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Cognitive functioning after medial frontal lobe damage including the anterior cingulate cortex: A preliminary investigation

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Abstract

Two patients with medial frontal lobe damage involving the anterior cingulate cortex (ACC) performed a range of cognitive tasks, including tests of executive function and anterior attention. Both patients lesions extended beyond the ACC, therefore caution needs to be exerted in ascribing observed deficits to the ACC alone. Patient performance was compared with age and education matched healthy controls. Both patients showed intact intellectual, memory, and language abilities. No clear-cut abnormalities were noted in visuoperceptual functions. Speed of information processing was mildly reduced only in Patient 2 (bilateral ACC lesion). The patients demonstrated weak or impaired performance only on selective executive function tests. Performance on anterior attention tasks was satisfactory. We tentatively suggest that our findings are inconsistent with anterior attention theories of ACC function based on neuroimaging findings. We propose that the data may imply that the ACC does not have a central role in cognition. We speculate that our findings may be compatible with the view that the ACC integrates cognitive processing with autonomic functioning to guide behaviour.

Keywords: Anterior cingulate cortex; Cognition

1. Introduction

Extensive neuroimaging research has demonstrated a role of the anterior cingulate cortex (ACC) in cognitive, emotional, and autonomic functions. Previous research has identified a distinction between dorsal and ventral ACC mediating cognitive and affective functions, respectively (Bush, Luu, & Posner, 2000; Devinsky, Morrell, & Vogt, 1995). The specific nature of the ACC's role in cognition is under debate. Few studies have investigated cognitive functioning in patients with relatively circumscribed lesions of the ACC.

2. Neuroimaging studies

Numerous theories of the cognitive role of the ACC have been proposed on the basis of functional neuroimaging findings. For example, Paus and colleagues have suggested that ACC activation reflects task difficulty (Paus, Koski, Caramanos, & Westbury, 1998). Others have argued that the ACC has a top down conflict resolution role in selection for action and is activated when the 'Supervisory Attentional System' is required (Posner & Digirolamo, 1998; Posner & Petersen, 1990; Shallice, 2002). An alternative view offered by Carter and colleagues emphasises the ACC's role in conflict monitoring (Botvinick, Cohen, & Carter, 2004; Carter et al., 2000; Macdonald, Cohen, Stenger, & Carter, 2000), principally utilising the Stroop task. Some studies have suggested that the ACC mediates

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action outcome evaluation and reward based action selection (e.g., Bush et al., 2002). Furthermore, Critchley, Corfield, Chandler, Mathias, and Dolan (2000), Critchley, Mathias, and Dolan (2001), and Critchley et al. (2003) have proposed that the ACC is necessary for the integration of autonomic responses with behavioural effort and does not play a primary role in cognition. Interestingly, a recent study of ACC/paracingulate morphology found that the more common leftward paracingulate sulcus asymmetry was associated with better performance across executive tasks. They suggested that the leftward pattern of folding is associated with a non-specific performance advantage on cognitively demanding executive function tasks, possibly due to differences in functional interactions between AC/paracingulate cortex and connected frontal regions (Fornito et al., 2004).

3. Psychophysiological and computational modelling studies

Holroyd and colleagues have published a number of interesting studies reporting psychophysiological and computational modelling data (Holroyd & Coles, 2002; Holroyd, Nieuwenhuis, Yeung, & Cohen, 2003; Miltner et al., 2003; Nieuwenhuis, Holroyd, Mol, & Coles, 2004a; Nieuwenhuis, Yeung, Holroyd, Schurger, & Cohen, 2004b). These studies have focused on a component of human electrical brain activity ("error-related negativity," ERN or NE) and its magnetic equivalent (the mERN) that is associated with error-processing. This activity has been thought to be generated within the ACC. It is proposed that the mesencephalic dopamine system conveys to the ACC a negative reward prediction error-signal when ongoing events are suddenly worse than expected. The ACC then generates the ERN and modifies performance on the task at hand. These findings endorse the error-detection account of ACC function implicit in the ERN model of Holroyd and colleagues (Pailing & Segalowitz, 2004). Interestingly, this account has been challenged by the conflict monitoring theory which claims that the ERN reflects ACC activity in the detection of response conflict (Gehring & Fencsik, 2001; Van Veen & Carter, 2002). Moreover, Van Veen, Holroyd, Cohen, Stenger, and Carter (2004) failed to find evidence in favour of the ACCs involvement in error-detection. This suggests that the ACCs exact role in cognition remains debatable and needs to be informed by lesion studies.

4. Lesion studies

There is a paucity of research investigating neuropsychological functioning in patients with ACC lesions. The current literature comprises only single case or small-scaled studies and provides equivocal support for the ACCs role in cognition, specifically executive abilities. Several studies have investigated patients who underwent bilateral anterior cingulotomy as a psychosurgical technique for relief of chronic pain, intractable obsessive-compulsive disorder (OCD) and/or major depression. These studies have provided inconsistent results, with some showing no cognitive deficits (Corkin, 1979), and others demonstrating deficits on tasks assessing visuospatial skills (e.g., Damasio & Van Hoesen, 1986; Ochsner et al., 2001; Vilkki, 1981) or attention (e.g., Cohen, Kaplan, Moser, Jenkins, & Wilkinson, 1999; Janer & Pardo, 1991; LaPlane, Degos, Baulac, & Gray, 1981). These deficits typically improve or resolve within weeks or months post surgery (Cohen et al., 1999; Janer & Pardo, 1991).

Swick and colleagues (Swick & Jovanovic, 2002; Swick & Turken, 2002; Turken & Swick, 1999) have studied two patients, one with a unilateral right mid caudal ACC lesion (DL) and the other with a left rostral to mid dorsal ACC lesion (RN). Three variations of the Stroop task were administered to both patients and revealed a dissociation in their response to Stroop performance. Patient DL performed with a high level of accuracy on interference trials but was slow in responding. In contrast, Patient RN was impaired in inhibiting dominant responses, with increased susceptibility to interference in high conflict blocks (Swick & Jovanovic, 2002). The authors concluded that these findings suggest topographic specificity of function within the ACC, with the mid-ACC subserving a general arousal function and separate regions mediating executive control processes that reduce the effects of conflict, consistent with Carter and colleagues' emphasis on the ACCs role in conflict monitoring (Swick & Jovanovic, 2002). The notion of functional specialisation within the ACC is supported by an earlier study, which documented deficits in executive tasks when using manual but not vocal responses in patient DL (Turken & Swick, 1999).

Stemmer and colleagues (Stemmer, Segalowitz, Witzke, & Schoenle, 2003) described five patients with a ruptured aneurysm of the ACoA who subsequently underwent clipping. All patients had lesions encompassing the anterior communicating artery and thus including the ACC, the medial prefrontal cortex and other related subcortical areas. These patients were cognitively impaired and not able to produce ERN, yet they were able to detect their errors on an experimental task. This result suggests that although the ACC is involved in the generation of ERN, the circuits outside the ACC region may support the error-detection itself. A recent study of four patients with ACC damage to regions similar to those implicated in cognitive control by imaging studies have been published. This study reported intact performance on two tasks of cognitive control, the Stroop test and a go–no go task (Fellows & Farah, 2005). On the basis of these results the authors suggest that the ACC does not necessarily play a role in cognitive control.

5. Aims

The aim of the present study was to investigate the role of the ACC in cognitive functioning. Two patients with medial frontal lobe lesions, primarily involving the ACC, completed a range of neuropsychological tasks, including tests of executive function and anterior attention which have been used in previous neuroimaging studies (e.g., Carter et al., 1998). Previous studies have reported impaired autonomic arousal in both patients (Critchley et al., 2003), and impaired Theory of Mind functioning in Patient 2 (Baird, Dewar, Critchley, Dolan, & Shallice, 2005).

6. Methods

6.1. Patients

Two patients were investigated in the Neuropsychology Department of the National Hospital for Neurology and Neurosurgery.

Patient 1 is a 28-year-old, left-handed female who had completed 15 years of education, including five years at university level. She underwent removal of a right prefrontal glioma. MRI revealed a unilateral right ACC lesion extending anteriorly toward the frontal pole (BA 32, 24), posteriorly to mid cingulate (BA 24) and inferiorly to involve the genual region (BA 32, 25, see Fig. 1A). There was also involvement of the anterior corpus callosum, anterior superior frontal gyrus, some of the supplementary motor area (medial BA 8) and some frontal white matter.

Patient 2 is a 39-year-old right-handed male who had completed 13 years of education. He underwent partial resection of an oligodendroglioma. The tumour involved the ACC bilaterally, including all of the left ACC (BA 32, 24) and spread diffusely through the left medial and lateral superior frontal gyri, right medial gyrus (BA 8), the gyrus rectus and orbitofrontal cortex (BA 11, 12), the medial thalamus and hypothalamus, insula cortex (BA 44), parahippocampal gyrus and left hippocampus. Diffuse changes were also noted in the superior temporal gyrus (BA 22) and anterior temporal pole (BA 38). On the right, the lesion involved genual and dorsal ACC (BA 32, 24), orbitofrontal cortex (BA 11), the subcallosal gyrus (BA 25) and anterior insula cortex (BA 44). While these changes were apparent on close radiological examination of MR images, Fig. 1B highlights the location of surgical debulking from a left dorsal approach.

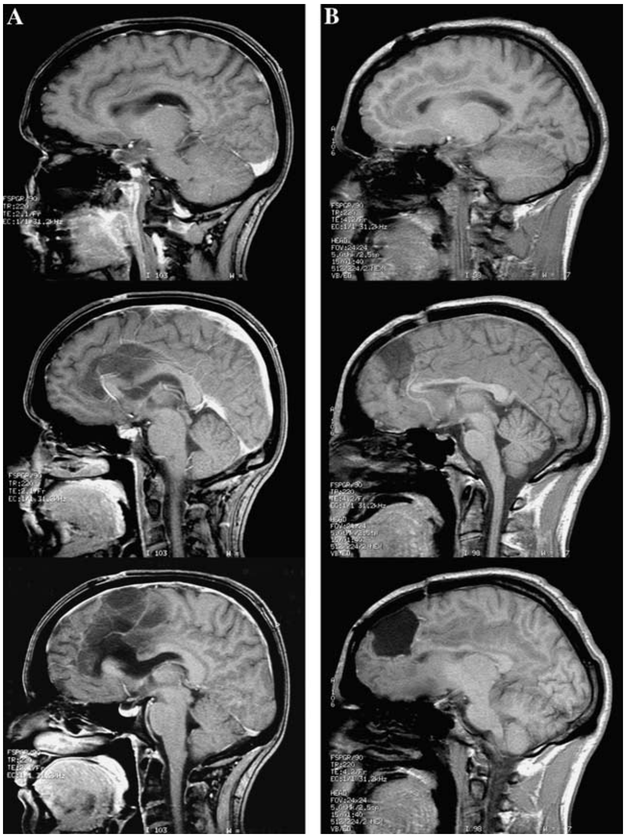

Fig. 1. MRI of lesion of (A) Patient 1, including unilateral right ACC lesion, and (B) Patient 2, including bilateral ACC lesion. For detailed description of lesions see text.

6.2. Controls

Patient performance on tests of intellect, memory, language, visuoperception, speed of information processing, and executive functions was compared with well-established norms. Performance on the Sustained Attention to Response Test (SART) was compared to eight age and education matched controls. Performance of Patient 1 on the Continuous Performance Test (AX-CPT) was compared with five age and education matched controls.

6.3. Measures

Neuropsychological assessment utilised measures of intellectual ability (Wechsler Adult Intelligence Scale [WAIS] Revised [WAIS-R]; Wechsler, 1955), memory (Recognition Memory Tests for words and faces; Warrington, 1984), nominal skills (Graded Naming Test; McKenna & Warrington, 1980), visuoperceptual skills (Object Decision subtest of the Visual Object and Space Perception Battery [VOSP]; Warrington & James, 1991), and speed of information processing (Digit Symbol Modalities test, Smith, 1982; Trail Making Test Part A; Army Individual Test Battery, 1944). Frontal executive tests comprised the Modified Card Sorting Test (Grant & Berg, 1981), Proverb interpretation, Stroop colour/word test (Trenerry, Crossen, DeBoe, & Leber, 1989), Trail Making Test Part B (Army Individual Test Battery, 1944), verbal fluency/controlled oral word association test (Benton, Hamsher, & Sivan, 1976) Cognitive Estimates Test (Shallice & Evans, 1978), Hayling and Brixton Tests (Burgess & Shallice, 1997, see Appendix A for a description of these tests), and the Six Elements Test from the Behavioural Assessment of the Dysexecutive Syndrome (BADS, Wilson, Alderman, Burgess, Emslie, & Evans, 1996, see Appendix A for a description of this test).

The SART (Robertson, Manly, Andrade, Baddeley, & Yiend, 1997) was administered to both patients. Patients were instructed to name digits on a computer screen except for a target. Two blocks of digits were presented following a nine trial practice block. Errors and reaction times of correct responses were recorded. Two errors were possible: commission errors, when a target numeral was named and omission errors, when a non-target numeral was not named.

A version of the Continuous Performance Test (AX-CPT, Carter et al., 1998) was administered to Patient 1. Sequences of letters were presented on a computer screen in cue-probe pairs. She was instructed to press a left button if she saw an 'X' but only if the previous letter was an 'A' (e.g., A…X) and to press a right button for all other letter combinations (e.g., K…X). Target trials (AX) occurred with a frequency of 70% (Carter et al., 1998) and were of principal interest. Non-target trials (AY, BX, and BY trials) each occurred with a frequency of 10%. This frequency manipulation has been hypothesised to produce higher levels of response competition in BX and AY trials than in AX and BY trials (Carter et al., 1998). Trials were presented continuously, in a pseudo-random order. Between cue and probe there were two delay conditions—1500 and 5700 ms. The shorter delay has been hypothesised to reduce working memory demands (Barch et al., 1997). Three blocks of 80 trials were administered, following a practice session of 20 trials. Response choice and RT was recorded.

6.4. Analysis

Patient performance on tests of intellect, memory, language, speed of cognition and executive functions was compared with well-established norms. Each patient's mean reaction time and number of commission errors in the SART was compared with controls using analyses of variance (ANOVA). In light of the finding that only one patient made omission errors, which were not made by any controls, a Mann–Whitey *U* test was used to compare this patient's performance with controls. This was necessary because there was no variance in the performance of controls.

Patient 1's performance on the AX-CPT was compared with controls using repeated measures ANOVA with 3 factors: *Conflict* (high-conflict, low-conflict), *Delay* (1500, 5700 ms), and *Group* (patient, control). To maximise the sensitivity of our results we chose not to use Mycroft, Mitchell, and Kay's (2002) suggested correction.

7. Results

7.1. Cognitive functions other than executive abilities

Table 1 shows patient performance on tests of intellectual, memory, language, visuoperceptual functions, and speed of information processing. Both patients showed normal intellectual, memory, language, and visuoperceptual functions. Speed of information processing was mildly reduced in Patient 2 only.

7.2. Executive abilities

Table 2 shows patient scores on executive tests. Both patients demonstrated weak or impaired performance only on some selective executive tests. Patient 1 demonstrated abnormal performance on only 2/10 executive tests. Specifically, her performance on the Hayling Sentence Completion Test was weak and she provided significantly elevated cognitive estimates. However, her performance on the other 8 executive tests was within normal limits. Patient 2 demonstrated abnormal performance on 3/10 executive tests. Consistent with Patient 1, his performance was impaired on the Hayling Sentence Completion Test. He also showed impaired performance on verbal fluency tests, and a weak

Table 1
Summary of neuropsychological tests scores

Task	Patient 1[A]	Patient 2[B]
VIQ (WAIS-R)	113	99
PIQ (WAIS-R)	112	113
RMT words (%ile)	50 (>75th)	49 (>75th)
RMT faces (%ile)	49 (= 95th)	50 (>95th)
RCFT copy (%ile)	28 (<1st)	35 (= 84th)
RCFT recall (%ile)	26 (= 73rd)	30 (>96th)
Story immediate recall[a] (%ile)	33 (25–50th)	35 (50–75th)
Story delayed recall[a] (%ile)	33 (= 50th)	33 (50–75th)
List learning total[b] (%ile)	63 (75–90th)	52 (25–50th)
Delay (%ile)[c]	15 (>90th)	12 (50–75th)
GNT (%ile)	25 (= 90th)	21 (= 50th)
Object decision (5% cut-off)	19 (>5%)	19 (>5%)
TMTA secs (%ile)	18 (80–90th)	37 (20–30th)
Digit symbol (ss)	14	7

Abbreviations used: WAIS, Wechsler Adult Intelligence Scale (Wechsler, 1955); RMT, Recognition Memory Test (Warrington, 1984); RCFT, Rey Complex Figure Test (Rey, 1941); [a] Story recall task from Assessment of Memory and Information Processing Battery (AMIPB, Coughlan and Hollows, 1985); [b] List Learning Task from AMIPB; [c] Recall after Interference from AMIPB; GNT, Graded Naming Test (McKenna & Warrington, 1980); Object Decision from the Visual Object and Space Perception Battery (Warrington & James, 1991); TMTA, Trail Making Test Part A (Army Individual Test Battery, 1944); %ile, percentile; secs, seconds; ss, scaled score.

[A] Patient 1 was seen over several sessions 3–13 weeks post surgery.

[B] Patient 2 was seen over several sessions approximately 4 years post surgery.

Table 2
Summary of standard clinical executive test scores

Executive task	Patient 1	Patient 2
MCST categories	6/6	6/6
Proverbs	8/8	6/8
Stroop colour/word (%ile)	112 (100)	94 (15–17th)[a]
TMTB (secs) (%ile)	44 (>90th)	86 (25–50th)
Hayling overall (ss)	7[a]	3[b]
Brixton (ss)	10	10
FAS total (%ile)	49 (66th)	24 (4th)[b]
Animals (%ile)	25 (73rd)	11 (2nd)[b]
CET	8[b]	1 (wnl)
BADS six elements (ps)	4	3

Abbreviations used: MCST, Modified Card Sorting Test (Nelson, 1976); TMTB, Trail Making Test Part B (Reitan & Wolfson, 1985); FAS, controlled oral word association test (Spreen & Strauss, 1998); CET, Cognitive Estimates Test (Shallice & Evans, 1978); BADS, Behavioural Assessment of the Dysexecutive Syndrome (Wilson et al., 1996); %ile, percentile; wnl, within normal limits; secs, seconds; ss, scaled score; ps, profile score (range 1–4, Control mean = 3.52, SD 0.80, see Wilson et al., 1996).

[a] Weak performance.

[b] Impaired performance.

Table 3
Sustained Attention to Response Test (SART)

SART	Patient 1	Patient 2	Controls $N = 8$
Commission errors (%) [maximum = 40]	4 (10%)	10 (25%)	3.9 (9.9%) SD = 3.1
Omission errors (%) [maximum = 320]	0	30 (9.5%)	0
Block 1 mean RT (SD)	402	643	388 (33.8)
Block 2 mean RT (SD)	417	704	409 (35.5)

SD, standard deviation; RT, reaction time.

performance on the Stroop test. However, his performance on the other 7 executive tests was intact.

7.3. *SART performance*

Table 3 shows patient performance on the SART compared with controls. Commission errors were made by both patients, but neither patient made significantly more errors than controls [$F(1,7) < 3.4$, $p > .1$]. Patient 2 made a small percentage of omission errors compared with no errors in patient 1 and controls, however, this difference was not statistically significant (Mann–Whitney *U* test, $p > .05$). Patient 2's mean reaction times for Block 1 and 2 were significantly slower than controls [$F(1,7) = 68.9$, $p < .0001$ and $F(1,7) = 39.5$, $p < .0005$, respectively]. In contrast, Patient 1's mean reaction times was in keeping with controls [$F(1,7) = 0.1$, $p > .05$].

7.4. *AXCPT performance: Patient 1*

In the RT data, there was a significant main effect of *Conflict*, with high-conflict trials being slower than low-conflict trials ($F(1,4) = 13.9$; $p < .05$), but no significant *Conflict* by *Group* interaction ($F < 1$). Analysis of the error data revealed a marginally significant main effect of *Conflict*, with high-conflict trials being more error-prone than low-conflict trials ($F(1,4) = 6.5$; $p = .06$), but again no significant *Conflict* by *Group* interaction ($F < 1$). These findings are illustrated in Fig. 2. The only significant effect involving the *Group* factor was a *Group* by *Delay* interaction in the RT data ($F(1,4) = 14.9$, $p < .05$). As controls responded on average 31 ms faster after the long delay than after the short delay, whereas patient 1 responded 50 ms slower. However, this interaction was not reliably affected by *Conflict* (*Group* × *Delay* × *Conflict* interaction: $F(1,4) = 3.4$, $p > .1$).

8. Discussion

This study explored the role of the ACC in cognition by investigating neuropsychological functioning in two patients with medial frontal lobe lesions involving the ACC. We are aware that the lesions of both patients extend beyond the ACC and that we cannot be certain of the exact role of the ACC in our findings. Another limitation of our study is the variation in lesion chronicity. Patient 1 was seen at an acute stage and Patient 2 at a chronic stage post surgery. However, it appears that there was no significant effect of chronicity of lesion. We will now discuss patient performance on neuropsychological tests in relation to previous studies of cognitive functioning in patients with ACC lesions.

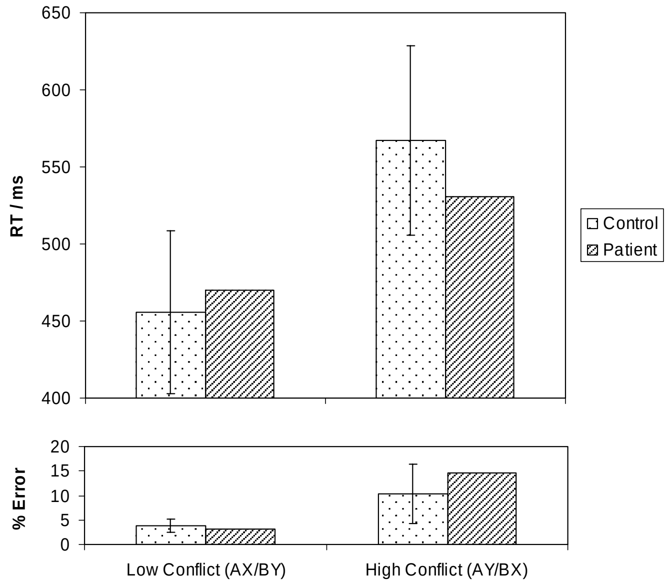

Fig. 2. Mean reaction times and error rates of Patient 1 and the control group in the low- and high-conflict trials of the AX-CPT. Error bars in the control data show 95% confidence intervals.

8.1. *Cognitive functions other than executive abilities*

Both patients showed intact intellectual, memory and language functions. Visuoperceptual functions also appear well preserved. Both patients performed well on the Object Decision test of visuoperception. Moreover they showed intact performance on a number of non-verbal tasks requiring high-level perceptual skills, such as PIQ, the visual recognition memory test for faces and the delayed recall of the Rey complex figure. Copying of the Rey complex figure was also intact in Patient 2 and selectively impaired in Patient 1. However, the significance of this result in Table 1 is unclear. Patient 1 had a preserved ability to recall the Rey complex figure and had a preserved performance on a number of perceptual tasks. Speed of information processing was mildly reduced only in Patient 2. These findings are consistent with previous studies documenting intact intellectual, language, and memory functions in patients following cingulotomy (Cohen et al., 1999; Janer & Pardo, 1991; Ochsner et al., 2001). For example, several studies have shown intact intellectual functioning as assessed by the WAIS or WAIS-R in patients undergoing bilateral cingulotomy for OCD, chronic pain and/or depression (Cohen et al., 1999; Janer & Pardo, 1991; Ochsner et al., 2001). Normal performance on the Boston Naming test has also been demonstrated in such patients (Cohen et al., 1999; Ochsner et al., 2001). Memory function has typically been assessed using the Wechsler Memory Scale and recall memory tests such as the Rey Auditory Verbal Learning test and Rey–Osterreith Figure, and found to be normal (Cohen et al., 1999; Janer & Pardo, 1991; Ochsner et al., 2001), although one study did find impaired memory for sequences in a tapping test (Faillace, Aleen, McQueen, & Northrup, 1971).

A reduced speed of information processing has been previously documented in studies of patients with ACC lesions (Cohen et al., 1999), while others have found no deficit. For example, Janer and Pardo (1991) reported normal performance on ‘reaction time probes of cognitive speed of information processing for linguistic, mathematic, and visuospatial dimensions’ in a patient after bilateral cingulotomy. These tasks required verbal responses about whether two simultaneously presented stimuli were the same or different, whereas our study utilised psychomotor measures of speed of information processing (Tail Making Part A test and Digit Symbol coding test). Thus, the difference in findings is likely to reflect task differences.

With regard to visual perception, contrasting findings are reported in the literature. This may reflect the range of measures that have been employed in patients with ACC lesions. Thus, Vilkki (1981) found impairment on Holtzman Inkblot technique requiring mental imagery in cingulotomy patients. Similarly, Ochsner et al. (2001) found impaired performance on tasks requiring mental rotation of images in a patient with bilateral cingulotomy. Other studies report visuospatial deficits in patients undergoing bilateral cingulotomy. Corkin (1979) found transient postoperative impairments on tests such as the Rey–Taylor Complex Figure copy. In contrast, Cohen et al. (1999) found intact performance in 12 bilateral cingulotomy patients on a range of visual tasks, including Judgement of Line Orientation and the Hooper Visual Organisation Test. In our patients we were unable to detect any clear-cut perceptual abnormality. These results suggest that ACC lesions do not appear to affect discriminatory visuoperceptual abilities per se. Rather, higher-level visual cognition involving rotation and mental imagery may be affected.

Overall, our data support the proposal that ACC lesions do not impair intellectual, memory, language, or visuoperceptual functions. Speed of information processing may be affected in some patients with ACC lesions. Although the lesions of both patients extended beyond the ACC, the lack of deficits suggests that this region does not play a significant role in these functions.

8.2. Executive abilities

Both patients demonstrated weak or impaired performance only on some selective executive tasks. It is noteworthy that performance on the majority of executive tests was normal. Patient 1, with a unilateral right ACC lesion, showed abnormal performance on only 2/10 executive tests. Specifically, her performance on one test of response inhibition was weak (Hayling Sentence Completion) and she demonstrated impaired Cognitive Estimates. Patient 2, with a bilateral ACC lesion, demonstrated abnormal performance on only 3/10 executive tests. Similar to Patient 1, his performance on the Hayling Sentence Completion Test was impaired. He also showed impaired performance on both verbal fluency tests, and a mildly weak performance on the Stroop test. The greater number of executive impairments expressed by Patient 2 may reflect that his ACC lesion was bilateral. While it is plausible that contralateral ACC activity may compensate following unilateral ACC damage, further research is required to explore whether bilateral lesions are more likely to result in executive impairments compared with unilateral ACC lesions.

In general, these findings are consistent with other studies that report circumscribed impairments on selective executive tests in patients with ACC lesions. For example, Cohen et al. (1999) and Janer and Pardo (1991) reported impaired verbal fluency and Stroop performance in patients after cingulotomy. However, intact performance on other executive tests, such as the Wisconsin Card Sorting Test, indicates that pervasive frontal executive dysfunction is not an essential consequence of ACC damage.

A number of studies examined Stroop performance in patients with ACC lesions with inconsistent findings. Transient postoperative impairments on the Stroop test are previously documented (e.g., Cohen et al., 1999; Janer & Pardo, 1991). Swick and Jovanovic (2002) found dissociation in Stroop performance in 2 patients with unilateral ACC lesions. Left ACC damage resulted in greater error rate on incongruent trials, while right ACC damage was associated with normal levels of interference and accurate performance on incongruent trials. This is in line with our finding of weak Stroop performance only in Patient 2 with a bilateral ACC lesion, predominantly involving the left ACC. In contrast, Patient 1, with a unilateral right ACC lesion, showed intact Stroop performance.

Interestingly, one study has suggested that Stroop test performance is dependent on the modality of response. Turken and Swick (1999) reported that in a patient with unilateral right ACC lesion, Stroop performance was intact when utilising vocal responses but impaired during motor responses, suggesting functional specialisation within the ACC. A recent study found intact performance on a computerised version of the classic Stroop test in four patients with ACC lesions due to stroke, including 3 unilateral left and one bilateral lesion (Fellows & Farah, 2005). In our study there was a dissociation as only Patient 2 with a bilateral lesion showed weak performance on the Stroop test, while Patient 1, with a unilateral right ACC lesion, showed intact Stroop performance. However, we cannot exclude that if a different version of the Stroop test was used, (e.g., an unblocked version with word reading and coloured naming in the same form), an impairment would not be found, as predicted by Stuss, Floden, Alexander, Levine, and Katz (2001). Overall, the role of the ACC in Stroop test performance remains controversial.

Remarkably, both patients performed normally on a range of executive tasks (e.g., Modified Card Sorting test, Brixton test, and proverbs), including the demanding Six Elements Test from the Behavioural Assessment of Dysexecutive Syndrome battery (Wilson et al., 1996). Overall, it appears that ACC lesions disrupt performance only on selective executive tasks, but the pattern of deficits does not appear to be uniform across patients. Further neuropsychological research in patients with ACC lesions is required to address the issue of potential 'executive function' specialisation within the ACC.

8.3. Anterior attention

Patient performance on the anterior attention tests, similar to tasks used in previous neuroimaging studies (e.g., Carter et al., 1998), was generally satisfactory. Patient error rates did not differ significantly from controls on the SART. Indeed, in terms of commission errors, the percentage was very similar between the 2 patients and controls. With regard to omission errors, Patient 1 (like controls) made no errors, while Patient 2 made a small percentage of errors which failed to reach statistical significance. Reaction times were in accordance with controls in Patient 1 and significantly slower in Patient 2, in keeping with his reduced speed of information processing. Our findings of satisfactory performance on the SART are consistent with those of a recent study which reported intact performance patients with ACC lesions on a similar computerised go–no go task (Fellows & Farah, 2005).

These findings were further replicated with the AX-CPT task in Patient 1. On the AX-CPT, the effect of the high-versus low-conflict trials did not differ between Patient 1 and controls. However, Patient 1 responded more slowly to the target after long delays compared with controls. Although only Patient 1 completed this task, this patient was in an acute stage post surgery and would be expected to show impaired performance if the ACC played a crucial role in mediating this function. Overall, the absence of any significant impairment on these anterior attention tasks is somewhat surprising given the findings of neuroimaging studies, and lends support to the notion that the ACC is not necessary for cognitive control, consistent with the findings of Fellows and Farah (2005).

8.4. Anterior cingulate cortex: Role in cognition

On the basis of neuroimaging findings, two main theories of the role of the ACC in cognition have been proposed, (1) conflict monitoring, and (2) anterior attention. The notion of conflict monitoring assumes that the ACC monitors the attentional requirements by evaluating the conflict between current and desired responses and engages other systems to modulate cognitive processing accordingly (e.g., Botvinick, Braver, Barch, Carter, & Cohen, 2001; Carter et al., 1998, 2000). This theory predicts impaired performance on cognitive tasks requiring conflict monitoring such as the Stroop test in patients with ACC lesions. Our findings do not unequivocally support this prediction. From two tests of conflict monitoring (Stroop test and Hayling Sentence Completion Test), Patient 1 showed a weak performance on only one (Hayling). In contrast, Patient 2 showed abnormal performance on both. Specifically, he showed impaired performance on the Hayling and a weak performance on the Stroop test. However, poor performance on these tasks may reflect impaired strategic processes subserved by other frontal regions (e.g., Stuss & Levine, 2002). Patient 2's lesion was more extensive. Thus, it is difficult to be certain of the ACCs role in conflict monitoring processes. Further lesion studies are required to clarify this.

The anterior attention account of ACC function suggests that the ACC directly allocates attentional resources to implement cognitive control (e.g., Posner & Digirolamo, 1998; Posner & Petersen, 1990). This theory predicts impaired performance on anterior attention tasks in patients with ACC lesions. Our findings do not support this notion. Both our patients showed satisfactory performance on a range of tasks requiring allocation of attentional resources (e.g., SART and Six Elements Test). Overall, these two theories have difficulty accounting for our patients' generally good performance on anterior attention and the majority of executive tasks. Previous animal research which found no evidence of ACC neuronal response during a conflict inducing task in macaques and recent findings by Fellows and Farah (2005) are also at odds with these two theories.

A relatively more recent account of ACC function has been proposed by Critchley and colleagues (Critchley et al., 2000, 2001, 2003, 2005). They suggest that the ACC is 'necessary for the appropriate generation of autonomic arousal during effortful cognitive and physical work.' This theory predicts impaired autonomic functioning and spared cognitive functioning in patients with ACC lesions. We have previously documented autonomic abnormalities in the two patients in this study (Critchley et al., 2003). Both patients showed abnormalities in autonomic cardiovascular responses with blunted autonomic arousal to mental stress during performance of cognitive (mental arithmetic) and motor tasks. In this study, we have failed to document any significant generalised cognitive impairment in both patients, the only exception being mild and isolated deficits in executive functions and speed of information processing. Critically, both patients performed satisfactorily even on very demanding tasks such as the SART. These findings are similar to those reported by Fellows and Farah (2005), who described four patients with intact performance on two cognitive control tasks (Stroop and go–no go tasks). Altogether, these findings appear to suggest that the ACC does not play a critical role in cognitive functioning. In these patients ACC lesions are associated with clear-cut abnormalities in behaviourally integrated autonomic responses. We therefore suggest that the ACC is involved in the generation of preparatory and facilitatory bodily arousal states during volitional behaviours, rather than having a primary role in associated cognitive computations. Clearly, more research is needed to corroborate this proposal.

In summary, we have provided a detailed investigation of neuropsychological performance, in particular executive, and anterior attention functions, in two patients with medial frontal lobe lesions involving the ACC. We found that cognitive functioning was generally intact in both patients. Patient performance on the majority of executive tests was normal. Selective deficits were found on only some executive tests. Performance on anterior attention tasks was also satisfactory. These findings are not in accordance with the anterior attention theory of ACC function based on neuroimaging findings. Rather, they are compatible with the view that the ACC integrates cognitive processing with autonomic functioning to guide behaviour. They suggest that the ACC does not have a specific cognitive role in accordance with the recently published study of Fellows and Farah (2005). However, patients with lesions in the ACC and cognitive impairments have also been documented (Stemmer et al., 2003). Since our patients had lesions extending beyond the ACC, we are aware that caution needs to be exerted in drawing firm conclusions from our study which adds to the ongoing debate of the role of the ACC in cognition.

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Appendix A

A.1. The Hayling and Brixton tests

The Hayling Sentence Completion Test consists of two sections, each with 15 sentences which are missing the last word. In Section 1 the subject is asked to complete the sentence sensibly as quickly as possible. For example, ‘the old house will be torn…down.’ In Section 2 the subject is asked to give a word that is unconnected to the sentence in every way, for example, ‘the captain wanted to stay with the sinking…lightbulb.’

The Brixton test consists of a 56 page stimulus book with each page showing the 10 circles set in two rows of five and numbered 1–10. On each page one circle is filled with a colour, and the position of this filled circle differs from page to page. The subject is asked to consider where the next filled position will be by trying to see a pattern or rule based on what they have seen on the previous pages (Burgess & Shallice, 1997).

A.2. The modified Six Elements Test from the Behavioural Assessment of the Dysexecutive Syndrome

The subject is asked to do three tasks (dictation, arithmetic, and picture naming) each of which is divided into two parts, A and B, making six sub tasks in total. The subject is required to attempt something from each of the six sub tasks within a 10 min period. One rule is to be followed and that is that they are not allowed to do two parts of the same task consecutively. For example, if naming one set of pictures (set A) they cannot switch to naming the other set of pictures (set B). They would need to do one set of arithmetic or dictation tasks first and then return to the other set of pictures later. It does not matter how well the subject performs the individual components, rather, the point of the test is to measure how well subjects can organise themselves. Three measures are obtained (i) number of sub tasks attempted (maximum 6), (ii) whether or not the rule was broken for each type of task (maximum = 3), and (iii) the maximum time spent on any one sub task (maximum 10 min; Burgess et al. in Wilson et al., 1996).

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