The Contribution of the Anterior Cingulate Cortex to Executive Processes in Cognition

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Synopsis

The anterior cingulate cortex (ACC), on the medial surface of the frontal lobes, has frequently been hypothesized to make critical contributions to the function of neural systems involved in the executive control of cognition. Three principal theories have been developed to account for this role. The first, inmotivated attentionï emphasizes the limbic identity of the ACC and the effects of
lesions to this area of the brain. The second, "attention allocation," emphasizes the fact that during functional neuroimaging studies activation of the ACC is seen during tasks that elicit incompatible response tendencies that must be resolved for correct performance. The third theory, "error detection," reflects the observation of a negative scalp potential occurring during incorrect responses which appears to have a medial frontal generator. The first and last theories suggest evaluative functions by the ACC in the service of control, while "attention allocation" suggests a strategic function. We have proposed that the data supporting all three theories can be reconciled if the ACC were detecting conflicting processes during task performance that might be associated with errors. In support of this hypothesis we describe results using event-related fMRI which confirm that the ACC does show error related activity but that the same region of the brain also shows increased response related activity during correct responses associated with response competition. This suggests a re-conceptualization of the contribution of the ACC to executive processes that support an evaluative role, specifically the on-line detection of processing conflicts that may be associated with deteriorating performance. Unresolved questions related to the contribution of this region to executive processes and potential future directions for research on the function of this region of the brain are discussed.

**Introduction**

With the development and widespread application of functional brain imaging over the past decade there has been a dramatic increase in interest in identifying the neural mechanisms underlying human cognition and behavior. Higher cognitive functions such as attention, memory and language functions have received particular emphasis (e.g. Posner and Abdullev, Cabeza and Nyberg). A common set of mental operations, termed executive functions, cut across these functional domains and have received a great deal of attention in these studies (Posner and Petersen, LaBerge, Baddeley, Shallice DiEsposito, Carter Cohen et al nature). Executive
functions comprise a broad class of mental processes involved in initiating and maintaining controlled information processing and co-ordinated actions. These processes include goal, or more broadly, context representation and maintenance, strategic processes such as attention allocation and stimulus-response mapping, and performance monitoring (Shallice 1988; Cohen et al 1992; Carter et al 1998.). These functions are essential for everyday cognition and behavior, and are notably vulnerable to brain injury and disease.

**Executive Control and The Anterior Cingulate Cortex**

One region of the brain which has consistently been associated with executive processes is the anterior cingulate cortex (ACC), on the medial frontal surface adjacent to the corpus callosum. The ACC has rich, bidirectional connections with the association cortex of the dorsolateral frontal, parietal, temporal pole and entorhinal cortices. It also receives rich projections from the amygdala. The ACC, in particular the cortex in the cingulate sulcus, also has rich efferent connections to multiple levels of the motor system, including SMA, pre-motor and motor cortex, and the anterior horn cells of the spinal cord (Dum and Strick, Morecraft). The laminar organization and connectivity of the ACC vary along its rostrocaudal extent and it has been hypothesized that this region of the brain is functionally heterogeneous, and involved in a range of functions including autonomic regulation, pain perception, and higher cognitive function. In this paper we focus on the contribution of regions of the ACC caudal to the genu of the corpus callosum higher cognitive processes. The unique connectivity of this region, and observations from brain injured subjects and functional neuroimaging studies, has led to the frequent claim that the ACC is a critical element in the neural system associated with executive processes and behavioral regulation (Mesalum, Posner and Petersen, DiEsposito). However the precise contribution of this region to this broad class of processes has not been well understood. As data have accumulated three distinct mechanisms by which the ACC may contribute to control have been proposed. These theories are 1) motivated attention, 2) attention for action and 3) error
detection. We will briefly review the evidence for each of these theories including the functional neuroimaging and electrophysiological literature related to the function of the ACC. We will then discuss a new, integrative theory of the contribution of the ACC to executive processes, based upon results of recent work from our laboratory. This new theory accommodates findings from a range of functional neuroimaging and electrophysiological studies, and reconciles, to some degree, the three competing theories mentioned above.

**Motivated Attention**

Speculation that the ACC was part of a network involved in the control of cognition, particularly spatial attention, actually precedes the ‘brain mapping’ era. Based upon the location of the ACC in Broca’s ‘great limbic lobe’ and reports of neglect associated with medial frontal lesions, Mesulam (1981) was the first to ascribe a specific role for the ACC during normal cognition. Specifically, Mesulam hypothesized that the ACC contributed a ‘motivational map’, to a neural network which included the thalamus and parietal cortex. The function of this network was to control the distribution of attention to locations in the visual field with the ACC providing a representation of the salience of a given location. The view that the ACC may contribute to ‘motivated’ attention has been echoed by a number of authors since (Devinsky, Mayberg, Drevets). The manner by which the ACC would compute the motivational significance of stimuli or the means by which it would influence attention allocation has not been made explicit however.

**Selective Attention**

Posner et al (1987) proposed an alternative view of the role of the ACC in executive processes
related to attention. This hypothesis arose out of a pioneering set of studies conducted by Posner and his colleagues using $^{15}$O H$_2$O PET during cognitive activation. ACC activity was observed during verb generation and word categorization tasks and was greater with high than low target frequencies in the latter task. Invoking the concept of attention to action, Posner hypothesized that the ACC strategically implemented processes which limit the potential conflicting actions taken towards stimuli.

Since these early studies activity in the ACC has been observed during the performance of a wide range of tasks engaging processes related to attention, memory, and language processing (e.g. see Cabeza and Nyberg for a review). ACC activation is not a ubiquitous finding, however. In studies using PET or fMRI to examine regional brain activity during cognitive performance, increased activity in the ACC is generally seen when tasks involve demands on selective attention, especially when subjects must 1) overcome a pre-potent response tendency, 2) under conditions of divided attention and dual task performance, 3) during novel, versus practiced task performance, and 4) during task performance which requires under-determined responding.

The classical task in which subjects must overcome a prepotent response tendency is the Stroop (1935) task, in which subjects must name the color of a word which is itself the name of a color. When the color and the word conflict (e.g. the word RED printed in blue ink), subjects are slower to respond and may occasionally err by naming the word, reflecting the competition which occurs between the required response, color naming, and the more automatic (but incorrect) response to a word, reading (Macleod 1991). Increased ACC activation during [15O]-H$_2$O PET in the incongruent condition, compared to color naming words where the word and color were the same (i.e. color congruent stimuli), was originally reported by Pardo et al (1990). ACC activation during incongruent stimuli compared to either congruent (Carter et al 1995) or color patches or neutral words (Bench et al 1993, Carter et al 1995) has since been reported by several investigators. Bush et al (1998) recently showed increased ACC activation in an fMRI
study in which subjects were required to report the number of words present in a display, when the words themselves were numbers which conflicted with the number of items. Taylor et al (1994) showed increased ACC activation when subjects responded with a learned association (say J when the letter P appears), compared to when subjects simply named the letter. Paus et al (1993) reported increased ACC activation under conditions where subjects were required to produce an anti-stimulus response, compared to when they produced a pro-stimulus response. Increased ACC activity was seen in an antisaccade versus a pro-saccade task and when subjects lifted a different finger to that touched by an investigator, compared to lifting the same finger. The go-no-go paradigm, in which subjects must withhold a frequent keypress to rarely occurring targets, also activates the ACC (Kawashima et al 1996, Casey et al 1997).

Increased ACC activity is observed when subjects are required to divide their attention across multiple features of a stimulus, compared to conditions in which subjects must focus on the occurrence of a single feature or a single stimulus. Corbetta et al (199) reported that ACC activity increased when subjects monitored for a change in one of several features of a visual display (color, size or motion) but not when they attended to just one feature. The same group reported an absence of ACC activation during vigilance per se, in a task where subjects monitored for the occurrence of an infrequent somatosensory stimulus (Pardo et al). Similarly increased ACC activity is seen during dual, compared to single task performance. DiEsposito et al (199) reported that when subjects performed a single, simple mental rotation task or a math task no ACC activation was observed, but when subjects were required to divide their attention and perform both tasks concomitantly robust ACC activation was observed.

A third set of conditions under which ACC activation is seen is during novel, versus practiced task performance. Raichle et al (1994) reported that during a verb-generate task, where subjects generate novel uses of nouns robust ACC activation is seen. However when they are permitted to generate stereotyped responses to the same list of nouns ACC activity was markedly reduced.
Similarly in the study by Paus et al (1993) ACC activation was greater when subjects performed tasks which involved novel stimulus-response pairings than when the pairings were highly practiced. Finally, in the study of Bush et al (1998) using a numeric Stroop task, ACC activity was greatest when subjects initially performed the task than when practiced. We observed similar effects of reduced ACC activity with practiced in a PET study of the color-word Stroop (unpublished data).

A final class of tasks which differentially activate the ACC are those which involve under-determined responding. In tasks such as verb generation and verbal fluency, as well as those which contrast during novel versus practiced conditions, subjects must choose from a set of responses (e.g. uses of nouns, words beginning with a particular letter), each of which is potentially correct. (Petersen et al 1988,1989, Friston et al 1993, Yetkin et al 1995). This has been referred to Botvinick et al (submitted) as under-determined-responding. Another example of a task which activates the ACC while eliciting under-determined responding is stem completion (Buckner et al 1995). In contrast, when subjects are permitted to generate stereotyped responses in tasks such as generate uses, responses are essentially determined by that produced on the previous presentation of a given noun, and ACC activity is much reduced (Raichle et al 1994).

The observation of increased activation under each of the experimental conditions outlined above is consistent with the hypothesis that the ACC implements processes which serve to reduce conflicts between potential responses to stimuli. Overcoming a pre-potent response tendency, divided attention and dual task performance, novel performance, and under-determined responding will all elicit response conflict and place demands upon such a cognitive system.
**Error Detection**

The two very different theories of Mesalum and Posner, motivated attention - an evaluative function, and attention to action - a strategic one, have dominated thinking about the contribution of the ACC to executive processes for over a decade. More recently however a third hypothesis has emerged. This theory, arising from electrophysiological studies of brain surface potentials, proposes a different kind of evaluative function for the ACC, that of an error detector.

Studies using cognitive evoked potentials (ERP’s) have observed a unique negativity, referred to as the error-related negativity, or ERN. Discovered concurrently by Falkenstein and by Ghering in 1990 (refs), this robust negative deflection of the scalp potential is observed approximately 75-150 msec after electromyographic evidence of a subject initiating an incorrect response. It is observed in response aligned averages of error trials occurring during a variety of speeded response tasks and response modalities (Ghering et al 1990, 1993, 1995, Dahaene et al 1994, Falkenstein et al 1991, 1995, Holroyd et al 1998). The ERN is largest when accuracy is emphasized in the task instructions, but is not dependent upon the subject receiving overt feedback regarding their performance (Falkenstein et al 1991, Dehaene et al 1994). Reaction times are longer for trials following an ERN, and the ERN is even observed when subjects begin to make an error (by dynamometer squeeze), but subsequently correct their response (Ghering et al 1993). A large ERN predicts a high likelihood that a subject will correct one of these partial errors. Most importantly, dipole modeling has shown that the ERN has a medial frontal generator, most likely the ACC (Dahaene et al 1995). This finding converges upon previous single unit and surface potential recording studies in the ACC of non-human primates showing increased firing rates during incorrect responses (Brooks 1986, Niki and Watanabe 1976). The results of studies of the ERN have led to the hypothesis that the ACC contributes to executive control by monitoring performance and detecting errors. It is hypothesized that this is implemented through a comparator process in which intended responses are compared to actual
responses. When a mismatch occurs, the ACC detects an error (Coles et al 1995, Falkenstein et al 1991, 1995) and signals other components of the executive system to enhance strategic processing (e.g. by increasing the allocation of attentional resources) and improve performance.

**Detecting Competition: An Integrative Theory Of ACC Function During Cognition**

While the early theory of Mesalum emphasized an evaluative role for the ACC, consistent with its limbic identity, the neuroimaging based theory of Posner emphasized a strategic function, implementing processes designed to reduce competition between incompatible responses. Studies of the ERN, however, again emphasize an evaluative function, albeit a very different one to that proposed by Mesalum. Rather than assigning salience to stimuli or locations, the ERN suggests that activity in the ACC provides an on-line mechanism for the brain to monitor its own performance.

How does one adjudicate between these competing theories? The electrophysiological evidence for error-related activity in the ACC seems compelling. However this theory is contradicted by many functional imaging studies using PET and fMRI during cognitive activation. These studies reveal robust increases in ACC activity during a whole range of tasks despite the fact that error rates for many of these tasks are extremely low. What, we may ask ourselves, could account for both sets of observations; that is, increases in ACC activity during errors, and increases in activity during correct trials of tasks such as the Stroop and verb generation? Rather than detecting errors per se, could the ACC instead be detecting conditions common to this set of tasks which might be associated with and perhaps predispose towards errors? The strategic function proposed by Posner, iattention to actioni, is hypothesized to serve to reduce conflicts between alternative responses to a stimulus. Could the ACC be detecting these conflicts, rather than (or in addition to) resolving them? Conflict would be expected to be particularly high during errors on tasks such as the Eriksen and go-no-go tasks that have been use to demonstrate
The ERN. This is because activity would simultaneously be occurring in both the correct and incorrect response channels. The observation that the ERN is greatest during partial errors which are subsequently corrected is consistent with this logic. Computational modeling, conducted within the PDP framework (Rumelhart and McClelland 1986) also supports this line of reasoning. Experiments using a PDP model of the Eriksen task, which has been widely used to generate the ERN, confirm that a high level of response competition is likely to occur during incorrect responses to such a task (Botvinick et al submitted). In addition, when the same measure of competition is computed across models of a range of tasks known to activate the ACC, including the Stroop task and stem completion, a pattern of activity with a comparable form and time course to the ERN is also observed. This supports our view that the ACC is detecting conflict, rather than errors, and that for a given task it would be expected to show increased response-related activity under conditions of conflict as well as during errors. If confirmed, this hypothesis would assign a specific evaluative function, conflict monitoring, to the ACC during normal cognition.

We have begun to use event-related fMRI to test this conflict monitoring hypothesis for the function of the ACC (Carter et al 1998). Consistent with the literature on the ERN, we predicted that the ACC would show error related activity. More importantly, however, we predicted that the ACC would also show increased activity during correct trials associated with response competition. Detecting response competition provides a more parsimonious mechanism for performance monitoring than a comparator mechanism, because rather than knowing both intended and actual responses, the ACC only needs summary knowledge of the state of the response system.

We scanned subjects in an event-related manner during two versions of the AX-CPT task (continuous performance task. The AX-CPT is a modified Continuous Performance Test (Rosvold and Mirsky 19) in which sequences of single letters are presented as cue-probe pairs.
During the task subjects were instructed to make a target response whenever the probe was an X preceded by a cue that was an A, and a non-target response to all other stimuli. Target (AX) trials occurred with 70% frequency and the 3 non-target trial types (AY, BX, BY) each occurred with 10% frequency. This frequency manipulation was introduced to produce higher levels of response competition on BX (non-A cue followed by X) and AY (A followed by non-X probe) trials than AX and BY (non-A cue followed by non-X probe). For BX trials, response competition occurs because the correct (non-target) response conflicts with the tendency to give a target response to an X probe (the correct response 87.5% of the time). In AY trials response competition occurs because subjects are primed to give a target response following an A (correct 87.5% of the time), and must override this tendency to give the correct, non-target response. AX and BY trials involve no such conflicts, and thus elicit less response competition. On half of the ten blocks of trials stimuli were degraded by removing 90% of the pixels, to increase error rates and allow us to examine ACC activity associated with incorrect responses. We used a slow rate of stimulus presentation and acquired multiple scans during a single trial which allowed us to examine the temporal dynamics of ACC activity in relationship to responses to the probe.

As predicted from ERP studies of the ERN, the ACC showed transient probe related activity which was greater on incorrect than correct trials. However, on correct trials, the same region of the ACC showed transient, probe related activity, which was greater on trials in which the task elicited response competition than on trials in which there was none. A highly significant subset of voxels showed both effects. This pattern of activity was specific to the ACC. The voxels showing these effects were primarily located along the ventral surface of the cingulate sulcus (BA 24cf, Vogt et al 1995, ventral cingulate motor area of Dum and Strick 1993). Interestingly dipole modeling indicates that this region of the ACC is the most likely source of the ERN (Dehaene et al 1994, Holroyd et al 1998) and it is also the location where Brooks (1986) observed error related activity during single unit recording studies of behaving monkeys. The region of activation did also extend partly onto the surface of the gyrus (BA 24bi) and onto the
dorsal bank of the sulcus (BA 32). Bilateral prefrontal regions (BA 9/46 and 44/45) and a premotor region showed some degree of error related activity, but none showed both error and competition effects. Since there was no main effect of task (degraded versus non-degraded), and error and competition related activity was transient and temporally related to the response to the probe, these effects are not likely to reflect non-specific responses to increased task difficulty, such as enhanced vigilance or arousal. Rather, the above results suggest that during normal cognition this region of the ACC serves a very specific evaluative function, in the service of executive control, detecting response competition, and indicating the need to implement strategic processes to maintain performance.

**Strategic Versus Evaluative Processes and the Anterior Cingulate Cortex**

Both the ERN literature and our own fMRI data suggest that the ACC serves an evaluative, rather than a strictly strategic function in the service of executive control. In our fMRI study, no region of the ACC showed greater activity during correct, than incorrect trials, as would be expected if it were implementing strategic functions. However, the type of evaluative function implied by these combined results is very different from the motivational map described by Mesalum (198). Rather than computing the salience of sensory representations in spatial co-ordinates, ACC activity seems to be reflecting the level of conflict present in the response system. On the other hand, to the degree that the presence of conflict reflects a need for control, activity in the ACC may indeed be considered to be motivational, with activity in this limbic brain region indicating that action is needed to reduce conflict and stabilize performance. In contrast to the hypothesis that the ACC implements selective attention, we propose that these processes are governed by regions of the brain other than the ACC.

**Future Directions and Unresolved Questions**
Our emerging understanding of the contribution of the ACC to executive processes during cognition suggests a specific evaluative function, detecting the occurrence of conflicts such as response competition which are normally associated with poor task performance and indicating the need to engage strategic processes. However, even if this is correct, many questions related to this function remain unanswered. For example it is not known whether the computation of conflict would occur in the ACC itself, or whether it would occur in other brain regions with which the ACC is connected. It is also not known whether the conflict detected by the ACC would be limited to response competition, or extend to other kinds of representational conflict. Botvinick (submitted) has pointed out that conflicts at a range of levels of representation, from the stimulus level to the conceptual level, could as an end result produce increased response competition. It is also possible that perceptual conflicts (such as occur during the congruent condition of the Stroop task, which has been shown to produce some ACC activation, Carter et al 1995, Bench et al 1993), or conceptual level conflicts might directly result in ACC activation.

Finally, we have not yet specified which regions of the brain would implement the strategic processes needed to reduce conflict, or how the activity of these regions is modulated by the ACC. Studies of the ERN show that trials after an ERN have longer reaction times, supporting the notion that ACC is associated at some point with changes in performance that reflect the engagement of strategic processes (ref). Does this modulation occur directly, via cortical-cortical connections between, for example the ACC and the dorsolateral prefrontal, parietal or entorhinal cortices, or is this modulated through neuromodulatory systems such as brainstem dopaminergic nuclei, with which the ACC has known functional connectivity. These unresolved questions will undoubtedly ensure that the further examination of the role of the ACC in executive processes during human cognition will remain an active area of investigation in cognitive neuroscience for many years to come.