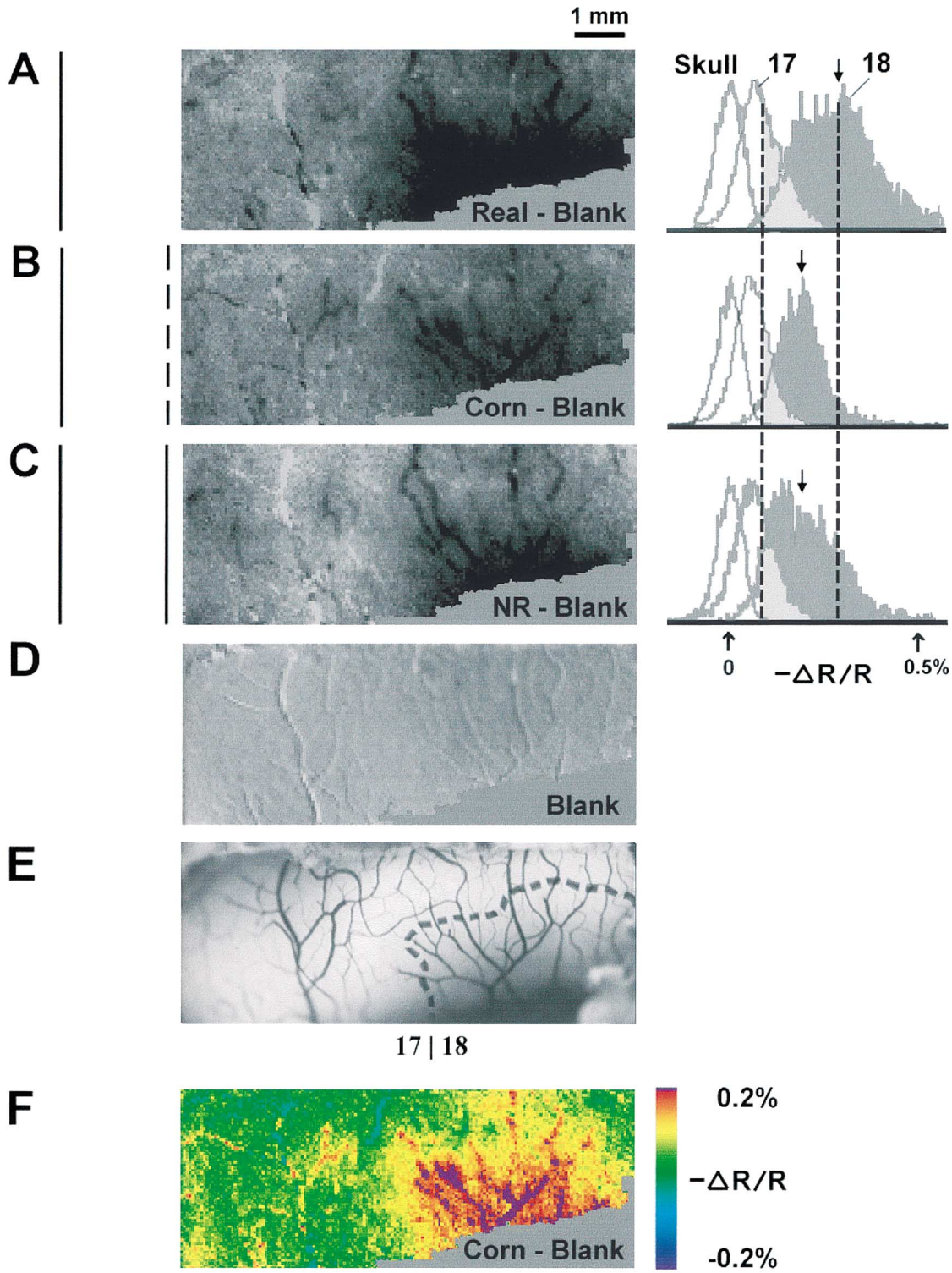

Fig. 4. Imaging Real and Illusory brightness response in Areas 17 and 18 (sum of 50 trials). Same case as shown in Fig. 3. Posterior to left, medial to top for (A–F). (A–C) Imaged responses to the Real, Cornsweet, and Narrow Real (NR) stimulation, respectively. Each condition is compared to the same Blank image shown in D. Horizontal contrast borders are at same locations as shown in Fig. 3E and F; their approximate positions relative to the imaged region are shown by solid and dotted lines at left of each image. Direct stimulation from the border should correspond to a region just beyond the left (posterior) end of the craniotomy. Negative changes in reflectance (dark areas) indicate more activation and positive changes in reflectance (light areas) indicate less activation. Images A–D scaled at $\pm 0.2\%$ change in reflectance. Zero change in reflectance (average gray) corresponds to no activation and is indicated by masked area in bottom right corner of each image. To right of each image are pixel distributions of Area 17, Area 18 (17/18 border shown by dotted line in (E)), and imaged skull (region not shown in image). Vertical dotted lines are provided for comparison of distributions. Left dotted line is upper limit of skull values. Right dotted line is median of Area 18 distribution obtained in response to Real condition. (D) Single condition image in response to Blank. (E) Blood vessel map with 17/18 border indicated (dotted line, from Fig. 3D). (F) Color-coded map of Cornsweet image shown in B.

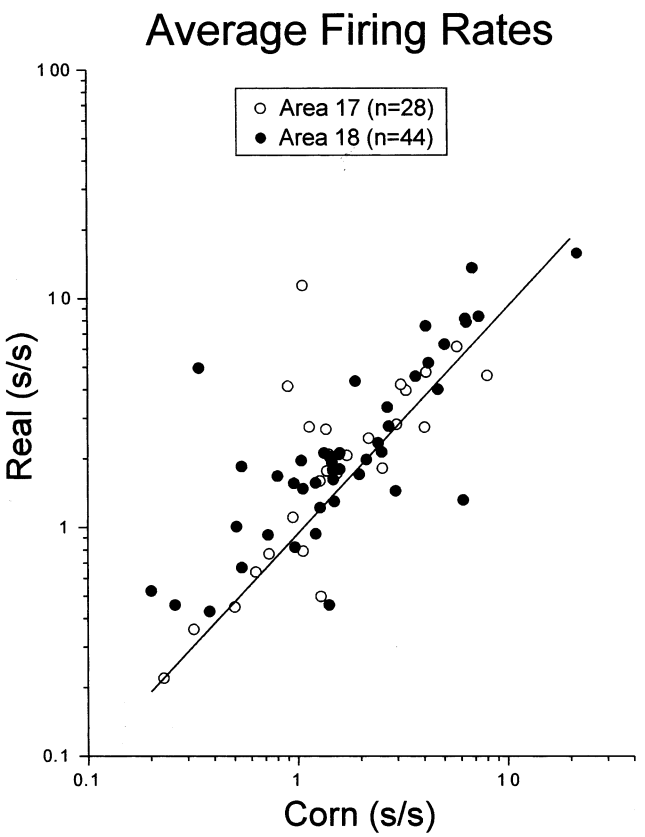

Fig. 5. Average firing rates during Cornsweet vs. Real stimulation for Area 17 cells (○, $n = 28$) and Area 18 cells (●, $n = 44$). Area 17 firing rates were not significantly different from Area 18 firing rates (for Real and for Cornsweet stimuli). Thus, the difference in imaged signal between Areas 17 and 18 is not due to average firing rate.

gray shading; median reflectance change 0.28%). Imaged response to the Cornsweet stimulus is shown in Fig. 4B. With Cornsweet stimulation, we also found greater activation in Area 18 than in Area 17 (99% of Area 18 pixels were above the upper limit of the skull distribution, versus 25% of Area 17 pixels; median reflectance change in Area 18: 0.18%, indicated by arrow above distribution). Although this Cornsweet activation was weaker than that found in the Real condition, it clearly exceeded the background level. Note that this significant level of activation occurred in the absence of direct luminance modulation of visual fields represented by imaged regions (Cornsweet border is at least 1 deg from imaged Area 18 and is outside the imaged region shown; see solid and dashed lines to the left of images in Fig. 4A–C and black dots in Fig. 3F). In Fig. 4C, we show imaged response to the Narrow Real stimulus. The Narrow Real stimulus produced a distribution of gray values in Areas 17 and 18 similar to that of the Cornsweet, as expected (94% of pixels above skull levels in Area 18: 30% of pixels above skull levels in Area 17; median reflectance change in Area 18: 0.19%, indicated by arrow above distribution). Thus all three brightness stimuli produced stronger imaged responses in Area 18 than Area 17.

For the same reasons stated for imaging the 17/18 border, it is unlikely that the imaged signals are due to cortical curvature as pixels overlying regions of curvature have been eliminated from consideration (gray masked area in lower right corners of images); moreover, our conclusions are not dependent upon precise thresholding of this region. In addition, the striking similarity between the regions preferentially responsive to low spatial frequency stimuli (Fig. 3C) and to Real, Cornsweet, and Narrow Real stimuli (but not to the Blank stimulus) suggests that these results are not artifactual. Furthermore, we also found similar preferential activation of Area 18 in response to Real, Cornsweet, and Narrow Real stimuli in two other cats that we imaged (not shown).

We considered the possibility that the differences observed between Area 17 and 18 activations were due to areal differences in basal firing rates or to areal differences in general responsiveness (e.g. via differential myelin content, via differential afferent innervation densities). We compared responses to Blank condition (single condition map, Fig. 4D) in Areas 17 and 18. Area 17/18 differences were not found in the Blank condition image (sum of 50 trials, Fig. 4D), illustrating that these differences did not result from subtracting a Blank that was itself not uniform. Blanks derived from individual blocks revealed similarly even blank maps (not shown). Furthermore, when we sampled electrophysiologically from these areas, we found no difference in the mean spontaneous firing rates of Area 17 and Area 18 cells (see Fig. 5). Neither did Area 18 necessarily show greater activation under all stimulation conditions tested (e.g. moving sinusoidal high spatial frequency gratings produced less activation in Area 18 than Area 17 as shown in Fig. 3A).

Since the Cornsweet brightness percept is induced distant from the contrast border, we wanted to know whether the imaged signal would decline or remain constant with increasing distance from the contrast border. We examined the signal magnitude across the imaged region of Area 17 and Area 18, a cortical area spanning several degrees of visual space (see Fig. 3D–F). These color-coded intensity values are shown in Fig. 4F. The presence of some activation (yellow pixels) at the far left edge of the image in Area 17 may indicate some direct influence of the border edge (cf. Fig. 3D–F). [Note that pixel values overlying blood vessels appear relatively saturated (e.g. purple pixels in Area 18).] However, throughout the remaining portions of Area 17, there is no obvious drop-off in imaged signal with cortical distance from the border. Neither is there any apparent decrease across the imaged region in Area 18 (mostly red pixels). Indeed, the imaged signal is reasonably constant across the imaged extents of both Areas 17 and 18. Furthermore, as shown below (Fig. 9),

neither did physiological responses decline with distance from the Cornsweet border. Thus, the relative constancy of both imaging and physiological response across (at least several degrees of) visual space are consistent with the encoding of a relatively uniform surface brightness percept.

Our imaging data demonstrate a border-induced brightness response obtained in the absence of direct luminance modulation. Similar to true luminance modulated response (Real), this illusory brightness response is greater in Area 18 than Area 17. This activation in Area 18 is not associated with areal differences in basal activation levels.

3.3. Single-unit recordings

To further explore the areal activation revealed by imaging, we recorded electrophysiologically from single units in imaged regions. We targeted recording locations within either Area 17 or Area 18 based on differential spatiotemporal response maps and by receptive field mapping. We studied single unit responses to the same Real, Cornsweet, Narrow Real, and Blank stimuli that were used for imaging. In keeping with imaging methodology, to ensure that recorded responses were not in direct response to border contrast, the contrast border was placed at least 1 deg of visual angle (typically 4–10 deg) away from the nearest edge of the classical receptive field (CRF). The edges of the CRF were determined by careful mapping (see Methods), and the focus and convergence of the eyes were checked frequently throughout each recording session. Although it is known that the size of receptive fields can increase with lower grating contrasts (e.g. Sceniak, Ringach, Hawken, & Shapley, 1999), most of the cells in our population were sufficiently distant from the Cornsweet border that direct luminance modulation of the receptive field was unlikely (see Fig. 9 below). Where there was doubt about the edge of the CRF, the CRF delineation was enlarged to encompass the questionable response.

To control for the possibility that responses merely reflect the noisiness of the data, as well as to ensure that responses were specific to the sign of the edge contrast, we used Blank (spontaneous) and Narrow Real stimulus conditions. Responses collected during blank screen presentation represent spontaneous levels of cortical activity. We hypothesized that the Narrow Real stimulus would produce an antiphase response in comparison to the Cornsweet.

Not all cells responded to these stimuli. Of the cells encountered, we estimate less than one in five responded to full field modulation of luminance. This need not be surprising given the well-described inhibitory subfields of many visual cortical cells and the low contrast of the stimuli (cf. DeYoe & Bartlett, 1980). Of those that responded to Real luminance modulation, even fewer responded to Cornsweet modulation. In our sampling procedure, we tested cells for response to Cornsweet only if they exhibited audible response to full-field luminance modulation. Thus, our sample does not include any cells that may have responded exclusively to Cornsweet.

We recorded responses to Real, Cornsweet, and Blank stimuli from a total of 28 cells in Area 17 and 44 cells in Area 18. Due to the low rates of response and subsequent extended periods of spike collection, we were not always able to hold each cell for all four conditions. Thus, responses to the Blank and Narrow Real stimuli were collected only for a subset of cells (Blank: Area 17, $n = 21$; Area 18, $n = 25$; Narrow Real: Area 17, $n = 12$; Area 18, $n = 28$). To investigate what aspects of single unit responses may correlate with perceived brightness, we examined three response characteristics: average firing rate, modulation response strength, and phase of response.

3.3.1. Differential 17/18 response is not predicted by average firing rate

We then examined whether the observed difference in imaged signal between Areas 17 and 18 is predicted by differences in firing rate. We found no significant difference between the average firing rates of Area 17 cells (Fig. 5, white dots, $n = 28$) and Area 18 cells (Fig. 5, black dots, $n = 44$). This was true for responses to both Real stimuli (Area 17: mean 2.59 spikes/s, range 0.22 to 11.39; Area 18: mean 3.19 spikes/s, range 0.43 to 15.78; Mann–Whitney U Test, $P = 0.8$) and Cornsweet stimuli (Area 17: mean 2.02 spikes/s, range 0.23–8.03; Area 18: mean 2.75 spikes/s, range 0.20–21.58; Mann–Whitney U Test, $P = 0.5$). Thus, differences in the imaged 17/18 responses were not paralleled by differences in mean firing rates of recorded Area 17 and 18 cells.

3.3.2. Cells show firing rate modulation to Cornsweet and Real stimulation

Another possible source of the differential imaging responses is the degree to which firing rate was modulated by changing stimulus brightness. To quantify this aspect, we fitted response histograms with sinusoids at one, two, and three times the temporal frequency of the stimulus (F1, F2, and F3 components). We reasoned that, although responses might be likely to modulate at the fundamental temporal frequency of the stimulus (F1), it was possible that other harmonics of this temporal frequency (F2, F3) could be relevant. The F1 modulation indices for Areas 17 and 18 ranged from 0.01 to 1.07 (Real: Area 17, mean 0.28, range 0.06–0.71; Area 18, mean 0.27, range 0.02–1.07; Cornsweet: Area 17, mean 0.07, range 0.01–0.20; Area 18, mean 0.07, range 0.01–0.38). Spontaneous modulation indices for F1 temporal frequency ranged from 0.01 to

0.15 in these areas (Area 17, mean 0.06, median 0.06, range 0.01–0.15; Area 18, mean 0.04, median 0.04, range 0.01–0.07).

Fig. 6 illustrates examples of electrophysiological responses recorded in Areas 17 (Fig. 6A,B) and 18 (Fig. 6C–F). We sometimes observed slow changes in cell firing rates that cycled in a similar manner to stimulus brightness (e.g. Fig. 6C). In many cases, responses to stimuli exhibited transient peaks that occurred in phase with the small increments or decrements in stimulus luminance (e.g. Fig. 6A). For responses with such strong transients (almost all in response to Real luminance modulation), the modulation index underestimates its response (i.e. the 'comb' index is larger, see Methods). These transient peaks were more common in responses to Real luminance modulation in Area 18 (roughly 10% of the cells in Area 17, 50% of the cells in Area 18), but were rare in the weaker Cornsweet and Narrow Real responses.

Of the cells in Area 17 that were well modulated by the Real luminance contrast stimulus, most were poorly modulated by the matching Cornsweet stimulus. Fig. 6A illustrates a typical Area 17 cell response (recorded in penetration 5 in Fig. 3). This cell exhibited a robust modulatory response (top PSTH, MI = 0.59) with strong transients associated with each of the 16 luminance steps of the Real stimulus condition. No modulation of response was found to an identically positioned

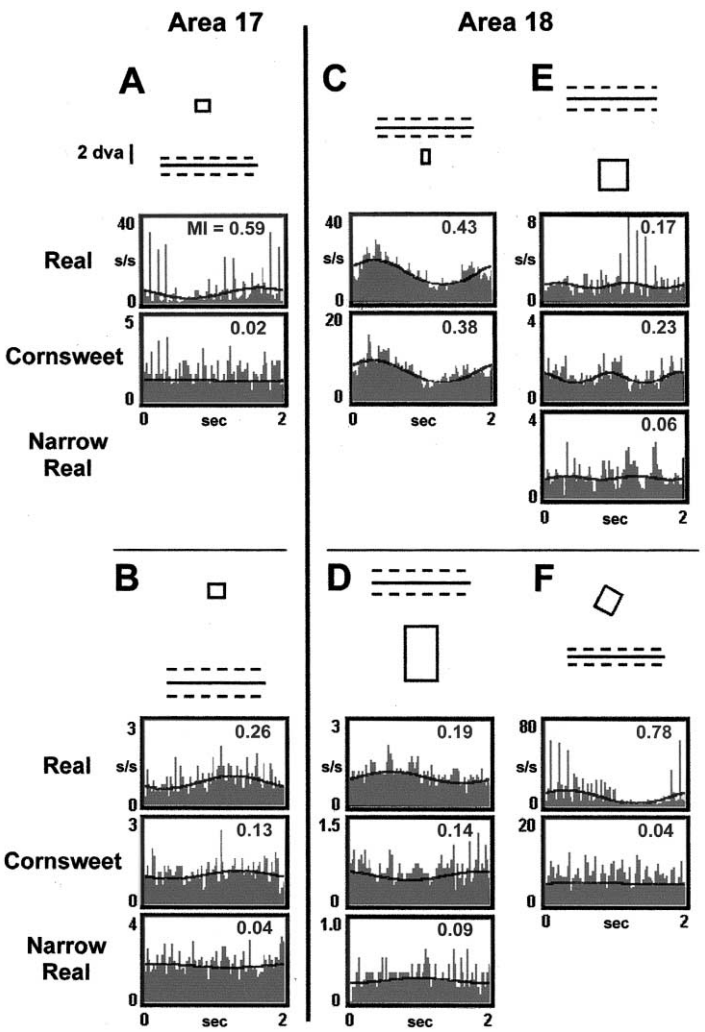

Fig. 6. Single unit responses to Real and Cornsweet stimuli. Response to Narrow Real, when tested, is also shown. In each of (A,B) (Area 17) and (C–F) (Area 18), stimulus border locations relative to receptive field are shown above. Peri-stimulus time histograms shown below (ordinate in spikes per second, 11 ms/bin; typically 300 cycles were presented). (A) Area 17 cell. The cell is well modulated by Real luminance but poorly by Cornsweet. Note the sharp transients in response in the Real PSTH that are in synchrony with step changes in luminance contrast of stimulus (see Section 2). (B) Area 17 cell. Cell shows moderate modulation to both Real and Cornsweet. This was the second-strongest Cornsweet modulation obtained in Area 17 sampling. (C–E) Area 18 cells. These cells show comparable modulation by Real and Cornsweet stimuli. In some cases, such as C, Cornsweet modulation in Area 18 could be pronounced (MI = 0.43) and clearly in-phase with Real modulation. Cell depicted in (E) is an F2 cell; the MI shown is calculated from its F2 component. Peak response of this cell to Real is 15 s/s. (F) Area 18 cell. Like the cell shown in (A), this cell responds well to the Real stimulus, but poorly to the Cornsweet.

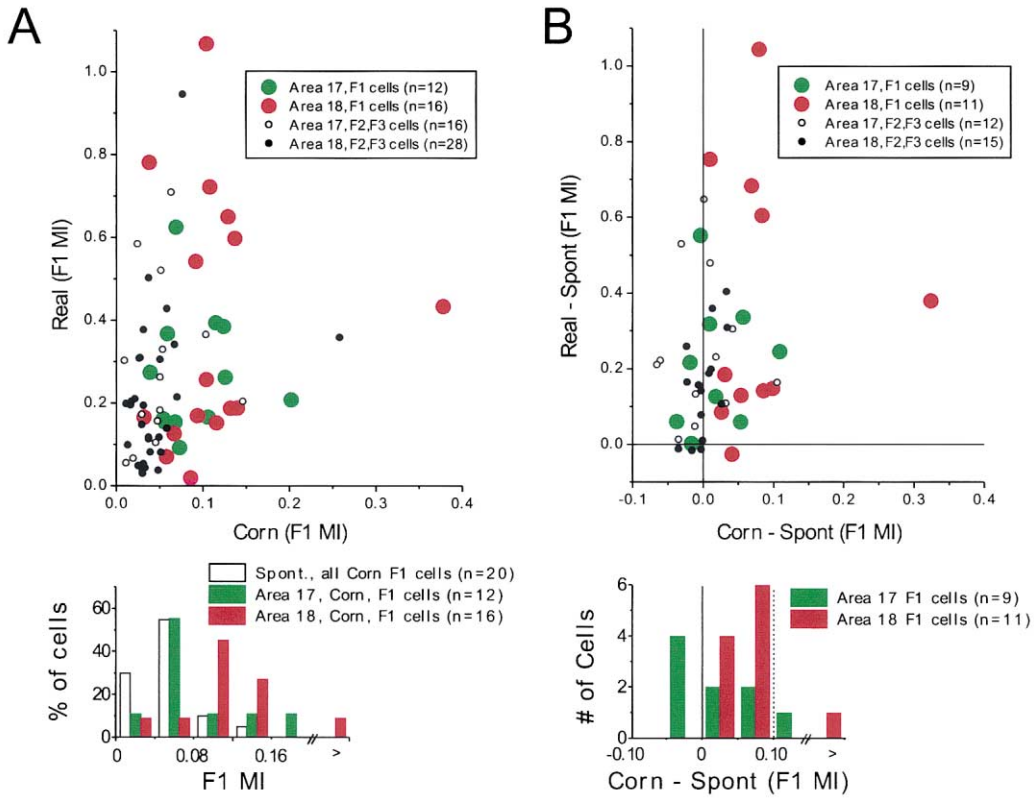

Fig. 7. Cornsweet vs. Real modulation responses. (A) Top: modulation indices of Area 17 ($n = 28$, white or green dots) and Area 18 (n = 44, black or red dots) cells to Cornsweet (abscissa) vs. Real (ordinate) stimuli. Red and green dots indicate F1 cells. Plotted values are F1 components of F1 cells (Area 17, green, $n = 12$; Area 18, red, $n = 16$) and F2, F3 cells (Area 17, white, $n = 16$; Area 18, black, $n = 28$). Only cells that exhibited F1 or F2 Real responses above the 95% confidence level (see Section 2) are included. Bottom: binned comparison of Area 17 (green) vs. 18 (red) Cornsweet responses of F1 cells. Spontaneous MIs (white) for the same cells are also shown ($n = 20$). (B) Top: spontaneous-subtracted responses of F1 cells. Each cell's Real and Cornsweet responses are subtracted against its own spontaneous index. Bottom: binned comparison of Area 17 (green) vs. Area 18 (red) spontaneous-subtracted Cornsweet responses of F1 cells. Each cell's Cornsweet response is subtracted against its own spontaneous index. Paired comparison of Cornsweet vs. spontaneous indices for the same cell is statistically significant for Area 18, but not Area 17 (Wilcoxon Signed Ranks Test, Area 18: $P < 0.002$, $n = 11$; Area 17; $P > 0.1$, $n = 9$).

Cornsweet stimulus (bottom PSTH, MI = 0.02). Fig. 6B illustrates the Area 17 cell with the second-largest modulation index to Cornsweet in our population (MI = 0.13), roughly comparable to its Real response (MI = 0.26). Note that the edge of its receptive field is 9 deg away from the Cornsweet border.

Cells in Area 18 also exhibited a clear modulation of response by the Real stimulus. While some of these cells were not modulated by the Cornsweet stimulus (Fig. 6F, recorded in site 6 in Fig. 3, MI = 0.04), others exhibited comparable responses to Real and Cornsweet (Fig. 6C MI = 0.38, Fig. 6D MI = 0.14, Fig. 6E MI = 0.23). Fig. 6E shows a cell with a strong Cornsweet response at twice the stimulus modulation frequency (F2). Some cells exhibited a Cornsweet response that was clearly in-phase with the Real response (Fig. 6B,C). Responses to the Narrow Real stimulus were generally weaker than those to the Cornsweet (Fig. 6B,D,E; also Fig. 10A).

To classify the cells, we defined 'F1 cells' as those cells with F1 components of the Cornsweet response larger than F2 and F3; F2 and F3 cells were similarly classified. Based on this classification, most cells in our population were either F1 cells (Area 17, $n = 12$; Area 18, $n = 16$) or F2 cells (Area 17, $n = 11$; Area 18, $n = 15$), and fewer were F3 cells (Area 17, $n = 5$; Area 18, $n = 13$). Since the F1 component of the response is at the modulation frequency of the stimulus and is thus correlated with brightness modulation, we chose to focus our analyses on these cells (of our F2 cell sample, only a few cells in Areas 17 and 18 exhibited significant responses).

3.3.3. Response to Cornsweet is significant in the Area 18 F1 cell population

To quantify the relative responses, we compared the F1 modulation indices of all cells in response to Real and Cornsweet stimuli. Fig. 7A, top, illustrates the distribution of F1 modulation indices of F1 cells in Area 17 ($n = 12$, green circles) and Area 18 ($n = 16$; red circles) in response to Real and Cornsweet stimuli. (For completeness, we also show our remaining data set: the

F1 component of F2 and F3 cells in Area 17 is indicated by open circles, $n = 16$, and those in Area 18 by filled circles, $n = 28$.) Most cells (69 out of 72) exhibited greater modulation to Real stimuli than to Cornsweet stimuli.

We then compared these distributions (Fig. 7A, bottom). Cornsweet modulation indices in Area 17 (F1 cells, green bars, $n = 12$) ranged from 0.03 to 0.20. Area 18 cells (F1 cells, red bars, $n = 16$) ranged from 0.01 to 0.38. To determine the significance of these collective modulations in Area 17 and 18, we compared them with modulation indices calculated from epochs of spontaneous activity (Blank stimulus, $n = 20$). These distributions indicate that the population of Area 18 Cornsweet responses are significantly different from spontaneous (Mann–Whitney U Test: $P < 0.002$) and that Area 17 population responses are also different from spontaneous, although with a lower significance (Mann–Whitney U Test: $P = 0.04$). In Fig. 7B, we show the subset of F1 cells in which both Cornsweet and spontaneous responses were measured (Area 17, $n = 9$; Area 18, $n = 11$). This response selection enables us to make paired comparisons between Cornsweet and spontaneous responses of the same cells. The responses of each cell to Real and Cornsweet are shown, relative to its own spontaneous index. This analysis shows that only Area 18 F1 cell Cornsweet responses were significantly greater than spontaneous (Wilcoxon Signed Ranks Test, Area 18: $P < 0.002$, $n = 11$; Area 17: $P > 0.1$, $n = 9$) when treated as a paired sample population. Thus, the Cornsweet response appears to be more significant in Area 18 than in Area 17.

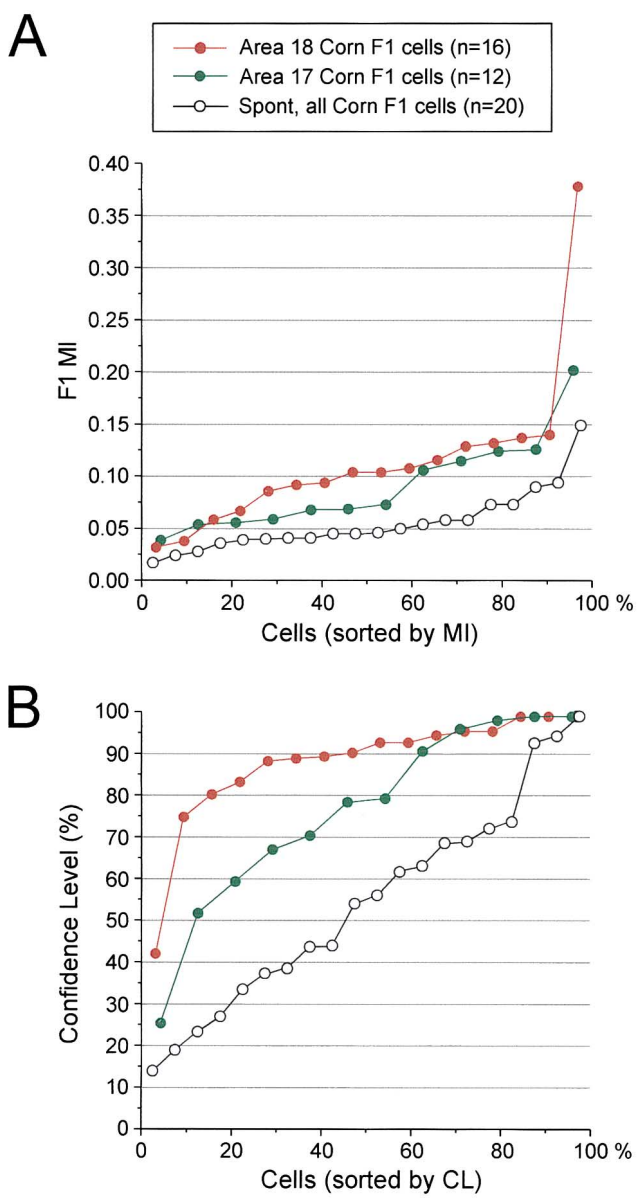

Fig. 8. Cornsweet vs. Spontaneous responses in Areas 17 and 18. (A) Modulation indices of F1 cells in Area 17 (green) and Area 18 (red) in response to Cornsweet. Spontaneous MIs in white. Cells are sorted along the abscissa by response strength. (B) Confidence levels of the above cells, determined by randomizing the ISI arrival order of spike trains. Five out of 16 cells in Area 18, and 4/12 cells in Area 17, are above the 95% confidence level.

To better illustrate the differences between Cornsweet and spontaneous responses in Area 18 (red) and Area 17 (green), we sorted responses by modulation index magnitude and plotted these in Fig. 8A. To be certain that our Cornsweet modulations were not merely 'chance' or random fluctuations in cellular firing activities, we applied a randomization ('bootstrap') statistical method to determine the significance of Cornsweet response on a cell-by-cell basis. This method is known to be an effective means to determine whether temporal changes in measured data may be reasonably explained by chance fluctuations (Manly, 1997). We generated for each cell a set of 100 randomized spike trains (see Section 2), calculated a modulation index for each, and generated a confidence measure for each recorded response. The sorted confidence levels of these responses are shown in Fig. 8B (ranking does not necessarily match that for response magnitude). At the 95% confidence limit, 5/16 cells in Area 18 and 4/12 cells in Area 17 showed significant modulation. At the 90% confidence limit, 9/16 cells in Area 18 and 5/12 cells in Area 17 showed significant modulation. This randomization analysis further supports our findings using other statistical approaches: that Cornsweet modulation responses are indeed present and significant, although weak, in a subset of cells in both Areas 17 and 18.

In addition to testing for the presence of Cornsweet responses in individual neurons, we also asked whether there is a collective (i.e. as a population) Cornsweet response. Specifically, we wondered whether the sum of Cornsweet responses might yield a significant response in phase with that of Real responses. We tested this by summing the fitted sinusoids of all Cornsweet re-

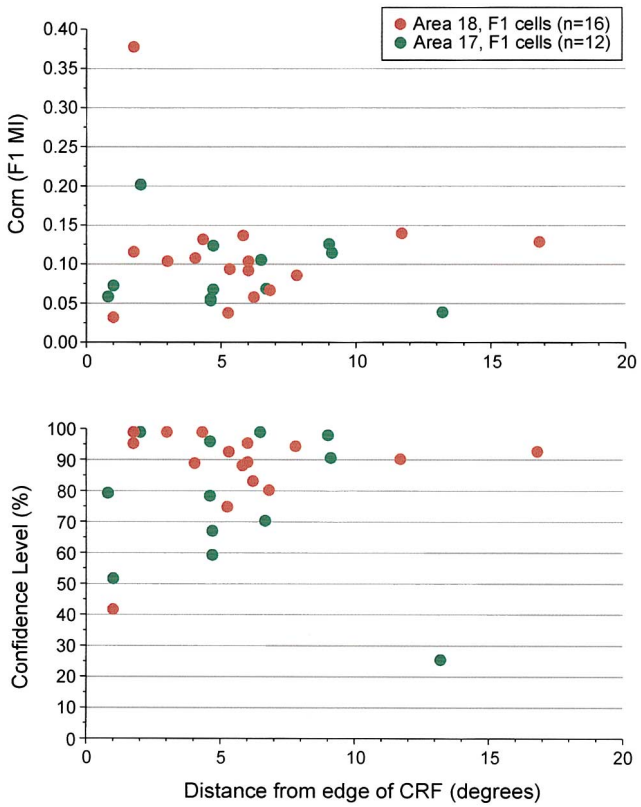

Fig. 9. Response to Cornsweet of Area 17 ($n = 12$) and Area 18 ($n = 16$) F1 cells as a function of distance from the contrast border. Ordinate, each cell's Cornsweet modulation index (top) and confidence level (bottom). Abscissa, distance from nearest edge of CRF to Cornsweet border in degrees. Significant modulations occur in both Areas 17 and 18 at distances over 5 deg from the edge of the CRF (7 deg from the CRF center), and a cell in Area 18 exhibits response at a distance of over 16 deg (20 deg from CRF center).

sponses, thereby producing a population Cornsweet response. The peak of this population sinusoid was significantly above chance levels for Area 18 but not for Area 17 (Area 18: $P = 0.015$, $n = 16$; Area 17: $P = 0.66$, $n = 12$). This significance was calculated by a bootstrap analysis in which we generated 1000 sinusoids using random pairings of magnitude and phase difference. For Area 18, this population sinusoid had a peak roughly in phase (48 deg offset) with the Real response. Thus, consistent with our results obtained from response magnitude (MI), the population Cornsweet response suggested a significant Cornsweet response in Area 18 but not Area 17.

3.3.4. The Cornsweet response is present at distant locations

Perceptually, the Cornsweet stimulus produces a brightness illusion that extends across the entire surface and is salient even at locations distant from the border. To examine the possible electrophysiological basis for this percept, we examined the strength of the Cornsweet response as a function of distance away from the border (distance between contrast border and edge of classical receptive field). Across the population, we did not find a clear relationship between response strength and distance from the border. As shown in Fig. 9, Cornsweet responses were found at a wide range of distances from the border. In Area 17, a few responses were recorded at distances up to 9 deg from the border to the edge of the CRF; in Area 18, Cornsweet responses were recorded at even larger distances (> 15 deg) from the border. The presence of these responses at a range of distances was seen both in terms of degrees of visual angle (Area 17, median = 4.7 deg, range 0.8–13.9 deg; Area 18, median = 4.7 deg, range 1–16.8 deg) and in units of receptive field width (Area 17, median = 2.8, range 0.5–7.25; Area 18, median = 1.6, range 0.2–5.1).

3.3.5. The Narrow Real response is in antiphase to the Cornsweet response in Area 18

During simultaneous contrast stimulation, it has been shown that some cells in Area 17 respond in antiphase to the luminance modulation of the surround (Rossi et al., 1996; Rossi & Paradiso, 1999), consistent with the signaling of perceived brightness during simultaneous contrast. Thus far, we have shown that there are cells whose responses are modulated by distant border contrast. However, are these cells sensitive to the perceived bright/dark phase of the stimulus? To test whether these responses are specific to perceived brightness, and not an indiscriminate response to a distant stimulus, we presented a Narrow Real stimulus for comparison. We reasoned that if a cell were merely responding to a distant luminance patch or any distant edge, then the response to the Cornsweet and Narrow Real stimuli should be in phase with each other. However, if a cell's response were correlated with perceived brightness, then its Narrow Real response should be opposite in sign to its Cornsweet response.

This expectation was supported by our data. Fig. 10A illustrates two examples of weak antiphase relationships between Cornsweet and Narrow Real responses (compare fitted sinusoids). Other examples can be seen in Fig. 6B,D,E. Fig. 10B, left, plots the distribution of Narrow Real responses (blue squares) and those of the Cornsweet (red circles) for cells in Area 18. The Narrow Real population is selected for F1 > F2,F3, the same criteria used to define the F1 cell Cornsweet population. (Narrow Real cells with F1 > F2,F3: Area 17, $n = 6$ of 12 cells; Area 18, $n = 13$ of 28 cells). Spontaneous indices for these cells are shown as open circles. Responses to the Narrow Real stimulus ranged from 0.058 to 0.201 in Area 17, mean 0.088; 0.034 to 0.290 in Area 18, mean 0.097. Consistent with the imaged response, the Narrow Real response is not significant when paired against its spontaneous index in Area 17, but it is significant in Area 18 (Wilcoxon

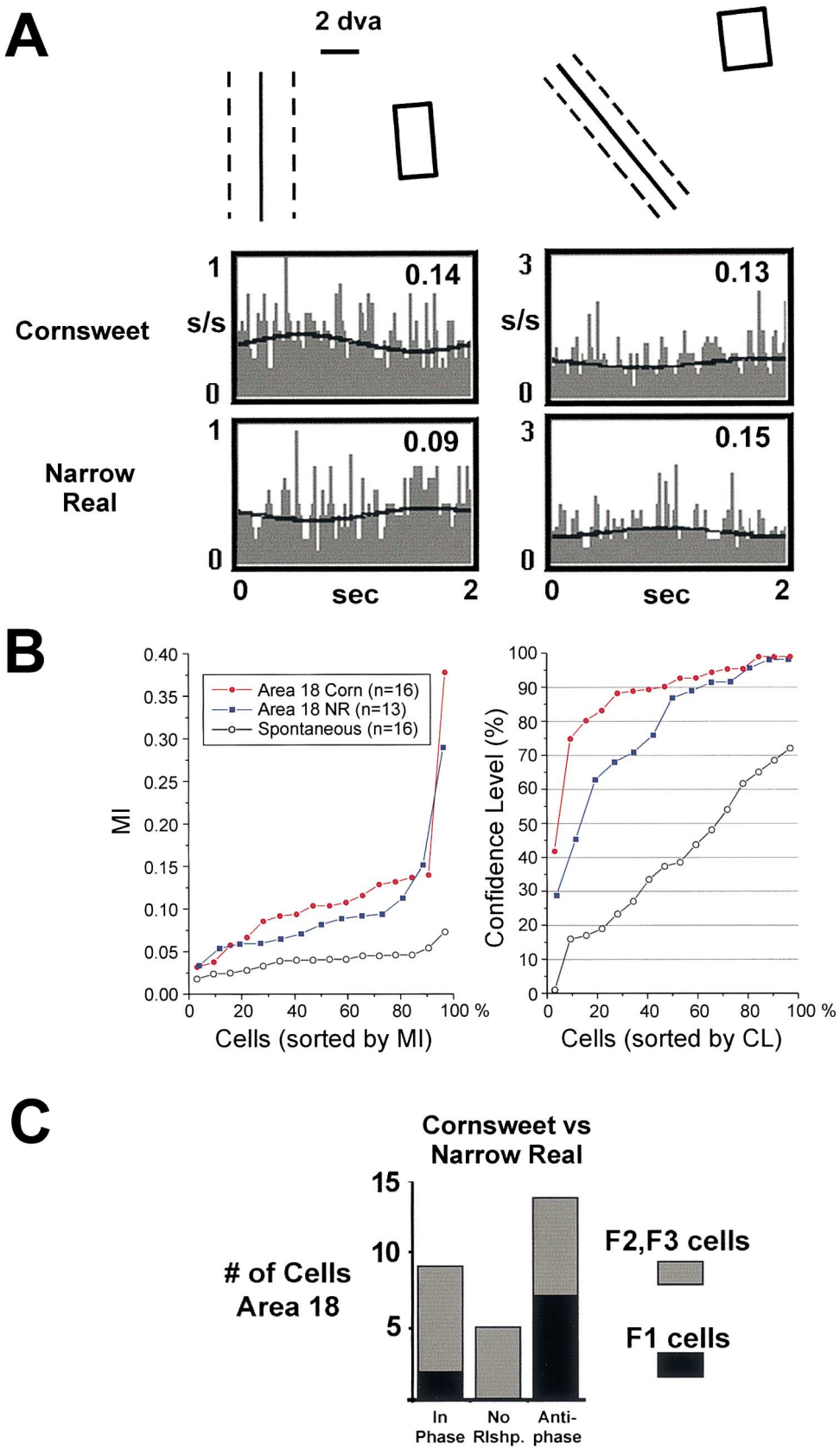

Fig. 10. Narrow Real vs. Cornsweet responses. (A) Examples of antiphase relationships between Cornsweet and Narrow Real response. Receptive field positions relative to contrast border shown above. Peri-stimulus time histograms illustrate antiphase relationship between Cornsweet and Narrow Real responses. See also Fig. 4B,D,E. (B) Left: modulation indices in Area 18 in response to Cornsweet (F1 cells, red circles) and Narrow Real (cells with Narrow Real MI F1 > F2,F3; blue squares). Spontaneous MIs of these cells in white (not all cells were tested with Blank). Right: confidence levels of the above cell responses. (C) In Area 18, seven out of nine F1 cells (14 out of 28 of all Area 18 cells) exhibit Cornsweet responses in antiphase with Narrow Real responses.

Signed Ranks Test, Area 17: $P > 0.1$, $n = 6$; Area 18: $P < 0.01$, $n = 8$). Also consistent with the imaging results, modulations to the Narrow Real were not significantly different from those to the Cornsweet (Mann–Whitney U Test, Area 17: $P = 0.9$; Area 18: $P > 0.2$). To determine the significance of individual Area 18 responses to the Narrow Real, the confidence levels of these responses calculated from randomization are plotted at Fig. 10B, right. In Area 18, 3/13 cells exhibited Narrow Real modulation greater than the 95% confidence level compared to 5/16 cells above the 95% confidence level for Area 18 Cornsweet responses. At the 90% confidence level these values are 5/13 for Narrow Real and 9/16 for Cornsweet. Thus, consistent with imaged results, the magnitudes of the Narrow Real responses were not significantly different from Cornsweet responses in Area 18.

Our Area 18 F1 population also suggested an antiphase relationship between Cornsweet and Narrow Real response (Fig. 10C). For this analysis, Cornsweet and Narrow Real response phases were pairwise compared for each Cornsweet cell. Area 17 cells were not included since there were too few with both significant Cornsweet and significant Narrow Real response. We divided the Area 18 data set into three bins: in-phase ($\pm$ 0–60 deg phase difference), antiphase ($\pm$ 120–180 deg phase difference), and neither in-phase nor antiphase ($\pm$ 60–120 deg phase difference). Of the 9 F1 cells in our Area 18 F1 population, 7 exhibited an antiphase relationship (Fig. 10C, black bars, $P(2,0,7) < 0.02$). Of all cells in Area 18, 14/28 exhibited this relationship (Fig. 10C, gray and black bars, $P(9,5,14) = 0.3$). While the number of cells is small, our results suggest that there are some cells (a population of F1 cells) whose phase relationships are consistent with percept.

4. Discussion

We have studied real and illusory brightness response in Areas 17 and 18 of the cat. We show that these selective cell responses are not merely chance fluctuations of neuronal spike trains. Although Cornsweet modulation responses are generally weak, in some cases they are comparable to Real luminance modulation responses. When population measures are considered via optical imaging and via multi-unit electrophysiological sampling, these collective Cornsweet modulations appear to be more evident in Area 18 rather Area 17. We further show that modulation responses to the Cornsweet stimulus are not due to direct stimulation of the CRF by the border contrast; they occur despite the absence of luminance modulation over the imaged/recorded areas. Furthermore, imaging and electrophysiological responses can be detected up to 15 deg or more from the inducing border (Figs. 4 and 9), consistent with the long-range perceptual effect of Cornsweet border induction. We obtain similar imaged responses with another illusory brightness stimulus, the Narrow Real stimulus. Also consistent with perception, we show that some single cell responses to Cornsweet and Narrow Real exhibit antiphase modulation relationships, suggesting a specificity of response to bright/dark phase of the brightness percept. Together, our results thus suggest the presence of single cells in Areas 17 and 18 that respond to the presence of distant border contrast, some of which are specific for brightness phase. These cells are more prevalent in Area 18 than Area 17.

Whether these edge-induced modulated responses are indeed the basis of 'brightness' perception in the cat remains to be studied. Cats are known to have a number of visual psychophysical capabilities and visual functional organizations similar to those of humans (e.g. Bravo, Blake, & Morrison, 1988; Payne, 1993; Lomber, Payne, Cornwell, & Long, 1996). Therefore, although we have not directly demonstrated a 'brightness' response per se in visual cortex, we argue that the presence of cortical response to distant border contrast modulations, which are known to induce brightness percepts in humans, and the phase specificity of some responses, is indicative of a neural basis of brightness response.

4.1. Imaging response to brightness change

Although low spatial frequency gratings have been used to obtain optical maps of color domains (blobs and thin stripes) in the primate (Ts'o et al., 1990; Roe & Ts'o, 1995, 1999) and of spatial frequency domains in the cat (Bonhoeffer et al., 1995; Shoham et al., 1997), no previous study has examined cortical response to large field luminance modulation with imaging methods. We have considered other possible sources of the observed 17/18 activation. One source to consider is the reported spontaneous background oscillations in cortical reflectance (roughly 0.1 Hz) (Mayhew et al., 1999). Since our stimuli were presented at temporal luminance modulations of 0.5 Hz, were randomly interleaved, and were averaged (50–60 trials over a period of approximately one hour), it is unlikely that such background oscillations would contribute in a significant and consistent way to our images. Furthermore, subtraction of the Blank condition from each of the Real and Cornsweet conditions should eliminate possible contribution of background slow temporal fluctuations to our stimulus-driven signal (Fig. 4). Our images are therefore not the result of inherent slow cortical oscillations. Our data also rules out the possibility that differential 17/18 activation may be due to differences in basal firing rates of cells in Areas 17 and 18, or to differential Area 17 versus 18 cortical magnification.

We considered the possibility that the receptive fields were directly activated by nonspecific light scatter within the eye. However, this explanation is not consistent with our results. Light scatter alone cannot account for the phase-specificity of the Cornsweet vs Narrow Real stimulus response (antiphase relationship). Both stimuli were controlled for total luminance (the total luminance level of our stimuli are constant across stimuli and constant within single stimulus conditions) and should have similar changes in light scatter, i.e. the light scatter should be in phase rather than antiphase. Furthermore, in a previous study in which the potential contribution of light scatter was examined, the addition of artificial pupils (which should reduce light scatter) did not diminish responses to simultaneous contrast stimuli (Rossi and Paradiso, 1996). These arguments suggest that the contribution due to light scatter is minimal and does not account for our findings.

We find it more likely that the imaged responses to Real luminance stimulation are a direct consequence of the spatiotemporal characteristics of the stimulus. As shown by our own data as well as those of others (Bonhoeffer et al., 1995; Shoham et al., 1997), Area 17 is much more weakly activated by low spatial frequencies. Thus, it may not be surprising to find preferential activation of Area 18 over Area 17 to such spatially uniform stimuli. It has also been suggested that Area 17 response is dominated by X-cell input and Area 18 by Y-cell input (Humphrey, Sur, Uhlrich, & Sherman, 1985; Ferster, 1990). The fact that X-cells commonly have strong suppressive surrounds (Bullier & Norton, 1979) is consistent with Area 17's relative quiescence to these large field stimuli.

That our imaged responses correlate more with firing activity modulation than overall firing activity per se is curious. Traditionally, an increase in optically imaged activation signal has been associated with an increase in overall firing rate. This association rests on the assumption that increase in neural firing rate brings about increasing metabolic demands and subsequent oxygen consumption. Recent reports suggest that optically imaged activations need not be necessarily associated with explicit neural firing (e.g. signals may reflect subthreshold activations (Das & Gilbert, 1995; Toth, Kim, Rao, & Sur, 1997; Bringuier, Chavane, Glaeser, & Fregnac, 1999). Our findings show that differential optical signals between Areas 17 and 18 can be obtained in the absence of obvious differences in average firing rates and that these differences may be more closely related to differences in firing rate modulation.

4.2. The role of Area 18 in border-induced brightness percepts

While spatiotemporal characteristics of the stimulus may underlie Area 18's preferential response to real luminance change, it is not sufficient to explain the imaged response in Area 18 to Cornsweet and Narrow Real stimuli. Our data suggest that the Area 18 response is directly related to distant border contrast. We have taken care to avoid direct luminance activation of the imaged area. By comparing activation levels to the same reference (either Blank response or skull reflectance) we feel comfortable that comparisons are both appropriate and interpretable. In conjunction with our electrophysiological findings, we suggest that these images represent illusory border-induced brightness response in cat visual cortex.

That border-induced brightness percepts are represented in Area 18 is consistent with its role as a higher order visual processing area. Area 18 has previously been implicated in the signaling of higher order contours (Sheth et al., 1996; Leventhal et al., 1998; Mareschal & Baker, 1998). It has also been compared to Area V2 in the primate, an area that has also been shown to process higher order illusory contours (Peterhans & von der Heydt, 1989; von der Heydt & Peterhans, 1989; Ramsden, Hung, & Roe, 2001; cf. Hirsch et al., 1995; Mendola et al., 1999). That V2 cells have been shown to co-signal real and illusory contours has prompted suggestions of common V2 circuitry underlying coding of these different stimuli (von der Heydt & Peterhans, 1989; Ramsden et al., 2001). The circuitry for generating 'illusory brightness' percepts in Area 18 is yet unknown. However, given the similarity of imaged response (preferential Area 18 activation) to both Real and Cornsweet stimuli and presence of single cells responsive to these stimuli, we suggest that similar border contrast circuitries may be evoked by both brightness stimuli. Indeed, the responses of some cells shown here in Area 18 may play a key role in the perceived brightness contrast equivalence.

Border induction is not the first brightness illusion found in early visual cortex. Previous studies using flanking luminance modulation (simultaneous contrast) (Rossi et al., 1996; Rossi & Paradiso, 1999) have reported significant neural modulation of Area 17 cells (75% of cells, $>25\%$ correlated with brightness). This suggests that at the very earliest cortical stage, neurons can respond to perceived brightness changes. These responses to simultaneous contrast, however, could be interpreted as arising from either surface contrast and/or explicit border signals. In our Cornsweet stimulus, surface contrast is absent and therefore brightness induction can only be attributed to the presence of the contrast border.

Together, these findings from Cornsweet and simultaneous contrast experiments suggest that brightness signaling in cat areas 17 and 18 may occur through two different mechanisms: border contrast induction and surface contrast induction. Our data suggest that these two mechanisms may not be invoked equally by Areas

17 and 18. Brightness responses that can potentially utilize surface contrast cues (i.e. simultaneous contrast) are known to be prevalent in Area 17 (Rossi et al., 1996). Because our border-dependent Cornsweet responses appear to be more robust in Area 18 than 17 (particularly when population measures are considered), Area 18 may play a greater role in signaling surface contrast due to border induction.

4.3. Mechanisms of border-induction

The neural circuitry underlying these distant brightness effects that we have described are yet unknown. However, interactions between oriented V1 and V2 cells and distant non-oriented V2 cells in cat (Hung et al., 1998) and primate visual cortex (Roe & Ts'o, 1999) suggest that signals could propagate from the contrast border via direct or indirect functional connections. Thus, this induction in Area 18 could be mediated by 18–17 and/or 18–18 border-to-surface propagation. Alternatively, it is possible that higher order brightness responses are the result of influences from higher cortical areas (De Weerd, Gattass, Desimone, & Ungerleider, 1995; Purves et al., 1999).

5. Conclusion

In conclusion, we report that brightness responses associated with distant border induction are evident in Area 18, and to a lesser extent in Area 17. We hypothesize that border-induced brightness in Area 18, in particular, may modulate simultaneous contrast brightness effects that manifest in Area 17. A balancing of brightness mechanisms in primary visual cortex (e.g. cat Area 17 or primate Area V1), coupled with border-induced associations in second visual cortex (e.g. cat Area 18 or primate Area V2), may underlie our ability to perceive proper contrast relationships between surfaces. Our finding of border influences upon surface representation is just one example of how the cortex can integrate multiple classes of information (e.g. contour and luminance) to enhance the percept provided by any individual class (e.g. luminance alone). These border and surface signals may be integrated by higher cortical areas, where responses to such brightness stimuli may be even more robust.

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