



Anterior cingulate cortex and the Stroop task: neuropsychological evidence for topographic specificity

Diane Swick^{a,b,*}, Jelena Jovanovic^{a,c}

^a Department of Neurology, VA Northern California Health Care System, University of California, Davis, CA, USA

^b Department of Neurology (127E), VANCHCS, 150 Muir Road, Martinez, CA 94553, USA

^c Department of Cognitive Science, VANCHCS, University of California, San Diego, 150 Muir Road, Martinez, CA 94553, USA

Received 10 January 2001; received in revised form 31 October 2001; accepted 16 November 2001

Abstract

Neuroimaging studies have implicated the anterior cingulate cortex (ACC) in many aspects of attention and cognition. Major theories of ACC function have proposed a role in conflict monitoring, executive control, response selection, and general arousal. Although the ACC is often treated as a unitary structure, extensive evidence suggests it exhibits anatomical and functional specificity. ACC activity during the Stroop color word interference task has been of particular interest. The purpose of the present study was to determine whether two different ACC subregions are *necessary* for intact color naming performance in the Stroop task. One experiment utilized blocked trial and mixed trial designs to emulate neuroimaging studies and to compare interference and facilitation effects, respectively. A third variant manipulated the probabilities of congruent and incongruent trials to alter levels of interference and cognitive control, or engagement of strategic processes, on a block by block basis. Two patients with focal lesions in either right mid-caudal (patient D.L.) or left rostral to mid-dorsal ACC (patient R.N.) exhibited distinctive performance profiles in these three versions of the Stroop task, providing further support for topographic specificity of function within the human ACC. Contrary to predictions from some neuroimaging experiments, damage to right mid-caudal ACC was associated with normal levels of interference and accurate performance on incongruent trials. Instead, D.L. showed reduced levels of facilitation relative to controls. Further, interference was not modulated by the probability manipulation in D.L., suggesting equivalently high levels of cognitive control in both conditions. Conversely, damage to left mid-dorsal ACC resulted in consistently lower accuracy on incongruent trials, indicating deficits in maintaining task set and inhibiting the automatic response. These results can help to constrain interpretations of ACC activations in functional imaging experiments of the Stroop task. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Attention; Executive function; Executive control; Response selection; Performance monitoring; Human

1. Introduction

Studies of the anterior cingulate cortex (ACC) have attracted an increasingly devoted following, given the ubiquity of ACC activations in neuroimaging investigations of cognition. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) experiments have detected increased blood flow in the anterior cingulate during a variety of cognitive tasks, including divided attention [11], verb generation [42], verbal fluency [12,14,17], novelty detection [18], working memory [44] and most notably, the Stroop task [2,6–8,15,23,26,36,43,53]. One interpretation of these results is that the ACC is important for attention and “selection of targets from competing inputs” [46]. This view of ACC function has been termed “attention to action” [59] or “selection for action” [42]. Posner and coworkers (e.g.

[47]) have adopted the Norman and Shallice [34] model of executive control as an explanatory construct for the function of the ACC. In Posner’s model of ACC function, executive control of the supervisory attentional system is orchestrated by the ACC and is required during situations in which automatic processes are inadequate, such as planning, error correction, novel responding, and overcoming habitual responses [47]. Thus, in the selection for action scheme, Posner and coworkers claim that the ACC implements control under difficult conditions where routine behavior must be suppressed.

Conversely, Carter and coworkers [7,29] suggest that the ACC monitors for response conflict, and it is the dorsolateral prefrontal cortex that actually implements cognitive control under conditions of high conflict. In this model, cognitive control is defined as the adaptability within the cognitive system that is required to make “appropriate adjustments in perceptual selection, response biasing, and the on-line maintenance of contextual information” [4]. Thus, based on

* Corresponding author. Tel.: +1-925-370-4081; fax: +1-925-229-2315.
E-mail address: diane@ebire.org (D. Swick).

neuroimaging results that observed differential activity in the ACC [7,29], the conflict monitoring hypothesis [4] proposes that the ACC is primarily recruited to detect conflict in the form of response competition. In contrast, the selection for action hypothesis [47] suggests that the ACC is engaged under all conditions that require cognitive control.

Other investigators have emphasized that the ACC can be partitioned into the rostral/ventral “affective” division (located approximately rostral and ventral to the genu of the corpus callosum) and the more dorsal/caudal “cognitive” division [5,16]. Based on an extensive review of the animal and human literatures, Vogt and coworkers [16,59] divided the ACC into further subdivisions involved in visceromotor control, vocalization, nociception, attention to action, and skeleto-motor control. Bush et al. [5] reviewed the neuroimaging literature and observed that rostral ACC activations occurred in emotional tasks and during symptom provocation in psychiatric patients (e.g. anxiety, obsessive compulsive disorder), while more dorsal and caudal ACC activity was elicited by cognitive tasks.

A related idea is that the ACC is more involved in arousal and affect, with only minor contributions to task-specific cognitive processing (see also [37,39,53]). Hence, the blood flow changes in PET studies may be due to task difficulty [39] and associated increases in anticipation [33] and anxiety [3]. Most ACC activations have been in difficult tasks associated with greater amounts of stress than the control conditions. Thus, any changes in cingulate activity may reflect manifestations of anxiety instead of specific attentional processes. Support for this idea was provided by a pharmacological manipulation (CCK4 injection) that increased subjective anxiety ratings, heart rate, and cerebral blood flow in the ACC [3]. Furthermore, another study demonstrated that anticipating the start of a cognitive task increased ACC blood flow as much as performing the task itself [33]. The peaks of both of these activations were located within what has been considered the cognitive subdivision.

Yet another alternative is that the ACC is related to higher-order motor control in a topographic fashion, with oculomotor, vocal, and manual responses eliciting activations from rostral to middle to caudal ACC, respectively [40]. This PET study required subjects to reverse an overlearned stimulus-response mapping and observed that separate regions of the ACC were engaged by each of the three response modalities [40]. We previously reported that the performance of patient D.L., with focal damage to right mid-caudal ACC, depended on the response modality used. Under the same requirements during tasks of selective and divided attention and a word-arrow variant of the Stroop, she was impaired when giving manual responses, but not vocal responses [56]. The caudal extent of her lesion includes the cingulate motor areas, in particular the manual motor control area in the scheme of Picard and Strick [45], but spares the vocal control area. Given the functional and anatomical heterogeneity of the ACC [16,19,59], the multiple hypotheses proposed here need not be mutually exclusive, a theme that is revisited

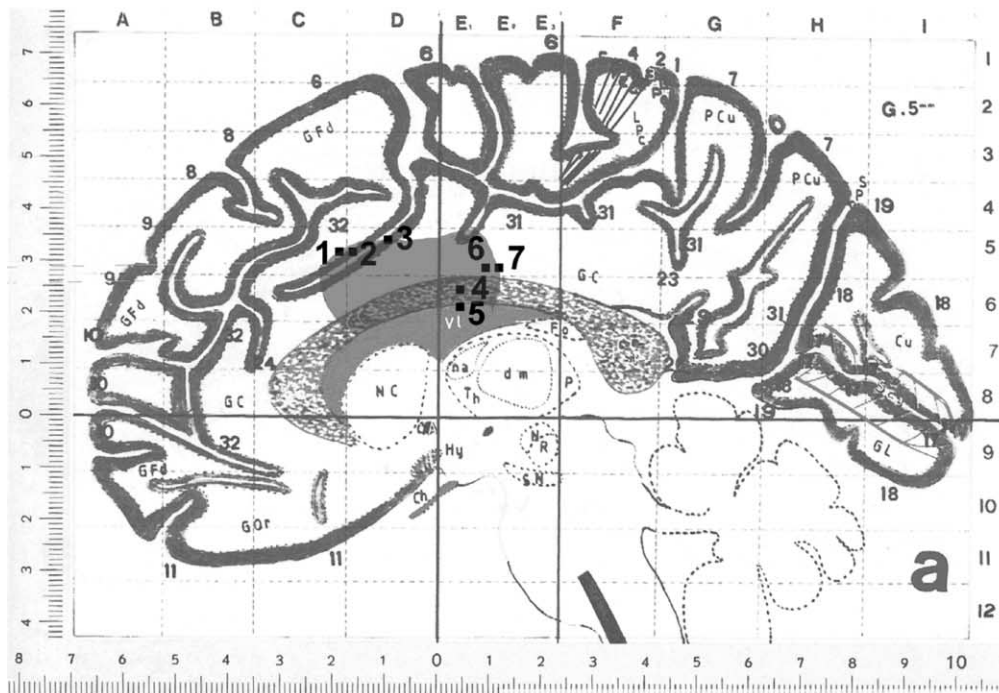
later in our discussion. Hence, case studies of patients with focal lesions in different subregions of the ACC are an important source of information on the topography of function within the human ACC.

The Stroop color-word interference task [49] is one of the most widely used experimental tasks in all of cognitive psychology (see [30] for comprehensive review). Subjects must name the ink color used to display color names or neutral stimuli. The ink color can either be congruent (e.g. “red” written in red ink) or incongruent (“red” written in blue ink). In this latter situation there is response conflict, since subjects must suppress the tendency to simply read the word. Subjects exhibit interference in the conflict condition through longer reaction times and more errors. Traditional explanations of Stroop interference have emphasized the automaticity of reading relative to color naming or the differential in speed of processing, but more recent parallel processing models have invoked simultaneous activation of word and color information, both of which converge on a common response mechanism (e.g. [9,28]). A differential in the *strength* of processing (due to training), with greater strength in the word reading pathway, was incorporated into the parallel distributed processing model of Cohen et al. [9]. Interference occurs when the word reading and color naming pathways produce conflicting activation at their point(s) of intersection. Facilitation ensues when activation in the two pathways is in agreement. The same processing mechanism accounts for both interference and facilitation effects in this model [9]. A conflicting hypothesis (so to speak) postulates that these two effects are mediated by separate, dissociable processing mechanisms [32].

The Stroop task has long been considered an index of executive control and frontal lobe function. For a number of years, it was thought to reflect the integrity of left frontal cortex [41]. However, Vendrell et al. [58] reported that lesions of *right* lateral prefrontal cortex correlated with increased Stroop errors, and that patients with left frontal lesions showed intact performance. An even more recent publication by Stuss and coworkers [50] suggested that left dorsolateral frontal lesions were associated with overall slowness and increased errors in color naming, but not a disproportionate increase in RTs or error rates during the incongruent condition. Instead, patients with damage in bilateral superior medial frontal cortex showed greater interference effects.

As mentioned above, neuroimaging studies of the Stroop task have implicated the ACC (see Fig. 1 for location of activation foci contained within the patients’ lesions). However, the performance of a patient given bilateral anterior cingulotomy as a treatment for severe depression [24] cast doubt upon the notion that the ACC is crucial for performance of the Stroop task. Compared to her pre-morbid performance, 2 weeks after surgery she showed no change in either naming latency or error rate in the incongruent condition (which was blocked). She was slower post-surgically,

Patient D.L.



Patient R.N.

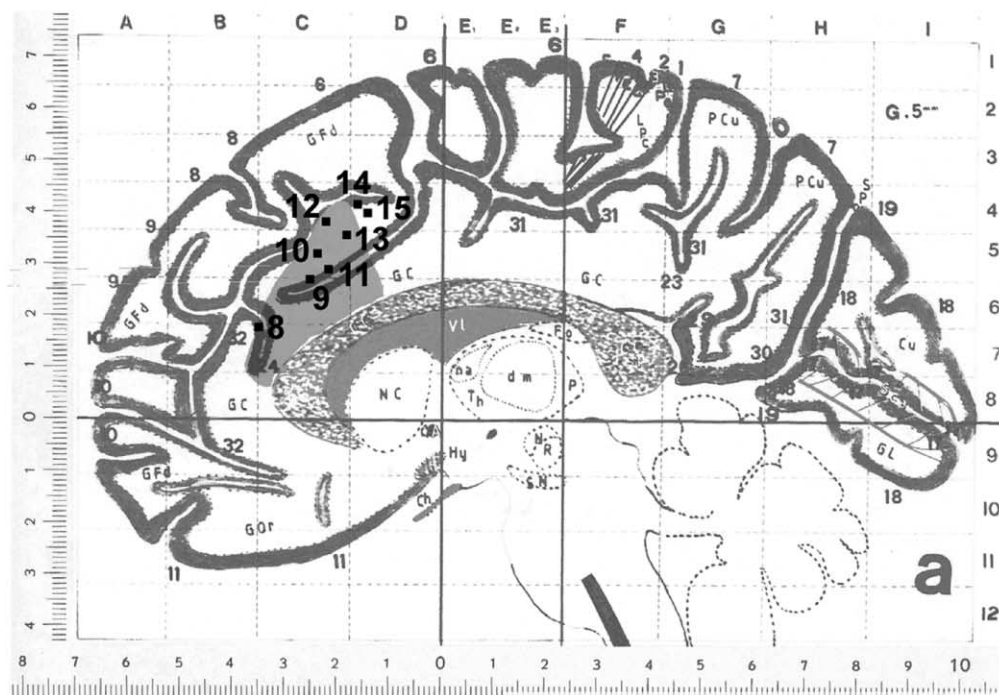


Fig. 1. The sagittal extent of the lesion is represented in gray shading on the Talairach and Tournoux coordinate system [52] for D.L. (top) and R.N. (bottom). Peaks of activation from 10 neuroimaging studies of the Stroop task are plotted inside the regions of damaged ACC for each patient. For ease of comparison, R.N.'s left hemisphere lesion is depicted on the right hemisphere section, although all activations are located in the left hemisphere or at midline. Within D.L.'s lesion are the following: 1, 2, incongruent–congruent blocks [36]; 3, counting Stroop, incongruent–neutral blocks [6]; 4, neutral word–neutral cross blocks [2]; 5, incongruent–neutral cross blocks [2]; 6, incongruent–neutral blocks [23]; 7, congruent–neutral blocks [8]. Within R.N.'s lesion are the following: 8, incongruent–neutral [53]; 9, incongruent–congruent blocks [43]; 10, incongruent–neutral blocks [23]; 11, incongruent–neutral blocks [8]; 12, high conflict, incongruent–congruent [26]; 13, incongruent–congruent blocks [43]; 14, high conflict, incongruent–congruent [7]; 15, incongruent–congruent blocks [15].

however, in naming the ink color of congruent words. Although the interference effect was actually diminished by cingulotomy, the authors interpreted the results as a reflection of ACC involvement in the task. Another null effect was reported by Stuss and coworkers [50], who did not find a relation between ACC damage and performance in the interference condition. The region associated with poorer performance in this study was located superior to the ACC [50]. On the other hand, patients with bilateral cingulotomies given for the treatment of intractable pain showed a higher interference index on the classic, original version of the Stroop [49], as compared to chronic pain patients without cingulotomies [10]. Another patient received bilateral cingulotomy for obsessive compulsive disorder and depression [35] and was tested 2 days prior to and 3 days after surgery in a computerized variant of the Stroop that used equal numbers of congruent, incongruent, and neutral trials. This patient's overall response times were significantly slower than controls both before and after surgery. However, most notable was her post-surgical increase in interference as measured by the difference between RTs on incongruent versus congruent trials [35]. Prior to surgery, she showed a smaller interference effect than controls, but post-surgically her interference effect was larger than controls. Interestingly, another patient with a right medial frontal tumor resection that included portions of the ACC was impaired on the clinical Stroop, but not a computerized single-trial variant [13].

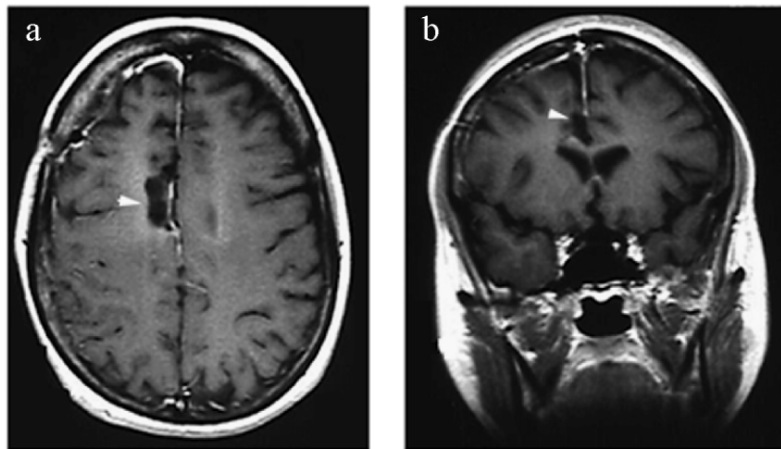
One possible reason for the discrepancy in this latter patient and in the literature at large is that the various formats of the Stroop test may place differing demands upon response selection, inhibition, and attentional processes. For example, a typical clinical version of the Stroop [54] requires subjects to read a list of 112 color words printed in incompatible colors on a sheet of paper; reading time is then compared to the time required to name the ink colors of incompatible words. Other formats include three conditions: reading of color words printed in black ink, naming color patches or XXX's, and color naming for incongruent words (reviewed in [27]). The various clinical versions of the Stroop utilize a blocked format with all stimuli presented on a single sheet of paper. Although neuroimaging experiments use the computerized, single trial presentation format, most of these studies have relied on blocked designs. Divergent results in the cingulotomy case studies mentioned above [24,35] could be due to the use of blocked versus mixed trial paradigms. In fact, Stuss and coworkers [50] predicted that deficits would emerge in ACC lesioned patients when randomly intermixed trial types were presented. Another consideration is the variable location of lesions within the ACC, which can also account for some of the disagreement in the neuropsychological results. A final factor is the chronicity of lesion, as well as its etiology.

To evaluate the *necessity* of ACC for conflict detection, response selection, and executive control processes, in the present study we tested two patients with focal ACC damage

on three versions of the Stroop color-word interference task. In Experiment 1, mixed blocks of trials (congruent, neutral, and incongruent) alternated with uniform blocks of either all congruent or all incongruent trials. The uniform blocks were included as a comparison to the blocked design of most neuroimaging experiments. The mixed blocks allowed a comparison of facilitation versus interference effects [32]. A double dissociation in the patients might indicate that separate ACC regions mediate Stroop facilitation and interference. Experiment 2 was modeled after the fMRI study of Carter et al. [7], in which all blocks had mixed trials (congruent and incongruent), but the probabilities of congruent and incongruent trials were manipulated from block to block. This design varied the level of response conflict for incongruent trials (higher in blocks with mostly congruent trials, lower in blocks with mostly incongruent trials) and the degree to which cognitive control was engaged (higher in mostly incongruent blocks, lower in mostly congruent blocks). The results of this event-related fMRI study demonstrated that the ACC showed enhanced activity to incongruent stimuli (versus congruent) in the high conflict condition, but not in the low conflict condition [7].

Each of the theories of ACC function has different predictions about the deficits that might be observed in patients with ACC lesions. The anticipation/arousal/task-difficulty class of theories [33,39,53] suggests that the ACC does not make a specific contribution to task performance, and hence the patients would not be expected to show impairments, unless these arousal factors assist in timely task performance. The executive control, or selection for action, hypothesis [46,47] would expect that the patients would exhibit greater interference (i.e. slower RTs) and increased error rates in the incongruent condition. Furthermore, strategic modulation of performance (in the high versus low conflict blocks of Experiment 2) would not be observed in the patients, since it is the ACC that implements adaptability in performance according to changing task demands, an executive control function. Like the selection for action hypothesis, the conflict monitoring hypothesis [7,29] also predicts greater interference and higher error rates. More specifically, and in contrast to the selection for action hypothesis [46,47], since the ACC was only activated during interference trials in the high conflict condition [7], decrements should be observed only in those blocks, and the implementation of strategies should not be altered. Topographic specificity is not implied by either of these models, but neuroanatomical and neuroimaging evidence for high-level motor control [37,40,45] predicts deficits in the color naming Stroop task only when the vocal control regions are damaged (since spoken responses are required). However, the present experiments do not directly test for a dissociation between manual and vocal responses, so our theoretical focus will be to compare the predictions generated by the conflict monitoring [7] and selection for action [47] hypotheses.

Patient D.L.



Patient R.N.

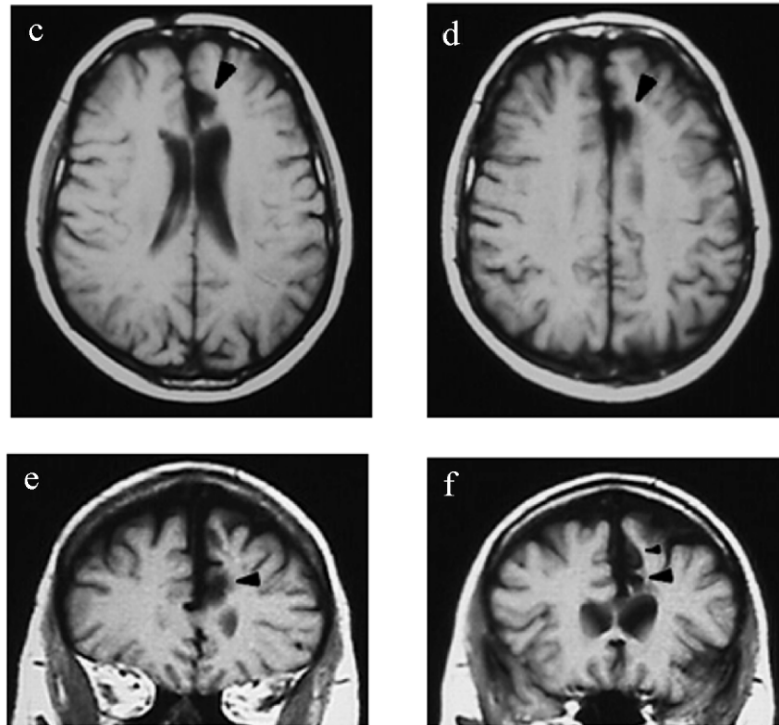


Fig. 2. MRI scans showing the lesions of patient D.L. (a, b) and patient R.N. (c–f). (a) Horizontal section at the level of the cingulate sulcus. The damaged area in the right hemisphere is indicated by a white arrowhead on the left side of the scan. (b) Coronal section of caudal ACC illustrating the lesion in the cingulate sulcus, while the paracingulate sulcus is intact. (c, d) Horizontal sections illustrating that R.N.'s lesion in the left ACC (indicated by black arrowheads) is ventral and rostral to that of D.L. (e, f) Coronal sections with ACC damage denoted by black arrowheads. In (f), the larger arrowhead shows the damage in the cingulate sulcus, while the smaller arrowhead above it indicates the lesion in the paracingulate sulcus, a more dorsal extent than in D.L.

2. Methods

2.1. Participants

Patient D.L. (right handed female, year of birth 1965, 12 years of education) had a tumor resected from the ACC of the

right hemisphere in 1990. The resulting lesion extends from the mid- to caudal portion of the ACC (Figs. 1 and 2). The caudal segment includes the cingulate motor area implicated in manual response control, located in the cingulate sulcus [40,45]. She has been and is currently taking anti-epileptic medications (Neurontin and Dilantin) to prevent seizures.

Patient R.N. (right handed male, year of birth 1931, 14 years of education) has a left hemisphere lesion extending from the rostral ACC (around the genu of the corpus callosum) to mid-ACC (Figs. 1 and 2), presumably due to occlusion of the pericallosal branch of the anterior cerebral artery. The rostral section of damage includes a small portion of the “emotional” ACC [6]. The mid to caudal extent of the lesion includes the vocal control areas of Picard and Strick [45] and Paus [40]. The damage also includes the rostral-most manual area in the Picard and Strick scheme [45], but no manual areas according to Paus and coworkers [39,40]. The date of the infarct is unknown, since neither R.N. nor his wife noted any behavioral changes suggesting the occurrence of a stroke.

For Experiment 1, D.L. (age 31) was compared to a group of six age-matched controls (mean age 30.3 years), and R.N. (age 66) was compared to a cohort of six older age-matched controls (mean age 65.3 years). For Experiment 2, D.L. (age 35) was compared to eight age-matched controls (mean age 36.8 years), and R.N. (age 69) was compared to eight older age-matched controls (mean age 67.0 years). All subjects were free from significant medical complications, substance abuse, psychiatric disturbances, and dementia.

2.2. Blocked versus mixed stroop

Stimuli were the words “red”, “blue”, “green”, and “yellow” printed in either the same color or different color ink. In two blocks (the blocked condition), all words were either in the congruent color (one block of 60 trials) or the incongruent color (one block of 60 trials). In three blocks of 60 trials each (the mixed condition), the trials were mixed with equal numbers of congruent, incongruent, and neutral trials (tree names: “oak”, “pine”, “maple”, and “walnut”). A practice block of 15 trials was administered (five trials each of congruent, incongruent, and neutral), then the order of the experimental blocks was as follows: mixed, congruous, mixed, incongruous, mixed. Stimulus duration was 500 ms, while the interstimulus interval (ISI) was 2 s. Subjects were instructed to name the ink color as quickly and accurately as possible. Voice onset latencies were recorded using a voice operated relay and microphone. Trials with vocal artifacts and premature triggers were excluded. RT and accuracy were analyzed using repeated measures ANOVAs. Data from D.L. and R.N. were compared to the range for each patient’s age-matched control group, and values falling outside the 95% confidence interval were considered significantly different from controls.

2.3. Stroop with probability manipulation

Stimuli were the words “red”, “blue”, “green”, and “yellow” printed in either the same color or different color ink. In three blocks of 60 trials each (the “high conflict” condition), 80% of the words were in the congruent color and 20% in the incongruent color. In three blocks (the “low

conflict” condition), 20% of the words were in the congruent color and 80% in the incongruent color. A practice block of 16 trials was administered (half congruent, half incongruent), then the order of the experimental blocks alternated between the high conflict and low conflict conditions. Stimulus duration was 500 ms, while the interstimulus interval (ISI) was 2 s. Subjects were instructed to name the ink color as quickly and accurately as possible. Voice onset latencies were recorded using a voice operated relay and microphone. Trials with vocal artifacts and premature triggers were excluded. RT and accuracy data in controls were analyzed using repeated measures ANOVAs with factors of condition (congruent, incongruent) and probability (80% congruent, 20% incongruent). An additional analysis examined the pattern of RTs on a block by block basis and included the factor of block (nos.1–3) as well as the variables condition and probability. The performance data from the patients were compared to the range for each patient’s age-matched control group, and values falling outside the 95% confidence interval were considered significantly different from controls.

3. Results

3.1. Stroop: blocked condition

All subjects were slower at naming the ink color during the incongruent block than the congruent block (Table 1). Mean RT data from the controls showed a significant main effect of condition: controls for D.L. [$F(1, 5) = 39.128$, $P < 0.005$]; controls for R.N. [$F(1, 5) = 29.646$, $P < 0.005$]. The overall RTs for D.L. were slower than those for her age-matched controls ($P < 0.05$), particularly during the congruent block ($P < 0.05$). Her RTs for the incongruent block fell with the 95% confidence interval for controls. Conversely, R.N. was faster overall than his control group ($P < 0.05$). Interference was expressed as a percentage [(incongruous RT – congruous RT)/congruous RT \times 100] to correct for these baseline RT differences. This interference effect was within the normal range for both ACC patients. Error rates were very low (Table 2), and D.L. did not differ from controls. However, R.N. had a significantly higher error rate than his controls for the incongruent block ($P < 0.05$).

Table 1
Mean RTs (ms) and the interference effect (%) for the anterior cingulate patients and their respective age-matched control groups for the blocked condition of the Stroop task. Standard errors are shown for the control data.

	Congruent	Incongruent	Interference (%)
D.L.	734.9 ^a	899.8	22.4
Controls (D.L.)	629.2 \pm 36.4	810.3 \pm 46.2	29.2 \pm 5.0
R.N.	569.3	766.8	34.7
Controls (R.N.)	688.5 \pm 49.7	833.8 \pm 28.7	23.0 \pm 5.6

^a Above the upper 95% confidence interval for controls.

Table 2

Error rates (%) for the anterior cingulate patients and their respective age-matched control groups for both conditions of the Stroop task.

	Blocked		Mixed		
	Congruent	Incongruent	Congruent	Neutral	Incongruent
D.L.	0.0	1.7	0.0	0.0	0.0 ^a
Controls (D.L.)	0.0	0.5 ± 0.5	0.0	0.6 ± 0.4	2.5 ± 0.7
R.N.	0.0	5.0 ^b	1.7	0.8	11.7 ^b
Controls (R.N.)	0.0	1.4 ± 0.9	0.0	0.8 ± 0.8	3.8 ± 1.6

^a Below the lower 95% confidence interval for controls. Standard errors are shown for the control data.

^b Above the upper 95% confidence interval for controls.

3.2. Stroop: mixed condition

Naming latencies for controls were slowest for incongruent trials, intermediate for neutral trials, and fastest for congruent trials (Table 3). A significant main effect of condition was observed: controls for D.L. [$F(2, 10) = 27.329$, $P < 0.005$]; controls for R.N. [$F(2, 10) = 20.045$, $P < 0.005$]. Planned comparisons (contrasts) indicated significant differences between congruent and incongruent ($P < 0.001$) and neutral and incongruent ($P < 0.01$) RTs for both control groups. The contrast between neutral and congruent, however, was significant only for the young controls for D.L. ($P < 0.05$), but not the older controls for R.N. ($P > 0.09$). The overall RTs for D.L. were again slower than those for controls ($P < 0.05$), but R.N. was not significantly faster than his control group in the mixed condition ($P > 0.1$). Interference and facilitation measures were obtained relative to neutral RTs: interference [(incongruous RT – neutral RT)/neutral RT × 100], and facilitation [(neutral RT – congruous RT)/neutral RT × 100]. The interference effect was within the normal range for both ACC patients. Percent facilitation for R.N. was within control levels (which were highly variable in the older group, ranging from –6.3 to 14.8%), but D.L. showed less benefit from trials presented in the congruent ink color ($P < 0.05$) than her controls. Error rates were very low (Table 2), and since D.L. made no errors, she was significantly more accurate than controls for the incongruent trials. R.N., however, was significantly less accurate for incongruent trials than his age-matched cohort ($P < 0.05$).

A direct comparison of the conflict effect in the blocked versus mixed trials was obtained by using the same percent

interference measure [(incongruous RT – congruous RT)/congruous RT × 100] for both conditions. The young control group for D.L. showed significantly greater interference in the blocked condition (29.2%) than in the mixed condition (19.1%; $P < 0.05$). D.L. also showed a similar modulation of performance in the two conditions (blocked = 22.4%; mixed = 9.6%). For the mixed trials, she fell within the range specified by the 95% confidence interval in her control group (9.5–28.6%), albeit barely. The older control group for R.N., on the other hand, did not show greater interference in the blocked (23.0%) compared to the mixed condition (24.3%; $P > 0.6$). R.N. showed a pattern more like the younger control group, with greater interference in the blocked condition (34.7%) than in the mixed condition (30.9%). For the mixed trials, he fell within the 95% confidence interval of his control group (8.8–39.8%).

3.3. Stroop: probability manipulation

All subjects exhibited slower naming latencies for incongruent stimuli than for congruent stimuli (see Table 4). The main effect of condition was highly significant: controls for D.L. [$F(1, 7) = 296.43$, $P < 0.0001$]; controls for R.N. [$F(1, 7) = 73.62$, $P < 0.0001$]. In an analysis that included all 16 controls, a main effect of probability was also observed [$F(1, 15) = 10.10$, $P < 0.01$], with faster RTs in the 20% congruent blocks, but note that this effect was modified by condition. Control subjects were faster on incongruent trials ($P < 0.0001$) but slower on congruent trials ($P < 0.05$) in the 20% congruent blocks compared to the 80% congruent blocks (RTs for incongruent trials, 20%: 724 + 31, 80%: 804 + 34; RTs for congruent trials, 20%:

Table 3

Mean RTs (ms) and the interference effect (%) for the anterior cingulate patients and their respective age-matched control groups for the mixed condition of the Stroop task^a

	Congruent	Neutral	Incongruent	Interference (%)	Facilitation (%)
D.L.	805.2	830.9	882.3	6.2	3.1 ^b
Controls (D.L.)	701.7 ± 43.1	754.5 ± 45.0	832.7 ± 46.4	10.6 ± 2.2	7.0 ± 1.3
R.N.	643.2	755.1	842.1	11.5	14.8
Controls (R.N.)	715.8 ± 52.6	767.0 ± 35.1	875.3 ± 30.2	14.6 ± 2.7	7.1 ± 3.4

^a Standard errors are shown for the control data.

^b Below the lower 95% confidence interval for controls.

Table 4

Mean RTs (ms) and the interference effect (%) for the anterior cingulate patients and their respective age-matched control groups for the probability Stroop task

	High conflict (80% congruent)			Low conflict (20% congruent)		
	Congruent	Incongruent	Interference (%)	Congruent	Incongruent	Interference (%)
D.L.	622.3	728.3	17.0 ^a	637.4	742.1	16.4
Controls (D.L.)	562.7 ± 43.1	755.5 ± 45.7	35.3 ± 3.4	582.5 ± 53.3	678.6 ± 52.7	17.4 ± 1.5
R.N.	503.2	683.0	35.7	541.9	683.2	26.1 ^b
Controls (R.N.)	628.7 ± 28.5	852.7 ± 45.5	35.8 ± 4.2	660.2 ± 32.8	770.2 ± 28.8	17.4 ± 3.5

^a Below the 99% confidence interval for controls. Standard errors are shown for the control data.

^b Above the upper 95% confidence interval for controls.

Table 5

Error rates (%) for the anterior cingulate patients and their respective age-matched control groups for both conditions of the Stroop task^a

	High conflict		Low conflict	
	Congruent	Incongruent	Congruent	Incongruent
D.L.	0.7	5.6	2.7 ^b	7.6 ^b
Controls (D.L.)	0.0	13.5 ± 3.8	0.0	2.8 ± 0.6
R.N.	0.0	22.2 ^b	0.0	10.6 ^b
Controls (R.N.)	0.0	8.0 ± 3.0	0.0	2.0 ± 0.5

^a Standard errors are shown for the control data.

^b Above the upper 99% confidence interval for controls.

621 + 32, 80%: 596 + 26). The main effect of probability only approached significance for the subgroup analyses: controls for D.L. [$F(1, 7) = 4.49, P < 0.08$]; controls for R.N. [$F(1, 7) = 5.10, P < 0.06$]. Most importantly, condition interacted with probability [$F(1, 15) = 46.36, P < 0.0001$], so that larger interference effects were observed in the 80% congruent (high conflict) blocks compared to the 20% congruent (low conflict) blocks. This was true for both young [$F(1, 7) = 31.82, P < 0.001$] and older control groups [$F(1, 7) = 18.28, P < 0.005$].

The overall mean RT for D.L. (683 ms) fell within the 95% confidence interval of her control group (590–700 ms), as did her RTs in the four separate conditions (Table 4). The overall mean RT for R.N. (603 ms) was significantly faster than his control group ($P < 0.01$), as it was outside the lower limit of the 99% confidence interval for the older controls (range 665–791 ms). Interference was expressed as a percentage [(incongruent RT – congruent RT)/congruent RT × 100] to correct for this baseline RT difference. Collapsed across probability, D.L. showed significantly less interference (16.7%) than controls (26.3%; $P < 0.01$). Of critical interest is the finding that her interference effect was normal in the 20% congruent blocks (the low conflict condition), but significantly *smaller* than that of controls in the high conflict condition with 80% congruent trials ($P < 0.01$; see Table 4). The controls for D.L. showed a modulation in performance based on the probability of incongruent trials [$F(1, 7) = 30.61, P < 0.001$], but D.L. did not. Conversely, R.N.'s interference effect was well-matched to that of controls for the high conflict condition, but he showed a greater interference effect than controls in the 20% congruent blocks

($P < 0.05$). The controls for R.N. exhibited a significant difference between the two probability conditions [$F(1, 7) = 29.43, P < 0.001$]. R.N. did as well, but to a lesser extent.

The accuracy data (Table 5) revealed higher error rates for incongruent stimuli: controls for D.L. [$F(1, 7) = 15.11, P < 0.01$]; controls for R.N. [$F(1, 7) = 8.76, P < 0.05$], and in the high conflict (80% congruent) blocks: controls for D.L. [$F(1, 7) = 9.91, P < 0.05$]; controls for R.N. [$F(1, 7) = 5.15, P < 0.06$]. None of the controls made any errors in the congruent condition. R.N. showed higher error rates than controls for incongruent trials in both probability conditions ($P < 0.01$), as he was well outside the 99% confidence intervals for controls (Table 5). Similar to controls, however, he was less accurate in the high conflict than the low conflict blocks. D.L., conversely, was less accurate in the low conflict blocks relative to the high conflict blocks, unlike controls. Furthermore, she made significantly more errors than controls for both congruent and incongruent trials in the low conflict (20% congruent) blocks. She made fewer errors than controls for incongruent trials in the high conflict blocks, although this did not reach significance.

4. Discussion

Neuroimaging studies have implicated the ACC in many aspects of attention and cognition. Although the ACC is often treated as a unitary structure, ample evidence indicates that it is heterogeneous in its cytoarchitectonics and anatomical connectivity [16,59]. The purpose of the present study was to determine whether two ACC subregions are

necessary for intact performance in the Stroop color word interference task. Two patients with focal lesions in different subregions of the ACC exhibited distinctive performance profiles in three versions of the Stroop task, providing further support for topographic specificity of function within the human ACC. One patient showed overall slowing in some conditions but normal interference effects, the other showed an impairment manifest as increased errors for incongruent trials. These results, which can help to constrain interpretations of ACC hemodynamic fluctuations in imaging experiments, will be discussed below in the context of existing theories of ACC function.

4.1. Blocked condition

In the blocked trial session, D.L. was slower overall, her interference was in the normal range, and she showed a very low error rate. D.L. was especially slow for the congruent block relative to controls, possibly indicating a reduced degree of facilitation when word and color were in agreement. Our results are consistent with MacLeod [30,32], who has suggested that Stroop interference and facilitation are mediated by separate systems. For example, manipulations of expectations for color words [57] or practice in integrated compared to separated versions of the Stroop [31] differentially affect the degree of interference, but not facilitation. Rather than being the flip side of interference, in which congruity helps in color naming, the view of MacLeod and coworkers [30–32] holds that facilitation is actually due to the inadvertent reading of color words. This could be even more apparent (and deliberate) in the 100% congruent condition of the present experiment, which was modeled on the blocked designs of many Stroop imaging studies.

D.L.'s results are inconsistent with the executive control and conflict monitoring hypotheses, both of which would predict increased interference and/or increased errors in the incongruent block, given that prior PET studies [2,23,36] have observed Stroop-related ACC activity in the precise region damaged in D.L. (see Fig. 1). Since her lesion spares the purported vocal response areas [40,45], intact performance on conflict trials when giving spoken responses can be seen as consistent with the topographic motor control idea. Stronger evidence for this position was provided by the previous findings of a dissociation between manual and vocal responses in patient D.L. [56]. In that study, she showed greater interference than controls in a word-arrow Stroop task when the responses were button presses, but not when responses were spoken. Similarly, she was less accurate than controls in selective attention and divided attention tasks with manual responses, but not with vocal responses [56]. Our interpretation of this dissociation is that decision processes, perhaps mediated by lateral prefrontal cortex, were intact, but response selection processes within the ACC manual control area were compromised by the lesion. As recently reviewed by Paus [37], mid and rostral ACC regions have connections with cortical and subcortical areas involved in

vocalization. Anatomical projections from caudal ACC to motor cortex and spinal cord are a defining feature of the cingulate motor areas for manual response control.

The overall slowing in D.L. could also be seen as consistent with the non-specific arousal/anticipation idea. Traditionally considered to be part of the limbic system, the cingulate gyrus may affect global aspects of motor behavior, a role that is separate from the more specific motor control functions of the cingulate motor areas (reviewed in [19]). In fact, recent neuroimaging findings well outside the cognitive realm lend support to the notion that much of the supracallosal ACC subserves a general arousal function [39,53]. Robust activations of the ACC were observed while subjects viewed photographs of romantic partners [1] and during sexual arousal in male subjects [48], and these activations show considerable overlap with some of those observed during the Stroop and other cognitive tasks. As noted by Paus and coworkers [39], the ACC is a major target of catecholaminergic neurons. Administration of alpha-methyl-*para*-tyrosine (AMPT), a drug that reduces catecholamine synthesis, eliminated the task-related blood flow activations in ACC during reversal of a previously practiced response mapping [38]. One interpretation of this effect is that changes in cingulate blood flow are dependent on the dopaminergic and noradrenergic systems, both of which have dense projections to the human ACC [21]. A parallel possibility is that AMPT decreased the subjects' anxiety level. Other studies have also examined the relationship between catecholamine function and activity in the ACC. For instance, schizophrenic patients failed to activate the ACC in a verbal fluency test, but apomorphine (a dopamine agonist) reversed this deficit [17].

In contrast to D.L., patient R.N. was faster overall, his interference was on the high end but within the normal range, and he committed significantly more errors. This would please proponents of the executive control (selection for action) hypothesis, since it suggests that he has defects in focusing attention on performing the appropriate task when competing sources of information are present. Thus, the left dorsal region of the ACC can be seen as contributing to the process of maintaining attentional set, which is considered an executive control function [32,47].

Whether R.N.'s deficit provides support for the conflict monitoring idea is more ambiguous. R.N. made more errors in the 100% incongruent condition, where cognitive control should have been high. Subjects typically realize when a block of trials is completely predictable and thus become more focused on color naming in the 100% incongruent condition.¹ The ACC was not engaged by conflict under conditions of high cognitive control [7]. A higher error rate under these circumstances could indicate a failure to maintain the necessary degree of control, which would support the selection for action hypothesis. Instead of the ACC, the

¹ Note that the controls' accuracy was significantly higher for incongruent trials in the blocked condition compared to the mixed condition [$F(1, 11) = 9.35, P < 0.02$; see Table 2].

conflict monitoring scheme has implicated dorsolateral prefrontal cortex (PFC) in implementing cognitive control [29], which in this case is maintaining task set. This idea was based on event-related fMRI results from a switching version of the Stroop, in which subjects had to randomly switch between color naming and word reading on a trial by trial basis [29]. Left dorsolateral PFC (but not ACC) was activated by cue instructions to perform the more difficult color naming task. Conversely, the ACC (but not PFC) was activated by the presentation of incongruent words. The ACC may signal the PFC to provide top-down control during performance of the Stroop task [29]. However, it is still difficult to reconcile R.N.'s elevated error rate here with a defect in conflict monitoring. More recent theorizing from the conflict monitoring camp [4] regarding the interactions between ACC and PFC will be discussed again later.

Another possibility is that R.N.'s performance might vary based on response output modality. His lesion includes the vocal response area [40,45] but spares the manual response area as defined by Paus [37,40]. Since the present Stroop task required spoken responses, R.N.'s deficit might be specific to giving vocal output. Crosson and coworkers [12] have implicated left paracingulate cortex (which was damaged in R.N.) in verbal response selection, based on an fMRI study of covert word generation. Other results from R.N. [55], however, demonstrated that he did not show a dissociation in performance between manual and vocal responses, although definitive evidence on this issue will await the results of future experiments in a larger group of patients.

4.2. Mixed trial condition

The patients showed comparable patterns of performance in the blocked and mixed conditions. D.L. was again slower overall and very accurate in her responses. She showed interference in the normal range but significantly *less* facilitation than controls, providing more direct support for the idea that facilitation and interference are mediated by separate mechanisms [32,57]. A similar effect was observed in the cingulotomy patient of Janer and Pardo [24], who was slower for congruent blocks after her surgery but showed no increase in RT for incongruent blocks. One possibility is that post-surgically, the patient engaged in accidental word reading (or deliberate "cheating") to a lesser extent and was thus (ironically) *more* focused on color naming. Also, note that enhanced ACC activity has been observed in comparisons of congruent versus neutral words in the Stroop task (e.g. [8]; see point no.7 in Fig. 1), with greater activity in the congruent relative to neutral condition (see also [2]). This, perhaps, can be seen as a correlate of facilitation, because faster RTs were observed on congruent compared to neutral trials in these studies [2,8]. Another possibility is that the ACC directs attention to the appropriate source of information regardless of conflict [32], since greater ACC activity has been elicited to both congruent and incongruent color words in comparison to neutral stimuli.

Similar to the blocked condition, the results of R.N. were in marked contrast to D.L. Although he showed normal interference, his error rate was once again elevated for incongruent trials. Since he was unable to suppress the automatic tendency to read the word, the left dorsal-mid ACC region damaged in R.N. appears to be important for inhibiting pre-potent responses in the Stroop color word task. On the other hand, his facilitation was within the range of his age-matched controls (albeit on the high end; but also note that facilitation was quite variable for the older adults). Word reading on congruent trials is likely to be more inadvertent and (less of a deliberate strategy) in the mixed condition than in the blocked condition, given the slower RTs in the former condition. A very interesting comparison between the two patients is not only in their susceptibility to interference, but also in their levels of facilitation. D.L. showed clear evidence for a dissociation: a reduction in facilitation but no undue ill effects for conflict, while R.N. appeared to skew his responses towards word reading, resulting in a greater error rate for incongruent trials and a tendency towards greater facilitation in congruent trials compared to neutral trials. So, then, does R.N. show a defect in conflict monitoring? Perhaps not, because he failed to maintain the appropriate task set and responded to the conflict by using a too-liberal strategy, not by showing a greater interference effect per se. This almost seems to be executive in nature. We examine this further in the next section.

4.3. Stroop probability manipulation

According to Carter et al. [7], in the 80% congruent (or high conflict) blocks, when cognitive control was supposedly low), the ACC was engaged for the rare incongruent trials. This fMRI finding would predict that patients D.L. and R.N. would exhibit signs of excessive susceptibility to interference in high conflict blocks, indicative of a deficit in conflict monitoring. Given the precise location of the ACC activation peak [7] in the vicinity of R.N.'s lesion (see point no.14 in Fig. 1), he should be especially prone to exhibit a deficit in this condition. In fact, R.N. showed overall RTs and interference within control levels, but once again his error rate was quite elevated. This does indeed provide some support for the conflict monitoring idea, but note that he was also less accurate for incongruent trials in all conditions.

Unlike for Experiment 1 (the blocked versus mixed trial conditions), which was run 4 years earlier, D.L. was matched to controls for overall RTs in the current Stroop task. Periodic participation in cognitive experiments over this time interval likely resulted in an improvement in her vocal response times. In common with her earlier findings, she showed a trend for fewer errors as well as significantly *less* interference than controls in the high conflict condition, which does not support the notion that her damaged ACC renders her unable to monitor for conflict.

In contrast to the high conflict condition, the ACC was not activated by the frequent incongruent trials in the low

conflict condition (20% congruent trials) of Carter et al. [7], when cognitive control was supposedly high. For these investigators, the ACC does not implement strategic processes that are engaged here to reduce conflict; for the executive control model of Posner and collaborators [5,46,47], it would do so. Another claim of the former researchers was that the ACC should *not* be activated for incongruent trials in the low conflict blocks, because cognitive control was strongly engaged to reduce the effects of conflict. Note, however, that these trials still resulted in an interference effect, meaning that conflict would still have to be detected and monitored. Under this logic, the incongruent words in the low conflict condition might have been expected to show an intermediate level of activation, but this was not the case [7]. Furthermore, MacLeod and MacDonald [32] suggested that cognitive control was not adequately manipulated in this study, since subjects' error rates were very low and did not differ between high conflict and low conflict blocks.

To briefly summarize the patients' results in the low conflict condition, both D.L. and R.N. showed worse performance than controls (selectively so for D.L., who was quite intact in all other conditions) when executive control processes were engaged, so this can be seen as providing some

support for the selection for action view. Specifically, D.L. showed normal interference but a higher error rate, which was quite rare for her. This might suggest that she was more prone to make word reading errors on incongruent trials when conflict was lower and a greater degree of cognitive control was required. R.N. committed more errors on incongruent trials than controls, consistent with his results in the previous experiments. He also showed greater interference in this condition.

On the basis of the combined results of the Stroop probability manipulation, we can say one of two things about executive control processes in D.L.: (1) either she exerts a very high degree of control in the mostly congruent blocks to reduce interference, and this is her strategy for dealing with high levels of conflict; or (2) since she shows the exact same interference rate for both high and low conflict conditions (unlike controls), she *is* deficient in strategically modulating her performance when the probabilities change. A block by block sub-analysis of RTs examined whether D.L. was capable of altering her pattern of responses with changes in stimulus probability (see Fig. 3a and b). Interestingly, D.L. started out showing her lowest interference in the first block, when she was especially slow for congruent

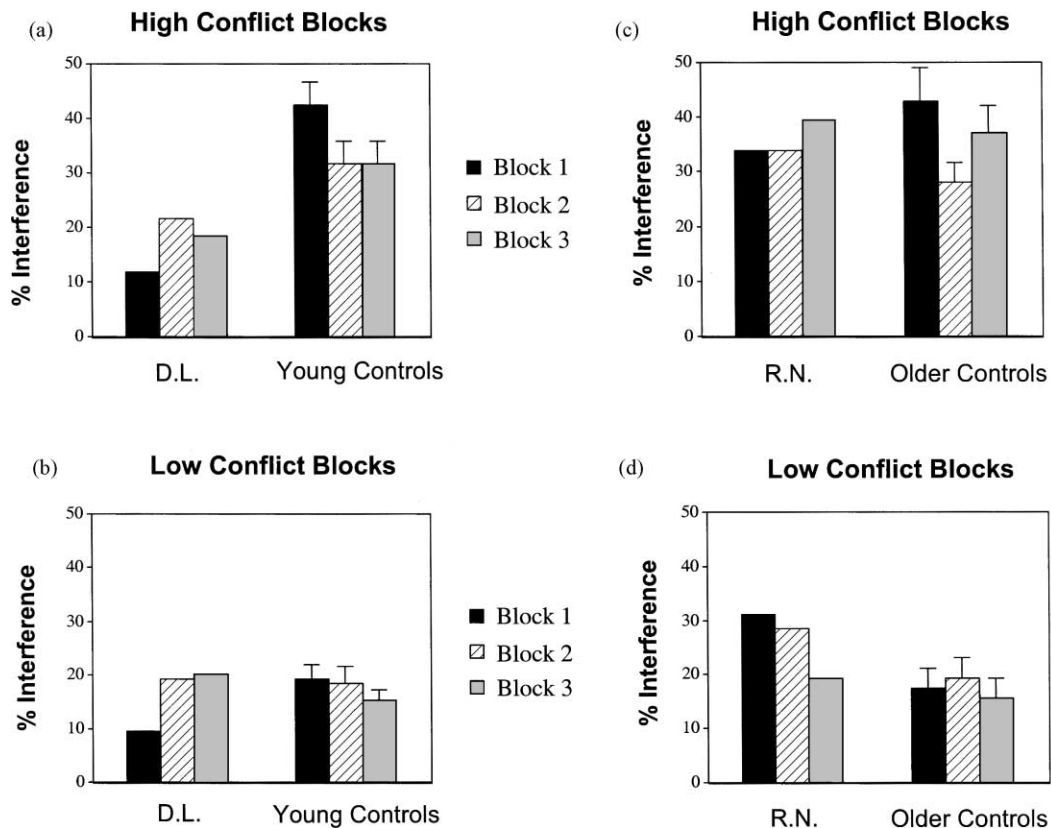


Fig. 3. Sub-analysis of the interference effect (percent interference) shown by block for patient D.L. and her age-matched controls (a, b) and for patient R.N. and his age-matched controls (c, d). In the high conflict condition, controls showed the greatest amount of interference for the first block [$F(2, 28) = 6.97, P < 0.01$], but this was not true of D.L. or of R.N., to a lesser extent. In the low conflict condition, interference across blocks was more stable in controls [$F(2, 28) = 1.33, P > 0.28$]. D.L. again showed smaller interference in the first relative to the subsequent blocks, while R.N.'s interference declined across blocks.

trials, then interference became greater in the second and third blocks when she sped up. This was the opposite of controls, who started out showing very high interference in the first block of the high conflict condition, then displayed a decrease once they got used to the rare incongruent trials. Thus, it does not appear that D.L. is completely incapable of modulating her performance based on condition. Hence, one interpretation is that D.L. adopted a conservative compensatory strategy (related to her low levels of facilitation) to reduce her susceptibility to conflict in demanding situations involving vocal response selection. Another possibility is raised by a single data point: her RTs on incongruent trials in the high conflict condition were actually *faster* than controls (by 28 ms) and slightly faster than her incongruent RTs in the low conflict blocks (by 14 ms).² Therefore, she appears to be more focused on color naming than controls and less distracted by incongruence when cognitive control is typically less engaged.

R.N. showed clear signs of modulating his performance based on probability, but to a lesser extent than his age-matched group (Fig. 3c and d). He exhibited greater interference than controls in the low conflict condition but was matched to the older adults in the high conflict blocks. This might be more reflective of a deficit in conflict monitoring, but it is quite difficult to separate this cognitive function from the ability to apply an effective strategy to reduce the negative effects of conflict. Parsing the role of the ACC in strategic versus evaluative executive processes on the basis of functional neuroimaging results or even the present lesion findings appears to be a challenging enterprise, as is predicting the consequences of ACC lesions on the basis of the conflict monitoring model. If the ACC is not able to effectively detect conflict, it cannot signal the dorsolateral PFC to implement the appropriate strategy. A more recent version of the theory proposes that "...ACC activation leads to shifts in cognitive control" ([4], p. 36) and predicts that "...acute lesions to the ACC should reduce ... frequency effects in the Stroop task..." ([4], p. 36). Actually, then, it *does* appear that the ACC is needed for shifts in strategy according to this model.

The lines between the conflict monitoring and selection for action camps are blurred, at least for the moment. This highlights the importance of placing the present lesion results in a larger context of frontal lobe function. In a meta-analysis of 107 PET studies, Koski and Paus [25] noted co-activation of dorsal ACC (area 32) and middle frontal gyrus. These two regions were co-activated to an even greater extent with increasing task difficulty. Both are likely to be critical parts of a network that contribute to performance in complex tasks such as the Stroop. In parallel distributed processing accounts of the Stroop [9],

simultaneous activation of conflicting word and color information can produce interference at multiple points of intersection. An important observation is that bilateral inferior frontal cortex (Brodmann areas 44/45) was activated at an *earlier* point in time than the ACC (during scan 2 rather than scan 3) in the high conflict condition of the Stroop [7]. One question that arises is, how can the ACC be detecting response conflict if the processes responsive to selection demands (attributed to the inferior frontal cortex) have already occurred before the ACC is engaged? The ACC can still be performing a monitoring function, but the response conflict that ultimately results in a longer RT for a given trial may actually be detected earlier in time. Electrophysiological recording techniques, with their superior temporal resolution, would be most useful in addressing these questions of directionality and time-course [20,22,51,60]. In fact, preliminary evidence suggests that R.N. shows an *enhanced* event-related potential (ERP) signal in response to incongruent stimuli [51]. His large conflict-related ERP indicates that the conflict must be detected elsewhere, so the damaged ACC cannot be a neural generator of the component. This observation, combined with his exaggerated behavioral interference effects, suggest the locus of the deficit is in the implementation of executive control processes that reduce the negative effects of conflict [47].

In conclusion, these experiments yielded neuropsychological evidence for topographic specificity of function within the human ACC. The two patients showed a dissociation in their response to Stroop interference. Damage to left mid-dorsal ACC resulted in a greater error rate on incongruent trials, and thus an impairment in the ability to inhibit the pre-potent response and maintain the relevant task set. In contrast, damage to right mid-caudal ACC was associated with normal levels of interference and mostly high levels of accuracy in the task, which required vocal responses. The overall slowing of D.L. in the blocked and mixed trial conditions suggests that the gyral surface of the mid-ACC may subserve a general arousal function [19,56], while her reduced levels of facilitation indicate that separate regions of the ACC may contribute to Stroop interference and facilitation effects. Whether any asymmetry exists between the left and right hemispheres of the ACC is currently unknown, and not an easily investigated issue. Focal lesions of the ACC are quite rare, cingulotomies are typically bilateral, and functional imaging activations are often bilateral (e.g. [26]) or very close to midline (e.g. [7]) and hence not easy to assign to left or right hemisphere. Future studies that examine functional connectivity and the temporal dynamics of ACC activity will be most informative.

Acknowledgements

This work was supported by Grant DC03424 from the National Institute on Deafness and Other Communication Disorders, NS17778 from the National Institute of Neurological

² Note that her age-matched controls were 77 ms *slower* for the same comparison, i.e. slower for incongruent trials in the high conflict compared to the low conflict blocks. D.L.'s 28 ms advantage over controls was not significant, but her pattern of performance was informative nonetheless.

Disorders and Stroke, and 98-47 CNS-QUA.05 from the James S. McDonnell Foundation. A preliminary version of Experiment 1 was presented at the 1997 meeting of the Cognitive Neuroscience Society. We thank Bob Knight and Bob Rafal for patient referrals, Victoria Stevens and Caitlin Roxby for their assistance, and And Turken for helpful discussions.

References

- [1] Bartels A, Zeki S. The neural basis of romantic love. *NeuroReport* 2000;11:3829–34.
- [2] Bench CJ, Frith CD, Grasby PM, Friston KJ, Paulesu E, Frackowiak RS, et al. Investigations of the functional anatomy of attention using the Stroop test. *Neuropsychologia* 1993;31:907–22.
- [3] Benkelfat C, Bradwejn J, Meyer E, Ellenbogen M, Milot S, Gjedde A, et al. Functional neuroanatomy of CCK4-induced anxiety in normal healthy volunteers. *American Journal of Psychiatry* 1995;152:1180–4.
- [4] Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD. Conflict monitoring and cognitive control. *Psychological Review*, in press.
- [5] Bush G, Luu P, Posner MI. Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences* 2000;4:215–22.
- [6] Bush G, Whalen PJ, Rosen BR, Jenike MA, McInerney SC, Rauch SL, et al. The counting Stroop: an interference task specialized for functional neuroimaging: validation study with functional MRI. *Human Brain Mapping* 1998;6:270–82.
- [7] Carter CS, Macdonald AM, Botvinick M, Ross LL, Stenger VA, Noll D, et al. Parsing executive processes: strategic versus evaluative functions of the anterior cingulate cortex. *Proceedings of the National Academy of Sciences* 2000;97:1944–8.
- [8] Carter CS, Mintun M, Cohen JD. Interference and facilitation effects during selective attention: an H₂¹⁵O PET study of stroop task performance. *Neuroimage* 1995;2:264–72.
- [9] Cohen JD, Dunbar K, McClelland JL. On the control of automatic processes: a parallel distributed processing model of the Stroop effect. *Psychological Review* 1990;97:332–61.
- [10] Cohen RA, Kaplan RF, Zuffante P, Moser DJ, Jenkins MA, Salloway S, et al. Alteration of intention and self-initiated action associated with bilateral anterior cingulotomy. *Journal of Neuropsychiatry and Clinical Neurosciences* 1999;11:444–53.
- [11] Corbetta M, Miezin FM, Dobmeyer S, Shulman GL, Petersen SE. Selective and divided attention during visual discriminations of shape, color, and speed: functional anatomy by positron emission tomography. *Journal of Neuroscience* 1991;11:2383–402.
- [12] Crosson B, Sadek JR, Bobholz JA, Gökçay D, Mohr CM, Leonard CM, et al. Activity in the paracingulate and cingulate sulci during word generation: an fMRI study of functional anatomy. *Cerebral Cortex* 1999;9:307–16.
- [13] Danckert J, Maruff P, Ymer C, Kinsella G, Yucel M, de Graaff S, et al. Goal-directed selective attention and response competition monitoring: evidence from unilateral parietal and anterior cingulate lesions. *Neuropsychology* 2000;14:16–28.
- [14] Davis KD, Taylor SJ, Crawley AP, Wood ML, Mikulis DJ. Functional MRI of pain- and attention-related activations in the human cingulate cortex. *Journal of Neurophysiology* 1997;77:3370–80.
- [15] Derbyshire SW, Vogt BA, Jones AK. Pain and Stroop interference tasks activate separate processing modules in anterior cingulate cortex. *Experimental Brain Research* 1998;18:52–60.
- [16] Devinsky O, Morrell MJ, Vogt BA. Contributions of anterior cingulate cortex to behaviour. *Brain* 1995;118:279–306.
- [17] Dolan RJ, Fletcher P, Frith CD, Friston KJ, Frackowiak RSJ, Grasby PM, et al. Dopaminergic modulation of impaired cognitive activation in the anterior cingulate cortex in schizophrenia. *Nature* 1995;378:180–2.
- [18] Downar J, Crawley AP, Mikulis DJ, Davis KD. A multimodal cortical network for the detection of changes in the sensory environment. *Nature Neuroscience* 2000;3:277–83.
- [19] Dum RP, Strick PL. Cingulate motor areas. In: Vogt BA, Gabriel M, editors. *Neurobiology of Cingulate Cortex and Limbic Thalamus: A Comprehensive Handbook*. Boston: Birkhauser, 1993. p. 415–41.
- [20] Falkenstein M, Hoormann J, Christ S, Hohnsbein J. ERP components on reaction errors and their functional significance: a tutorial. *Biological Psychology* 2000;51:87–107.
- [21] Gaspar P, Berger B, Febvret A, Vigny A, Henry JP. Catecholamine innervation of the human cerebral cortex as revealed by comparative immunohistochemistry of tyrosine hydroxylase and dopamine-beta-hydroxylase. *Journal of Comparative Neurology* 1989;279:249–71.
- [22] Gehring WJ, Knight RT. Prefrontal-cingulate interactions in action monitoring. *Nature Neuroscience* 2000;3:516–20.
- [23] George MS, Ketter TA, Parekh PI, Rosinsky N, Ring H, Casey BJ, et al. Post RM. Regional brain activity when selecting response despite interference: an H₂¹⁵O PET study of the Stroop and an emotional Stroop. *Human Brain Mapping* 1994;1:194–209.
- [24] Janer KW, Pardo JV. Deficits in selective attention following bilateral anterior cingulotomy. *Journal of Cognitive Neuroscience* 1991;3:231–41.
- [25] Koski L, Paus T. Functional connectivity of the anterior cingulate cortex within the human frontal lobe: a brain-mapping meta-analysis. *Experimental Brain Research* 2000;133:55–65.
- [26] Leung H-C, Skudlarski P, Gatenby JC, Peterson BS, Gore JC. An event-related functional MRI study of the Stroop color word interference task. *Cerebral Cortex* 2000;10:552–60.
- [27] Lezak MD. *Neuropsychological Assessment*, Third Edition. New York: Oxford University Press, 1995.
- [28] Logan GD. Attention and automaticity in Stroop and priming tasks: theory and data. *Cognitive Psychology* 1980;12:523–53.
- [29] MacDonald III AW, Cohen JD, Stenger VA, Carter CS. Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science* 2000;288:1835–8.
- [30] MacLeod CM. Half a century of research on the Stroop effect: an integrative review. *Psychological Bulletin* 1991;109:163–203.
- [31] MacLeod CM. Training on integrated versus separated Stroop tasks: the progression of interference and facilitation. *Memory and Cognition* 1998;26:201–11.
- [32] MacLeod CM, MacDonald PA. Interdimensional interference in the Stroop effect: uncovering the cognitive and neural anatomy of attention. *Trends in Cognitive Sciences* 2000;4:383–91.
- [33] Murtha S, Chertkow H, Beauregard M, Dixon R, Evans A. Anticipation causes increased blood flow to the anterior cingulate. *Human Brain Mapping* 1996;4:103–12.
- [34] Norman, DA, Shallice T. Attention to action: willed and automatic control of behavior. In: Schwartz GE, Shapiro D, editors. *Consciousness and Self-regulation*, vol. 4. New York: Plenum Press, 1986.
- [35] Ochsner KN, Kosslyn SM, Cosgrove GR, Cassem EH, Price BH, Nierenberg AA, et al. Deficits in visual cognition and attention following bilateral anterior cingulotomy. *Neuropsychologia* 2001;39:219–30.
- [36] Pardo JV, Pardo PJ, Janer KW, Raichle ME. The anterior cingulate cortex mediates processing selection in the Stroop attentional conflict paradigm. *Proceedings of the National Academy of Sciences* 1990;87:256–9.
- [37] Paus T. Primate anterior cingulate cortex: where motor control, drive and cognition interface. *Nature Reviews Neuroscience* 2001;2:417–24.
- [38] Paus T, Benkelfat C, Cumming P, Evans AC, Gjedde A, Petrides M, et al. Alpha-methyl-*para*-tyrosine (AMPT) attenuates task-specific CBF changes in human anterior cingulate cortex. *Society for Neuroscience Abstract* 1994;20:353.

- [39] Paus T, Koski L, Caramanos Z, Westbury C. Regional differences in the effects of task difficulty and motor output on blood flow response in the human anterior cingulate cortex: a review of 107 PET activation studies. *NeuroReport* 1998;9:R37–47.
- [40] Paus T, Petrides M, Evans AC, Meyer E. Role of the human anterior cingulate cortex in the control of oculomotor, manual, and speech responses: a positron emission tomography study. *Journal of Neurophysiology* 1993;70:453–69.
- [41] Perret E. The left frontal lobe of man and the suppression of habitual responses in verbal categorical behaviour. *Neuropsychologia* 1974;12:323–30.
- [42] Petersen SE, Fox PT, Posner MI, Mintun M, Raichle ME. Positron emission tomographic studies of the cortical anatomy of single-word processing. *Nature* 1988;331:585–9.
- [43] Peterson BS, Skudlarski P, Gatenby JC, Zhang H, Anderson AW, Gore JC, et al. An fMRI study of Stroop word-color interference: evidence for cingulate subregions subserving multiple distributed attentional systems. *Biological Psychiatry* 1999;45:1237–58.
- [44] Petit L, Courtney MC, Ungerleider LG, Haxby JV. Sustained activity in the medial wall during working memory delays. *Journal of Neuroscience* 1998;18:9429–37.
- [45] Picard N, Strick PL. Motor areas of the medial wall: a review of their location and functional activation. *Cerebral Cortex* 1996;6:342–53.
- [46] Posner MI. Attention: the mechanisms of consciousness. *Proceedings of the National Academy of Sciences* 1994;91:7398–403.
- [47] Posner MI, DiGirolamo GJ. Executive attention: conflict, target detection, and cognitive control. In: Parasuraman R, editor. *The Attentive Brain*. Cambridge, MA: MIT Press, 1998. p. 401–23.
- [48] Redouté J, Stoléru S, Grégoire M-C, Costes N, Cinotti L, Lavenne F, et al. Brain processing of visual sexual stimuli in human males. *Human Brain Mapping* 2000;11:162–77.
- [49] Stroop JR. Studies of interference in serial verbal reactions. *Journal of Experimental Psychology* 1935;18:643–62.
- [50] Stuss DT, Floden D, Alexander MP, Levine B, Katz D. Stroop performance in focal lesion patients: dissociation of processes and frontal lobe lesion location. *Neuropsychologia* 2001;39:771–86.
- [51] Swick D, Turken AU, Larsen J, Roxby C, Kopelovich JCS, Jovanovic J, et al. Anterior cingulate cortex: error monitoring or conflict monitoring? *Cognitive Neuroscience Abstract* 2001;8:72.
- [52] Talairach J, Tournoux P. *Co-planar Stereotaxic Atlas of the Human Brain*. Stuttgart: Thieme, 1988.
- [53] Taylor SF, Kornblum S, Lauber EJ, Minoshima S, Koeppe RA. Isolation of specific interference processing in the Stroop task: PET activation studies. *NeuroImage* 1997;6:81–92.
- [54] Trenerry MR, Crosson B, DeBoe J, Leber WR. *The Stroop Neuropsychological Screening Test*. In: *Psychological Assessment Resources*, Odessa, FL, 1989.
- [55] Turken AU, Swick D. Is response selection in the anterior cingulate cortex specific to output modality? *Society for Neuroscience Abstracts* 1998;24:1682.
- [56] Turken AU, Swick D. Response selection in the human anterior cingulate cortex. *Nature Neuroscience* 1999;2:920–4.
- [57] Tzelgov J, Henik A, Berger J. Controlling Stroop effects by manipulating expectations for color words. *Memory and Cognition* 1992;20:727–35.
- [58] Vendrell P, Junque C, Pujol J, Jurado MA, Molet J, Grafman J, et al. The role of prefrontal regions in the Stroop task. *Neuropsychologia* 1995;33:341–52.
- [59] Vogt BA, Finch DM, Olson CR. Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions. *Cerebral Cortex* 1992;2:435–43.
- [60] West R, Alain C. Effects of task context and fluctuations of attention on neural activity supporting performance of the Stroop task. *Brain Research* 2000;873:102–11.