Focusing on the Anterior Cingulate Cortex

Effects of Focal Lesions on Cognitive Performance

Diane Swick and And U. Turken

Attentional control over behavior is important for flexible and adaptive responding in a complex environment. Automatic, habitual responses are inadequate during situations in which multiple goals and sources of information must be maintained simultaneously, such as during planning and decision making, the avoidance and correction of erroneous responses, novel responding, and the resolution of conflict. These executive control functions, as assessed by neuropsychological tests, are often compromised in individuals with injuries in the frontal lobes (Stuss & Alexander, 2000). The lateral prefrontal cortex (PFC) is thought to play a critical role in executive control processes by exerting top-down influences over other brain regions involved in sensory and motor processing (Miller & Cohen, 2001).

In addition, neuroimaging investigations have highlighted the importance of the anterior cingulate cortex (ACC). Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) experiments have detected enhanced neural activity in the ACC during the performance of tasks that demand high levels of attentional control (Bush, Luu, & Posner, 2000). The ACC is densely interconnected with other frontal lobe regions, especially the mid-dorsolateral PFC, as well as parietal and motor cortices (Bates & Goldman-Rakic, 1993; Dum & Strick, 1993; Vogt & Pandya, 1987). Meta-analyses of multiple neuroimaging studies have shown that ACC and lateral PFC are coactive in demanding task conditions (Duncan & Owen, 2000; Koski & Paus, 2000). These observations have prompted the suggestion that the ACC is a key component of the neural mechanisms that mediate executive control over thought and behavior (Posner, 1994; Posner & Petersen, 1990). Anatomical and physiological abnormalities in the ACC have been observed in disorders ranging from schizophrenia and Parkinson's disease to clinical depression and obsessive-compulsive disorder. Theoretical accounts of the symptoms in these conditions all indicate a critical role for the ACC in brain function (Benes, 2000; Frith, 1992; Mayberg, 1997), which has yet to be elucidated in a specific manner.

Studying the effects of neurological damage is a powerful method of investigating brain function in humans. By detailing the abilities that are spared and compromised after focal injury to a specific brain area, conclusions can be reached about the role of that region. Fur-
ther, the functional significance of results from neuroimaging studies can be tested directly in neuropsychological experiments. There have been relatively few reports of focal ACC lesions (e.g., Cohen et al., 1999; Corkin, Twitchell, & Sullivan, 1979; Danckert et al., 2000; Janer & Pardo, 1991; Ochsner et al., 2001), due to the rare occurrence of isolated lesions to this region. Most studies have tested patients who underwent cingulotomy, a psychosurgical procedure occasionally performed on individuals with psychiatric disorders or chronic pain. The occurrence of preexisting, severe, and intractable psychiatric illnesses complicates the interpretation of results in these individuals.

We have tested two patients with focal ACC lesions in a series of experimental tasks designed to assess high-level attentional control over perceptual, cognitive, and motor processes, in the sense originally defined by Norman and Shallice (1986). Our objectives were to investigate the nature of ACC involvement in the control of attention, and to test the validity of conclusions drawn from neuroimaging findings. Patient R.N., a 69-year-old righthanded male, has a left-hemisphere lesion extending from rostral ACC (around the genu of the corpus callosum) to mid-ACC (Figure 29.1A, 29.1B) due to occlusion of the pericallosal

**FIGURE 29.1.** MRI scans showing the lesions of patient R.N. (A, B) and patient D.L. (C, D). (A) Horizontal section illustrating the lesion in left ACC (black arrowhead). (B) 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. (C) Horizontal section at the level of the cingulate sulcus. The damaged area in the right hemisphere is indicated by a white arrowhead on the left side of the scan. (D) Coronal section of caudal ACC illustrating the lesion in the cingulate sulcus, while the paracingulate sulcus is intact.
branch of the anterior cerebral artery. Patient D.L. is a 35-year-old right-handed female who had a tumor resected from the right ACC. The resulting lesion extends from the mid- to caudal portion of the ACC (Figure 29.1C, 29.1D). Many foci of activation from neuroimaging studies are located within R.N.'s or D.L.'s lesions (Figure 29.2). Behavioral testing in these patients can be informative about the necessity of the ACC for particular executive control functions, and event-related potential (ERP) recordings can enrich our understanding of the temporal parameters underlying any attentional deficits that might be observed. Scalp-recorded ERPs have excellent temporal resolution, but their spatial resolution is relatively poor. However, the plausible neural generators for a given ERP component can be constrained if it is absent or altered in patients with focal brain lesions (Swick & Knight, 1998). Such an approach can also speak to the question whether the contribution of ACC to attentional control occurs only in later stages of performance or if it extends to the sensory domain as well.

Specifically, we sought to investigate whether an intact ACC is necessary to carry out individual cognitive control functions such as conflict detection, error monitoring, response selection, and/or task switching, or whether the ACC subserves a more general control function that can be defined as “responsiveness to task difficulty.” In addition, we used the divergence in lesion location in the two patients to test whether anatomical specificity of func-
tion can be demonstrated. If the ACC is a nodal point for the large-scale attentional networks in the frontal lobes, then focal ACC damage should result in performance deficits in multiple task domains. If the ACC contributes to some aspects of performance but not others, such dissociations would favor the view of multiple interactive processes, rather than a single control module. Also, such findings would support the notion that the ACC is a functionally heterogeneous structure (Paus, 2001) and is not likely to be the sole locus for executive control mechanisms. The functions under study here include the detection of conflict between competing response alternatives, monitoring for errors in performance, flexible adjustment of performance strategy, and switching attention between stimulus dimensions, all of which are important measures of attentional control. The chapter addresses a series of ongoing controversies in the functional neuroimaging literature over the interpretation of hemodynamic changes that occur within the ACC during the performance of specific cognitive and motor tasks.

CONFLICTS OR ERRORS?

One enduring debate about the role of the ACC in attentional control is whether conflict monitoring and error monitoring can be viewed as unitary (Carter et al., 1998, 2000) or distinct (Coles, Scheffers, & Holroyd, 2001; Falkenstein, Hoormann, Christ, & Hohnsbein, 2000) functions of the ACC. Models postulating that error monitoring can be viewed as separate from conflict monitoring are based on ERP data, although recent fMRI results have lent support to this stance as well (Braver, Barch, Gray, Molfese, & Snyder, 2001; Garavan, Ross, Kaufman, & Stein, 2003; Ullsperger & von Cramon, 2001). The error-related negativity (ERN) component of the ERP is recorded from frontocentral midline electrodes when subjects make errors in speeded reaction-time tasks (Falkenstein, Hohnsbein, Hoorman, & Blanke, 1990; Gehring, Goss, Coles, Meyer, & Donchin, 1993). The ERN is a measure of performance monitoring that seems to be independent of response conflict, because it is observed in very simple tasks without conflicting response alternatives (Falkenstein et al., 2000). Thorough reviews on the ERN, error processing, and the ACC are provided by Holroyd, Nieuwenhuis, Mars, and Coles (Chapter 16, this volume) and by Luu and Pederson (Chapter 17, this volume).

On the other hand, the conflict-monitoring hypothesis suggests that the primary function of the ACC's cognitive subdivision (as defined by Devinsky, Morrell, & Vogt, 1995) is to detect response conflict, based on imaging results during tasks such as divided attention (Corbetta, Miezin, Dombmeyer, Shulman, & Petersen, 1991), flanker interference (Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999), and the color-word Stroop interference task (Carter et al., 2000; Milham et al., 2002; Pardo, Pardo, Janer, & Raichle, 1999). One such study used the continuous performance test and observed that the same region of dorsal ACC showed increases in activity during error trials as well as correct trials with high levels of conflict (Carter et al., 1998). Because mistakes are more likely to occur when competing response tendencies must be resolved, errors are considered to be a subset of conflict-monitoring processes in this model.

Lesion studies can help to adjudicate between these alternative views. The lesion in Patient R.N. is located in the dorsal ACC region implicated in conflict detection (Carter et al., 1998), with the rostral-most extent impinging upon the affective subdivision, which has been linked to error processing (Bush et al., 2000). The damage in Patient D.L. is more caudally located and includes the caudal cingulate motor area (CMA) involved in controlling
Effects of Focal Lesions on Cognitive Performance

(a) \[
\begin{array}{c}
\text{RIGHT} \\
\text{LEFT}
\end{array}
\]
Congruent Incongruent

(b) \[
\begin{array}{c}
\text{WORD} \\
\text{cue (350 ms)}
\end{array}
\]
1500 ms ISF
\[
\begin{array}{c}
\text{RIGHT} \\
\text{stimulus (350 ms)}
\end{array}
\]
Press Right Button response

FIGURE 29.3. (a) Examples of the stimuli used in the word–arrow Stroop task. The word and the arrow indicated the same response on congruent trials and the opposite response on incongruent trials. In the blocked version, subjects responded to either the word or the arrow by giving a vocal or a manual response. These four conditions were administered in separate blocks. (b) In the switching version used in the ERP study, only manual responses were given. The attended stimulus dimension was cued on each trial by presentation of the cue word ("arrow" or "word") for 350 msec, followed 1,500 msec later by the word–arrow stimulus display.

the selection of manual responses (Paus, Petrides, Evans, & Meyer, 1993). A recent ERP study tested whether error-related and conflict-related activity within the ACC are separable phenomena (Swick & Turken, 2002). The experiment used a word–arrow variant of the Stroop conflict paradigm designed to investigate the relationship between response modality (manual or vocal) and the compatibility between stimuli and responses (Baldo, Shimamura, & Prinzmetal, 1998). We modified the original design, in which subjects attended to words or arrows in separate blocks, to a switching version, in which the attended stimulus dimension (word or arrow) was cued on each trial (Figure 29.3). First, we examined the status of error monitoring by asking whether the ERN component on incorrect trials, and subsequent compensatory behaviors, were impaired in R.N. Second, we examined whether the N2 component, related to the detection of competing response tendencies (Kopp, Rist, & Mattler, 1996), was diminished, as predicted by the conflict-monitoring hypothesis (Carter et al., 2000). If not, this would suggest that ACC activations might not reflect activity that is strictly time-locked to conflict detection processes.

Figure 29.4A illustrates that control subjects generated a negative potential (the ERN) in the ERP recordings for error trials, which was greater than the response for correct trials. The ERN peaked at ~65 msec after incorrect responses and was largest at the fronto-central midline electrodes (FCz, Cz). In the stimulus-locked ERP averages, controls generated a potential (the N2) that was more negative-going for correct conflict trials than for correct congruent trials (Figure 29.4B). The onset of the N2 component was at ~350 msec and its peak at 450 msec poststimulus. R.N. showed a dissociation between ERPs related to conflict and error processing. Figure 29.4B illustrates that the amplitude of his N2 component to correct incongruent stimuli was enhanced relative to controls. By contrast, R.N. exhibited a reduc-
tion in the amplitude of the ERN component to incorrect responses, such that it did not differ from the "correct-related negativity" (or CRN) for accurate responses (Figure 29.4A). Thus, R.N. did not show a difference between response-locked ERP activity on correct and incorrect trials. In addition, R.N. showed a deficit in correcting his erroneous responses, 78% corrected versus 88% for controls.

One viewpoint about action-monitoring processes is that the CRN may signal the outcome of a general, response-related monitoring process, and the ERN reflects this generic monitoring process plus error-specific activity (Ford, 1999). If this is the case, ACC damage eliminated the error-specific activity in R.N. (reduced ERN) but spared the general monitoring process (intact CRN). Some fMRI studies (Kiehl, Liddle, & Hopfinger, 2000; Menon, Adleman, White, Glover, & Reiss, 2001) have reported error-related activity in the ACC that is rostral to the cognitive subdivision. In addition, recent studies have linked the ERN to negative affective responses (Luu, Collins, & Tucker, 2000) and to financial loss in a gambling task (Gehring & Willoughby, 2002). If R.N. showed a dampened affective response to errors, his motivation to self-correct could have been reduced. Because the more rostral and ventral ACC regions are considered part of the affective subdivision, the ERN may largely reflect emotional processing rather than a cognitive operation. This interpretation is supported by the abolition of all ERN activity in patients with lesions of ventromedial PFC that included ventral ACC (Swick et al., 2001).

Along with the enhancement of conflict-detection processes as measured by the N2, R.N.'s behavioral performance in the Stroop task was impaired. He showed elevated interference effects and lower accuracy relative to controls. One explanation for these findings is that R.N. has an impairment in engaging the control processes that reduce the effects of response conflict. It appears that intact brain regions detected the conflict at the same time as controls, as indicated by N2 onset latency, but were recruited for prolonged evaluation and conflict-resolution processes. 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 PFC and the basal ganglia (BG) are able to represent stimulus-response mappings and 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

![FIGURE 29.4. Dissociation of error-related and conflict-related ERPs in R.N. (a) The ERN and CRN in the response-locked waves at frontocentral midline electrodes (FCz and Cz). Response onset occurs at the vertical bar (time = 0 msec), tic marks are 200 msec, and negative is plotted upward. (b) ERPs related to conflict (N2) in the stimulus-locked waves at FCz and Cz. Stimulus onset occurs at the vertical bar (time = 0 msec).]
Effects of Focal Lesions on Cognitive Performance

(a) ERRORS

Controls

Patient D.L.

(b) CONFLICT

Controls

Patient D.L.

FIGURE 29.5. Caudal ACC lesion resulted in reduction of both (a) ERN and (b) N2 in patient D.L. relative to age-matched controls. Details as in Figure 29.4.

with the proposal that PFC and BG detect incompatible response options on incongruent trials and signal conflict-resolution processes, perhaps in caudal ACC and SMA.

Preliminary data from patient D.L. (Swick & Turken, 2004), with damage in the right caudal ACC, revealed a diminution of both ERN and N2 relative to age-matched controls (Figure 29.5). This is supportive of the view that these processes do overlap to some extent but are not entirely co-localized within the ACC (Ullsperger & von Cramon, 2001). Thus, the scalp-recorded ERN is influenced by neural generators in both perigenual ACC extending dorsally into Brodmann area 32 as well as in mid-to-caudal ACC. Conversely, N2 amplitude was diminished only by caudal ACC damage. Previous behavioral results in D.L. demonstrated that she showed significant performance decrements when giving manual responses in the word–arrow Stroop task (Turken & Swick, 1999). However, her performance was comparable to controls when giving vocal responses, even when arbitrary response mappings were used, suggesting that her executive control functions were intact. Those findings demonstrated that caudal ACC is not critical for attentional control processes, because D.L. could produce the correct decisions in each task. Rather, this region is important for manual response control. Taken together, these results support a somatotopic organization of the ACC based on response modality (Paus et al., 1993; Picard & Strick, 1996) and provide neuropsychological evidence for functional specialization within the human ACC.

CONFLICT OR CONTROL?

The N2 results in R.N. indicate that the dorsal ACC does not generate conflict-related activity that occurs prior to the behavioral response. Nevertheless, numerous imaging studies have observed increased ACC activity during incongruent conditions of the Stroop task (reviewed in MacLeod & MacDonald, 2000). The conflict-monitoring hypothesis suggests that the ACC detects response conflict, then signals the dorsolateral PFC to implement the control functions (MacDonald, Cohen, Stenger, & Carter, 2000), such as greater focusing of attention. On the other hand, the executive control view maintains that ACC implements control under difficult conditions where routine behavior must be suppressed (Posner & DiGirolamo, 1998). One missing link is when, exactly, the ACC comes online to implement this control (or to signal other regions to do so).

To evaluate the necessity of ACC for conflict detection and attentional control processes, the ACC patients were tested on three versions of the color–word Stroop task with
vocal responses (Swick & Jovanovic, 2002). Although many foci of activation from neuroimaging studies are located within D.L.’s and R.N.’s lesions (Figure 29.2), prior findings of regional specialization within ACC (Turken & Swick, 1999) led us to predict different results in the two patients. In one experiment, mixed blocks of trials (congruent, neutral, incongruent) alternated with uniform blocks of either all congruent or all incongruent trials. The third version was modeled after the study of Carter and colleagues (2000), in which the probabilities of congruent and incongruent trials were manipulated from block to block. This design varied the level of response conflict (high in blocks with mostly congruent trials; low in blocks with mostly incongruent trials) and the degree to which executive control processes were engaged (low in mostly congruent blocks; high in mostly incongruent blocks).

Results in D.L. indicated that damage to caudal ACC was not associated with excessive interference effects for vocal responses, in accord with previous results (Turken & Swick, 1999). Furthermore, her interference was not modulated by the probability manipulation: D.L. exhibited less interference than controls in the high-conflict condition, suggesting equivalently high levels of cognitive control in both conditions. Conversely, damage to dorsal ACC resulted in consistently lower accuracy on incongruent trials, indicating that R.N. showed a deficit in inhibiting the automatic response. R.N. also showed greater interference than did controls in the low-conflict condition, suggesting that dorsal ACC implements the strategic processes engaged here to reduce conflict (Posner, 1994). Thus, subregions of ACC appear to have separable functions, with the caudal area involved in high-level motor control for manual responses and the more rostral and dorsal regions involved in conflict-resolution and attentional-control processes under difficult task conditions.

**RESPONSE CONFLICT OR TASK DIFFICULTY?**

Another unresolved issue is whether the rubric of “response conflict” is able to account for the totality of the ACC literature, or whether a more general idea such as “task difficulty” is a better fit to the data. In the next experiment, the Eriksen flanker task was used to further investigate selective attention and response competition. In this task, subjects are slower to respond when a central target letter is surrounded by incongruent flanker letters than if the flankers are congruent or neutral (Eriksen & Eriksen, 1974). Neither D.L. nor R.N. showed an increase in flanker interference relative to their age-matched control groups (Turken, 2000). An additional analysis was performed to investigate the effects of the preceding stimulus on the current response. The Gratton effect (Gratton, Coles, & Donchin, 1992) is a reduction in the behavioral costs of interference after response conflict on the previous trial, presumably due to an adjustment in performance strategy, where more weight is put into top-down control processes. For controls, the standard Gratton effect was obtained: Flanker interference was reduced if the preceding trial was incongruent. D.L. showed increased interference when responding with the left (contralateral) hand to incongruent stimuli preceded by a congruent stimulus trial. This suggests that D.L. has compromised control over motor response conflicts, possibly expressed more strongly on the contralateral side, as would be expected from the fact that her lesion includes the caudal CMA region implicated in manual response control (Paus et al., 1993). This is also consistent with our previous report with this patient (Turken & Swick, 1999). That she showed the Gratton effect has two consequences. First, it suggests that she is capable of using strategic control processes to compensate for the effect of her lesion on motor response control. Second, it indicates the caudal CMA is not likely to be the source of the warning signal that would trigger a high-level control process by the lateral PFC.
In contrast, R.N.’s performance was comparable to his controls’. He showed normal interference and Gratton effects in the flanker task, which would argue against a deficit in either manual response control or flexible adjustment of performance strategy. How do we reconcile these seemingly disparate findings with R.N.? He was not impaired in the Eriksen flanker task, yet he showed deficits in the classic color-word Stroop and the cued version of the word-arrow Stroop. Are there differences in the conflict operations tapped by Stroop and flanker tasks (Fan, Flombaum, McCandliss, Thomas, & Posner, 2003)? Could the general construct of “task difficulty” or the recruitment of another attentional control function account for the differences?

**ATTENTIONAL SWITCHING**

To pursue this latter question, we investigated mental flexibility, as indexed by the ability to switch successfully between stimulus dimensions (Swick & Turkcan, 2004). Here, we compared the cued word-arrow Stroop (Figure 29.3B) to a version where the attended dimension remained constant throughout a block. Overall performance in the blocked condition was compared to the condition where switches were needed randomly on a trial-by-trial basis. Furthermore, we examined whether R.N. would show large costs in terms of longer reaction times (RTs), lower accuracy, and altered ERPs on trials that require switching versus 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.

R.N. performed better than did controls in the blocked version of the task, as he was significantly faster, more accurate, and less affected by conflicting information (Swick & Turkcan, 2004). Thus, the left dorsal ACC is not essential for response-selection mechanisms or for conflict-monitoring functions. In contrast, R.N. was quite impaired when the stimulus dimension was cued on each trial, requiring rapid, unpredictable switches of attention. 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. In addition, 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 poststimulus, compared to only 400 msec poststimulus 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 & Shallice, 1986) or of a task demand node (Cohen, Dunbar, & McClelland, 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, Woodward, Laurens, & Liddle, 2001). Other imaging experiments have reported switching-related activations which overlap with the dorsal ACC region damaged in R.N. (Dove, Pollman, Schubert, Wiggins, & von Cramon, 2000; Kimberg, Aguirre, & D'Esposito, 2000). These findings were not predicted by the conflict-monitoring hypothesis, which postulates that the dorsal ACC’s domain is limited to detection of motor conflicts and not conflicts between different task sets.

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, Koski, Caramanos,
DEFICITS OF ATTENTION

& Westbury, 1998). This hypothesis can also encompass R.N.'s prior results in the classic Stroop task, where he committed more errors than did controls on incongruent trials, indicating a deficit in inhibiting the prepotent word-reading response (Swick & Jovanovic, 2002). In the color-word Stroop, the irrelevant word-reading response is much more automatic than the arrow button-press response in the word–arrow experiment. This account views the dorsal ACC as a bridge between lateral PFC and ventromedial PFC regions. If lateral PFC signals that more cognitive resources need to be recruited, dorsal ACC relays the message to rostral ACC and other ventromedial regions, leading to a general increase in arousal, reflected in enhanced activity in the autonomic nervous system (Critchley et al., 2003) and in brainstem nuclei such as the locus coeruleus (Aston-Jones, Rajkowski, & Cohen, 1999). The alerted brainstem nuclei trigger an increase in cortical arousal (Foote & Morrison, 1987), which results in enhanced concentration, thus improving performance in difficult situations.

ACC, SCHIZOPHRENIA, AND ERROR MONITORING

As cited previously, a number of investigations into neurological and psychiatric disorders have indicated abnormalities in various subregions of the ACC as correlates of these conditions. As a particular example, the neuropsychological deficits associated with schizophrenia have been challenging for researchers to characterize and interpret, and a coherent theoretical framework for explaining them has only begun to evolve over recent years (Frith, 1992). Numerous studies have documented abnormalities in the ACC in patients with schizophrenia (Benes, 2000). Better characterization of how these abnormalities are related to the symptoms of schizophrenia can thus help us make advances in both schizophrenia research and the understanding of ACC function. Our recent work has aimed to follow this approach (Turken, Vuilleumier, Mathalon, Swick, & Ford, 2003). Using a specially designed task, we investigated the relation between disorders in self-monitoring, which have been proposed to be one of the key functions of ACC, and other measures of executive attention (conflict resolution, task set preparation, and task switching). A group of high-functioning patients with schizophrenia showed a specific deficit in monitoring the consequences of their actions, as assessed by their ability to correct their erroneous responses in the absence of external feedback on accuracy. This finding successfully replicated earlier reports demonstrating the same phenomenon (Frith & Done, 1989; Malenka, Angel, Hampton, & Berger, 1982). In contrast, the other measures of executive attention did not show a significant worsening of performance for the patients compared to controls. These findings have two implications. First, one of the primary effects of ACC dysfunction in schizophrenia might be specifically related to the ability to monitor self-initiated cognitive processes and actions, which is crucial for volitional activity, while possibly sparing to some extent other attention control processes. Second, and in a broader sense, such a finding provides further support for the notion that error monitoring and conflict resolution are dissociable processes with distinct neural bases.

CONCLUSIONS

As has been noted, each approach to the study of brain function has unique benefits as well as particular shortcomings. Therefore, converging evidence from parallel lines of research allow us to validate findings produced by a particular area of research and produce novel hypotheses that can be tested using a combination of the existing methods. Our research
provides an example of this approach. The question whether error monitoring and conflict resolution might be related but distinct psychological processes, with emphasis on how they relate to ACC function, has primarily been motivated by ERP and functional neuroimaging findings with normal populations. In another vein, the notion that the ACC has multiple anatomically and functionally defined subregions has emerged mostly from animal research (Devinsky et al., 1995), from the analysis of its patterns of connectivity with other regions (Bates & Goldman-Rakic, 1993), and from its differential response to task manipulations and coactivation with other brain regions in neuroimaging studies (Koski & Paus, 2000). Whether ACC activations in cognitive studies reflect the execution of specific cognitive operations or a more general contribution whenever task demands increase is another question motivated by imaging studies.

One approach for future work is to combine fMRI and ERP studies in the same groups of patients to distinguish between direct and distal effects of ACC lesions. Lesions might disrupt the functioning of larger networks, rather than compromise a particular operation carried out by the damaged area itself. Whole brain imaging, together with newer approaches to network analysis, can provide clues. This approach can also reveal the mechanisms of recovery of function after brain damage.

Another tactic for further neuropsychological experimentation is the comparison of different patient groups, such as ventral ACC, dorsal ACC, and lateral PFC, to look for the existence of double dissociations. Along these lines, the use of newer structural mapping techniques, including three-dimensional reconstruction methods (Frank, Damasio, & Grabowski, 1997), diffusion-tensor imaging (Conturo et al., 1999), and voxel-based lesion-symptom mapping (Bates et al., 2003) can refine the ability to quantify and localize the brain lesions. These methods can help to determine which part of the lesion is primarily responsible for a particular behavioral deficit. The combination of anatomically precise structural MRI with ERPs will allow more accurate localization of the neural generators.

Finally, ERP and fMRI studies can be designed to test hypotheses that have emerged from our patient findings. The neuropsychological data provide support for topographic specialization of control functions within the ACC. Furthermore, the lesion results suggest that there is not a single locus for attentional control in the brain.

ACKNOWLEDGMENTS

This work was supported by Grant No. DC03424 from the National Institute on Deafness and Other Communication Disorders and No. 98-47 CNS-QUA.05 from the James S. McDonnell Foundation (Diane Swick), and by Grant No. 5 F32 NS43961-02 from the National Institutes of Health (Aud U. Turken). Thanks to Robert Knight and Robert Rafal for patient referrals, and Jelena Jovanovic, Jonathan Kopelowich, Jary Larsen, Kim Miller, and Caitlin Roxby for their assistance.

REFERENCES


DEFICITS OF ATTENTION


