Is anterior cingulate cortex necessary for cognitive control?

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Summary

Functional neuroimaging studies in normal humans suggest that dorsal anterior cingulate cortex (dACC) plays an important role in cognitive control. This brain area is reliably activated when tasks require the ongoing adjustment of the allocation of attention. The dACC has come to occupy a central role in theories of attention and cognitive control, which hold that dACC either monitors response conflict, signalling the need for adjustments in cognitive processes, or directly mediates such adjustments. However, functional imaging results cannot establish that a brain area is necessary for a particular cognitive process. This requires evidence from loss-of-function studies. Here we assessed cognitive control in four human subjects with damage to dACC and 12 age- and education-matched control subjects using several measures drawn from the functional imaging literature. All four subjects with dACC damage showed normal adjustments in performance following manipulation of response conflict in both Stroop and go–no go tasks. Furthermore, damage to the dACC did not impair the phenomenon of post-error slowing, nor alter the ability to adjust performance in response to explicit speed or accuracy instructions. Thus, cognitive control, as assessed by four different measures in two different tasks, appears to be intact in these subjects, arguing against a necessary role for dACC in this process.

Introduction

Interest in the cognitive functions of dorsal anterior cingulate cortex (dACC) was awakened after early PET studies showed an unexpected association between attention-demanding cognitive processing and dACC activation (e.g. Posner *et al.*, 1988). Subsequent research with PET and functional MRI (fMRI) showed that dACC is reliably activated when tasks require the ongoing adjustment of cognitive resource allocation (Botvinick *et al.*, 1999; Paus, 2001), a set of processes known as 'cognitive control'. The dACC has come to occupy a key role in two major theories of cognitive control (Posner and DiGirolamo, 1998; Botvinick *et al.*, 2001). According to the 'conflict monitoring' account of dACC function (Carter *et al.*, 2000; MacDonald *et al.*, 2000; Botvinick *et al.*, 2001; Milham *et al.*, 2003), the dACC monitors the need for attentional resources by evaluating the level of conflict between current and desired responses and engaging other systems to modulate cognitive processing

accordingly. According to the 'anterior attentional system' account (Pardo *et al.*, 1990; Gehring *et al.*, 1993; Posner and DiGirolamo, 1998; Peterson *et al.*, 1999), the dACC implements cognitive control directly by allocating attentional resources. In either case, dACC is hypothesized to play a critical role in cognitive control.

Functional neuroimaging can provide evidence that activity in a particular brain area is associated with a particular cognitive function, but does not allow inferences about whether an area is necessary for this function. This question can be addressed by studying patients with lesions of the dACC. Given the postulated central role of this region in two widely held theories of cognitive control, one might expect that deficits in attentional control and/or conflict monitoring should be readily demonstrable in subjects with such damage. However, the neuropsychological literature on the effects of dACC damage is inconsistent at best. For example,

although many functional imaging studies have demonstrated increased activation in the dACC during performance of the Stroop task (Pardo *et al.*, 1990; Carter *et al.*, 1995, 2000; Leung *et al.*, 2000), two fairly large lesion studies have failed to find a systematic effect of dACC damage on the size of the Stroop effect (Vendrell *et al.*, 1995; Stuss *et al.*, 2001). On the other hand, the much more focal lesion induced by cingulotomy has been reported to result in mild impairment on this measure (Cohen *et al.*, 1999), although older studies of similar populations reported intact performance on various other tests of executive function (Ballantine *et al.*, 1977; Corkin *et al.*, 1979). Smaller studies or case reports have also yielded variable results. For example, Janer and Pardo (1991) found only 'subtle and ephemeral' deficits in a patient studied pre- and post-cingulotomy on tasks found to elicit dACC activations in their early PET work (including the Stroop task) that had largely resolved by 8 months post-surgery. A case study measuring event-related potentials in response to errors provided some evidence that conflict monitoring was intact in a patient with unilateral dACC damage (Swick and Turken, 2002), while a series of two patients with unilateral dACC damage found deficits in performance of Stroop-type tasks, but that were response modality specific (Swick and Jovanovic, 2002).

There are difficulties in interpreting existing lesion studies: all share the problem of small sample size, imposed by the fact that dACC damage is relatively rare. Secondly, lesion location varies, and there are several lines of evidence that suggest that the functional divisions of the dACC occur at a relatively fine grain (Paus *et al.*, 1993; Bush *et al.*, 2000; Koski and Paus, 2000; Paus, 2001; Swick and Jovanovic, 2002). Strong tests of hypotheses derived from functional imaging findings require a patient population in which the lesions involve the brain area implicated by imaging studies. Finally, the behavioural measures of cognitive control and/or conflict monitoring have varied across studies, and may not have been optimal for detecting deficits in these particular processes. Current theories of cognitive control do not make strong predictions about overall ability to perform attention-demanding tasks. The cognitive system can perceive, attend, recall and respond even if it cannot adjust attention according to task demands. Thus, depending on where normal subjects adaptively set their attention relative to the patients' default levels of attention, patients with difficulty in cognitive control might be overall more or less accurate than normal. While tasks such as the Stroop task invoke cognitive control, it is not clear that the usual performance measures (such as the Stroop effect in the standard version of the task) would necessarily be systematically affected by dACC damage.

Ever more refined experimental approaches emerging from the functional imaging literature now provide tools to isolate cognitive control from other processes involved in performing tasks such as the Stroop task (Botvinick *et al.*, 1999; Carter *et al.*, 2000; Durston *et al.*, 2002), and should provide a more definitive test of the hypothesized role of the dACC in cognitive control. To our knowledge, only one study of subjects with dACC damage has explicitly manipulated the need for cognitive control in humans (Swick and Jovanovic, 2002). This study found reduced modulation of the Stroop effect as a function of incongruent stimulus frequency in one subject with unilateral dACC damage, and absent modulation in another. A consistent finding that even unilateral dACC damage results in the loss of cognitive control would constitute compelling evidence for the cognitive control theories of dACC function. We therefore followed up this report in a larger population, relating lesion location directly to functional imaging activations, and adding multiple converging measures of cognitive control. In order to isolate cognitive control from other task demands, we used the same tasks and behavioural measures that have been used in the functional imaging studies of cognitive control. The goal was to test whether the dACC plays a necessary role in cognitive control.

Methods

Subjects performed two different tasks in which demand for cognitive control can be varied: the classic Stroop colour-word naming task, and the go–no go task. As in the imaging literature, cognitive control ability was isolated by varying the need for attentional control within task. Subjects' capability for cognitive control could be assessed by comparing performance on the attention-demanding trials when they were frequent and cognitive control was highly engaged (keeping response conflict low), and when they were infrequent and cognitive control was therefore less engaged, resulting in high conflict on the incongruent trials. The Stroop task evoked a sufficient number of errors to allow examination of another indicator of cognitive control, post-error slowing. Differences in performance between high and low conflict blocks and post-error slowing are both measures of conflict-mediated cognitive control, i.e. adjustments in cognitive resource allocation caused by on-line detection of increased conflict. We also included a manipulation intended to assess patients' ability to control cognitive resource allocation strategically, by administering the go–no go task twice, once with instructions favouring speed over accuracy and once favouring accuracy over speed.

Subjects

Four participants with damage involving the dACC were identified through the patient database of the University of Pennsylvania's Center for Cognitive Neuroscience. All had suffered ischaemic stroke of the anterior cerebral artery or its pericallosal branch a range of 0.5–7 years prior to testing. One dACC subject was taking phenytoin, and another levitiracetam for well-controlled seizure disorders; the remaining two were taking no medications. Twelve age- and education-matched control subjects were recruited by advertisement. Controls were not taking psychoactive medication, and were free of current or past psychiatric or neurological illness as determined by history and screening neurological examination. Controls scored at least 28 out of 30 on the Mini-Mental Status Examination (Folstein *et al.*, 1983) and <16 on the Beck Depression Inventory. IQ was estimated by means of the National Adult Reading Test (NART). A summary of the background information for all participants is provided in Table 1. There were no significant

Table 1 *Subject characteristics*

Group	Age (years)	Education (years)	ANART IQ
dACC group ($n = 4$)	44.3 (6.9)	13.3 (1.5)	118 (7)
Controls ($n = 12$)	48.8 (10.3)	14.9 (2.8)	120 (8)

All values are the mean (SD); ANART = American National Adult Reading Test.

differences between the dACC-damaged group and controls on the measured demographic variables [analysis of variance (ANOVA), all $P > 0.19$].

All subjects provided written, informed consent prior to participation in the study, in accordance with the Declaration of Helsinki, and were paid a nominal fee for their time. The study protocol was approved by the Institutional Review Board of the University of Pennsylvania.

Lesion analysis

Lesions were traced from T1-weighted, multi-planar MRIs onto the standard Montreal Neurological Institute brain by a neurologist experienced in image analysis, using MRIcro software (Rorden and Brett, 2000). MRIcro software was also used to generate the lesion overlap images.

Tasks
Stroop colour naming task

This computerized version of the classic Stroop task required subjects to name one of five colours of ink in which single words were printed, as they were shown on the screen one at a time. All words were the names of the same five colours; hence, all trials were either congruent (ink colour and word the same) or incongruent (ink colour and word different). Stimuli were on screen until the subject answered, with an inter-trial interval of 1000 ms. The onset of the verbal response was recorded by a microphone connected to a PsyScope button box (http://psyscope.psy.cmu.edu). Subjects had 70 practice trials, with equal numbers of congruent and incongruent stimuli. This was followed by two blocks of 100 trials each separated by a rest period; the first, low conflict, block had 80 incongruent trials and 20 congruent trials. In the second, high conflict, block, this ratio was reversed. The ratio of incongruent to congruent trials in the two conflict conditions is that employed in two previous studies that have examined the role of the dACC in conflict monitoring (Carter *et al.*, 2000; Swick and Jovanovic, 2002).

Go–no go task

A computerized go–no go task required subjects to press the space bar with their right hand when a single digit appeared in the centre of the screen. When the number 4 appeared, no bar press was to be made. The stimulus was displayed for 1000 ms, with a 500 ms inter-stimulus interval. Four blocks of 200 trials each were administered to each subject, separated by other tasks within the 2 h testing session. The first two blocks were done under accuracy instructions, the second two under speed instructions. Twenty practice trials preceded each block, after which the speed or accuracy instructions were again emphasized. Within each block, the frequency of no go stimuli was varied (average one in eight, versus average five in eight) to provide runs of high and low conflict conditions, arranged either ABA or BAB, counterbalanced across blocks. Both tasks were programmed

on a Macintosh computer, using PsyScope software (http://psyscope.psy.cmu.edu; Cohen *et al.*, 1993).

Statistical analysis

Outliers (>3 SD from the mean) were removed from the raw response time (RT) data prior to further analysis. The reported mean RTs are for correct trials. RT data entered into the analysis are mean values of a large number of observations in each subject, and as such will tend to be normally distributed according to the central limit theorem. Parametric statistical tests were therefore employed. Error rates were treated in the same way, except that they were first log-transformed to conform better to a normal distribution, where necessary. The key analyses examine the degree to which performance was modulated under conditions that were expected to require varying degrees of cognitive control, rather than absolute task performance. Initial analysis assessed the effect of group membership and level of conflict on the Stroop interference effect and go–no go error rates using repeated measures ANOVA, with significance set at $P < 0.05$, two tailed. This analysis supported the null hypothesis, which could in principle be due to inadequate statistical power to detect differences in performance between the two groups. We therefore also directly tested the alternative hypotheses that dACC subjects do modulate performance in response to changes in level of conflict, errors and explicit instruction. This was done by examining whether the observed change in performance in each of two conditions, in each task, was greater than zero, with paired t tests or one-group t tests, as appropriate. Significance was set at $P < 0.05$, one tailed. The number of Stroop task errors committed by dACC subjects varied considerably (range 4–11), violating the assumption of constant variance underlying standard t tests. The t value for each subject was therefore normalized for the variance in each sample, before being combined to examine the group effect for post-error slowing. Because the small sample size makes it difficult to be certain that the data are approximately normally distributed, key analyses were also confirmed using non-parametric tests. Finally, the performance of individual subjects with dACC damage was compared with the range of performance observed in the control group.

Results
Lesion analysis

Four subjects with damage involving the dACC were compared with 12 age- and education-matched controls. Demographic information is provided in Table 1. The lesions in three cases were confined to the left hemisphere, and in a fourth case were bilateral; all were the chronic result of ischaemic stroke. Figure 1 shows the lesion location for each subject, and the lesion overlap for all four subjects in relation to activations during a variety of attention-demanding cognitive tasks as summarized in a meta-analysis of functional neuroimaging studies (Bush *et al.*, 2000). As indicated in the figure, such studies have reported foci of activation over a relatively large area of the dorsal medial frontal lobe, but concentrated in dACC. Three of the four subjects in the present study, including the subject with bilateral injury, have damage that includes the majority of these activation foci. The damage in the fourth subject involves the more ventral
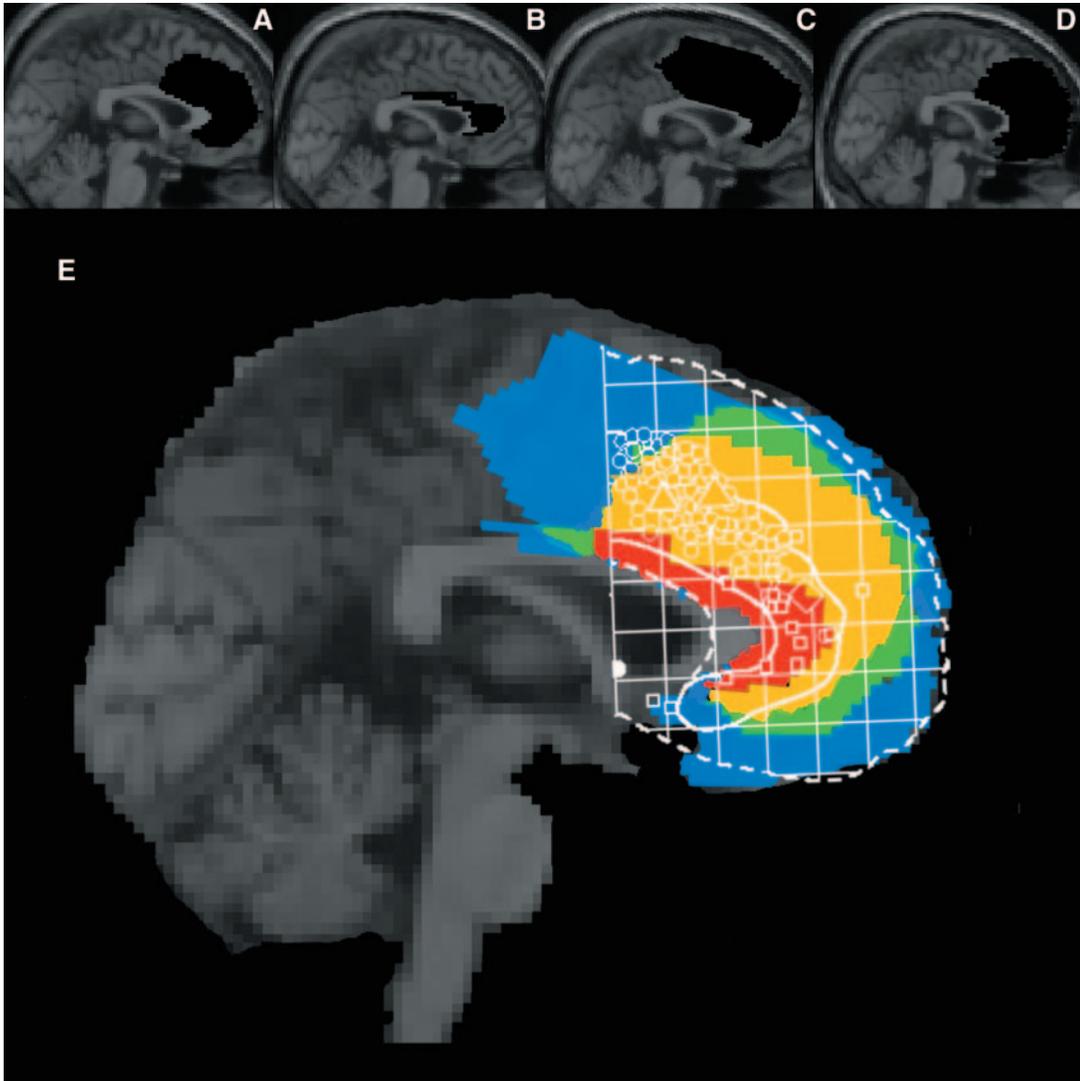
Fig. 1 Sagittal views of the standard Montreal Neurological Institute (MNI) brain showing the location of the lesion in each dACC subject. Two subjects (**A** and **B**) had focal damage primarily confined to the left dACC. One (**C**) had more extensive injury to the left cingulate and supplementary motor area, with involvement of the corpus callosum. The fourth subject (**D**) had suffered bilateral anterior cerebral artery infarction, with extensive damage to medial frontal structures, including medial orbitofrontal cortex, ventral dACC and fronto-polar areas bilaterally. This subject was included because she appears to have extensive damage to the dACC bilaterally. We reasoned that while any impairment this subject manifested could not necessarily be attributed to dACC damage, intact performance would be strong evidence that the dACC was not necessary for the cognitive processes being examined. An overlap view of the lesions of all four subjects is shown beneath (**E**): blue indicates areas damaged in a single subject, green in two, orange three and red all four subjects. A sketch of the areas activated in a variety of functional neuroimaging experiments using a variety of attention-demanding tasks, as summarized in the meta-analysis of Bush *et al.* (2000), is overlaid for comparison. Circles indicate activations in cognitive tasks, squares activations in tasks with emotional content.

part of dACC, corresponding to activation foci found in at least some imaging studies of tasks requiring cognitive control.

An alternative definition of the region of the dACC that is important for cognitive control, again derived from the functional imaging literature, is that region of the cingulate cortex anterior to the plane of the anterior commissure and posterior to the genu of the corpus callosum, including the adjacent cingulate sulcus (Botvinick *et al.*, 1999). All four subjects have damage to most or all of this region; in the subject with bilateral damage, this area appears to be damaged in its entirety in both hemispheres.

High versus low conflict

Although subjects with dACC damage were slower than controls on the Stroop task, their capacity to adjust cognitive control in response to changes in level of response conflict was indistinguishable from that of control subjects (Table 2, Fig. 2A). Repeated measures ANOVA with condition (incongruent, congruent) and conflict level (high, low) as

Table 2 *Results of the Stroop task under high and low conflict conditions*

Group	High conflict block				Low conflict block			
	Incongruent RT (ms)	Congruent RT (ms)	Interference (ms)	Errors	Incongruent RT (ms)	Congruent RT (ms)	Interference (ms)	Errors
dACC	938 (117)	749 (94)	193 (38)	12.5 (6.5)	981 (184)	843 (151)	137 (33)	6.0 (6)
Controls	837 (145)	665 (115)	171 (62)	10.4 (7.8)	808 (112)	702 (100)	106 (50)	2.8 (3)

All values are the mean (SD). Errors are expressed as a percentage of incongruent trials. RT = reaction time.
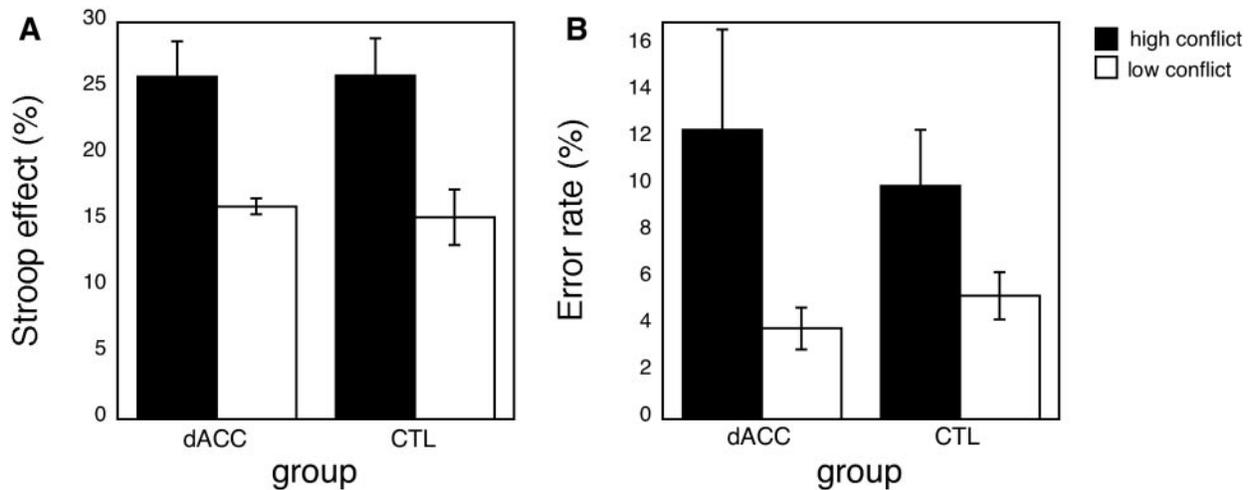

Fig. 2 Modulation of the Stroop effect (expressed as mean percentage change from congruent trial RT; **A**) and go–no go error rate (expressed as mean percentage of no go trials; **B**) as a function of conflict level. Subjects with dACC lesions modulated performance to the same degree as controls in response to changes in the frequency of incongruent trials in both tasks. Error bars show the SEM.

the within-subjects measures and group as the between-subjects measure was performed on the mean RT data for each block. The dACC subjects were slower in general, indicated by a main effect of group [$F(1,28) = 6.5, P < 0.05$]. There was also a significant main effect of condition [$F(1,28) = 9.5, P < 0.01$] and of conflict level [$F(1,28) = 7.4, P < 0.05$]. The effect of condition was modulated by conflict level [$F(1,28) = 4.9, P < 0.05$], reflecting the fact that both the control group ($P < 0.05$) and the dACC group ($P = 0.05$) were slower on congruent trials in the setting of low conflict. Neither group showed a systematic change in incongruent RT with level of conflict ($P > 0.15$). Crucially, there was neither a group × condition interaction [$F(1,28) = 0.6, P = 0.8$] nor an interaction between group, condition and conflict level [$F(1,28) = 0.06, P = 0.8$]. Error rates (expressed as a percentage of incongruent trials in each block, and log-transformed) followed a similar pattern. There was no significant effect of group [$F(1,14) = 1.3, P = 0.28$] but a significant effect of conflict level [$F(1,14) = 21.1, P < 0.01$], and no interaction [$F(1,14) = 0.1, P = 0.76$]. Non-parametric analyses confirmed the main finding: the mean change in RT between high and low conflict conditions did not differ significantly across the two groups (Mann–Whitney U test, $U = 20, P = 0.63$).

Thus, the modulation of performance in response to change in conflict level in the Stroop task was similar in both dACC

subjects and controls. It is, of course, not logically possible to prove the null hypothesis; could this lack of a detectable difference be due to inadequate statistical power in light of the small sample size? Inspection of the data (Figs 2 and 3) argues against this interpretation, and we went on to address this issue statistically as directly as possible by asking whether the dACC group showed a statistically significant increase in the size of the Stroop effect in the high, compared with the low conflict condition. One-tailed paired t tests indicated that such an increase was detectable in dACC subjects and in controls (Fig. 2A; control, $t = 8.5, P < 0.01$; dACC, $t = 3.1, P < 0.05$), providing further evidence that both groups consistently modulated their performance in response to changes in conflict level, and showing that this effect was robust enough to be statistically detectable within the group of four dACC subjects. Finally, given the variation in lesion extent and laterality in the dACC subjects, performance of each individual was also examined. The modulation of performance in all four dACC subjects was as least as great as that of control subjects (Fig. 3A). The size of the Stroop effect was larger in the high conflict compared with the low conflict condition for all 12 control subjects, and all four dACC subjects.

The go–no go task included high and low frequency no go conditions, to allow comparison of low and high conflict
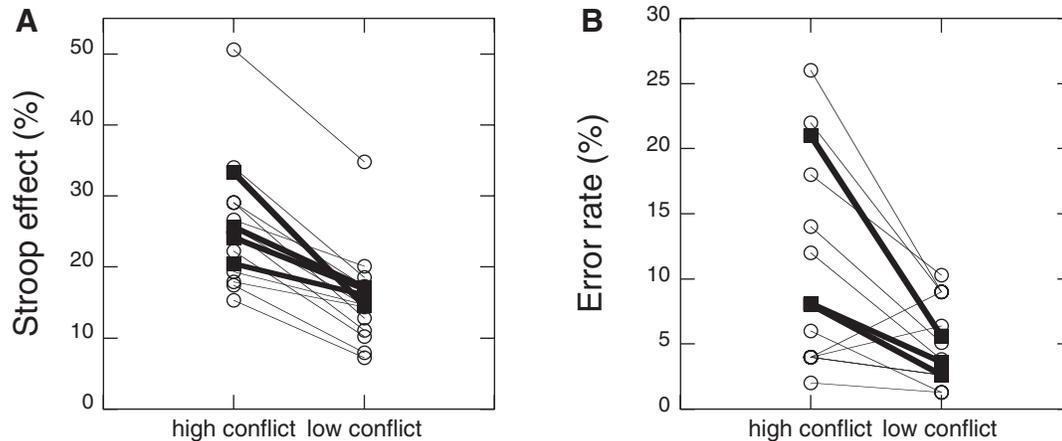
Fig. 3 Modulation of performance by level of conflict in individual subjects. (**A**) The effect of changing conflict level on the Stroop effect (expressed as percentage change from congruent trial RT). (**B**) The effect on error rates (expressed as a percentage of no go trials) in the go–no go task. Control values are represented by the open circles and thin lines. The dACC subjects are shown by filled squares and thick lines.

conditions in this task as well. A similar approach has been used in a prior fMRI study that found that dACC activity varied with the level of conflict (Durston *et al.*, 2002). As in that study, we focused on error rates, and found them to increase under high conflict conditions. Controls had average error rates of 10 ± 8% in the high conflict condition, and 5.3 ± 3.3% in the low conflict condition (collapsed across instruction conditions). One subject declined to complete the entire battery of tests, and so complete data are only available for three of the dACC subjects, including the subject with bilateral damage. The average error rate for this group of dACC subjects was 12.4 ± 7.5% under high conflict, and 3.9 ± 1.5% under low conflict (Fig. 2B). Error rates did not differ across groups [log-transformed rates; $F(1,13) = 0.12$, $P = 0.73$], but there was a main effect of conflict level [$F(1,13) = 17$, $P < 0.01$]. Crucially, there was no interaction between group and conflict level [$F(1,13) = 1.8$, $P = 0.21$], a finding also supported by non-parametric analyses (change in error rate by conflict level did not differ across groups, Mann–Whitney U test, U = 12, $P = 0.38$). As in the Stroop task, we went on to ask whether the dACC subjects showed statistically detectable evidence of a change in error rate in the two conditions. Both the control group and the dACC group had significantly higher error rates in the high conflict than in the low conflict condition (paired *t* test on log-transformed data, control group, $t = 2.9$, $P < 0.05$; dACC group, $t = 7.3$, $P < 0.05$). As in the Stroop task, the variation in error rates according to conflict level for individual dACC subjects fell within the control range (Fig. 3B; all three dACC subjects and 10 of 12 control subjects had higher error rates in the high conflict compared with the low conflict condition). The partial data that are available for the dACC subject who did not complete all conditions (trials under accuracy conditions only) indicate a pattern similar to the rest of the dACC group, with an error rate of 3.6% in the low conflict condition and 6.1% in the high conflict condition.

Mean RTs for go trials were also examined: the dACC subjects were slower overall, with a significant main effect of group [$F(1,26) = 17$, $P < 0.001$]. There was no main effect of conflict level [$F(1,26) = 0.9$, $P = 0.34$], nor was there a significant interaction of group × conflict level [$F(1,26) = 1.8$, $P = 0.2$]. Non-parametric analysis confirmed that the change in RT as a function of conflict level did not differ detectably across groups (Mann–Whitney U test, U = 12, $P = 0.38$). The fact that the error rate was significantly influenced by conflict level while RT was not, and that these effects were not influenced by the presence of dACC damage, argues that performance in both groups is altered in response to changes in the degree of response conflict beyond a simple speed–accuracy tradeoff.

Post-error slowing

Slowing of RT on the trial following an error is considered a manifestation of cognitive control. The effect of error commission (on incongruent trials) on performance on the subsequent trial in the Stroop task was examined in both groups. The control group was limited to those who made ≥3 errors (*n* = 9); all dACC subjects made at least that many errors. dACC subjects were on average 11.4% slower on correct post-error trials than on correct trials that did not follow an error [difference >0, one group, one-tailed *t* test (normalized for unequal variance) $t = 2.11$, $P = 0.06$]. Controls slowed an average of 3.5% on the post-error trial. This was not significantly different from 0 ($t = 1.0$, $P = 0.33$). At the individual level, seven of nine control subjects and all four dACC subjects were on average slower on post-error trials, compared with trials that did not follow errors.

Speed and accuracy instructions

Cognitive control can be variably engaged on the basis of task instruction. If the dACC plays a necessary role in

Table 3 *Results of the go–no go task under speed or accuracy instructions*

Group	Speed instructions		Accuracy instructions	
	RT (ms)	Error rate	RT (ms)	Error rate
dACC	476 (109)	5.1 (1.0)	538 (124)	4.5 (0.9)
Controls	377 (47)	8.2 (6.0)	422 (42)	4.2 (1.9)

All values are the mean (SD). Error rates are expressed as a percentage of no go trials.

implementing cognitive control (but not if it serves solely as a conflict monitor), this predicts that lesions to the dACC should lead to an impaired ability to modulate performance when instructions change. As shown in Table 3, while subjects with dACC lesions were overall slower in both instruction conditions on the go–no go task, as a group their performance modulation in response to instructions was not significantly different from controls. Both groups made few errors; mean error rates under the different instruction conditions were not detectably different [log-transformed error rates, $F_{(1,26)} = 1.5$, $P = 0.24$]. Mean RT showed a trend toward an effect of instruction [$F_{(1,26)} = 3.8$, $P = 0.06$], which critically did not interact significantly with group [$F_{(1,26)} = 0.1$, $P = 0.74$]. At an individual level, 10 of 12 control subjects and two of three dACC subjects (including the subject with bilateral damage) were either faster, or made more errors, or both under speed than accuracy instructions. The remaining dACC subject had very low error rates in both conditions (speed 0.045, accuracy 0.05), and her overall RT performance was bested by only two of the control subjects. Instruction did not interact systematically with group and conflict level terms either in RT or in error rates (all $F < 0.3$, $P > 0.57$); the data in Figs 2B and 3B are therefore collapsed across instruction conditions for simplicity of presentation.

Discussion

Is the dACC necessary for cognitive control? The present study attempted to answer this question by assessing the effects of dACC damage on cognitive control in four patients, operationalizing cognitive control in terms of the same manipulations and measures used in the imaging literature. Specifically, we administered two tasks commonly used in imaging studies of cognitive control, the Stroop task and the go–no go task, and examined the effects of the proportion of attention-demanding trials (low proportions/low control/high conflict versus high proportions/high control/low conflict), the effects of errors on the speed of the subsequent response and the effects of explicit instruction concerning the speed–accuracy tradeoff. dACC damage did not systematically impair cognitive control so measured. Indeed, even extensive, bilateral damage to the dACC and adjacent medial frontal lobe structures was not sufficient to impair cognitive control discriminably.

A previous study of two subjects with unilateral dACC damage had somewhat different findings, using the same Stroop task (Swick and Jovanovic, 2002). One individual with right dACC damage failed to modulate her performance between high and low conflict blocks, and a left dACC-damaged subject showed less modulation than six control subjects. When compared with our larger group of control subjects, the latter subject's degree of modulation falls within the normal range. The total lack of modulation shown by the first subject may have been the result of an idiosyncratic emphasis on accuracy, consistent with her paradoxically more accurate performance than controls in the high conflict condition. Intact post-error slowing has been reported in a single case with focal right dACC damage (Swick and Turken, 2002), in keeping with the findings of the present study. The accumulating evidence indicates that damage to the dACC, even when bilateral, need not affect cognitive control.

As five of six subjects tested to date have had unilateral damage, one possible explanation of these results is that one intact hemisphere is sufficient for normal performance. However, the subject with bilateral dACC damage reported here performed within the normal range on all four measures of cognitive control, arguing against such an interpretation.

What, then, is the function of the dACC? A number of studies have provided alternative interpretations of the role this region may play. These have focused on the motivational, emotional and/or reward-related processes that are often part of the optimal performance of cognitive tasks, and as such might be confounded with cognitive control (Gehring and Fencsik, 2001; Bush *et al.*, 2002; Shidara and Richmond, 2002). Single unit recordings in monkeys have produced evidence that many neurons in the dACC encode information about the likelihood that a response will be rewarded (Koyama *et al.*, 2001; Shidara and Richmond, 2002). Very recently, similar evidence has been provided by single unit recordings in humans undergoing cingulotomy; further, post-cingulotomy, the same subjects were impaired at reward-guided response selection (Williams *et al.*, 2004). This last finding is also consistent with the effect of dACC lesions in macaques on reward-guided responding (Hadland *et al.*, 2003). Interestingly, in support of the present findings, a detailed single unit study in macaques found no evidence that dACC neurons selectively respond to response conflict in two different conflict-inducing tasks (Nakamura *et al.*, 2004).

Another plausible alternative account of dACC function concerns its role in controlling the autonomic nervous system. Critchley *et al.* recently have provided converging evidence for a role for the dACC in controlling the autonomic responses that accompany cognitive effort in humans (Critchley *et al.*, 2003; Critchley, 2004). dACC activation has also been found in response to mild hypoglycaemia, a condition associated with important changes in autonomic tone, but with no apparent cognitive or emotional demands (Teves *et al.*, 2004), and in pharmacologically induced anxiety (Benkelfat *et al.*, 1995). An autonomic function

of dACC is also consistent with recent fMRI studies of the Stroop task that have confirmed the rapid diminution of dACC activation in response to practice, in the face of the continued requirement for (and behavioural evidence of) cognitive control (Milham *et al.*, 2003; Erickson *et al.*, 2004). The control of autonomic tone is a variable that is generally neither measured nor controlled for, and is likely to be correlated with, but not necessary for cognitive control. (This is not to say that modulation of autonomic tone is irrelevant to optimal performance in general; it simply may not be necessary to perform effectively predominantly cognitive tasks such as the Stroop or go–no go task.)

Either of these alternatives may prove to be the explanation for the discrepancy between findings from lesion and functional imaging studies concerning the role of the dACC in cognitive control. While both animal and human work argues that the dACC is not a functionally unitary structure (Turken and Swick, 1999; Barch *et al.*, 2001; Paus, 2001; Shidara and Richmond, 2002; Swick and Jovanovic, 2002), the present study provides evidence that cognitive control is not amongst the necessary functions of this brain area.

It has long been noted that imaging cannot provide evidence that a brain area is necessary for performing a cognitive operation (e.g. Frackowiak *et al.*, 1997). Correlated activation may reflect brain activity that is non-essential or even epiphenomenal with respect to the function of interest. Nevertheless, in practice, the brain regions implicated by imaging and lesion studies usually coincide. It is therefore surprising that the dACC, which has been associated with cognitive control through a number of carefully designed imaging studies, appears unnecessary for that function.

Acknowledgements

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