Introduction
Dysfunction of the ACC in several psychiatric diseases has been a common finding in the last several years. In schizophrenia, for example, ACC dysfunction has been described in functional imaging studies using several different paradigms like e.g. verbal fluency tasks (Dolan et al. 1995), Stroop conflict tasks (Yucel et al. 2002), error processing (Suggest referencing Carter et al., 2002 American Journal of Psychiatry paper here as well) (Laurens et al. 2003) or tone discrimination tasks (Holcomb et al., 2000). Evidence for an involvement of the ACC in the pathophysiology of schizophrenia also comes from ERP-studies (Mulert et al. 2001) or post-mortem anatomical studies (Benes 1999). Based on these findings, concepts have been developed to explain the role of the ACC in the pathophysiology of schizophrenia (Benes 2000; Tamminga et al. 2000).
In addition, altered ACC activations have been described in an increasing number of other psychiatric diseases with functional imaging: in depression (Mayberg et al. 1997), autism (Deb and Thompson 1998), posttraumatic stress disorder (Lanius et al. 2003) or obsessive compulsive disorder (Ursu et al. 2003). The findings of altered ACC activity in a number of different psychiatric diseases in different kinds of paradigms further underlines the need for a better understanding of ACC function and dysfunction.

ACC Dysfunction: Apathy And Negative Symptoms
One traditional approach to understanding the role of a particular cerebral structure is to carefully observe patients who have a circumscribed lesion. Patients with bilateral lesions of the ACC are often in an akinetic mute state. They are profoundly apathetic (Mega and Cohenour 1997; Mega
and Cummings 1997). Patients appear awake but they do not display emotions, showing complete indifference to their circumstances. The loss of spontaneous activity is associated with the involvement of the supplementary motor cortex and the cingulate motor area. If these regions are spared, motor activity is normal, but patients demonstrate the loss of motivation to engage in a task. Patients can be led by the examiner to engage in a task but will fail to self-generate sustained, directed attention. These patients lack cognitive motivation (Laplane et al. 1981). Interestingly, some patients recover from ACC infarction and describe the initial muteness as a “loss of will”: “Nothing mattered” (Damasio and Van Hoesen 1983).

In schizophrenia, symptoms can be described as “positive” or “negative” (Andreasen 1990). Positive symptoms are, for example, delusions or hallucinations. Negative symptoms include loss of interest or apathy. Interestingly, a correlation of ACC dysfunction and negative symptoms in schizophrenia has been described in a large study (n=39) of drug naïve patients (Ashton et al. 2000). In a different study, a lack of activation of the mesial frontal cortex (including parts of the cingulate gyrus) occurred only in patients with high scores for negative symptoms (Andreasen et al. 1992). In addition, reduced gray matter volume in patients with prominent negative symptoms has been found in the anterior cingulate and medial frontal gyri (Sigmundsson et al. 2001). Taken together, these findings suggest that a primary defect in the ACC of schizophrenic patients (including an altered cytoarchitecture and connectivity) might be associated with negative symptoms like apathy or loss of interest. Accordingly, in analogy to patients with large macroscopical lesions of the ACC, a diminished cognitive motivation might contribute to a low level of performance in schizophrenia in cognitive tasks.

Table 1. LORETA-activations of the HEI-group

<table>
<thead>
<tr>
<th>Time</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>p-value</th>
<th>localisation</th>
<th>Brodmann area</th>
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<tr>
<td>92-132 ms</td>
<td>-3</td>
<td>10</td>
<td>29</td>
<td>5.20*</td>
<td>ACC</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>-38</td>
<td>-67</td>
<td>50</td>
<td>4.99*</td>
<td>Gyrus parietalis superior</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>31</td>
<td>50</td>
<td>4.94*</td>
<td>Gyrus frontalis superior</td>
<td>8</td>
</tr>
</tbody>
</table>

Recent ERP Studies
In the last few years, we have described a double peak configuration of the N1-potential in auditory choice reaction tasks. Patients with schizophrenia show a reduced amplitude of the second peak (Mulert et al. 2001; Mulert 2002). Source localisation, both with LORETA or BESA (Gallinat et al. 2002; Mulert et al. 2001) has suggested a generator in the auditory cortex for the early peak (90-100 ms post-stimulus) and a generator in the ACC for the second peak (130-140 ms post-stimulus).
Errors, Conflicts, and the Brain

In the statistical comparison between patients with schizophrenia and healthy controls, patients showed a significant reduction of ACC activity. Patients with schizophrenia did show worse performance with significantly increased reaction times (mean: 615 ms versus 428 ms, p=0.001). However, a similar situation with reduced N1-amplitudes and diminished ACC activity was observed in the comparison of healthy subjects with long reaction times versus healthy subjects with short reaction times (Mulert et al. 2003a). Since it is known that motivation and effort are related to both reaction times and N1-amplitude (Wilkinson 1967), one could wonder whether differences in the motivation of the healthy volunteers might have influenced the results. In fact, using the same paradigm, we recently described a significant effect of the amount of effort exerted by subjects on their reaction times, N1 amplitudes and ACC activity (Mulert et al. 2003b). In this study, 35 healthy volunteers participated. Three runs of the task were performed: one with the instruction to stay relaxed during the task (relaxed condition, RC), one with the instruction to press the respective button as fast and as precisely as possible (effort condition, EC), and one control run with no action required at all (control condition, CC). The individual degree of spending effort or being relaxed during the task was registered with a questionnaire after each run. For all subjects, the auditory evoked N1 potentials were significantly different in the three runs, with highest amplitudes in the EC-run (9.72 µV) and lowest in the CC-run (8.40 µV). Subjects with especially high effort increase in the EC-run in comparison to the RC-run (HEI-group, n = 12) showed highest amplitudes (11.60 µV) during the EC-run. This group did also show shorter reaction times (mean 369 ms ±69 versus 415 ms ±70) than the subjects with low effort increase (LEI-group). In the LORETA-analysis, the HEI group showed significantly increased current source density in the ACC (t= 5.2; Talairach coordinates x, y, z: -3, 10, 29), in the superior parietal gyrus (t = 4.99; -38, -67, 50) and in the superior frontal gyrus (t = 4.99; 18, 31, 50), see Table 1.

Conclusion
Reduced performance in cognitive tasks like choice reaction paradigms can result from disturbed ACC function associated with reduced cognitive motivation. This is probably the case in schizophrenia: several lines of evidence, including post-mortem anatomical studies, suggest ACC disturbance in this disease. However, since different levels of cognitive motivation, associated with different activation levels of the ACC, also exist within the group of healthy subjects, it might well be possible that not every finding of reduced ACC activity in psychiatric patients is related to an underlying brain pathology. Therefore, an assessment of the effort level during the execution of a task might be desirable.

References
Errors can be dissociated from conflict: Implications for theories of performance monitoring

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Neuroimaging studies of cognition have indicated that the anterior cingulate cortex (ACC) is strongly activated in numerous executive control tasks, but neuropsychological studies can determine the conditions in which the ACC is essential for performance. An ongoing controversy in the performance monitoring literature is whether conflict detection and error monitoring can be viewed as unitary functions performed by the same region of the ACC, or whether these processes can be functionally and anatomically dissociated. To directly assess these alternatives, a patient with focal lesion of rostral to mid-dorsal ACC was compared to controls in an event-related potential (ERP) study designed to examine errors, conflicts, and task switches. The patient showed a reduction in the error-related negativity (ERN) component after incorrect responses, accompanied by lower error correction rates. Conversely, the stimulus-locked N2 component on correct conflict trials was enhanced. Thus, the ERN is functionally different from conflict-related neural activity reflected in the N2. These data support the emerging notion that error monitoring and conflict monitoring are dissociated within the ACC, with the more rostral, perigenual region related to affective evaluation of erroneous responses. Conflicts compromised performance only when rapid attentional switches between alternative stimulus dimensions were required, indicating a role in set-switching. The results provide further evidence for the existence of functional specialization in the ACC.
Introduction
The anterior cingulate cortex (ACC) has been proposed to be an essential part of the anterior attention system (Posner and Petersen, 1988). However, the precise functions of this structure are an ongoing matter of debate among researchers using event-related potential (ERP) and functional magnetic resonance imaging (fMRI) methodologies. Monitoring for errors in performance, and detecting conflict between competing response alternatives, have been proposed as two of its roles. A controversial issue is whether these processes can be viewed as unitary (Carter et al, 1998, 2000) or distinct (Falkenstein et al, 2000; Coles et al, 2001) functions of the ACC. Models postulating that error monitoring can be viewed as separate from conflict monitoring are based on ERP data. The error-related negativity (ERN) component is generated when subjects make errors in speeded reaction time tasks (Falkenstein et al, 1990; Gehring et al, 1993). The ERN is a measure of performance monitoring that seems to be independent of response conflict, since it is observed in very simple choice reaction time tasks (Falkenstein et al, 2000). On the other hand, the conflict monitoring hypothesis suggests that the primary function of the ACC is to detect response conflict, based on positron emission tomography (PET) and fMRI results during tasks such as divided attention (Corbetta et al, 1991), flanker interference (Botvinick et al, 1999), and the color-word Stroop (Pardo et al, 1990; Carter et al, 2000; Milham et al, 2002). Furthermore, a dorsal region of the ACC showed increases in activity during error trials as well as correct trials with high levels of conflict (Carter et al, 1998). Since errors are more likely to occur when competing response tendencies must be resolved, they are considered to be a subset of conflict monitoring processes in this model.

Yet, detection of errors and conflicts does not tell the entire story of ACC function. Neuroanatomical and physiological studies in primates have revealed a high degree of topographic specialization, with subdivisions involved in visceromotor and skeletomotor control, vocalization, and pain, as well as attention (Devinsky et al, 1995). The rostral/ventral division has been linked to autonomic function and emotion, and the more dorsal/caudal region has been associated with cognition and higher-order motor control (Bush et al, 2000; Paus, 2001). Involvement of the ACC in arousal and affect is not a new idea. In 1937, the “limbic lobe” was proposed to be the anatomical basis of emotions, and the cingulate cortex was included in the “circuit of Papez” (Papez, 1937). Some researchers propose this as a major function, with only minor contributions to task-specific cognitive processing (Paus, 2001). Hence, hemodynamic changes during cognitive experiments may be due to task difficulty (Paus et al, 1998) and associated increases in anticipation (Murtha et al, 1996) and anxiety (Benkelfat et al, 1995). The peaks of activation in these articles are located within the cognitive subdivision of the ACC.

A recent experiment suggested that visceromotor control functions might not be confined to ventral ACC regions in humans. Activity in the dorsal ACC was sensitive to sympathetic modulation of heart rate, independent of cognitive and motor-related activity (Critchley et al, 2003). In addition, patients with ACC lesions showed diminished autonomic arousal to mental stress compared to controls. These authors concluded that the ACC is involved in modulation of bodily arousal states in response to current context, but this effect may be mediated through projections to ventral ACC area 25 (Devinsky et al, 1995).

Therefore, this report adopts the view that ascribing a single function to the ACC is an untenable position. Motor control, affect, autonomic function, and higher cognitive functions including error and conflict processing can all be considered part of the ACC’s repertoire. Some of these processes have overlapping representations within the ACC, and some of these processes can be dissociated (see also Ullsperger and von Cramon, 2001). The goal of the present study is to assess whether error monitoring and conflict monitoring can be dissociated in a patient with a unilateral lesion restricted to the dorsal ACC (Swick and Turken, 2002). The rostral extent of lesion encroaches into the ACC area implicated in error detection by fMRI results (Kiehl et al, 2000; Menon et al, 2001).
Three major questions were posed by the current experiments. First, we asked whether the ERN and subsequent compensatory behaviors are impaired in R.N. Second, we examined if the N2 component related to the detection of competing response tendencies is diminished, as predicted by the conflict monitoring hypothesis (Carter et al, 2000). If not, this would suggest that ACC activations observed in Stroop-like tasks do not reflect activity that is strictly time-locked to conflict detection processes. Finally, we investigated mental flexibility, as indexed by the ability to switch successfully between stimulus dimensions. Overall performance in the condition where the attended dimension remained constant throughout a block was compared to the condition where switches were needed randomly on a trial-by-trial basis. Further, we examined whether R.N. would show large costs in terms of longer RTs, lower accuracy, and altered ERPs on trials that require switching vs. those that repeat the same attended stimulus. If so, this would suggest that the ACC is critical for switching attention between relevant stimulus dimensions, which is another executive control function.

Materials and Methods
Participants
Patient R.N. (age 69, 14 yrs education) has a unilateral lesion extending from left rostral ACC (around the genu of the corpus callosum) to mid-ACC (Figure 1). He presented at the Neurology Clinic with a complaint of headaches, but no alteration in cognitive status. An MRI was recommended, and a chronic lesion was apparent. The dorsal extent of R.N.’s lesion is in paralimbic ACC, which is above the cingulate sulcus and includes area 32 (Paus et al, 1998). The rostral (perigenual) extent of the damage is considered supracallosal (Z>2) limbic ACC. The posterior motor areas (Y<10) are spared. The lesion was presumably due to occlusion of the pericallosal branch of the anterior cerebral artery. The date of the infarct is unknown, since neither R.N. nor his wife noted any behavioral changes suggesting the occurrence of a stroke. Eight controls (mean age 67.0 yrs, 14.9 yrs education) were tested for comparison to R.N. All participants were free from significant medical complications, substance abuse, psychiatric disturbances, and dementia. All subjects signed informed consent statements approved by the Institutional Review Boards of the Martinez VA and UC Davis.

Figure 1.
MRI scans from Patient R.N. Left - Horizontal section illustrating the lesion in the left ACC (black arrowhead). Right - Coronal section with ACC damage. The larger arrowhead shows the damage in the cingulate sulcus, while the smaller arrowhead above it indicates the lesion in the paracingulate sulcus.

Stimuli and Behavioral Tasks
Exp. 1 (Blocked): Stimulus displays consisted of a word and an arrow located above and below the center of the screen. The arrow pointed either to the left or right, and the word was either “LEFT” or “RIGHT.” The positions of the word and arrow were varied randomly from trial to trial. The stimuli were preceded by a fixation cross presented for 500 msec, followed by a delay period of either 500 or 750 msec. The stimulus remained on the screen until a response was given, and the next trial started 1300-1700 msec later. Either manual or vocal responses were required in separate blocks; only the manual responses will be reported here. There were two manual conditions with different instructions: (1) Arrow: press the left or right button corresponding to the direction of the
Errors, Conflicts, and the Brain

arrow, ignoring the word; (2) Word: press the button indicated by the word, ignoring the arrow. In all conditions, the word and arrow stimuli could be congruent or incongruent, with equal numbers of each randomly intermixed. Two blocks (48 trials each) of each condition were administered in random order.

Exp. 2 (Cued): The stimulus displays and response instructions were the same as in Exp. 1. What differed was that each trial started with a cue word (“arrow” or “word”) presented in the center of the screen for 350 msec, followed by the stimulus 1500 msec later. The cue indicated which of the two stimuli was the relevant, to-be-attended dimension. The cue varied randomly from trial to trial, and stimulus displays (presented for 350 msec) could be congruent or incongruent (50% probability for each). Subjects were told to respond as fast as possible without making an excessive number of errors. They were also encouraged to quickly correct themselves after making an error. The interval from stimulus onset to the beginning of the next trial was 3125 msec (SOA from onset of stimulus display to onset of next trial cue). Subjects were given a maximum time interval of 2000 msec for their first response, and error corrections were allowed at any time before the end of the trial. There were a total of 12 blocks of each with 64 trials.

ERP Recording and Analysis

During Exp. 2, EEG was recorded using an Electro-Cap with 48 tin electrodes. Forty-four scalp channels, 2 EOG electrodes, and the right mastoid were referenced to the left mastoid. The EEG was amplified (x50,000), filtered (0.1-80 Hz), and continuously digitized at a 256 Hz sampling rate. Twenty-nine channels were selected for further analysis. Data were re-referenced to the average of the mastoids off-line and digitally low-pass filtered (20 Hz). Trials containing eye movement, excessive peak-to-peak deflections, or amplifier blocking were automatically rejected. Trials with blinks were corrected with an adaptive filtering algorithm (Dale, 1994). Stimulus-locked and response-locked averages were computed for individual subjects; group averages were computed for controls and compared to R.N. A digital filter of 2-10 Hz was also applied to the response-locked averages to isolate the ERN from temporally overlapping slow positive potentials (Luu and Tucker, 2001). ERPs were quantified by computing peak amplitudes or mean amplitudes in defined latency windows relative to a 100 msec pre-stimulus baseline (-100 to 0 msec) or a 200 msec pre-response baseline (-400 to -200 msec). The data were statistically evaluated with repeated measures ANOVAs, using Greenhouse-Geisser corrections for multiple comparisons. Data from R.N. were compared to the range for his age-matched control group, and values falling outside the 95% confidence interval were considered significantly different from controls.

Results

Blocked Condition: Behavioral Performance

Behavioral data are illustrated in Table 1. For RT, there was a significant main effect of congruity \([F(1.6)=14.25, p<.01]\), and a congruity X stimulus interaction \([F(1.6)=8.18, p<.03]\). The conflict effect was larger in the attend word than the attend arrow condition. Since Patient R.N. (442 msec) was significantly faster than controls (531 msec; \(p<.01\)), interference was also expressed as a percentage \((\text{incongruous RT} - \text{congruous RT})/\text{congruous RT} \times 100\). Overall, R.N. showed significantly smaller interference effects than controls (7.4% vs. 3.8% for R.N, \(p<.05\)). R.N.’s error rates were well-matched to those of controls.

Cued Condition: Behavioral Performance

There was a main effect of congruity \([F(1.7)=81.10, p<.0001]\), and the congruity X stimulus interaction approached significance \([F(1.7)=5.01, p=.06]\). R.N. performed as well as controls for congruent stimuli, but his RTs for incongruent stimuli were slower. R.N. showed excessive interference effects for both the word and arrow conditions, in contrast to his above average performance in the blocked version of the Stroop. Likewise, he showed a higher error rate than controls for incongruent trials in the attend arrow condition (\(p<.01\)).
9 Pathology of Performance Monitoring

Table 1. Mean RTs (msec) and error rates (%) for congruent (Con) and incongruent (Incon) stimuli, and the interference effect (%Int), for patient R.N. and his age-matched control group for the blocked and cued conditions of word-arrow Stroop task. Note: ** = above the upper 99% confidence interval for controls.

<table>
<thead>
<tr>
<th></th>
<th>Attend Arrow</th>
<th></th>
<th>Attend Word</th>
<th></th>
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</thead>
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<td></td>
<td>Con</td>
<td>Incon</td>
<td>%Int</td>
<td>Con</td>
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<tr>
<td>mean RTs</td>
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<td></td>
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<tr>
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<td>512</td>
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<tr>
<td>R.N.</td>
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<td>449</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
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<td>CUED</td>
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<td></td>
</tr>
<tr>
<td>mean RTs</td>
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<td></td>
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<td>Controls</td>
<td>467</td>
<td>507</td>
<td>8.1</td>
<td>476</td>
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<td>R.N.</td>
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<td>489</td>
<td>7.4</td>
<td>452</td>
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<td>no switch</td>
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<tr>
<td>Controls</td>
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<td>489</td>
<td>7.4</td>
<td>452</td>
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<tr>
<td>R.N.</td>
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<tr>
<td>switch</td>
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<tr>
<td>Controls</td>
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<tr>
<td>R.N.</td>
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<td>19.5**</td>
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<td>Errors</td>
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</tr>
<tr>
<td>Controls</td>
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<td>8.6</td>
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<tr>
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<td>17.7**</td>
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<td>7.2</td>
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<td>11.0**</td>
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<td>Controls</td>
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<td>23.2**</td>
<td></td>
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</table>

The main effect of switching was significant \(F(1,7)=21.78, \ p<.003\), with faster responses on no switch trials (479 msec) than on switch trials (520 msec). For accuracy, the interaction between switching and congruity \(F(1,7)=10.59, \ p<.02\) reflected more errors on incongruent trials in the switch (12.4%) vs. the no switch condition (9.8%). R.N. exhibited exaggerated switching costs relative to controls, which were evident as disproportionate increases for RTs in the incongruent attend word condition and for errors in the incongruent attend arrow condition. Switching costs (switch RTs - no switch RTs) for R.N. and controls were comparable in the attend arrow conditions but not the attend word incongruent condition (controls: 40 msec, R.N.: 94 msec; \(p<.01\)). A similar difference measure was calculated for errors (switch % errors - no switch % errors). R.N. showed exaggerated switching costs in the incongruent attend arrow condition (controls: 1.5%, R.N.: 12.2%; \(p<.01\)).

For measures of compensatory behavior, R.N. showed post-error slowing comparable to controls. Likewise, he did not show an elevated percentage of erroneous corrections ("corrections" of correct responses). However, he was impaired (\(p<.05\)) at correcting his errors (77.9% vs. 88.0% in controls).

Cued Condition: ERPs

The ERN peaked at 65 msec in the controls’ response-locked ERPs (Figure 2A). A negative component was also observed on correct trials, the "correct-related negativity” or CRN (Ford, 1999). ERN peak amplitude was measured at 6 midline electrodes (Fz, FCz, Cz, CPz, Pz, POz) in the 20-125 msec post-response interval. The mean ERN measured at these sites (-3.8 µV) was significantly greater than the CRN (-1.8 µV), \(F(1,7)=16.46, \ p<.005\). Conversely, R.N. did not show a difference in amplitude between correct and error trials (-1.4 µV for both). This relationship
also held for measurements at individual electrodes (ERN/CRN at FCz: -3.1/-3.8 for R.N., -5.5/-3.3 for controls; at Cz: -3.3/-3.7 for R.N., -4.9/-2.7 for controls).

The effects of interference were evident as an N2-type component peaking at 450 msec in the stimulus-locked waves (Figure 2B). The N2 for incongruent stimuli was less positive than for congruent from 350-500 msec \([F(1,7)=117.67, p<.0001]\). R.N. showed a delay in N2 latency (524 vs. 449 msec) and an increase in its amplitude, as measured in the difference waves (incongruent – congruent). However, N2 onset was identical in controls and R.N. in the attend word condition (~350 msec), suggesting that R.N.’s brain detected the conflict at the same time as controls, but engaged in prolonged evaluation and conflict resolution processes.

The effects of switching between attended stimulus dimensions were evaluated by measuring mean amplitudes in 100 msec windows in the stimulus-locked waves. No switch trials yielded larger positive potentials than switch trials between 300-500 msec in controls. There were no interactive effects of stimulus type or congruity. R.N. showed protracted effects of switching that extended until 800 msec at the frontal electrode sites, clearly visible in the subtraction waveforms (Figure 3). R.N. showed significantly more negative-going difference waves than controls from 500 to 800 msec (\(p<.01\)).

### Discussion

A dissociation between error monitoring and conflict monitoring processes was observed in a patient with focal damage in the dorsal ACC, with the rostral-most extent in the affective subdivision. Patient R.N. showed above average performance in a Stroop-like task when the attended stimulus dimension was blocked. In contrast, he exhibited impairments when the attended dimension was cued on a trial-to-trial basis. He also showed a deficit in correcting erroneous responses and a reduction in the amplitude of the ERN. Conversely, the N2 to correct incongruent stimuli was enhanced, suggesting that the dorsal ACC does not generate this component. Below we discuss the hypothesized roles of the ACC in three executive control functions.
Error Monitoring
The ACC has been implicated as a critical generator of the ERN. In the patient, ERN and CRN amplitude were indistinguishable. If these two components arise from the exact same neural source, the ACC could be viewed as a modulator of the ERN but not as the primary generator. In this view, the ERN generator can no longer distinguish between correct responses and errors due to lack of input from the ACC. Another interpretation draws on the notion that ERN and CRN are related, but not identical (Ford, 1999; Falkenstein et al, 2001). Here, CRN is thought to signal the outcome of a general, response-related monitoring process, and ERN reflects this generic monitoring process plus error-specific activity. Thus, ACC damage eliminated the error-specific activity but spared the general monitoring process in R.N. Some neuroimaging groups (Kiehl et al, 2000; Menon et al, 2001) have reported error-related activity in the ACC that is rostral to the cognitive subdivision, and the ERN has been associated with negative affective responses (Luu et al, 2000). If R.N. showed a dampened affective response to errors, his motivation to self-correct could have been reduced.

Conflict Monitoring
R.N. performed better than controls in the blocked version of the task, as he was significantly faster, more accurate, and less affected by conflicting information. One interpretation of this finding is that he did not notice any inconsistencies in the stimulus displays, implying that he is impaired in conflict monitoring. However, our explanation is that R.N. showed superior focused attention in this task relative to controls. Although the attended dimension was known in advance, the position of the word and arrow were unpredictable from trial to trial, so subjects had to attend to the correct stimulus on incongruent trials. Thus, the left dorsal ACC was not essential for response selection mechanisms or for conflict monitoring functions. In contrast, R.N. was quite impaired when the attended stimulus dimension was cued on each trial, requiring rapid, unpredictable switches of attention.

An N2-type component was observed on correct incongruent trials. The N2 was not only intact following dorsal ACC lesion but was, in fact, enhanced. Of critical importance is the dissociation between error and conflict: ERN amplitude was reduced but N2 was increased. One explanation could be an impairment in engaging the control processes that reduce the effects of response conflict. This observation, combined with his exaggerated behavioral interference effects, suggest a deficit in the recruitment of inhibitory processes under difficult task conditions. We hypothesize that intact regions in lateral prefrontal cortex (PFC) are able to detect response conflict, but damage to the dorsal ACC renders him impaired in response inhibition, which may be due to disconnection from cingulate and supplementary motor areas (SMA). Our findings are consistent with the proposal that the PFC detects incompatible response options on incongruent trials and signals conflict resolution processes, perhaps in caudal ACC and SMA.

![Figure 4](image-url)
Errors, Conflicts, and the Brain

However, Yeung (2003) proposed that a lesion-induced reduction in attentional capacity can account for the ERN/N2 dissociation if one assumes faulty, but residual, ACC function. R.N.’s left hemisphere is damaged, but his right ACC is intact. Another criticism of the results recognizes the limitations of generalizing from a single-case study to a major theory of performance monitoring. Further study with a larger number of patients is certainly desirable. On this note, Figure 4 shows preliminary data from another patient with damage in the right caudal ACC (lesion described in Turken and Swick, 1999). In contrast to R.N., Patient D.L. shows a diminution of both ERN and N2 relative to her younger age-matched control group. This is supportive of the view that these processes do overlap to some extent, but are not entirely co-localized within the ACC (Ullsperger and von Cramon, 2001).

Attentional Switching

Relative to controls, R.N. showed significantly elevated interference effects and lower accuracy in the switching Stroop task, unlike his stellar performance in the blocked version. This pattern of results suggests that dorsal ACC plays a role in inhibition of the inappropriate response under conditions that require switching between attended stimulus dimensions. Additionally, R.N. exhibited exaggerated costs for RT and accuracy on switch relative to no switch trials. He also showed a prolonged ERP effect on switch trials, lasting until 800 msec post-stimulus, compared to only 400 msec post-stimulus in controls. Although R.N. can execute the attend word/attend arrow tasks themselves, he cannot easily shift between the two tasks. Advance configuration of task set involves activation of an appropriate schema (Norman and Shallice, 1986) or of a task demand node (Cohen et al, 1990), both of which can be seen as top-down control functions. Thus, dorsal ACC does not appear to be necessary for conflict monitoring per se, but it is important for unpredictable switches of attention when the task involves response conflict. These results complement an fMRI study in which a reverse Stroop effect was induced by rapid switches between color naming and word reading tasks (Ruff et al, 2001). Other imaging experiments have reported switching-related activations which overlap with the dorsal ACC region damaged in R.N. (Dove et al, 2000; Kimberg et al, 2000).

A related explanation for R.N.’s discrepant performance in the blocked and cued Stroop is the idea that the ACC responds to increased levels of arousal during more cognitively demanding tasks and is recruited under conditions of greater task difficulty (Paus et al, 1998, 2001). This hypothesis can also encompass R.N.’s prior results. In three different versions of the Stroop color-word task, R.N. showed consistently lower accuracy on incongruent trials, indicating a deficit in inhibiting the pre-potent word reading response (Swick and Jovanovic, 2002). In the color-word Stroop, the irrelevant word reading response is much more automatic than the arrow button press response in the current experiment.

Implications for Theories of Performance Monitoring

In light of the evidence for topographic specificity, the precise location of a particular hemodynamic response or ERP dipole solution within the ACC is an important issue to consider. For example, an ERN dipole in subgenual ACC is not likely to reflect the same processes as a dipole that borders on the pre-SMA. In agreement with others (Falkenstein et al., 2001; Luu et al, 2003), we suggest that the ERN and the CRN are not identical, and that ERN is comprised of signals from two distinct generators: one from rostral ACC that is specific to errors, and another in caudal ACC that may support more general response monitoring functions. Likewise, R.N.’s data demonstrate that ERN and N2 have dissociable generators. However, there is probably some degree of overlap, given that damage to caudal ACC resulted in the reduction of both components. Finally, as others have shown, ERN does not appear to be closely related to corrective behavior under some conditions. Furthermore, behavioral measures of performance adjustment (e.g., error correction, post-error slowing) do not seem to be closely related. The cognitive, motor, and
affective processes that comprise the performance monitoring system are quite complex and worthy of further study.

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Errors, Conflicts, and the Brain

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