Trial-by-Trial Coupling of Concurrent Electroencephalogram and Functional Magnetic Resonance Imaging Identifies the Dynamics of Performance Monitoring

Stefan Debener,1,2,* Markus Ullsperger,3,* Markus Siegel,1 Katja Fiehler,3,4 D. Yves von Cramon,1 and Andreas K. Engel1

1Institute of Neurophysiology and Pathophysiology, Center of Experimental Medicine, University Medical Center, Hamburg University, D-20246 Hamburg, Germany, 2Medical Research Council Institute of Hearing Research Southampton, Royal South Hants Hospital, SO 14 0YG Southampton Hants, United Kingdom, 3Department of Cognitive Neurology, Max-Planck Institute for Human Cognitive and Brain Sciences, D-04103 Leipzig, Germany, and 4Cognitive Psychophysiology Laboratory, Department of Psychology, Philips-University Marburg, D-35032 Marburg, Germany

Goal-directed behavior requires the continuous monitoring and dynamic adjustment of ongoing actions. Here, we report a direct coupling between the event-related electroencephalogram (EEG), functional magnetic resonance imaging (fMRI), and behavioral measures of performance monitoring in humans. By applying independent component analysis to EEG signals recorded simultaneously with fMRI, we found the single-trial error-related negativity of the EEG to be systematically related to behavior in the subsequent trial, thereby reflecting immediate behavioral adjustments of a cognitive performance monitoring system. Moreover, this trial-by-trial EEG measure of performance monitoring predicted the fMRI activity in the rostral cingulate zone, a brain region thought to play a key role in processing of response errors. We conclude that investigations of the dynamic coupling between EEG and fMRI provide a powerful approach for the study of higher order brain functions.

Key words: fMRI; EEG; anterior cingulate cortex; performance monitoring; ICA; error processing

Introduction

In a rapidly changing environment, goal-directed behavior requires the monitoring and dynamic adjustment of ongoing actions. Erroneous actions, in particular, are highly informative for successful adjustments of future behavior (Ridderinkhof et al., 2004). Accordingly, neural correlates of performance monitoring have been studied extensively in humans by means of electroencephalogram (EEG) and functional magnetic resonance (MR) imaging (fMRI). One of the EEG signatures is the error-related negativity (ERN), an event-related brain potential (ERP) peaking within 100 ms after erroneous responses (Falkenstein et al., 1990; Gehring et al., 1993). fMRI studies consistently implicate the posterior frontomedian cortex in processing of response errors, negative feedback, response conflict, and decision uncertainty (Ridderinkhof et al., 2004). Informed by both ERN and fMRI research, the current view is that error processing is accomplished by a fundamental performance monitoring system signaling the need for behavioral adjustments in the service of action outcome optimization (Ridderinkhof et al., 2004; Ullsperger and von Cramon, 2004).

A common notion is that performance monitoring is a dynamic process that systematically fluctuates over time. Behavioral adjustments can, for instance, lead to prolonged reaction times (RTs) on trials subsequent to errors, thereby reflecting a more cautious response mode (Rabbitt, 1966; Ridderinkhof et al., 2004). This view is supported by fMRI work showing that enhanced activity in the posterior frontomedian cortex predicts greater subsequent posterior slowing (Garavan et al., 2002; Kerns et al., 2004). For the ERN, this question is difficult to address, because ERPs usually are derived by averaging across trials. To account for this problem, independent component (IC) analysis (ICA) can be applied, a statistical source separation technique suitable for single-trial EEG analysis (Makeig et al., 2002, 2004). If the ERN indeed reflects performance monitoring, ICA-filtered trial-to-trial variations of its amplitude should go along with systematic behavioral changes in the same trial and particularly in subsequent trials. Based on a previous account (Gehring et al., 1993), we predicted greater single-trial ERN amplitudes after errors, reflecting a change to a more conservative response strategy in subsequent trials.

EEG source localization studies (Dehaene et al., 1994; Ullsperger and von Cramon, 2001) have suggested the posterior frontomedian cortex as neural generator of the ERN. However, these analyses do not inform on whether the ERN is related to hemodynamic changes of error monitoring. To date, it remains poorly understood how hemodynamic and electrophysiological correlates of cognitive processes relate to each other. Regarding the relationship between electrophysiological measures and...
fMRI, local field potentials recorded in the visual cortex of anesthetized monkeys have been shown to predict the local fMRI blood-oxygen-level-dependent (BOLD) signal (Logothetis et al., 2001). Here, we tested whether the electrophysiological correlate of performance monitoring systematically predicts the BOLD response in the rostral cingulate zone (RCZ) of the posterior frontomedian cortex. To address both the dynamic variability of performance monitoring and the relationship between its hemodynamic and electrical signatures, we performed a single-trial analysis of simultaneous EEG/fMRI measurements. We thereby avoided the usual problem that within-subject behavior fluctuates across separate recording sessions (Ullsperger and von Cramon, 2001).

Materials and Methods

Participants. Eighteen healthy right-handed volunteers participated in the experiment. As a result of technical malfunction and thus incomplete recordings of either EEG or fMRI, data from five subjects had to be discarded. The final sample consisted of eight females and five males (22–29 years of age; mean age, 25.2 years). Written informed consent before the start of the experiment was obtained from each participant according to the declaration of Helsinki.

Behavioral task. Stimuli were presented using Presentation 0.76 (Neurobehavioral Systems, San Francisco, CA) and appeared on a back-projection screen mounted inside the scanner bore behind the participants head. A speeded modified flanker task was used known to yield sufficient error rates to study the ERN (see Fig. 1). Participants were presented with a fixation mark at the center of the screen, after which four horizontal flanker arrows appeared for 110 ms. The arrows were 0.46° tall and 1.08° wide and appeared 0.52° and 1.04° above and below the screen center. The target arrow was presented for 30 ms in the center of the flanker arrows; its onset was delayed by 80 ms from the onset of the flanker. In 50% of the 400 trials, the flankers pointed in the same direction as the target (compatible trials), and in the other half of the trials in the opposite direction (incompatible trials). Compatible and incompatible trials appeared in randomized order. Participants were instructed to respond with maximal speed and accuracy to the target arrow with the response hand indicated by the arrow direction. Whenever participants responded after an individual, dynamically adapting response deadline, a symbolic feedback was presented for 1400 ms after target onset, instructing participants to speed up. The average intertrial interval amounted to 6 s; for the remaining time, the fixation mark was presented. The trials were interspersed with a total of 32 nontones, during which only the fixation cross was presented and no response was required. Trials occurred at multiple, systematically offset time points (range, 0–1.5 s) in relation to fMRI data acquisition to improve temporal resolution (Josephs et al., 1997; Miezin et al., 2000).

Simultaneous EEG/fMRI recording. Imaging was performed at 3 tesla on a Siemens (Erlangen, Germany) Trio system equipped with the standard bird cage head coil. Twenty-two functional slices were obtained parallel to the anterior commissure–posterior commissure line (thickness, 4 mm; interslice gap, 1 mm) using a gradient-echo planar imaging (EPI) sequence with an echo time of 30 ms, a flip angle of 90°, a repetition time (TR) of 2000 ms, and an acquisition bandwidth of 100 kHz. Acquisition of the slices was arranged such that they all were acquired within 1500 ms and were followed by a 500 ms no-acquisition period to complete the TR. This was done to visually monitor proper recording of the EEG signal during MR scanning and to include for each TR a nongradient contaminated baseline period into the EEG recordings (Fig. S1, available at www.jneurosci.org as supplemental material). The fMRI matrix acquired was 64 × 64 with a field of view of 19.2 cm, resulting in an in-plane resolution of 3 × 3 mm². A total of 1300 volumes was acquired. Functional data were motion-corrected off-line with the Siemens motion correction protocol. Before the functional runs, anatomical modified driven equilibrium Fourier transform (MDEFT) and EPI-T1 slices in the plane with functional images were collected.

Continuous EEG data were collected from 30 standard scalp sites using the BrainAmps MR plus, a high-input impedance amplifier specifically designed for recordings in high magnetic fields (BrainProducts, Munich, Germany). Sintered Ag/AgCl ring electrodes with built-in 5 kΩ resistors were used and mounted into an electrode cap according to the 10–20 system (Falk Minow Services, Herrsching, Germany). Two additional electrodes were placed below the left eye and on the lower back to monitor eyeblinks and electrocardiograms, respectively. Electrode impedances were maintained below 10 kΩ before recordings. The nonmagnetic EEG amplifier was fixed beside the head coil and powered by a rechargeable power pack placed outside the scanner bore. The subject’s head was immobilized using vacuum cushions and sponge pads. The amplified EEG signals were transmitted with a fiber optic cable to a recording personal computer placed outside the scanner room. All 32 channels were recorded with FCz as reference. Although this is an unusual reference site for fMRI studies, it allowed us to keep the difference between recording reference and “active” electrodes small, thereby minimizing the chance of amplifier saturation. The data were recorded with a passband of 0.016–250 Hz and digitized with 5000 samples per second at 16 bit with 0.5 μV resolution (dynamic range, 16.38 mV).

EEG data analysis. EEG data were corrected for MR gradient and ballistocardiac artifacts by applying modified versions of the algorithms proposed by Allen and colleagues (Allen et al., 1998, 2000). Gradient artifacts were removed as implemented in Vision Analyzer 1.04 software (BrainProducts) by subtracting an artifact template from the 40 Hz low-pass-filtered data, using a baseline-corrected sliding average of 20 consecutive volumes. This resulted in EEGs denoised for MR gradients, as shown for representative 10 s traces in Figure S1 (available at www.jneurosci.org as supplemental material). Further processing of the 250 Hz downsampled data was performed using Matlab 6.5 (MathWorks, Natick, MA) and EEGLAB 4.51 (Delorme and Makeig, 2004), a freely available open source software toolbox (EEGLAB toolbox for single-trial EEG data analysis, Swartz Center for Computational Neurosciences, La Jolla, CA; http://www.sccn.ucsd.edu/eeeglab). The EEGLAB plug-in FMRIB 1.0 (Niazy et al., 2005) (FMRIB EEGLAB plug-in for removal of fMRI-related artifacts, Center for functional MRI of the Brain, Oxford, UK; http://www.fmrib.ox.ac.uk/~rami/fmribplugin) was used for 0.4–35 Hz filtered data to remove ballistocardiac artifacts. Based on the identified heartbeat events, an artifact template was defined as the median across a sliding window of 30 heartbeats centered around the heartbeat event being processed. As a result, EEG data denoised for ballistocardiac artifacts were derived but with common EEG artifacts such as eyeblinks still being present (Fig. S1, available at www.jneurosci.org as supplemental material).

The MR-denoised EEG data were re-referenced to common average, and stimulus- and response-locked ERPs were calculated separately for the experimental conditions of interest. The time-locking event for all stimuli-locked analyses was the target arrow onset within a ±200–0 ms. For response-locked ERPs, we used a baseline from −600 to −400 ms to avoid contamination of the baseline period with stimulus-evoked potentials. Stimulus-locked ERPs clearly indicated the common ERP morphology (i.e., an N1 at occipital channels, a P300 at parietal channels, and the ERN at frontocentral channels), altogether confirming reasonable data quality (Fig. S2a, available at www.jneurosci.org as supplemental material). Grand mean ERP images were computed by color-coding the single-trial amplitudes aligned to stimulus onset, smoothed with a moving average across 30 adjacent trials (Delorme and Makeig, 2004). Topographical inspection of both scalp ERPs and reaction-time-sorted ERP images clearly indicated a contamination of the event-related portion of the signal with different artifacts (Fig. S2, available at www.jneurosci.org as supplemental material). In addition to the typical eyeblink artifacts, a strong response-locked exogenous artifact was visible at temporal sites, as characterized by a reversed polarity between left and right hemisphere channels. This event-related artifact probably was caused by button-press-related small body movements and related current induction. For this and other reasons, it was inevitable to linearly decompose the response-related process of interest from these and further signal contributions. We performed extended infomax ICA (Bell and Sejnowski, 1995; Lee et al., 1999) on the MR-denoised single-subject continuous EEG data. ICA finds an unmixing square matrix of the size of the number of channels, which, when matrix-multiplied with the raw
data, reveals maximally temporally independent activations. A weight change of $10^{-7}$ as stop criterion resulted in stable decompositions after <800 iterations. Each IC can be characterized by a time course (IC activation) and a topography (IC map), the latter being given by the inverse weights. The 30 ICs for each subject were screened for maps resembling the typical frontocentral radial ERN topography and a contribution to the ERP difference between incompatible error and incompatible correct trials, that is, a larger negative deflection at the response interval for erroneous trials. This resulted in identification of one IC for each subject, presumably reflecting the contribution of the neural correlate of performance monitoring to the scalp EEG. Figure S3 (available at www.jneurosci.org as supplemental material) shows the individual IC maps identified along with the average map, after root mean square normalization of individual maps (see Fig. 2a). For each subject, the selected IC was then back-projected to the scalp to reveal unique polarity information and microvolt scaling. Figure S4 (available at www.jneurosci.org as supplemental material) shows the resulting ERPs and ERP images. Compared with the original scalp data (Fig. S2, available at www.jneurosci.org as supplemental material), spatiotemporally overlapping contributions were now absent in the IC ERPs and ERP images.

To model the neural source of the selected ICs, the grand average IC map was submitted to BESA 2000, version 4.2 (MEGIS, Graefeling, Germany). A standardized finite element model (FEM), as provided by BESA, was used. It was created from an averaged head of 24 individual MRIs in Talairach space, and this head was also used for display purposes. BESA, was used. It was created from an averaged head of 24 individual MRIs in Talairach space, and this head was also used for display purposes.

The Dynamics of Performance Monitoring

Statistical analysis. Randomization statistics based on 1000 repetitions were performed to identify significant power changes in the time–frequency plane relative to baseline activity in the EEG. This analysis was applied separately to each subject and each condition. In addition, randomization statistics on the time–frequency power differences between incompatible error and incompatible correct conditions were performed. To summarize these results for the group of 13 subjects, binomial statistical analysis was applied.

The statistical analysis of the association between single-trial EEG amplitudes and reaction times was achieved by determining the linear regression slopes between single-trial amplitudes and reaction time values (see Fig. 3c). Separate analyses were performed for the current trial, that is, single-trial amplitudes were related to reaction times of the same trial and to the following trial. In the latter case, single-trial amplitude values were associated to reaction times whenever the following trial belonged to the same stimulus condition. For group analysis, the resulting individual slopes were tested against zero (see Fig. 3d) by applying one-sided $t$ tests for conditions in which a prediction could be made on the basis of the performance monitoring model.

The statistical analysis of fMRI data was based on a least squares estimation using the general linear model for serially autocorrelated observations (random effects model) (Friston et al., 1995; Worsley and Friston, 1995; Aguirre et al., 1997; Zarahn et al., 1997). Event-related designs were implemented, that is, the hemodynamic response design was modeled by the experimental conditions for each stimulus (event = onset of stimulus presentation). The measured signal was described by a convolution of the temporal stimulus distribution and the hemodynamic response function. The design matrix was generated using a synthetic hemodynamic response function and its first and second derivative and a response delay of 6 s (Friston et al., 1998). The model equation, including the observation data, the design matrix, and the error term, was convolved with a 4 Gaussian units. The estimated effective degrees of freedom were estimated as described by Worsley and Friston (1995). In the following, contrast maps, that is, estimates of the raw-score differences among specified conditions, were generated for each subject. The individual functional datasets were all aligned to the same stereotactic reference space, and a group analysis was performed. For multisection analysis, the random-effects analysis can be effected as a one-sample $t$ test on the resulting contrast images across subjects and sessions (Worsley and Friston, 1995; Holmes and Friston, 1998). Subsequently, $t$ values were transformed into z scores. The design matrix consisted of onset vectors for compatible correct, incompatible correct, and incompatible erroneous trials. Trials involving late response feedbacks and nonevents formed two additional onset vectors. The six translational and rotational motion correction parameters provided by the Siemens motion correction protocol were included as regressors. As in previous studies (Ullsperger and von Cramon, 2001, 2004), analysis of error-related brain activity was performed by contrasting incompatible erroneous with incompatible correct trials, thus extracting specific signal increases on errors. Conflict-related activity should cancel out, because response conflict occurs on both incompatible correct and erroneous trials. To minimize the probability of false positives (type I error), only voxels with a $z$ score $>3.09$ ($p < 0.001$, uncorrected) and with a volume $>180$ mm$^3$ (five voxels) were considered as activated voxels (Brauer et al., 2001).
In a second analysis testing whether the single-trial ERN measure covaries with the fMRI signal, a parametric design was used (Büchel et al., 1996, 1998). The single-trial amplitudes vector was used as a parameter referring to the onsets of all responses in the task, regardless of their accuracy and speed. The design matrix furthermore contained two onset vectors for late-response feedbacks and nonevents. The six translational and rotational motion correction parameters were included as additional regressors.

**Results**

**Behavioral results**

While participants underwent concurrent EEG and fMRI data acquisition, they performed a speeded flanker task. They were required to respond with button-presses according to the direction indicated by a centrally presented target arrow, which was surrounded by irrelevant but distracting flanker arrows (Fig. 1). Participants made errors on 0.58% (SEM, 0.16) of compatible and 17.23% (SEM, 2.17) of incompatible trials (significant difference; \( t_{(12)} = 7.75; p < 0.0001 \)). The number of compatible errors was insufficient for meaningful statistical analyses, such that this stimulus–response type was excluded from further analysis. Hit reaction times were 380.8 ms (SEM, 7.9) for compatible and 445.0 ms (SEM, 8.1) for incompatible trials (significant difference; \( t_{(12)} = 21.26; p < 0.0001 \)). The mean deadline was 475.7 ms (SEM, 17.7). It was missed in 9.46% (SEM, 1.8) of compatible and in 27.69% (SEM, 3.50) of incompatible trials. Error reaction times for incompatible trials were 388.2 ms (SEM, 9.8), thus being significantly shorter than for incompatible correct trials (\( t_{(12)} = 4.41; p < 0.001 \)). In sum, these behavioral results are consistent with previous findings for flanker tasks (Eriksen and Eriksen, 1974; Ullsperger and von Cramon, 2001). Importantly, there was a sufficient numbers of errors for incompatible trials to allow meaningful data analyses.

**EEG signal analysis and identification of independent component related to performance monitoring**

After denoising the EEG from MR gradient and ballistocardiographic artifacts, ERPs were computed (Fig. S1, available at www.jneurosci.org as supplemental material). As expected, a frontocentral ERN was clearly visible for incompatible error trials but strongly reduced, if not absent, for the correct response conditions (Fig. S2, available at www.jneurosci.org as supplemental material). To separate ERN-related EEG signals from other brain processes and artifacts, we performed ICA on each subject’s MR-denosed raw EEG data (Bell and Sejnowski, 1995). ICA returns a set of spatial filters, which yield component activations that are maximally temporally independent from each other. In each subject, we identified one IC that met the following two criteria and therefore was the best candidate to account for the ERN. First, the IC...
should have a near-radial central topography. Second, its backprojected ERP time course should yield a more negative deflection at the response interval in the incompatible error compared with the incompatible correct condition. The topographies of the selected ICs for each subject are shown in the supplemental material (Fig. S3, available at www.jneurosci.org). Independent components reflecting the parietal error positivity (Pe) or the N200 were not observed.

We performed several analyses to test whether the IC selected for each subject indeed reflects the spatial and temporal characteristics of the ERN. First, we performed fMRI-informed source modeling of the grand average IC map (Fig. 2a,c). A single equivalent current dipole was seeded into the RCZ, with the exact location taken from the conventional second-level fMRI analysis contrasting incompatible error and incompatible correct trials [Talairach coordinates ($x$, $y$, $z$) = 0, 20, 30] (Table 1) (see Fig. 5). This source dipole accounted for 90.2% of the variance (Fig. 2c). Seeding additional dipoles into other cortical areas identified by the same fMRI analysis (lateral prefrontal cortex, left anterior insula) did not improve the model fit, suggesting that the identified ICs represent activity originating in the RCZ.

Second, grand mean ERPs of the back-projected IC activations revealed a clear ERP in the incompatible error condition (Fig. 2b). These IC ERPs strongly resembled those from the original scalp channel data, but their topography appeared now free of artifact contributions (Fig. S4, available at www.jneurosci.org as supplemental material). Typically, the ERPs showed a polarity reversal at outer electrodes (e.g., F7/8, P7/8) (see Fig. S4, available at www.jneurosci.org as supplemental material), which, taking into account the common average reference, supports the notion that the selected IC can be explained by a single equivalent dipole located in the RCZ.

Third, we explored the EEG signal on a single-trial level. ERPs are usually derived by averaging across trials, which prevents the study of trial-by-trial variations of the EEG signal. To overcome this limitation, so-called ERP images were computed showing the respective single-trial IC activations sorted by reaction time. These analyses demonstrate a good signal-to-noise ratio, because time–frequency analysis revealed a prominent theta power increase (Fig. 2). ERP images and ERP time courses related to error monitoring covary with the single-trial EEG signals (Fig. 3). Note the low number of events for the ERN and the parietal ERP component (Pe) in the control trials for compatible correct trials. Here, short RTs were associated with high single-trial amplitudes ($b = 5.48; p = 0.002$; one-sided $t$ test). Interestingly, the opposite relationship was found for incompatible correct trials. Here, short RTs were associated with small single-trrial amplitudes ($b = -2.14; p = 0.046$), consistent with previous findings for the ERN in speeded tasks using a deadline procedure (Luu et al., 2000). However, these effects did not remain significant when RT and single-trial amplitude outliers (values $> 3$ SD) and trials following a late feedback were excluded from the analysis (incompatible errors, $b = 2.61, p = 0.103$; incompatible correct, $b = -2.01, p = 0.140$).

More importantly, we identified a clear relationship between ERN dynamics and subsequent behavioral adjustments. We found that higher single-trial amplitudes were associated with longer RTs on conflict trials after errors (Fig. 3c,d). Thus, activity variations of the performance monitoring system, as estimated by the single-trial EEG measure, significantly predicted posterior slowing ($b = -5.38; p = 0.043$). After exclusion of outliers and trials followed by the late feedback, this effect was even more pronounced ($b = -5.90; p = 0.032$). Moreover, this effect could not be explained by a correlation between RTs on errors and RTs on subsequent trials, which was absent (second level mean; $r = 0.06; NS$). The present analysis thus demonstrates that posterior slowing (Rabbitt, 1966) was driven by postresponse electrophysiological activity in the RCZ.

<table>
<thead>
<tr>
<th>Table 1. Results of fMRI analyses</th>
<th>Coordinates</th>
<th>HEMISPHERE</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>z value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional analysis contrasting incompatible error versus incompatible correct</td>
<td>Rostro cingulate zone (z24)</td>
<td>Left</td>
<td>-2</td>
<td>20</td>
<td>30</td>
<td>4.02*</td>
</tr>
<tr>
<td>Inferior anterior insula</td>
<td>Left</td>
<td>-29</td>
<td>12</td>
<td>-12</td>
<td>6.63</td>
<td></td>
</tr>
<tr>
<td>Superior frontal gyrus (6/8)</td>
<td>Left</td>
<td>12</td>
<td>11</td>
<td>57</td>
<td>3.76*</td>
<td></td>
</tr>
<tr>
<td>Sulcal frontalis inferior (9/46)</td>
<td>Left</td>
<td>-29</td>
<td>36</td>
<td>27</td>
<td>3.54*</td>
<td></td>
</tr>
<tr>
<td>EGG-informed analysis</td>
<td>Rostro cingulate zone (32/6/8)</td>
<td>0</td>
<td>17</td>
<td>42</td>
<td>-3.86*</td>
<td></td>
</tr>
</tbody>
</table>

The table shows conventional random effects analysis modeling compatible correct, incompatible correct, and incompatible error trials with separate onset vectors. Contrast incompatible correct versus compatible correct is shown. Parametric analysis used single-trial amplitude quantification of error-related independent component of the EEG data set. Brodmann areas are in parentheses. *$p < 0.001$ and spatial extent criterion met.

Single-trial EEG amplitudes and the dynamics of performance monitoring
A key prediction that can be derived from performance monitoring models is that physiological signatures of error monitoring should predict behavioral adjustments at the single-trial level. To address this, ERN magnitude was obtained in every single trial by taking peak-to-peak measures of the 2–10 Hz bandpass-filtered IC signals (Fig. 3a). We examined the relationship of the resulting single-trial amplitudes for each subject (Fig. 3b) to behavior (Fig. 3c). For incompatible errors, the single-trial amplitude was significantly correlated with reaction time, such that short RTs were associated with high single-trial amplitudes ($b = 5.48; p = 0.002$; one-sided $t$ test). Interestingly, the opposite relationship was found for incompatible correct trials. Here, short RTs were associated with small single-trial amplitudes ($b = -2.14; p = 0.046$), consistent with previous findings for the ERN in speeded tasks using a deadline procedure (Luu et al., 2000). However, these effects did not remain significant when RT and single-trial amplitude outliers (values $> 3$ SD) and trials following a late feedback were excluded from the analysis (incompatible errors, $b = 2.61, p = 0.103$; incompatible correct, $b = -2.01, p = 0.140$).

More importantly, we identified a clear relationship between ERN dynamics and subsequent behavioral adjustments. We found that higher single-trial amplitudes were associated with longer RTs on conflict trials after errors (Fig. 3c,d). Thus, activity variations of the performance monitoring system, as estimated by the single-trial EEG measure, significantly predicted posterior slowing ($b = -5.38; p = 0.043$). After exclusion of outliers and trials followed by the late feedback, this effect was even more pronounced ($b = -5.90; p = 0.032$). Moreover, this effect could not be explained by a correlation between RTs on errors and RTs on subsequent trials, which was absent (second level mean; $r = 0.06; NS$). The present analysis thus demonstrates that posterior slowing (Rabbitt, 1966) was driven by postresponse electrophysiological activity in the RCZ.

Trial-by-trial coupling of EEG and fMRI
A key question in the present context is whether hemodynamic signals related to error monitoring covary with the single-trial ERN (Nunez and Silberstein, 2000; Logothetis et al., 2001). If present, such a relationship should only be found in brain regions specifically involved in performance monitoring. To this end, we used the EEG single-trial amplitude to predict the fMRI BOLD signal. To take into account the slow time course of fMRI BOLD, the single-trial EEG amplitudes were convolved with the hemodynamic response function at button-press onset times. The following parametric random effects fMRI analysis identified a significant correlation of the single-trial amplitude with the BOLD response specifically in the RCZ (Fig. 4, Table 1). The direction of
RCZ, the conventional fMRI contrast revealed additional brain structures, such as insular and lateral prefrontal cortex (Fig. 5, Table 1). The conventional contrast extracted error-specific signal increases, whereas performance-monitoring-related activations present in both correct and incorrect trials cancelled out to a large degree. The EEG-informed fMRI analysis, on the other hand, was more specific to variations of the monitoring signal itself. These differences in process specificity might also account for the observation that the maxima of the RCZ foci were separated by ~12 mm in inferior–superior direction (Ullsperger and von Cramon, 2001). However, with the given the between-plane resolution, a functional interpretation of this finding remains speculative.

Discussion

The present study demonstrates an event-related trial-by-trial coupling of simultaneously recorded EEG, fMRI, and behavior in humans. The major advantage of simultaneous recordings is that these different measures are studied under identical sensory and motivational conditions, thereby allowing the investigation of trial-by-trial fluctuations. We found the single-trial ERN to be systematically related to ensuing behavioral adjustments. As predicted by performance-monitoring models, the ERN seems to signify the likelihood that the action outcome is worse than expected (Holroyd et al., 2004; Brown and Braver, 2005). On error trials, this likelihood estimate has been suggested to be driven primarily by postresponse conflict between executed and concurrently activated response tendencies (Yeung et al., 2004). Moreover, the single-trial ERN amplitude reflects activation of the RCZ neurons involved in controlling subsequent adjustments. This finding is paralleled by invasive recordings showing that performance adjustments are preceded by enhanced firing rates of RCZ neurons (Shima and Tanji, 1998; Williams et al., 2004). Our finding that posterror slowing was predicted by the single-trial ERN has not been reported in previous studies, in which this relationship was investigated by the study of the averaged ERN and correlations across subjects. At the group level, however, many other factors may contribute to averaged ERN amplitude variations (e.g., skull thickness, variations of the cingulate sulcus, and trait factors) (Pailing and Segalowitz, 2004). Moreover, the EEG-informed approach as well as the conventional fMRI analysis identified the observed relationship confirmed that trials with greater absolute single-trial ERN amplitudes were associated with stronger BOLD responses in the RCZ. Although the EEG-informed approach as well as the conventional fMRI analysis identified the
for behavioral adjustments. The ability to measure the dynamics of the monitoring signal will significantly facilitate addressing its relationship to immediate and long-term control adjustments (Ridderinkhof et al., 2004).

The peak-to-peak measure used to quantify performance-monitoring-related EEG activity takes into account the ERN and the subsequent positive peak, which is also maximal at frontocentral sites. This frontocentral positive EEG deflection seems to result from activity in the RCZ as well, which is consistent with a previous source localization study (van Veen and Carter, 2002). Note that this positivity should not be confused with the parietal error positivity Pe (Falkenstein et al., 1990, 2000), which was not captured in the ICA decomposition. Furthermore, it has been hypothesized that ERN and preresponse N200 on correct trials may both reflect similar processes, namely response conflict monitoring (Yeung et al., 2004). We did not obtain a reliable N200 conflict effect in our data; in particular, we found no IC reflecting an N200 modulation. Usually, the N200 preresponse conflict effect is very small (up to 2 µV) (van Veen and Carter, 2002), and we therefore may have missed it as a result of the recording environment or the limited number of electrodes. The relationship between ERN and the N200 conflict effect remains an open question that should be optimally addressed by ICA decomposition of high-density EEG data acquired outside the MR environment.

For resting conditions, it has been shown previously that simultaneous EEG and fMRI BOLD can reveal systematic correlations (Goldman et al., 2002; Laufs et al., 2003). The event-related trial-by-trial correlation approach here presents a new strategy for integrating EEG and fMRI. Alternative approaches such as fMRI-informed ERP dipole seeding (Ullsperger and von Cramon, 2001; Thees et al., 2003) implicitly assume a tight link between the neural generators of ERPs and fMRI activation foci. However, as exemplified by the present study, conventional fMRI contrasts may well reveal cortical regions that do not comprise neuronal sources of the ERP and vice versa (Nunez and Silberstein, 2000). Because fMRI BOLD and ERP components can differ with regard to their sensitivity to experimental manipulations, fMRI-informed dipole seeding is not necessarily a valid solution of the inverse problem in EEG.

High magnetic fields provide adverse conditions for EEG recordings. Application of ICA offers a practical solution to minimize artifacts and to identify functionally meaningful EEG activity on a trial-by-trial basis (Debener et al., 2005; Makeig et al., 2002, 2004). The identified IC reflected all features of the ERN, including scalp topography, ERP morphology, and time–frequency characteristics. We also found that the fMRI-informed dipole seeding approach confirmed the RCZ as the major source of the selected ICA correlate of the ERN. This latter finding also validates the main assumption of ICA as applied to EEG data. Under favorable circumstances, a clean independent component should reflect the ongoing activity of a synchronous piece of cortex expressing a dipolar projection. More importantly, we conclude that the covariation of the single-trial ERN measure with the fMRI BOLD response in the RCZ strongly supports the proposed RCZ source of the ERN (Holroyd et al., 2004; Ridderinkhof et al., 2004; Ullsperger and von Cramon, 2004). Thus, the fMRI signal and the ICA single-trial correlate of the ERN appear to reflect directly related neuronal and metabolic processes in the RCZ. Our data fit well with animal research on a coupling between BOLD and local field potentials (Logothetis et al., 2001; Logothetis, 2003), the latter being known to be the basis of the scalp-recorded EEG (Nunez and Silberstein, 2000).

The joint study of electrophysiological and hemodynamic signatures of regional event-related brain activity seems very promising because future studies may succeed in identifying multiple functionally relevant ICs. This would allow to relate several IC time courses to regional fMRI activation, thereby holding great potential to address two cardinal questions in the field of cognitive neuroscience. First, concurrent single-trial EEG/fMRI will facilitate addressing the dynamic interplay between ongoing and event-related brain activity (Arieli et al., 1996; Makeig et al., 2002). Second, adding electrophysiological information provides high temporal precision and thus helps to shape models on how cognitive processes are dynamically implemented in distinct cortical areas (Stephan et al., 2004). By successfully demonstrating a trial-by-trial coupling of noninvasive event-related EEG and fMRI, new avenues are opened for future experiments that address the dynamics of information processing within both anatomically and functionally defined neural networks.

References


Supplemental Material

Trial-by-trial coupling of concurrent EEG and fMRI identifies the dynamics of performance monitoring
By Stefan Debener, Markus Ullsperger, Markus Siegel, Katja Fiehler, D. Yves von Cramon, and Andreas K. Engel

Supplemental Figure 1. Exemplary time series of EEG data after recording (upper row), after correction for MR gradient artifacts (middle row), and after correction for ballistocardiac artifacts (lower row).
Supplemental Figure 2. Stimulus-locked grand mean average waveforms of scalp-recorded ERP data for the three stimulus-response conditions (green = compatible correct, blue = incompatible correct, red = incompatible error). The lower part depicts the ERP images for the three stimulus-response conditions. Trials are sorted by ascending reaction time, as indicated by the black sigmoid curve.
Supplemental Figure 3. Scalp topography maps of the independent component accounting for performance-monitoring-related EEG activity shown for each individual subject and for the grand mean average across subjects (root mean square normalized).
Supplemental Figure 4. Stimulus-locked grand mean average waveforms of the EEG time course resulting from backprojection of the independent component related to performance monitoring, shown for the three stimulus-response conditions (color code as in Supplemental Fig. 2). The lower part depicts the ERP images for the three stimulus-response conditions. Trials are sorted by ascending reaction time, as indicated by the black sigmoid curve.