Dynamic Interactions between Large-Scale Brain Networks Predict Behavioral Adaptation after Perceptual Errors

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Failures to perceive visual stimuli lead to errors in decision making. Different theoretical accounts implicate either medial frontal (MF) cognitive control processes or prestimulus occipital (OC) cortical oscillatory dynamics in errors during perceptual tasks. Here, we show that these 2 previously unconnected theoretical accounts can be reconciled, and the brain regions described by the 2 theories have complimentary and interactive roles in supporting error adaptation. Using a perceptual discrimination task and time-frequency network-based analyses of electroencephalography data, we show that perceptual anticipation and posterior top-down control mechanisms recruit distinct but interacting brain networks. MF sites were a hub for theta-band networks and theta-alpha coupling elicited after errors, whereas occipital sites were a network hub during stimulus anticipation and alpha-gamma coupling. Granger causality analyses revealed that these networks communicate in their preferred direction and frequency band: response-related MF → OC interactions occurred in the theta band, whereas stimulus anticipation-related OC → MF interactions occurred in the alpha band. Subjects with stronger network interactions were more likely to improve performance after errors. These findings demonstrate that multiple large-scale brain networks interact dynamically and in a directionally specific manner in different frequency bands to support flexible behavior adaptation during perceptual decision making.

Keywords: alpha band, cognitive control, networks, theta band, top-down

Introduction

One of the primary functions of the human nervous system is to adapt behavior according to changes in the environment. Momentary failures to perceive and respond appropriately to the environment reflect "hiccups" in monitoring and behavioral control that range from mildly annoying (not seeing your glasses on your desk) to potentially dangerous (not seeing a bicyclist while driving a car). Over the past few decades, 2 prominent accounts for why perceptual errors occur have developed largely independently of each other, and their literatures have seen little intersection.

One account focuses on top-down cognitive control processes and is centered around the medial frontal (MF) cortex (Botvinick et al. 2001; Ridderinkhof et al. 2004; Egner 2007). This cognitive control network is hypothesized to monitor behavior and the environment for errors or negative feedback and to send "top-down" signals to recruit other prefrontal and sensory regions to bias goal-directed information processing. Although researchers have slightly different interpretations of precisely what the error-related signals reflect and top-down mechanisms that they elicit (Holroyd and Coles 2002; van Veen and Carter 2002; Ridderinkhof et al. 2004; Brown and Braver 2005; Rushworth and Behrens 2008), they all predict that errors result from lapses in control and that errors activate MF-based top-down control mechanisms to improve performance. Electrophysiological activation of the MF-centered cognitive control system seems to be expressed through MF theta-band (4–8 Hz) oscillatory activity, as well as oscillatory synchronization between MF and lateral prefrontal cortex (Luu and Tucker 2001; Trujillo and Allen 2007; Hanslmayr et al. 2008; Cavanagh et al. 2009; Cohen, van Gaal, et al. 2009; Mazaheri et al. 2009; Cohen 2011). A separate account of errors in perceptual tasks focuses on reduced stimulus-evoked and stimulus-preceding activity in occipital cortex (OC) and posterior parietal regions (Weissman et al. 2006; Bressler et al. 2008; Walsh et al. 2011). This literature suggests that errors arise because of ongoing endogenous fluctuations in rhythmic neural activity in the alpha band (8–12 Hz) (Monto et al. 2008; Mathewson et al. 2009; van Rullen et al. 2011), such that erroneous responses follow stimuli that are perceived during brief periods of relatively less organized visual cortical processing. Prestimulus fluctuations predict perceptual accuracy (Mazaheri et al. 2009), reaction time (van Rullen et al. 2011), and perceptual confidence (Macdonald et al. 2011). Again, different researchers have proposed slightly different interpretations of how prestimulus neural activity leads to performance variability (Klimesch et al. 2007; Haegens et al. 2011; Mathewson et al. 2011; van Rullen et al. 2011), but all accounts predict that certain configurations of endogenous rhythmic neural activity make upcoming stimuli less likely to be fully and accurately processed.

The purpose of our study was 2-fold. First, to examine how these 2 largely unconnected theories, which focus on different brain regions (posterior vs. anterior) and different brain rhythms (theta vs. alpha), might be reconciled into a more unified account of error adaptation during perceptual performance. Second, to characterize the local and large-scale cortical networks that are ignited by perceptual errors and anticipation of upcoming stimuli, how these networks interact, and how the functioning of those networks might predict posterror adaptation. After replicating previous findings regarding how MF theta and posterior alpha dynamics are related to task performance, we performed 3 sets of novel analyses to test the following hypotheses. First, we predicted that MF theta and OC alpha coordinate local networks that operate in higher frequency bands. This hypothesis was tested by examining whether cross-frequency coupling was present and modulated by region and task performance. Second, we predicted that MF and OC electrodes are hubs in large-scale networks in the theta and alpha frequency bands. This hypothesis was tested by examining whether cross-frequency coupling was present and modulated by region and task performance.

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alpha band, respectively, that are activated by signals for performance adjustments such as errors and stimulus anticipation. We tested this hypothesis by examining how large-scale oscillatory synchrony networks unfold over time, space, and frequency (using analyses based on graph theory) and how these networks predict behavioral performance. Finally, we predicted that these networks communicate with each other in their preferred frequency bands and in time periods in which they are most active, specifically, MF → OC in the theta band during responses and errors and OC → MF in the alpha band during stimulus anticipation. This hypothesis was tested with Granger causality, a measure of directed synchronization.

Materials and Methods

Subjects

Nineteen subjects (aged 18–30, 5 male) from the University of Amsterdam community participated in this study in exchange for course credit or 14 Euros. The study was approved by the local ethics committee, and subjects signed an informed consent document. Subjects had normal or corrected-to-normal vision and were self-reported free of neurological disorders and history of physical head trauma.

Task

Subjects performed a simple visual discrimination task, in which they had to report whether a brieﬂy presented target stimulus was a square (visual angle of 0.74° × 0.74°) or a diamond (i.e., the same square but tilted by 45°) by pressing a left or right response button (counterbalanced across subjects). The target (duration = 17 ms) was always followed by a metatrace mask (duration = 200 ms, visual angle of 1.24°, see Fig. 1) to reduce its visibility. The interstimulus interval between target and mask was set at 67 ms; pilot testing revealed that these parameters resulted in an approximate 25% error rate across subjects. Subjects received performance feedback after every trial with an auditory tone presented at the time of the button press for 17 ms (400 or 600 Hz, counterbalanced across subjects). The intertrial interval (response to next trial) was fixed at 1017 ms to isolate preparatory/anticipatory neural processes leading up to the next trial. During the intertrial interval, a fixation cross was presented. Stimuli were white presented on a black background.

![Figure 1](http://cercor.oxfordjournals.org/)

**Figure 1.** Task design (A) and behavioral data (B). Each circle/dot in B is a subject. Error bars are standard errors of the mean.

EEG Data Collection

Electroencephalography (EEG) data were acquired at 512 Hz using a BioSemi ActiveTwo 64 channels system (BioSemi, Amsterdam, the Netherlands, for more hardware details, see bisosemi.com) placed according to the international 10-20 system, from both earlobes, and from electromyography (EMG) electrodes placed on the thumb muscles. Offline, EEG data were high-pass ﬁltered at 0.5 Hz, rereferenced to the average of the earlobe electrodes for preprocessing, and then epoched from −1.5 to +2 s surrounding each trial. All trials were visually inspected, and those containing EMG or other artifacts not related to blinks were manually removed. Independent components analysis was performed using eeglab software (Delorme and Makeig 2004), and components containing blink/oculomotor artifacts or other artifacts that could be clearly distinguished from brain-driven EEG signals were subtracted from the data.

Trials containing partial errors (those in which subjects made a correct response but activated the muscle corresponding to the incorrect response) were removed from the data because our unpublished results and previous studies (Coles et al. 1985, 1995) suggest that these trials elicit qualitatively distinct patterns of brain activity compared with correct responses without partial errors. Identification of partial errors was done via an algorithm and conﬁrmed by visual inspection. The derivative of the EMG signal from each hand was ﬁrst Z-transformed. This allowed us to base identiﬁcation on EMG variance and thus eliminate hand- and subject-speciﬁc differences in impedance, signal amplitude, etc. A partial error was marked when the normalized derivative of the EMG on the hand not used to make the response exceeded one standard deviation in the time between 200 ms poststimulus onset and the actual button press. The peak of the partial error must also have been more than 2 times the largest peak from −300 ms to stimulus onset (this would eliminate trials in which noisy EMG produced apparent partial errors). On average, 12.35% of correct trials were identiﬁed as containing partial errors (range: 3.88–28.16%).

Examining long-range functional connectivity in EEG is hindered by volume conduction—the phenomenon that deep but powerful brain electrical activities contribute to the signal recorded over many electrodes. Volume conduction makes it difﬁcult to disentangle synchronization between different sources of brain activity from synchronization between different electrodes measuring activity from the same brain sources. However, volume-conducted activity has a broad and low spatial frequency structure and therefore is minimized through spatial ﬁltering methods such as current-source-density or cortical source estimation. Current-source-density is a spatial ﬁlter that increases topographical selectivity by effectively subtracting out spatially broad and therefore likely volume-conducted effects. This approach has been validated for investigating interelectrode synchronization (Srinivasan et al. 2007; Winter et al. 2007) and is an appropriate method for examining synchronization dynamics of large-scale cortical networks during cognition. The units of the data after this transform are mV/cm², although power data here were converted to decibel (see below).

EEG Time-Frequency Decomposition

All analyses were performed in matlab. Single-trial data were ﬁrst decomposed into their time–frequency representation by multiplying the power spectrum of the EEG (obtained from the fast Fourier transform) by the power spectrum of complex Morlet wavelets (\(e^{2\pi tf} e^{-f^2/2\sigma^2}\)), where \(t\) is time, \(f\) is frequency, which increased from 1 to 20 Hz in 20 logarithmically spaced steps, and \(\sigma\) deﬁnes the width of each frequency band, set according to 6/(2\(\pi f_\text{max}\)) [thus, 6 cycles], and then taking the inverse fast Fourier transform (this is mathematically equivalent to time-domain convolution but is considerably faster). From the resulting complex signal, an estimate of frequency band-speciﬁc power at each time point was deﬁned as the squared magnitude of the result of the convolution \(Z(\text{real} [z(t)]^2 + \text{imag} [z(t)]^2)\) and an estimate of frequency band-speciﬁc phase at each time point was taken as the angle of the convolution result. Relatively long epochs were cut from the continuous EEG data (~1.5 s to 2 s) to allow edge artifacts due to sudden transitions in signal values between trials to subside outside the window of interest. Taking long epochs and trimming edge artifacts is
preferred over, for example, Hanning window tapering because the latter method attenuates real signal, whereas the former does not. We also examined higher frequency activity from 20 to 100 Hz in 40 logarithmically spaced steps, using a multitaper approach in which wavelets were windowed with a series of orthogonal Slepian tapers and the resulting time-varying power spectra were averaged. This approach provides frequency-domain smearing and thus may be more sensitive for detecting temporally transient or broadband changes in high-frequency oscillation power. However, we observed no significant increases in task-related gamma activity and synchronization (possibly related to the brief stimulus duration). Hoogenboom et al. (2006). Cross-frequency coupling results, however, demonstrate that there was indeed task-related gamma activity over posterior electrodes, but the transient nature of these gamma "bursts" were such that they were significantly synchronized with alpha phase but were sufficiently jittered that they were difficult to observe in response-locked trial averaging.

Power was normalized using a decibel (dB) transform (dB power = 10 × log10 [power/baseline]), where the baseline activity was taken as the average power at each frequency band, averaged across conditions, from −300 to −100 ms prestimulus. Conversion to a dB scale ensures that data across all frequencies, time points, electrodes, conditions, and subjects are in the same scale and thus comparable.

**Time-Frequency Power Statistics**

Statistics were performed by *t*-tests. Black areas in time-frequency plots enclose regions in which contiguous pixels were significantly different from intertrial-interval baseline at *P* < 0.01 (two-tailed) for at least 300 ms and at least 3 consecutive frequency bins. Shaded areas in time series plots denote differences across conditions.

**Large-Scale Networks Analyses**

Frequency band–specific phase synchronization (functional connectivity) was computed according to $\theta_j = \sum h_t e^{i\theta_h_t}$, where *n* is the number of trials, and $\theta_j$ and $\theta_h$ are the phase angles of electrodes *j* and *h*. This is an index at each time–frequency point of the consistency of phase angle differences between 2 electrodes over trials. This was computed between each pair of electrodes. Subsequently, synchronizaton values were taken into an analysis of network activity based on principles of graph theory. Graph theory provides a mathematical framework with which to conceptualize and quantify local and global network characteristics. Applied to EEG, each electrode is considered a node, and each possible connection between pairs of electrodes is considered a vertex. Each node could have a maximum of 63 vertices (connections to all electrodes minus itself). However, only vertices that are robust (i.e., reflecting strong functional connectivity) should be considered. Thus, a threshold is applied (described below), and each electrode can be assigned a value—termed synchronization degree—according to the number of suprathreshold vertices it has (i.e., the number of electrodes with which there is robust functional connectivity). Electrodes with relatively large synchronization degree may be considered a "hub" or intersection for information flow. Synchronization degree was computed separately for each frequency band–specific time, electrode, and condition. The threshold was set to one standard deviation above the median of each subject’s interregional phase synchronization distribution, thus producing an empirical subject-specific thresholding approach. Preliminary testing demonstrated that different thresholds had minimal effect on the overall topographical distributions and condition differences. Statistical tests were conducted as described for power.

**Granger Causality (Directed Synchronization)**

Granger causality estimates the directed synchronization between 2 regions. It is defined as the log of a ratio of error variances from a univariate autoregression model, in which current values of, for example, FCz/FC1/FC2 activity (averaged together in the time domain prior to the analysis) are predicted from preceding values of FCz activity, and a bivariate autoregression model, in which current values of FCz/1/2 activity are predicted from preceding values of FCz/1/2 and also Oz/O1/O2 activity. The null hypothesis—that the history of signals from occipital electrodes do not contribute to current signals at frontal electrodes—would therefore result in a Granger causality estimate of 0. For the frequency domain, the power spectrum of the autoregression coefficients was computed and passed through a transfer function from which frequency band–specific error variance ratios could be estimated (Dhamala et al. 2008) (the same frequency bands were used as in the wavelet transform analysis). Due to the large number of analysis windows tested (moving windows over time, separately for each trial, condition, and subject), it was not feasible to select order and window sizes based on, for example, Bayes information criterion. We therefore averaged across 2 sets of parameters for the analysis, one with an order of 8 and a window of 200 ms and one with an order of 12 and a window of 500 ms. The former parameter set optimizes temporal specificity and the latter parameter set optimizes frequency specificity. Thus, together, these results provide a balance between temporal and frequency resolutions. Note that because the same parameters were applied to all conditions, time windows, and subjects, no biases were introduced via differential parameter selection. Granger causality estimates were then taken to the group level, and statistical tests were conducted as described for power. Granger causality was computed in matlab based on published equations (e.g., Dhamala et al. 2008).

Granger causality relies on autoregressive modeling, which in turn assumes that data are stationary in the time window used for autoregression modeling. Because of the extremely large number of windows tested (moving windows over time, separately for each trial, condition, and subject), it was not feasible to visually inspect each data sequence for stationarity. We thus used 2 automated procedures for assessing nonstationarity, KPSS and ADF, both from the Granger Causality Matlab toolbox (Seth 2010), which is available for free download on the internet. On average, 0.49% of windows were identified as possibly containing nonstationary data. This did not differ between conditions (repeated-measures analysis of variance [ANOVA]: $F_{2,30} = 0.94, P = 0.365$).

**Cross-Frequency Coupling Analyses**

We quantified cross-frequency coupling by testing whether fluctuations in power of higher frequencies was nonuniformly distributed over the phase of slower oscillations (Canolty et al. 2006; Cohen, Axmacher, et al. 2009a, b). Specifically, we extracted the phase of MF theta (defined as a wavelet with center frequency of 6 Hz, at electrode FCz) and alpha (wavelet with center frequency of 12 Hz, at electrode Oz) from each single trial. Subsequently, the power time series from 20 logarithmically spaced frequencies ranging from 60 to 200 Hz from each single trial. We next tested whether power values were nonuniformly distributed over lower frequency phase ($\sum_{a=1}^{6} \theta_a$, where *a* are power values, *θ* are phase values, and *t* are time points), from 600 ms temporal windows surrounding 200 ms time points from −300 to 1300 ms peri-response (thus, −600 to 0 ms, −400 to 200 ms, etc.). Because a nonuniform distribution of power over phase can occur if phase values are nonuniformly distributed within a time window (e.g., even in absence of cross-frequency coupling) and because these resulting modulation values have no inherently interpretable meaning (because they scale with power, which differs across subjects and frequency bands), a nonparametric step is required before cross-subject averaging and statistics. We therefore performed permutation testing to obtain the likelihood of each time-frequency cross-frequency coupling value occurring due to chance. Five hundred iterations were performed in which the power time series was cut randomly and the second part of the time series was placed before the first part, and the modulation was recomputed. This procedure therefore preserves both the power and phase time series but shuffles them with respect to each other. The actual observed cross-frequency coupling was recomputed as the normalized distance away from this permuted distribution. Thus, the modulation becomes a Z value that can be interpreted as a regular parametric statistic. This entire procedure was done separately for each time–frequency–electrode point. Although time consuming (>20 h per subject), it ensures that the cross-frequency coupling results were due to the precise timing of the relationship between high frequency power and lower frequency phase and were not due to changes in overall power or phase distribution. To
focus on task-related changes in cross-frequency coupling, data were baseline subtracted, using the preresponse period. The pattern of condition differences was the same when using uncorrected values.

Overview of Analysis Scheme
Multiple comparisons is an important issue for EEG studies, particularly when many analyses are performed, as in our study. We therefore adopted an hypothesis-driven analysis protocol to reduce the chance of false positives. First, we had clear hypotheses of the electrodes to use based on previous studies (e.g., Cohen, van Gaal, et al. 2009), namely occipital (average of O1/O2/Oz) and frontocentral (FC1/FC2/FCz) electrodes (note that averaging across multiple electrodes also decreases the chance of spurious findings by increasing signal-to-noise). For these specific electrodes only, we computed time-frequency maps for our brain measures of interest (power, cross-frequency-coupling, synchrony, graph, and granger causality). Based on previous findings, we were specifically interested in the theta and alpha bands. The precise time-frequency boundaries were selected based on the average across all conditions, thus this selection procedure was orthogonal to potential condition differences. Thereafter, to examine condition-specific differences, we focused only on these specific time-frequency windows. Exploratory analyses (e.g., brain-behavior correlations across time) ARE explicitly noted. Finally, we provide the $P$ values of results so the strength of the effects can be individually evaluated.

Behavior Analyses
We quantified individual differences in error adjustment using the following expression: $(N_{Ec}/(N_{Ec} + N_{Ee}))$, where $N$ is trial number, $Ee$ is error trials followed by error trials, and $Ec$ is error trials followed by correct trials. This approach normalizes for trial number thus preventing the results from being skewed by the number of total errors, which was different across subjects. In all correlations between EEG data and posterror adjustment, we used Spearman’s correlations.

Results
Behavioral Performance
Subjects made errors on 25.5% of trials (standard error of the mean 2.8%). We separated errors in which subjects made a correct response in the following trial (i.e., error–correct trial pair, "Ec") from those in which subjects made another error in the following trial (error–error trial pair, "Ee"). These errors were contrasted with trials in which subjects were correct on both the current and the subsequent trials ("Cc"). After errors, subjects were more likely to make another error than expected by chance ($t_{18} = -3.14, P = 0.0056$; Fig. 1B), as previously observed (Mathewson et al. 2009), and as expected given the fluctuating nature of control processes (Monto et al. 2008). As an individual differences measure of the extent to which subjects improved their performance after errors, we computed the ratio of Ec trials to all error trials (called “behavior error adaptation” in Figures).

Electrode-Specific Activity and Local Networks
We first examined electrode-specific oscillation power (i.e., the strength of local frequency band–specific activity). As expected based on previous studies (Luu and Tucker 2001; Cavanagh et al. 2009), response-related theta-band power was maximal over MF electrode FCz (mean time and frequency: 254 ms postresponse and 4.32 Hz; Fig. 2A1,A2) and was stronger after errors compared with correct responses (Cc vs. Ec trials; $P < 0.01$ from –100 to 700 ms peri-response; Fig. 2C1). Error-related MF theta power was also stronger when subjects successfully adapted their behavior on the following trial (Ec vs. Ee trials; $P < 0.01$ from –175 to 150 ms; Fig. 2C1). We also observed the expected pattern of stimulus-related activity over posterior regions: An initial theta power increase (mean time and frequency: 343 ms poststimulus and 3.82 Hz; Fig. 2B1,B2) and alpha power suppression, although there were no significant condition differences in alpha (Fig. 2B2). Robust sustained gamma (30–80 Hz) activity was not observed in the trial-averaged plots (Fig. 2A3–B3), although, as described later, task-related gamma was temporally synchronized with alpha phase (i.e., cross-frequency coupling) and therefore difficult to assess in trial averaging. Finally, we replicated the finding that prestimulus OC alpha phase predicts accuracy during trials with high but not low alpha power (see Supplementary Fig. S1), as previously reported (Mathewson et al. 2009). Together, these findings confirm expected patterns of results from both the cognitive control literature and the posterior alpha phase literature.

We next correlated electrode-specific oscillation power with behavioral performance. To reduce multiple comparisons, we correlated behavioral and neural indices of error adaptation only in time–frequency windows in which there was a significant difference in neural activity between Ec and Ee conditions. We found that subjects who engaged MF theta more strongly after errors were less likely to make subsequent errors ($r = 0.68, P = 0.002$; Fig. 2C2). In the time window of significant Ec–Ee activity for OC sites, correlation with behavior was marginally significant ($r = 0.45, P = 0.053$; Fig. 2D2). In a subsequent exploratory analysis, we computed the time course of this brain–behavior correlation, which showed the correlation to be maximal around the time of the response for MF (Fig. 2C3, –150 to 150 ms) and maximal in the preresponse/poststimulus period for OC (Fig. 2D3, –175 to –75 ms).

Oscillation dynamics recorded from a single electrode may also reflect how those oscillations are used to group local neural networks that fluctuate in higher frequency bands (Canolty and Knight 2010). Therefore, we tested our prediction that MF theta and OC alpha coordinate higher frequency task-related oscillatory activity. MF theta phase was coupled to MF alpha power (peak at 10 Hz) maximally at 500 ms after the response ($t_{18} = 5.04, P < 0.001$; Fig. 3A1,C), was significantly stronger for Ec compared with Cc responses ($t_{18} = 3.63, P = 0.0019$), and was stronger for Ec compared with Ec trials ($t_{18} = 3.22, P = 0.0047$; Fig. 3A2). MF theta phase was also coupled to gamma ($P < 0.01$ from 60 to 70 Hz at 300 ms) but was not different between conditions or at other time points. Thus, MF theta–alpha coupling was strongest for Ec, slightly weaker for Ee, and weakest for Cc trials, highlighting that local MF networks code for just-made errors as well as whether those errors are used to adapt subsequent performance.

In contrast, OC alpha phase was coupled to spatially broad posterior gamma power from 300 to 700 ms after the response (condition average: 15–40 Hz, $t_{18} = 2.96, P = 0.015$; Fig. 3B1,C) and, in contrast to frontal cross-frequency coupling, was significantly stronger for Cc and Ec trials compared with Ec trials (i.e., posterior alpha–gamma coupling was weakest when subjects made 2 consecutive errors; $P < 0.01$ from 13.5 to 70 Hz; Fig. 3B2). OC cross-frequency coupling was not significantly different between Cc and Ec conditions (all $P$’s over time $>0.13$), indicating that local OC network activity predicts accuracy on the upcoming trial, but is not related to accuracy of the just-made response. Because cross-frequency coupling
strengths are based on the precise timing between higher frequency power and lower frequency phase and because of the data-driven bootstrapping procedure, these results could not be attributed to differences in frequency band-specific power across condition or region.

We next tested whether cross-frequency coupling was related to error adaptation. As with the power correlation analyses, we initially tested correlations in the time-frequency windows in which there were significant condition differences. MF theta-alpha coupling significantly predicted error adaptation at 500 ms ($r = 0.54$, $P = 0.018$, Fig. 3D2), but OC alpha-gamma coupling did not significantly predict error adaptation at 300-700 ms ($r = 0.378$, $P = 0.156$). Subsequent exploratory correlation time course analyses revealed that MF theta-alpha coupling was correlated with error adaptation selectively at 500 ms (Fig. 3D2), and OC alpha-gamma coupling predicted error adaptation during stimulus presentation and response. Because of the exploratory nature of this time course analysis, future studies should verify whether the observed OC alpha-gamma coupling is indeed robustly correlated with posterror accuracy around stimulus presentation and the response.

**Figure 2.** Local oscillation power reveals differential MF and OC dynamics during the task. A1 and B1 show topographical distributions of lower frequency (2-8 Hz) power around the time of the response (A1) and stimulus (B1). A2 and B2 show time-frequency power plots averaged across all 3 conditions for lower frequencies and A3 and B3 for higher frequencies. Black lines encircle regions of significance relative to baseline (−300 to −100 ms prestimulus, averaged across conditions) at $P < 0.01$. (C, D) Line plots in C1 and D1 show 2-8 Hz activity separately for each condition. Solid horizontal lines on the bottom depict time windows in which conditions differed at $P < 0.01$. MF and OC power difference between Ec and Ee trials correlated with error adaptation (error adaptation is defined as $N_{Ec}/(N_{Ee} + N_{Ec})$) (each dot in C2, D2 is a subject and the line is the best linear fit). Temporal windows for correlations in C3 and D3 were taken from times in which Ec-Ee was significant.

**Large-Scale Brain Networks for Cognitive Control and Stimulus Anticipation**

We tested our second prediction—that MF and OC are hubs in large-scale networks that are activated by performance errors and stimulus anticipation—by applying principles of graph theory to the time-frequency phase synchrony data. Graph theory is increasingly used to investigate the network...
Figure 3. Cross-frequency coupling (CFC) in MF and OC. (A) Theta-band phase from FC1, FCz, and FC2 (MF electrodes) was coupled with alpha power over MF regions (topographical maps in C, top row) during the response and intertrial interval (time-frequency plot in A1 shows coupling profile at electrode FCz), but only during error trials, particularly for Ec trials. A2 shows CFC modulation (averaged Z values across subjects) over frequencies at electrode FCz. Black and gray lines show frequency bands in which significant differences were observed at \( P < 0.01 \). B1, B2, same as A but for CFC with alpha phase and power measured at electrode Oz, which exhibited robust alpha-gamma coupling that was weakest for Ee trials, and not different between Cc and Ec trials. C shows topographical maps of CFC with midfrontal theta phase (upper panel) and occipital alpha phase (lower panel) (electrodes used for seeds are illustrated in gray). D1 show the correlation between MF theta-alpha coupling and error adaptation; D2 shows the time course of this CFC-behavior correlation.
organization of the brain, typically during resting-state or with structural data (Bullmore and Sporns 2009). However, neurocognitive processes are not stable over time and frequency but rather ebb and fluctuate with task demands. We therefore extended graph theory into the time-frequency domain by considering that graph properties can change not only over space but also over time and frequency. We focus on the synchronization degree—the parameter from graph theory that describes the richness of connectivity (based on oscillatory phase synchronization) that each electrode has with other electrodes. Thus, larger synchronization degrees suggest that region is a stronger hub for large-scale network connectivity, while holding other graph parameters constant across time, frequency, and condition. Synchronization degree is defined as the number of suprathreshold task-related functional connections each electrode has with all other electrodes; the threshold is defined uniquely for each subject and frequency band and is independent of task condition.

We focused on MF and OC areas are potential hubs for large-scale network formation based on prior findings (Cohen, van Gaal, et al. 2009) and the localization of response- and stimulus-related power dynamics (Fig. 2A1,B1). MF was a hub for theta-band networks that were maximal around the time of the response (Fig. 4A1). Response-related MF theta network size increased after Ec compared with Cc (P < 0.01 from −150 to 750 ms) and Ec compared with Ec (P < 0.01 from −500 to 1500 ms; Fig. 4A2). Seeded topographical synchrony maps show that the MF-based network was primarily connected with lateral and anterior prefrontal regions, sensory-motor, and occipital regions (Fig. 4E).

OC was a hub for alpha-band networks during stimulus anticipation, as well as delta and theta-band networks around the time of the response and stimulus onset (Fig. 4B1). In the alpha band, there was an increase in network size for Ec compared with Ec trials (P < 0.01 in several time windows from −500 to 1150 ms, Fig. 4B2). OC alpha-band network sizes were not different between Ec and Cc trials, further highlighting that alpha predicts the accuracy of the upcoming trial and is not related to the just-made response. In lower frequencies (2–8 Hz), there was an increase in stimulus-related network size (see the poststimulus period in Fig. 4B1,B2, and the preresponse period, which contains temporally jittered stimulus onsets) and following the response. There was a tonic decrease in theta- and alpha-band networks during Ec trials (P < 0.01 from −500 to 1500 ms), though network size was greater for Cc compared with Ec trials in lower frequencies after the response (P < 0.01 from 125 to 575 ms). Seeded synchrony topographical maps show that the OC-based network was primarily connected with midfrontal, parietal, and lateral occipital regions (Fig. 4E). This pattern of OC alpha network dynamics occurred in absence of changes in OC alpha power. Thus, large-scale alpha networks can form through their specific timing (oscillatory phase synchrony) rather than solely increases or decreases in site-specific power (Palva S and Palva JM 2011).

As predicted, large-scale network dynamics correlated strongly with individual differences in behavior adaptation. At time periods in which we observed a significant Ec – Ec difference in synchronization degree, subjects with larger MF and OC networks in both theta and alpha bands were more likely to improve performance after errors (see scatter plots in Fig. 4C1,D1). Exploratory correlation time course analysis revealed that behavior correlations with theta-band networks were high and stable throughout the trial for both MF and OC regions, whereas brain-behavior correlations with alpha-band networks were maximal around stimulus anticipation for both regions (black time course correlation in Fig. 4C2,D2). This pattern of correlations was different from that with power, for which significant brain-behavior correlations were temporally specific to the time of the response. Control analyses confirmed that these results were not due to differences in trial number, band-specific oscillation power, or signal-to-noise ratio across trials or between trials. Within condition, these variables did not correlate consistently with synchronization degree (Supplementary Fig. S2). The results were also present when statistically regressing out trial count from the behavioral error adaptation measure (Supplementary Fig. S2).

Directed Synchronization Between Frontal and Occipital Networks
To gain deeper insight into the directional flow of the temporal interactions between OC and MF and to test our third main prediction that these 2 networks communicate with each other in their preferred frequency bands, we applied time-frequency Granger causality (Cohen, van Gaal, et al. 2009) as a confirmatory follow-up analysis to estimate directional synchronization between frontal and occipital sites. This provides a more direct test of bottom-up (occipital → frontal) versus top-down (frontal → occipital) influences. Statistics were done using repeated-measures ANOVA with factors direction (MF → OC vs. OC → MF) and frequency band (2–8 vs. 10–15 Hz, taken from 0 to 500 ms and 200–600 ms, respectively, based on results from the graph-coefficients analyses), on the differences between conditions (Ec – Cc). Thus, the tests were not focused on the fit of the Granger causality models to the data per se but rather on the relative strength of directional coupling between conditions.

In general, MF → OC directed synchrony was maximal in the theta band around the time of the response (Fig. 5), was significantly stronger compared with OC → MF theta-band directed synchrony (F1,18 = 8.91, P = 0.008), and was stronger in the theta band compared with the alpha band (F1,18 = 9.72, P = 0.006). Importantly, there was a significant direction × accuracy interaction (repeated-measures ANOVA; F1,18 = 7.09, P = 0.016), such that theta-band MF → OC directed synchrony was stronger for Ec compared with Cc trials (t18 = 2.19, P = 0.0421), whereas alpha-band OC → MF directed synchrony was stronger for Ec compared with Ec trials (t18 = 2.22, P = 0.0395). There were no correlations with behavior adaptation, although there also were no significant differences between Ec and Ec trials. These findings are consistent with the idea that MF regions use theta to send top-down control signals, whereas OC regions use alpha to support stimulus anticipation.

Discussion
Flexible behavior requires the ability to rapidly evaluate errors and engage posterror adaptation mechanisms. Here, we show that large-scale brain networks related to cognitive control centered around MF, and stimulus preparation centered around OC, interact to support posterror behavior adjustments. MF theta networks were associated with errors, whereas OC alpha networks were associated with upcoming correct responses, but activity in both networks predicted behavior adaptation. These findings link literatures that have previously had little interaction and demonstrate that multiple brain networks support task performance in distinct but cooperative ways.
Figure 4. Synchronization degree—a property of graphs that quantifies the extent to which each node (electrode) acts as a hub for large-scale connectivity—change over time, frequency, and condition. A1 and B1 show condition-averaged time-frequency plots of synchronization degree for MF (A) and OC (B) sites. Hotter colors indicate stronger frequency band-specific networks linked to those areas. MF networks were prominent in the theta band after the response, whereas OC networks were prominent in the theta band after the stimulus, and in the alpha band between the response and the next stimulus. Line plots in A2 and B2 show frequency band-specific synchronization degrees for different conditions. Horizontal bars at bottom indicate condition differences at \( P < 0.01 \) with a minimum of 50 ms contiguously significant points. (C,D) Synchronization degrees correlated with individual differences in performance adaptation after errors. As in Figure 2, correlations were based on times of significant Ec – Ee differences. C2 and D2 show the time course of the correlations. These correlations could not be attributed to trial count, oscillation power, or signal-to-noise ratio because synchronization degree did not correlate with these variables (see Supplementary Fig. S2). (E) shows seeded synchrony topographical maps for the OC-based network and the MF-based network for 2 frequency bands (theta and alpha) (electrodes used for seeds are illustrated in gray).
It has been known for decades that the MF cortex including anterior cingulate is involved in flexible behavior adaptation. A highly influential model of the neural mechanisms of flexible behavioral adaptation proposes that the MF cortex detects conflicts or errors and signals to the lateral prefrontal cortex that behavioral adjustments are required (Botvinick et al. 2001; Holroyd and Coles 2002). Theta-band oscillations have been identified as a physiologically plausible medium for this signal (Trujillo and Allen 2007; Hanslmayr et al. 2008; Marco-Pallares et al. 2008; Cavanagh et al. 2009; Christie and Tata 2009; Mazaheri et al. 2009). Others have suggested that MF cortex might also directly implement some aspects of behavior adaptation by modulating motor threshold or sensory processing (Egner 2007; Rushworth et al. 2007; Danielmeier et al. 2011). Consistent with this, error-related and conflict-related theta-band synchrony has been observed between MF and OC (Cohen, van Gaal, et al. 2009), MF and lateral prefrontal cortex (Hanslmayr et al. 2008; Cavanagh et al. 2009), and MF and the ventral striatum (Cohen, Axmacher, et al. 2009a, b). Our findings extend this literature by demonstrating that MF theta coordinates both local (cross-frequency coupling) and large-scale (synchronisation degree) networks that code for recent errors and correlate with error adaptation. Indeed, given more widespread brain-behavior correlations for MF-based networks compared with MF electrode-specific power, MF-based networks may be more relevant for error adaptation than the local MF activity.

The relation between prestimulus posterior alpha phase and visual perception accuracy has been examined for over 40 years (for review, see Klimesch et al. 2007). Slightly different theories have been put forth to account for this relationship (Klimesch et al. 2007; Jensen and Mazaheri 2010; Mathewson et al. 2011), but the central underlying axiom is that alpha reflects rhythmic fluctuations in cortical inhibition, and if stimuli happen to reach visual cortex during temporal windows of relative inexcitability, those stimuli will be suboptimally processed therefore increasing the chance of errors. Much of this work has focused on electrode-specific analyses, typically over occipital or parietal regions. Our results suggest that these posterior sites are key hubs to coordinate large-scale networks that utilize alpha-band oscillations.

Surprisingly, these 2 approaches—MF cognitive control and posterior alpha phase—have developed mostly independently of each other, although they account for similar behavioral phenomena. Recently, however, some integration between these 2 literatures is beginning to emerge in the literature. For example, Carp and Compton (2009) showed that posterror posterior alpha power dynamics (which failed to show an increase during the intertrial interval as in often observed), correlated with posterror slowing, although they did not examine a relationship between posterior alpha dynamics and frontal dynamics at the single-trial level as was done here. Although not specifically related to oscillatory electrophysiological mechanisms, Walsh et al. (2011) used functional magnetic resonance imaging to suggest that conflict-related hemodynamic activity in MF regions interacts with attention-related activity in parietal regions to support postconflict adaptation. Our findings provide a more direct bridge between these literatures, by demonstrating that MF and OC regions coordinate local networks (cross-frequency coupling) and operate as hubs for large-scale brain networks (from graph-based analyses), which interact using their preferred frequency bands (from Granger causality analyses) during perceptual discrimination task performance. These 2 networks make complimentary functional contributions, with MF networks coding both for accuracy of the just-made response as well as its functional significance for the upcoming trial and OC networks involved in preparing the system for upcoming perceptual accuracy.

Figure 5. Granger causality demonstrates that MF → OC and OC → MF directed synchrony occur separately in time and frequency. MF → OC was maximal in lower frequencies around the time of the response (A1), whereas OC → MF directed synchrony was maximal in the alpha band prior to the upcoming stimulus, and just after the response in lower frequencies (B1). Granger causal values are squared in the time–frequency plot to highlight color scaling; statistics are based on raw values. MF → OC synchrony was stronger for Ec compared with Cc trials in the theta band, whereas OC → MF synchrony was stronger for Cc compared with Ec trials in the alpha band (see time courses in A2 and B2).
These literatures seem to focus on different primary sources of errors. The MF cognitive control literature generally assumes that errors result from lapses in MF-related control processes, whereas the OC alpha literature generally assumes that the origin of the error depends largely on the quality of the sensory evidence. These are not mutually exclusive sources of errors, and in many tasks used to study performance monitoring, lapses in control processes and poor sensory evidence evaluation may co-occur. Thus, the brain networks involved in control and sensory evaluation may both be involved and interacting during these tasks. Indeed, it has recently been suggested that the human performance monitoring system involves an evaluation mechanism that takes the source of the error into account (Maier et al. 2011) and that the specific adaptation mechanism followed by the error is influenced by that (Danielmeier and Ullsperger 2011).

Bridging these 2 theoretical and methodological approaches may prove mutually beneficial because the MF top-down control account has a rich history of psychological and theoretical interpretation (Ridderinkhof et al. 2004), and the OC prestimulus alpha account has a rich history of neurobiological interpretation and methodological rigor (Klimesch et al. 2007; VanRullen et al. 2011).

Interest in how cross-frequency coupling may reflect neural information processing schemes has increased recently (Osipova et al. 2008; Canolty and Knight 2010; Voytek et al. 2011). We observed cross-frequency coupling to be region-, frequency band-, and process-specific: MF theta-alpha coupling supports both error detection and error correction mechanisms, whereas OC alpha-gamma coupling supports preparatory processes that predict accuracy in the upcoming trial. This is consistent with previous reports implicating frontol theta-alpha coupling in negative feedback learning (Cohen, Elger, et al. 2009) and posterior alpha-gamma coupling during active visual processing (Osipova et al. 2008; Voytek et al. 2011). The posterior alpha-gamma coupling is consistent with a model from Mazaheri and Jensen (2010) that proposes that alpha oscillations serve as a "rhythmic pulse" to regulate local processing, which would be reflected in gamma power and increased spiking activity (Haegens et al. 2011). Methodologically, the presence of alpha-gamma and theta-gamma cross-frequency-coupling in absence of significant stimulus-related gamma in cross-trial averaging may help explain why gamma is not always observed (Hoogenboom et al. 2006). Specifically, if gamma occurs in bursts that are synchronized with alpha phase—but alpha is not perfectly phase-reset by the stimulus—these gamma bursts may average out in cross-trial averaging but would be apparent when locking the data to alpha phase. A similar pattern of findings was obtained by Osipova et al. (2008).

Oscillations have been hypothesized to support integration of large-scale networks (Buzsaki and Draguhn 2004; Fries 2005; Hipp et al. 2011) and control of top-down information flow (Engel et al. 2001). For example, alpha-band activity is thought to selectively route the flow of information according to task goals by selectively inhibiting brain areas representing task-irrelevant or distracting information (Jensen and Mazaheri 2010; Haegens et al. 2011). This may be the physiological mechanism by which task-relevant areas become functionally coupled and decoupled according to task demands (Egner and Hirsch 2005; Chadick and Gazzaley 2011). Less is known about the role of MF theta in coordinating large-scale networks, although these and recent findings (Cohen, van Gaal, et al. 2009; Cavanagh et al. 2010; Cohen 2011) implicated MF theta as a fulcrum for prefrontal cortex-based top-down control networks involved in flexible adaptation of behavior after errors or negative feedback.

Limitations

We focused on posterror accuracy and not posterror slowing. Although both are used in cognitive control studies, these behavioral phenomena seem to be driven by different cognitive processes (Gehring and Knight 2000; Danielmeier and Ullsperger 2011). Posterror slowing might be driven by motor inhibition (Danielmeier and Ullsperger 2011) or nonspecific orienting responses after infrequent events (Notebaert et al. 2009; Verguts et al. 2011). In contrast, posterror accuracy change might be more related to attentional or control processes. Indeed, posterror slowing and posterror accuracy measures do not always correlate and follow a different time course (see Danielmeier and Ullsperger 2011). In our own data set, we found these measures to be nonsignificantly correlated ($r = 0.056$, $P = 0.819$), although there was some posterror slowing ($P = 0.0492$).

Relatedly, one might expect accuracy to increase after errors. Indeed, in cognitive control tasks, posterror correction is often reported (Cho et al. 2009; Danielmeier and Ullsperger 2011), but posterror reductions in accuracy are also reported (Rabbitt and Rodgers 1977; Fiehler et al. 2005; Mathewson et al. 2009). Danielmeier and Ullsperger (2011) recently suggested 2 reasons why subjects might fail to correct their errors in some tasks: short intertrial intervals (1.017 s in our study); and perceptual difficulty of the task, for example, when stimuli are degraded and difficult to encode. Maier et al. (2011) came to a similar conclusion. They suggested that the adaptation mechanism depends on the source of the error. Thus, some errors might trigger selective adaptation in behavior (increase in performance), whereas others do not (or even decrease performance).

Another limitation is that the present experimental design did not allow us to separate internally versus externally generated error signals (i.e., response-related from feedback-related activity). However, previous work has shown that both internally signaled response errors and negative performance feedback elicit similar patterns of MF theta dynamics and that these theta dynamics predict posterror and postfeedback adjustments (Cavanagh et al. 2009, 2010; van de Vijver et al. 2011).

Conclusion

In conclusion, the present findings implicate MF cortex as the fulcrum of a neural network involved in monitoring behavior for errors and theta-band oscillations as a putative neurophysiological mechanism by which MF cortex engages specific and widespread networks for implementing flexible performance adaptation. These findings also implicate OC as a fulcrum for a neural network involved stimulus anticipation and alpha band (as well as theta/delta bands) oscillations as its mechanism of operation and communication. This frequency-band "multiplexing" of information may facilitate the emergence of multiple functionally interacting networks that are crucial for fast behavioral adaptation after errors.
Supplementary Material

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

Funding

M.X.C. is supported by a Vidi grant from the Netherlands Organization for Scientific Research (NWO). S.v.G. is supported by a Rubicon grant from the NWO.

Notes

The authors thank Claudia Arena for assistance with data collection and Tobias Donner and Heleen Slagter for critical comments on the manuscript. Conflict of Interest: None declared.

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