



Anatomy of an error: ERP and fMRI

Daniel H. Mathalon^{a,b,*}, Susan L. Whitfield^c, Judith M. Ford^{d,e}

^a Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA

^b Psychiatry Service, Veterans Affairs Connecticut Healthcare System, West Haven, CT, 06516, USA

^c Department of Psychology, Stanford University, Stanford, CA, USA

^d Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305-5550, USA

^e Psychiatry Service, Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA

Abstract

Successful inhibition of pre-potent responses involves conflict; failed inhibition involves both conflict and errors, complicating the study of errors. Event-related potential (ERP) and functional magnetic resonance imaging (fMRI) data were collected while ten subjects (26–55 years old) performed a Go/NoGo task, with pre-potent responses (88% Go) and inhibition of responses (12% NoGo). We measured error-related negativity (ERN) to false alarms (FA), correct-related negativity (CRN) to hits, NoGo N2 to correct rejections (CR) and Go N2 to hits. ERP difference scores were derived (ERN-CRN; NoGoN2-GoN2) for correlating with fMRI contrasts (FA–hits; CR–hits). Age effects were removed from ERN and N2 difference scores, and conflict effects, reflected in N2 difference scores, were removed from ERN. The resulting ERN correlated with fMRI activations in both caudal and rostral anterior cingulate cortex (ACC), while N2 correlated with fMRI activations in caudal ACC and in executive control regions including dorsolateral prefrontal cortex. Thus, error and conflict monitoring may be dissociable, subserved by both overlapping and distinct ACC regions.
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1. Introduction

About 10 years ago, two laboratories reported a unique brain response to errors, the error-related negativity (ERN) (Gehring et al., 1993) and the negativity associated with errors (Ne) (Falkenstein et al., 1991). This negative component of the event-related brain

* Corresponding author. Tel.: +1-203-932-5711x5539; fax: +1-203-937-3886.

E-mail address: daniel.mathalon@yale.edu (D.H. Mathalon).

potential (ERP) starts at the onset of the overt error response, peaks ≈ 100 ms thereafter, and is maximal at frontocentral midline scalp sites (Gehring et al., 1993; Kopp et al., 1996; Kopp and Rist, 1999). Although it is generated when the subject knows the correct response but fails to execute it (Dehaene et al., 1994), it is dissociable from error awareness (Nieuwenhuis et al., 2001). It is independent of corrective motor responses, occurring after errors of commission in Go/NoGo tasks even though no corrective actions are possible (Falkenstein et al., 1995; Scheffers et al., 1996; Falkenstein et al., 2000), and also occurring in response to external error feedback (Miltner et al., 1997; Badgaiyan and Posner, 1998; Luu et al., 2000). The ERN was interpreted as a reflection of error detection or attempted error inhibition, resulting from a comparison of the actual and intended responses (Gehring et al., 1993; Scheffers et al., 1996; Scheffers and Coles, 2000). That there might be such an error detection system was proposed by Rabbitt (1966) to explain our attempts to correct our errors “in flight” before they are complete.

1.1. ERN: error monitoring and conflict monitoring

Although the initial view of the ERN was that it reflected an error-monitoring system in the brain, an alternative theoretical account of the ERN that has gained prominence in recent years is that it reflects the detection of response conflict, rather than errors per se (Carter et al., 1998; Botvinick et al., 1999; Cohen et al., 2000; Botvinick et al., 2001). Carter et al. (1998) first reported functional magnetic resonance image (fMRI) activation in the anterior cingulate cortex (ACC) associated with errors of commission in the AX-continuous performance task (AX-CPT) and showed that this same ACC particle was activated to correct trials that were high in conflict. They argued that errors were simply a special case of response conflict in which the incorrect response channel prevailed in its competition with the correct response channel. The conflict hypothesis of the ERN, formalized by Botvinick et al. (2001), postulated that the ERN is emitted by the ACC as part of a conflict monitoring system that detects high degrees of response competition and recruits greater top-down control from the dorsolateral prefrontal cortex (DLPFC) to improve task performance and reduce conflict. In spite of conflict on *correct* trials, the ERN does not occur on these trials, possibly because response conflict is resolved before a correct response is emitted (Nieuwenhuis et al., 2003). An ERP reflection of conflict on correct trials is best seen in the stimulus-locked ERPs prior to response execution, perhaps as an N2 component—the second major negative component of the ERP, peaking between 200 and 400 ms. A study by van Veen and Carter (2002a) provided support for this hypothesis by showing conflict modulation of the N2 component of the stimulus-locked ERP.

1.2. N2 and conflict

The N2 was first linked to response conflict when it was shown to be associated with successful response inhibition in Go/NoGo tasks (for review see Falkenstein et al., 1999). Indeed, it has been suggested that the ERN might be a delayed NoGo N2; that is, ERN ‘may reflect a late and hence unsuccessful attempt to inhibit the false alarm’ (Falkenstein et al., 1999, p. 271). However, Falkenstein et al. compared ERPs associated with successful (N2) and unsuccessful (ERN) response inhibitions in visual and auditory Go/NoGo tasks and

found that N2 and ERN can be distinguished based on scalp topography, sensory modality and group performance differences. Nevertheless, using dipole source localization analyses, van Veen and Carter (2002a) could not distinguish N2 and ERN elicited during a choice reaction time (RT) task, locating the source of both in the same area of the ACC.

The fact that an enhanced N2 is elicited by correct responses to high response-competition trials in choice RT tasks (van Veen and Carter, 2002a) and correctly withheld responses to NoGo trials in Go/NoGo tasks (Falkenstein et al., 1999) is consistent with the view that the stimulus-locked N2 reflects conflict in both tasks. Although Go/NoGo tasks involve the monitoring and inhibition of a single response, whereas choice RT tasks involve monitoring competition between two or more responses, Go/NoGo tasks can be considered to evoke conflict between competing responses in the sense that participants must choose to go or not to go based on the stimulus presented. Competition between emitting a response or withholding it generates conflict on NoGo trials, particularly when highly probable Go trials create a pre-potent tendency to respond. Indeed, participants must inhibit the pre-potent Go response on NoGo trials just as they must inhibit the pre-potent tendency to read the color words in a Stroop task or respond in accord with incongruent flankers in the Eriksen flankers task. Thus, both the Go/NoGo task and choice RT tasks, such as the Stroop or flankers tasks, involve conflict and require some degree of pre-potent response inhibition. A further argument supporting the induction of conflict on the NoGo trials is the fact that NoGo P300 is later than the Go P300 (e.g., Pfefferbaum and Ford, 1988), consistent with other examples of a time cost associated with high conflict trials in choice RT tasks.

1.3. Brain areas associated with error and conflict monitoring

As mentioned above, fMRI has been used to distinguish errors and response conflict. Although Carter et al. (1998) showed the same region of the ACC was activated by conflict and errors, more recent fMRI studies (Kiehl et al., 2000; Braver et al., 2001; Ullsperger and von Cramon, 2001) have shown distinct areas of the ACC to be activated by conflict and by errors, suggesting potentially dissociable processes. However, the precise locations of these differential ACC activations to conflict and to errors have not been consistent across studies. For example, at least two studies (Kiehl et al., 2000; Braver et al., 2001) have localized conflict to caudal ACC and errors to rostral ACC. In contrast, Ullsperger and von Cramon (2001) showed that while both errors and response competition activated the frontomedian wall during the flankers task, errors preferentially activated the motor (caudal) region of ACC. To examine if the ERN recorded from the same subjects could have been generated in caudal ACC, a single dipole was placed there and found to account for 91% of the variance. Perhaps because this task did not elicit a large N2 on correct trials, no dipole analysis of the N2 was reported. However, van Veen and Carter (2002a) used dipole source analysis to model the generators of both N2 and ERN. They localized them both to caudal ACC, consistent with fMRI activations on conflict and error trials reported by others (Carter et al., 1998; Kiehl et al., 2000; Menon et al., 2001). They were unable to localize the ERN to the rostral ACC, which some fMRI studies have shown to be selectively activated by errors (Kiehl et al., 2000; Braver et al., 2001; Menon et al., 2001), but they did localize a generator of the later positivity associated with errors, or Pe (Falkenstein et al., 1995), to the rostral ACC. van Veen and Carter (2002b) suggested that the contribution of ACC activity to the

generation of the ERN could reflect a more general role of the ACC in conflict detection, rather than error detection per se. Despite these results, the controversy surrounding the role of ACC in conflict versus error detection remains unresolved.

Other frontal lobe structures have also been indirectly implicated in the generation of the ERN. While patients with DLPFC lesions have normal amplitude ERNs following errors compared to age-matched controls, they also have “ERNs” on correct trials (Gehring and Knight, 2000). Similarly, abnormally large ERNs on correct trials, sometimes referred to as ‘CRNs’, have been observed in patients with schizophrenia (Kopp and Rist, 1999; Alain et al., 2002; Mathalon et al., 2002), a disorder known to be associated with DLPFC dysfunction (e.g., Weinberger and Berman, 1996; Goldman-Rakic and Selemon, 1997). Thus, DLPFC input appears to be critical for modulating the ERN signal differentially to correct and error responses. Indeed, bilateral activation of the DLPFC might also contribute to the ERN and could be mistakenly modeled as a single midline dipole in ACC. Similarly, bilateral activation of supplementary motor area (BA6) and pre-supplementary motor area (BA8), which are both preferentially activated to errors (Kiehl et al., 2000; Menon et al., 2001), could also be misrepresented by a single midline dipole in a typical equivalent-dipole model.

While it is unlikely that activity in the basal ganglia could contribute directly to the ERN, it may contribute indirectly (Holroyd and Coles, 2002). Indeed Parkinson’s Disease patients, who are known to have dopaminergic deficits in the basal ganglia, have reduced ERN amplitudes (Falkenstein et al., 2001; Holroyd and Coles, 2002), as do the elderly (Nieuwenhuis et al., 2002; Mathalon et al., 2003) in whom dopaminergic tone is also diminished (Arnsten et al., 1995; van Dyck et al., 2001). Dopaminergic neurons in the basal ganglia exhibit a phasic response when important predictions fail (Schultz et al., 1998). Moreover, one basal ganglia structure, the caudate, has been implicated in stopping an error in progress (Rubia et al., 2001). Another possible source indirectly contributing to the ERN is the cerebellum, which has a well-documented role in motor control and ‘in flight’ error adjustments (Schmanhmann, 1997).

1.4. *Distinguishing between N2 and ERN*

While dipole localization studies provide one approach to distinguishing response conflict reflected in N2 from error detection reflected in ERN, dipole models do not provide unique solutions to the inverse problem. The scalp surface topography of an ERP can be equally well accounted for by many alternative dipole models that may vary greatly in both the number of dipoles and their locations. To further examine the distinction between conflict and error processing, we have adopted a regression analysis approach to isolate ERN variance that is independent of the N2, with subsequent correlation of these Go/NoGo ERP components (N2 and N2-adjusted ERN) with fMRI activations collected during a separate Go/NoGo scan session. fMRI activity associated with successful and unsuccessful response inhibition is likely to reflect more than just response conflict and error monitoring. It may include differential activity associated with sensation, perception, response selection, self-evaluation, planning for the next trial and any number of other processes happening in the 6 s it takes for the hemodynamic response to peak and the subsequent 6–12 s it takes to return to its baseline state. Correlation of these fMRI activations with ERP components allows a relatively focused interrogation of those brain activations that specifically covary

with the electrophysiological indices of conflict and error processing that emerge and resolve within the first 400 ms following stimulus presentation (N2) or erroneous response execution (ERN).

1.5. Goals of the paper

To focus on those brain regions predominantly engaged by error monitoring, we correlated ERN data with fMRI activations from *unsuccessful* response inhibitions. Similarly, to focus on brain regions involved with conflict monitoring, we correlated NoGo N2 data with fMRI activations from *successful* response inhibitions. Because errors are typically associated with conflict, we removed from the ERN the variance it shares with N2 and examined the correlations of this relatively “conflict-free” measure of error processing with fMRI error activations.

2. Methods

2.1. Participants

In separate sessions, we recorded ERPs and fMRI while ten healthy subjects (age: mean = 38.0 years, range = 26–55 years) performed a Go/NoGo task. All gave written informed consent after procedures had been fully described. Subjects were recruited by newspaper advertisements and word-of-mouth, screened by telephone using questions from the Structured Clinical Interview for DSM-IV (SCID) (First et al., 1995), and were excluded for any significant history of Axis I psychiatric illness, significant head injury (loss of consciousness >30 min or resulting in neurological sequelae) or neurological or other medical illnesses compromising the central nervous system. All of the subjects were right handed. No subject reported vision problems.

2.2. Task

In order to engage response conflict and elicit NoGo errors, we established a strong pre-potent bias to respond to Go stimuli. To build up expectancy for Go stimuli, we skewed stimulus probabilities, pre-trained subjects to respond to the stimulus that subsequently became the NoGo stimulus and emphasized speed over accuracy. Subjects viewed an irregular sequence of *K* (12%) and *X* (88%) stimuli, presented for 100 ms each. The stimulus onset asynchrony (SOA) was 1, 2 or 3 s, with each SOA occurring with equal probability. The interval between two *K* stimuli (the event of interest) varied between 7 and 24 s. The letters were presented in green Helvetica font, presented on a black background and subtended a visual angle of $\approx 2^\circ$. This is similar to a paradigm used by Kiehl et al. (2000).

Participants responded with the right index finger each time an *X* was presented and withheld responding to *K*s. There were 42 *K* stimuli and 288 *X* stimuli.

This task was identical for ERP and fMRI except that participants were supine in the scanner and seated in the ERP recording booth and that the scanner environment was noisier.

2.3. Behavioral data acquisition, processing and analysis

A pressure-sensitive piezo-electric transducer fit inside the plastic cylinder in which the right index finger rested. It produced a continuous measure of response activity, was sensitive to vigor or acceleration of the response and was used to record motor responses. A very low criterion for motor responses was set (>15% of the rolling average amplitude for the 20 surrounding trials) such that a slow and weak response to a *K* would register as an error, as would a very brisk, but partial response. The sensitivity of this response device to partial errors likely increased the number of errors we observed, relative to a standard all-or-none button press device.

2.4. ERP data acquisition, processing and analysis

2.4.1. ERP acquisition

Subjects were seated in a comfortable chair in a sound attenuating, electrically shielded booth. Electroencephalogram (EEG) data were recorded from 24 scalp sites (Fp1, Fpz, Fp2, F3a, Fza, F4a, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, Oz, O2) referenced to linked mastoids, but only data from the central nine sites (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4) are reported here. Vertical electro-oculogram (EOG) was recorded from electrodes placed above and below the right eye and horizontal EOG was recorded from electrodes placed at the outer canthus of each eye. Data were sampled every 2 ms (500 Hz) with a band-pass filter of 0.05–30 Hz.

2.4.2. ERP processing and analysis

Single-trials were corrected for the effects of eye blinks and eye movements based on correlations of the VEOG and HEOG with the EEG recorded at each electrode site (Gratton et al., 1983) before baseline correction. Trials exceeding $\pm 100 \mu\text{V}$ were then rejected. Data were low pass filtered at 12 Hz before peaks were identified and measured. NoGo N2 was measured as the maximum negativity between 150 and 400 ms, post-stimulus, in the stimulus-synchronized ERPs to successful response inhibitions. ERN was measured as the maximum negativity between 24 and 200 ms post-response in the response-synchronized ERPs to unsuccessful response inhibitions (i.e., false alarms). Both were measured relative to a -100 to 0 ms baseline. For further comparison of ERN with NoGo N2, we also measured ERN in the stimulus-synchronized averages of the false alarm trials between 150 and 400 ms. Univariate repeated measures analyses of variance (ANOVA) were performed for accuracy (NoGo N2 versus ERN), anterior-posterior scalp site (A-P: frontal, central, parietal) and lateral scalp site (Lat: left, middle, right) for peak amplitudes and latencies. The association between NoGo N2 and ERN amplitudes was assessed using Pearson correlation coefficients.

2.5. fMRI data acquisition, processing and analysis

2.5.1. fMRI acquisition

Images were acquired on a GE 3 Tesla MRI scanner using a custom made head coil. Subjects' heads were stabilized with a bite bar made from their dental impression. After

shimming (Kim et al., 2000), functional images were acquired with a spiral gradient-echo sequence (Glover and Lai, 1998) in the axial plane oriented parallel to the anterior commissure-posterior commissure (AC-PC) line prescribed from the midsagittal slice of a previously acquired SPGR anatomic sequence. 24 slices (6 mm thick, 0 mm gap) were acquired with each 1.5 s TR (TE = 30 ms, NSA = 1, FOV = 24 cm; flip angle = 70°, bandwidth = 100 kHz; matrix = 64 × 64). Voxel dimensions were 3.75 × 3.75 × 6 mm. Images corresponding to the first four TRs were discarded from further analysis to eliminate non-equilibrium effects.

2.5.2. *fMRI processing*

Image processing was performed with Statistical Parametric Mapping (SPM99) (<http://www.fil.ion.ucl.ac.uk/spm/spm99.html>). Raw data were reconstructed and slice-time corrected. Functional images were re-oriented based on their relation to a template brain in a standard coordinate system (Talarach/Montreal Neurological Institute (MNI) templates supplied in SPM99) and their origin was set to the AC based on its location on the mid-sagittal slice of the high resolution SPGR image. Functional images were motion corrected by re-aligning all scans to the first scan. The mean functional image was normalized to the MNI echo-planar image (EPI) template using a 12-parameter affine transformation and 4 × 5 × 4 nonlinear basis functions, and the resulting parameters were used to anatomically normalize all individual functional images in the time series. The images were subsequently resliced to 4 × 4 × 4 mm³ using sinc interpolation and then spatially smoothed with a Gaussian filter, 10 mm FWHM. Smoothing facilitated inter-subject averaging by minimizing differences in functional and gyral anatomy, enhanced the signal-to-noise ratio and satisfied the assumptions of Gaussian random field theory implemented in SPM 99. During model estimation, low frequency noise was removed with a temporal high pass filter (cut-off based on SPM defaults) and grand mean scaling was implemented to adjust images for global differences in image intensity across subjects.

2.5.3. *fMRI analysis*

For individual subject (first-level) analyses, a fixed effects event-related design was implemented using multiple linear regression time series analyses (Holmes et al., 1996) to determine the location and extent of brain activations. The hemodynamic responses were modeled using the SPM canonical hemodynamic response function (two γ functions) with a temporal derivative term. For most subjects, four event types were modeled: X hits and errors of omission, and K correct rejections and false alarms. However, some subjects had no errors of omission, so these events could not be modeled for those subjects. Rests (the first and last 14 scans) were not included in this analysis. We used a height threshold of $P < 0.05$, uncorrected and an extent threshold of six contiguous voxels. We contrasted: (1) false alarms–hits; (2) correct rejections–hits; (3) false alarms–correct rejections. In addition to whole-brain effects, a major focus of the fMRI analysis was on ACC activations during both false alarms and correct rejections. To this end, using the small volume correction option in SPM99, we interrogated 15 mm radius spheres around published ACC centroids of activation preferentially associated with errors (Kiehl et al., 2000; Menon et al., 2001; Ullsperger and von Cramon, 2001) or in one case, with errors and conflict (Carter et al., 1998). These centroids are listed in Table 1.

Table 1
Anterior cingulate cortex coordinates for centroids of interest

Authors	Contrast*	MNI coordinates (x, y, z)	ACC region
Ullsperger and von Cramon (2001)	FA-CR	7, 8, 32	CMA
Kiehl et al. (2001)	FA-CR	4, 22, 40	Caudal
	FA-CR	−8, 45, 15	Rostral
	FA-0	4, 22, 40	Caudal
	FA-0	12, 36, 12	Rostral
Menon et al. (2001)	Error processing	10, 34, 22	Posterior caudal
Carter et al. (1998)	Conflict + error processing	4, 24, 48	Caudal

* FA, false alarm; CR, correct rejections; 0, implicit baseline.

2.5.4. fMRI/ERP correlation analysis

The major intent of this paper was to use the ERP to focus on the activations associated with conflict monitoring as reflected in N2 and those activations associated with error monitoring as reflected in ERN. Because the fMRI activations focus on contrasts between conditions, analogous contrasts were generated for the ERPs to provide parallel measures for correlating with the fMRI measures. Thus, in the correlational analyses below, ERN is expressed as the difference score between ERN (to false alarms) and CRN (to hits), and NoGo N2 is expressed as the difference score between NoGo N2 (to correct rejections) and Go N2 (to hits).

Because conflict almost always accompanies errors (Carter et al., 1998) and because age is associated with ERN amplitude (Mathalon et al., 2003), we isolated ERN variance that was unassociated with both age and NoGo N2 variance using multiple regression analysis. To do this, we regressed ERN scores (ERN at Cz–CRN at Cz) on both age and N2 scores (NoGo N2 at Cz–Go N2 at Cz) and saved the residuals. These residual ‘N2- and age-adjusted’ ERN scores reflected error-related neuroelectric activity that was independent of variation in age and conflict processing as indexed by the NoGo N2. Similarly, we regressed N2 scores on age and saved the residuals, resulting in adjusted N2 scores that indexed conflict-related neuroelectric activity independent of age. Two correlational analyses were performed using the simple regression option in SPM99: (1) ERN (N2- and age-adjusted) versus fMRI contrast (false alarms–hits); and (2) N2 (age-adjusted) versus fMRI contrast (correct rejections–hits).

3. Results

3.1. Behavioral performance

As can be seen in Table 2, subjects made a large number of false alarm errors, probably due to the strong pre-potent bias to respond to Go stimuli and the highly sensitive response device. Also, more errors were committed in the fMRI than ERP environment, probably due to the stress associated with the MRI environment.

Table 2
Number of trials

	Mean	S.D.	Min	Max
<i>False alarm errors to K</i>				
fMRI environment	21.8	10.4	8	30
ERP environment	17.4	7.8	5	27
<i>Hits to X</i>				
fMRI environment	285	4.6	273	288
ERP environment	265	15.4	239	285
<i>Correct rejections to K</i>				
fMRI environment	20.2	6.1	12	34
ERP environment	24.6	7.8	25	37

3.2. ERPs

As can be seen in Fig. 1, where response-synchronized ERPs to hits and false alarms are overlaid, false alarms elicited an ERN that peaked ≈ 125 ms post-response and was largest at Cz. In Fig. 2, stimulus-synchronized ERPs to correct rejections, false alarms and hits are overlaid, revealing a large NoGo N2 to correct rejections and an even larger N2/ERN complex to false alarms (referred to as ‘stimulus-synchronized ERN’) that was maximal at Cz. In two separate three-way (accuracy \times anterior – posterior scalp site \times lateral scalp site) repeated-measure ANOVAs, we compared (1) stimulus-synchronized NoGo N2 to response-synchronized ERN and (2) stimulus-synchronized NoGo N2 to stimulus-synchronized ERN. Results of these ANOVAs are presented in Table 3. Even with each averaged using its own best method (response-synchronized for ERN and stimulus-synchronized for N2), the ERN ($-6.5 \mu\text{V}$) is considerably larger than the NoGo N2 ($-2.4 \mu\text{V}$), perhaps due to the overlapping positivity of the large NoGo P300 attenuating the negativity of the NoGo N2. Comparison of N2 and ERN in both the response- and stimulus-synchronized averages revealed differences in scalp distribution along the A-P dimension (Table 3). Nevertheless, these two components measured at Cz are strongly correlated ($r = 0.86$, $P = 0.001$), indicating that subjects who produce a larger conflict-related NoGo N2 on correct rejection trials also produce larger response-locked ERNs on false alarm trials. The large stimulus-synchronized ERN on false alarm trials appears to contain both N2 and ERN components (see Fig. 2 at Fz for evidence of two distinct components that blur together at Cz) and is significantly correlated with the response-locked ERN ($r = 0.76$, $P < 0.02$) and the stimulus-locked NoGo N2 to correct rejections ($r = 0.89$, $P < 0.0006$). This suggests that the stimulus-synchronized ERN is a relatively noisy component due to sub-optimal stimulus-locked averaging of response-related activity. Indeed, when the NoGo N2 to correct rejections is regressed on both the stimulus- and response-synchronized ERNs in a multiple regression, a predictive relationship is observed for the ERN derived from the stimulus-locked ($P = 0.03$) averages, but less for the response-locked ($P = 0.07$). Thus, the stimulus-locked ERN/N2 complex is more tightly coupled to stimulus-locked NoGo N2 on correct rejection trials than it is to the response-locked ERN on false alarm trials.

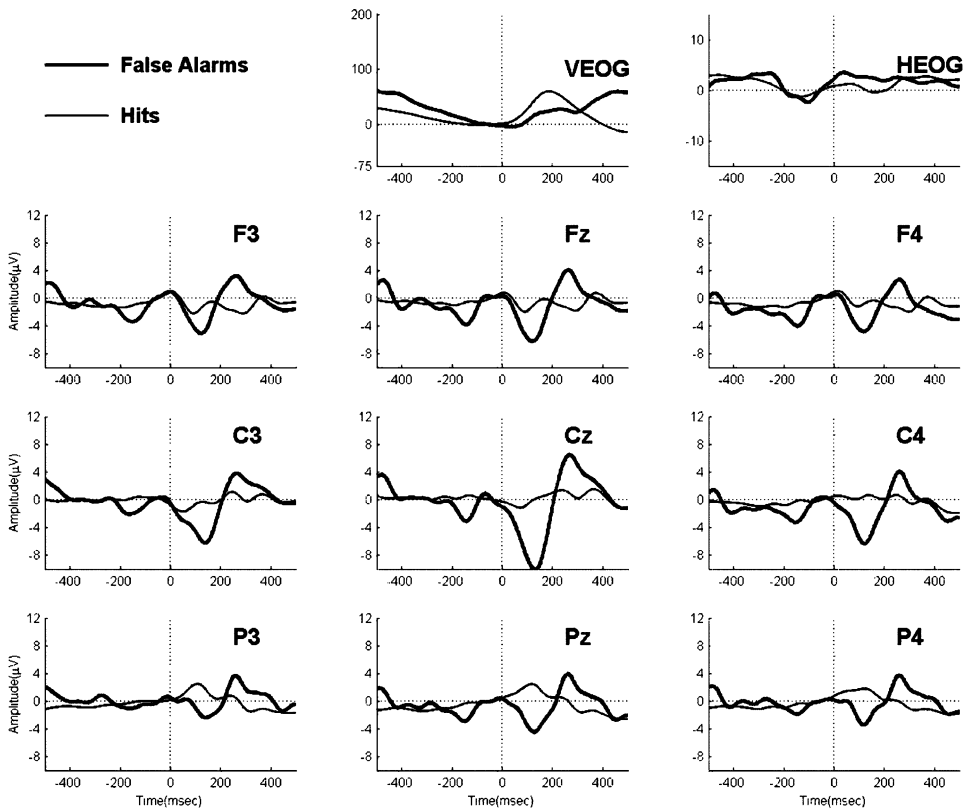


Fig. 1. Response-synchronized ERPs overlaid to false alarms and hits. Response occurred at 0 ms. Negative is plotted down.

The ERP difference scores (ERN-CRN versus NoGo N2-Go N2) are somewhat less highly correlated ($r = 0.69$, $P < 0.02$) than the single condition ERP components ($r = 0.86$, $P = 0.001$), with the correlation indicating that the ERN and NoGo N2 difference scores shared $\approx 50\%$ of their variance. In an effort to isolate error-specific physiological variance from conflict-related variance, we deprived the response-locked ERN difference score of the variance it shared with the NoGo N2 difference score using simple linear regression. As suggested above in the ANOVA results, the mean ERN difference score (mean = -10.40 , S.E. = 1.99) was significantly less than zero ($t(9) = -5.23$, $P < 0.0005$), indicating a significant effect of response accuracy (i.e., ERN < CRN). In order to determine whether this ERN-CRN difference score remained significantly less than zero after its regression on the NoGo N2 difference score, the intercept of the regression line was tested against zero. This intercept gives the estimated mean of the ERN difference score when the NoGo N2 difference score is equal to zero (i.e., when there is no ERP indication of response inhibition-related conflict). The ERN difference score intercept ($B_0 = -8.29$, S.E._{B0} = 1.71) was not as negative as the mean ERN difference score and its S.E. was

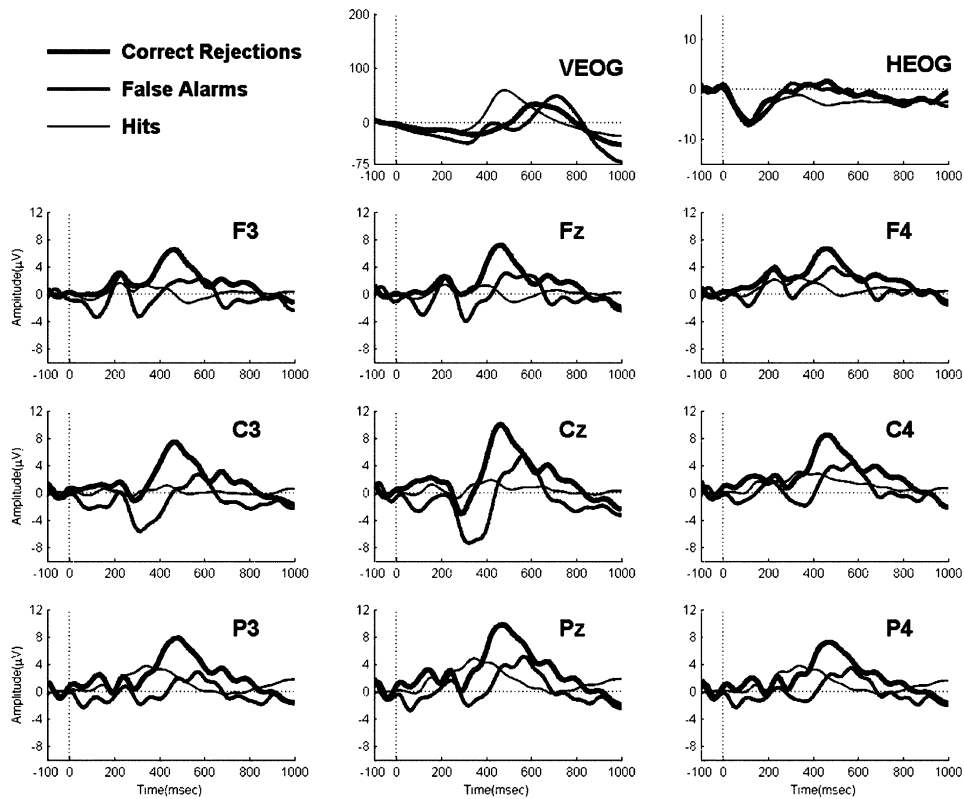


Fig. 2. Stimulus-synchronized ERPs overlaid to correction rejections, false alarms and hits. Stimulus occurred at 0 ms. Negative is plotted down.

smaller, indicating that accounting for its relationship with the NoGo N2 reduced the effect of response accuracy and also reduced its variance. Nonetheless, this intercept remained significantly less than zero ($t(9) = 4.85$, $P < 0.001$), indicating that a significant response accuracy effect persisted even when the conflict reflected by the NoGo N2 difference score was equal to zero. The residual ERN-CRN difference scores were further regressed on age to remove age-related variance. The adjusted ERN difference scores (adjusted for NoGo N2 and age) were subsequently used in correlational analyses.

3.3. fMRI

Many regions in the frontal and parietal lobes and in the ACC were more activated to correct rejections than hits (correct rejections–hits), particularly in the right hemisphere, reflecting a combination of response conflict, response inhibition and stimulus improbability (Fig. 3, $P < 0.001$, uncorrected; Table 4). As can be seen in Fig. 4 and Table 4, many regions were more activated to false alarms than hits (false alarms–hits), reflecting error detection, response conflict and all the sensory and cognitive processes listed above. However, the

Table 3
ANOVAs: ERN versus NoGo N2 amplitudes and latencies

Source	df	F-Value	p(G-G)*
<i>N2 amplitude (stimulus-synchronized) versus ERN amplitude (response-synchronized)</i>			
Accuracy	1,18	17.42	0.002
Anterior-posterior	2,18	8.31	0.004
Laterality	2,18	7.88	0.004
Accuracy*anterior-posterior	2,18	21.83	0.000
Accuracy*laterality	2,18	2.67	0.118
Anterior-posterior*laterality	4,36	6.17	0.007
Accuracy*anterior-posterior*laterality	4,36	2.14	0.162
<i>N2 amplitude (stimulus-synchronized) versus ERN amplitude (stimulus-synchronized)</i>			
Accuracy	1,18	5.38	0.046
Anterior-posterior	2,18	7.16	0.008
Laterality	2,18	5.73	0.014
Accuracy*anterior-posterior	2,18	3.00	0.093
Accuracy*laterality	2,18	4.13	0.066
Anterior-posterior*laterality	4,36	7.42	0.008
Accuracy*anterior-posterior*laterality	4,36	1.72	0.211
<i>N2 latency (stimulus-synchronized) versus ERN latency (stimulus-synchronized)</i>			
Accuracy	1,18	2.93	0.121
Anterior-posterior	2,18	4.93	0.033
Laterality	2,18	0.62	0.536
Accuracy*anterior-posterior	2,18	3.51	0.063
Accuracy*laterality	2,18	8.39	0.004
Anterior-posterior*laterality	4,36	1.05	0.376
Accuracy*anterior-posterior*laterality	4,36	0.88	0.464

* G-G, Greenhouse-Geisser correction for non-sphericity.

$P < 0.001$ (uncorrected) threshold used for the correct rejection–hits contrast revealed no significant activations for the false alarms–hits contrast; hence, we lowered the threshold to $P < 0.05$ (uncorrected). To visualize the differences in these activations, they are displayed in Figs. 3 and 4, but with different thresholds. The focussed analysis on ACC centroids implicated in prior studies showed ACC activations in the false alarms–hits contrast. The results of this analysis appear in Table 5.

Direct comparisons of false alarm errors with correct rejections (false alarms–correct rejections) revealed only a few brain regions (bilateral BA6, left BA5, BA30) to be more activated by errors than by correct rejections, possibly reflecting the large effort needed to inhibit responses on NoGo trials in this paradigm. In light of the much stronger widespread activations observed to successful response inhibitions relative to false alarms, direct comparisons were not particularly informative.

3.4. ERP versus fMRI

The major intent of this paper was to use ERP–fMRI correlations to focus the fMRI activations on those areas associated with conflict monitoring as reflected by the NoGo

Table 4
Brain regions in which activations are significant ($P < 0.05$, unc; extent = 6) for false alarms–hits and correct rejections–hits

Region	Correct rejections–hits		False alarms–hits	
	BA	<i>N</i>	BA	<i>N</i>
<i>(a) Left hemisphere</i>				
Inferior frontal gyrus	9, 13, 44, 45, 46, 47	106	13, 47	29
Medial frontal gyrus	6, 8, 9, 10, 11, 32	123	8	1
Middle frontal gyrus	6, 8, 9, 10, 11, 46, 47	56		
Superior frontal gyrus	6, 8, 9, 10	76		4
Paracentral gyrus	31	9		
Precentral gyrus	6, 9, 44	20		
Extra-nuclear	13, 47	10		
Anterior cingulate cortex	9, 24, 32, 42	62		2
Cingulate gyrus	24, 31, 32	48		1
Parahippocampus	AMYG, HC, 19, 27, 34	22		1
Uncus	AMYG	1		
Inferior occipital gyrus	17, 18, 19	12		
Middle occipital gyrus	18, 19, 37	23		
Superior occipital gyrus		1		
Lingual gyrus	18, 19	17		
Inferior parietal lobe	39, 40	30	40	12
Supramarginal gyrus	39, 40	27	40	5
Cuneus				
Precuneus	7	21		
Fusiform gyrus		26		
Sub-lobar			13	7
Inferior temporal gyrus	20, 21, 37	15		
Middle temporal gyrus	19, 21, 37, 38, 39	90		
Superior temporal gyrus	13, 222, 38, 39	97	22, 38	27
Sub-gyral	HC, 20	5		
Sub-callosal gyrus	34	1		
Lentiform nucleus (globus pallidus)		37		
Lentiform nucleus (putamen)		92		
Thalamus		40		
Caudate	Head, body	31		
Insula	13, 47	34		
Clastrum		21		
Brainstem	Midbrain, pons	43	Midbrain, pons	47
Cerebellum	Anterior	15	Anterior	7
	Posterior	29		
<i>(b) Right hemisphere</i>				
Inferior frontal gyrus	6, 9, 10, 13, 44, 45, 46, 47	152	13, 47	41
Medial frontal gyrus	6, 8, 9, 10, 11, 32	163	8	13
Middle frontal gyrus	6, 8, 9, 10, 12, 46, 47	205	11	1
Superior frontal gyrus	6, 8, 9, 10	132	6,8	6
Paracentral gyrus	5, 6, 31	10		

Table 4 (Continued)

Region	Correct rejections–hits		False alarms–hits	
	BA	<i>N</i>	BA	<i>N</i>
Precentral gyrus	6, 9, 44	75	44	2
Extra-nuclear	13, 47	11		
Anterior cingulate cortex	10, 24, 32, 42	74	32	3
Cingulate gyrus	23, 24, 31, 32	115	23, 32	13
Parahippocampus	AMYG, HC, 19, 27, 34, 35, 36, 37	34	27, 30	9
Uncus	AMYG, 28	3		
Middle occipital gyrus	18, 19, 37	14		
Inferior occipital gyrus	28, 29	7		
Superior occipital gyrus	19, 39	5		
Lingual gyrus	18, 19	13		2
Inferior parietal lobe	7, 39, 40	120	40	24
Superior parietal lobe	7, 40	47		
Supramarginal gyrus	40	19	40	4
Cuneus	7, 19	5		
Precuneus	7, 19, 31, 39	121		
Fusiform gyrus	20, 37	6		
Sub-lobar	HC, AMYG	9	13	4
Post-central gyrus	5, 40	7		
Angular gyrus	39	13		
Inferior temporal gyrus	20, 37	11		
Middle temporal gyrus	19, 21, 37, 39	65		1
Superior temporal gyrus	13, 22, 38, 39	88	22, 38	33
Sub-gyral	6, 8, 10, 39, 40	16		3
Sub-callosal gyrus	47	5		
Lentiform nucleus (globus pallidus)		34		
Lentiform nucleus (putamen)		90		
Thalamus		63		
Caudate	Head, body, tail	42		
Insula	13, 47	40	13	7
Clastrum		15		
Brainstem	Midbrain, pons	64	Midbrain, pons	30
Cerebellum	Anterior	77	Anterior	14
	Posterior	31		

Brain regions and Brodmann areas (BA) are given as described by Lancaster et al. (2000). Number of voxels (*N*) activated in each region is listed. Activations in fluid and white matter were excluded.

N2 (age-adjusted) and those uniquely associated with error monitoring as reflected by the ERN (age- and N2-adjusted). To the extent that these ERP components correlated with different regions of fMRI activity, we might infer that the processes they reflect are also different. In Fig. 4, we show in red the brain regions where the activations in the false alarms–hits contrast were significantly correlated with the adjusted ERN scores. This figure shows that subjects with larger ERNs had greater activations in both rostral and caudal regions of the ACC, with the caudal region extending substantially into BA 8 (Table 6). In Fig. 3, we show in green the brain regions where activations in the correct rejections–hits

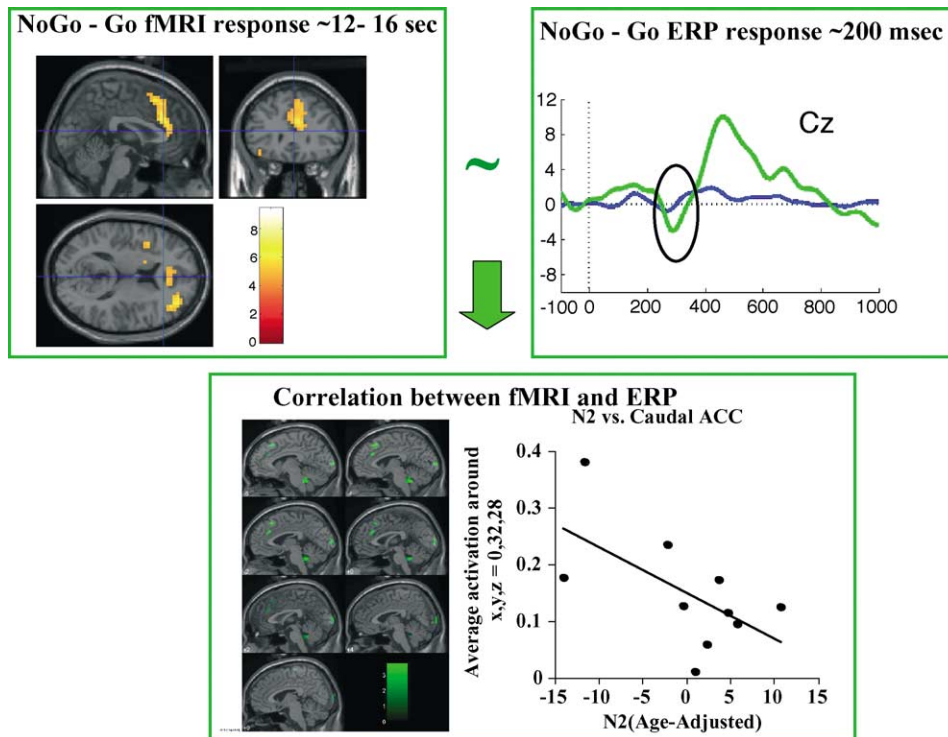


Fig. 3. fMRI, ERP and fMRI/ERP correlations for correct rejections (NoGo)–hits (Go) comparisons. Three-planar view for fMRI ($P < 0.001$, uncorrected) (upper left), ERPs overlaid correct rejections and hits from Cz (upper right), fMRI and ERP correlations ERP correlations ($P < 0.05$, uncorrected, extent 6) focussing on ACC (lower left), scatter plot showing that subjects with larger age-adjusted N2 scores have greater caudal ACC activation.

contrast were significantly correlated with the adjusted N2. This figure shows that subjects with larger N2s had greater activations in caudal ACC, including a more superior cluster extending into BA8. In Table 7, we show the results of the analysis focussed on specific ACC centroids from the literature. The ERN was significantly correlated with false alarm activations in voxels located in the vicinity of both the caudal and rostral ACC centroids, although the spatial extent of these local clusters of activation was somewhat larger in the rostral ACC (see Table 7 and Fig. 4). In contrast, the N2 was significantly correlated with correct rejection activations in voxels located in the vicinity of the caudal ACC centroids; only 2 voxels showed significant correlations in the vicinity of the rostral ACC centroid (Table 7), and these voxels failed to form a contiguous cluster in the rostral ACC exceeding our extent threshold of 6 voxels (Fig. 3). Thus, while significant clusters of correlations were observed in the caudal ACC/BA 8 for both the ERN and the N2, only the ERN showed a substantial cluster of correlations in the rostral ACC. In addition, it is noteworthy that the Carter et al. (1998) ACC/BA 8 centroid that was activated by both errors and conflict is associated with both ERN and N2.

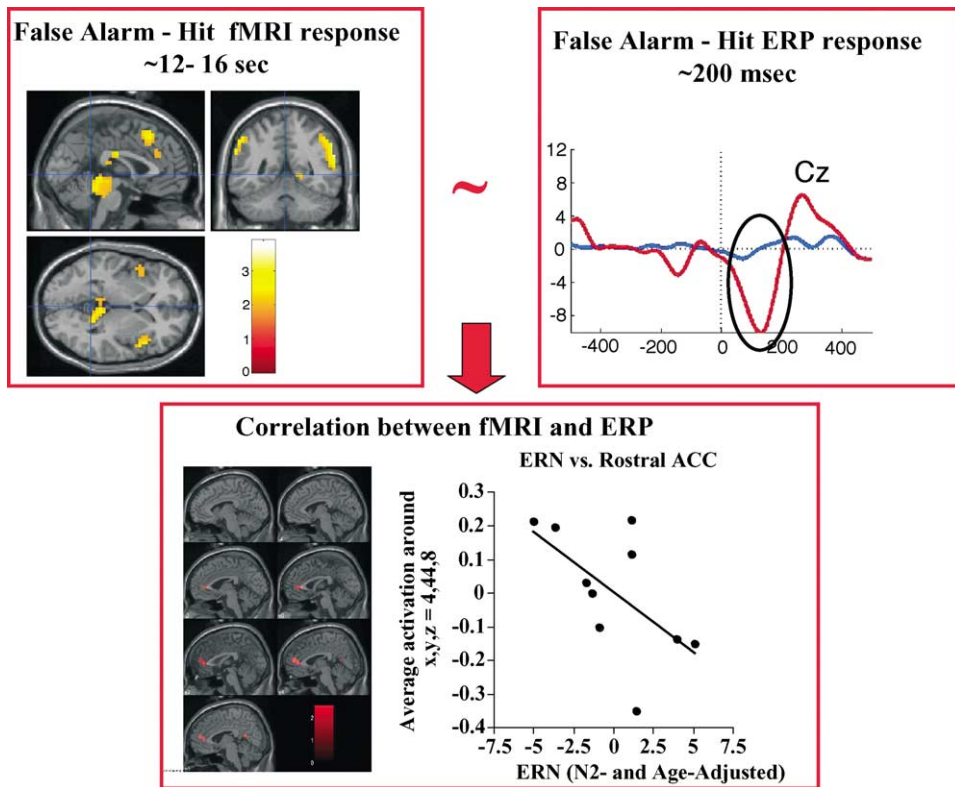


Fig. 4. fMRI, ERP and fMRI/ERP correlations for false alarms (NoGo)–hits (Go) comparisons. Three-planar view for fMRI ($P < 0.05$, uncorrected) (upper left), ERPs overlaid false alarms and hits from Cz (upper right), fMRI and ERP correlations ERP correlations ($P < 0.05$, uncorrected, extent 6) focussing on ACC (lower left), scatter plot showing that subjects with larger N2- and age-adjusted ERN scores have greater rostral ACC activation.

4. Discussion

4.1. ERP data

As expected, errors were associated with a large ERN, especially at Cz where it peaked 125 ms after the response. Also as expected, correct rejections were associated with a large N2 peaking ≈ 300 ms after the stimulus. Because correct rejections, by definition, have no motor response, response-synchronized averages could not be calculated. However, the scalp distributions of N2 measured from stimulus-synchronized averages were different from ERN measured from both response-synchronized and stimulus-synchronized averages. Although the practice of using scalp topography differences to infer differences in neural generators has recently been challenged (Urbach and Kutas, 2002), the different scalp distributions observed for ERN and N2 would traditionally be considered evidence for different neural sources that likely reflect different cognitive processes. This is con-

Table 5
Anterior cingulate cortex (ACC) centroid analyses of Correct Rejection and False Alarm fMRI contrasts*

	Correct Rejections - Hits				False Alarms - Hits			
	Activated Centroid			N	Activated Centroid			N
	x	y	z		x	y	z	
Kiehl et al. (2000)	8	28	28	226	4	20	52	58
Caudal ACC (4, 22, 49)	−4	28	32		0	32	28	
	12	20	52					
	12	12	40					
Kiehl et al. (2000)	4	36	20	244	0	36	24	1
Rostral ACC (−8, 45, 15)	−8	40	20					
	−12	52	28					
Ullsperger and von Cramon (2001)	8	28	28	174	4	24	44	25
Cingulate Motor Area (7, 18, 32)	−4	28	32		0	32	28	
	12	12	40					
Menon et al. (2001)	8	28	28	220	0	32	28	9
Posterior Caudal ACC (10, 34, 22)	24	44	28		4	36	24	
	12	48	28					
Carter et al. (1998)	12	16	52	233	8	20	56	70
Caudal ACC/BA 8 (4, 24, 481)	0	28	36					

* Montreal Neurological Institute (MNI) Coordinates.

sistent with the data presented by Falkenstein et al. (1999) who concluded that conflict monitoring reflected in N2 engages different processes from error monitoring reflected in ERN. However, it is not consistent with the dipole localization data presented by van Veen and Carter (2002a) nor with their suggestion that error monitoring and conflict monitoring are subserved by the same region of the ACC.

4.2. fMRI data

Although fMRI activations were greater during correct rejections than errors, similar regions were activated during both. Because of our a priori focus on ACC activation on error trials, we specifically interrogated ACC centroids published by Kiehl et al. (2000) using the same Go/NoGo task, by Carter et al. (1998) using a paradigm where errors were less immediately obvious to the subjects, by Ullsperger and von Cramon (2001) using a flankers task and by Menon et al. (2001) using a Go/NoGo task. In this way, we confirmed the involvement of rostral, caudal and motor ACC during both false alarms and correct rejections. Because ACC showed even greater activations during correct rejections, it was difficult to isolate error monitoring from conflict monitoring in the fMRI analysis.

4.3. ERP and fMRI correlations

In this paper, we present a new approach to distinguishing between error monitoring and conflict monitoring using a combination of ERP and fMRI data. The fMRI and ERP

Table 6
Brain regions in which activations ($P < 0.05$, unc) for an fMRI contrast are correlated with an ERP component contrast

Region	Conflict monitoring without age		Error monitoring without age and conflict monitoring	
	BA	<i>N</i>	BA	<i>N</i>
ERP contrast:	NoGoN2-GoN2 (age-adjusted)		ERN-CRN (N2- and age-adjusted)	
versus fMRI contrast:	Correct rejections–hits, $P < 0.05$, unc		False alarms–hits, $P < 0.05$ unc	
<i>Left hemisphere</i>				
Inferior frontal gyrus	10, 46	4		
Middle frontal gyrus	6, 9, 10, 46	12		
Superior frontal gyrus	6, 8, 10	9		
Pre-central gyrus	9	1		
Medial frontal gyrus	8	3		
Anterior cingulate	32	3		
Cingulate gyrus	32	1		
Middle occipital gyrus	18	1		
Cuneus	18	3		
Brainstem	Pons	1		
Cerebellum	Anterior	16		
<i>Right hemisphere</i>				
Middle frontal gyrus			10	4
Superior frontal gyrus	6	1		
Pre-central gyrus	4, 6	3		
Cingulate gyrus			32, 42	8
Posterior cingulate			23	3
Uncus	28	3		
Cuneus	18	3		
Middle temporal gyrus	21	9		
Superior temporal gyrus	13, 21, 22, 38	16		
Inferior parietal lobule	40	2		
Parahippocampus	18	1		
Brainstem	Pons	1		
Cerebellum	Anterior	2		

Brain regions and Brodmann areas (BA) are given as described by Lancaster et al. (2000). Number of voxels (*N*) activated in each region is listed. Activations in fluid and white matter were excluded.

data considered alone each suggest that false alarms and correct rejections engaged somewhat different cognitive processes and underlying neural circuits, in spite of considerable conceptual, neuroanatomical and neurophysiological overlap between error monitoring and conflict monitoring. This conclusion is underscored when ERP and fMRI data are correlated. This correlational analysis allowed us to focus narrowly on those brain activations associated with conflict monitoring reflected in N2, with error monitoring reflected in ERN, and especially those activations associated with error monitoring after the effects of conflict monitoring as reflected in N2 were removed.

Table 7

	Correct Rejections - Hits				False Alarms - Hits			
	Activated Centroid			N	Activated Centroid			N
	x	y	z		x	y	z	
Kiehl et al. (2000)	−4	24	48	9	12	32	48	2
Caudal ACC (4, 22, 49)	0	32	28	3				
Kiehl et al. (2000)	0	36	24	2	4	44	8	11
Rostral ACC (−8, 45, 15)								
Ullsperger and von Cramon (2001)	0	32	28	2				
Cingulate Motor Area (7, 18, 32)								
Menon et al. (2001)	0	32	28	4	8	44	12	1
Posterior Caudal ACC (10, 34, 22)								
Carter et al. (1998)	−4	24	48	9	12	36	48	6
Caudal ACC/BA 8 (4, 24, 481)	0	28	36					

4.3.1. ERN and fMRI correlations

ERN and NoGo N2 were highly correlated, suggesting a tight coupling between the brain's response to successful response inhibition and the brain's response to false alarm errors. Nonetheless, by regressing out the NoGo N2 difference score from the ERN difference score, we were able to isolate the residual ERN variance that was unrelated to the physiological response to conflict ($\approx 50\%$ of the ERN variance was unrelated to the NoGo N2 conflict response). This gave us a relatively 'pure' measure of the electrophysiological response to errors with which to probe the fMRI false alarm–hit contrasts. The resulting ERN-specific correlations implicated activity in both caudal ACC/BA 8 and rostral ACC, whereas the N2-specific correlations implicated activity in regions of caudal ACC/BA 8 but not rostral ACC. Thus, the rostral ACC activity during false alarm errors was uniquely associated with larger ERNs, consistent with the finding of Kiehl et al. (2000). Rostral ACC is a region of ACC sometimes associated with negative affect, perhaps related to the narcissistic blow associated with errors (Bush et al., 2000). The ERN was also associated with the caudal ACC/BA 8 region implicated in prior fMRI studies of error processing, but was not associated with other regions implicated in error processing including the DLPFC (Carter et al., 1998; Gehring and Knight, 2000; Mathalon et al., 2002) and the striatum (Falkenstein et al., 2001; Holroyd and Coles, 2002), perhaps due to the small sample size limiting our power to detect these relationships.

Involvement of ACC with error monitoring is consistent with dipole localization analyses (Dehaene et al., 1994; Miltner et al., 1997; Badgaiyan and Posner, 1998; Holroyd et al., 1998; Luu et al., 2000), as well as with a literature showing patients with ACC lesions to have reduced error awareness (Turken and Swick, 1999) and diminished or absent ERNs following errors (Stemmers et al., 2000).

It is important to comment on the apparent inconsistency in the data reported for the simple fMRI contrasts and the data reported for the correlations between the simple fMRI contrasts and the ERP amplitudes: While the activation map for the contrast of errors minus correct

hits indicated caudal ACC activity, the map of the correlations between this contrast and the ERN-CRN difference indicated that the strongest correlations were observed in the rostral ACC. We offer the following explanation for the caudal activation seen during simple error contrast: By their nature, errors include conflict associated with response-inhibition and conflict associated with making an error. The conflict associated with response inhibition may have contributed some caudal activation to the rostral activation we expected to see for errors. Our correlation procedure suppressed the caudal activation and enhanced the rostral activation through two separate effects. First, by isolating the ERN variance that was independent of the N2, we minimized the contribution of response-inhibition conflict from ERN. Second, by correlating this ‘conflict-free’ ERN with the error activations, we were able to ‘pull-out’ activations in rostral cingulate that were not apparent for the whole group of subjects, because not all subjects had rostral cingulate activation during errors-only subjects with large ERNs had strong rostral ACC activation. With this joint method, activations associated with errors moved from a more caudal focus (seen in the simple contrast maps) to a more rostral focus (seen in the correlation maps).

4.3.2. N2 and fMRI correlations

Subjects with larger N2s to correct rejections had greater caudal ACC/BA 8 and DLPFC activations, suggesting a role of both conflict and control (Carter et al., 1998) in the NoGo N2. Also, subjects with larger N2s had greater visual cortex activation, suggesting a positive role of visual processing in averting errors.

5. Conclusions

While these data are consistent with the literature and the theory surrounding error and conflict monitoring, we are aware that these relationships could be due, in part, to ‘third variables’. For example, it is possible that other variables such as age, head size, IQ, etc. might have contributed to the relationships we observed. While we attempted to remove the effects of age, other variables may continue to contribute. Also, it is important to note that we used a response device that resulted in the inclusion of partial errors, or errors that were not successfully ‘corrected in flight’.

Our fMRI and ERP data suggest that error and conflict monitoring are at least partially subserved by the same frontal neural circuitry, perhaps because errors are typically accompanied by conflict. When the shared variance between N2 and ERN was removed from the ERN, yielding a relatively ‘conflict-free’ measure of error monitoring, it was associated with false alarm related fMRI activity in both rostral ACC and caudal ACC/BA 8, as well as BA 10 and posterior cingulate. Previous studies have implicated rostral ACC (Braver et al, 2001; Kiehl et al, 2000), caudal ACC and/or BA 8 (Carter et al, 1998; Kiehl et al, 2000; Menon et al, 2001; Ullsperger and von Cramon, 2001), and BA 10 (Kiehl et al, 2000) in error processing. N2, however, was also associated with caudal ACC and BA 8 regions, as well as several executive control regions of the brain, such as DLPFC (MacDonald et al., 2000) and inferior parietal lobule (Garavan et al., 1999), consistent with the idea that error monitoring and conflict monitoring are subserved by some of the same medial frontal lobe regions but also engage some distinct neural circuitry. In particular, our ERP-fMRI corre-

lational analysis suggests that despite overlap between conflict and error processing, there are some brain regions including the rostral ACC that may be selectively engaged by error processing, independent of conflict processing. This method of correlating ERP amplitudes with fMRI activations across subjects allowed us to focus on the activations that were associated with the brief moment in time when the brain's neuroelectric response to errors was most evident. Whether this would be observed within a single subject on a trial-to-trial basis awaits improvements in simultaneous recording of fMRI and ERP methodology. Nevertheless, this analysis is an example of how we might start to combine ERP and fMRI data to distinguish between brain activations associated with complex and overlapping cognitive processes.

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