Reorganization of Oscillatory Activity in Human Parietal Cortex during Spatial Updating

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Single-neuron recordings have shown that the posterior parietal cortex (PPC) processes spatial information in many frames of reference, including gaze-centered, head-centered, body-centered, and intermediate coding frames. At the population level, rhythmic neuronal synchronization may provide a mechanism by which PPC could selectively emphasize the task-relevant reference frame in spatial processing. Using magnetoencephalography, we tested this hypothesis by studying the modulations in oscillatory activity in a spatial updating task. Human subjects had to remember the location of a target, briefly flashed left or right of central fixation. Next, they refixated and then, after a further memory delay, made a saccade to the memorized target location. We observed gammaband (>40 Hz) synchronization and alpha-band (8–12 Hz) desynchronization in contralateral occipital and parietal areas, both showing updating in a gaze-centered reference frame but with fast and slow time courses, respectively. Furthermore, after updating, ipsilateral areas showed less alpha desynchronization when they had been contralateral to the target before updating. Taken together, our results suggest that power in the gamma band is instantly reorganized to encode task-relevant visuomotor space in a gaze-centered reference frame, while power in the alpha band reflects a regulatory mechanism actively facilitating the gating of the saccade target and inhibiting the original stimulus representation.

Keywords: alpha band, gamma band, magnetoencephalography, saccade, reference frame

Introduction

The posterior parietal cortex (PPC) plays an important role in the transformation of spatial representations from perception to action. In particular, activity in the lateral intraparietal area (LIP) of monkey PPC and homologous areas in the human PPC has been associated with specialized spatial functions, including the control of spatial attention (Silver and Kastner 2009; Bisley and Goldberg 2010; Liu et al. 2010), working memory (Pesaran et al. 2002; Curtis et al. 2004), and saccade planning (Sereno et al. 2001; Andersen and Buneo 2002; Zhang and Barash 2004; Liu et al. 2010).

The neural architecture of LIP is characterized by primarily eye-based gaze-centered response fields (Andersen and Buneo 2002; Patel et al. 2010). Furthermore, within the gaze-centered neuronal population of LIP, activity has been demonstrated to remap in order to compensate for intervening saccades (Duhamel et al. 1992; Colby et al. 1995; Medendorp et al. 2003; Merriam et al. 2003). Gain field modulations, the scaling of neuronal firing rates by eye and head position, have been suggested to implicitly transform these spatial representations into other gaze-independent (e.g., head/body-centered) reference frames (Andersen et al. 1985; Chang et al. 2009).

At the population level, rhythmic neuronal synchronization may provide a mechanism to selectively amplify and gate behaviorally relevant representations in parietal processing (Buzsáki 2006). In general, gamma-band oscillations (>40 Hz) have been implicated in active local processing, maintaining and emphasizing a neural representation (Fries 2009), while alpha-band oscillations (8–12 Hz) reflect functional inhibition and gating (Klimesch et al. 2007; Jensen and Mazaheri 2010).

With regard to monkey area LIP, intracranial local field potential recordings have shown that neurons synchronize their activity in a spatially tuned manner during the coding of a working memory for a saccade (Pesaran et al. 2002). Using magnetoencephalography (MEG), corresponding observations have been made in human PPC, indicating a bias of spectral power to contralateral target locations (Medendorp et al. 2007; Van Der Werf et al. 2008, 2009, 2010; Hinkley et al. 2011). But without varying eye position, the question remains unanswered whether these oscillations are related to the construction of a gaze-independent spatial representation or are a manifestation of the saccade goal encoded in gaze-centered coordinates.

To discriminate between these 2 possibilities, we applied MEG to record oscillatory brain activity from human subjects while they produced intervening saccades between viewing a goal target and generating an eye movement toward its remembered location. While the target remained stable in gaze-independent coordinates (i.e., relative to head/body), its remembered location must be updated to compensate for the intervening saccade in gaze-centered coordinates. By exploiting the hemispheric lateralization of the power in the various frequency bands, we compared conditions in which the remembered location of the target reverses sides relative to the gaze-fixation point versus conditions in which the target remains at the same side after the intervening eye movement.

Our results show that parietal gamma-band synchronization is immediately biased toward the new goal direction, consistent with spatial updating of the goal direction in a gaze-centered reference frame. Power modulations in the alpha band are in line with a regulatory mechanism for spatial updating, slowly inhibiting the retrospective target representation, and facilitating the updated target representation for the saccade. Taken together, our findings suggest a reorganization of oscillatory activity during spatial updating.

Materials and Methods

Participants

Twenty-two naïve participants (7 females/15 males; mean age 26.5 years), free of any neurological or psychiatric disorders, volunteered to...
participate in the study. All participants provided written consent according to guidelines of the local ethics committee (CMO Committee on Research Involving Humans subjects, region Arnhem-Nijmegen, the Netherlands).

**MEG Recordings**

Participants sat upright in the MEG system, viewing a stimulus screen that was positioned 40 cm in front of them. Stimuli were generated with Presentation 9.10 software (Neurobehavioral Systems Inc. Albany, NY). Using an LCD video projector (SANYO PLC-XP41, 60 Hz refresh rate), these stimuli were projected onto the screen via 2 front-silvered mirrors. MEG data were recorded continuously using a whole-head system with 275 axial gradiometers (CTF Systems Inc., Port Coquitlam, Canada). Head position with respect to the sensor array was continuously measured using localization coils fixed at anatomical landmarks (the nasion and at the left and right ear canal). Horizontal and vertical electrooculograms (EOGs) were recorded using electrodes placed below and above the left eye and at the bilateral outer canthi. Impedance of all electrodes was kept below 5 kΩ. During the experiment, the EOG recordings were continuously inspected to ensure that participants were vigilant and correctly performing the task. Furthermore, the electrocardiogram (ECG) was recorded with electrodes (impedance < 50 kΩ) attached above the right clavicle and under the last false rib on the left side. All signals were low-pass filtered at 300 Hz, sampled at 1200 Hz, and then saved to disk.

For each participant, a full-brain anatomical magnetic resonance image (MRI) was acquired using a standard inversion prepared 3D T₁-weighted scan sequence (flip angle = 15°; voxel size: 1.0 mm in-plane, 256 × 256, 164 slices; time repetition = 0.76 s; time echo = 5.3 ms). A 1.5-T whole-body scanner (Siemens, Erlangen, Germany) was used to record the anatomical MRIs, with reference markers at the same locations as during the MEG recording, to allow alignment of the individual MEG and MRI data in later analyses.

**Experimental Paradigm**

Subjects performed an intervening-saccade task, shown in Figure 1. Each trial began with the subject fixating centrally at a small white cross presented on the screen. After a baseline period of 1.5 s, a target stimulus was flashed for 100 ms in the left or right visual hemifield, horizontally at a mean eccentricity of 3° or 9°, and positioned vertically at a polar angle < 45° relative to the horizontal meridian. Targets were jittered slightly in eccentricity (2° visual angle) to make them less predictable. After a 2-s delay period (the first delay period), the fixation cross jumped to a new position, at a horizontal eccentricity of 3°, 9°, or 15° (jitter 2°), in either the left or the right visual field, unpredictable to the subject. Subjects were instructed to immediately saccade to the new fixation position (i.e., the intervening saccade), which was presented for a duration of 2 s (second delay period). The offset of the fixation cross signaled the subjects to look at the remembered location of target. The refixation positions were chosen such that the desired amplitude of this saccade was on average 6° (jittered in the interval 4-8°). Subsequently, after 0.7 s later, the central fixation cross reappeared, indicating the start of a new trial. Trials were presented in 20 blocks of 30 trials each, with the different blocks separated by a brief self-paced resting period.

Essentially, the paradigm had 4 different conditions regarding the remembered location of the target relative to gaze before and after the intervening saccade. It either remained to the right (RR condition) or remained to the left (LL) or it shifted from right to left (LR) or moved from left to right (LR). In contrast, during the intervening-saccade task, the location of the target is invariant in a gaze-independent coding frame, such as a head-, body-, or world-fixed frame.

**Behavioral Analysis**

EOG data from each subject were inspected online to ensure high vigilance levels and correct performance of the task. Figure 1B shows the EOG traces (horizontal component) of a typical subject during 20 trials of each of the 4 conditions. A schematic representation of the respective target (o) and fixation position (+) is flanked on the right-hand side. For each condition, the subject keeps stable fixation during the first delay period. The subsequent intervening saccade brings the eyes’ fixation point either to the left or to the right of the remembered target location, which is subsequently well maintained till the end of the second delay period. The saccade to the remembered target location is made after the fixation spot was turned off. Note that, for every remembered target position, there are opposing eye movement vectors with about equal amplitudes. Trials with eye movements larger than the noise level of the EOG recordings (2× standard deviation [SD] = 1.0°) during fixation period were discarded. Also trials in which subjects blinked or performed incorrectly otherwise were excluded from further analysis. The EOG recordings in all 22 subjects confirmed that they followed the instructions correctly in most trials. There was no significant difference in the number of rejected trials among the 4 task conditions, specified above (one-way ANOVA, F<sub>3,68</sub> = 2.4, P > 0.05). On average 398 ± 89 (SD) trials per participant were accepted for further analysis (LL 97 ± 24 (SD) trials; LR 101 ± 23 trials; RR 98 ± 23 trials; RL 101 ± 21 trials). Begin and end times of the intervening refixation saccades were based upon visual inspection, accounting for noise level of the EOG system (Van Der Werf et al. 2008). Based on the same criteria, reaction times for the memory-guided target-directed saccades (LL: 181 ms; RR: 185 ms; LR: 187 ms; RL: 182 ms) did not differ between the 4 conditions (one-way ANOVA, F<sub>3,68</sub> = 2.0, P > 0.05).

**MEG Data Analysis**

Data were analyzed using Fieldtrip software (http://www.ru.nl/ neuro-imaging/fieldtrip), an open source Matlab toolbox for neurophysiological...
data analysis developed at the Donders Institute for Brain, Cognition and Behaviour. From the trials that survived the exclusion criteria described above, data segments that contained muscle activity or jump artifacts in the SQUIDs were excluded using semiautomatic artifact rejection routines.

For the sensor-level analysis, an estimate of the planar gradient was calculated for each sensor (Bastiaansen and Knoesche 2000). The horizontal and vertical components of the planar gradients estimated using the signals from the neighboring sensors approximate the signal measured by MEG systems with planar gradiometers. The planar field gradient simplifies the interpretation of the sensor-level data since the maximal signal is located above the source (Hamalainen et al. 1993). Power spectra were computed separately for the horizontal and vertical planar gradients of the MEG field at each sensor location, and the sum of both was computed to obtain the power at each sensor location irrespective of the orientation of the gradient.

With these data, we also took several measures to protect our results against oculomuscular distortions, including microsaccades, which have been shown to produce high-frequency artifacts (Yuval-Greenberg et al. 2008; Jerbi et al. 2009). First, we refrained from analyzing data during which the intervening or final saccade was made. Second, we used independent component analysis (ICA) to clean the sensor-level data of cardiovascular artifacts as well as any remaining eye-muscle artifacts due to the eccentric fixation during the second delay period in our paradigm. More specifically, we excluded the components that correlated the highest \( r > 0.15 \) with either the EOG or the ECG signal and had a spatial topography associated with ocular or cardiac magnetic effects (Barbati et al. 2004). Also components whose effects were topographically located around the eyes were excluded from the data. Finally, we balanced our contrasts (see below) to rule out effects of eccentric gaze fixation during the second delay.

Time-frequency representations (TFRs), estimating the time course in power, were computed using a Fourier approach, applying a tapered window. Because the gamma band is typically much wider and therefore better characterized with more spectral concentration (Hoogenboom et al. 2006), we analyzed 2 frequency ranges separately. For the lower frequency band (5–10 Hz), we used a Hanning taper, and a time window of 0.5 s, sliding through the trials in steps of 0.05 s. This resulted in a spectral smoothing of roughly 3 Hz. For the higher frequency band (40–130 Hz), we applied a multitaper approach (Percival and Walden 1993) using 11 orthogonal Slepian tapers and an analysis window of 0.4 s, also sliding through the trials in steps of 0.05 s. This resulted in a spectral smoothing of approximately 14 Hz.

To localize the neural sources of the various spectral components, we applied an adaptive spatial filtering (or beamforming) technique (Dynamic Imaging of Coherent Sources) (Gross et al. 2001; Liljestrom et al. 2005). First, we divided a template brain volume (International Consortium for Brain Mapping template; Montreal Neurological Institute (MRI), Montreal, Canada) into a regular 1 cm 3D grid. We then warped each subject’s MRI to fit this template MRI and the template’s grid, after which we warped the grid back to fit the subject’s original MRI to obtain a grid in MNI coordinates for each subject. This procedure allowed us to directly compare grid points across subjects in MNI space without the need to normalize. For each subject and for each grid point, a spatial filter was constructed that passes activity from this location with unit gain, while attenuating activity from other locations (Gross et al. 2001). This filter was computed from forward modeling with respect to dipolar sources at each grid point (the lead field matrix) and the cross spectral density between all combinations of sensors at the frequency of interest. We used realistic single-sphere head models from each subject’s individual MRI to calculate the lead field matrix (Nolte et al. 2003). For every single subject, the source power was estimated to the same baseline interval that was used for the sensor-level analysis.

Statistical Inferences

We computed the task-related changes in power in various frequency bands relative to average power in the baseline period (see Fig. 1). The high-frequency baseline power was computed over the period from -0.4 to -0.2 prior to the presentation of the stimulus, using a 0.4 s wide sliding window. The low-frequency baseline was determined across the interval -0.35 to -0.25 s, using a 0.5 s sliding time window. Thus, in effect, the baseline period was equal for both frequency ranges: -0.6 to 0 s prior to stimulus onset. We expressed the difference in log power between the respective delay periods and the baseline as a \( t \)-score for each subject and for each condition. The resulting \( t \)-scores were transformed into \( z \)-scores (Bauer et al. 2006; Medendorp et al. 2007) to obtain normalized estimates of power differences. The resulting \( z \)-scores, which are now well normalized for intrasubject variance, were pooled across subjects \( (z_{\text{group}} = \frac{1}{\sqrt{N}} \sum z_i \) with \( z_i \) being the \( z \)-score of the \( i \)th subject).

In the first delay, statistical significance of the power modulations was tested at the sensor level by using a nonparametric clustering procedure (Nichols and Holmes 2002; Maris and Oostenveld 2007). We chose our frequency ranges of interest to be 8–12 Hz for the alpha band and 40–60 Hz for the gamma band. These frequency ranges are compatible with previous reports (Medendorp et al. 2007; Van Der Werf et al. 2010). In this procedure, cluster-level test statistic is defined by pooling the \( z \)-scores of neighboring sensors showing the same effect in a given time-frequency window of interest. In a nonparametric statistical test, the type I error rate is controlled by evaluating the cluster-level test statistic under the randomization null distribution of the maximum cluster-level test statistic. In our analysis, this was obtained by randomly permuting the data between 2 conditions within every participant. By creating a reference distribution from 1000 random sets of permutations, the \( P \) value was estimated as the proportion of the elements in the randomization null distribution exceeding the observed maximum cluster-level test statistic. The significant channels were used for further analysis of the power changes during the second delay, that is, after the intervening saccade, using the randomization approach in the time-frequency domain rather than on the sensor level. A nonparametric approach was also applied to test for statistical significance at the source level, clustering together neighboring voxels exhibiting a similar effect in a predefined volume of interest, comprising of the occipital and parietal cortices. More specifically, we predefined the region of interest (ROI) using the WFU pickatlas (http://fmr.i.wfubmc.edu/), including the angular gyrus, superior parietal cortex, inferior parietal cortex, postcentral sulcus, cuneus, precuneus, superior occipital cortex, middle occipital cortex, inferior occipital cortex, calcarine sulcus, supramarginal sulcus, and the lingual sulcus.

Isolating Task-Dependent Spectral Power

The paradigm was designed with 8 different types of trials. Table 1 provides an overview of the screen positions (horizontal components) of the target position (T) and the gaze refixation location (G), with the initial central fixation at 0°. Recall that in the actual task, the respective positions were jittered slightly. The 8 different trial types can be divided into RR, RL, LL, and LR conditions, as described above. In our analyses, we exploited the hemifield-specific lateralization of power of power to compare conditions in which the target shifts sides relative to gaze (RL, LL, RL, RR).
Ge$sensors covering the right hemisphere: Gi$fixation (Ge) in a similar manner, using the following formulas for the gaze-independent target representation (Gi) and the direction of eye paradigm. We computed the direction selectivity of power for both the specific changes in power during the second delay period of our pooled across hemispheres, resulting in the combined hemisphere-calculations for the sensors covering the left hemisphere, we only dependent target representations are enhanced. For the corresponding opposing gaze-centered (or updated) target directions, these gaze-direction. Because in this comparison, P1 and P4 and P5 and P8 have a rightward gaze direction and P5 and P8 trials with a leftward gaze direction, resulting in a subtraction of potential effects due to gaze direction. Because in this comparison, P1 and P4 and P5 and P8 have opposing gaze-centered (or updated) target directions, these gaze-dependent target representations are enhanced. For the corresponding calculations for the sensors covering the left hemisphere, we only flipped the sign in the above equations. The isolated contributions were pooled across hemispheres, resulting in the combined hemisphere-specific changes in power during the second delay period of our paradigm. We computed the direction selectivity of power for both the gaze-independent target representation (Gi) and the direction of eye fixation (Ge) in a similar manner, using the following formulas for the sensors covering the right hemisphere: Gi = (P4 - P1) + (P8 - P5), in which Pi represents the power during the second delay in trial type i in Table 1. Because P1 and P4 represent trials in which the stimulus was presented to the right and P5 and P8 trials with the stimulus to the left, this comparison effectively subtracts out potential effects of a head-centered target encoding. Similarly, during the second delay, P1 and P4 reflect power of trials with a rightward gaze direction and P5 and P8 trials with a leftward gaze direction, resulting in a subtraction of potential effects due to gaze direction. Because in this comparison, P1 and P4 and P5 and P8 have opposing gaze-centered (or updated) target directions, these gaze-dependent target representations are enhanced. For the corresponding calculations for the sensors covering the left hemisphere, we flipped the signs in the equations. We pooled the power effects across hemispheres.

Results
We examined the role of neuronal synchronization in the representation of memorized visual targets across intervening eye movements. In our test, subjects fixated at a central point, while a target was briefly cued into the retinal periphery. After a delay, subjects switched fixation points (the intervening saccade) and then after another delay looked to the remembered location of the target. On half of the trials, the intervening saccade made the remembered location of target change sides relative to the gaze line, while on the other half of the trials, the remembered target stayed on the same side relative to gaze. We assessed the laterality of spectral power during the second delay interval to characterize the oscillatory activity in terms of gaze-dependent target updating (Gd), gaze-independent target coding (Gi), and gaze direction (Ge).

Contralateral Gamma-Band Activity after Target Presentation
We start the description of our results with a focus on the high-frequency power modulations (>40 Hz) during the first delay interval. During this interval subjects have to memorize a location of a target that served as a goal only after an intervening eye movement, which could be directed either leftward or rightward. Because the z-scores are calculated against an arbitrary task-irrelevant baseline, we show and interpret the data by contrasting different experimental conditions within hemispheres. Figure 2A shows the scalp topography of 40–60 Hz gamma-band activity, averaged across subjects, during 4 consecutive nonoverlapping time intervals, each covering 0.5 s of the first delay interval. Regions with warmer (red) colors (positive z-scores) show a preference for contralateral targets; regions with cooler (blue) color (negative z-scores) have a bias for ipsilateral targets. The stimulus response, observed in the time interval 0–0.5 s, is reflected by a clear contralateral bias in power in both posterior hemispheres (40–60 Hz; 0–0.5 s; P < 0.05; significant sensors are marked). This preference vanishes almost completely during the next 0.5 s but then builds up again to significant values during the last second of the delay interval (40–60 Hz; 1.0–2.0 s; P < 0.05; significant sensors are marked).

Figure 2B, middle panel, shows the scalp topography of the mean power changes over time 1.0–2.0 s and frequency 40–60 Hz. The 2 symmetric subsets of posterior sensors (marked by dots) were subjected to a time-frequency analysis, shown by the left- and right-hand panels in Figure 2B, in the same color format. Based on the symmetry of these panels, the spectrograms were pooled across hemispheres, resulting in the combined hemisphere-specific changes in power for contralateral versus ipsilateral targets (Fig. 2B, bottom panel).

As shown, in response to the target cue, the posterior sensors show a clear directional bias, across a 40–120 Hz frequency range, peaking in the 40–60 Hz range with a stronger synchronization at sensors contralateral than ipsilateral to targets. Source localization methods (ROI-restricted beamforming, see Materials and Methods) of the most responsive periods revealed the direction-selective activity in the gamma band to originate mainly from occipital areas, with some spread to parietal areas (40–60 Hz; 0–0.5 s; P < 0.05) (see Fig. 2B, bottom-left panel). During the delay interval, this power selectivity was sustained exclusively in the 40–60 Hz band, gradually increasing in strength toward the end of this period. The source of this narrow gamma-band activation was localized exclusively to extrastriate occipital areas (40–60 Hz; 1.0–2.0 s; P < 0.05) (see Fig. 2B, bottom-right panel). In absence of any visual stimulation during the first delay, and without the incentive to plan a targeting saccade, this effect can be interpreted as a direction-selective working memory for contralateral targets.

Gamma-Band Synchronization Reorganizes during Spatial Updating
The crucial manipulation in this experiment was the intervening eye movement, which subjects produced between viewing the target and executing the eye movement toward its remembered location. If the target location is coded relative to gaze, its memory trace must be remapped to maintain the integrity of the information in this frame across the eye movement. The outcome of this process should manifest itself as a retuning of the directional selectivity of spectral power during the second delay for conditions changing the direction of the target relative to gaze. More specifically, this reorganization of spectral power should operate across hemispheres when the intervening saccade changes the side of the
target relative to gaze and within a hemisphere when the target remains on the same side. On the other hand, the location of the target would remain in the same hemifield relative to the head and body, that is, in gaze-independent coordinates. Thus, if the directional selectivity of the spectral power, as observed during the first delay period, reflects the side of the target relative to the head or body, there is no need for a hemispheric reorganization of neuronal synchronization after the intervening saccade. Despite these clear predictions, however, it is also important to realize that subjects adopted a new eye position during the second delay period, which may also put its signature on the observed spectral power.

A bias in spectral power during the second delay period, therefore, could reflect the outcome of gaze-dependent target updating (Gd), the persistence of a gaze-independent target representation (Gi), or the result of maintaining eccentric eye fixation (Ge). We determined each of these 3 components on the basis of selecting different subsets of trials, which were selected such that contributions of the other 2 factors are neutralized in terms of hemifield (for details, see Materials and Methods). Furthermore, the power modulations during the second delay period were analyzed in alignment with the end time of the intervening saccade (when the refixation was stable). Figure 3 shows the results of these analyses, plotting scalp topography (left column), time-resolved power changes in relation to each component (right column), and the source reconstruction of the task-modulated oscillatory source (Fig. 3D). Contralateral and ipsilateral biases in spectral power are color coded in red and blue, respectively.

Figure 3A (left) shows the selective power modulations due to gaze-dependent target updating (Gd), in the form of more spectral power in the gamma band for contralateral than ipsilateral targets (0.25-1.25 s after refixation was completed) at posterior sensors, at the 60-80 Hz frequency range. The TFR of the marked sensor groups, which were determined based on the activity during the first delay, is shown in the right panel, pooled across hemispheres. The spectrograms clearly demonstrate that the contralateral selectivity of power in the 60-80 Hz gamma band is a sustained and significant effect ($P < 0.05$; nonsignificant time-frequency tiles are masked at an opacity of 0.5), coding the gaze-centered direction of the target, which is equivalent to the direction of the pending saccade. It is further noteworthy that the updated gaze-centered representation during the second delay is found at a higher frequency range than the gamma-band frequency that reflected the memorized target location before the intervening eye movement. The source of the 60-80 Hz gamma-band activity was exclusively found in the PPC ($P < 0.05$; 0.5-1.0 s; 60-80 Hz; ROI-restricted beamforming, see Materials and Methods) (Fig. 3D).

Recall that in our task the location of the target is spatially constant in a gaze-independent coding frame, such as a head-, body-, or world-fixed frame. Figure 3B demonstrates the lack of evidence for the alternative hypothesis, showing the absence of a persisting gaze-independent target representation (Gi) in

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**Figure 2.** A 40-60 Hz gamma band encodes the working memory for the location of the flashed target during the first delay. (A) Topographical representation of the direction-selective 40-60 Hz gamma band over time, in consecutive 0.5 s time windows. Warmer (red) color coding represents a bias toward contralateral presented stimuli; cooler (blue) color coding represents a bias toward ipsilateral presented stimuli. Marked sensors show a significant effect ($P < 0.05$, see Materials and Methods). (B) Direction-selective time-frequency resolved power changes during the first delay, for the sensors marked in the top-middle panel. The top-middle panel shows the topographical representation of the 40-60 Hz gamma band pooled across subjects during the 1.0- to 2.0-s period after stimulus presentation. Top-left and -right panels show the TFRs of the selected sensors covering the left and right hemisphere, respectively. The bottom-middle panel shows the TFR in the gamma band (40-130 Hz) range pooled across hemispheres. Time $t = 0$ and vertical line, stimulus presentation; at $t = 2.0$ s the fixation cross jumps to a new position. The bottom-left and -right panels show ROI-restricted source reconstructions of the 40-80 Hz and 40-60 Hz gamma band during the first 0.5 s, and the 1.0- to 2.0-s period after stimulus presentation, respectively. Color format as in A. Only significant voxels are shown ($P < 0.05$, see Materials and Methods). CS, central sulcus; PO, Parietooccipital sulcus; IPS, intraparietal sulcus. The solid line demarcates the visible part of the ROI.
oscillatory activity after the intervening saccade, in both topography of the 60–80 Hz band and in the TFR of the sensors of interest. Thus, the gamma band reorganizes in a gaze-centered reference frame during spatial updating.

Figure 3C plots the directional selectivity of power modulations due to the maintenance of an eccentric gaze direction (Ge) during the second delay, irrespective of target location. The data indicate a sustained selectivity for gaze direction (in the form of lower power in the hemisphere contralateral than ipsilateral to gaze direction) that is mostly confined to the 100–130 Hz frequency range, with only a marginal effect in the 60–80 Hz gamma band ($P < 0.05$).

In summary, the gaze-centered updates of the saccade target are seen in the relative increases of contralateral power in the 60–80 Hz gamma band observed during the second delay, while eccentric eye position leaves a signature by the substantial contralateral decrease in 100–130 Hz gamma-band power and minor power reduction in the 60–80 Hz range.

**Alpha-Band Selectivity after Target Presentation**

We also analyzed the spectral power changes in the lower frequencies (5–40 Hz) for the 2 delays separately. Figure 4 shows the results of the first delay interval, in the format of Figure 2, with cooler colors reflecting a relative contralateral desynchronization.

The top panel (Fig. 4A), demonstrating the temporal evolution of the alpha-band (8–12 Hz) topography in successive time intervals, reveals significantly lower power values in relation to contralateral stimuli (8–12 Hz; 0–0.5 s; $P < 0.05$; significant sensors are marked). This selectivity is then sustained for about 1 s in the delay (8–12 Hz; 0.5–1.5 s; significant sensors are marked) and then disappears, prior to the refixation. Figure 4B, middle panel, shows the mean alpha power during the 0.5- to 1.5-s period, which excludes the effects related to visual processing. Significant sensors are marked, and their TFRs, averaged for each hemisphere, are shown by the left- and right-hand panels. Because of their similarity, we pooled the $z$-scores of both hemispheres (Fig. 4B, bottom panel). As shown, the directional alpha-band tuning starts roughly at 0.3 s and fades away again at about 1.2 s. ROI-restricted source localization (see Materials and Methods) revealed the occipital cortex as the source of this alpha-band selectivity (0.5–1.5 s; 8–12 Hz; $P < 0.05$) (Figure 4B, right-lower corner). Because subjects wait for the moment of the refixation (see Materials and Methods), which shows up by a relocation of the fixation cross to the left or right of central fixation, the absence of the hemispheric bias in the later stage of the trial may reflect full-field visuospatial attention.

Additional low-frequency effects in the beta band ($\sim$20 Hz) seem to follow a similar modulation as the alpha band, albeit at an apparent slightly different time course. The transient theta increase at $\sim$6 Hz and its harmonics at $\sim$12 and 24 Hz immediately after stimulus presentation are likely to be related to the visually evoked event-related field (Medendorp et al. 2007).

**Alpha-Band Power Reflects Hemispheric Inhibition and Engagement after Updating**

As for the power at the higher frequencies, we analyzed the task-dependent contribution to the power at the lower frequencies during the second delay from stable gaze-fixation onward, isolating the effects of gaze-dependent target updating (Gd), from gaze-independent target coding (Gi) and gaze-direction coding (Ge). Statistical inferences were based on the TFR, taken from the channels identified during the first delay (see Materials and Methods).

Figure 5 illustrates the results, with the left column plotting the topographic distribution of alpha-band power (10–12 Hz), the middle column demonstrating the time-resolved power changes at the 5–40 Hz frequency range during this time interval and the right column showing the sources of the alpha-band activity.
Figure 4. Alpha-band modulations during the first delay interval. Format as in Figure 2; blue color coding indicating lower power for contralateral than ipsilateral targets. (A) Temporal evolution of the alpha-band topography (8–12 Hz). Significant sensors are marked \( p < 0.05 \). (B) Time-frequency resolved power modulations for the sensors marked in the top-middle panel (8–12 Hz, 0.5–1.5 s). Right bottom panel shows the ROI-restricted source reconstruction of the alpha band during the 0.5- to 1.5-s time period. Only significant voxels are shown \( p < 0.05 \). The solid line demarcates the visible part of the ROI.

Figure 5. The alpha band (8–12 Hz) facilitates the gaze-dependent representation while inhibiting the gaze-independent target representation. Format as in Figure 3. Nonsignificant time-frequency tiles are masked with opacity of 0.5. (A) Reorganization of alpha-band desynchronization during spatial updating in a gaze-dependent reference frame. Cooler (blue) color coding represents a decrease of alpha-band power for targets contralateral relative to gaze. (B) Alpha-band synchronization in a gaze-independent reference frame. Warmer (red) color coding represents an increase of power for contralateral presented stimuli, independent of the current gaze position. (C) Gaze position does not modulate alpha-band power. Cooler (blue) color coding, a relative alpha decrease for contralateral gaze direction.
modulations (ROI-restricted beamforming, see Materials and Methods). Figure 5A, left panel, shows lower alpha-band synchronization for targets being contralateral than ipsilateral to the new gaze fixation. Across hemispheres (middle panel), this bias at the selected sensors (based on the first delay) arises at about 0.25 s after refixation and persists throughout the delay. The right-hand panel shows the location of the alpha source in occipital cortex.

Figure 5B, left panel, demonstrates the topographic power distribution of the same alpha-band frequency as in A, but now in terms of gaze-independent (i.e., head- or body-centric) target coding. This analysis revealed a relative alpha power increase to targets that were initially presented in the contralateral field, at the start of the trial, of which both the temporal dynamics (middle panel) and the source localization (right panel) resemble that of the gaze-centered suppression effect in A. Therefore, under the assumption that a relative increase in alpha-band power reflects cortical inhibition, we could explain the Gi effects as the inhibition of the hemisphere contralateral to the location of the target before the intervening eye movement. Before we further proceed with this explanation, Figure 5C demonstrates the isolated gaze-direction effect, which only shows a broadband transient effect around and after gaze stabilization, most likely evoked by the visual presentation of the refixation cross.

How do the suppression effects due to gaze-dependent updating in Figure 5A relate to the gaze-independent power enhancements in Figure 5B? The bar plots in Figure 6 show the average response of the marked sensor groups during the second delay for conditions of within and across hemifield updating, relative to the direction of gaze. In both conditions and in both the contralateral and the ipsilateral hemispheres, there is a strong alpha power reduction relative to baseline. Because baseline levels are arbitrary and difficult to interpret, we prefer to compare the alpha levels across experimental conditions and within hemispheres. For within hemifield updating, the bars confirm a stronger desynchronization at contralateral sensors compared with ipsilateral sensors (paired \( t \)-test, \( t = -2.1, P < 0.05 \)), consistent with a stronger engagement of the hemisphere that is contralateral to the target after the updating. Likewise, for updating across hemifields, there is stronger desynchronization at contralateral than ipsilateral sensors after the target updating (paired \( t \)-test, \( t = 4.6, P < 0.01 \)). However, whereas the contralateral sensors show no significant power differences between the 2 updating conditions (paired \( t \)-test, \( t = 0.2, P = 0.8 \)), the ipsilateral sensors are significantly less desynchronized (paired \( t \)-test, \( t = 2.1, P < 0.05 \)) when comparing across versus within hemifield updating. The ipsilateral sensors after across hemifield updating in fact covered the hemisphere contralateral to the target before updating. Therefore, we can interpret their relative enhancement compared with the within updating condition as an active suppression of the hemisphere that coded the target before it was remapped to the other hemisphere. Alternatively, we could regard this result as a stronger disinhibition over ipsilateral sensors during within hemifield updating compared with between hemifield updating.

**Discussion**

We investigated the reference frames of oscillatory activity in parietal cortex during visual processing, spatial updating, and saccade planning. By introducing a change of fixation between stimulus presentation and the final memory-guided saccade, we could relate the direction selectivity of various frequency bands to spatial updating in a gaze-centered reference frame, spatial coding in a gaze-independent reference frame, or as an eye position (i.e., eccentric gaze) effect.

In the higher frequencies, strong biases in spectral power were observed in both the first (before refixation) and the second (after refixation) delay periods. Since the first delay was free of any explicit directional saccade planning, the observed direction-selective 40–60 Hz gamma band can be interpreted as a working memory of the target (Howard et al. 2003; Jokisch and Jensen 2007), being reverberated strongest when closest to the point of refixation (Fig. 2). The source of this activity was localized to extrastriate occipital areas and not to the saccade-related areas of the PPC, adding evidence to the sensory nature of this working memory trace (Nakamura and Colby 2000, 2002). This observation seems at odds with previous human neuroimaging work (Medendorp et al. 2005; Merriam et al. 2003) and nonhuman primate electrophysiology (Duhamel et al. 1992; Mazzoni et al. 1996), showing PPC activation when...
visual targets have to be kept in memory. Methodologically, if both regions would oscillate in a coherent fashion, the source reconstruction would be drawn toward the stronger source, here the occipital source (Van Veen et al. 1997). On the other hand, the present paradigm also differs from these earlier studies not only in timing but also in stimulus material. For example, most previous studies did not impose a first memory delay and thus required no sustained stimulus maintenance prior to the intervening eye movement (Duhamel et al. 1992; Merriam et al. 2003). Other studies using delays have used visual distracters (Medendorp et al. 2003), adding more attentional demands and thus more parietal involvement to the task (Silver and Kastner 2009). In other words, as long as the retinotopic coordinates of a visual memory trace remain stable, PPC may be less involved in representing it than extrastriate occipital areas.

After refixation, when the target is the goal of the next saccade, the target representation was updated in a gaze-centered reference frame, as expressed by a bias in 60–80 Hz power (see Fig. 3A), originating from contralateral PPC. No evidence was found for a gaze-independent reference frame in parietal gamma-band tuning (Fig. 3B). This finding shows that gamma-band activity reorganizes to account for intervening eye movements, maintaining the constancy of the internal representation of visuomotor space (Medendorp 2010). The posterior parietal location of this gamma-band source is in line with previous blood oxygen level–dependent and TMS studies showing that the PPC encodes and updates targets of eye movements in a gaze-centered reference frame (Colby et al. 1995; Medendorp et al. 2003, 2005; Merriam et al. 2003; Morris et al. 2007; Patel et al. 2010).

Another cortical structure that is widely accepted to play a role in (memory-guided) saccades and spatial updating are the frontal eye fields (FEFs), in both humans and nonhuman primates (Bruce and Goldberg 1985; Dias and Segraves 1999; Curtis and D’Esposito 2006; Sommer and Wurtz 2008; Prime et al. 2010; Medendorp et al. 2011). Using intracranial EEG, Lachaux et al. (2006) also observed frontal gamma-band activity during oculomotor planning (Jerbi et al. 2010). Our topographical representations of the second delay also hint at frontal activity in a gaze-dependent reference frame (Fig. 3A). Because our source analysis only included parietofrontal areas (see Materials and Methods), and thus excluded the FEF, we cannot make any further claim about the involvement of the FEF in this study. Generally speaking, however, it has been argued that the power of the oscillatory activity in the FEF is smaller than in parietal areas; also the orientation and size of the FEFs may prevent a reliable demonstration of their involvement in particular tasks (Jerbi et al. 2008).

Our results indicate that the high-frequency oscillatory activity may be an instrumental mechanism in implementing spatial updating, which is here dictated by the metrics of the saccade. Due to the short moments of inhibition and excitation in a cycle of a high-frequency rhythm, neurons can rapidly change their functional connectivity—and herewith information transfer—on a millisecond time scale. During the short time windows of excitation, effective communication can exist if a receiving group is oscillating in synchrony (Fries 2005). The shift in frequency and the reallocation of the oscillatory activity in the gamma band after the intervening saccade could be initiated by a synchronizing event, most likely by the efference copy of the saccadic motor command (Rajkai et al. 2008; Sommer and Wurtz 2008; Melloni et al. 2009). Together, the presaccadic oscillatory activity from extrastriate areas and the synchronizing event of the intervening saccade could have caused a spatially updated oscillatory activity of higher frequency in the PPC. The frequency of the updated oscillatory activity may also depend on the size of the network involved (Buschman and Miller 2007). Prior to updating, the sensory trace must be reactivated to feed from occipital into higher order areas like PPC, where efference copies for updating arrive. In contrast, after the updating, the target representation can be maintained locally in PPC because it has become the goal of the next saccade, in a frequency range consistent with previous reports (Pesaran et al. 2002; Medendorp et al. 2007; Van Der Werf et al. 2008, 2010).

One further important aspect that may not be left out in our discussion is related to changes in eye position. Although we found clear evidence for a gaze-dependent reference frame, we also contrasted leftward and rightward gaze fixations to assess the spectral signature of eye position. We found the eye-position effects in primarily a 100–130 Hz gamma band, indicating a decrease of power for contralateral gaze directions (Fig. 3C). This gamma band is different from the gamma band coding the spatial representation (Fig. 3A), confirming that the latter is not an eye-position effect (cortical or ocular). From single-unit literature it is known that parietal neurons modulate their activity as a function of eye, head, and hand position (Andersen et al. 1985; Brotchie et al. 1995; Chang et al. 2009). These modulations express themselves as a gain change; that is, an increase or decrease of the firing rate of individual neurons, without distorting the spatial tuning of the recorded neurons. As such, gain fields have a weighting effect, controlling the influence of individual neurons on the population output (Blohm and Crawford 2009). Because gamma-band synchronisation is thought to provide the brain with a mechanism for gain control (Tiesinga et al. 2004; Fries et al. 2007; Womelsdorf and Fries 2007; Gregoriou et al. 2009), one could speculate that the observed gamma-band modulation is functionally related to the gain fields observed in monkey electrophysiology. Individual neurons could then be spiking in a favorable or an unfavorable phase of a local gamma cycle, allowing for a proper weighting of the input signals. This mechanism of phase coding also allows for a quick read out of spiking information without the need for the integration of spike trains (Fries et al. 2007). The finding that gain fields are topographically organized in at least 2 parietal areas (Siegel et al. 2003) also fit the present observation. Unfortunately, we were not able to reconstruct the source of this activity.

In the lower frequencies, stimulus presentation induced an alpha-band lateralization that persisted for a longer time period than the initial broadband gamma response (Fig. 4B). Nonetheless, the alpha-band bias was not sustained throughout the first delay, indicating that these oscillations are involved in processing the stimulus without actually encoding a representation of it (Van Der Werf et al. 2008). For example, if the alpha-band desynchronization reflects the focus of attention, these findings fit the notion that attention drawn by the stimulus persists for a while (Okada and Salenius 1998; Worden et al. 2000; Golomb et al. 2008; Van Der Werf et al. 2008; van Gerven and Jensen 2009; Van Der Werf et al. 2010). However, toward the end of the first delay, spatial attention must be directed toward the whole visual field because the location of the new fixation cross cannot be anticipated by the subject. As spatial
attention is no longer on the remembered stimulus position, it would be important to maintain the coordinates of the target in working memory. Indeed, during this period, the 40–60 Hz gamma band originating from extrastriate occipital areas showed an increase in power. Interestingly, Wyart and Tallon-Baudry (2009) observed gamma-band activity in similar cortical regions during a visual decision task, in which subjects had to indicate the presence or absence of a stimulus. The authors observed functionally dissociable alpha- and gamma-band activities, with the alpha band reflecting the spotlight of visual attention and the gamma band reflecting the perceptual bias in extrastriate occipital areas. Here, we add evidence for their reasoning that the functional mechanisms implemented by gamma and alpha can operate independently from each other, with one increasing the general excitability of an area (alpha) and the other reflecting a sensory memory trace or prediction (gamma).

After the intervening eye movement, the alpha Gd and Gi showed slowly developing biases (Fig. 5A,B), which one could interpret as coding neuronal target representations in both gaze- and nongaze-centered reference frames. However, when trying to unify this with observations in the first delay, we do not consider this interpretation very likely. As a more simple interpretation, the slowly developing sustained decrease in the hemisphere contralateral to the direction of the saccade target (Gd effect) is due to the direction of spatial attention, which is now aligned with the direction of saccade planning. Note that this happened at a slower time scale than the updated gamma-band activity, which could be related to recent findings showing that attentional facilitation lingers for a while in old retinotopic coordinates after the saccade (Golomb et al. 2008, 2010). Concurrently, in the hemisphere that was (and during the first delay) engaged in maintaining the spatial location of the target, a relative increase of alpha power slowly builds up, yielding the Gi effect (see Figs 5B and 6). Along this line, the Gi effect therefore supports the notion that alpha-band synchronization reflects the inhibition of task-interfering areas (Pfurtscheller et al. 1996; Klimesch et al. 2007; Tuladhar et al. 2007; Mccuwenisen et al. 2010). Yet, as we already pointed out in the Results, the Gi effect can also be interpreted in terms of a stronger disinhibition of ipsilateral regions (Fig. 6), consistent with the recruitment of the hemisphere that codes the target.

Finally, several previous studies have referred to the topographic modulations in the alpha band as retinotopic modulations (Worden et al. 2000; Kelly et al. 2006). However, because these studies did not vary eye position, any inference as to whether these topographic modulations are related to a gaze-centered (retinotopic) frame of reference is unwarranted. Compared with these studies, the present study is novel in that it has truly decoded the spatial reference frame in which the alpha band (and gamma band) operates during cortical processing.

We conclude that alpha- and gamma-band oscillations play distinct roles in the maintenance and updating of spatial goals during an intervening eye movement. Power in the gamma band is instantaneously reorganized to encode task-relevant space in a gaze-centered reference frame, while power in the alpha may reflect slower attentional processes that might act independently when necessary.

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Notes
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References


