

Conflict effects without conflict in anterior cingulate cortex: Multiple response effects and context specific representations

Joshua W. Brown*

Department of Psychological and Brain Sciences, Indiana University, 1101 E Tenth St., Bloomington, IN 47405, USA

ARTICLE INFO

Article history:

Received 27 June 2008

Revised 16 March 2009

Accepted 8 April 2009

Available online 16 April 2009

ABSTRACT

The error likelihood computational model of anterior cingulate cortex (ACC) (Brown, J.W., Braver, T.S., 2005. Learned predictions of error likelihood in the anterior cingulate cortex. *Science* 307: 1118–1121) has successfully predicted error likelihood effects, risk prediction effects, and how individual differences in conflict and error likelihood effects vary with trait differences in risk aversion. The same computational model now makes a further prediction that apparent conflict effects in ACC may result in part from an increasing number of simultaneously active responses, regardless of whether or not the cued responses are mutually incompatible. In Experiment 1, the model prediction was tested with a modification of the Eriksen flanker task, in which some task conditions require two otherwise mutually incompatible responses to be generated simultaneously. In that case, the two response processes are no longer in conflict with each other. The results showed small but significant medial PFC effects in the incongruent vs. congruent contrast, despite the absence of response conflict, consistent with model predictions. This is the multiple response effect. Nonetheless, actual response conflict led to greater ACC activation, suggesting that conflict effects are specific to particular task contexts. In Experiment 2, results from a change signal task suggested that the context dependence of conflict signals does not depend on error likelihood effects. Instead, inputs to ACC may reflect complex and task specific representations of motor acts, such as bimanual responses. Overall, the results suggest the existence of a richer set of motor signals monitored by medial PFC and are consistent with distinct effects of multiple responses, conflict, and error likelihood in medial PFC.

© 2009 Elsevier Inc. All rights reserved.

Introduction

The last decade has seen an emerging agreement that the medial prefrontal cortex (mPFC) and anterior cingulate cortex (ACC) in particular are critically involved in performance monitoring. These regions seem to form the monitoring component of a general system of executive or supervisory control (Norman and Shallice, 1986), which monitors the behavioral state and adjusts higher level goals accordingly. Initial primate studies showed error detection signals in monkey anterior cingulate (Gemba et al., 1986). The error-related negativity, or ERN (Gehring et al., 1990; Hohnsbein et al., 1989), provided evidence of a human analogue, with a source localized to the medial prefrontal cortex (Dehaene et al., 1994). A series of subsequent high-profile studies argued for a reconceptualization of the error detection signal as resulting from conflict between mutually incompatible response plans (Botvinick et al., 1999; Carter et al., 1998; MacDonald et al., 2000). Our own more recent work combines computational neural modeling, fMRI, and cognitive psychology to argue for a further reconceptualization of the performance monitoring

system as predicting the likelihood that the current action will result in an error (Brown and Braver, 2005).

In Brown and Braver (2005), we posed a context specificity question that helped motivate the search for anticipatory error likelihood effects in ACC. If a subject performs a task that induces response conflict, such as the Eriksen flanker task (Eriksen and Eriksen, 1974), the subject must press either the left or the right index finger button, but not both. Then if the subject leaves the experiment and goes riding a bicycle, the subject might come to a stop sign and have to activate the brake levers with both index fingers simultaneously. In that case, will the ACC show greater response conflict effects in the Eriksen task than while bicycling? If so, then how does the ACC know when two responses are in conflict with each other, vs. when they are not?

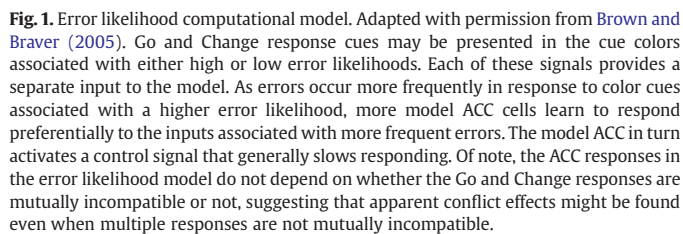
The error likelihood model

The error likelihood computational neural model that originally predicted error likelihood effects (Brown and Braver, 2005) has provided a rich source of ongoing predictions. The model works as follows (Fig. 1). First, inputs represent plans to move given a particular response cue, which may be associated with a high or low likelihood of an error. The cue signals in the original model consisted of colored

* Fax: +1 812 855 4691.

E-mail address: jwmbrown@indiana.edu.

URL: <http://www.indiana.edu/~cclab>.



The model was originally simulated to perform a change signal task (Brown and Braver, 2005), which dissociates error commission, response conflict, and error likelihood. Briefly, subjects are instructed to respond with a button press of the left or right index finger corresponding to the direction of an arrow that appears in the center of the screen. One one-third of the trials, a second arrow appears that is larger than the first arrow and above it, and points in the opposite direction. The appearance of the second arrow instructs the subject to, if possible, withhold the response to the first arrow and instead substitute a response to the second arrow. The change signal delay (CSD) is the time difference between the onset of the first and second arrows. The likelihood of an error can be increased by increasing the

Error likelihood signals may in turn drive risk aversion, a function that depends on ACC (Magno et al., 2006; Paulus and Frank, 2006). To explore this issue, after the error likelihood computational model was published, we manipulated it to simulate variations in both error likelihood and the potential severity of the error, should an error occur. Risk may be defined as a function of both error likelihood and the severity of the consequences of an error (Saaty, 1987). The severity of an error, i.e. the magnitude of its consequences, was represented in the model by the magnitude of the error signal that trained ACC. Small consequences, such as failing to win a small amount of money due to an incorrect response, were represented by a small error training signal. Large consequences, such as failing to win a larger amount of money, were represented by a proportionally larger error training signal in the model. The computational neural model predicted that the ACC would learn to be sensitive to increases in both error likelihood and the potential severity of the consequences, as predicted by a paired color cue associated with the error likelihood and response consequence severity, even when no error actually occurs. This prediction that was subsequently confirmed with fMRI, even in the absence of task difficulty effects as indexed by RT (Brown and Braver, 2007). Furthermore, we found that the error likelihood and anticipated error consequence effects were notably absent in those individuals who were most likely to engage in risky behavior (Brown and Braver, 2007). That finding in turn suggested that ACC may not only detect the risk of a behavior but also bias decision-making against risky choices, and it suggested why some studies may fail to show error likelihood effects (Nieuwenhuis et al., 2007), due to individual differences in risk aversion across a population. We returned again to the error likelihood model and simulated the individual differences in risk aversion as resulting from stronger or weaker learning signals driven by error commission. The model then accounted for the individual differences in error likelihood and predicted error consequence effects. Furthermore, the computational model predicted that a higher learning rate from errors would increase error likelihood effects but, surprisingly, that conflict effects would weaken, as ACC representations became sharpened and less responsive to general increases in the number of planned responses. This counter-intuitive inverse relationship between conflict and error likelihood effects, as predicted by the computational model (Brown and Braver, 2008), agreed with fMRI findings (Brown and Braver, 2007). Nevertheless, despite the repeated predictive success of the error likelihood model, subsequent behavioral studies have suggested that multiple monitoring signals of conflict and error likelihood detection might function somewhat independently of each other (Brown, In Press).

The error likelihood computational model makes a further prediction, namely the *multiple response effect* described above. Specifically, Fig. 1 shows that the model ACC responds directly to multiple response plans (from the input layers) rather than response conflict *per se* at the response layer. Conflict effects occur in the model as response cues indicate a greater *quantity* of different responses to

be prepared, even though one of the cued responses is inappropriate and will lead to an error if executed. The key point is that in the model, an increasing quantity of response cues will increase ACC activity associated with the cued responses and will lead to apparent conflict effects in the model ACC, *even if the task is changed at the response level so that the responses are no longer mutually incompatible*. This is due to the simple fact that the model ACC is agnostic about whether the two responses being prepared are mutually incompatible or not. This means that previous simulations of the model that predict response conflict effects can be interpreted as predictions of a multiple response effect, given that the model makes no computational distinction between conflicting vs. non-conflicting responses (Brown and Braver, 2005). This model prediction can thus be stated as follows: *apparent conflict effects in ACC reflect in part an increasing number of response plans, regardless of mutual incompatibility*. This re-interpretation of conflict effects has been proposed previously based on studies of macaque ACC and supplementary eye fields (Nakamura et al., 2005; Olson and Gettner, 2002), in which the co-activation of multiple direction-selective cells representing different movement directions leads to greater average activity than a single movement representation across the population of cells. This would lead to apparent conflict effects at the population level, despite the fact that individual cells may not represent conflict *per se*. These are strong predictions by the model. The remainder of this paper describes a test of the prediction. In short, the results confirm the model prediction of multiple response effects regardless of conflict but also suggest that conflict and error likelihood prediction may reflect distinct neural processes.

The current study used modified versions of two well-known tasks that have been used to study response conflict: firstly, the Eriksen flanker task (Eriksen and Eriksen, 1974), and secondly, the change signal task (Brown and Braver, 2005; Husain et al., 2003), which derives from the stop signal task (Logan, 1985). Both of these tasks have shown response conflict effects in ACC with fMRI (Botvinick et al., 1999; Brown and Braver, 2005).

The first question to be addressed is whether or not ACC activity remains increased when two mutually incompatible responses are no longer mutually incompatible. The Eriksen flanker task (Eriksen and Eriksen, 1974) was modified by crossing congruent and incongruent stimuli with a prior task cue of “MIDDLE” vs. “ALL”, in which the cue varies randomly for each trial (Fig. 2). In the MIDDLE condition, subjects are instructed to respond to the middle of the five arrowheads and essentially perform the classical Eriksen flanker task. In the ALL condition, subjects are instructed to respond to both the middle and flanking arrowheads. In other words, if the middle stimulus differs from the flankers (i.e. an incongruent stimulus), then

responses to both are to be made simultaneously. Simultaneous responses are deemed correct if both are generated sometime before the response deadline, regardless of which response is generated first. The contrast between congruent and incongruent stimuli in the MIDDLE condition yields the response conflict effect. The contrast between congruent and incongruent stimuli in the ALL condition yields the multiple response effect, in which the quantity of simultaneous responses is increased (two responses for “incongruent” trials vs. one response for “congruent” trials). Of note, the quantity of cues remains the same for both congruent and incongruent trials in the modified Eriksen task: there are five arrows presented side-by-side in each case, so any effects could not be attributed to a greater quantity of cues in one condition vs. the other. If an ACC effect of incongruent > congruent is found in the Eriksen ALL condition, then at least part of what is currently known as the conflict effect in ACC may actually not depend on the presence of response conflict, but rather on the presence of multiple planned responses, even if one of those planned responses is not executed. Also, if an interaction is found such that the contrast incongruent > congruent shows larger effects in the Eriksen MIDDLE than ALL condition, then ACC response conflict effects must depend on task context, as indicated by the prior MIDDLE or ALL cue.

The second question to be addressed, assuming that conflict effects depend on task context, is how the task dependency comes about. There are two alternative possibilities here. First, it is possible that conflict effects represent error likelihood. In the “ALL” condition, if errors do not occur for incongruent stimuli, then reduced ACC activity in the incongruent ALL condition compared with the incongruent MIDDLE condition would be consistent with lower perceived error likelihood. In that case, the regions of ACC that show conflict effects should also show error likelihood effects. An alternative hypothesis is that context dependency arises from the inputs to ACC, which may be specific to the task context. In this case, the requirement to press both buttons simultaneously in the incongruent ALL condition might be represented as a single bimanual motor act (Kermadi et al., 1998). There would be only a single input to ACC, namely the bimanual act representation, which would afford no conflict signal. If so, then it may be possible to demonstrate response conflict effects between bimanual vs. unimanual representations. This prediction could be tested by looking for ACC activity when a bimanual response countermands, and therefore conflicts with, a unimanual response.

A modification of the change signal task (Brown and Braver, 2005) allows both error likelihood and the context dependency of conflict, including potential conflict between unimanual and bimanual responses, to be tested simultaneously. The change signal task (Brown and Braver, 2005) was modified (Fig. 3) by crossing the conditions with an additional factor of “LAST” vs. “ALL”, which varies randomly from one trial to the next. In the LAST condition, subjects are instructed to perform the change signal task as in previous studies (Brown and Braver, 2007; Brown and Braver, 2005), in which they respond in the direction of the first arrow by default but substitute a response to the second arrow if it appears subsequent to the onset of the first arrow. Subjects respond with button presses by the left and/or right index fingers. In the ALL condition, subjects are instructed to respond to the first arrow and also the second arrow, if it appears. Thus, the appearance of the second arrow in the ALL condition provides the same stimuli that elicit response conflict, except that the responses to the first and second arrows are no longer mutually incompatible. Instead, the left and right index finger responses must be executed simultaneously as in the modified Eriksen task above. The contrast between one vs. two arrows (i.e. the Go vs. Change condition) in the LAST cue condition, restricted to correct trials only, yields the response conflict effect. The contrast between one vs. two arrows (i.e. the Go vs. Change condition) in the ALL cue condition, restricted to correct trials only, would be expected to yield ACC activity consistent with a multiple response effect, and also consistent with a conflict

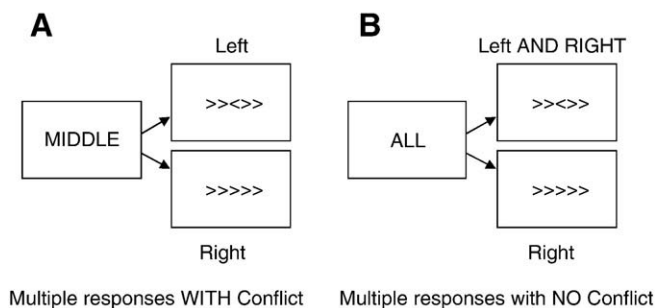


Fig. 2. Modified Eriksen flanker task. Adapted from Eriksen and Eriksen (1974). Each trial begins with a cue indicating whether multiple responses are (A) mutually incompatible (“MIDDLE” cue), or (B) mutually compatible (“ALL” cue). Subjects respond to the Eriksen cues with a button press by the left, right, or both index fingers. The four flanking arrows on either side of the middle arrow always point in the same direction for a given trial. The middle arrow may point in the same or opposite direction as the flankers. For the MIDDLE condition, subjects must respond only to the direction of the center of the five arrows. For the ALL condition, subjects must respond to all arrow directions present.

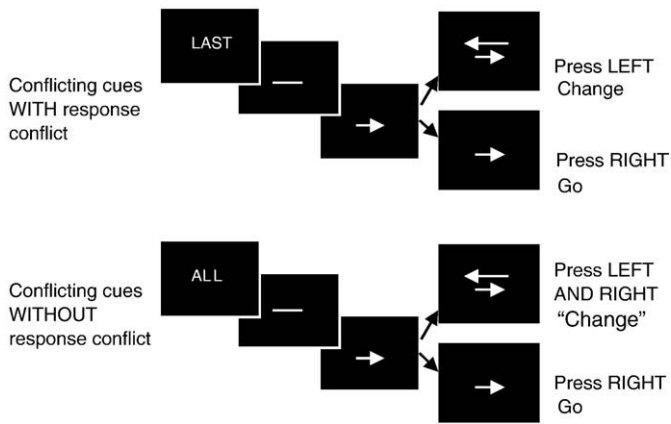


Fig. 3. Modified change signal task. Adapted from Brown and Braver (2005). Subjects respond with a button press by the left index finger for left pointing arrows and the right index finger for right pointing arrows. Each trial begins with a cue indicating whether multiple response are mutually incompatible (LAST) or not mutually incompatible (ALL). For the LAST trials, a change signal (second arrow) indicates that the subject must withhold the response to the first arrow. For the ALL trials, a change signal indicates that subject must respond with both index fingers simultaneously.

effect if there exists conflict between the original unimanual response and the bimanual response cued by the appearance of the second arrow. Of note, errors of commission are unlikely in the ALL condition, because no cues require a response to be withheld. The contrast between high vs. low error likelihood correct Go trials in the LAST condition yields the error likelihood effect (Brown and Braver, 2005). In the remainder of the paper, the Eriksen task results first demonstrate the multiple response effect (i.e. conflict effects even when no state of conflict exists), and second that response conflict depends on task context. Finally, the change signal task results demonstrate that the context dependency is primarily due to the presence of complex, bimanual task representations rather than error likelihood effects.

Materials and methods

Subjects ($N=20$, 11 females, mean age 21.9, range 18–42) performed a modified change signal task (Brown and Braver, 2005) and a modified Eriksen flanker task (Eriksen and Eriksen, 1974). Subjects were all right-handed. Two subjects were excluded from further analysis in the Eriksen task for failing to perform correct trials in the Eriksen Incongruent ALL condition. All procedures were approved by the Indiana University Human Subjects Committee. All subjects provided informed consent in accordance with the principles of the Declaration of Helsinki.

Subjects performed four successive blocks of the change signal task and two successive blocks of the Eriksen task. The order was counterbalanced across subjects. Each block lasted 8 min and began and ended with 30 s of a screen with a white “+” symbol fixation on blank (black) background.

Experiment 1: Eriksen task

For the modified Eriksen task (Eriksen and Eriksen, 1974), subjects performed two blocks of 82 trials each, for a total of 164 trials. Each trial begins with a cue (“MIDDLE” or “ALL”, equally likely, randomly intermixed) in the center of the screen, in white letters on a black background, with 18 point courier font, for 1000 ms. Then the screen is blank for 1000 ms. Afterwards, the Eriksen task cue appears for 1000 ms (the response deadline), in the same white 18 pt. Courier font. The Eriksen task stimuli consisted of a central arrow “>” or “<”, surrounded by two flanking arrows on each side (Fig. 2). Congruent and incongruent target stimuli are equally likely and randomly

intermixed. Subjects must respond only to the middle stimulus in the MIDDLE condition or to both the middle and flanker stimuli in the ALL condition. For a response to be considered correct, all and only the appropriate responses must be generated before the response deadline. Then feedback of “Correct” or “Error” is given in the center of the screen for 500 ms, and then the screen is blank for 500 ms. Thus the total minimum trial duration is 4 s. The ITI was jittered by adding a 2000, 4000, or 6000 ms blank screen delay after each trial, with $p=0.40$ of successive 2000 ms jitter delays, resulting in an exponential jitter distribution for optimal efficiency of estimating event-related responses (Dale, 1999). GLM regressors for subsequent fMRI analysis consisted of Error trials and all combinations of the ALL vs. MIDDLE condition and the Incongruent vs. Congruent conditions, for a total of five event-related regressors.

Experiment 2: change signal task

The change signal task was modified from Brown and Braver (2005), as shown in Fig. 3. Each change signal task block included 82 trials, for a total of 328 change signal task trials. Each trial begins with a cue “LAST” or “ALL” in 18 pt Courier font in the center of the screen. The cue colors were either white or blue (RGB 128, 128, 255) for all stimuli of a given trial. The cue remained visible for 1000 ms, after which it was replaced by colored dashes “—” in the center of the screen for 1000 ms. Immediately following the dashes, the Go signal was presented in the center of the screen until a response deadline of 1000 ms. The Go signal consisted of two dashes and an arrowhead (e.g. “<--”) pointing left or right. On one-third of trials, a Change signal appeared after a delay. The change signal consisted of an arrow larger than the Go signal and above it, and pointing in the opposite direction. The Change signal instructed subjects to, if possible, withhold the response to the Go signal and instead respond to the Change signal. The Change Signal Delay (CSD) was the time interval between the onset of the Go and Change signal arrows. CSDs were initially set to 250 ms in the low error likelihood condition and 400 ms in the high error likelihood condition. The cue colors were paired with a corresponding error likelihood condition, and the mapping was counterbalanced across subjects. CSDs were updated with an asymmetric staircase algorithm after each Change signal trial in the last condition to achieve target error rates of 5% and 50% in the low and high error likelihood conditions, respectively. The maximum increment or decrement of each CSD was 50 ms. The change signal remained visible until the Go signal disappeared. After that, the screen was blank for 1000 ms. The ITI is jittered as for the Eriksen task above. GLM regressors for subsequent fMRI analysis consisted of Change/Error trials, No-response errors in Go trials, and all combinations of High vs. Low error likelihood, the LAST vs. ALL condition, and the Go (i.e. tasks with no change signal) vs. Change conditions, for a total of ten event-related regressors.

fMRI methods

Subjects were scanned with a Siemens Trio 3 T scanner, with an 8-channel coil. Functional images were acquired with a standard EPI sequence (volume TR = 2 secs, slice thickness = 3 mm, TE = 25 ms, slice gap = 0.75 mm, voxel size 3.4375 in plane, flip angle = 70, FOV = 220 mm, 33 slices). The slices were oriented 30° transverse to coronal from the AC–PC line for whole brain coverage. Each block consisted of 240 scans, plus 4 earlier scans that were discarded while waiting for the scanner to reach equilibrium. High resolution T1 images (160 sagittal slices, whole brain coverage) were acquired from each subject after functional runs were complete.

Analysis was performed mainly in SPM5, with BET2 from FSL (Smith et al., 2004) used for skull-stripping the T1 images to improve co-registration. Functional images underwent slice timing correction and realignment to the mean functional. Anatomical

images were co-registered to the MNI 152 atlas, and the functionals were then co-registered to the atlas using the parameters derived from the anatomical co-registration to the atlas. In this way the functional images were transformed into atlas space. Functional images were smoothed with a 3D isotropic Gaussian kernel with an 8 mm FWHM. These constituted the input to the event-related estimation of the GLMs. The GLMs also included nuisance covariates consisting of a mean, linear trend, and the 6 degrees of movement freedom estimated during the functional image realignment. GLM regressors were constructed from zero-duration impulse functions aligned on the scan during which the first response occurred, or aligned on the scan during which the target cue appeared if no response occurred. These impulse functions were convolved with a canonical hemodynamic response function (Friston et al., 1999) to generate the GLM regressors.

Results

Behavioral results

There are several different kinds of errors that subjects can make. In general, an error is recorded if the wrong button is pressed, or if two button presses were required but only one button was pressed before the response deadline. No-response errors are counted separately from other errors and occur when no button is pressed at all before the response deadline. Due to the nature of the tasks in the ALL conditions, an initial response followed by the other response was considered correct, regardless of which response was made first. Response times (Fig. 4) are analyzed from correct trials only and are based on the time of the first response if multiple correct buttons are pressed.

Eriksen task

Error rates in the Eriksen task for congruent vs. incongruent stimuli in the MIDDLE condition were 0.8% and 8.0%, respectively, yielding a significant incongruity effect ($F(1,17, \text{MSe} = 0.0016) = 31.36, p < 0.001$). For the Eriksen ALL condition, congruent vs. incongruent error rates were 3.5% and 9.5%, respectively, yielding a significant incongruity effect ($F(1,17, \text{MSe} = 0.0045) = 7.17, p < 0.02$). The no-response rate in the Eriksen task was 4.8% and did not differ between MIDDLE and ALL conditions ($F(1,17, \text{MSe} = 0.0013) = 3.086, p = 0.10$).

For the Eriksen task, response time conflict effects in correct trials were found in the MIDDLE condition for incongruent (625 ms) vs. congruent (540 ms) $F(1,17, \text{MSe} = 851) = 76.9, p < 0.001$. Likewise, there was an effect of increasing response quantity in the absence of response conflict for incongruent (586 ms) vs. congruent (554 ms) $F(1,17, \text{MSe} = 1029) = 8.86, p < 0.01$ (Fig. 4A).

Change signal task

For the change signal task, the mean CSD in High vs. Low Change trials was 450 vs. 199 ms. ($t(19) = 11.39, p < 0.001$). The same High and Low CSDs were used for both LAST and ALL conditions, but they were updated only based on responses in the LAST condition, so the targeted high and low error rates did not apply to the ALL condition. For the Change signal LAST condition, the overall error rate (including errors of both commission and omission) was 54.6% (30.2% commission, 24.4% omission) in the High/Last/Change condition and 20.6% (5.8% commission, 14.8% omission) in the Low/Last/Change condition. The overall error rate in the high error likelihood condition was close to the target of 50%, but the overall error rate in the low error likelihood condition was higher than the target 5%, due to a number of errors of omission which could not be entirely compensated for by reducing the CSD in that condition. The omission error rate was 19.6% in the LAST condition and 19.1% in the ALL condition, which included both trials with no response and trials with responses made after the deadline. Errors of commission or partial response occurred in 19.4% of High/Change/ALL trials, 0.7% of High/Go/ALL trials, 12.2% of Low/Change/ALL trials, and 0.9% of Low/Go/ALL trials.

For the change signal task, response time conflict effects were found in the LAST condition for incongruent (774 ms) vs. congruent (712 ms) $F(1,19, \text{MSe} = 8294) = 9.48, p < 0.01$. However, there was no effect of increasing response quantity in the ALL condition for incongruent (714 ms) vs. congruent (701 ms) $F(1,19, \text{MSe} = 4433) = 0.80, p = 0.38$ (Fig. 4B).

Sequential effects in the Eriksen task

The effects of response conflict are often seen most clearly in how conflict in one trial affects control in the subsequent rather than the current trial (Botvinick et al., 1999; Brown et al., 2007; Jones et al., 2002). For the Eriksen task, conflict would be expected to lead to slowing in the subsequent trial. Specifically, correct incongruent vs. congruent trials in the MIDDLE condition should lead to slower subsequent MIDDLE/Congruent/Correct trial RTs. Of note, these conditions can include exact stimulus repeats, which might lead to priming effects that speed up subsequent RT when the first trial is congruent (Mayr et al., 2003). To control for this confound, exact stimulus repeat sequences were excluded from the sequential effect analysis. The results showed that in the MIDDLE condition, incongruity significantly slowed subsequent trial MIDDLE/Congruent/Correct RT ($F(1,17, \text{MSe} = 4227) = 27.22, p < 0.001$), consistent with a conflict effect in the MIDDLE condition. In contrast, incongruity in the ALL condition did not slow subsequent trial MIDDLE/Congruent/Correct RTs ($F(1,16, \text{MSe} = 4601) = 2.01, p = 0.18$). Likewise, incongruity in the ALL condition did not slow subsequent trial ALL/Congruent/Correct RTs ($F(1,16, \text{MSe} = 3976) = 0.00, p = 0.98$). Some

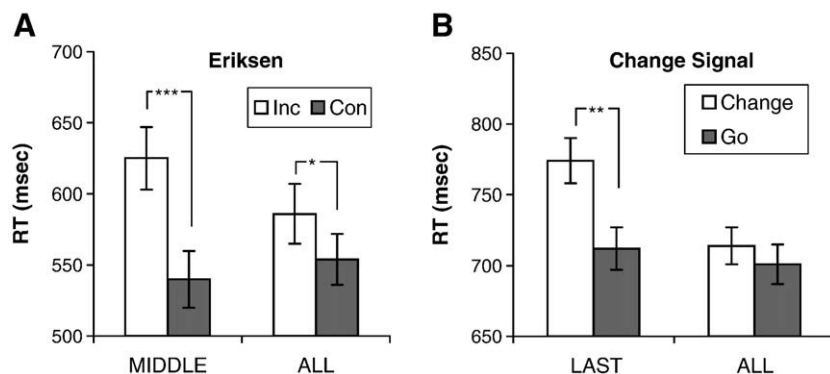


Fig. 4. Behavioral results from each task. (A) Incongruity effects on response times in the modified Eriksen task. Incongruity effects are seen in both the MIDDLE and ALL conditions. (B) Incongruity effects on response times in the change signal task. An incongruity effect is seen in the LAST but not the ALL condition, despite the fact that strong ACC effects are seen in both LAST and ALL conditions (Fig. 5 below).

subjects (2–3) were excluded from these analyses due to missing conditions, as the particular combinations of conditions and sequences were complex and therefore infrequent. Subjects with at least one trial per condition were included in the sequential effect analyses.

Sequential effects in the change signal task

In the change signal task LAST condition, there was a trend toward correct change vs. go trials leading to RT slowing in subsequent LAST/Go/Correct trials ($F(1,19, \text{MSe}=7039)=3.60, p=0.07$), consistent with a conflict-induced slowing effect. If the previous trial is ALL instead, there is likewise an effect of previous congruency ($F(1,19, \text{MSe}=3039)=7.44, p<0.02$). This result holds even if response repetitions are excluded ($F(1,16, \text{MSe}=5811)=7.89, p<0.02$). However, if the subsequent condition is ALL/Go/Correct trials, and response repetitions are removed, then preceding ALL/Correct Change vs. Go trials do not lead to subsequent trial RT slowing ($F(1,13, \text{MSe}=4802)=0.01, p=0.93$). Several subjects were excluded from these analyses due to missing conditions. Overall, the results of the change signal task suggest that incongruency effects leading to subsequent trial control effects occur in both the LAST and the ALL conditions, and these are seen in subsequent LAST trials. This is consistent with the presence of response conflict effects between unimanual and bimanual response representations in ACC.

Incongruency in the ALL condition led to significant slowing in subsequent trials in the Change Signal but not the Eriksen tasks. This suggests the presence of response conflict between unimanual vs. bimanual responses in the Change signal but not Eriksen tasks. To explicitly compare the difference between the two tasks, the effect of incongruent vs. congruent ALL/Correct trials on subsequent LAST or MIDDLE Congruent/Correct trials was compared between the Eriksen and change signal tasks. The interaction however was not significant ($F(1,17, \text{MSe}=2898)=0.48, p=0.50$).

fMRI results

Conflict effects

The first part of the fMRI data analysis involves identifying a region of medial PFC in which response conflict effects are found. For maximum sensitivity, the search region is limited to Brodmann's areas 24 and 32, which requires less correction for multiple comparisons than a whole brain search. The family-wise error (FWE) corrected p -value for $\alpha=0.05$ in BA 24/32 is $\alpha=1.0593 \times 10^{-5}$. This is the alpha value yielded by SPM5 for a small-volume correction based on the region including BA 24/32, as determined by WFU PickAtlas (Lancaster et al., 2000; Maldjian et al., 2003). When a conjunction of two independent effects is tested against the global null hypothesis, the α for each effect is the square root of the FWE corrected α values

(Friston et al., 2005). In this case, $\alpha=0.0033$ for each voxel. In other words, a candidate voxel must pass both independent tests to be considered significant vs. the global null hypothesis that no conflict effects are present. By applying this criterion to the conflict contrasts in the change signal and Eriksen tasks, the analysis identified a single region in bilateral ACC, in BA 32 at MNI 4, 16, 46 (Fig. 5A). Of note, the region of significant effects extends from BA 32 dorsally into BA 8, consistent with previous studies of conflict effects (Rushworth et al., 2002). Confirmatory analysis showed conflict effects in this region to each pass the corrected threshold ($\alpha<0.0033$) for conjunctions (change signal task: $t(19)=3.51, p<0.003$; Eriksen task $t(17)=3.89, p<0.002$), as shown in Fig. 5B. A whole brain analysis was also performed using the same method to look for regions showing a conflict effect in both tasks. For this test, the corrected threshold for each test was a more stringent $\alpha=6.186 \times 10^{-4}$, because the number of multiple comparisons was greater. No frontal regions showed significant effects with this whole brain test. Overall, this analysis is consistent with reports that ACC signals response conflict in the classical versions of the Eriksen and change signal tasks, as found in previous work (Botvinick et al., 1999; Brown and Braver, 2007; Brown and Braver, 2005).

The next question is whether ACC region shows conflict effects in the Eriksen ALL condition, in which multiple responses are generated, but they are not in conflict with each other according to the definition of the task rules. For the Eriksen task, the relevant contrast was ALL/Inc/Correct – ALL/Cong/Correct. The effect was small but significant ($t(17)=2.22, p<0.05$), as shown in Fig. 5B. This is a multiple response effect, as predicted *a priori* by the error likelihood computational model, in which apparent conflict effects remain even when task rules are changed such that the responses are no longer mutually incompatible. The multiple response effect accounted for over 50% of the magnitude of the conflict effect in this case (0.109 vs. 0.055% signal change for conflict and multiple response effects, respectively).

Despite the significance of the multiple response effect, it does not completely account for response conflict effects. This is seen by subtracting the multiple response effect from the conflict effect, i.e. (MIDDLE/Inc/Correct – MIDDLE/Cong/Correct) – (ALL/Inc/Correct – ALL/Cong/Correct). This contrast is also significant ($t(17)=2.22, p<0.05$). As a whole, these results from Experiment 1 suggest three conclusions. First, the error likelihood model prediction is partly correct, in that there is a multiple response effect in ACC as predicted. Second, the multiple response effect is smaller than the response conflict effect and so cannot fully account for response conflict effects. Third, response conflict effects are therefore dependent on the particular task context in which the movements are performed, in the sense that the ACC somehow knows when two responses are mutually incompatible, vs. when they are not.

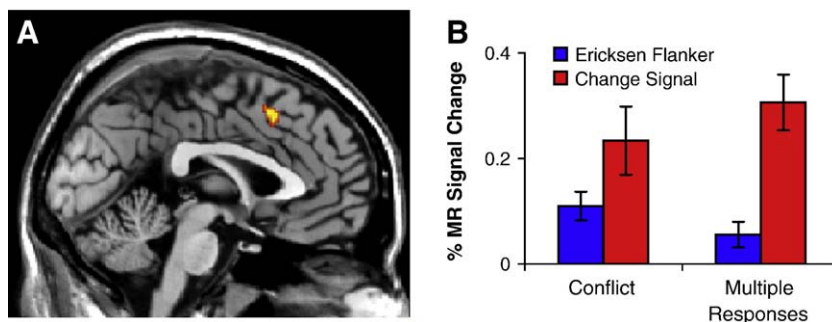


Fig. 5. fMRI results. (A) Region overlapping ACC defined by voxels that show conflict effects in both the Change Signal (LAST condition) and Eriksen (MIDDLE condition) tasks. (B) ROI analysis confirms the conflict effects. In the Eriksen task, incongruent response cues lead to greater ACC activation even in the multiple response condition, consistent with the predictions of the error likelihood computational model. In the change signal task, incongruent response cues also lead to greater ACC activation, which may reflect a multiple response effect as well as conflict between unimanual and bimanual response representations.

Error likelihood or conflict between complex responses?

Now the question remains as to what accounts for the context dependence of conflict effects. One possibility is that context dependence reflects a learned prediction of lower error likelihood in the non-conflicting task context. An alternative possibility is that complex, bimanual movements in the ALL condition reflect a single motor representation (Kermadi et al., 1998) as input to the ACC, which replaces the separate left and right response representations that may otherwise activate the ACC in the MIDDLE condition. This could account for weaker incongruity effects in the ACC for the ALL relative to the MIDDLE condition in Experiment 1, i.e. why the multiple response effect could not completely account for the conflict effect.

Analysis of the change signal task revealed no error likelihood effect in the identified ACC conflict region (High – Low contrast, restricted to LAST/Correct/Go trials), $t(19) = 0.21$, $p = 0.83$. Nevertheless, additional analyses were performed to look for error likelihood effects and yielded weaker effects in the medial PFC (MNI-10, 42, 42; $p < 0.005$ uncorrected), similar to previous findings (Brown and Braver, 2007; Brown and Braver, 2005, 2008). There is a potential confound, however, as pointed out recently (Nieuwenhuis et al., 2007), namely that error likelihood as predicted by the task cue may be confounded with the difficulty of actual task performance, which may covary with RT. Our more recent studies have shown error likelihood effects even in the absence of RT effects (Brown and Braver, 2007), although a catch trial design shows that error likelihood effects only occur when a response is generated (Krawitz et al., 2008). In the present study, RT was slightly higher in the High vs. Low LAST/Correct/Go conditions (717 vs. 705 ms, $t(19) = 2.20$, $p < 0.05$). To control for the effect of RT, the GLMs were reestimated with RT included as a nuisance covariate that parametrically modulated copies of each regressor that had been included in the original GLMs. This error likelihood effect remained significant ($t(19) = 3.26$, $p < 0.005$ uncorrected), suggesting that the error likelihood effect was not confounded with RT. Overall, the results suggests that the region showing conflict effects does not reflect underlying error likelihood effects, consistent with recent behavioral findings that conflict and error likelihood effects may reflect distinct underlying processes (Brown, In Press).

Next, the ACC conflict region was analyzed to look for the response conflict effect, but in the ALL condition, in which the response cued by the change signal (i.e. second arrow) does *not* conflict with the response cued by the go signal (i.e. first arrow). The contrast is Change minus Go in the ALL/Correct condition. The effect was highly significant ($t(19) = 5.67$, $p = 10^{-5}$), as seen in Fig. 5B, despite the absence of an obvious response conflict between the first and second arrows in this ALL condition. Nonetheless, the effect is consistent with the behavioral finding showing conflict-induced slowing in subsequent trials after correct Change vs. Go trials in the ALL condition (see Behavioral results).

Discussion

The results of the change signal task and Eriksen task together challenge the notion of medial PFC as solely a conflict detector. The finding of an incongruity effect in the Eriksen task ALL condition in particular suggests that at least part of the apparent conflict effects may instead be due to the presence of multiple planned response representations, regardless of response conflict. Response conflict can occur when a less frequent response must be generated (Braver et al., 2001), but it is unlikely that the incongruity effect in the ALL condition is due to the greater frequency of a unimanual rather than bimanual response, because they were equally likely in the ALL condition. This finding is consistent with earlier reports of multiple response effects in monkey medial PFC (Nakamura et al., 2005; Olson and Gettner, 2002) but challenges the interpretation of incongruity effects in medial PFC that have previously been construed as reflecting

a computation of response conflict (Botvinick et al., 2001; Botvinick et al., 1999; Carter et al., 1998).

The results of the change signal task, and especially in the ALL condition, suggest a paradoxical conclusion that conflict may exist between the first arrow and the second arrow responses, even though the two responses can (and should) be executed simultaneously. How can this be? One possibility is that the response representation activated by the first arrow is not a simple mapping of arrow stimulus to corresponding button press, but instead it is a complex mapping of arrow to button press *and* suppression of the opposite button press. This would be an example of a complex bimanual movement representation (Kermadi et al., 1998) that is specific to a particular task context. In that case, the response to the second arrow would present a conflict between the suppression cued by the first arrow and the execution cued by the second arrow. For this reason, a contribution of response conflict to the incongruity effect in the change signal ALL condition cannot be completely ruled out, although the results are also consistent with a multiple response effect as found in the Eriksen task ALL condition. If response conflict is present in the change signal ALL condition, then response conflict effects cannot be limited to conflict between simple movements, but must instead depend on complex sets of movements that may occur in specific contexts.

Nonetheless, this account based on response conflict cannot accommodate the findings of an incongruity effect in the Eriksen task ALL condition, because in the Eriksen task, there is no asynchrony in the presentation of a unimanual vs. bimanual response cue. So the incongruent stimulus in the Eriksen task does not constitute a countermand of a preceding congruent stimulus as it does in the change signal task, which implies that the unimanual response representation would not be activated in the first place. This in turn implies that the multiple response effect found in the Eriksen task ALL condition is not confounded with response conflict. If the Eriksen task were modified so that the center and flanker stimuli were presented asynchronously, i.e. flankers before center or *vice versa*, then an initial movement or active suppression might be countermanded by the final response to the complete stimulus, and this might lead to the larger ACC activation.

Another possible explanation of incongruity effects in the change signal ALL condition is the number of response cues. In the change signal task, incongruity involves a greater number of response cues (i.e. a second arrow). This is in contrast to the number of response cues in the Eriksen task, which is the same for congruent and incongruent stimuli. Thus, part of the multiple response effect may be due to the presence of a greater number of response cues. In any case, the multiple response effect and a potential multiple response cue effect are both distinct from a conflict effect. While many studies of tasks such as no-go and stop signals have controlled for the quantity of stimuli simultaneously presented (Braver et al., 2001; Husain et al., 2003; Rubia et al., 2001), others including our own use additional stimuli to cue the response inhibition (Brown and Braver, 2005; Stuphorn et al., 2000). When an increasing number of stimuli are presented and cue different responses, caution is warranted before increased ACC activity is automatically interpreted as a response conflict effect. Similarly, visual search tasks that include greater quantities of distractors and show corresponding increases in ACC activity may reflect in part this multiple response cue effect rather than response conflict (Magno et al., 2006). In the change signal task used here, the multiple cues in the ALL condition are associated with response conflict in the LAST condition. This means that the possibility of some generalization across task conditions as a source of the conflict effect in the ALL condition cannot be ruled out, and this could also account for the multiple response effect. Nonetheless, conflict effects were significantly larger in the Eriksen MIDDLE relative to the ALL condition, consistent with response conflict effects having a dependence on task context.

The present study was motivated in part by predictions of the error likelihood computational model. One of the model predictions, the

multiple response effect in ACC, was supported by the results. Nonetheless, other results suggesting complex bimanual movement representations go beyond the model as simulated and suggest how the model may be extended. If the model simulation were provided a richer set of bimanual response representations, it may well show effects consistent with conflict in the change signal ALL condition. Nonetheless, the finding of greater incongruency effects in the Eriksen MIDDLE relative to ALL condition, combined with the lack of an error likelihood effect in the identified ACC region, is difficult to reconcile with the predictions of the error likelihood model. The results are instead consistent with partly distinct neural mechanisms underlying conflict and error likelihood signals within ACC, as suggested by recent behavioral studies (Brown, *In Press*). Thus, the error likelihood model proves both its utility in making testable predictions, many of which have been confirmed (Brown and Braver, 2007; Brown and Braver, 2005, 2008), as well as its limitations on some counts. Forthcoming computational modeling work provides a more complete model of ACC effects as resulting from predictions of the probable outcomes of a planned response (Alexander and Brown, *in prep*).

The present study addresses the question of how the ACC knows when two responses are in conflict with each other. In computational models of response conflict, this issue is often taken for granted, as the mutual incompatibility of simulated responses is assumed (Botvinick et al., 2001; Brown et al., 2007; Jones et al., 2002). The current results suggest that the inputs to ACC are not simple, direct representations of a primary motor action. Instead, they may be task specific and complex, consisting of multiple coordinated movements represented as a single coherent act. The richness and specificity of inputs to ACC may allow conflict, error likelihood, and other effects found in ACC to be specific to individual tasks and behavioral contexts. ACC encompasses a large number of cells over a large swath of pericallosal cortex. Rather than computing a single scalar conflict signal, the ACC may compute a variety of context dependent monitoring signals, which may account for why the effects observed with fMRI seem to spread beyond a single column of cortical surface real estate.

Acknowledgments

Supported by A NARSAD Young Investigator Award, the Sidney R. Baer, Jr. Foundation, AFOSR FA9550-07-1-0454, and NIH/NIDA R03 DA023462-01. The author thanks E. Dinh for help with data collection, and S. Nieuwenhuis and three anonymous reviewers for very helpful comments.

References

- Botvinick, M.M., Nystrom, L., Fissel, K., Carter, C.S., Cohen, J.D., 1999. Conflict monitoring versus selection-for-action in anterior cingulate cortex. *Nature* 402, 179–181.
- Botvinick, M.M., Braver, T.S., Barch, D.M., Carter, C.S., Cohen, J.C., 2001. Conflict monitoring and cognitive control. *Psychol. Rev.* 108, 624–652.
- Braver, T.S., Barch, D.M., Gray, J.R., Molfese, D.L., Snyder, A., 2001. Anterior cingulate cortex and response conflict: effects of frequency, inhibition, and errors. *Cereb. Cortex* 11, 825–836.
- Brown, J., *In Press*. Multiple cognitive control effects of error likelihood and conflict. *Psychol. Res.* doi:10.1007/s00426-008-0198-7.
- Brown, J.W., Braver, T.S., 2005. Learned predictions of error likelihood in the anterior cingulate cortex. *Science* 307, 1118–1121.
- Brown, J., Braver, T.S., 2007. Risk prediction and aversion by anterior cingulate cortex. *Cogn. Affect. Behav. Neurosci.* 7, 266–277.
- Brown, J.W., Braver, T.S., 2008. A computational model of risk, conflict, and individual difference effects in the anterior cingulate cortex. *Brain Res.* 1202, 99–108.
- Brown, J., Reynolds, J., Braver, T.S., 2007. A computational model of fractionated conflict-control mechanisms in task switching. *Cogn. Psychol.* 55, 37–85.
- Carter, C.S., Braver, T.S., Barch, D.M., Botvinick, M.M., Noll, D.C., Cohen, J.D., 1998. Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science* 280, 747–749.
- Dale, A.M., 1999. Optimal experimental design for event-related fMRI. *Hum. Brain Mapp.* 8, 109–114.
- Dehaene, S., Posner, M.I., Tucker, D.M., 1994. Localization of a neural system for error detection and compensation. *Psychol. Sci.* 5, 303–306.
- Eriksen, B.A., Eriksen, C.W., 1974. Effects of noise letters upon the identification of a target letter in a nonsearch task. *Percept. Psychophys.* 16, 143–149.
- Friston, K.J., Holmes, A., Ashburner, J., 1999. Statistical Parametric Mapping (SPM) (available at <http://www.fil.ion.ucl.ac.uk/spm>).
- Friston, K.J., Penny, W.D., Glaser, D.E., 2005. Conjunction revisited. *NeuroImage* 25, 661–667.
- Gehring, W.J., Coles, M.G.H., Meyer, D.E., Donchin, E., 1990. The error-related negativity: an event-related potential accompanying errors. *Psychophysiology* 27, S34.
- Gemba, H., Sasaki, K., Brooks, V.B., 1986. 'Error' potentials in limbic cortex (anterior cingulate area 24) of monkeys during motor learning. *Neurosci. Lett.* 70, 223–227.
- Hohsain, J., Falkenstein, M., Hoorman, J., 1989. Error processing in visual and auditory choice reaction tasks. *J. Psychophysiol.* 3, 32.
- Husain, M., Parton, A., Hodgson, T.L., Mort, D., Rees, G., 2003. Self-control during response conflict by human supplementary eye field. *Nat. Neurosci.* 6, 117–118.
- Jones, A.D., Cho, R., Nystrom, L.E., Cohen, J.D., Braver, T.S., 2002. A computational model of anterior cingulate function in speeded response tasks: effects of frequency, sequence, and conflict. *Cogn. Affect. Behav. Neurosci.* 2, 300–317.
- Kermadi, I., Liu, Y., Tempini, A., Calciati, E., Rouiller, E.M., 1998. Neuronal activity in the primate supplementary motor area and the primary motor cortex in relation to spatio-temporal bimanual coordination. *Somatosens. Mot. Res.* 15, 287–308.
- Krawitz, A., Braver, T.S., Brown, J.W., 2008. The influence of working memory on error-likelihood prediction in the anterior cingulate cortex. *Cognitive Neuroscience Society*, San Francisco, CA.
- Lancaster, J.L., Woldorff, M.G., Parsons, L.M., Liotti, M., Freitas, C.S., Rainey, L., Kochunov, P.V., Nickerson, D., Mikiten, S.A., Fox, P.T., 2000. Automated Talairach atlas labels for functional brain mapping. *Hum. Brain Mapp.* 10, 120–131.
- Logan, G.D., 1985. On the ability to inhibit simple thoughts and actions: II. Stop-signal studies of repetition priming. *J. Exp. Psychol.* 11, 675–691.
- MacDonald, A.W., Cohen, J.D., Stenger, V.A., Carter, C.S., 2000. Dissociating the role of the dorsolateral prefrontal cortex and anterior cingulate cortex in cognitive control. *Science* 288, 1835–1838.
- Magno, E., Foxe, J.J., Molholm, S., Robertson, I.H., Garavan, H., 2006. The anterior cingulate and error avoidance. *J. Neurosci.* 26, 4769–4773.
- Maldjian, J.A., Laurienti, P.J., Kraft, R.A., Burdette, J.H., 2003. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *NeuroImage* 19, 1233–1239.
- Mayr, U., Awh, E., Laurey, P., 2003. Conflict adaptation effects in the absence of executive control. *Nat. Neurosci.* 6, 450–452.
- Nakamura, K., Roesch, M.R., Olson, C.R., 2005. Neuronal activity in macaque SEF and ACC during performance of tasks involving conflict. *J. Neurophysiol.* 93, 884–908.
- Nieuwenhuis, S., Schweizer, T., Mars, R.B., Botvinick, M.M., Hajcak, G., 2007. Error-likelihood prediction in the medial frontal cortex: a critical evaluation. *Cereb. Cortex* 17, 1570–1581.
- Norman, D., Shallice, T., 1986. Attention to action: willed and automatic control of behavior. In: Davidson, R., Schwartz, G., Shapiro, D. (Eds.), *Consciousness and Self Regulation: Advances in Research and Theory*. Plenum, New York.
- Olson, C.R., Gettner, S.N., 2002. Neuronal activity related to rule and conflict in macaque supplementary eye field. *Physiol. Behav.* 77, 663–670.
- Paulus, M.P., Frank, L.R., 2006. Anterior cingulate activity modulates nonlinear decision weight function of uncertain prospects. *NeuroImage* 30, 668–677.
- Rubia, K., Russell, T., Overmeyer, S., Brammer, M.J., Bullmore, E.T., Sharma, T., Simmons, A., Williams, S.C., Giampietro, V., Andrew, C.M., Taylor, E., 2001. Mapping motor inhibition: conjunctive brain activations across different versions of go/no-go and stop tasks. *NeuroImage* 13, 250–261.
- Rushworth, M.F., Hadland, K.A., Paus, T., Sipila, P.K., 2002. Role of the human medial frontal cortex in task switching: a combined fMRI and TMS study. *J. Neurophysiol.* 87, 2577–2592.
- Saaty, T.L., 1987. Risk – its priority and probability: the analytic hierarchy process. *Risk Anal.* 7, 159–172.
- Smith, S.M., Jenkinson, M., Woolrich, M.W., Beckmann, C.F., Behrens, T.E., Johansen-Berg, H., Bannister, P.R., De Luca, M., Drobnjak, I., Flitney, D.E., Niaz, R.K., Saunders, J., Vickers, J., Zhang, Y., De Stefano, N., Brady, J.M., Matthews, P.M., 2004. Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage* 23 (Suppl 1), S208–219.
- Stuphorn, V., Taylor, T.L., Schall, J.D., 2000. Performance monitoring by the supplementary eye field. *Nature* 408, 857–860.