

Anterior Cingulate Cortex and Response Conflict: Effects of Response Modality and Processing Domain

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Studies of a variety of higher cognitive functions consistently activate a region of anterior cingulate cortex (ACC), situated posterior to the genu and superior to the corpus callosum. However, it is not clear whether the same ACC region is activated for all response modalities (e.g. vocal and manual) and/or all processing domains (e.g. verbal and spatial). To explore this question, we used rapid event-related functional magnetic resonance imaging and a spatial Stroop task with conditions tapping both verbal and spatial processing. We also employed novel methods that allowed us to acquire the accuracy and reaction times of both manual and vocal responses. We found one large ACC region that demonstrated significant response conflict effects with both vocal and manual responses, and three ACC regions that demonstrated significant response conflict effects with both spatial and verbal processing. We did not find any ACC regions that demonstrated activity selective to either a specific response modality or processing domain. Thus, our results suggest that the same regions of ACC are responsive to conflict arising with both manual and vocal output and with both spatial and verbal processing.

Introduction

The role of the anterior cingulate cortex (ACC) in higher cognition has received a great deal of attention in recent years. In part, this is because studies of a wide range of higher cognitive functions, including working memory, verbal fluency, selective attention, and long-term memory have consistently found activation of the ACC. More specifically, the region typically activated in these studies is situated posterior to the genu of the ACC, and superior to the corpus callosum. In the nomenclature of Picard and Strick, this ACC region is located in the rostral cingulate zone (rCZ) (Picard and Strick, 1996). In recent work, we have proposed a hypothesis as to why this region of the ACC is activated in a wide range of cognitive tasks. Specifically, we have hypothesized that this ACC region is active under a range of task conditions because it evaluates the demand for cognitive control by monitoring for the occurrence of response conflict in information processing. A number of studies now provide support for this hypothesis (Carter *et al.*, 1998; Botvinick *et al.*, 1999, 2001; Barch *et al.*, 2000; Carter *et al.*, 2000; Braver *et al.*, 2001). However, an additional question is whether this ACC region is functionally homogeneous, or whether it can be further functionally segregated along some domain, such as the nature of the response to be made or the nature of the processing domain. In particular, the goals of this study were to determine whether or not the same ACC region responds to conflict in across response modalities (e.g. both vocal and manual) and/or across processing domains (e.g. verbal and spatial).

As noted above, our hypothesis about ACC function is that it serves to evaluate the demand for cognitive control by monitor-

ing for response conflict or crosstalk in information processing. By crosstalk we mean interference or interactions in the processing of two stimuli or responses that occurs when the pathways for this processing overlap. Thus, our hypothesis predicts that the ACC should be active whenever there is a high degree of competition between incompatible responses. A number of studies now provide support for this hypothesis, demonstrating activation of a similar ACC region in a variety of task domains that all elicit response conflict. These task domains can be loosely grouped into three categories. First, this ACC region is active in task conditions in which a prepotent response tendency has to be overcome, such as in studies of the Stroop task and the Go/No-go task (Pardo *et al.*, 1990; Bench *et al.*, 1993; Paus *et al.*, 1993; Taylor *et al.*, 1994, 1997; Carter *et al.*, 1995, 2000; Kawashima *et al.*, 1996; Casey *et al.*, 1997; George *et al.*, 1997; Bush *et al.*, 1998; Derbyshire *et al.*, 1998; Botvinick *et al.*, 1999; Brown *et al.*, 1999; Konishi *et al.*, 1999; Peterson *et al.*, 1999; Braver *et al.*, 2001). Second, this ACC region is active in task conditions when the response to be made is not fully constrained by the task context, such as in studies of verb generation, verbal fluency, and stem completion (Petersen *et al.*, 1989; Frith *et al.*, 1991, 1993; Friston *et al.*, 1993; Raichle *et al.*, 1994; Buckner *et al.*, 1995; Yetkin *et al.*, 1995; Warburton *et al.*, 1996; Phelps *et al.*, 1997; Thompson-Schill *et al.*, 1997; Crosson *et al.*, 1999). Lastly, ACC activity is also commonly found when individuals produce errors, a situation that typically either elicits, or is the result of, response conflict (Hohnsbein *et al.*, 1989; Gehring *et al.*, 1990; Dahaene *et al.*, 1994; Carter *et al.*, 1998; Kiehl *et al.*, 2000).

Although a growing body of evidence supports the hypothesis that the ACC is responsive to conflict in information processing, a number of questions about the role of the ACC in cognition remain. In particular, one important issue is whether the same ACC region responds to conflict in all response modalities. There are a number of reasons to raise this question. First, in prior work, Paus and colleagues found that response conflict tasks using oculomotor, manual and speech responses activated slightly different ACC regions (Paus *et al.*, 1993). Paus found that oculomotor and speech responses activated regions in the rostral ACC, speech responses activated regions in the intermediate ACC, and manual response activated regions in the caudal ACC. These researchers argued that this pattern was consistent with data on the somatotopic organization of cingulate cortex in monkeys, and interpreted their results as consistent with the hypothesis that the ACC participates in facilitating appropriate motor responses, and inhibiting inappropriate ones. However, since only peak activations were reported, the extent of overlap in ACC regions activated by different response modalities was not clear.

A second reason to ask whether the location of activity within

the rCZ is somatotopically mapped is a more recent review article by Picard and Strick (Picard and Strick, 1996). In this work, Picard and Strick reviewed positron emission tomography (PET) studies demonstrating activation changes in the medial wall of the human cortex. Picard and Strick divided these studies into ones that used either simple or complex motor tasks, defining a complex motor task as one 'characterized by additional motor or cognitive demands such as the selection of a motor response, and the acquisition of a conditioned association'. Picard and Strick concluded that there was evidence for some somatotopic organization of ACC activations associated with particular output modalities for both simple and complex tasks, as well as differences in the anatomic location of activations associated with simple versus complex motor tasks. In addition, Paus *et al.* provided another recent review of the ACC literature, concluding that there was evidence for hand-arm responses activating a more caudal cingulate region, and non hand-arm responses activating a more rostral cingulate region (Paus *et al.*, 1998). However, the somatotopic mappings suggested by Picard and Strick versus Paus are slightly different, with Picard and Strick suggesting additional arm regions within the zone Paus suggested contained primarily speech or non arm-hand representations. Further, for the majority of the studies in both reviews, activation peaks for different response modalities were obtained from different studies. Thus, it is difficult to know what contribution differences in task design, imaging, and anatomical localization methods may have made to differences in the location of activations.

A third reason to ask whether the location of activity in the rCZ is somatotopically mapped is the results of a recent study by Turken and Swick (Turken and Swick, 1999). These authors report work with a focal right ACC lesion patient. The paradigms used to assess the patient included both tasks that should elicit response conflict (e.g. the Stroop, a divided attention task) and more simple response preparation tasks. Across all three tasks, both simple and complex, the patient exhibited a selective impairment in responding when manual, but not vocal responses were required. On the surface, the results of this study are consistent with the hypothesis that the ACC may exhibit somatotopic mapping. However, the precise location of the lesion in this patient may actually not correspond to the region of ACC typically activated by response conflict. Specifically, the lesion was primarily located in BA 24, and included the dorsal and ventral banks of the cingulate sulcus, but did not extend into the paracingulate sulcus. In addition, the lesion did not extend into the supplementary motor area (SMA), but did extend down to the corpus callosum. Thus, the majority of the lesion in this patient may actually lie below the rostral cingulate zone identified by Picard and Strick, which was located mainly in BA 32, with some extension into dorsal BA 24. As noted above, the rostral cingulate zone is the area we believe is most strongly associated with the monitoring of conflict. Further, the lesion in this patient clearly extended into the caudal cingulate zone identified by Picard and Strick, which they associated more with the production of simple as compared to complex manual responses.

As described above, several lines of evidence suggest that there may be somatotopic mapping of ACC activations associated with response conflict. However, an update of Picard and Strick's review provides a somewhat different picture regarding somatotopic organization within the rostral cingulate zone. Specifically, in Tables 1-3, we list the locations of ACC activations from the tasks that Picard and Strick categorized as

Table 1
Stereotactic coordinates of activations in ACC for vocal responses

Reference	Comparison	ACL ^a		
		X	Y	Z
(Barch <i>et al.</i> , 1999)	generate words-read words	1	27	38
(Barch <i>et al.</i> , 2000)	generate words: high-low selection	2	30	14
	generate words: weak-dominant response	3	28	29
(Baker <i>et al.</i> , 1997)	generate words-repeat words	-4	18	36
(Bench <i>et al.</i> , 1993)	Stroop task: incongruent-cross control	4	-4	20
	Stroop task: word control-cross control	10	-4	24
	Stroop task: incongruent-cross control	18	40	4
	Stroop task: incongruent-cross control	20	42	8
	Stroop task: incongruent-cross control	22	42	12
(Brown <i>et al.</i> , 1999)	Stroop task: incongruent-color naming	8	23	35
	Stroop task: incongruent-color naming	-4	14	35
(Buckner <i>et al.</i> , 1995)	stem completion-fixation	6	20	30
(Carter <i>et al.</i> , 1995)	Stroop task: incongruent-neutral	-8	22	28
	Stroop task: incongruent-neutral	12	44	20
(Carter <i>et al.</i> , 2000)	Stroop task: expectancy (mostly congruent, mostly incongruent) trial type (congruent, incongruent) scan with trial	0	15	41
(Derbyshire <i>et al.</i> , 1998)	Stroop task: incongruent-congruent	-2	14	40
	Stroop task: incongruent-congruent	0	2	48
(de Zubicaray <i>et al.</i> , 1998)	random letter generation-recite alphabet	6	14	42
	random letter generation-recite alphabet	3	31	20
(Dye <i>et al.</i> , 1999)	generate words-repeat words	2	26	40
(Friston <i>et al.</i> , 1993)	generate words-repeat letters	-2	18	24
(Frith <i>et al.</i> , 1991)	generate words-repeat words	4	23	36
(George <i>et al.</i> , 1994)	Stroop task: incongruent-naming color bars	-20	0	28
	Stroop task: incongruent-naming color bars	-22	24	32
	Stroop task: incongruent-naming color bars	26	-10	28
(George <i>et al.</i> , 1997)	Stroop task: incongruent-naming color bars	-22	8	28
(Grasby <i>et al.</i> , 1993)	word retrieval from memory-rest	8	22	28
	Word retrieval from memory-rest	8	18	32
(Pardo <i>et al.</i> , 1990)	Stroop task: incongruent-congruent trials	10	19	32
	Stroop task: incongruent-trials	7	17	32
	Stroop task: incongruent-congruent trials	17	25	30
	Stroop task: incongruent-congruent trials	13	44	22
(Paus <i>et al.</i> , 1993)	word association: reversal-rest	1	13	48
	word association: reversal-rest	7	20	38
	word association: reversal-fixation	9	34	13
	word association: reversal-fixation	4	15	49
	word association: reversal-overpracticed	4	30	17
	word association: reversal-overpracticed	7	34	22
	word association: reversal-overpracticed	1	22	49
	word association: reversal-overpracticed	3	18	44
	word association: reversal-overpracticed	5	20	36
(Petersen <i>et al.</i> , 1989)	generate words-repeat words	6	14	41
	generate words-repeat words	2	24	30
	generate words-repeat words	7	18	41
	generate words-repeat words	11	21	30
(Peterson <i>et al.</i> , 1999)	Stroop task: incongruent-congruent	-7	26	27
	Stroop task: incongruent-congruent	-7	18	36
	Stroop task: incongruent-congruent	7	26	27
(Phelps <i>et al.</i> , 1997)	generate words-repeat words	-4	20	40
	generate words-repeat words	4	17	27
	generate words-repeat words	-12	17	27
(Petrides <i>et al.</i> , 1993)	random number generation-counting	11	25	22
(Raichle <i>et al.</i> , 1994)	naive generate words-practiced generate words	-4	28	36
(Sergent <i>et al.</i> , 1992)	letter sound discrimination-object discrimination	4	18	31
(Taylor <i>et al.</i> , 1994)	incongruent-congruent letter naming	10	14	43
(Taylor <i>et al.</i> , 1997)	Stroop task: incongruent-neutral	-3	35	18
(Thompson-Schill <i>et al.</i> , 1997)	generate words: high selection-low selection	-4	11	45
(Vandenberghe <i>et al.</i> , 1997)	attend to two-attend to one feature	-10	20	32
(Warburton <i>et al.</i> , 1996)	word generation-word comparison	-12	6	44
	word generation-listening	-12	14	48
	word generation-listening	4	16	20
Average coordinates	verbal responses	3	20	31

^aACL = Anterior cingulate location.

complex, as well additional studies we could find that fell into any of the categories of tasks outlined above (inhibition of

Table 2

Stereotactic coordinates of activations in ACC for manual responses

Reference	Comparison	ACC region of interest		
		X	Y	Z
(Botvinick <i>et al.</i> , 1999)	Eriksen flanker task: incongruent–congruent	–2	28	31
(Bush <i>et al.</i> , 1998)	counting Stroop task: incongruent–neutral	12	9	34
(Carter <i>et al.</i> , 1998)	CPT-AX: high–low conflict trials	4	25	43
(Corbetta <i>et al.</i> , 1991)	divided attention–passive control	–7	23	34
	divided attention–passive control	–11	45	24
(Deiber <i>et al.</i> , 1991)	random–fixed joystick movements	8	34	32
(Frith <i>et al.</i> , 1991)	random–directed finger movements	3	16	34
(Garavan <i>et al.</i> , 1999)	Go/No-go task: correct no-go trials–fixation	1	16	42
(Hyder <i>et al.</i> , 1997)	random–directed finger movements	12	16	23
	random–directed finger movements	10	19	36
(Jenkins <i>et al.</i> , 1994)	new key press sequence–rest	4	22	28
	new–learned key press sequence	6	30	28
(Jueptner <i>et al.</i> , 1997)	random–fixed key press sequence	–2	4	48
	random–fixed key press sequence	6	16	32
	new–fixed key press sequence	4	16	36
(Jueptner <i>et al.</i> , 1997)	new–learned key press sequence	2	20	28
	new–attend to learned key press sequence	–2	16	44
	new–attend to learned key press sequence	18	34	–4
(Kawashima <i>et al.</i> , 1996)	Go/No-go–response selection	8	6	42
	Go/No-go–response selection	–4	9	38
	Go/No-go–response selection	–4	5	30
(Kiehl <i>et al.</i> , 2001)	Go/No-go: errors–fixation	4	22	40
	Go/No-go: errors–fixation	12	36	12
	Go/No-go: correct rejections–fixation	4	8	45
	Go/No-go: errors–correct rejections	4	22	40
	Go/No-go: errors–correct rejections	–8	45	15
	Go/No-go: correct hits–fixation	6	20	40
(Klingberg, 1998)	auditory/visual dual task–control	0	16	44
(Klingberg and Roland, 1997)	Go/No-go–passive control	–2	16	45
(Paus <i>et al.</i> , 1993)	condition key press: reversal–fixation	4	5	49
	condition key press: reversal–overpracticed	15	8	49
	opposite finger movement–rest	5	–4	48
	opposite–directed finger movement	1	22	38
	opposite–directed finger movement	5	10	45
(Petrides <i>et al.</i> , 1993)	self-ordered pointing–directed pointing	7	34	26
	self-ordered pointing–directed pointing	3	29	29
	self-ordered pointing–directed pointing	9	24	40
	conditional pointing–directed pointing	5	30	21
(Playford <i>et al.</i> , 1992)	random joystick movement–rest	4	27	24
	random joystick movement–rest	2	25	28
(Samuel <i>et al.</i> , 1998)	random joystick movement–rest	–4	4	44
(Vandenberghe <i>et al.</i> , 1999)	reversed–recognized stimulus/response associations	–18	20	32
	reversed–recognized stimulus/response associations	–12	22	48
(Whalen <i>et al.</i> , 1998)	counting Stroop task: neutral–fixation	9	–6	46
	counting Stroop task: neutral–fixation	–3	–6	50
(Zatorre <i>et al.</i> , 1992)	alternate key press–rest	7	8	42
(Zatorre <i>et al.</i> , 1994)	conditional key press–repetitive key press	8	18	29
	conditional key press–repetitive key press	1	24	42
	conditional key press–repetitive key press	5	36	26
Average coordinates	manual responses	3	19	35

prepotent response, underdetermined responding, commission of errors), and which provided standardized stereotactic coordinates in the reference frame of Talairach and Tournoux for their ACC activations. Figure 1 plots these activations on a mid-sagittal slice from the Talairach coordinate system.

As can be seen in Figure 1, there is a large area of rCZ in which activations associated with both manual and vocal responses are intermixed, with no clear visual evidence for somatotopic organization within this region of the rCZ. However, Picard and Strick suggested that there may be two subdivisions of the rCZ, an anterior one (rCZa) and a posterior one (rCZp), each of which

Table 3

Stereotactic coordinates of activations in ACC for oculomotor responses

Reference	Comparison	Anterior cingulate location		
		X	Y	Z
(Anderson <i>et al.</i> , 1994)	remembered saccades–reflexive saccades	8	4	44
(Doricchi <i>et al.</i> , 1997)	antisaccade–fixation	4	32	20
	antisaccade–fixation	–2	26	16
	antisaccade–prosaccade	–6	26	12
	antisaccade–prosaccade	2	26	16
(O'Driscoll <i>et al.</i> , 1995)	antisaccade–prosaccade	–2	10	44
(Paus <i>et al.</i> , 1993)	conditional saccades: reversal–overpracticed	7	27	29
	conditional saccades: reversal–fixation	8	29	22
	conditional saccades: reversal–fixation	9	32	12
	opposite–targeted saccades	1	10	42
(Sweeney <i>et al.</i> , 1996)	antisaccade–prosaccade	–4	28	–4
Average coordinates	oculomotor responses	2	24	23

may have separate regions for face and arm representations. In addition, Picard and Strick suggested that the caudal cingulate zone (just in front of and behind the Vca line) primarily contains arm representations. Thus, similar to Picard and Strick, we separated the reviewed activations into three subregions: (i) caudal cingulate zone (cCZ: posterior to $Y = +6$ and $+29$ mm $< Z < +46$ mm); (ii) posterior rostral cingulate zone (rCZp: $+5$ mm $< Y < +26$ mm, $+26$ mm $< Z < +51$ mm); and (iii) anterior rostral cingulate zone (rCZa: $+24$ mm $< Y < +26$ mm; $+9$ mm $< Z < +41$ mm). Seven activations fell within the cCZ, of which five were associated with manual and two with vocal/eye responses, providing some evidence consistent with the hypothesis that the cCZ contains arm representations. In both the rCZa and the rCZp, Picard and Strick suggested that the arm representations were caudal to the face representations. If this were true, then activations associated with manual, as compared with vocal or eye responses, should have more posterior Y coordinate values and/or more superior Z coordinate values. To evaluate the presence or absence of somatotopy in these rCZ subdivisions quantitatively, we compared the Y and Z coordinates for manual versus vocal/eye responses using t -tests. For the rCZp, these analyses did not indicate any significant differences in either the Y (manual $M = 16.3$; vocal/eye $M = 17.1$) or Z (manual $M = 38.7$; vocal/eye $M = 36.1$) coordinates ($P < 0.10$). Similarly, for the rCZa region, these analyses again did not indicate any significant differences in either the Y (manual $M = 34$; vocal/eye $M = 31.1$) or Z (manual $M = 24.3$; vocal/eye $M = 21.8$) coordinates ($P < 0.10$). Thus, with the inclusion of more recent studies assessing response conflict, no clear evidence emerges for somatotopy in either the rCZa or the rCZp.

A second issue regarding activity in the rCZ is whether the same ACC region responds to conflict in all processing domains (e.g. verbal and spatial). Other regions of cortex demonstrate evidence for lateralized activation in response to differences in processing domain. For example, inferior frontal cortex (BA 44/6) shows relatively greater right sided activation for non-verbal processing, but relatively greater left-sided activation for verbal processing (D'Esposito *et al.*, 1998; Kelley *et al.*, 1998). Thus, one might hypothesize that the ACC might demonstrate a similar lateralization of function, with the right ACC being more responsive to conflict arising with non-verbal processing, while left ACC might be more responsive to conflict arising from verbal processing. Unfortunately, there is little research to date relevant to addressing this hypothesis. The vast majority of the

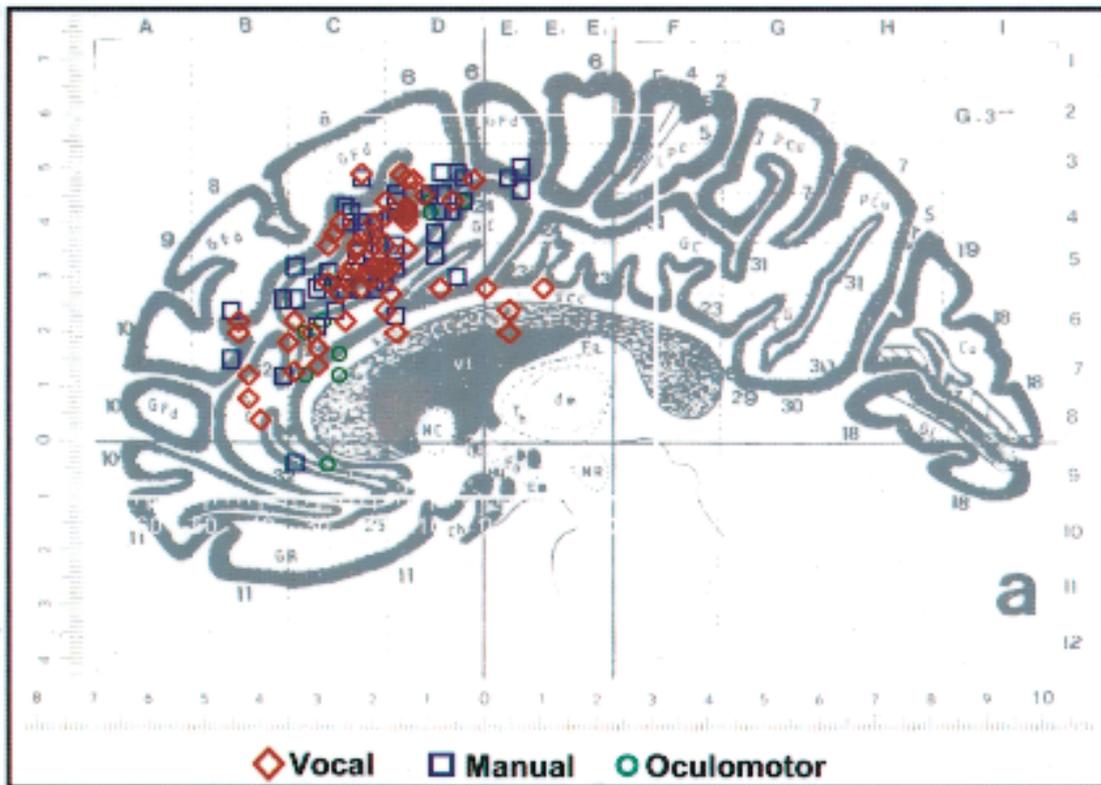


Figure 1. Plot of ACC activations associated with different response modalities in Talairach space (see Table 1 for coordinates).

studies that have examined inhibition of a prepotent response, underdetermined responding, or errors have used verbal processing. In the imaging domain, the exception to this is studies that have examined antisaccades, which can be conceived of as non-verbal processing. However, these antisaccade studies have primarily used eye movements as the response modality. Thus, it is impossible to determine whether the location of ACC activity in such studies reflects the nature of the processing or the modality of the response. The Turken and Swick study of the ACC lesion study did include conditions in their Stroop task that could be conceived of as both verbal (e.g. attend to the word) and non-verbal (e.g. attend to direction of the arrow). However, their patient showed impairment in both the word and arrow conditions when manual responses were required, although the pattern of impairment was slightly different in the two conditions.

As described above, our review of the literature suggests that, while there is reason to question whether the location of activity in the rCZ is somatotopically mapped, the research to date does not provide a clear answer to this question. In addition, there is almost no evidence to date regarding whether the location of ACC activity might vary according to the nature of the processing domain. Thus, the goal of the current study was to test directly these two hypotheses in healthy individuals using event-related functional magnetic resonance imaging (fMRI). Specifically, we used a version of the spatial Stroop task that allowed us to fully cross processing domain (e.g. verbal versus non-verbal) with response modality (e.g. vocal versus manual). In addition, we used fMRI methods that allowed us to acquire both the content and the latency of participants oral responses in vocal response conditions.

Materials and Methods

Participants

Thirteen neurologically normal right-handed subjects participated in this study. Subjects were seven males and six females, with a mean age of 23 (range 19–33 years). Subjects were paid \$25 an hour for participation, and gave informed consent in accordance with guidelines set by the Human Studies Committee at Washington University. Because of technical problems, behavioral data from one subject and imaging data from a separate subject were unusable, and thus these subjects were excluded from analysis.

Behavioral Procedures and Cognitive Tasks

A Power Macintosh computer (Apple, Cupertino, CA) and PsyScope software (Cohen *et al.*, 1993) displayed all visual stimuli. A LCD projector (Sharp, model XGE850) projected stimuli onto a screen placed at the head of the bore. Subjects viewed the screen via a mirror fastened to the head coil. Subjects responded either by pushing a fiber-optic light-sensitive key-press connected to a PsyScope Button Box (Carnegie Mellon University, Pittsburgh, PA) that recorded both accuracy and reaction time, or by making an overt vocal response (described in more detail below). Stimuli appeared for 1000 ms, followed by a 2200 ms inter-trial interval.

We used a factorial design, fully crossing two spatial Stroop tasks (attend to location, attend to word) with two response types (manual, vocal) and four trial types (fixation, congruent, neutral, incongruent). In all task conditions, subjects were presented with a word either to the right or left of a central fixation point. In the attend to location task (referred to as 'location'), subjects were told to respond to the location of the word, and ignore its content. In the attend to word task (referred to as 'word'), subjects were told to respond to the content of the word and ignore its location. For fixation trials for both tasks, subjects simply saw a centrally presented fixation cross. For congruent trials in both tasks, subjects saw either the word 'right' presented to the right of fixation, or the word 'left' presented to the left of fixation. For incongruent trials in

both tasks, subjects saw either the word 'right' presented to the left of fixation or the word 'left' presented to the right of fixation. In neutral trials for the location task, subjects saw the words 'home' and 'great' presented either to the left or right of fixation. In neutral trials for the word task, subjects saw the words 'right' and 'left' presented in the center of the computer screen. Participants were asked to make a manual response on half of the trials, pressing either the right or left button of the fiber-optic button box. Participants were asked to make a vocal response on the remaining trials, saying either 'right' or 'left' aloud. Trials were blocked by task and response modality, such that each participant performed two runs of each of the following (with order counterbalanced across participants): (i) location, manual response; (ii) location, vocal response; (iii) word, manual response; and (iv) word, vocal response. During each run, the four trial types (fixation, congruent, neutral, incongruent) were presented equally often in a continuous series of 112 intermixed trials. To allow rapid event-related analyses (Dale and Buckner, 1997), trial types were pseudorandomly intermixed with first-order counterbalancing (each trial type followed every other trial type equally often). Four different such pseudorandomly intermixed orders were created, and used twice for each subject (once for a word run and once for a location run). List order was counterbalanced across subjects. To create a stable task baseline, each functional run began with 16 s of visual fixation and ended with an additional 35.2 s of visual fixation.

Acquisition of Vocal Responses

Participants' overt vocal responses were acquired through the use of an elastic tube and a condenser microphone. The elastic tube was positioned over the participant's mouth and taped to the head coil. The elastic tube ran the length of the participant's body to the door of the scanner room. The condenser microphone was taped to the inside of the elastic tube at the end near the scanner door and run under the scanner door. The signal from the microphone was then split, going both into a standard tape-recorder (to record the content of the participant's response) and into the PsyScope button box attached to the Macintosh computer running PsyScope software. The connection into the button box allowed a voice-activated response key to record the reaction time of the participant's vocal response. Normally, the noise generated by fast changing echo-planar gradients preclude accurate acquisition of overt vocal responses. To avoid this, a quiet interval of 800 ms was interleaved with each frame acquisition ($T_R = 2400$ ms + 800 ms Quiet = 3200 ms trial) (Akbudak *et al.*, 1999). Although such a quiet period was not needed for manual responses, the identical procedure was used for both manual and vocal response runs to enhance comparability across different response modalities. The accuracy of participant's performance in the vocal response condition was coded by listening to the tape-recordings made during the scanning session.

Scanning Procedures

Images were acquired on a Siemens 1.5 Tesla Vision System (Erlangen, Germany) with a standard circularly polarized head coil. A pillow and tape were used to minimize head movement. Headphones dampened scanner noise and enabled communication with participants. Structural images were acquired using a high resolution (1.2511 mm) sagittal 3-D MP-RAGE (Mugler and Brookeman, 1990) T_1 -weighted sequence ($T_R = 9.7$ ms, $T_E = 4$ ms, flip = 12, $T_1 = 300$ ms). Functional images were acquired using an asymmetric spin-echo echo-planar sequence ($T_R = 2400$ ms, Quiet Period = 800 ms, $T_E = 50$ ms, flip = 90). During each functional scanning run 128 sets of 16 contiguous, 8 mm thick axial images were acquired parallel to the anterior-posterior commissure plane (3.75×3.75 mm in-plane resolution), allowing complete brain coverage at a high signal-to-noise ratio (Conturo *et al.*, 1996). Each run lasted ~7 min, with a 2 min rest period between runs.

Movement Estimation and Correction

Functional images were corrected for movement using a six-parameter rigid-body rotation and translation correction (Friston *et al.*, 1994; Snyder, 1996). Two sets of estimated movement parameters (Pitch, Roll, Yaw, X , Y , Z) were obtained from this algorithm. The first set was the difference of the current image from the immediately preceding image, which will be referred to as incremental movement. The second set was the differ-

ence of the current image from the reference image (the first image acquired), which will be referred to as absolute movement. For Pitch, Roll and Yaw, the parameters are expressed in degrees. For X , Y and Z the parameters are expressed in millimeters. The absolute values of these estimates were used to examine the degree of increased movement associated with producing overt vocal responses. We analyzed the movement data using two-factor ANOVAs, with image as the random factor (all images acquired were analyzed), task (location, word) and response modality (manual, vocal) as within-subject factors and the six movement parameters (Pitch, Roll, Yaw, X , Y , Z) as dependent variables. For absolute movement, there were no significant main effects of either task or response modality. This result is consistent with our prior research demonstrating no increase in absolute movement during overt vocal responding (Barch *et al.*, 1999, 2000). For incremental movement, the ANOVAs demonstrated no significant main effects of task, but significantly main effects of response modality for all six parameters (all P s < 0.05). For all parameters, incremental movement was greater during vocal than manual responding. However, the magnitude of incremental movement during vocal responding was still relatively small, again consistent with the results of our prior research on overt vocal responding (Barch *et al.*, 1999, 2000).

Susceptibility Artifacts

To assess potential reductions in signal-to-noise (SNR) associated with overt vocal responses, we quantified SNR by calculating the mean SNR (mean/variance) for each participant, for each slice location, separately for vocal and manual response runs. Paired-sample t -tests indicated significantly reduced SNR during vocal compared to manual responses for 12 out of the 16 slices ($P < 0.05$). To determine the magnitude of the SNR reduction, we calculated the average percent decrease in SNR $\{[(\text{Manual SNR} - \text{Vocal SNR})/\text{Manual SNR}] \times 100\}$ across participants for each slice. The average decrease in SNR ranged from 0 to 22% across slices ($M = 11\%$), and was relatively small (e.g. < 10%) in the more superior slices. However, the reduction in SNR did increase in the more inferior slices, which is not surprising given that these slices are closer to the throat and mouth region.

Image Analysis Procedures

Functional imaging data were analyzed according to the following procedures. Following movement correction, all functional images were scaled to achieve a whole-brain mode value (used in place of mean because of its reduced sensitivity to variation in brain margin definition) of 1000 for each scanning run (to reduce the effect of scanner drift or instability). Functional images were then resampled into 3 mm isotropic voxels, transformed into standardized atlas space (Talairach and Tournoux, 1988), and smoothed with a Gaussian filter (6 mm FWHM). A General Linear Model (Friston *et al.*, 1994; Worsley and Friston, 1995; Josephs *et al.*, 1997; Zarahn *et al.*, 1997; Miezin *et al.*, 2000) was used to analyze the pre-processed data on a voxel-by-voxel basis. Estimates of the magnitudes of each effect were derived from the model. Specifically, the seven time-points following the stimulus were cross-correlated with a series of five lagged hemodynamic response functions, each separated by 1 s, in order to account for possible variation in the onset of the hemodynamic response function (Boynton *et al.*, 1996; Dale and Buckner, 1997; Buckner *et al.*, 1998). These magnitude estimates were then analyzed using appropriately designed ANOVAs and t -tests (as described in more detail below), treating subject as a random effect. Statistical parametric maps of the voxel-wise t - and F -values were thresholded for significance using a cluster-size algorithm (Forman *et al.*, 1995). This algorithm takes account of the spatial extent of activation to correct for multiple comparisons. The specific thresholds used for each analysis are described below. In graphic displays, all effects are described in terms of percent signal change. Percent signal change was defined as signal magnitude divided by the mean signal intensity across all functional runs of the intercept term of the linear model.

Results

Behavioral Data Analyses

The behavioral data acquired during the scanning session, both

errors and reaction times for correct responses, were analyzed using three-way ANOVAs with task (location, word), response modality (manual, vocal) and trial type (congruent, neutral and incongruent) as within-subject factors. The error rates for this task were very low (Fig. 2), although the ANOVA indicated a main effect of trial type [$F(2,20) = 14.46, P < 0.01$], and a two-way interaction between task and response modality [$F(1,10) = 10.06, P < 0.01$], which was further moderated by a three-way interaction between task, response modality, and trial type [$F(2,20) = 9.02, P < 0.01$]. The main effect of trial type reflected the fact that there were more errors in the incongruent condition than either the neutral or congruent conditions, which did not differ. The three-way interaction resulted from there being a bigger increase in errors from the neutral to incongruent condition for manual as compared to vocal responses in the word task, but a bigger increase in errors in the incongruent condition for vocal as compared to manual responses in the location task. For the RT (reaction time) ANOVA, all main effects and interactions were significant, including the three-way interaction between task, response modality and trial type [$F(2,20) = 23.56, P < 0.01$]. Planned contrasts indicated that the main effect of trial type was significant for both vocal [$F(2,20) = 16.08, P < 0.01$] and manual responses [$F(2,20) = 10.75, P < 0.01$] in the location task and both vocal [$F(2,20) = 6.29, P < 0.01$] and manual [$F(2,20) = 74.23, P < 0.01$] responses in the word task. However, as can be seen in Figure 2, the three-way interaction between task, response modality and trial type resulted from there being a greater slowing of RT between the neutral and incongruent condition for vocal as compared to manual responses in the location task, but a greater slowing of RT between the neutral and incongruent trial types for manual than vocal responses in the word task.

The above analyses of the behavioral data utilized RT measures for vocal responses acquired during the course of fMRI scanning. To determine whether these RT data were valid, we ran an additional 12 subjects in the identical tasks outside of the scanner. The results for these 12 subjects were essentially identical to those with the data acquired in the scanner, including three-way interactions between task, response modality and trial type for both RT [$F(2,22) = 9.10, P < 0.001$] and errors [$F(2,22) = 7.39, P < 0.01$]. To quantitatively assess the similarities of the RT

data acquired in and outside of the fMRI scanner, we conducted an ANOVA on the RTs, with session (in scanner, out of scanner) as a between-subject factor. There was a main effect of session [$F(1,21) = 22.08, P < 0.01$] with overall faster RTs outside of the scanner. In addition, there was a session response modality interaction [$F(1,21) = 24.91, P < 0.01$]. This interaction reflected the fact that although overall RTs were slower for both manual and vocal response in the scanner as compared to out of the scanner, the slowdown was greater for vocal than manual responses. There were no other interactions between session and any of the other factors.

Common ACC Regions Responsive to Conflict for Vocal and Manual Responses

We began the analysis of the fMRI data by looking for ACC regions that displayed significant effects of response competition with *both* vocal and manual responses. Our hypotheses were specifically focused on the ACC, thus we focused on voxels falling within either the rCZ or cCZ as defined by Picard and Strick (1996). However, we also examined voxels falling within pre-SMA and SMA as comparison regions, again as defined by Picard and Strick. More specifically, we defined a voxel as being within the rCZ if its Tailarach coordinates placed it within BA 32 superior to $Z = +10$ mm and anterior to $Y = +5$ mm, or within BA 24 superior to $Z = +10$ mm and anterior to $Y = +15$ mm. We defined a voxel as falling within the cCZ if its Tailarach coordinates placed it within BA 24 with a Y coordinate between $+5$ and -15 mm and a Z coordinate between $+30$ and $+45$ m. We defined a voxel as falling within pre-SMA if its Tailarach coordinates placed it within BA 6 anterior to $Y = 0$ mm, and as falling within SMA if its Tailarach coordinates placed it within BA 6 posterior to $Y = 0$ mm.

To examine our hypotheses, we performed 'conjunction' analyses similar to those described by Friston and colleagues (Price and Friston, 1997; Friston *et al.*, 1999). To do so, we conducted paired *t*-tests on all voxels (separately for vocal and manual responses) and examined only those voxels within ACC, SMA, and pre-SMA that demonstrated a significantly greater magnitude of response in the incongruent condition as compared to the neutral condition independently for both vocal and manual responses. Because of the conjunctive nature of this

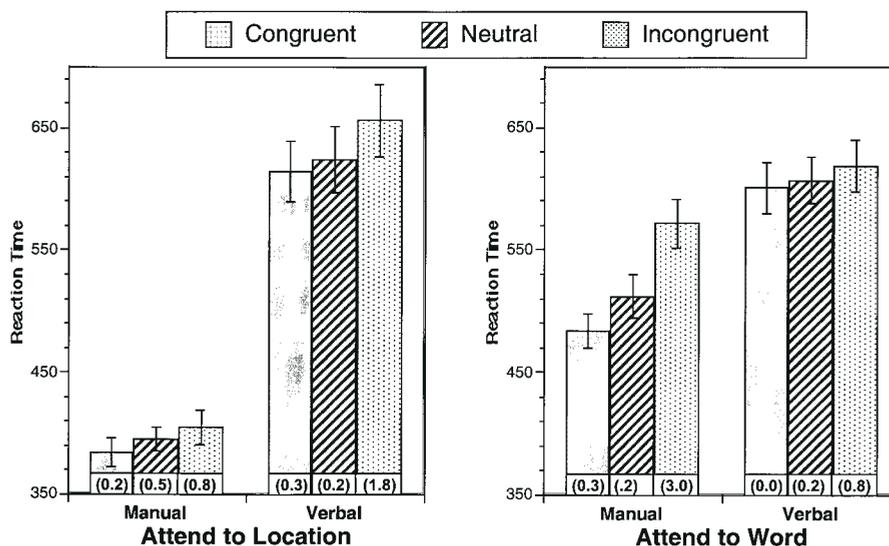


Figure 2. Graph plotting reaction times for behavioral data acquired during fMRI scanning. Error rates are shown at the bottom of the graph bar for each condition.

analyses, we set the P -value threshold for the analysis of each individual response modality at $P < 0.05$ and four voxels. However, requiring a conjunction of significance in both the vocal and manual response condition actually leads to significance threshold of $P < 0.0025$ (0.05×0.05). As shown in Table 4, this analysis identified a region of ACC that demonstrated significant response competition effects for both manual and vocal responses, located in the rCZ. Figure 3 displays the time courses for this ACC region. For both vocal and manual responses, ACC activity was greater during incongruent trials than during neutral trials.

One criticism that might be leveled against the above analysis is the possibility that we found a common ACC region responsive to conflict for both manual and vocal responses because covert articulation may have been engaged in at least one of the manual response conditions (e.g. attend to word, manual response). One might make a similar argument for participants having engaged in 'covert' arm movements in at least one of the vocal response conditions (e.g. attend to location). To address this possibility, we conducted a second analysis examining only the manual response condition we thought least likely to engage any covert articulation (i.e. attend to location, manual response) and the vocal response condition we thought least likely to engage any covert arm movements (i.e. attend to word, vocal response). We used conjunction analyses identical to those described above to identify ACC and SMA voxels that demonstrated significant response conflict effects in *both* the attend to location-manual response condition and the attend to word-vocal response conditions. In general, this analysis produced results similar to those described above. Specifically, as shown in Table 4, we found two regions of ACC and a region of SMA that demonstrated significant response conflict effects for both the location-manual and word-vocal tasks. One of the ACC regions was in the posterior rCZ, and one was in the anterior rCZ.

Different ACC Regions Responsive to Conflict for Vocal Versus Manual Responses

To identify ACC regions demonstrating response competition effects selectively for only one of the two response modalities (e.g. manual or vocal), we conducted two-factor ANOVAs on each voxel, with trial type (neutral, incongruent) and response modality (manual, vocal) as within subject factors. We then examined those voxels demonstrating significant interactions between trial type and response modality. We used a more liberal threshold for this analysis ($P < 0.01$ and four voxels), to protect against null results due to an overly conservative threshold. This analysis did not identify any regions in ACC that demonstrated conflict effects in one response modality and not the other. However, this lack of an effect in ACC did not reflect an inability to identify any region showing such an interaction. Although these areas were not the focus of this study, we see regions in the cerebellum, inferior frontal cortex, parietal cortex, and SMA that demonstrated significant response conflict effects (e.g. greater event-related activity to incongruent than neutral trials) for manual, but not vocal responses. We also saw a region of middle frontal gyrus that demonstrated significant response conflict effects for vocal but not manual responses.

As noted above, a criticism that might be leveled against the above interaction analysis is the possibility that we failed to find ACC regions responsive in one modality and not the other because covert articulation may have been engaged in at least one of the manual response conditions (e.g. attend to word, manual response) or because 'covert' arm movements may have

Table 4
Regions demonstrating significant response conflict effects in conjunction analyses

Regions of interest	Brodman area(s)	X ^a	Y ^a	Z ^a	No. of voxels
Both vocal and manual responses					
Anterior cingulate	24/32	7.5	9	42	29
Location-manual and word-vocal					
Anterior cingulate	24	1.5	18	24	9
Anterior cingulate	24/32	7.5	9	42	28
SMA	6	-13.5	0	54	4
Both word and location tasks					
Anterior cingulate	24	7.5	21	24	8
Anterior cingulate	24/32	10.5	3	42	11
Anterior cingulate	32	4.5	15	39	14
SMA	6	-13.5	0	54	4
Pre-SMA	8	-4.5	21	48	8

^aX, Y and Z are coordinates in a standard stereotactic space (Talairach and Tournoux, 1988) in which positive values refer to regions right of (X), anterior to (Y) and superior to (Z) the anterior commissure (AC).

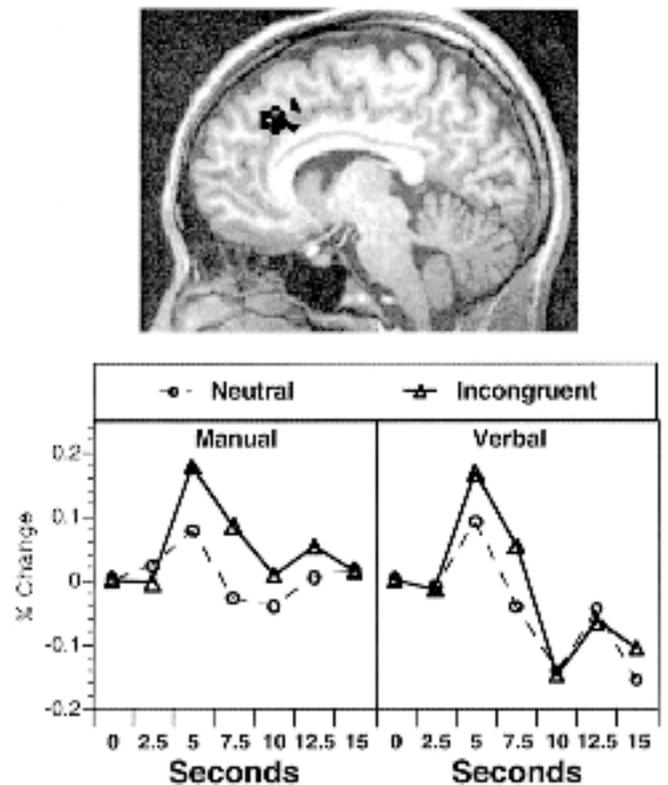


Figure 3. ACC regions exhibiting significantly response conflict effects (greater event-related activation to incongruent than neutral trials) for both manual and vocal responses. Insets plot percent signal change (averaged across all voxels within a ROI) for the seven time points following the onset of the stimulus, separately for neutral and incongruent trials.

occurred in at least one of the vocal response conditions (e.g. attend to location). Thus, to again address this possibility, we conducted an additional analysis comparing the manual response condition we thought would be least likely to engage any covert articulation (i.e. attend to location, manual response) and the vocal response condition we thought would be least likely to engage any covert arm movements (i.e. attend to word, vocal response). Specifically, we conducted voxel-wise two-factor ANOVAs on each voxel, with trial type (neutral, incongruent) and condition (location-manual vs word-vocal) as within-

subject factors. Even with this more stringent analysis, we did not find any ACC regions showing response conflict effects in one of the conditions and not the other. Again, however, although these regions were not the focus of this study, we did see areas in primary motor cortex, frontal insula, and middle frontal gyrus (Table 5) that demonstrated significant response conflict effects (i.e. greater event-related activity to incongruent than neutral trials) for manual but not vocal responses. In addition, we found regions of visual cortex, temporal cortex and inferior and middle frontal cortex that demonstrated significant response conflict effects for vocal but not manual responses.

Our results are somewhat in conflict with previous findings by Paus and colleagues. To determine whether such differences might be related to analysis strategies, we also analyzed the data in a manner similar to Paus *et al.* Specifically, we conducted separate subtractions (incongruent - neutral) for manual and vocal responses, and identified peaks of activation separately for each response modality. A voxel was identified as a peak if it occurred with a cluster of at least four significantly activated voxels and was located at least 12 mm from any other peak of activation. For this analysis, we used the same significance threshold as in our first 'conjunction' analyses ($P < 0.05$). Without the additional constraint of the conjunction, this is a liberal threshold. However, we choose to err on the side of identifying potential false positives with good power to detect differences in the peaks of ACC activity as a function of response modality, as to provide the fairest comparison to the study by Paus and colleagues. These analyses identified three peaks of ACC activity for response conflict effects with manual responses: (i) BA 24 ($X = -10, Y = 3, Z = 36$); (ii) BA 24 ($X = 1, Y = 9, Z = 36$); and (iii) BA 32 ($X = 19, Y = 36, Z = 24$). For vocal responses, we identified two peaks of activation: (i) BA 32 ($X = 7, Y = 3, Z = 42$) and (ii) BA 32 ($X = 4, Y = 39, Z = 27$). These peaks for manual versus vocal responses do not show a clear dissociation in terms of a rostral/caudal dimension. Thus, even using a similar analyses approach, our findings still differ from Paus and colleagues.

Common ACC Regions Responsive to Conflict in Both the Location or Word Task

We next investigated ACC regions that displayed significant effects of response competition for *both* the word and location tasks. To do so, we again performed 'conjunction' analyses. We again conducted paired *t*-tests on all voxels (separately for the location and word tasks) and examined only those voxels in ACC, SMA or pre-SMA that demonstrated a significantly greater magnitude of response in the incongruent condition as compared to the neutral condition for both the word and location tasks. As shown in Table 4, this analysis identified three regions of ACC, a region of SMA and a region of pre-SMA that demonstrated significant response competition effects for both the word and location tasks. Not surprisingly, two of these ACC regions were very similar in location to the one identified in the conjunction analysis for vocal and manual responses. The other ACC region was more rostral, falling in the anterior portion of the rCZ. As can be seen in Figure 4, the time courses of the cortical response for these ACC regions indicated that for both the word and location tasks, ACC activity was greater during incongruent trials than during neutral trials.

Different ACC Regions Responsive to Conflict in the Location Versus Word Task

To identify ACC regions demonstrating response competition effects for only one of the two tasks (e.g. word or location), we

Table 5
Regions demonstrating selective response conflict effects in disjunction analyses

Regions of interest	Brodman area(s)	X ^a	Y ^a	Z ^a	No. of voxels
Manual but not vocal responses					
Cerebellum	–	–1.5	–66	–15	4
Inferior frontal cortex	47	–28.5	15	–3	4
Inferior frontal cortex	44/6	49.5	6	9	6
Superior parietal cortex	40	31.5	–36	45	5
SMA	6	10.5	–21	54	4
Vocal but not manual responses					
Middle frontal cortex	9	25.5	18	39	4
Location–manual but not word–vocal	24	1.5	18	21	4
Primary motor cortex	1/2	46.5	–24	30	4
Inferior frontal cortex	45	–22.5	30	3	4
Middle frontal cortex	46/9	–40.5	36	24	5
Word–vocal but not location–manual					
Visual cortex	18	–7.5	–78	0	9
Visual cortex	18	10.5	–81	0	9
Temporal cortex	21	58.5	–21	–21	4
Temporal cortex	21/22	–64.5	–51	6	4
Inferior frontal cortex	47	–49.5	24	–6	6
Middle frontal cortex	9	13.5	60	27	4
Word but not location task					
Visual cortex	17/18	–7.5	–81	–3	38
Visual cortex	17	–7.5	–90	–12	4
Visual cortex	17/18	13.5	–81	0	28
Visual cortex	18	1.5	–81	12	11
Cerebellum	–	–16.5	–57	–9	4
Parietal cortex	40	–61.5	–24	24	4

^aX, Y, and Z are coordinates in a standard stereotactic space (Talairach and Tournoux, 1988) in which positive values refer to regions right of (X), anterior to (Y), and superior to (Z) the anterior commissure (AC).

conducted two-factor ANOVAs on each voxel within ACC and SMA, with trial type (neutral, incongruent) and task (attend to word, attend to location) as within-subject factors. We then examined those voxels demonstrating significant interactions between trial type and task ($P < 0.01$). We did not find any regions in ACC that demonstrated task-selective conflict effects. Again, however, this lack of an effect in ACC did not reflect an inability to identify any region showing such an interaction. Although not the focus of this study, we did see a number of regions that demonstrated significant response conflict effects for the word task, but not the location task, including regions in visual cortex, cerebellum and parietal cortex (Table 5).

Somatotopy in Primary Motor and Somatosensory Cortex

The current study did not find any evidence for somatotopic mapping of conflict associated activation in ACC, although we did find some evidence for regions in SMA responding selectively to conflict with manual responses. However, to be in a better position to interpret the absence of clear somatotopy in ACC activations, we assessed our ability to identify somatotopic organization of activation in primary motor and somatosensory cortex, as well as supplementary motor cortex. Both human and animal data indicate that somatotopy should be present in primary motor cortex and SMA. Thus, demonstration of such results in the current study would suggest that our methods and design provided the power to detect somatotopic mapping where it is known to exist. Thus, we used paired *t*-tests to identify regions more responsive to manual than verbal responses, collapsing across task and trial type ($P < 0.01$ and four voxels). We identified regions more responsive to vocal than manual responses in the same manner, collapsing across task and trial type. As shown in Figure 5, we were able to see clear somato-

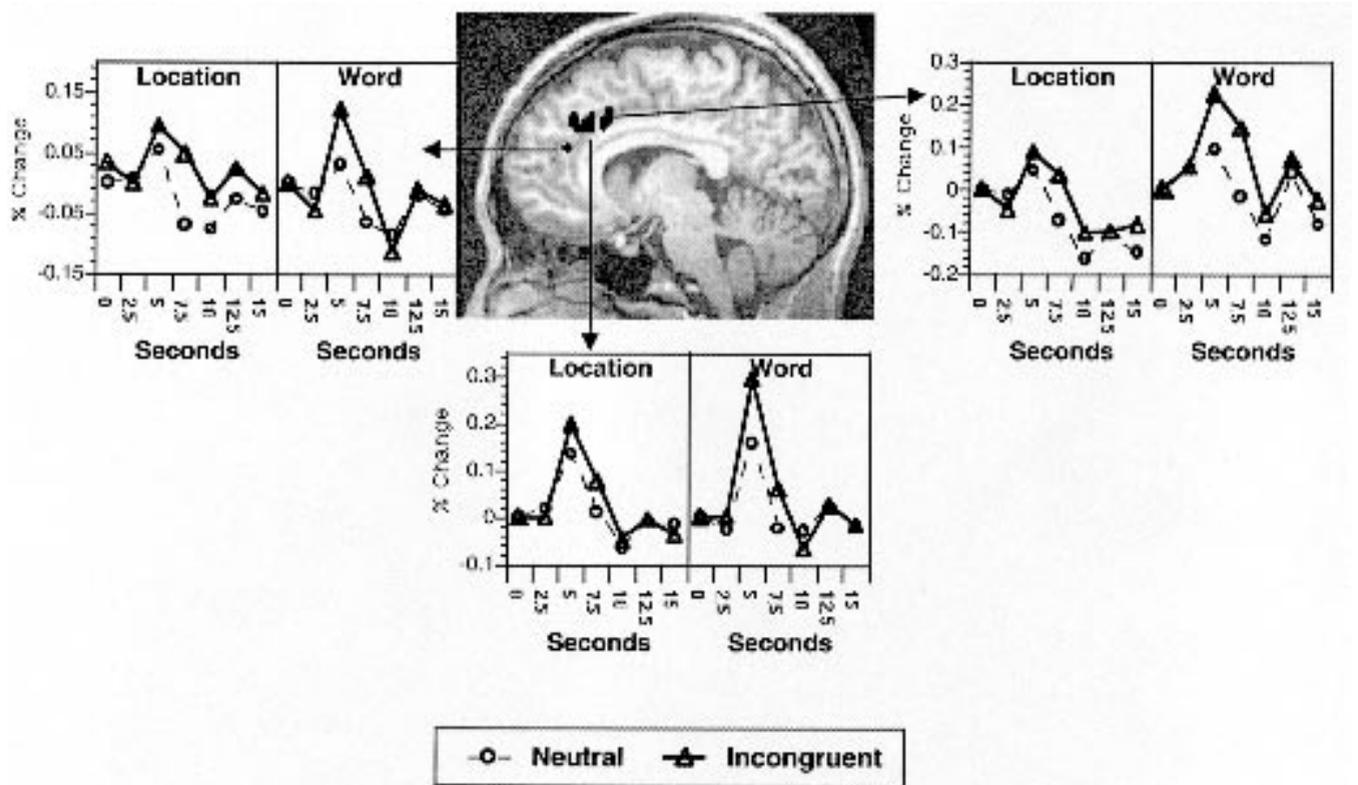


Figure 4. ACC regions exhibiting significantly response conflict effects (greater event-related activation to incongruent than neutral trials) for both the word and location tasks. The insets plot percent signal change (averaged across all voxels within a ROI) for the seven time points following the onset of the stimulus, separately for neutral and incongruent trials.

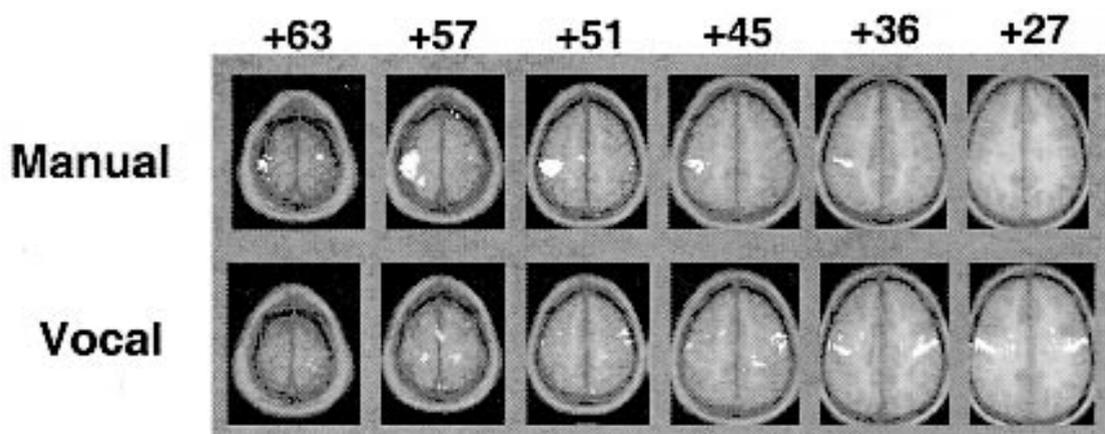


Figure 5. Regions within primary motor and supplementary motor cortex, demonstrating differential activation as a function of response modality.

topic organization of activations in primary motor cortex. Specifically, activations associated with the right-handed button press were clearly left lateralized and superior to the activations associated with vocal responding, which were more bilateral. In addition, within SMA we identified a region associated with manual responding that was located posterior to an SMA region associated with vocal responding, a pattern that conforms well with prior studies on somatotopic mapping in SMA (Picard and Strick, 1996).

Discussion

The major results of this study were that we identified regions of

the ACC, within the rCZ, that demonstrated significant response conflict effects across response modalities and across processing domains. More specifically, we found a region of the posterior rCZ that demonstrated significant response conflict effects (greater activity during incongruent than neutral trials) for both manual and vocal responses. In addition, we found three regions of the ACC, one in the anterior rCZ and two in the posterior rCZ, that demonstrated significant response conflict effects for both verbal and non-verbal processing. Further, we did not find any ACC regions that demonstrated either response modality-specific or processing domain-specific response conflict effects. In contrast, we were able to identify clear differences in the

regions of activations associated with manual versus vocal responses in primary motor and somatosensory cortex, regions known to display such somatotopic mapping.

These results of the current study in regards to the rCZ conflict with the conclusions drawn by Picard and Strick in their review of the literature, which suggested that there were different regions of both the anterior (rCZa) and posterior (rCZp) rostral cingulate zones associated with manual versus vocal responses, and that such differences are of a magnitude capable of being detected in group averaged analyses. As described above, we did not find any evidence for such somatotopy within either rCZa or rCZp. As such, our current findings are consistent with the review of the literature we presented in the Introduction, which suggested that ACC activity as a function of response conflict for both vocal and manual responses occurred throughout the rCZ, without clear somatotopic mapping. We should note, however, that the results of our study do not preclude the possibility that a finer grained somatotopy might be present in rCZ activations, such as might be detected in single subjects analyses or with a higher resolution magnet. However, our results are *not* consistent with the hypothesis that rCZ activations in response to conflict are somatotopically organized on a scale such as that suggested by Picard and Strick, who reviewed studies using group averaged data.

The ACC activation we identified as responsive to conflict for both vocal and manual responses fell within what Picard and Strick would designate the rCZ. However, one might still wonder about the presence of somatotopy within the caudal cCZ. Picard and Strick and Paus have defined the cCZ somewhat differently. Paus has defined the border between the caudal and rostral ACC as $Y = +10$ mm, irrespective of the Z coordinate. In addition, Paus has suggested that activations associated with *either* simple or complex manual responses should segregate to the cCZ. The centroid for our ACC ROI demonstrating response conflict effects for *both* vocal and manual responses fell within the cCZ as defined by Paus. Thus, our results are not consistent with Paus' suggestion that activations associated with complex manual responses are localized to cCZ while activations associated with vocal and eye movement responses are located more rostrally. In contrast to Paus, Picard and Strick define the border between the rCZ and cCZ in terms of both the anterior/posterior (approximately $Y = +5$ mm) and inferior/superior (approximately $Z = +45$ mm) dimensions. Further, Picard and Strick suggested that the cCZ is primarily activated by simple manual responses. However, when we collapsed across conflict conditions (e.g. congruent, neutral and incongruent) and simply compared manual to verbal responses, we did not find selective activation of cCZ for manual responses, although we did find evidence for somatotopic mapping in primary motor cortex and SMA. Further, inspection of the activation maps computed separately for vocal and manual responses indicated activation of the cCZ in all task conditions for both vocal and manual responses. The activation of cCZ (as defined by Picard and Strick) for vocal responses is somewhat surprising, and suggests that further research is needed to determine whether this finding replicates and to clarify the functional role of cCZ activity in humans.

We also did not find any evidence for laterality differences in ACC activation as a function of processing domain (i.e. verbal versus non-verbal). As noted in the Introduction, some cortical regions, such as the inferior frontal cortex, have shown evidence of lateralization of activation as a function of processing domain (D'Esposito *et al.*, 1998). However, other frontal regions, such as dorsolateral prefrontal cortex (DLPFC) show much less evidence

for lateralization of activation as a function of processing domain (D'Esposito *et al.*, 1998). Interestingly, the rostral ACC has known strong reciprocal connectivity with dorsolateral prefrontal cortex (Devinsky *et al.*, 1995). As such, our finding of common ACC regions activated by response conflict with both vocal and manual responses, and with both verbal and non-verbal processing may actually be consistent with our hypothesis regarding the role that ACC activation may play in cognitive control. Specifically, we have hypothesized that a conflict signal from the ACC may help recruit additional cognitive control functions that may be carried out by other brain regions or systems, such as the dorsolateral prefrontal cortex. Consistent with this view, many of the tasks that elicit ACC activation also elicit dorsolateral prefrontal cortex activation (Carter *et al.*, 1995; Braver *et al.*, 1997, 2001; Cohen *et al.*, 1997; Corbetta *et al.*, 1991). Thus, it may be that the ACC serves to help determine when regions such as the dorsolateral prefrontal cortex needs to come on line to provide needed biasing in favor of task-relevant processing. As noted above, the same regions of DLPFC appear to be active for processing in multiple different domain and with all response output modalities (D'Esposito *et al.*, 1998). As such, we may not see evidence for somatotopic mapping of ACC regions responsive to conflict if their function is to engage control mechanisms supported by other cortical regions that are involved in multiple processing domains and with multiple output modalities.

The current study and the review of the literature in the Introduction was specifically designed to examine the relationship between response conflict and ACC activation. However, the review presented in the Introduction did not include studies examining a type of task that often elicits ACC activation, namely working memory tasks. It is possible that the ACC activations during such working memory studies reflects the presence of response conflict in such paradigms. However, since these working memory studies did not explicitly include conditions that varied the degree of response conflict, we did not feel that it was fair to include them in a review of ACC activations associated with response conflict. Further, the vast majority of working memory studies have used manual responses, making it difficult to compare the location of ACC activations as a function of response modality. Nonetheless, as reviewed by Petit *et al.* (Petit *et al.*, 1998), many of the ACC activations in working memory studies fall very close to the ACC regions identified in the current study. More interestingly, Petit found that activity in rCZ during both spatial ($X = 6$, $Y = 9$, $Z = 36$) and face ($X = 5$, $Y = 7$, $Z = 33$) working memory tasks was sustained during the delay period in which participants had to hold information on line. One possible explanation for this sustained rCZ activity during the delay period, suggested by Petit, is that it reflects the fact that participants do not yet know what the final motor response will be, and thus are preparing to respond with either a right or left button press. Thus, in terms of our response conflict hypothesis, this simultaneous activation of motor programs associated with both a right and left button press may generate conflict between incompatible motor representations. However, at present this is a *post hoc* explanation for the presence of rCZ activity during working memory tasks, and additional research is needed to determine whether or not rCZ activation in working memory tasks reflects response conflict.

Notes

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