Functional Architecture of Eye Position Gain Fields in Visual Association Cortex of Behaving Monkey

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Siegel, Ralph M., Milena Raffi, Raymond E. Phinney, Jessica A. Turner, and Gábor Jandó. Functional architecture of eye position gain fields in visual association cortex of behaving monkey. J Neurophysiol 90: 1279–1294, 2003. First published April 2, 2003; 10.1152/jn.01179.2002. In the behaving monkey, inferior parietal lobe cortical neurons combine visual information with eye position signals. However, an organized topographic map of these neurons’ properties has never been demonstrated. Intrinsic optical imaging revealed a functional architecture for the effect of eye position on the visual response to radial optic flow. The map was distributed across two subdivisions of the inferior parietal lobule, area 7a and the dorsal prelunate area, DP. Area 7a contains a representation of the lower eye position gain fields while area DP represents the upper eye position gain fields. Horizontal eye position is represented orthogonal to the vertical eye position across the medial lateral extents of the cortices. Similar topographies were found in three hemispheres of two monkeys; the horizontal and vertical gain field representations were not isotropic with a greater modulation found with the vertical. Monte Carlo methods demonstrated the significance of the maps, and they were verified in part using multiunit recordings. The novel topographic organization of this association cortex area provides a substrate for constructing representations of surrounding space for perception and the guidance of motor behaviors.

INTRODUCTION

Classical studies of the primate inferior parietal lobule began with shrapnel injuries during World War I (Critchley 1953; Head and Holmes 1911). Modern electrophysiological measurements revealed the subdivisions and defined the neuronal properties of the inferior parietal lobule available to construct representations of surrounding visual space (Andersen et al. 1985; Heilman et al. 1993; Siegel and Read 1997a). The inferior parietal lobules of the macaque monkey cortices have two visual association areas that lie on the cortical gyrii, area 7a and the dorsal prelunate (DP) area (Siegel and Read 1997b). The receptive fields of electrically recorded single neurons in monkeys for these regions often approach 60° in size, can be bilateral, and, at least those of area 7a, are selective to navigational optic flow (Motter and Mountcastle 1981; Read and Siegel 1997; Siegel and Read 1997a). The gain of the visual responses of inferior parietal lobule neurons is modulated by the position of the eye in the orbit and the monkey’s behavioral state (Andersen et al. 1985; Bushnell et al. 1981; Read and Siegel 1997). There has been no evidence from any measurements of single cells for a mapping of these properties across the inferior parietal lobule’s surface in the behaving monkey (Andersen et al. 1990; Blatt et al. 1990). Anatomical projections between the inferior parietal lobule and the frontal and temporal lobes suggest that there may be topographies. The projections are patterned regions of interdigitated columns and regions of overlap (Andersen et al. 1990; Cavada and Goldman-Rakic 1989; Lewis and Van Essen 2000). When retrograde tracers are injected in two projective areas (e.g., area 8 and 46), stripes of overlapping cell bodies that can diverge are found in area 7a (Andersen et al. 1990). Such projection patterns elsewhere [e.g., between V1 and V2 (Ts’o et al. 2001)] have been correlated with functional architectures and could indicate the presence of similar organizing principles in the inferior parietal lobule. Given the relatively small surface area of the cortical regions in the inferior parietal lobule and the large receptive and gain fields, the paucity of published electrophysiological mapping data might simply indicate that the orbital gain fields overlap substantially across the surface and have no topography. Alternatively the single-unit methodology may be technically unable to unveil a functional architecture in chronic behaving monkey studies because there are substantial errors in the localization of electrode penetrations over the 1 or 2 yr needed for recording (Andersen et al. 1990; Siegel and Read 1997a). Another possibility is the relationship of gaze direction to cortical topography may be dynamic in ways that require large areas to be examined simultaneously (or nearly so) for these properties. The absence of explicit knowledge for an inferior parietal lobule functional architecture has substantially hindered an exploration of how the underlying circuitry can compute a neuronal correlate for spatial cognition.

Optical imaging utilizes light to assess the oxygenation of hemoglobin (Hb) and thus indirectly measure neuronal metabolism and activity. This technology permits multiple measurements over an extended period of time and space in the behaving monkey (Shoyerman et al. 2000) and allows for a direct assessment of maps in the inferior parietal lobule. In the current study, intrinsic optical imaging has revealed a novel map of eye position modulating visual responses in the inferior parietal lobule. This architecture is discussed in terms of constraints on subsequent spatial perceptual and motor processing.

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M E T H O D S

Surgical details

Two monkeys were prepared for chronic behavioral studies using standard methods (Siegel and Read 1997a). The use of the artificial dura permits long-term studies and followed published methods (Shoyerman et al. 2000) with modifications as described here. During the implant surgery performed under sterile conditions and isoflurane (0.5–2% in O₂) anesthesia, the animal was given ceftriaxone sodium antibiotic (Rocephin, Roche, 100–150 mg · kg⁻¹ · d⁻¹), mannitol (25% 1 ml/kg iv), and furosimide (1 mg/kg im) prior to opening the dura. The latter two minimized cerebral edema. The artificial dura was found to have a small tear, as well as expansion and compression artifacts. Major veins and arteries could be distinguished based on the presence of pulsations.

In some experiments, another stimulus set was utilized to examine upper and lower gaze field tuning. Two fixation positions [e.g., (0, 10°) and (0, -10°)] were used; over the fixation, one of two different optic flows (expansion, compression, clockwise and counterclockwise) was presented in each trial. The fixation conditions for which expansion and compression optic flow was presented were analyzed as part of the current study; the remaining data serve as the basis for a study of optic flow (Raffi and Siegel 2002; M. Raffi and R. M. Siegel, unpublished data).

Optical imaging technique

The monkey’s head was firmly attached to a floating Newport air table via an implant made of Palacos R radiopaque bone cement (No. 12-0001, Smith+Nephew Richards, Memphis, TN) over the skull held with ≤20 Synthes (Paoli, PA) titanium screws. This implant was made in a recovery surgery 1–6 mo prior to the artificial dura implant. The implant covered the skull from the occipital notch to the frontal bone and laterally replaced the insertion points of the temporalis muscles. Embedded in the cement was a custom stainless steel t-bar fixture with a 6.35 × 50 × 30 mm hardened steel plate in the frontal plane. This combination provided exceptional rigidity. The camera was also attached to the Newport table using off-the-shelf components.

Intrinsic optical imaging methods were used to study the cortical topography (Shoyerman et al. 2000). The macroscope, somewhat based on optical principles of Ratzlaff and Grinvald (1991), consisted of a Nikon Nikkor AF Micro 60 mm/2.8 D lens and a 50 mm Nikon 1.2 lens (No. 385083) as the objective. Unlike the Ratzlaff/Grinvald macroscope where the matched lenses are focused at infinity, the 60 mm Nikkor Micro lens focused on the inverted image from the 50 mm objective lens. Adjusting the focal plane of the 60 mm Nikkor lens permitted variation of the magnification as well as an unusually long, 30–80 mm, working distance while maintaining a narrow depth of field. Images were taken from two monkeys who had 20 mm diameter chambers implanted over a trephination in the skull (as described in the preceding text), based on magnetic resonance images (Fig. 2, A and B). The chamber was filled with 0.9% saline and hydraulically sealed with a glass plate for optical imaging.

Typically 750 × 480 pixel images were collected at 605 nm with 17.3 μm/pixel resolution at a depth of 500 μm below surface capillaries (imaged with green light). These were resampled to provide a 34.6 μm/pixel resolution. The data were not spatially or temporally filtered other than the reduction of the spatial resolution by a factor of two to avoid inducing spatial distortions or filtering artifacts. Major veins and arteries could be distinguished based on the presence of pulsations.

Image analysis

The Optical Imaging 2001 system (Rehovot, Israel) was used to collect optical data. Data collection was initiated by first collecting a reference image in the interval between trials while the monkey was
not in the task. This reference image served to set the amplifiers’ gains and offsets. Two hundred and fifty six frames at 30 Hz were averaged; a reference image was collected every 16 trials (~160 s). This reference image was stored in memory and subtracted from incoming images in real-time by the optical imaging system. This difference image was digitized by the imaging system and stored on disk. Off-line, the reference image and difference image were combined to provide measurements of total reflectance with ≤16 bits precision. Optical images were collected for every trial. At the same time, a behavioral control computer kept records of the animal’s performance (Siegel and Read 1997a) and was synchronized with the optical-imaging system via a set of digital lines. An IBM SP2 computer and

FIG. 2. First stage of analysis of gain fields from monkey 1, right hemisphere (M1R). A: 3-dimensional reconstruction of the sulcal and gyral patterns from magnetic resonance images. The intraparietal sulcus (IPS) joins with the lunate sulcus (LS) (heavy black line). The 20 mm diameter chamber is shown (white circle) with the recording region in the black rectangle. B: angioarchitectonics of the region of interest taken with 540 nm illumination. The large vessel at the top of the image lies over the intraparietal sulcus (IPS). A draining vein lies between the dorsal apex and the most dorsal portion of the superior temporal sulcus (STS) and was used to delimit the image into area 7a and DP. The superior temporal sulcus can be observed with a dissection microscope to begin just to the right of the “STS” label. C: the cocktail response is the average evoked response to stimulus onset across all conditions using 605 nm illumination. D: the single condition map varies both as a function of the location on the cortex and the eye position. The average evoked response displayed for each position had the cocktail response subtracted. The location of each image indicates the position of the fixation and optic flow stimulus. Dataset 3/20/2000/gm; the range of the gray scale for C is (-1.1%) and for D is (-0.2%,0.2%).
an imaging package (Khoral Research, Albuquerque, NM) were used for subsequent analysis and display. All trials for which the monkey incorrectly performed the trial (e.g., eye movement, incorrect lever movement) were rejected from the data set. A typical run would result in 30–90 trials per condition or 270–1,200 trials each day.

BASELINE NORMALIZATION ANALYSIS (BNA). A regression analysis was utilized. It normalized each trial’s data by a baseline value collected at the start of the trial. The evoked reflectance signal was quantified by subtracting the “baseline” image (averaged for 1,000 to 0 ms relative to stimulus onset) from the signal averaged over the 2,000–3,000 ms after stimulus onset. At this time the monkey was fixing an initial red target and holding back the manipulandum. The resulting difference image for the ith presentation was expressed as a percentage change from the “baseline.” Thus the percentage change in reflectance was

\[ D_{i,J}(J) = \frac{E_{i,J}(J) - B_{i,J}(J)}{B_{i,J}(J)} \] (1)

where the mean evoked response was

\[ E_{i,J}(J) = \frac{\sum_{t=2000}^{1000 \text{ ms}} U(J)}{N} \]

is the number of frames in the interval (2,000, 3,000) and similarly for the mean baseline response \( B_{i,J}(J) \). Four hundred to 1,200 images corresponding to all behaviorally correct trials were collected per experiment.

Data from some trials needed to be rejected as outliers, either from excessive movement of the monkey’s torso, which could move the brain slightly, or from an error in the data collection system. Failure to perform this rejection could result in a topography that would be dominated by the gargantuan signal from one aberrant trial. This rejection was performed off-line by an automated algorithm. A mask was superimposed on each of these images solely to perform off-line automated trial rejection (Fig. 3). The mask served to exclude large blood vessels and dimly illuminated cortex from the rejection procedures. The masked image was computed with the following heuristic. The mean reference image (Fig. 3A) on a pixel-by-pixel basis of the −26–52 reference images were computed. From this average image, the mean ± SD of all its pixel values was computed. The pixels of the image were thresholded to 1 if they were one-half of a SD greater than the mean to form the mask and to 0 otherwise (Fig. 3B). This mask excluded the larger blood vessels. This binary mask was then multiplied on a pixel-by-pixel basis with the individual difference images from each trial and the mean ± SD of this masked collection of pixels was thus computed. The distribution of the means of the masked regions followed a reasonable approximation to a normal distribution (Fig. 3D), and only trials that fell within one SD of the mean were further analyzed. A plot of the mean versus the SD yielded a parabolic-like curve, which was further utilized for automated rejection (Fig. 3D). Points that had SDs within 0.1% of the value 0 were rejected; such trials arose from an error in the data collection software and were <1% of the total trials. This parabolic relationship is expected from a normal distribution of the pixels’ values within each image and could be exploited in the future for additional higher order noise based analysis. In short, trials for which the mean evoked signal was >1 SD from the mean of all evoked signals were rejected to remove outliers. These varied between 10 and 20% of the behaviorally correct trials. This automated approach differs from earlier studies for which trial rejection was performed manually (Grinvald et al. 1991) or not at all (Vneek et al. 1999).

The mean image for each stimulus condition was computed resulting in nine average images per experiment corresponding to the nine fixation points. Parameter maps were constructed using standard linear regression methods (PROC GLM, SAS, Durham, NC) on individual pixel values (Fig. 4). The nine average images in units of percentage change in luminance (units of %) were used. For every pixel, the equation

\[ D_{i,J}(J) = \alpha_{i,J}(J)E_{i} + \alpha_{i,J}(I)E_{i} + \beta_{i,J} + \epsilon_{i,J} \] (2)

was evaluated, where \( D_{i,J}(J) \) is the ith trial’s change in reflectance for the \((I,J)\) pixel (%), \( \alpha_{i,J}(J) \) and \( \alpha_{i,J}(I) \) are the slopes of the regression for each pixel (%/°), \( \beta_{i,J} \) is the intercept for each pixel (%), \( \epsilon_{i,J} \) is the error values, and \( E_{i} \) and \( E_{i} \) are the fixation point (and stimulus center) position. This equation defines a plane with a maximum slope of \( \sqrt{\alpha_{i,j}^2 + \alpha_{i,j}^2} \) at an angle of \( \theta \) = arctan \( (\alpha_{i,k}/\alpha_{i,j}) \) relative to the x axis [indices \((J,J)\) omitted here for clarity]. As the optical signal is the negative of the expected rate of neuronal firing (Shtoyerman et al. 2000), the angle maps were constructed by multiplying each slope parameter by −1 prior to computing the quadrant for each arctan. The same parameter maps were obtained whether the average single condition images were used or all the individual trials were used in the regression, presumably because the error is approximately a normal distribution about the mean. Generally the average single-condition images were used to reduce computational requirements. Regions of interest (ROIs) were chosen for simple computations of means and SDs as described in RESULTS. A Monte Carlo analysis was used to establish the error for this entire analysis. In summary, the BNA was
devised to examine the changes in the optical signal from a defined baseline and is analogous to electrophysiological studies where the changes in firing rate relative to baseline are assessed (Read and Siegel 1997).

RESULTS

An image of M1R’s exposed cortex (Fig. 2A) taken with green (540 nm) illumination reveals the angioarchitectonics of the inferior parietal lobule (Figs. 2B and 7A). To reduce the contribution of the blood vessels to the signal and to emphasize the oxygenation signal (Shtoyerman et al. 2000), the cortex was imaged at a wavelength of 605 nm with a modified macroscope (Ratzlaff and Grinvald 1991) at a depth of 500 μm.

Prior single-unit studies have established that both area 7a and DP neurons have “gain fields” (Andersen et al. 1985, 1990; Colby and Goldberg 1999; Read and Siegel 1997). The concept of a gain field means that the amplitude of a response to a visual stimulus can be increased or decreased by the position of the eye in the orbit. To determine if there was a cortical topography of the gain field, two monkeys performed the motion detection task with the fixation point placed in one of nine locations in a 20 × 20° grid (Fig. 1C) while a 13 × 8 mm region of cortex was imaged. An expansion navigational optic flow stimulus was presented 2,000 ms after fixation point onset and was always centered over the fixation point.

Time course of optical signal

In the inferior parietal lobules of the monkeys performing the task, the time course of the optical signal differed from that typically reported in primary visual cortex in behaving animals. In primary visual cortex studies, the initial event triggering the alteration in blood flow that underlies the optical signal is the actual visual mapping stimulus (Shtoyerman et al. 2000). In the reaction task used here, there were multiple retinal and extra-retinal events that could alter the neural activity of inferior parietal lobe and hence the hemoglobin and optical signal. The initial relevant event in the recording sequence is the onset of the fixation point closely followed (<500 ms) by the saccadic eye movement to the fixation point and the hand pulling the key. Both area 7a and DP neurons are sensitive to eye position, fixation point onsets, and the planning of motor activity (Andersen et al. 1985, 1987, 1990; Siegel and Read 1997a), so it was not unexpected that these three events taken together were correlated with changes in the optical signal measured at 605 nm (Fig. 6). The ROI in the two images is illustrated in the line drawing above each time course. Tem-
temporal signals were computed by spatially averaging an $2 \times 2$ mm square region of cortex but not averaging in time. Often, but not always, there was a negative dip in the optical signal followed by a positive overshoot (e.g., dark thick line of Fig. 6A). The timing and amplitude of the initial changes over the first 1,000 ms of the trial was variable across experiments reflecting the uncontrolled behavioral state prior to fixation (cf. Fig. 6, A and B, for $M1R$ and $M2L$, respectively.) Variation was found both within animals and within cortical areas, hence the differences in Fig. 6, $A$ and $B$, were not simply a result of the cortical region or animal studied. The baseline period from $-1,000$ to $0$ ms before the stimulus was used to normalize the optical signal, as complete behavioral control was obtained just before this interval and the time course was reasonably similar.

Based on gain field single-unit work (Siegel and Read 1997a), the optical signal should modulate as a function of the position of the eye in the orbit and the visual stimulus. To evaluate the optical correlate of the gain field effect, expansion or compression flow stimuli were presented in a $2 \times 2$ factorial design with either up or down fixations in $M1R$ and $M2L$. The flow stimulus began 2 s after the fixation point and was centered over that location (Fig. 6). Although there is variability in the time course prior to the $(-1000,0)$ interval, at that time, the time courses converge indicating that the optical signal is similar across the different fixations. For the area DP region of Fig. 6A, at $-1,000$ ms after stimulus onset, the optical time course depended on the type of optic flow for upward fixation (cf. the heavy and thin black lines). The differential response to the optic flows was also found for downward fixation (cf. heavy and thin gray lines.) For the 7a region of Fig. 6B, the dependence of the optical signal on the type of optic flow is best seen for the downward (gray lines) fixation. For this particular patch of cortex, there is a weak dependence of the signal on the visual stimulus.

Across experiments, maximal differences were seen in the 2,000 to 3,000 ms interval following the onset of the visual stimulus. Hence the 2,000 to 3,000 ms interval after flow onset was used as a measure of the underlying visually evoked neural activity; optical measurements were expressed as the percentage change from the baseline signal and were the basis of the baseline normalization analysis.

This type of experiment was repeated over 10 times in $M1R$ and 6 times in $M2L$. The reflectance signal depended on the expansion and compression stimulus as well as eye position. The modulation depended on the position on the cortex. Indeed this optical tuning in area DP is the first evidence for optical flow selectivity in DP. These results suggest a mapping of optical flow as well as gain fields across the inferior parietal lobe, which serves as the basis of another study under preparation (Raffi and Siegel 2002). The remainder of the current report only examines the effect of eye position on the expansion optic-flow-evoked response.

**FIG. 5.** Gain field maps for the crown of the inferior parietal lobule. $A$: parameter map for the direction of the maximal gain field response $\arctan(-\alpha_y, -\alpha_x)$. Area 7a and area DP have representations of the lower and upper gain fields, respectively. As one progresses counter-clockwise from the ventral part of 7a, the gain field tuning goes clockwise from lower left to upper right angles of gaze. To compute the final map, the slopes were multiplied by $-1$ prior to computing the angle, to correct for the optical signal being the inverse of the expected neural activity (Shinoyama et al. 2000). Inset shows the color direction scale. Contralateral (red) is to the left and ipsilateral (blue) to the right of the colored circle. The thin squares show the region of interest. These data were collected 19 days after chamber placement. $B$: parameter map for the direction of maximal gain field response for day 63. Data of Fig. 6, $A$ and $B$. Again, area 7a represents upper field and DP represents lower field with a horizontal gradient running dorsal to ventral. (The thin dashed line indicates the lower and right edges of the cortex studied in $A$.) $C$: parameter map for the direction of maximal gain field response for day 18. The angle was derived from horizontal and vertical coefficient maps for data of Fig. 7, $D$ and $E$, respectively. (Datasets for $A$: 3/20/2000/g; $B$: 05/02/2000/gm; $C$: 19/03/2000-gm.)
Cortical topography of optical signal

To explore the dependence of the reflectance on eye position, only expansion optic flow was used. The monkeys performed the fraction of structure detection task for nine different fixations on a 20×20° grid (Fig. 1C). In each case, the expansion stimulus was centered over the fixation point. Two experiments in M1R are presented in Figs. 2/4 and Fig. 7. For M1R, averaging across all fixation conditions, the modulation in the reflected light over the baseline was −0.5% and varied across the cortex (Figs. 2C and 7B). There was a smaller (−0.1%) amplitude light evoked response that depended on the monkey’s eye position (Figs. 2D and 7F). The reflected light varied both as a function of the particular eye position and the particular location on the cortex, suggesting there was a cortical topography for the gain field. The two experiments performed 1 day apart have similar effects in the single condition maps (cf. Figs. 2 and 7). Thus when the fixation and the stimulus were at the upper right on the screen (10°,10°), a bright signal was found at the right portion of area 7a. When the fixation and stimulus were at lower left on the screen (−10°,−10°), a bright signal was found in the right portion of DP (Figs. 2D and 7F). There was a clear border between 7a and DP at the blood vessels that runs across the middle of the images. By low-power microscopic examination, it was determined that the superior temporal sulcus did not extend that far dorsally, so that the border ran under the large vessel but across a flat cortical surface. Thus in both experiments there appears to be a discontinuity in the representation underneath this blood vessel.

To combine the data from these nine maps, the mean optical

FIG. 6.  Time course of the optical signal. The optical signals were averaged for −2×2 mm of cortex. To determine if the visual responses depended on both the visual stimulus and eye position (i.e., gain field), the response to 2 different optic flows centered on the fovea was obtained in a 2×2 factorial design with two different angles of gaze (0,10°) and (0,−10°). The animal indicated a change in the fraction of structure for the optic flow. The time course diverged for the different conditions after −500 ms. The first gray bar indicates the period that the baseline was computed; the second gray bar in B indicates the time that visual responses were assessed. The time −2,000 ms corresponds to the fixation point onset; optic flow onset occurs at 0 ms. The brightness of the lines is used to encode fixation up vs. fixation down; the thickness of the lines are used to indicate expansion versus compression. A: data from M1R. The sketch shows the relationship of the region of interest in the dorsal prelunate area (DP) to the vasculature. There is a clear difference in the amplitude and time course of the signal for the expansion vs. compression stimulus for the upward gaze position. Altering the eye position alters the difference between the expansion and compression stimulus. B: data from M2L. The sketch shows the relationship of the region of interest in 7a to the vasculature. There is a clear difference in the amplitude and time course of the signal for the expansion vs. compression stimulus for the lower gaze position. Altering the eye position alters the difference between the expansion and compression stimulus. All data were expressed as a 0.1 percentage change from the baseline time period. Error bars are SEs. The small bar in each sketch is 1 mm. C: the task events are indicated relative to the time course in B. The change to unstructured optical flow occurred at a random time in the interval [4000, 5000 ms] followed by the key release in an additional [150, 800 ms] time window. The change to unstructured motion and the key release occurred after the end of optical data collection.
signal at every pixel was linearly regressed on the orbital position using the baseline normalization analysis (METHODS).

Maps of the regression parameters were constructed. The intercept parameter map (Figs. 4A and 7C) is the change in measured light expected when the monkey was fixating straight ahead and the stimulus was over the fixation point. The map of the vertical slopes (αx) of the regression (Figs. 4C and 7E for M1R) illustrate how the optical signal depended on the vertical fixation position. DP had predominantly negative values for the vertical regression coefficient, whereas 7a had positive values. This means that fixation in the upper visual field leads to smaller (i.e., more negative) optical signals in DP. Similarly, the positive vertical coefficient values in area 7a indicate a maximal reflected light response for upper field fixations. There is also a horizontal eye position dependence of the reflected light (αy) which can best be seen in DP (Figs. 4B and 7D, which depict the horizontal slope, αy). For example in Fig. 4B, most of area 7a and DP have similar horizontal tuning except for the most lateral part of DP, which is darker.

The horizontal and vertical coefficient parameter maps were transformed from rectangular to polar coordinates (METHODS). In polar coordinates, each pixel was represented by a polar vector with an amplitude (Fig. 4D, data not shown for Fig. 7) and angle (Fig. 5, A–C). The “amplitude map” was constant across the imaged regions outside of the blood vessels and suggests that the optical signal strength is constant across the imaged region. To compute an “angle map” that reflected the underlying neuronal electrical activity, the sign of the slopes was changed to account for the negative relationship between the 605 nm signal and the neuronal signal (Shtoyerman et al. 2000); the angle map illustrates the gain fields’ dependence on eye position and cortical location. The angle map had two clearly demarcated gain fields within the 13 × 8 mm image. ROIs are indicated for each map; the angle corresponding to that ROI is indicated in small type above and below each image. According to the angle map, neurons in DP should increase firing rate when a visual stimulus was presented over the fovea while the monkey was looking up; similarly neurons of 7a should be best activated when looking down and to the left. This 7a/downward and DP/upward split of the imaged regions was modulated within each region by the horizontal eye position. As one progresses counterclockwise from ventral DP, the direction of gain field tuning progresses clockwise. As the strength of the horizontal modulation was variable between the two experiments, the smoothness and completeness of the representation varies. A more lateral image of the gain field map taken from a third experiment in M1R is illustrated in Fig. 4F; the gain field extends to the most posterior portions of DP that can be imaged; in this one lateral view, there appears to be another shift in the gain field in the more lateral portions of DP and 7a. In each of the three examples of the gain field map of M1R (Fig. 5), upper and lower field gain breakdown is seen. The horizontal tuning is weaker and more variable between these different experiments.

Comparison of maps across days

This main result of a division in the gain field between area 7a and DP was reproduced within M1R by collecting 14 maps over a period of 78 days. Two ROIs, one in area 7a and one in area DP were initially chosen for analysis (Fig. 8). The ROIs were placed so as to be observed in as many day’s data as possible (for comparisons between days) and to be roughly the same distance from the junction of the intra-parietal and lunate sulci as well as equidistant from the large vessel in the middle of the chamber. This was to make the effect of vessel induced pulsations equivalent for the two locations. The medial-lateral position was arbitrarily selected. A ROI was chosen to be -2 × 2-mm square. The circular mean and standard error of the gain field for the ROIs was 283 ± 11° for area 7a, and 99 ± 8° for area DP. The locations and means for six additional ROIs were computed as summarized in Fig. 8 to sample across the cortex in an unbiased manner. Using the total of eight ROIs, there are a few key observations. The area 7a and DP regions clearly had differences in terms of upper and lower field representation at all positions. There appeared to be a slight trend for further modulation along the horizontal direction within each cortical field which might have been obscured by the averaging across days.

The measurements for the ROIs in area 7a and DP were compared for the most lateral position with a Watson’s F test for circular means and were significantly different (P < 0.01, DF = 11). The mean difference between the 7a and DP tuning on a day by day basis was 190 ± 17° and was significantly different from a uniform circular distribution. Thus DP and 7a have significantly different gain field representations for these two ROIs, with DP expected to have stronger electrophysiological responses for upper fixations and area 7a having a stronger expected gain field representation for lower field fixations. Additional paired comparisons were made for each matched medial-lateral positions and each was found to be different for the upper and lower positions.

Monte Carlo analysis

To get an independent estimate of the reproducibility of the measurements and analysis within a day, Monte Carlo methods were used (METHODS). The data from some of the full nine position gain field experiments were tested. The core idea behind the Monte Carlo study was to test the hypothesis that the maps were specifically linked to the stimulus conditions. More formally, the null hypothesis was that there was no relationship between the stimulus presentation and the resulting maps.

To test this hypothesis, two manipulations were compared. In the first manipulation, half of the data were randomly selected from the original data and the map computed. The other half of the data were used for another map. The second manipulation was to randomly assign a stimulus condition to each trial for half the data and compute the map; the remaining

FIG. 7. A second gain field map recorded from M1R. A: green light image of cortex, B: cocktail response (average response) of cortex across all gaze angles, C: intercept parameter map of regression, D: horizontal coefficient of regression, E: vertical coefficient of regression, F: the single condition maps varies both as a function of the location on the cortex and the eye position. The average evoked response displayed for each position had the cocktail response subtracted. The location of each image indicates the position of the fixation and optic flow stimulus. The number in the top left corner indicates the gray scale range. (Data set for 19-03-2000/grand.)
data were used to construct another map continuing this randomization. (Formally, one would say that the data were randomly assigned to the stimulus conditions without replacement.) Thus the specific relationship between the actual data and the stimulus used to collect it was destroyed. Maps were then constructed for the resulting “new” data set (Fig. 9).

Each pass through the data set then provided four new maps; two were made respecting the relationship between the data and the stimuli and two with disrupted relationships. Two populations of parameter maps were constructed in this way, and the stimuli and two with disrupted relationships. Two were made respecting the relationship between the data and the stimulus used to collect it was destroyed. Maps were then constructed for the resulting “new” data set (Fig. 9).

For the data of Fig. 2, this procedure was repeated for 115 surrogate sets yielding 230 new maps. Additional ROIs could have been chosen; however, the Monte Carlo analysis was too computationally intensive to permit this. Maps were generated and the same ROI were sampled. Circular means and errors were computed. A comparison in the two distributions was computed using a using a circular Watson $F$-test analysis. (Oriana Software, Kovach Computing Services, Anglesey, Wales).

For the data of Fig. 2, the bootstrap circular mean and standard error was $132 \pm 2.2^\circ$ for the area 7a ROI and was $42 + 1.8^\circ$ for the area DP ROI. For comparison, if the optical measurements were randomly assigned to a stimulus, the circular standard error had a high value of 76 and 78° for DP and 7a, respectively. The distribution of directions was essentially flat for the randomized data. These random versus the bootstrap distributions were significantly different ($P < 0.0001$).

Similar results were found for two other days tested a few weeks apart showing that within a single day, the maps had within day errors of $<5^\circ$.

**Replication in a second monkey**

**Gain field maps.** The gain field map was replicated in two hemispheres of a second animal using the BNA (the data of M2R and M2L). The quality and number of the maps in M2R was few and of poorer quality than the other maps due to the subdural bleed. Nonetheless the primary result of an upper-lower gain field separation between 7a and DP could be confirmed (Fig. 10A for M2R). The reds and yellow of the gain fields in area 7a indicate lower field effects while the blues and purples in DP indicate the upper gain field. As before, the numbers at the edge of the images represent the average for the ROIs, which appropriately correspond to the upper and lower gain fields. In M2L, the chamber placement was more lateral and the image is at a higher magnification. Hence the union of the IPS and LS are beyond the left of the panel (Fig. 10B). Gain field maps were again obtained with the upper and lower gain field divisions. The periodicity seen in M2R (Fig. 10A) is perhaps reminiscent of ocular dominance periodicity in primary visual cortex. However, the present study does not provide any source for this structure and it was only seen in this one map.

**ROI analysis.** The circular mean and SE data for ROIs of M2R in 7a and DP were $240 \pm 23$ and $75 \pm 8^°$, $n = 4$, respectively; these two ROIs were significantly different ($P < 0.01$, DF = 6, Watson’s $F$ test). In M2L, the ROIs were picked to be similar to that of M1R with the means for the ROIs being $310 \pm 26$ and $94 \pm 19^°$, $n = 5$, for 7a and DP, respectively; the ROIs were significant at $P < 0.01$, DF = 8, Watson’s $F$ test. The upper and lower breakdown between area 7a and DP was found in all these data to agree for all three hemispheres.

**Monte Carlo analysis.** The reproducibility of the maps within a day using the Monte Carlo analysis in M2R was similar to that of M1R (circular SE of $4^°$). A Monte Carlo analysis was also performed in M2L with an approximately doubled error. Thus we estimate that in three hemispheres the error of our measurement within a 2 × 2-mm region is $\sim 4^°$.

In summary, our optical recordings have shown area 7a and area DP have gain field tuning. At least for the two regions imaged, there appears to be a division of labor with 7a representing the lower gain field and DP representing the upper gain field. There is also modulation with the horizontal eye position.
Electrophysiological confirmation of eye position maps

Typically, for optical imaging experiments, single-unit recordings are made to “verify” the optical responses correspond to classically defined electrophysiological responses (Shmuel and Grinvald 1996; Shtoyerman et al. 2000). This approach has worked very well in V1 where there is a columnar architecture for orientation and ocular dominance. The optical signal only indicates reflected light from the upper layers, and it is reasonable to assume that the bulk of the changes in reflected light arise from metabolic changes in the smallest processes with the largest surface-area to volume ratio (Frostig et al. 1990; Malonek and Grinvald 1996; Malonek et al. 1997).

Low-impedance electrodes were introduced through the artificial dura and measurements of gain fields were made. Recordings were only made in one animal, M1R; the number of penetrations with the artificial dura was minimized because the electrodes caused a small pinhole in the artificial dura. In our hands, the artificial dura often self-sealed, but at times, air could seep in under the artificial dura. This lead to concerns about subdural infections compromising the continuation of the studies; although this never occurred. As well, even though the

Fig. 9. Monte Carlo analysis of parameter maps. The data of Fig. 2 were analyzed multiple times either respecting (A) or disrupting (C) the relationships between the stimuli and optical images. B shows the original parameter map and the ROIs used in the quantified portion of the analysis. In A, the upper and lower field breakdowns are maintained between 7a and DP, although the colors are not precisely the same for each exemplar generated by choosing data at random from the original data set. In C, the tuning varies widely between each exemplar. D: distribution of directional tuning for the ROIs. The labels “rand DP” and “rand 7a” refer to the exemplars where the relationship between the collected images and stimuli are randomized (i.e., disrupted). The labels “DP” and “7a” refer to the data where the relationship between the 2 is respected. These circular distributions are compared using a circular $\chi^2$ test (see text).
size of the bubbles were small (being ~1 mm in diameter), they precluded any optical recording from 2 day to 1 wk while they were being reabsorbed.

The multiunit response to the alteration of eye position (Fig. 11) appeared similar to the responses obtained from single-unit recordings as reported elsewhere (Read and Siegel 1997). Gain fields in area 7a may be linear or humped (Read and Siegel 1997), and so a quadratic stepwise regression model was used; the stepwise selection only permits coefficients significant different from 0 at $P < 0.05$ to remain in the model (Read and Siegel 1997). Both the peristimulus time histograms as well as the regression surfaces are illustrated (Fig. 11). After the approach from single-unit studies on optic flow in the inferior parietal lobule (Phinney and Siegel 2000; Read and Siegel 1997), baseline activity was evaluated for 1 s prior to stimulus onset. The response of the multiunit activity was evaluated over 1 s immediately after stimulus onset to combine phasic and tonic responses. To reduce variability caused by any instability of the recordings, the baseline rate was subtracted from the evoked response on a trial-by-trial basis.

Sample recordings from area 7a (Fig. 11, A and B) and DP (Fig. 11, C and D) illustrate the type of tuning found electrically. The gain field tuning of these cells was similar to that reported elsewhere with these stimuli (Read and Siegel 1997).

Cells were recorded from a 5 mm strip in DP (9 penetrations) and a 1.25 mm strip in 7a (5 penetrations) in hemisphere
**MIR (Fig. 12A).** The region from which the area 7a recordings are taken is indicated by ■, while the region for which the DP recordings are taken is indicated by □. Twelve of 54 area 7a multiunit recordings (22%), and 14/56 (25%) of area DP multiunit recordings were found to significantly depend on the position of the eye in the orbit. In 7a, half of the neurons had significant linear coefficients, while the other six had only significant quadratic components. In DP, 11 of the cells only had a significant linear component; 3 were purely quadratic and 2 had both a linear and quadratic components. For the purely linear cells, the direction of the gain fields could be summarized by the vertical and horizontal slopes; for the purely quadratic cells, the gain field was symmetric in the vertical and horizontal and the gain field was assigned a coordinate of (0,0°). For the neurons with both a linear and quadratic component, the gain field was appropriately corrected to place the peak in the appropriate quadrant (Fig. 12B). The 7a recordings sites were mostly in the lower contralateral lower field while the DP recordings were mostly in the ipsilateral upper field.

As a population, the area 7a and DP neurons were statistically different. The significance between the DP and the 7a population regressions were computed three different ways. First, a Mann-Whitney test was used to determine if each of the regression coefficients were different across areas; all effects were significant at $P < 0.05$, except for the second-order “$y” coefficient ($\alpha_{yy}$). Second, a canonical discriminant analysis (SAS PROC CANDIS, Durham, NC), which considers a linear combination of all five regression coefficients, was used. The sum $0.08* + 16.3*_{y} + 4.16 *_{y} - 17.4 *_{xx} + 1.44 *_{yy}$ was significantly different for the two populations at $P < 0.001$. Last, to determine the eye position for which the activity was maximal, the slope coefficients from each recording were converted into polar coordinates. The electrophysiological circular mean and standard error was $231 \pm 30^\circ (n = 5)$ and $27 \pm 30^\circ (n = 10)$, for 7a and DP, respectively. The directional tunings for the two areas were significantly different ($P < 0.05$; DF = 3, Watson’s $F$ test). Thus the directional tuning from the electrical recordings was able to discriminate between area 7a and DP, a novel finding not yet reported from electrophysiological recordings. The lack of any report of this in earlier studies may be because of the poor spatial electrode localization in earlier work obscured such effects.

Figure 12 illustrates both the average signal for the optical ROI and for the electrophysiological data. In comparison to the optical data, the multiunit data replicated the upper and lower gain field divisions between 7a and DP; the ipsilateral-contralateral distinctions did not match that of the optical data. This may be due to the disparity in location of the optical and electrical recording sites or differences in the source of the electrical and optical signals (Logothetis et al. 2001). Ideally, simultaneous, multisite, tangential electrode penetrations should be made within area 7a and DP to precisely match the two types of data.

**DISCUSSION**

These experiments provide evidence for a functional architecture of orbital gain fields in area 7a and area DP of the inferior parietal lobe of the behaving monkey.

**Relationship between optical signal and underlying activity**

Key to the demonstration of these maps was the utilization of intrinsic optical imaging at 605 nm. The signal at this wavelength scales with the level of reduced-Hb (Frostig et al. 1990; Malonek and Grinvald 1996; Malonek et al. 1997). The optical signals mostly mirror the metabolism of the small neuronal elements such as presynaptic fibers, boutons and dendrites (Logothetis et al. 2001). Those elements have the smallest diameters and hence the largest surface-area-to-volume and maximal contribution to the oxidative metabolism. Hence the intrinsic optical signals are most similar to local field potentials (Logothetis et al. 2001). The question is how much of this signal is above threshold and will be impressed onto the spiking neuronal activity. There is a substantial literature in primary visual cortex that supports the assertion that intrinsic signals ultimately reflect outputs from cells (i.e., spiking). The principles underlying the source of the optical signal derived from striate studies should also be applicable to the current studies in inferior parietal lobe.

Our electrical measurements indeed confirm the optical results. The upper and lower gaze field division of representation between area 7a and DP are found with both methodologies. The optical parameter maps in one chamber were confirmed using multiunit electrophysiological recordings. Multiunit recordings were made as the tip impedance needed to be low ($\sim 300$ kΩ) to permit piercing of the artificial dura. The percentage of selective cells was lower as compared earlier studies (Andersen et al. 1990; Read and Siegel 1997; Siegel and Read 1997a), perhaps because the stimuli parameters (e.g., retinal...
stimulus location, type of optic flow) used in the present study were not optimized for each recording site. A second reason for the lower number of significantly tuned recordings between the two studies is that multiunit data can sum the contributions of single cells with disparate tunings resulting in a broadened and nonsignificant response. Despite these technical limitations, there was a reasonable match between the multiunit cell physiology and the optical maps.

Confirmation of finer details of the maps, such as the horizontal modulation of the gain field, were not made in that it would have required repeated penetrations and damage to the artificial dura. Given that the optical methods provide a detailed map and the substantial body of evidence supporting the neural underpinnings of these maps, we were restricted and conservative in the electrical recordings; mostly serving to verify the signal in two ROIs.

Time course of the optical signal

The time course of the signal in this association cortical region shows novel properties as compared with earlier measures of the striate cortex. In our studies, the initiation of the task, known from electrophysiological data to activate parietal neurons (Andersen et al. 1990; Motter and Mountcastle 1981; Read and Siegel 1997; Siegel and Read 1997a) led to a biphasic wave on which the test visual responses ride. Once behavioral control was achieved, the baseline optical signal was similar across different fixation conditions. When the optic flow stimulus started, there was a difference in the signal starting at ~1,000 ms for the expansion versus the compres- sion stimuli; this difference depended on whether the animal was looking up or down as well as the region of the cortex. [The interaction between the optical flow and the eye position tuning is the subject of work in progress (Raffi and Siegel 2002)]. This later visual signal was dependent on the position in the orbit in a manner reminiscent of gain fields described from electrophysiological studies. Thus both visual input and eye position contributes to the optical response.

Baseline normalization analysis model

For any single location, the strength of the optical signal depended on the eye position in the orbit. This dependence was modeled as a linear function. Other models might have been used, as ~40% of inferior parietal lobule neurons have peaked nonlinear gain fields (Andersen et al. 1985; Read and Siegel 1997). In preliminary analysis, higher-order functions such as a quadratic were used. The qualitative results in terms of an upper and lower field breakdown between area DP and 7a were similar; it was difficult to justify the higher-order model on a pixel-by-pixel basis as the signal to noise was low. Hence the data were modeled with the linear regression, and a Monte Carlo analysis was used to validate the model parameters.

The effect of eye position on the visual response was visualized with parameter maps. A positive dependence of the expected neuronal responses on eye position was found in DP, whereas the negative relation was found in 7a. This does not mean that DP exclusively represents upper field eye positions. Rather the results indicate that DP is modulated by both upward and downward eye positions and that upward positions leads to an increase in neural activity with downward leading to a decrease in activity. Similarly 7a is modulated by both upper and lower eye positions with an opposite sign to that of DP. Interestingly, these parameter maps indicate that when the point of regard for the eyes is in the upper visual field, both areas should be modulated; similarly both are active for lower fixations. Thus either projections from DP or 7a can provide information needed by recipient cortical zones. It is also possible that areas such as area 46 and 8a that receive interdigitated projection from both DP and 7a (Andersen et al. 1990) could use these complementary signals in a push-pull fashion (cf., Grossberg and Kuperstein 1986). It is tempting to speculate that this differential signal computed from both 7a and DP could provide a more reliable signal to other cortices representing visual space or planning motor behaviors.

Nature of the topographic representation of the gain field

The gain field topography was found in three hemispheres of two animals. In all three monkeys, the upper and lower gain field representation was found distributed between 7a and DP. This was shown using the nine position gain field test in all three animals. The upper and lower representation was the strongest topography, whereas the contra/ipsi-lateral representation was markedly weaker. One possibility that could explain the weaker contra/ipsi-lateral representation is that it is in the more lateral 20 mm of 7a and DP that cannot be imaged in these experiments due to the chamber placement. For example, the ipsilateral lower gain fields could extend right up to the area 7a/7b border. The scant data that were acquired suggest that this is not the case (Fig. 5B), although additional data are certainly needed to resolve this issue. In some experiments, the contra/ipsilateral modulation is clear, and there appears to be an almost complete representation of the contralateral gain field; whereas in others the contra/ipsilateral representation is scarcely evident. The hemodynamic response and/or the noise in the optical signal may preclude a repeatable measurement or there is plasticity in this portion of the representation. Imaging with voltage-sensitive sensors that more faithfully represent the signals in both space and time may resolve whether there is indeed a contra/ipsi representation.

In the animal for which extensive mappings were performed, the maps were not precisely the same day to day as evaluated across the 3 mo of recordings. In comparison, the fine structure of ocular dominance is exquisitely reproducible across months of recordings in striate cortex (Shohtyarman et al. 2000). The experimental procedures are essentially the same in the striate study as in the present study of the inferior parietal lobule; eye position control is similar, the wavelength of light is the same; the species are the same. Possible sources for the variation in the inferior parietal lobule maps appear to be linked to the cortical areas under study; the inferior parietal lobule areas receive both highly processed visual signals from dorsal and ventral stream areas as well as feedback from the frontal areas. It is clearly possible that the inferior parietal lobule maps are modulated by the state of the animal’s attentional, intentional, or vigilance systems. The possibility that the monkey’s behavioral state could cause plasticity on a day-to-day basis needs to be considered. Specific experiments to address the effect of these factors on maps in the inferior parietal lobule will be necessary.
The gain that lies ventral to the recording chambers that have not been functionally periodic (Shtoyerman et al. 2000). The inferior visual or motion direction) found mapped within the retinotopy [e.g., V1 (Tootell et al. 1982), MT (Albright et al. 1984), or have had retinotopy as their most coarse representation basis other cortical maps in the visual system described to present a functional architecture for the inferior parietal lobe association cortex. All of these subdivisions by some into a dorsal and ventral area. Others considered V4 one cortical area. Even today there is not a accepted opinion of whether V4d and V4v are one or two areas (Pinon et al. 1998; Tootell and Hadjikhani 2001; Van Essen 2003). Thus the designation of the areas 7a and DP as those with lower and upper gain fields respectively should be taken as an operational and functional definition, which will require additional anatomical analysis.

**Novel functional architecture**

The topographical maps are evidence of a functional architecture for the inferior parietal lobe association cortex. All other cortical maps in the visual system described to present have had retinotopy as their most coarse representation basis [e.g., V1 (Tootell et al. 1982), MT (Albright et al. 1984), or MST (Tanaka et al. 1986)] with columns (e.g., ocular dominance or motion direction) found mapped within the retinotopy with a 1 mm periodicity (Shtoyerman et al. 2000). The inferior parietal lobule maps are novel in that they are the first primate cortical visual map that uses eye position as its most coarse basis. Indeed, to our knowledge there is no report of a eye-position topography to date. The transformation from a retinotopic map to an eye position based gain map is evidence for an intermediate step in the transformation from visual to motor coordinates. The circuits subsuming the generation of this novel map likely utilize cortical feedback as 7a and DP do not have direct projections from subcortical structures that represent eye position (Siegel and Read 1997b). If the principles governing multiple scales of functional architectures in early vision hold for this association cortex, then the large-scaled gain field functional architecture described here may serve as the scaffolding on which other sensory, attentional, and intentional maps may be embedded at finer columnar scales. These distributed multi-scaled representations of visual and eye position can be then combined to construct appropriate perceptual and motor signals in recipient cortical areas (Pouget and Sejnowski 1997; Siegel 1998; Zhang and Sejnowski 1999).

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