Neural Representation During Visually Guided Reaching in Macaque Posterior Parietal Cortex

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Heider B, Karnik A, Ramalingam N, Siegel RM. Neural representation during visually guided reaching in macaque posterior parietal cortex. J Neurophysiol 104: 3494–3509, 2010. First published September 15, 2010; doi:10.1152/jn.01050.2009. Visually guided hand movements in primates require an interconnected network of various cortical areas. Single unit firing rate from area 7a and dorsal prelunate (DP) neurons of macaque posterior parietal cortex (PPC) was recorded during reaching movements to targets at variable locations and under different eye position conditions. In the eye position–varied task, the reach target was always foveated; thus eye position varied with reach target location. In the retinal-varied task, the monkey reached to targets at variable retinotopic locations while eye position was kept constant in the center. Spatial tuning was examined with respect to temporal (task epoch) and contextual (task condition) aspects, and response fields were compared. The analysis showed distinct tuning types. The majority of neurons changed their gain field tuning and retinotopic tuning between different phases of the task. Between the onset of visual stimulation and the preparatory phase (before the go signal), about one half the neurons altered their firing rate significantly. Spatial response fields during preparation and initiation epochs were strongly influenced by the task condition (eye position varied vs. retinal varied), supporting a strong role of eye position during visually guided reaching. DP neurons, classically considered visual, showed reach related modulation similar to 7a neurons. This study shows that both area 7a and DP are modulated during reaching behavior in primates. The various tuning types in both areas suggest distinct populations recruiting different circuits during visually guided reaching.

INTRODUCTION

Primates rely heavily on the visual guidance of limb movements for foraging and social interactions. They have to select a visual target, move the eyes to the target, and finally follow with the hand to the target (Desmurget and Grafton 2000). This reaching process requires transformations between coordinate systems in time with multiple computational steps involved (Shadmehr and Wise 2005). Areas of the posterior parietal cortex (PPC) play a critical role in the transformation between vision and action by combining signals from various cortical areas.

Eye position modulates visual neural responsiveness of PPC neurons (Andersen and Mountcastle 1983; Andersen et al. 1985, 1990b; Read and Siegel 1997; Salinas and Sejnowski 2001). Reaching studies of the parietal reach region (PRR) suggest that visually guided arm movements are planned in eye-centered coordinates (Batista et al. 1999; Buneo et al. 2002; Scherberger et al. 2005; Snyder et al. 2006). In this study, eye position was either varied together with the reach target so that reaching was made to foveated targets, or fixation was kept constant on the center so that reaching was made to nonfoveated targets. The goal of this study was to explore the specific spatial and temporal relationships between visual, preparatory and reach signals in two regions of the PPC. Area 7a and the nearby dorsal prelunate (DP), which is at the most posterior end of the PPC and believed to be strongly visual, were examined. The DP region has strong feedforward connections to area 7a (Andersen et al. 1990a; Cavada and Goldman-Rakic 1989a), but also receives signals from other parietal, frontal, and extrastriate visual areas (Stepniewska et al. 2005).

The first hypothesis tested whether eye position and retinotopic tuning of 7a and DP neurons were affected by task phase, especially preparation and initiation of the reaching movement. If different mechanisms or inputs contributed to various signals in PPC such as eye position and motor planning, we might expect differential effects on spatial tuning for the visual, preparatory, and movement initiation phases of the task. The second hypothesis examined the spatial parameters during preparation and initiation of the reaching movement between the two task conditions, that is, whether the reach targets were foveated. Planning and executing a reach movements to targets in the same body-centered, but different eye-centered coordinates, might yield distinct spatial tunings of 7a and DP neurons because both areas are strongly altered by gain fields.

We implemented an “approach” (Gardner et al. 2007), also called “radial” (Fattori et al. 2005) reaching movement, in which the hand starts from a position close to the animal’s trunk and moves in three dimensions (3D) toward the reach target, as used in an area 7a study by MacKay (1992). We used optic flow field stimuli as reach targets. This stimulus ensured that we activated 7a and DP neurons optimally and allowed to study the influence of the reach-related signals modulating these visual responses. The delayed reaching task evaluated visual stimulus presentation, eye position, preparation, and initiation of the arm movement activity.

METHODS

Animal preparation

Two male rhesus monkeys (M1R, 11 kg; M3R, 8.5 kg; age ~10 yr) were trained on a visually guided reaching task. All procedures conformed to the National Institutes of Health Guide for the Care and Use of Laboratory Animals; Rutgers University Animal Care and Facilities Committee approved all experimental protocols.

Each animal was prepared for electrophysiological recordings by attaching a head post and recording chamber in separate surgeries. All surgeries were performed under sterile conditions with isoflurane

3494

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The NIMH Cortex software (//www.cortex.salk.edu) displayed the stimuli, controlled the behavioral variables, and was synchronized to the analog spike collection system that was programmed using Matlab (MathWorks, Natick, MA) in conjunction with a PCMCIA-based A/D converter (NI DAQCard-6036E, National Instruments, Austin, TX) in a PC-based system.

**Stimuli and behavioral task**

The fixation dot consisted of a small (0.8° diam) red square. The visual reach targets were circular patches of moving dots (12° diam). These were either expansion (76%) or compression (24%) optic flow patches, which consisted of 128 dots (0.1° diam) with an equivalent angular velocity of 6°/s and a point life of 532 ms. The optic flow patches were displayed in one of nine positions within a 3 × 3 grid (step 12°, total 36 × 36° area).

The monkeys performed two versions of the reaching task. In the eye position–varied task (EVAR; Fig. 2A), the small fixation dot and the optic flow reach target were presented together in one of the nine positions to test the effect of eye position. The optic flow patch was presented behind the fixation dot, which was visible throughout the task. Thus the reach target was always foveated ensuring that angle of gaze and reach position varied jointly, whereas the locus of retinotopic stimulation remained constant over the fovea. In the retinal-varied anesthesia. Both monkeys had been previously used for intrinsic optical imaging of posterior parietal cortex and had imaging chambers (diameter 20 mm) implanted over their right hemisphere (Heider et al. 2005; Siegel et al. 2003) contralateral to the left hand used for reaching. This permitted visual identification of areas 7a and DP in the chamber. At the conclusion of the optical imaging studies and before recording, the transparent artificial dura was removed, and the natural dura was allowed to grow back over the brain. If necessary, systemic prophylactic antibiotics were given for this procedure (Ceftriaxone, 50 mg/kg). A stainless steel adapter was attached to the optical chamber to hold the stage and microdrive and allow precise, targeted electrode penetrations into designated areas (Fig. 1).

**Experimental setup**

During the experiment, the animal’s head was fixed with the head post attached to a specially designed primate chair that allowed free movement of the upper limbs. A touch-sensitive panel (Elo TouchSystems, Menlo Park, CA) positioned 30 or 35 cm (depending on each monkey’s arm length) from the animal’s eyes recorded the reaching endpoints. Distance from the launching position to the touch screen was 35–40 cm (depending on the end position of the target). The reach distance from the start panel to the nine end positions was not varied in a systematic manner. The experiments were performed in a completely dark room. However, a faint luminosity of the touch screen could not be completely eliminated even at the lowest brightness settings and completely black background. Thus the monkey could only perceive his hand when it had reached and partially occluded the reach target.
task (RVAR; Fig. 2B), the fixation dot always appeared in the center of the screen (primary position 0, 0°), and the optic flow target was displayed in one of the nine positions. Thus the reach target was not foveated, except for the center target, and retinotopic stimulation was varied. In both tasks, the monkeys were required to touch the targets within the 12°-target diameter.

The temporal sequence of task events was always as follows (Fig. 2C). A trial started only when the left hand rested on the touch-sensitive launching panel. Then, the fixation dot appeared and the monkey started fixating within 500 ms. After 1,500 ms, the optic flow target was displayed. Randomized between 2,000 and 3,000 ms after stimulus onset, the structured optic flow changed to unstructured motion; thus the duration of the delay period was variable. Within a 600-ms reaction time, the animal made a hand movement to the target. Once the hand landed on the touch screen, the monkey had to hold his hand on the optic flow target for 1,500 ms. The target remained in place during this period. A drop of juice rewarded the animal for successful completion of the trial.

If the monkey did not acquire fixation within the 500-ms time, the trial was aborted, and a new trial started after 500 ms. Launching the hand incorrectly, that is, too early before or too late after the stimulus changed, terminated the trial immediately. The monkey performed a minimum of 10 trials per condition (total of 90 correct responses for either RVAR or EVAR task). The two tasks were performed in separate blocks of trials with their order varied.

An infrared eye camera (ISCAN, Cambridge, MA) in conjunction with the NIMH Cortex system monitored and collected eye position noninvasively at 60 Hz. The eye movement window was kept at 4° to control fixation; this value conforms to other reaching studies (Batista and Andersen 2001; Battaglia-Mayer et al. 2001, 2005; Marzocchi et al. 2008; Scherberger et al. 2003; Snyder et al. 2006). If the monkey fixated outside this window, the trial aborted immediately.

The eye movements were examined off-line at two time points (stimulus onset and lift hand) in the two tasks. One experiment shows typical eye movement traces for two task conditions (Fig. 3). The average eye position traces (10 trials) at the lift hand event for the nine reaching locations are plotted. Although fixation was not as precise as in pure fixation tasks (Andersen et al. 1985, 1990a; Goldberg et al. 2002; Siegel and Read 1997), we could find no bias with different stimulus presentations, hence the larger 4° fixation window. In the EVAR task, no eye movements were associated with the different fixation positions at the lift hand event (Fig. 3A). Most importantly, in the RVAR task, there was no biased eye movement toward the optic flow target at the time of hand lift (Fig. 3B). The average horizontal and vertical eye position from each experiment were transformed into vectors to quantify these effects (Fig. 3, C and D). The difference in vector amplitude 500 ms before and after lift hand was computed. In the example shown, eye position shifts averaged 1° for the EVAR task and 0.8° for the RVAR task. In comparison, eye position shifts at the onset of the optic flow stimulus were on average 2.2° in the EVAR and 1.5° in the RVAR task. These findings were similar across experiments. Thus changes in eye position at the time of the reach event were minimal and could not be responsible for differences in neural activity between tasks.

Neural recordings

Neural responses were recorded extracellularly with platinum-iridium electrodes (UEPSEGSG2N5G, FHC, Bowdoinham, ME) with an impedance of 0.5–2.5 MΩ. Penetrations were oriented orthogonal...
to the cortical surface. The electrode was advanced using a hydraulic motor drive (David Kopf Instruments, Tujunga, CA). After passing through the dura, the depth of the first occurrence of neural activity was recorded, and recordings were confined to 2,000 μm from the top of neural activity. We also recorded activity when retracting the electrode to confirm depth measurements in case of dimpling. Aver-

age depth of all recordings was 1,140 ± 565 (SD) μm (n = 155). Per
penetration, about one to five units were recorded. Because the sulcal pattern of the PPC was visible through the transparent dura, the two cortical regions of interest could be located without killing the animal (Fig. 1). Area 7a was operationally defined as the cortex between the intraparietal sulcus (IPS) and the end of the superior temporal sulcus (STS) in agreement with earlier studies (Heider et al. 2005; Siegel et al. 2003). DP was defined as the region between the STS and the lunate sulcus (LS).

Neural activity was amplified (Model 1800 Microelectrode AC Amplifier, A-M Systems, Carlsborg, WA), fed through a Humbreg 50/60 Hz noise eliminator (AutoMate Scientific, Berkeley, CA), band-pass filtered (300–20,000 Hz), digitized at 40 KHz, and spikes separated off-line with spike sorting software (Off-line Sorter 1.39, Plexon, Dallas, TX). All subsequent quantitative analyses were done on the off-line sorted data. Units were isolated on-line with a dual-window discriminator (BAK, Germantown, MD) to assess neural selectivity during recording.

To obtain a sample as unbiased as possible, activity from all neurons that could be sufficiently isolated were recorded regardless of whether a neuron displayed a preference for the visual or reach aspect of the task. In about one half of all units recorded, preference for type of motion (expansion, compression, and 2 rotational fields) was tested with a centrally presented large field optic flow patch (20° diam). Most area 7a or DP neurons responded robustly to either expansion or compression optic flows as reported previously (Merchant et al. 2001; Read and Siegel 1997; Siegel and Read 1997); thus these two types of stimulus were used for the majority of units. In instances where visual preference for type of optic flow could not clearly be established from the on-line neural response, expansion flow was used.

Spike analyses

Analog data were analyzed off-line with the Plexon software, and spikes were identified by comparing waveforms over the course of the experiment in conjunction with Khoros (Khoral Research, Albuquerque, NM) and custom UNIX-based software. Spike rasters were synchronized to different task events (Fig. 2C, dashed lines), and the firing rate for the epochs of interest was calculated (Anderson and Siegel 1999; Siegel and Read 1997): 1) baseline activity during fixation before stimulus onset; 2) after stimulus onset to determine visual responsiveness (visual epoch); 3) before cue to lift (i.e., stimulus change) to determine movement prepa-
ration activity before the reach movement (preparatory epoch); and 4) after lift hand from starting panel to determine reach initiation activity (reach epoch). For the baseline, visual, and preparatory epochs, 500-ms intervals were used. For the reach epoch, a 300-ms interval was used to avoid contamination from the tactile or visual cues when the hand touched the screen.

Categorical regressions

To directly quantify the spatial relationship between the different epochs on a neuron-by-neuron basis, a multiple step procedure was followed. The individual firing rates for all four epochs was first computed. To simultaneously examine the dependency of firing rate on type of epoch and reach target position, a stepwise categorical quadratic regression model was applied. The model for the firing rate was

\[
A(x, y, E, i) = a_0[E]x + a_1[E]y + a_2[E]xy + a_3[E]x^2 + a_4[E]y^2 + b[E] + e_i
\]

\[
A(x, y, E, i)
\]

is the firing rate for the \(i\)th trial. \(E\) is the epoch under consideration, which has four categorical values, corresponding to the baseline, visual, preparation, and reach epochs. \(x\) and \(y\) are the positions of the target on the screen in degrees of visual arc. \(a_0[E]\) refers to the four categorical coefficients for the linear dependence on the horizontal position. \(a_3[E]x^2\) refers to the four possible categorical coefficients for the second-order dependence on the horizontal position. Similar terms are found for the vertical \(a_1[E]y\) and \(a_4[E]y^2\) coefficients and the interaction term \(a_{xy}[E]xy\). \(b[E]\) is the intercept that can differ for the four categorical epochs. \(e_i\) is the error for the \(i\)th trial. The coefficients (e.g., \(a_0[E]\)) were selected using a stepwise algo-

rithm that determined whether the quartet of coefficients was significantly different from zero. At the conclusion of the stepwise algorithm, only coefficients remained that were statistically significant from zero at \(P < 0.05\). The categorical regression was implemented using procedures GLMOD and REG (SAS Institute, Cary, NC). This analysis thus concluded with values that were significant at \(P < 0.05\).

TIME-DEPENDENT TUNING. The combination of significant regres-
sion parameters determined the tuning type for each neuron. Neurons with uniform firing rates across target positions (P) but different mean firing rates across epochs (E) were termed type E. Neurons with significantly different spatial parameters (\(a_x\), \(a_y\), \(a_{xx}\), \(a_{xy}\)) across epochs have multiplicative interactions between position and epoch and were termed multiplicative type E×P. These cell response fields changed shape between epochs that is, their eye position (EVAR task) or retinotopic (RVAR task) spatial tuning was altered as the task progressed. Finally, there were nonsignificant cells with neither epoch nor position effects (NS). Two other tuning types could potentially result from the categorical regression analysis but were not encountered: I) cells that had at least one significant spatial parameter and maintained the same firing rate between epochs (type P) and 2) cells with at least one significant spatial parameter, which remained con-
stant across epochs, and significant changes in overall firing rate between epochs (E+P).

TASK-DEPENDENT TUNING. To examine the effects of task on neural reactivitiy, categorical regressions examined the effect of task (T, RVAR vs. EVAR) and position (P) separately during the preparatory and reach epochs, because they represent crucial stages of the reaching task. This analysis again showed three different interaction types. Neurons with uniform firing rates across positions but different mean firing rates between tasks were called type T. Neurons that changed spatial parameters between tasks (multiplicative type T×P) had response fields that differed significantly between tasks. Nonsign-
ificant cells (type NS) that had neither task nor position effects were also found. Again, there were no pure position cells (type P) nor were there any additive cells (type T+P).

Both the time-dependent and the task-dependent population spatial parameters were computed for the multiplicative types. For cells with significant linear horizontal and vertical coefficients (\(a_x\), \(a_y\)), the direction of spatial tuning was summarized by the x- and y-vectors. The population spatial parameters were assessed with circular statistics. First, the resulting vectors were transformed into polar coordinates, that is, \(\theta = \arctan (a_y/a_x)\) with the convention of 0° (360°) corresponding to the right position “East” (12, 0°) with a counter-
clockwise rotation. For the population of vectors, the Hotelling one-sample test (Batschelet 1981; Zar 1984) determined whether vectors were distributed nonuniformly. This statistic uses the ampli-
tude and the direction of the angular tuning. Therefore a weakly spatially tuned cell (i.e., with small linear coefficients) contributes less to the statistic than a strongly tuned cell for a given direction. Significance level for the resulting F-test was set at \(P < 0.05\). To examine changes in spatial tuning, the directions of the difference vectors (\(a_{xxsep} - a_{xx\text{prep}}\), \(a_{xysep} - a_{xy\text{prep}}\)) were computed between the preparatory and visual epoch. Such a comparison shows modulation early and late in the delay period and thus reflects increasing influ-
ences from nonvisual signals.
In cells with mixed linear and quadratic coefficients, the dimensions of the resulting response fields were determined based on the combination of significant parameters \((a_x, a_y, a_{xx}, a_{yy})\), similar to previous studies (Heider et al. 2005; Quraishi et al. 2007). Cells that had a quadratic dependence along both the horizontal and vertical had a local maximum (“peak,” negative \(a_{xx}\) and \(a_{yy}\) terms), a local minimum (“trough,” positive \(a_{xx}\) and \(a_{yy}\) terms), or a “saddle” shaped response field (different signs for \(a_{xx}\) and \(a_{yy}\) terms). For the two latter combinations, the highest firing rate is located in the periphery of visual space. Thus for cells with quadratic coefficients, the preferred direction (maximum response) can only be established for cells with negative quadratic coefficients (peaks) and without interaction parameters \((a_{xy})\). To visualize the spatial tuning for each significant cell, response fields derived from the quadratic, and linear coefficients were created.

To determine whether neural responses differed between two epochs (visual vs. preparatory) on a trial-by-trial basis, the firing rate was computed for the two epochs averaged across all nine positions. The averaged firing rate was compared with a paired \(t\)-test generating a probability value, \(P\). The number of neurons with a probability of \(P < 0.05\) was calculated. This analysis is called paired analysis throughout the paper. For comparison of cell type distributions, a \(\chi^2\) test was used with a significance level of \(P < 0.05\).

**RESULTS**

**Behavioral data**

Behavioral measurements consisted of reach endpoint accuracy relative to the center of the target and response times. Endpoints on the screen from one experiment (EVAR and RVAR) are plotted in Fig. 4. This example shows that reaching was more accurate (i.e., closer to the target center) in the EVAR than RVAR task. A paired comparison of the vectors derived from the horizontal and vertical endpoint positions confirmed that accuracy was indeed greater in the EVAR task when the reach target was foveated (\(t\)-test, \(P = 0.007\)). The lower endpoint accuracy in the RVAR task may be the result of the larger difference between reach endpoint and fovea and the known gaze-dependent errors when pointing to peripheral targets (Henriques and Crawford 2000).

Two behavioral time segments were computed for all experiments: reaction time (RT), that is, the period from the change in optic flow to the hand lift, and movement time (MT) from the hand lift to the moment the hand touched the screen. These two time segments were compared between the RVAR and EVAR task for 98 recordings where both tasks were completed (Fig. 5). Within an experimental recording, MTs from start panel to touch screen were significantly shorter in the RVAR task (\(t\)-test, \(P < 0.001\)) than in the EVAR task (Fig. 5A).

For the RTs (Fig. 5B), there were no significant differences between the EVAR and the RVAR tasks with respect to the mean. The pairwise plots examined how these behavioral parameters varied on a day-by-day basis. Both movement times and reaction times varied between experiments but were significantly correlated between tasks within a day (Fig. 5, A

**FIG. 4.** Reach endpoints of 1 typical experiment (\(n = 90\) trials, MFR256.C01) during the EVAR task (A, ○) and the RVAR task (B, ●). Dashed circles indicate circumference of optic flow patches (diameter 12°).

**FIG. 5.** Distribution and scatter plots of mean behavioral times (\(T\)) for the 2 tasks (\(T_{EVAR}\); EVAR, \(T_{RVAR}\); RVAR). ○, behavioral times that were significantly different (\(T_{EVAR}\) vs. \(T_{RVAR}\)) with Student’s \(t\)-test; ●, nonsignificant values. Along each axis, histograms show distribution of behavioral times for the significant (filled bars) and nonsignificant (open bars) values. The angled histograms represent \(T_{EVAR} - T_{RVAR}\). A: movement times (time from hand lift to touch). B: reaction times (time from stimulus change to hand lift). Each dot represents the mean of the behavioral times during 1 recording run (90 trials).
Some days, the monkey responded very fast, whereas on other days, reaction and movement times were slower in both tasks. The two animals differed in their mean detection and travel times but showed the same task effects.

Across all experiments, the average reach velocity was ~1.2 m/s, which lies well within published data for fast, ballistic reaching (Churchland et al. 2006; Gardner et al. 2007; Kurata and Hoshi 2002). These behavioral reach data were obtained largely without visual feedback (Desmurget and Grafton 2000; Vercher et al. 1994), because the monkey could not see his hand until it reached the touch screen. The slower speed (i.e., longer movements times) found when reaching to foveated targets in the EVAR task matches published studies in humans (Prablanc et al. 1986). These behavioral differences between the two task conditions suggest different computational strategies and have to be considered when interpreting the single unit data (Moran and Schwartz 1999; Snyder et al. 2006).

Electrophysiological dataset

The main goal of this study was to examine the spatial relationship between baseline, visual, preparatory, and reach signals in area 7a and DP. The statistical analyses thus focused on temporal (epochs), spatial (reach target position), and contextual (task condition) aspects of the neural response. A total of 164 units (90 in M1R, 74 in M3R; 99 in area 7a, 65 in DP) were studied quantitatively using the EVAR task. For the RVAR task, 119 units were studied (62 in M1R, 57 in M3R; 65 in area 7a, 54 in DP). For a total of 98 cells, both the RVAR and EVAR tasks were completed (53 in 7a; 45 in DP).

The data are presented three ways. First, the epoch-based analysis and modeled response fields are exemplified for one area 7a and one DP cell. Second, the epoch-based analysis examines temporal and spatial aspects within the EVAR and RVAR tasks for the population of neurons. Third, the EVAR and RVAR tasks are compared directly during preparatory and reach epochs to show the effect of eye position.

Single unit activity synchronized to task epochs

EVAR task. The 7a neuron (Fig. 6, A–D) responded strongly during all epochs in the EVAR task. The baseline activity before stimulus onset was strongest for the contralateral (left) eye positions (Fig. 6A, light gray–shaded bars). The neuron responded with a transient burst of activity to the onset of the visual stimulus for the contralateral and lower eye positions (Fig. 6A, dark gray–shaded bars). The baseline and visual activity resulted in two differently shaped response fields (Fig. 6B). During the preparatory epoch, the spatial preference remained constant, with higher activity for the contralateral and lower eye positions (Fig. 6, C and D). After the lift hand event, the spatial preference shifted upward toward the midline (Fig. 6, C and D).

The DP neuron (Fig. 6, E–H) had a weak spatial tuning during the baseline fixation epoch with elevated activity for the lower ipsilateral (right) eye positions (Fig. 6E). Steep increases in activity were observed at stimulus onset for the contralateral and ipsilateral eye positions (Fig. 6E), resulting in a saddle shaped response field (Fig. 6F). This eye position tuning changed during the preparatory epoch (Fig. 6G) with a preference for lower contralateral targets. During the reach epoch, firing increased further for the lower center position (Fig. 6G) and changed the shape of the response field (Fig. 6H).

The spatial tuning across time for both neurons is shown by plotting the linear coefficients (Fig. 7). The 7a neuron (Fig. 7A) started with an upper contralateral eye position tuning during baseline (B) and shifted to a lower contralateral tuning when the stimulus appeared (V). During the preparatory epoch, this tuning moved toward the vertical midline (P) and finally upward toward the center after the monkey launched the reaching movement (R). The DP neuron (Fig. 7B) shifted eye position tuning from lower ipsilateral (B) to contralateral (V, P) and back to the lower ipsilateral eye positions (R) as the task progressed.

RVAR task. The 7a neuron exhibited a distinct retinotopic tuning when fixation was kept constant on the center position (Fig. 8, A–D). Baseline tuning was flat (Fig. 8, A and B) as expected. At stimulus onset, the neuron fired for targets appearing in the lower contralateral visual field (Fig. 8A), resulting in a peaked response field (Fig. 8B). During the preparatory epoch, the retinotopic tuning remained in the lower contralateral visual field (Fig. 8, C and D) and then moved further upward toward the midline (Fig. 8, C and D) during the reach epoch.

The DP neuron’s response field was flat during the baseline period (Fig. 8, E and F). Stimuli appearing in the center and ipsilateral visual field yielded increased neural activity (Fig. 8E), resulting in a peaked response field for the visual epoch (Fig. 8F). The preparatory epoch was characterized by strongly elevated activity for the upper ipsilateral retinotopic targets yielding a steeply tilted response field (Fig. 8, G and H). After the lift hand event, the firing rate sharply decreased, especially for those positions that showed peak firing during the preparatory epoch (Fig. 8G). During the reach epoch, the highest firing rates were seen for the lower ipsilateral targets (Fig. 8, G and H).

The corresponding plot of the linear coefficients for the 7a neuron during the RVAR task (Fig. 9A) shows how the cell’s spatial preference started in the center during baseline (B) and moved toward the lower contralateral visual field after stimulus onset (V). During preparation (P) and initiation of the reach (R), the retinotopic spatial tuning shifted back toward the center. The DP neuron (Fig. 9B) switched its retinotopic spatial tuning from center (B) toward the ipsilateral visual field at stimulus onset (V), further ipsilateral during preparation (P), and downward during reach (R).

Comparison of spatial tuning between epochs

These two example neurons show the complex interactions between reach target location and epoch. Area 7a and DP neurons altered their spatial eye position and retinotopic tuning during the task. To quantify such changes for the population of recorded neurons, different tuning types were determined using the results of the categorical regression. Cells were classified as 1) having significant changes in overall firing rate without spatial tuning (type E), 2) having time-variant spatial tuning (type E×P), or 3) cells without effects (type NS).

EVAR task. The majority of cells (70%, 114/164) showed an effect of epoch and/or position as quantified by the statistical categorical regression (Fig. 10A). The distribution of the two
tuning types (E, E×P) did not differ significantly between areas. Area 7a and DP also contained neurons that did not respond during any of the selected epochs (NS, total: 30%; 50/164; 7a: 35%; 35/99; DP: 23%, 15/65). The type E neurons showed flat spatial tuning and significant differences in intercepts between at least two epochs (total: 10%; 17/164; 7a: 12%, 12/99; DP: 8%, 5/65). Comparison of intercepts between visual and preparatory epochs did not show significant differences.

The multiplicative (type E×P) neurons comprised 59% of the cells (total: 97/164; 7a: 52%; 52/99, DP: 69%, 45/65). These cells were fit with at least one significant spatial param-
The multiplicative (type E×P) neurons comprised 45% (total: 54/119; 7a: 45%, 29/65; DP: 46%, 25/54) of the cells. Pure linear modulation was present in 30% (16/54), whereas 33% (18/54) of E×P neurons had an additional quadratic dependence. For population of purely linear cells, angular tuning was uniformly distributed. Significant interaction terms were present in 22% (12/54) of the E×P neurons. Among the 54 E×P cells, 43 had significant spatial parameters for the visual, preparatory, and/or reach epoch. With the paired analysis, it was found that 52% of the E×P neurons (7a: 14/54; DP: 14/54) significantly changed their firing between the visual and preparatory epoch.

In summary, the regression analysis provided a robust quantitative measure of the differential effects of epoch on a neuron-by-neuron basis during the EVAR and RVAR tasks. About two thirds of the cells were altered by epoch as the task progressed, more often in form of changes in spatial tuning than in form of gain changes. Although the stimulus on the screen provided constant visual stimulation throughout the task, additional spatially tuned inputs related to the preparatory and reach event impacted these neurons’ activity.

Comparison of single unit activity between RVAR and EVAR task

Neural activity during the preparatory and reach epochs was directly compared on a neuron-by-neuron basis for conditions where the location of the reach targets was identical, but reach movements were made under different combinations of eye and retinal information. In the EVAR task, the monkey reached to a foveated target; thus eye position varied concurrently with reach target position, whereas the retinotopic stimulation remained constant on the fovea. In the RVAR task, the target was not foveated (except for the center position) and the retinotopic stimulation varied. A subset of 98 cells was analyzed in which both the EVAR and RVAR tasks were tested. Categorical regressions determined the effects between the two factors: task condition (T, EVAR vs. RVAR) and position (P, 9 reach target positions). These effects were determined separately for each of the four epochs, but the focus will be on the preparatory and reach epochs. Neurons were grouped according to whether they changed their tuning in the task or spatial domain.
Baseline and Visual Epochs. Firing rate for the center position was compared between EVAR and RVAR tasks to identify possible contributions from attentional or other effects between the two task blocks. For both epochs, firing rates did not differ significantly between the two tasks.

Preparatory Epoch. This epoch is characterized by an absence of sensory or motor changes. The monkey is fixating, a structured optic flow stimulus is displayed, and the hand is resting on the launching panel. During this epoch, the task factor affected 76% (74/98) of the cells significantly (Fig. 11A),
suggesting that the majority of cells changed their tuning or gain depending on whether the hand was going to be moved to a foveated or peripheral reach target. The two tuning types (T, \(T/H_{11003}P\)) were distributed evenly between area 7a and DP. About one quarter of the neurons were not affected by either factor (NS, total: 24%, 24/98; 7a: 30%, 16/53; DP: 18%, 8/45). The type T was observed in 30% of the cells (29/98; 7a: 30%, 16/53; DP: 29%, 13/45). These cells differed in their mean firing rates between RVAR and EVAR conditions but had flat spatial tuning. Intercepts did not differ significantly between the two conditions for this group.

The multiplicative type \(T/H_{11003}P\) was present in 46% of cells (total: 45/98; 7a: 40%, 21/53; DP: 53%, 24/45). In this group of neurons, identical reach targets yielded different spatial tuning during the preparation of the reaching movement. Typical response fields of 7a cells are shown in Fig. 12A. This cell showed peak firing for upper ipsilateral retinotopic targets (positive vertical and horizontal coefficients) during the RVAR task. When reaching was performed to foveated targets (EVAR), spatial preference shifted toward eye positions along vertical midline (Fig. 12E, gray arrow). Another DP cell example fired mostly for targets in the contralateral hemispace during RVAR condition and moved its preference toward the upper contralateral space during EVAR condition (Fig. 12, B and F, gray arrow).

Similar to the analysis of the E\(\times\)P cells, the T\(\times\)P cells during the preparatory epoch were fit with at least one significant spatial parameter \((a_x, a_y, a_{xy}, a_{xx}, a_{yy})\) during both tasks. Sixteen of these 45 cells (36%) were only linearly modulated by the target position. Angular tuning distribution for these purely linear T\(\times\)P cells was uniform. Directions of spatial shifts between linear parameters for the EVAR and RVAR conditions were also uniform. Another 40% of T\(\times\)P neurons (18/45) had an additional quadratic dependence in at least one dimension. Significant interaction terms were present in 27% (12/45).

REACH EPOCH. This epoch differed from the preparatory epoch by the additional sensory and motor changes (visual stimulus change and the onset of hand movement initiation). The majority of the cells (total: 81%, 79/98; 7a: 79%, 42/53; DP: 82%, 37/45) showed significant task effects (Fig. 11B), confirming the hypothesis that the activity during movement initiation was strongly affected by the task condition, that is, whether the monkey was going to reach to a foveally or eccentrically presented stimulus. There were no significant differences in distribution of the T and T\(\times\)P types between the two areas. Nonsignificant cells comprised 19% of the population (NS, total: 19/98; 7a: 21%, 11/53; DP: 18%, 8/45). About one quarter of the cells were type T neurons (total: 27% 26/98; 7a: 28%, 15/53; DP: 24%, 11/45). Intercepts between RVAR and EVAR conditions for this group did not differ significantly.

More than one half of the cells were of the multiplicative type \(T\times P\) (total: 54%, 53/98; 7a: 51%, 27/53; DP: 58%, 26/45). Thus identical reach target positions yielded varying spatial preferences depending on whether the target was foveated or not. The area 7a cell changed spatial preference from upper to lower contralateral reach positions between EVAR and RVAR conditions.
and RVAR task (Fig. 12, C and E, black arrow). The DP cell shifted preference from upper to lower reach positions between RVAR and EVAR tasks (Fig. 12, D and F, black arrow). Seventeen of these 53 cells (32%) were only linearly modulated by the target position and had a uniform distribution of spatial tuning. Spatial shifts between EVAR and RVAR conditions were also distributed uniformly. Another 38% of the T×P neurons (20/53) had an additional quadratic dependence in at least one axis. Significant interaction terms were present in 28% (15/53) of the T×P neurons.

**DISCUSSION**

Combined findings from various studies have lead to the general consensus that PPC neurons are involved in goal-directed behaviors including attentional and motor planning signals (Andersen et al. 1997; Burnod et al. 1999; Coulthard et al. 2008; Rozi et al. 2008; Snyder et al. 2006). This study builds on prior reaching studies in area 7a (Battaglia-Mayer et al. 2005, 2007; Blum 1985; MacKay 1992; Mountcastle et al. 1975; Rushworth et al. 1997) and expands our knowledge about PPC neurons, including DP. First, spatial tuning was quantitatively compared between the baseline, visual, preparatory, and initiation phases of the reaching task. Modeled response fields show the changes in spatial tuning over time. Second, area 7a and DP neurons were classified into subpopulations with distinct spatial and temporal tuning properties. Third, the role of eye position on reaching activity was examined by having the monkeys reach to foveated (EVAR task) or nonfoveated (RVAR task) targets. Fourth, and importantly, DP was identified as containing neurons that are modulated during the planning and initiation phases of the reaching task.

**Methodological considerations**

In this study, reaching movements occurred in a radial (3D) manner. This differs from a lateral reach, where the monkey starts the reach from a target on the screen and then lifts the hand briefly off the screen to move to the next target on a plane, as used in many reaching studies (Batista and Andersen 2001; Battaglia-Mayer et al. 2005, 2007; Scherberger and Andersen 2007; Snyder et al. 2006). A radial reach more closely resembles a natural movement (MacKay 1992). Because the animal was fixating before making the reach movement, the hand could not be seen until it hit the screen and partially occluded the optic flow target.

**Neural responses during different epochs**

About one half of the neurons responded to the onset of the visual stimulus and showed effects of eye and retinal position, as demonstrated previously (Battaglia-Mayer et al. 2007; Fischer and Boch 1981a,b; Maguire and Baizer 1984; Merchant et al. 2001; Mountcastle et al. 1987; Read and Siegel 1997; Siegel and Read 1997; Youakim et al. 2001). Within each task condition (EVAR or RVAR), we assume that the initial visually dominated response was affected by multiple signals during the preparatory and reach epochs.

**PREPARATORY RESPONSES.** The preparatory epoch was operationally defined as the 500 ms before the cue to reach. Changes in neural firing during this delay epoch were not contaminated by overt sensory events or motor behaviors. The visual stimulus was a constant optic flow, and the hand remained at a resting position. As the target appeared on the screen several seconds before the cue to reach, the monkey had enough time to shift his attention and anticipate the upcoming reach cue. It is very likely that the preparation of the reaching movement began as soon as the fixation spot and/or reaching target appeared on the screen. Thus the preparatory epoch likely represents a phase of movement preparation, during which integration of multiple signals can occur.

First, the spatial locus of attention has been shown to alter neural activity in area 7a and DP (Bender and Youakim 2001; Bushnell et al. 1981; Mountcastle et al. 1981; Quraishi et al. 2007; Raffi and Siegel 2005; Steinmetz and Constantinidis 1995). In the EVAR task, attention was overtly directed because the reach target was always foveated, whereas in the RVAR task, attention was covertly directed to the nonfoveated reach target (Bushnell et al. 1981; Quraishi et al. 2007; Steinmetz et al. 1994). Covert and overt attention are likely to modulate neural responses during the RVAR and EVAR conditions, respectively. However, the variety of neural response types suggests that the preparatory modulation went beyond mere attentional enhancement or suppression of the visual signal (Sakata et al. 1995). Recent findings in lateral intraparietal area (LIP) showed that motor planning and attentional processes can be separated anatomically (Liu et al. 2010). Studies in PRR also strongly suggest that motor planning can be distinguished from attentional modulation because it is dependent on the effector (Calton et al. 2002; Snyder et al. 2006).

Second, this study also showed that motor planning likely contributed to the preparatory signal through known anatomi-
cal feedforward and feedback pathways (Andersen 1997; Scherberger et al. 2005). It has been proposed that parietal cortex represents an early stage in movement planning (Snyder et al. 2000). Covert movement planning during a memory or delay period modulates neurons in 7a (Snyder et al. 1997). Thus both area 7a and DP form part of a larger neural network that is crucial for transforming visual spatial information into a motor plan (Scherberger and Andersen 2007).

REACH RESPONSES. The firing rate during the reach epoch likely had both overt sensory and motor contributions, because the monkey detected the stimulus change, initiated the hand movement, and moved his hand toward the target. Changes in spatial tuning could derive from joint proprioception, because primates are quite accurate in localizing their limbs in 3D space even in absence of visual or tactile inputs (Baraduc et al. 2001; Ghika et al. 1995; Kalaska 1988; Prud’homme and Kalaska 1994; Ren et al. 2006; Scheidt et al. 2005). Such inputs are likely to be conveyed through other parietal areas that respond to somatosensory and proprioceptive manipulations (Breveglieri et al. 2006; Fattori et al. 2001; Ferraina et al. 1997, 2001; Johnson et al. 1996). An important contribution to the reach signal could derive from efference copy or corollary discharge (Hyvärinen 1982; Mountcastle et al. 1975; Rushworth et al. 1997). Indirect feedback from motor cortices through areas 7b or 5 might be involved in such signals (Gardner et al. 2007). These multiple signals are combined in time to monitor and modulate ongoing reaching movements (Beurze et al. 2007). These modulatory signals likely propagate to DP through strong reciprocal connections with area 7a and other parietal and frontal areas (Andersen et al. 1990a; Cavada and Goldman-Rakic 1989b; Stepniewska et al. 2005). Thus this population of PPC neurons integrates information from multiple cortical sources to calculate the sensorimotor transformation.

Sensorimotor transformation and classification of neurons

The majority of studied area 7a and DP neurons modulated their firing rate during the baseline, visual, preparatory, and/or reach epochs. Categorical regression methods were used to classify neurons into different tuning types based on interactions between epoch and position. In the EVAR task, a small proportion of neurons (~10%) were modulated by the epoch but were not spatially tuned (E-type cells). During the RVAR task, a slightly higher proportion of this tuning type was found. Large receptive fields that extend beyond the display could explain nonselectivity to retinotopic position. Overall, cells of this type could reflect a gain signal from motor planning (Bullock et al. 1998; Snyder et al. 1998) or from nonspatial attentional modulation.

A substantial number of spatially tuned cells changed their spatial preference (eye position tuning or retinotopic tuning) during progression of either task (E×P). During the EVAR conditions, 59% of the neurons started with a certain eye position preference at baseline and stimulus onset and altered their spatial tuning as the monkey prepared and executed his reach movement. In the RVAR task, 45% changed their retinotopic tuning. This suggests a predominance of gain field...
tuning over retinotopic tuning in the population of neurons, which is in agreement with earlier studies (Heider et al. 2005; Read and Siegel 1997; Siegel et al. 2003). Substantial changes in spatial tuning occurred between the visual and preparatory epoch for both conditions. These changes could arise from spatially tuned attentional or planning signals based on other coordinate frames (e.g., arm-centered, head-centered) originating from frontal or other parietal areas (Pesaran et al. 2006; Rozzi et al. 2006). These signals modulated and changed the eye position and retinotopic tuning that prevailed during the early “visual” phase of the task. Reach-related modulation, when the hand was lifted off the start position, could further be attributed to a combination of sensory (e.g., visual, proprioceptive) and motor signals as suggested for other parietal areas (Breveglieri et al. 2008).

Thus shifts in spatial tuning could represent highly specific feedback from spatially tuned neurons in other cortical areas. Alternatively, initial generation or on-line modification of the motor command could arise within area 7a or DP to guide the ensuing reach movement. Such motor commands need to be generated in conjunction with visual information. This could involve intracortical circuitry within area 7a and/or DP, consistent with lesion and imaging studies that support the role of parietal cortex in on-line adjustment of reaching movements under visual control (Buxbaum and Coslett 1998; Desmurget et al. 1999; Pisella et al. 2000).

**Contextual dependence of the sensorimotor transformations**

To achieve accurate reaching performance, information from various sources (e.g., visual, proprioceptive, efference copy) is updated continuously, allowing comparison of targeted with actual movement (Desmurget et al. 1998). Previous studies have shown that gaze direction and retinotopic location of a visual target modulate neural activity in both area 7a and DP neurons (Andersen et al. 1985, 1990a; Bremmer et al. 1997; Heider et al. 2005; Read and Siegel 1997; Siegel et al. 2003, 2007). To separate the contributions of retinotopic and gain field signals, the loci of fixation and retinal stimuli were systematically varied and quantitatively assessed.

Behavioral effects of reaching to nonfoveated targets consisted of decreased reaching accuracy and shorter movement times, suggesting involvement of distinct neural populations. This also supports macro-level description of recruitment of different neural networks for foveal versus peripheral reaching assessed with event-related functional MRI and human lesion studies (Clavagnier et al. 2007; Pisella et al. 2009). Behavioral differences between the tasks could also be caused by differences in activity within the same population of neurons. For example, parietal area 5 cells combine signals from multiple sources to encode information about change of movement trajectory (Archambault et al. 2009; Chen et al. 2009).

Human psychophysical findings support a strong coupling between gaze direction and pointing movements (Admiraal et al. 2004; Dijkerman et al. 2006; Henriques et al. 1998; Noggers and Bekkering 2001). When the gaze is held steady on the reach target, efference copy and ocular proprioception allow greater accuracy in reaching (Lewis et al. 1998; Wilmut et al. 2006). When the gaze is off the reach target, other sensory signals such as arm proprioception exert a more prominent influence (Rossetti et al. 1995), which are likely to recruit different neural populations. Visually guided reaching thus involves ongoing comparison of different sensory inputs (e.g., visual vs. proprioceptive) to achieve maximum reach endpoint accuracy. Foveating the target could lead to longer movement times because of on-line corrective processes that combine ocular and retinal signals (Béduard and Proteau 2004; Desmurget and Grafton 2000). It has also been suggested that neurons in parietal cortex use retinal error signal that reflect the difference between target and hand position (Magescas et al. 2009). These error signals could be represented by PPC neurons during the different reach task conditions.

Direct comparisons of spatial tuning between RVAR and EVAR conditions during the preparatory and reach epochs showed distinct populations of cells. Spatial tuning during preparation and initiation epochs differed between RVAR and EVAR conditions for about one half of all neurons (T×P neurons). Task-related spatial changes in representations of reach planning and execution have been described for other parts of the cortex (Jouffrais and Boussaoud 1999; Schwartz et al. 1988). For example, motor cortex neurons are strongly affected by the kinetics of the arm movements (Scott and Kalaska 1997; Scott et al. 1997). Because the movement times in this study differed substantially between RVAR and EVAR conditions, the trajectories were not identical between the two task conditions.

These contextual effects can also be discussed with respect to different coordinate frames. Under both task conditions, reach movements were made to the same target location relative to the body (e.g., head, shoulders, or hands) but to different locations relative to the eye. If hand-centered signals dominated the 7a and DP responses, the spatial tuning would be similar between RVAR and EVAR conditions. If neural responses during reaching were dominated by eye-centered signals, spatial tuning would differ because eye position relative to the reach target (i.e., hand position) varied between RVAR and EVAR tasks. This was the case for the majority of cells, suggesting that eye position modulated tuning of these cells during the preparation and initiation of the reach movement. The changes of spatial tuning over time (between epochs) suggest that the initial eye position and retinotopic visual signals are affected later during the task by other reach-related signals. It is also likely that 7a and DP neurons use mixed coordinate frames, for example, a combination of hand-centered and eye-centered coordinates, as suggested for premotor and PRR neurons (Batista et al. 2007; Chang and Snyder 2010).

**Reach-related activity in dorsal prelunate and area 7a neurons**

Neurons in area 7a are strongly visual but show substantial modulation from extraretinal sources such as eye position (Andersen et al. 1990b; Read and Siegel 1997), attention (Constantinidis and Steinmetz 2001; Mountcastle et al. 1981; Qurashi et al. 2007; Raffi and Siegel 2005; Steinmetz and Constantinidis 1995; Steinmetz et al. 1994), and visually guided, goal-directed hand movements (Battaglia-Mayer et al. 2007; MacKay 1992; Rozzi et al. 2008; Rushworth et al. 1997).

DP neurons also showed modulation during preparation and initiation of reach movements, which was an unexpected result of this study. Properties of DP neurons strongly resembled
those of area 7a with respect to temporal (epoch-based) and contextual (task-related) effects. Thus these results support a role for DP neurons that goes beyond the merely visual (Fischer and Boch 1981a; Mountcastle et al. 1987; Tanaka et al. 1986). Although DP is lower in an anatomically defined hierarchy than area 7a (Andersen et al. 1990a; Felleman and Van Essen 1991), it receives modulatory feedback from other parietal and frontal areas (Lewis and Van Essen 2000). The possibility that DP, and perhaps 7a, receive these signals via reentry (Edelman 1989) suggests a powerful role of these processes.

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DISCLOSURES

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