Cortical Temporal Dynamics of Visually Guided Behavior

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Little is known about the temporal dynamics of cortical activation during visually guided behavior. We measured changes in brain activity in human posterior parietal cortex (PPC) and premotor cortex (PMC) during saccades and visually guided reaching using magnetoencephalography (MEG) and novel time–frequency reconstructions of MEG (tMEG) data. Results indicate that early high-gamma activity over the frontal eye fields (FEFs) was present during saccade preparation, and high-gamma activity progressed from the supplementary and FEFs to visual cortex during saccade execution. In contrast, early high-gamma activity over dorsal PMC and late beta activity in primary motor cortex and PPC were unique to reach preparation. During reaching, high-gamma activity progressed from sensorimotor cortex and PMC to parietooccipital cortex. These unique spatial–temporal processing patterns reflect the known connectivity of 2 different sensorimotor networks in macaques. The onset and duration of activity in these areas provides direct evidence for concurrent serial and parallel processing in the human brain during the integration of the sensorimotor inputs necessary for visually guided performance.

Keywords: arm, magnetoencephalography, motor intention, parietal, premotor, saccades

Introduction

When acting on the visual world, information that enters the eye must be translated into a motor command, a function that theoretically occurs in a network of brain regions that includes posterior parietal cortex (PPC) and premotor cortex (PMC). Several lines of evidence indicate that PPC and PMC integrate sensorimotor information during visually guided behavior. Studies of neural response properties in these regions reveal that many of the neurons in PPC and PMC respond to either visual or somatosensory stimulation (Colby et al. 1996; Padberg et al. 2005) or a combination of both (Iriki et al. 1996; Duhamel et al. 1998; Graziano et al. 2000). Many parietal neurons active during reaching and saccades also encode the direction and endpoint of an intended movement in visual space (Mazzoni et al. 1996; Buneo et al. 2002). In addition, both PPC and PMC are projection targets for neurons within sensory and motor cortex (Blatt et al. 1990; Shipp et al. 1998, Lewis and Van Essen 2000). These receptive field properties and connection patterns suggest that sensory and motor information converge in PPC and PMC in order to guide the formation of a specific type of movement such as a reach or a saccade.

Furthermore, the receptive fields of these neurons tend to be anchored to a specific body structure such as the arm or hand (Iriki et al. 1996; Graziano et al. 1997; Duhamel et al. 1998). For example, cortical areas in the superior parietal lobule of the monkey with an expanded representation of the forelimb such as Brodmann’s Area 5 (BA5; Pons et al. 1985; Padberg et al. 2007) contain neurons that increase activity during visually guided reaching movements but not saccadic eye movements (Snyder et al. 1997; Calton et al. 2002). Thus, it has been hypothesized that PPC and PMC are functionally organized into regions that are involved in the action of a specific body structure (Colby and Goldberg 1999; Andersen and Buneo 2002). Additional support for this hypothesis comes from the pattern of interconnections between effector-specific regions of PPC and PMC. Parietal areas active during saccades (such as lateral intraparietal area [LIP]) project to oculomotor regions of PMC, such as the supplementary and frontal eye fields (FEFs) (Bullier et al. 1996; Lewis and Van Essen 2000). In contrast, parietal areas that contain neurons with motor receptive fields active during reaching (including medial intraparietal area [MIP] and V6A) have afferent connections that extend not only to neighboring parietal fields with similar tactile receptive field properties (such as BA5; Selzter and Pandya 1986; Shipp et al. 1998) but also to regions of dorsal premotor (PMd) and ventral premotor (PMv) PMC that are active during forelimb movements (Caminiti et al. 1999).

Studies of connections between effector-specific regions of PPC and PMC in the macaque have provided insight into processing networks that subserve the transformation of visual information into a motor program. While results from human neuroimaging studies using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have provided some evidence of sensorimotor integration and effector specificity in the human neocortex (Bremner et al. 2001; Simon et al. 2002; Astafiev et al. 2003), the relatively poor temporal resolution of these techniques precludes the examination of real-time cortical interaction during visually guided behavior.

Here, we used time–frequency reconstructions of magnetoencephalography (tMEG) data to measure preparatory and executive processing in human PPC and PMC during visually cued saccade and reach tasks known to produce activity in these regions (Calton et al. 2002; Astafiev et al. 2003). tMEG refers to the algorithmic reconstructions of brain source localizations across time derived from noninvasive magnetoencephalography (MEG) sensor recordings. We hypothesize that the connection patterns identified in the macaque reflect effector-specific networks subserving movement preparation and execution. The temporal and spatial resolution of tMEG allowed us to examine the oscillatory, spatial, and temporal dynamics of these putatively homologous effector-specific networks in human cortex.

Materials and Methods

Participants

Data were acquired from 8 healthy volunteers from the University of California, San Francisco (5 men, 3 women, all right handed). Participants...
were screened for neurological conditions as well as contraindications for MEG. Written consent from each participant was obtained prior to the experiment. All procedures were approved by the Committee on Human Research at the University of California, San Francisco.

**Task**

Subjects performed a modified cue-delay-target task (Calton et al. 2002) during MEG recordings. Stimuli were generated on a PC using Presentation software (www.neurobs.com/presentation) and were projected into the magnetically shielded room using a Christie LX41 (Christie Digital, Cypress) at a display rate of 60 Hz onto a screen using a series of mirrors. Between trials, subjects rested their right hand on a point (crosshairs) at the center of the screen and maintained fixation on the same crosshairs. At the beginning of every trial, a peripheral cue arrow color coded for movement type (blue arrow for reach or yellow arrow for saccade) was presented for 200 ms on either the left or right side of the screen. At target onset (variable ISI: 800-1400 ms) a white arrow appeared in the same location as the cue which instructed the subject to execute the prepared movement by pointing or making a saccade to either the left or right hand target location (Supplementary Fig. 1). The cue and target arrow were always congruent on all trials, and no antimovements were made by participants during the imaging session.

For saccadic eye movements, subjects made a saccade in the direction indicated by the arrow to 1 of 2 buttons embedded in either side of the stimulus display. For reaching movements, subjects guided their right hand to 1 of 2 buttons embedded in either side of the stimulus display. Eye movements were monitored through concurrent vertical and horizontal electrooculograms (EOG), and reaction times (RTs) for saccade trials were measured based on the onset and offset of a ballistic eye movement in the EOG data. Subjects were trained prior to data collection to maintain fixation at the center of the screen during reaching trials and to keep hand position constant (at the fixation target at the center of the screen) during saccade trials. EOG data were also used to identify and discard epochs where fixation was not maintained between trials or epochs where erroneous saccades were generated (i.e., during reach trials; Supplementary Fig. 2). Hand position was monitored by the experimenter through video recordings of task performance, and runs where subjects failed to maintain proper positioning were discarded and collected again. RTs for reach trials were evaluated relative to completion of the button press. A long intertrial interval (randomized 3600–3900 ms) was used to ensure that subjects had a sufficient length of time to return to the starting position. In total, 200 epochs of variable duration (200–5100 ms) were collected for each trial type (800 trials total per subject).

**Behavioral Performance**

Movement execution RT was recorded for both saccade trials (from target onset to saccade as measured using concurrent EOG) and arm movements (from target onset to button press). Average RT for saccadic eye movements was 217.7 ms (standard error [SE] = 24.5 ms) and 269.3 ms (SE = 18.8 ms) for left and right saccade execution, respectively. Average RTs for left reach execution was 752.7 ms (SE = 85.5 ms), and average RT for right reach execution was 685.8 ms (SE = 65.8 ms). Repeated-measures within-subject analysis of variance demonstrated a main effect for movement type ($P < 0.0001$), where subjects were faster to respond during saccade trials versus reach trials to either direction. However, there was no main effect for direction ($P = 0.74$) and no significant interaction between the 2 ($F = 1.26, P = 0.27$). Error rates for each participant were very low (~5%), precluding the analysis of error trials.

**Data Acquisition**

MEG recordings were done using a 275-channel CTF Omega 2000 whole-head biomagnetometer system with third-order gradient correction (VSM MedTech). Coils were placed at the nasion and 1 cm rostral to the left and right periauricular points in the direction of the nasion in order to localize the position of the head relative to the sensor array. These points were later coregistered to a high-resolution structural MR image through a spherical single-shell head model. Scan sessions where head movement exceeded 2 mm within a run were discarded and repeated. Data were collected using a sample rate of 1200 Hz.

**Analysis**

All trials were corrected for noise artifact and head movement, and error trials were discarded. Artifact detection was performed visually by removing channels with excessive scatter and removing trials with eye blinks, saccades, EMG noise, or other obvious artifacts (MEG sensor signal amplitude exceeding 10 pT). Neural sources were spatiotemporally estimated using a time-frequency optimized adaptive spatial filtering technique implemented in the Neurodynamic Utility Toolbox for MEG (NUTMEG; http://bl.ualcs.edu) using the shared computing cluster at the California Institute for Quantitative Biomedical Research (www.qb3.org). This approach allowed us to observe induced (non phase-locked) responses, measured as either a significant negative or positive change in the modulation of oscillatory activity. A tomographic volume of source locations (voxels) was computed through an adaptive spatial filter (with a lead field resolution of 5 mm) that weights each location relative to the signal of the MEG sensors (Dalal et al. 2008). Source power for each location was derived through a noise-corrected pseudo-$F$ statistic expressed in logarithmic units (decibels; dB; Dalal et al. 2008) effectively comparing the magnitude of the signal during an ‘active’ experimental time window versus a baseline ‘control’ window (see Robinson and Vrba 1999; Dalal et al. 2008).

Experimental time windows during the movement preparation and movement execution periods (either reach or saccade to either the left or right) were compared versus a resting (intertrial) baseline window of the same length. Data were passed through a filter bank and partitioned into partially overlapping time windows using broad windows optimized for capturing spectral peaks in the MEG signal (Guggisberg et al. 2007; Dalal et al. 2008). Time-frequency windows of 250 ms with a 50 ms step size were estimated in the alpha (8–12 Hz), low beta (12–20 Hz), high beta (20–35 Hz), and gamma (35–55 Hz) frequency bands, with smaller sliding time windows (100 ms with 25 ms steps) computed for the high gamma (65–90 Hz) and ultra high gamma (90–115 Hz) frequency bands (Guggisberg et al. 2007; Dalal et al. 2008). Oscillations between 55 and 65 Hz were not reconstructed due to contamination in the data by line noise and visual projector artifacts (e.g., refresh rate) within this range (60 Hz). Changes in oscillatory power during the periods of movement preparation and execution (either reach or saccade to either the left or right) were computed in each frequency band relative to signal power during the intertrial interval (250 ms ITI window, 8–55 Hz; 100 ms ITI window, 65–115 Hz). Data were analyzed in a stimulus-locked design (0 ms = visual cue) for both periods of movement preparation (reach and saccade). For the period of movement execution, data were analyzed in both a stimulus-locked design (0 ms = visual target) as well as a response-locked design (0 ms = movement) in order to evaluate changes in oscillatory activity that occur prior to movement completion (reach and saccade). Measuring changes in signal power (in decibels) over time allowed us to identify both the onset and peak of activity over a specific brain region following a given event.

A high-resolution anatomical MRI was obtained for each subject and spatially normalized to a standard Montreal Neurological Institute (MNI) template brain using SPM2 (http://www.fil.ion.ucl.ac.uk/spm/software/spm2) with the resulting parameters being applied to each individual subject’s beamformer volume through NUTMEG. Group analyses to evaluate effects at the second level were performed with statistical nonparametric mapping (SnPM; Singh et al. 2003). To minimize spatial frequency noise in the beamformer volumes, average and variance maps for each individual time window were calculated and smoothed using a Gaussian kernel with a width of 20 ms (FWHM = 20 mm full-width at half-maximum (Barnes et al. 2004; Guggisberg et al. 2007; Dalal et al. 2008). From these volumes, a pseudo-$F$ statistic is obtained for each voxel, time window, and frequency band. SnPM does not depend on a normal distribution of power change values across subjects. Correction for multiple comparisons (multiple voxels and time windows) was performed by obtaining a permuted distribution (through $2^k$ possible combinations of negations) and estimating the.
significance of each pseudo-$F$ value from its position in this permuted distribution. We report peak activity in the group analysis as $P < 0.05$, corrected for multiple comparisons whenever possible. In order to identify additional regions active within this frontoparietal network below the corrected threshold, a more liberal threshold (significant at $P < 0.01$, uncorrected) was also applied. The details of this approach have been described elsewhere (Singh et al. 2003; Dalal et al. 2008). An example of a group analysis from the time-frequency reconstructions of MEG data obtained by adaptive spatial filtering methods is shown in Supplementary Figure S3.

RESULTS

We identified onset, peak, and duration of activity over a cortical area in discrete frequency ranges across subjects (see Supplementary Fig. 3; Supplementary Video 1). Significant group increases and decreases in oscillatory activity (when compared with a within-trial resting baseline) were identified for 4 active states (saccade preparation, reach preparation, saccade execution, and reach execution). In agreement with the existing electroencephalography (EEG)/MEG literature, changes (decreases) in beta (12–35 Hz) power were largely confined to primary sensory and motor regions of the cortex (for a review, see Pfurtscheller and Lopes de Silva 1999), while significant power increases in a range greater than 65 Hz (in the high gamma band, associated with complex cognitive function and sensory integration; Tallon-Baudry and Bertrand 1999) localized to multiple cortical regions in the parietal and frontal lobes. We also identified significant group differences in oscillatory activity between saccade and reach preparation conditions.

Saccade Preparation

Following the appearance of a peripheral visual cue instructing subjects to prepare a movement of the eyes to the left or the right (cue onset $= 0$ ms, white line in Fig. 1A–E), the onset of activity across cortical areas occurred at different points in time in different frequency ranges. Cortical activity following the visual cue appeared first over visual cortex and PMC and was followed by activity in extrastriate cortex, PPC, and ultimately prefrontal cortex (Supplementary Videos 1,2).

0 ms (Cue Onset)–250 ms

During the first $250 \text{ ms}$ following the presentation of a saccade cue, significant decreases in alpha (8–12 Hz) and low-beta band power localized to regions of visual cortex in the hemisphere contralateral to the visual field being stimulated. In the high-gamma range (65–90 Hz) an increase in power was observed with an onset of 110 ms in right PMC for both left and right saccade preparation trials. This increase in high-gamma power, which peaked at 187.5 ms following the cue, and localized to a region over the superior frontal sulcus of the right hemisphere (Fig. 1A) was not observed during reach preparation (Fig. 1F–J). This region of the superior frontal sulcus has been identified in both human fMRI (Astafiev et al. 2003) and MEG studies (McDowell et al. 2005; Herdman and Ryan 2007) as the human FEFs (Table 1). High-gamma activity over the right FEF was present for both saccadic eye movements to the left (Fig. 1A) and right (Supplementary Fig. 4A). Following high-gamma activity over the FEF, we localized a decrease in power in the low-beta band over extrastriate visual cortex beginning 225 ms postcue that peaked at 425 ms (Fig. 1B; Table 1). For both left and right saccade preparation, activity in extrastriate cortex was always contralateral to the visual field being stimulated (Fig. 1B, Supplementary Fig. 4B).

250–400 ms

Following activity in FEF and extrastriate visual cortex, 275 ms after the visual cue appeared, a decrease in low-beta power localized to a region of caudal PPC contralateral to the visual field being stimulated (Fig. 1C; Table 1). At $350 \text{ ms}$ postcue, an additional region of activity localized to caudal PPC in the hemisphere ipsilateral to the cue (Fig. 1D; Table 1). Following onset, activity in caudal PPC was sustained throughout saccade preparation. This pattern of activity, with the onset of activity in the contralateral hemisphere preceding activity in the ipsilateral hemisphere, was the same for both saccade preparation directions (Fig. 1C,D; Supplementary Fig. 4C,D). This region of caudal PPC has been previously identified in human fMRI studies as a possible homolog of saccade-selective macaque area LIP (Sereno et al. 2001; Astafiev et al. 2003).

400–625 ms

Beginning at $425 \text{ ms}$ following the cue, we observed an increase in low-beta power over the right middle frontal gyrus for both right and left cue trials (Fig. 1E; Supplementary Fig. 4E; see Supplementary Video 1). Based on the MNI coordinates, this increase in low-beta power is likely in dorsolateral prefrontal cortex (DLPFC; BA46/9; Table 1). Following onset, this right DLPFC activity was present throughout saccade preparation. Low-beta activity in DLPFC during this period consists of power increases, as opposed to a decrease in the same frequency range at earlier time points over caudal PPC (Fig. 1A–E).

Reach Preparation Period

The timing of activity during the reach preparation period showed some similarity to the latency and duration of activity during saccade preparation; however, additional areas were active in the low-beta band when subjects prepared a movement of the arm. Following the cue to prepare a reaching movement (cue onset $= 0$ ms; white line in Fig. 1F–J) a decrease in low-beta power in visual cortex was followed by an increase in high-gamma power over PMC, with subsequent changes in low-beta power over PPC, primary motor cortex (M1; Supplementary Fig. 3) and DLPFC (see Supplementary Videos 3,4). Unique to the period of reach preparation, an increase in low-beta power over DLPFC was followed by significant changes in low-beta power in 2 additional regions of parietal cortex not active during the period of saccade preparation.

0 ms (Cue Onset)–250 ms

Following activity in visual cortex in the alpha band at 150 ms postcue (data not shown), low-beta activity with an onset of 225 ms postcue localized to the same region of extrastriate visual cortex active during saccade preparation (Table 1). This decrease in power peaked at $425 \text{ ms}$ (Fig. 1F; Supplementary Fig. 4F), with a latency and duration similar to activity observed during saccade preparation in this location.

250–400 ms

Later activity was identified in both PMC and PPC (Fig. 1G–J; see Supplementary Videos 3,4) during reach preparation. We observed an increase in high-gamma power over a dorsal region
of PMC (PMd) in the left hemisphere (contralateral to the responding arm, Fig. 1G) with an onset of 262.5 ms and an offset of 362.5 ms for both cue directions (Fig. 1G). This activity in PMd in the left hemisphere was present in both movement preparation directions (Fig. 1G, Supplementary Fig. 4G). Activity in the FEF was absent during reach preparation (Fig. 2A).

At 275 ms following cue presentation, a decrease in low-beta power localized to an area of PPC in the hemisphere contralateral to the visual field in which the cue appeared and was followed by an additional region of activity at 337.5 ms postcue over ipsilateral caudal PPC (Fig. 1H,I). The duration of this beta activity in bilateral caudal PPC was from 300 ms until the presentation of the target. In human fMRI studies, similar regions of caudal PPC have been shown to be active during visually guided reaching (Astafiev et al. 2003; Connolly et al. 2003). The same region of caudal PPC was active in the low- 

![Figure 1. Time-frequency group reconstructions for the period of left saccade (A–E) and left reach (F–J) movement preparation. Time-frequency spectrograms are reconstructed during a specific time window (white box) for the peak voxel in each region. During saccade preparation to the left (dark gray horizontal line, panels A–E), a yellow cue arrow appeared in the left visual field (cue onset = 0 ms; white vertical line) with a duration of 200 ms (yellow horizontal line). Following the cue to saccade, sources localized to (in order of onset of activity): the right FEF (panel A), right extrastriate cortex (panel B), right caudal PPC (panel C), left caudal PPC (panel D), and the right DLPFC (panel E). During reach preparation to the left (dark gray horizontal line, panels F–J), a blue arrow cue appeared on the left hand side of the screen (cue onset = 0 ms; white vertical line) with a duration of 200 ms (blue horizontal line). Following the cue to reach, sources localized to (in order of onset of activity): right visual cortex (panel F), left PMd (panel G), right caudal PPC (panel H), left caudal PPC (panel I), and right DLPFC (panel J). Cortical activity consisted of significant increases (as in FEF, PMd, and DLPFC, in red) or reductions (as in visual and PPC, in blue) in oscillatory power. All functional maps are thresholded (75% maximum power, in dB) and superimposed on a rendering of the MNI template brain through MRICro (http://www.sph.sc.edu/comd/rorden/mricro.html).](http://cercor.oxfordjournals.org/)

522 Cortical Dynamics of Visually Guided Behavior • Hinkley et al.
Saccade preparation (Fig. 1 with an onset of 300 ms for either movement direction) beta band during both saccade and reach preparation (Table 1), with an onset of 300 ms for either movement direction (Fig. 1H,I; Supplementary Fig. 4H,I).

400–625 ms
Beginning 450 ms following the onset of the reach cue, increases in low-beta power localized to the same portion of right DLPFC active during saccade preparation (Fig. 1J; Supplementary Fig. 4J; Table 1). A direct comparison was also made between the period of reach preparation and saccade preparation in order to identify regions specific for preparing a movement of the arm (Fig. 3). Just prior to target onset (525 ms postcue), a power decrease in the high-beta band (20–35 Hz) over primary motor cortex of the left hemisphere was significantly greater during reach than saccade preparation (Fig. 3A). At 575 ms postcue, decreases in low-beta power over PPC in the anterior intraparietal sulcus (likely in BA5; Table 1) and the medial wall of right PPC (likely BA7m; Table 1) was significantly greater during reach preparation than saccade preparation (Fig. 3B,C). Previous human fMRI studies have demonstrated activity within rostral parietal areas (such as BA5) in response to visually guided movements of the forearm (Levy et al. 2007; Hinkley et al. 2009). Decreases in beta power over M1, BA5 and Area 7M persisted until reach execution (Fig. 3). Although a decrease in low-beta power can be seen over both BA5 and BA7M during saccade preparation, this downward modulation in the beta band was significantly greater during the period of reach preparation in both regions (Fig. 2B). No significant changes in activity were identified when a direct comparison was made between the saccade preparation period and corresponding points in reach preparation as a baseline.

Saccade Execution Period
Saccade execution was initiated following the appearance of a white target arrow in the same location that the cue arrow was presented. Following this target arrow (target arrow = 0 ms, white line in Fig. 4A–F), activity was observed in both the low-beta (12–20 Hz) and high-gamma bands (65–90 Hz) across visual cortex, PPC, and PMC (Supplementary Videos 5,6). This progression of activity were identifiable during movements of the eyes to either the left (Fig. 4A–F) or right (Supplementary Fig. 5A–F). Similar patterns of activity were seen in the response-locked analysis, following the initial onset of the saccade (initial movement = 0 ms, white line in Supplementary Fig. 6) and prior to movement completion (return back to fixation).

Target Onset (0 ms)–400 ms
At a mean latency of 337.5 ms following the presentation of the target arrow an increase in high-gamma power localized to the cortex of the medial wall of the frontal lobe (Fig. 4A, Supplementary Fig. 5A). This region, which is likely the human supplementary eye fields (SEF; Table 1), was active during both leftward and rightward saccade execution periods with a response duration of 250 ms. A similar pattern of induced activity in the high-gamma range was also seen in the response-locked analysis. Prior to an eye movement back to fixation in the response-locked analysis, an early peak of activity in the 65–90 Hz range localized to the SEFs (Supplementary Fig. 6A).
activity in the SEF. In the frontal lobe, 2 peaks of high-gamma identified 3 peaks of activity in the high-gamma range following comparisons. In the saccade response-locked analysis, we also region of occipital cortex (Fig. 4).

Following the increase in high-gamma activity over the SEF, we also seen following activity in the high-gamma range following activity in cortical areas with earlier latencies may contribute to the decrease in low-beta power shown here. Conventions as in Figure 1.

400–600 ms
Following the increase in high-gamma activity over the SEF, we identified an increase in high-gamma power over the right FEF at 437.5 ms following the target (Fig. 4B; Table 1) and the left FEF at 450 ms (Fig. 4G; Table 1) during saccade execution in either direction. In addition to high-gamma activity in the FEF, an increase in high-gamma power was present over a large region of occipital cortex (Fig. 4D) 487.5 ms following saccade target presentation (Table 1; P < 0.02 corrected for multiple comparisons). In the saccade response-locked analysis, we also identified 3 peaks of activity in the high-gamma range following activity in the SEF. In the frontal lobe, 2 peaks of high-gamma activity were localized to the left and right FEFs (Supplementary Fig. 6B,C). Induced activity over primary visual cortex was also seen following activity in the SEF, concurrent with changes in high-gamma power over the FEF bilaterally (Supplementary Fig. 6D). Propagating waves of high-gamma activity between the SEF and FEF during saccades have been previously reported in humans using recordings from cortical surface electrodes (Lachaux et al. 2006).

600–850 ms
A significant decrease in low-beta power with a peak latency of 625 ms localized to bilateral PPC during both leftward and rightward saccade execution and continued throughout the saccade execution period (Fig. 4E,F). Peak activity in caudal PPC preceded the average RT for the saccade return to fixation (796 ms). This significant decrease in beta power prior to movement completion was also identified in the response-locked analysis. Over similar locations of the parietal lobe, peaks in beta power reduction localized to the right and left caudal PPC (Supplementary Fig. 6E,F). Like the stimulus-locked analysis, changes in beta power over caudal PPC in the response-locked analysis followed transient increases in high-gamma activity over occipital and frontal cortex. The location of these sources overlaps with regions of caudal PPC active during saccade preparation and reach execution.

**Reach Execution Period**
Following the reach preparation period, a target arrow appeared in the same location as the cue, instructing subjects to reach for the right or left target button using the right hand. Following the presentation of the target arrow (target arrow = 0 ms, white line in Fig. 4G–M), cortical activity in the beta (12–35 Hz) and high-gamma bands (65–90 Hz) appeared over PMC, occipital, and parietal cortices (Supplementary Videos 7,8) while subjects executed an arm movement, prior to button press (mean button press latency = 71.9 (212) ms; white line in Supplementary Fig. 7). A similar pattern of activity was observed when subjects moved their right arm to a target on the left (Fig. 4G–M) and the right (Supplementary Fig. 5G–M).

**Target Onset (0 ms)–500 ms**
Following the target arrow, a significant decrease in high-beta (20–35 Hz) power localized to left M1 (P < 0.004 corrected for multiple comparisons) at 400 ms posttarget and right M1 (left reaching movements, P < 0.012; right reaching movements, P < 0.02, all corrected for multiple comparisons) 450 ms following target onset (Fig. 4G,H; Table 1). Activity in bilateral M1 was sustained throughout the entire period of reach execution (Fig. 4G,H). Although activity in M1 was persistent throughout the movement, a peak in activity was localized prior to the response. This initial activity over bilateral M1 was also present prior to the button press in the response-locked analysis (Supplementary Fig. 7A,B).

500–625 ms
Two peaks of activity in the high-gamma range were identified during reach execution, beginning 500 ms following target onset. First, an increase in high-gamma power at 587.5 ms (with a duration of 150 ms) localized to a region of the inferior frontal gyrus (Fig. 4I; Table 1) likely in PMv cortex. Second, 625 ms following target onset, high-gamma activity increased over left sensorimotor cortex (SMC; Fig. 4I) for either reach direction and was sustained throughout the reach. A large number of voxels within SMC were statistically significant (Fig. 4I), suggesting that this activity represents synchronized activity in multiple fields, including primary motor cortex and the anterior parietal somatosensory fields (BA 3a, 3b, 1, and 2; Table 1). In the response-locked analysis, similar peaks in high-gamma activity confirmed that this activity occurred during the visually guided reach. Prior to button press (white line; Supplementary Fig. 7) a transient increase in power in the 65–90 Hz range was present over PMv (Supplementary Fig. 7C) and SMC (Supplementary Fig. 7E) that followed peaks in beta power over M1 bilaterally.

625–850 ms
Beginning 600 ms following target onset, 3 sources (an increase in high-gamma band power and 2 significant decreases in low-
beta band activity) localized to 3 distinct regions of PPC (Fig. 4K–M). In the high-gamma range at 687.5 ms, increased activity localized to cortex in the parietooccipital (PO) sulcus (Fig. 4I; Table 1). High-frequency activity in PO in conjunction with PMv and SMC may serve to integrate information across visual and somatosensory domains during movement, as synchronized oscillatory activity greater than 40 Hz has been implicated in the binding of incoming sensory inputs to guide behavior (Tallon-Baudry and Bertrand 1999; Engel and Singer 2001). Second, significant decreases in low-beta power localized to a region of PPC (Fig. 4K) in the hemisphere contralateral to the target location (RH, left reach: 625 ms, P < 0.043 corrected for multiple comparisons; LH, right reach: 825 ms, P < 0.02 corrected for multiple comparisons) at a latency and in a location similar to the high-gamma activity in PO (Table 1). Finally, at a mean latency of 800 ms following target onset, a significant decrease in power over PPC in the hemisphere ipsilateral to the target (Fig. 4M) was identified (LH, left reach: 725 ms; RH, right reach: 875 ms).

Although these peaks in activity in the stimulus-locked analysis occur within PPC and PO occurred relatively late in reach execution (following activity in M1, PMd, and SMC but prior to the average RT for button press), transient increases in beta power and high-gamma power were also present in the response-locked analysis immediately prior to the button press. Increased activity in these regions was localized prior to movement completion (Supplementary Fig. 7, white line) over caudal PPC bilaterally (Supplementary Fig. 7EG) and PO of the left hemisphere (Supplementary Fig. 7D). The peaks in activity we identify in the stimulus-locked analysis over frontal and parietal cortex occurred prior to the button press in the response-locked analysis, during the visually guided reach and were not associated with completing the movement itself.

**DISCUSSION**

Using MEG, we measured the spectrottemporal cortical dynamics in 2 networks specialized for visually guided saccades and reaching. This study is the first of its kind to use tMEG to dissociate networks (timing and location of activity in specific frequency ranges) specialized for these 2 movement types. The level of detail provided by the time-frequency analysis of MEG sensor data allow us to directly address questions about serial and parallel processing in discrete cortical regions on a millisecond timescale, which is not possible using techniques like fMRI, PET, or EEG.

Responses in some brain regions (such as visual cortex and DLPFC) were invariant across effector types, likely related to stimulus properties or attentional processing. However, multiple regions of PPC and PMC were active during only one type of movement (SEF and FEF for saccades; PMd, PMv, BA5, and 7m for reaching), and these 2 networks showed unique temporal dynamics. These “effector-specific” patterns are prominent in both the beta (12–35 Hz) and high-gamma (65–90 Hz) frequency bands. In addition, while the onset and peak of activity often differed across areas, consistent with serial information processing, power changes were sustained over hundreds of milliseconds in many cortical regions, suggesting that some of these processes took place in parallel. We hypothesize that the flow of information within these networks is related to the temporal dynamics of the activity that we observed in response to saccade and reach preparation and execution (Fig. 5). This hypothesis is consistent with connections of putatively homologous regions subserving similar movements in the macaque monkey.

**Effector-Specific Networks**

Previous studies of visually guided behavior have provided a sense of the complex organization of parietal and PMC involved in movements of the eyes and forearm (Simon et al. 2002; Astafiev et al. 2003; Hinkley et al. 2009). Here, we extend this work, outlining the temporal dynamics of activity in these regions. We hypothesize that the activity identified in the tMEG reconstructions illustrate in real time the progression of activity across a network. Our findings suggest the presence of effector-specific frontoparietal networks in humans, similar to those described in macaque monkey neocortex.

For example, unique to saccade preparation was an increase in the high-gamma band localized to the right FEF (Fig. 5). During saccade execution, high-gamma activity was observed in SEF and subsequently in visual cortex and FEF bilaterally, followed by a low-beta power decrease over caudal PPC. This progression of high-gamma activity across SEF, FEF, and visual cortex during saccade execution (Fig. 5, right column) is consistent with known connections in macaque cortex, where efferent projections from the SEF synapse on regions of the FEF (Schall et al. 1993). FEF and visual cortex in nonhuman primates, in turn, project to caudal regions of PPC serving saccades (such as area LIP; Blatt et al. 1990; Lewis and Van Essen 2000). These connections are distinct from the connections between frontal and parietal areas involved in visually guided forelimb movements in nonhuman primates.

During the generation of a reach, multiple regions of the frontoparietal cortex were uniquely active. For reach preparation, high-gamma activity increased in left dorsal PMC prior to low-beta activity in BA5 and BA7m in PPC (Fig. 5). At reach target onset, initial low-beta activity in M1 was followed by an increase in high-gamma power over SMC, PO, and area PMv in the hemisphere contralateral to the limb in motion, a pattern of activity not present during saccade execution (Fig. 5). Reach-specific activity in SMC, PO, and PMv was followed by changes in low-beta power over caudal PPC bilaterally. In the macaque monkey, premotor, sensorimotor, and PO cortical fields involved in visually guided forelimb movements are projection targets for primary motor cortex (Shipp et al. 1998; Dancause et al. 2006; Stepniewska et al. 2006). Inputs from PMv, SMC, and PO, in turn, converge on PPC areas involved in reaching, such as MIP and V6A (Caminiti et al. 1999). Collectively, the results of the present study combined with data from nonhuman primate neuroanatomy suggest that in macaques and humans premotor corticofugal fields (SEF, FEF, and PMv) direct signals to posterior parietal cortical fields (caudal PPC) during visually guided behaviors.

As in previous fMRI studies, patterns of activity overlapped to some extent (see Levy et al. 2007; Hinkley et al. 2009). In both the saccade and reach preparation conditions activity occurred in visual and prefrontal cortex (Fig. 5, left column, hatched bars). Early beta activity over the occipital lobe likely represents processing of the visual cue, a finding previously reported in an MEG study of movement preparation (McDowell et al. 2005). During both reaching and saccade preparation, activity was also identified in right DLPFC, a region involved in the maintenance of visuospatial representations to guide
Figure 4. Stimulus-locked group analysis of the data during both the left saccade execution period (dark gray horizontal line, panels A–F) and the reach execution period (dark gray horizontal line, panels G–M). Movement execution was signaled when a white target arrow in the left visual field (at 0 ms) with a duration of 1000 ms (yellow horizontal
behavior (Levy and Goldman-Rakic 2000). Increased beta power in DLPFC was only present during movement preparation and subsequently ramped down following the onset of the target, suggesting that this activity was associated with goal maintenance irrespective of response modality. Increased beta power in DLPFC during both saccade and reach preparation supports the hypothesis that this region is released from inhibition following activity in PPC and PMC (Pastötter et al. 2008), a hypothesis based on connectivity data from DLPFC, PPC, and PMC in the macaque brain (Petrides 2005).

Sensorimotor Integration

Based on the timing and distribution of activity during movement preparation and execution, we can infer a pattern of integration of inputs from the eyes and hands involving PPC and PMC. For example, during the period of movement preparation, which required a visual cue to be transformed into a movement of the eyes or arm, early activity in premotor and visual cortex progressed to regions of PPC bilaterally (Fig. 5), suggesting that activity observed at earlier latencies in modality-specific areas are integrated in caudal PPC. Specifically, the changes in low-beta power over the caudal regions of PPC occurred ~100 ms after activity over extrastriate visual cortex, suggesting that input from visual cortex is processed in PPC during visually guided movement. Similarly, activity in PMC was also relayed to caudal PPC during movement preparation, as the high-gamma increase over right FEF for saccades and left PMd for reaching occurred ~100 ms earlier than changes in low-beta activity over caudal regions of PPC. This temporal distribution of activity is consistent with the notion that prefrontal cortex can act as a top-down influence on information being processed in the parietal lobe (Knight 1984; Brass et al. 2005).

In addition, our data suggest that information processed during reach preparation in caudal PPC and M1 is relayed to rostral and medial parietal fields prior to movement onset. We observed changes in activity over caudal PPC and M1 before activity in parietal areas 5 and 7M. Human MRI studies have shown activity in the rostral regions of parietal cortex (including BA5) that play a preferred role in visually guided reaching (Levy et al. 2007; Hinkley et al. 2009). The late activity we see in BA5 and BA7M indicate that anterior parietal fields active during arm movements come on-line during the very late period of reach preparation. In nonhuman primates, both BA5 and BA7M are reciprocally connected with M1, PMC, and caudal PPC (Shipp et al. 1998; Caminiti et al. 1999; Padberg et al. 2007). The temporal pattern of activity we identified in human cortex suggests that, as in the macaque, human PPC and PMC are sites of integration of specific sensory, motor, and cognitive signals needed to produce a movement.

Serial versus Parallel Processing

In the nonhuman primate literature exquisite diagrams of information processing have been developed through models of neuroanatomical data (Felleman and van Essen 1991; Kaas and Garragthy 1991). However, the progression of activity across the brain during visually guided behavior in real time has yet to be shown. In the present study, we identified both serial and parallel processes based on the difference in the timing of peak activity between brain regions within tMEG reconstructions. Serial processing was observed, for example, during the period of movement preparation when high-gamma activity in effector-specific premotor cortical fields (FEF, PMd) peaked prior to low-beta activity in caudal PPC. These serial patterns of processing are consistent with electrophysiological recording data from macaque monkey cortex that shows propagating waves of activity between motor cortical fields during visually guided reaching tasks (Rubino et al. 2006).

In contrast, several researchers have presented experimental evidence of parallel cortical processing, where spatially disparate brain regions are active during overlapping periods of time. For example, in the somatosensory system of both

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Figure 5. Summary of the stages of processing during movement preparation (left column) and execution (right column). Areas were active during both movement types (in hatched bars) or specialized for either arm movements (in dark gray) or eye movements (in light gray). The peak of activity in a single area is marked in black (vertical line). Regions with high-gamma activity are outlined in white. During saccade preparation, FEF activity occurs prior to activity in areas LIP/PRR. During reach preparation, processing in PMd precceeds activity in areas LIP/PRR in the caudal parietal lobe and then to M1, which in turn is followed by activity in both BA5 and BA7M. During saccade execution, SEF activity precedes processing in FEF and visual cortex, which in turn is followed by activity in areas LIP/PRR prior to the return movement back to the origin. During reach execution, bilateral activity in M1 precedes activity in left SMC, PO, and PMv. Activity in sensorimotor and visual cortex is followed by processing in parietal areas LIP/PRR while the limb is in motion.
human and nonhuman primates, a model of parallel processing has been developed based on observations of simultaneous neural activity in brain regions originally hypothesized to be hierarchically organized, such as S1 (3b) and S2/PV (Zhang et al. 1996; Karhu and Tesche 1999). For visually guided behavior, Naranjo et al. (2007) observed activity across PPC and PMc in EEG time series data from visually guided arm movements. They proposed that temporally overlapping activation across PPC (SPL and Area 7M) and motor cortex (PMd, M1) during reach preparation was indicative of parallel processing during sensorimotor transformations.

Our findings, with relatively high spatiotemporal resolution, reveal a more detailed temporal structure within the frontal-parietal network during arm movements. Although activity over PMd during reach preparation overlapped in time across M1 and caudal PPC, changes in oscillatory activity in PMd were only identified in the high-gamma band, while changes in M1 and caudal PPC were only significant in the beta range (Fig. 5). In our data set, divergent patterns of activity in different frequency ranges (high-gamma, beta) demonstrate the complexity of cortical processing. Therefore, while activity can be measured in a given cortical field using PET/fMRI/EEG, this activity can actually occupy one or more different frequency ranges with putatively different functions (Pfurtscheller et al. 2003). The observation of simultaneous serial and parallel processing in the brain is consistent with an emerging hypothesis from work in both human EEG/MEG and nonhuman primate electrophysiological recordings where serial and parallel processes operate concurrently in order to maximize cortical resources (Bullier and Nowak 1995; Inui et al. 2006).

The results of the present study demonstrate that effector-specific cortical processing occurs across both spatial and finely tuned temporal levels. Our tMEG data reveal that temporal information in visuomotor transformations can be encoded through 2 different mechanisms. First, posterior parietal and premotor networks specific for the use of a single-effector are well defined when oscillatory brain activity in the gamma range is separated from spatially overlapping, low-frequency (beta) activity. Second, the onset and duration of activity across brain areas provides information about how these signals interact in the brain to guide a movement of the eyes or the forelimb toward a visual location. Sustained activity (in, e.g., primary motor cortex during reach preparation) suggests that inputs can be processed in parallel even in brain regions that are recruited at different points in time (BA5, DLPFC, and 7m during the same period). This is a clear example in vivo of what has been suggested based on neuroanatomical work from nonhuman primates—that complex cognitive functions such as visuomotor transformation are not only represented by processing within specific cortical fields but also by areas that are connected and interact with each other.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

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Notes

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