

How does preparation influence cognitive control?

Informative cues guide cortico-subcortical systems for conflict resolution.

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**Abstract**

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Behavioral research has demonstrated that the demands placed on cognitive control mechanisms are significantly reduced when cues give the opportunity to prepare for the upcoming processes. Currently, the neurocognitive bases of preparation are not fully understood, as most neuroimaging investigations of cognitive control do not separate preparation from execution. The current fMRI investigation separately examined processes associated with preparing for response conflict from those associated with response execution, using a modified version of the Preparing to Overcome a Prepotent Response (POP) task. The addition of non-informative cues allowed us to map the neural networks involved in the preparation for conflict and the influence of such preparatory processes. Data from 42 individuals showed that the presence of preparatory cues reduced the cognitive demands associated with overcoming a prepotent response, as evidenced

both by significant cue X congruency interactions in behavioral data, and by reduced patterns of neural activation for response override trials that were followed by informative preparatory cues. Preparation to override a was associated with engagement of a distributed network typically associated with cognitive control, including the dorsolateral prefrontal cortex, anterior cingulate cortex, inferior parietal lobes, and striatum. Interestingly, many of these regions were not subsequently recruited during conflict resolution following informative cues. In contrast, when conflict resolution occurred “on the fly” (following noninformative cues), response inhibition regions became activated during task execution, namely the right inferior frontal cortex and globus pallidus. Individual differences analyses showed that better performance (as indexed by faster RTs) with and without preparatory cuing was underpinned by largely non-overlapping neural networks, with cued execution being associated with striatal activity, whereas execution “on the fly” was more broadly associated with recruitment of a cortical and subcortical control network. These results show both qualitative and quantitative differences in the neurocognitive processes associated with executing controlled behaviors with and without preparation.

## 1. Introduction

### 1.1 The importance of understanding preparation in cognitive control

Humans spend considerable neural and cognitive resources making predictions about upcoming events. Such predictions allow us not only to process information efficiently, but also to prepare for situations in which successful behavior requires additional *cognitive control*.

Cognitive control is a construct used to describe general top-down processes that coordinate neural computations to successfully achieve goal-directed behavior, such as making the proper motor response, in the face of conflicting sensory stimuli or competing behavioral responses.

While the nature of preparation remains debated (see discussion below), it undoubtedly influences the ability to resolve conflict. Thus, understanding the neurocomputations that support preparatory processes is essential to a complete understanding of cognitive control.

Traditionally, cognitive control has been studied using a variety of tasks that require additional mental effort to either inhibit an automatic or dominant response (e.g., the Stroop task: Stroop, 1935), and the Simon task: Craft & Simon, 1970), or to switch between possible responses (e.g., the Task Switching paradigm: Monsell, 2003). However, most paradigms used to measure cognitive control present the task-relevant information at the same time a task-relevant response is required. One critical limitation of this approach is that it does not take into account the role of preparation for conflict, discussed herein. A relatively straightforward way to do so is to present cues with varying information about the task-desired response *before* the target stimuli on which the controlled behavior must be executed. One can then measure the neurocognitive mechanisms associated with the processing of such cues and their impact on subsequent performance.

Currently, only a relatively small body of neuroimaging work on cognitive control has investigated the neural bases of preparatory processes. For example, in an fMRI investigation of cued task-switching, Ruge and colleagues found that providing a cue ahead of target stimuli indicating that a switch trial was forthcoming reduced the overall cost associated with switching tasks (as indexed by slowed response times during switch trials; Ruge et al., 2005; Ruge, Jamadar, Zimmermann, & Karayanidis, 2013). The authors report that this preparatory cue processing was associated with activation of frontal and parietal brain networks, which were then reactivated during the execution of the target stimulus. Thus, it is possible that cues that signal an upcoming task allow for all task-related regions to go “online” before the actual task is presented. Similarly, another investigation using cued task-switching found that regions that become active during preparatory cue processing (primarily prefrontal, parietal, and pre-SMA) also became active during the execution of the task-switch following no preparation, but to a greater extent (Shi, Zhou, Müller, & Schubert, 2010). From this, the authors conclude that it is in fact possible to separate activity unique to “a subset of the general task-preparation related regions” that activate less strongly during preparation than during execution (p. 1263) and that providing cues with stimulus-response mapping information ahead of a target leads to enhanced task-switching performance. While this body of work has begun to provide important answers about the nature of neural processes that govern preparation in cognitive control, many questions remain to be answered. For instance, the majority of task-switching paradigms require switching between equally weighted (i.e., equibiased) tasks. Thus, providing a cue ahead of the task essentially amounts to providing critical information for completing the task (stimulus-response mappings) before the stimulus is presented. It is not clear from these tasks whether or not that information also allows an individual to begin to deploy more controlled processes, such as those

necessary for overriding a prepotent or dominant response. Thus, investigations making use of unequally biased responses provide further insights into the neural bases of preparatory control processes. The current study aimed to investigate whether preparatory cues for overriding a dominant response allows one to deploy in advance control processes that would otherwise deal with such conflict “on the fly.”

## **1.2 A cued response override task**

The Preparing to Overcome Prepotent Response (POP) task employed herein was originally designed to investigate such preparatory cue processing (Barber & Carter, 2005). This task capitalizes on both the spatial compatibility of stimulus-response features to generate a prepotent response, similar to the commonly used Simon task, and on the frequency with which congruent and incongruent responses occur, to manipulate the extent to which a given trial requires automatic or controlled responding. Specifically, the congruent condition involves pressing a key to indicate the direction the target arrow is pointing, with the button and response hand that is on the same side as the direction indicated by the arrow (i.e., press the “A” key on the left side of the keyboard with your left hand if the arrow is pointing to the left). The prepotency of this response pattern is enhanced by the fact that the majority of trials in the paradigm (75%) are congruent. The critical manipulation in the original POP task is the presence of a cue that indicates whether the subsequent stimulus will be congruent, or in rare cases (25% of the time), will require an *incongruent* response (with the hand/button in the opposite direction that the arrow is pointing), thus requiring the override of the prepotent response via the resolution of conflicting stimulus-response (SR) associations. In theory, providing a cue ahead of an incongruent response trial allows for neural networks to engage earlier in processes related to overcoming the more automatic, prepotent response, despite the fact that a specific response

cannot be planned before the stimulus is presented. Previous studies using the POP task have shown that cued preparatory processing engages the neural networks associated more broadly with cognitive control and conflict monitoring (Barber & Carter, 2005). Specifically, Barber & Carter (2005) found that bilateral dorsolateral prefrontal cortex (dlPFC) was more active during the presentation of an incongruent cue to override (incongruent *preparation*) than during a congruent one, whereas the *execution* of a cued incongruent trial included regions in the anterior cingulate cortex (ACC) and superior parietal lobule that were not recruited in preparation. These findings are somewhat inconsistent with the cued task-switching literature described above, which has shown that the areas activated during cue processing are also active during execution. A plausible explanation for these divergent findings is that different preparatory processes occur depending on whether cues provide a means for anticipating specific types of conflict (such as in the Barber and Carter investigation) or only provide a means for activating stimulus-response patterns (as is seen in the task-switching literature). In other words, an incongruent cue during the traditional POP task both provides the correct stimulus-response mapping, and explicitly signals the need to override a dominant response to the upcoming stimulus, whereas the cue in task-switching paradigms simply signals the stimulus-response mapping. Moreover, the control processes being deployed in the two tasks (mental set shifting versus dominant response override) may trigger highly distinct neural preparatory processes, as suggested by previous investigations. Cues that are informative enough to signal the type of forthcoming conflict may recruit specific cognitive control processes early during preparation such as conflict monitoring, while less informative cues may trigger general preparation such as attention or tonic alertness (Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008). Although the results summarized above provide a critical beginning to our understanding of the preparatory override processes, the

original POP paradigm and existing task-switching investigations do not allow for the direct comparison of these different types of preparatory processes. Thus, the influence of the measured preparatory responses can be better evaluated with a direct, within-subjects comparison of two conditions, one where the cue signals the trial type (informative cue) and another where the cue does not provide information about trial type and instead only signals a known forthcoming task (noninformative cue).

To more systematically isolate the neurocognitive mechanisms associated with preparing for response conflict, a modified version of the POP task was created. In this modified version, the information indicating whether a congruent or incongruent response was appropriate was either presented before the trial (i.e., as an informative colored cue, consistent with the original POP design) or at the same time as the arrow stimulus (target arrows themselves were colored), following a noninformative white cue. The inclusion of the noninformative cue that only signaled the onset of an upcoming stimulus allowed for a better investigation of the nature of preparatory neurocomputations. Specifically, this condition allowed for the estimation of preparation for conflict, as it occurs in paradigms with unequally biased responses. Furthermore, this design allows the comparison of three qualitatively different mechanisms involved in the resolution of conflict: (1) Anticipatory neurocomputations for conflict resolution during an incongruent response (as measured over the time at which a cue indicates an incongruent trial), (2) Executing the command to override the stronger and more automatic response during incongruent trials following previous preparation, and (3) Executing an incongruent response “on the fly” without trial-type preparation (i.e., noninformative cue or only task preparation).

### **1.3 Experimental predictions**

We predict that the extent to which preparatory neurocomputations will share features in common with cued task-switching (e.g., Ruge et al., 2005) or the specific network involved in preparing to override a dominant congruent response (Barber & Carter, 2005) will depend on how much information can be extracted from the cues (trial informative versus noninformative cues). Thus, we make the novel prediction that noninformative cues will recruit a more general task network reflecting automatic or equibiased S-R mapping, while informative cues will result in the early recruitment of networks associated with specific anticipatory processes for selecting between automatic or dominant S-R representations. This prediction should be further supported by results indicating that preparation to informative cues should differ based on the level of control necessary for the proper execution of the forthcoming task via the correct S-R activation. In other words, incongruent informative cues should elicit distinct activation profiles from those seen in congruent informative cues. Specifically, we expect incongruent informative cues to result in the strongest recruitment of a distributed frontoparietal network, which has been previously implicated in the rapid deployment (ms by ms) of cognitive control. Furthermore, the effects of preparation during incongruent informative cues should result in reduced behavioral and neural costs during the response phase, due to facilitation in overriding the dominant response (as opposed to those trials where overriding needs to happen “on the fly” because the preceding cue was uninformative about trial type).

In summary, the current study aims to extend our understanding of the role of preparatory processing in cognitive control by isolating the processes specific to preparation for conflict resolution to behaviorally biased responses. Furthermore, this study’s experimental manipulations allow us to measure the effects of such preparation on the eventual deployment of the “override” response. Taken together, this design will allow us to make stronger inferences

about the neurocognitive mechanism or mechanisms by which preparatory processes ameliorate the demands associated with cognitive control.

## **2. Methods**

### **2.1 Participants**

Data were collected from 42 healthy, right handed participants (30 female, mean age = 22.31 years) recruited from the University of Washington undergraduate student population. Six participants (5 female) were excluded from neuroimaging analyses due to excessive head motion (4+ mm). Data from the remaining 36 participants are described herein. All participants gave informed consent prior to participating in the study, as outlined by the University of Washington's Institutional Review Board, and received monetary compensation for their time.

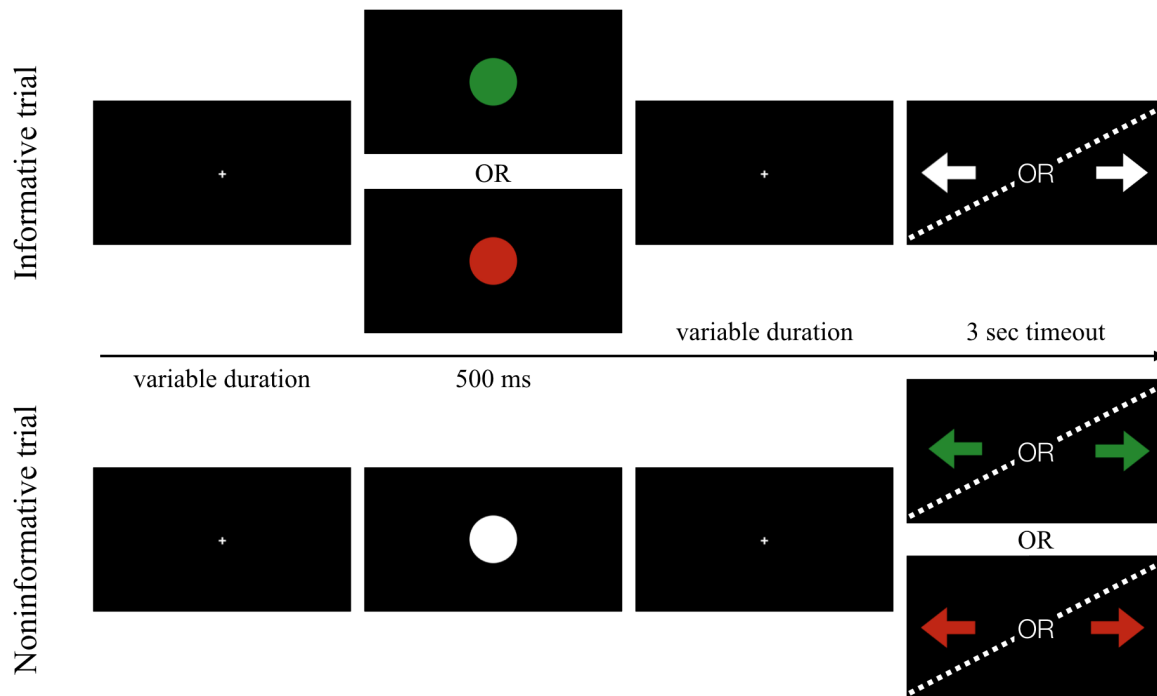
### **2.2 Materials**

The modified POP task consisted of 80 trials, each of which began with a circle-shaped cue that was later followed by an arrow-shaped target stimulus. Half of the trials included “informative” cues which indicated which type of task was coming next (congruent: green circles, incongruent: red circles), consistent with the original POP design. The other half of the trials included “noninformative” cues (white circles) which did not provide information regarding the upcoming target stimulus. Informative and noninformative trials were presented in blocks of 10 trials, in pseudorandomized order. Each block began with a prompt indicating block type, presented on the screen for 3 seconds. The timing for informative and noninformative trials was identical and is described in detail below.

**2.2.1 Informative cue condition.** Each informative trial began with either a green (75% of trials) or red (25% of trials) circle appearing centrally on the screen for 500 milliseconds. Each circle was followed by a fixation of variable duration (2-10 seconds) to allow an accurate

estimation of activation for cues and arrows separately (Dale, 1999). After the variable delay, a white arrow facing either to the left (50%) or to the right (50%) was presented. Participants were asked to press a button with the hand corresponding to the direction in which the arrow was pointing for trials where the cue was green (congruent trials), and respond in the opposite direction of the arrow for trials where the cue was red (incongruent trials). The strength of the congruent SR association was reinforced in two ways: (1) the on-screen placement of the arrows corresponded to the direction in which they were pointing. For example, a left-facing arrow was also placed near the left-most margin of the screen; and (2) congruent trials, or those with the green cue preceding the arrow, made up the majority of the trials (75%), making the most common response the one that was congruent with the arrow. Participants had three seconds to respond to each arrow before the trial was recorded as an error (e.g., “no response”). Behavioral response times and accuracies were collected for all participants. Following each response, a centered crosshair appeared between trials for a time randomly varying between 2 and 10 seconds to reduce collinearity between phases (Dale, 1999).

**2.2.2 Noninformative cue condition.** The timing and order of presentation of noninformative POP trials were identical to the informative trials. The critical manipulation involved the point at which the task-relevant information was presented. Specifically, each noninformative trial began with a white circle that did not provide information about whether the arrow task would be congruent or incongruent. Subsequently, the arrows themselves were presented in either green (congruent trials, 75%) or red (incongruent trials, 25%) indicating what the expected response was. All other trial features remained identical to informative trials. A sample figure with detailed trial time-course activity is presented below in Figure 1.



*Figure 1.* Sample of trial informative and noninformative conditions with time-course information.

### 2.3 Procedure

All participants completed the Edinburgh Handedness Inventory (Oldfield, 1971) and received a short behavioral practice (20 trials) for the fMRI task one day prior to their scan. The fMRI POP task was conducted in two scanner acquisition runs, each consisting of two informative and two noninformative blocks, with each block containing 10 trials. At the beginning of each block, participants were presented with a block cue to inform them if they would be performing informative or noninformative trials for that block. For both informative and noninformative blocks, participants were asked to attend carefully to the cue and to respond as quickly and accurately as possible to the proceeding arrow. An angled mirror reflecting a projector screen at the back of the scanner bore allowed participants to view the experimental task.

## 2.4 Neuroimaging Methods

**2.4.1 fMRI Data Acquisition.** Structural and functional volumes were obtained using a whole-body 3.0 T Philips Achieva scanner at the Integrative Brain Imaging Center (IBIC) of the University of Washington. Structural images were acquired using a T1-weighted MPRAGE sequence. A T2\*-weighted echo-planar (EPI) sequence was used for functional volume acquisition, with time repetition (TR) = 1000 milliseconds, time echo (TE) = 30 milliseconds, flip angle = 60°, and field of view (FOV) = 24 cm. Seventeen 5 millimeter slices aligned to the anterior commissure-posterior commissure (AC-PC line) were acquired per volume, with a 1-millimeter gap between slices. Each oblique slice was a matrix of 80x80 voxels with an in-plane resolution of 3x3 mm.

**2.4.2 fMRI Data Processing and Analysis.** Data were analyzed using SPM8 (Wellcome Trust Centre for Neuroimaging, Cambridge, UK). All functional volumes were corrected for slice timing acquisition, corrected for motion, normalized to the Montreal Neurological Institute (MNI) template, resampled to 2 mm<sup>3</sup> voxels, and smoothed using an 8 mm Gaussian kernel.

Analyses were conducted using a mass-univariate general linear model (GLM) as implemented in SPM8 (Penny, Friston, Ashburner, Kiebel, & Nichols, 2011). Single-subject models were generated with the following 9 independent regressors: congruent cues, incongruent cues, neutral cues, informative-cued congruent arrows, informative-cued incongruent arrows, noninformative-cued congruent arrows, noninformative-cued incongruent arrows, incorrect trial cues, and incorrect trial arrows. Second-level models were generated by comparing the parameters estimates of first-level models using subjects as the random factor. All activation analyses are reported at the height threshold of  $p < 0.001$ , with a minimum distribution of activation of at least 20 contiguous voxels.

**2.4.2.1 Individual differences analysis of neuroimaging data with behavioral response times.** In order to better understand the impact of preparatory processes on conflict resolution during execution, a correlation analysis between brain activity at the time of execution and behavioral response times was conducted. Specifically, this relation between brain activity and behavior was assessed on a voxel-wise basis using random-effects multiple regression models, where response times to incongruent trials for informative and noninformative cues were entered as independent variables. For this analysis, the dependent variables of interest were the contrast of parameter estimates for incongruent execution following informative cues and for incongruent execution following noninformative cues. These analyses are reported at the height threshold of  $p < 0.001$ , with a minimum distribution of activation of at least 20 contiguous voxels.

### **3. Results**

#### **3.1 Behavioral Results**

All participants performed well above chance (minimum accuracy = 86%, mean = 96%). Two 2 X 2 analyses of variance (ANOVAs) were conducted measuring response times for correct trials only and accuracies separately. As anticipated, there was a main effect of congruency on response times, with longer times observed for incongruent trials than for congruent trials [ $F(1, 41) = 46.00, p < 0.01$ ]. A main effect of cuing was also detected, with longer response times observed for trials in the noninformative condition than in the informative condition [ $F(1, 41) = 61.32, p < 0.01$ ]. Importantly, a significant interaction in response times was observed between congruency and type of cuing [ $F(1, 41) = 4.80, p < 0.05$ ]. Follow-up analyses confirmed that significantly smaller differences between incongruent and congruent trials were observed in the informative cue condition [ $t(41) = -2.19, p < 0.05$ ] suggesting that

preparatory cuing significantly ameliorated the demands associated with overriding a prepotent response re. Response times for each condition in the 2 x 2 design are depicted in Figure 2.

ANOVAs conducted on accuracies revealed only a main effect of congruency, with significantly lower accuracies for incongruent trials than congruent trials across cuing conditions [ $F(1,41) = 20.89, p < 0.01$ ]. There were not other significant effects on accuracy, which is not particularly surprising giving the low variability in accuracies overall.

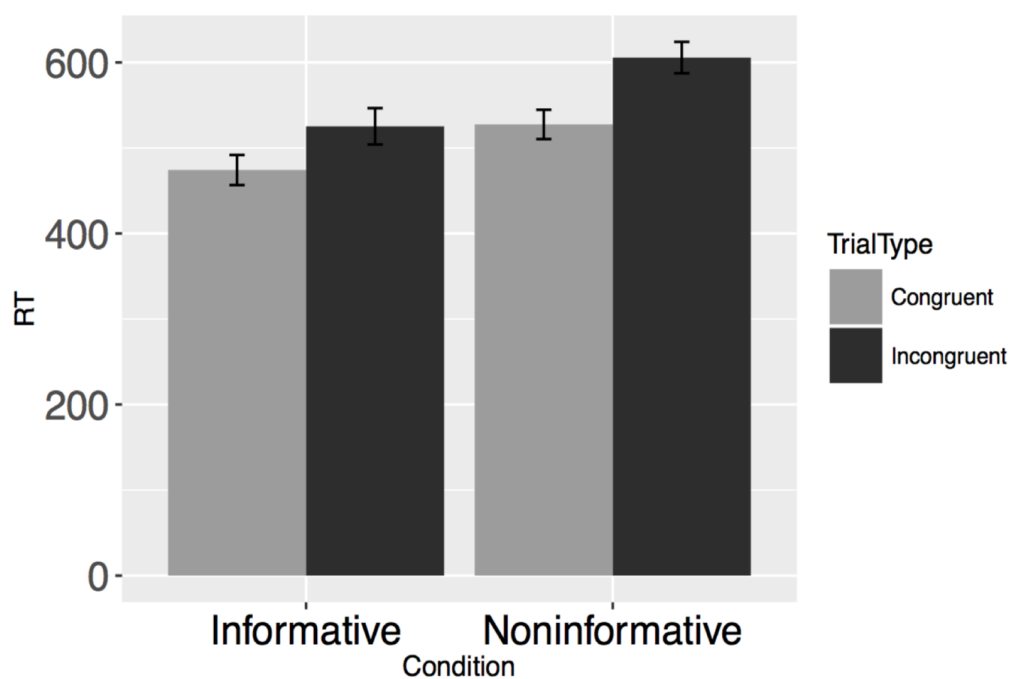


Figure 2. Response time (RT, in milliseconds) for each condition and trial type. Error bars represent one standard error of the mean.

## 3.2 Neuroimaging Results

### 3.2.1 General linear model results.

**3.2.1.1 Contrast A: Informative cue processing.** Preparatory mechanisms to specific trials were assessed by comparing patterns of neural activation in response to all informative cues to patterns of neural activity elicited by all noninformative cues. This contrast revealed that

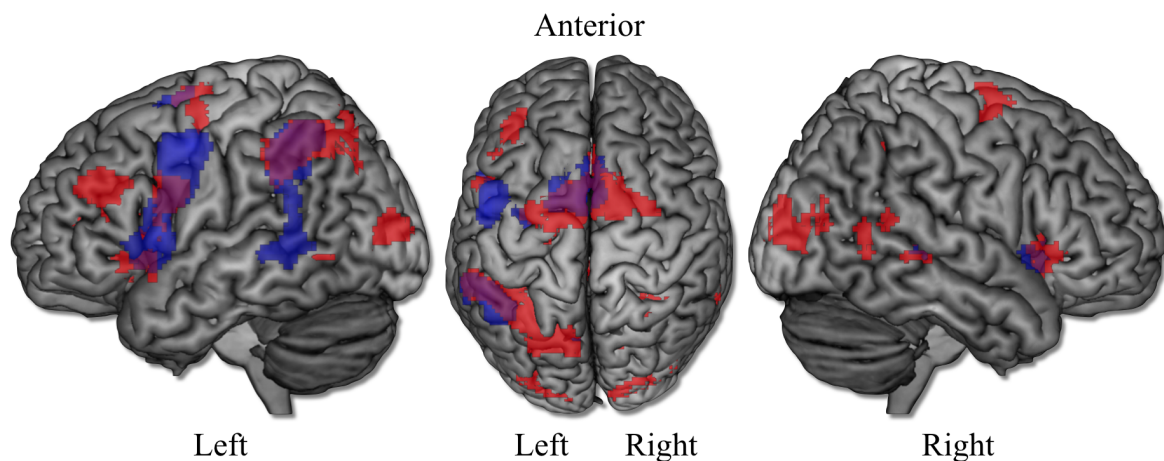
informative cue processing resulted in more activation in a distributed network of regions including a frontoparietal network to a greater extent than did the processing of noninformative cues. Specifically, informative cues resulted in greater brain activity in (1) a bilateral frontal network including the superior frontal gyrus, dorsal and middle cingulate cortex (dACC and MCC), and anterior insula (aI), and (2) left lateralized parietal regions including the inferior parietal lobe (IPL) and intraparietal sulcus (IPS). This is consistent with our prediction that cued preparation that is trial specific, irrespective of whether it involves controlled (override) or automatic (dominant) responding, engages the same networks that are involved generally in cognitive control. There were no voxels in which noninformative cues elicited greater activation than informative cues.

**3.2.1.2 Contrast B: Override cue processing.** The brain regions associated specifically with preparing to overcome response conflict were measured by comparing patterns of activation during override cue processing (preceding incongruent trials) to those observed during congruent cue processing. This contrast showed that override (incongruent) cue processing was associated with greater activation than congruent cue processing in a frontoparietal network similar to that described in Contrast A (above). Specifically, greater activation was again observed in (1) bilateral frontal regions including the anterior and middle cingulate cortex, and insula, and (2) left parietal regions including the IPL and IPS. Additional activation specifically for preparation to override response conflict was observed in the left dorsolateral prefrontal cortex, as well as in the subcortical regions of the right dorsal striatum (not pictured in the cortical rendering). There were no voxels in which congruent cues elicited greater activation than incongruent, override cues. Comparisons of Contrast A (informative cue processing, in blue) and Contrast B (override

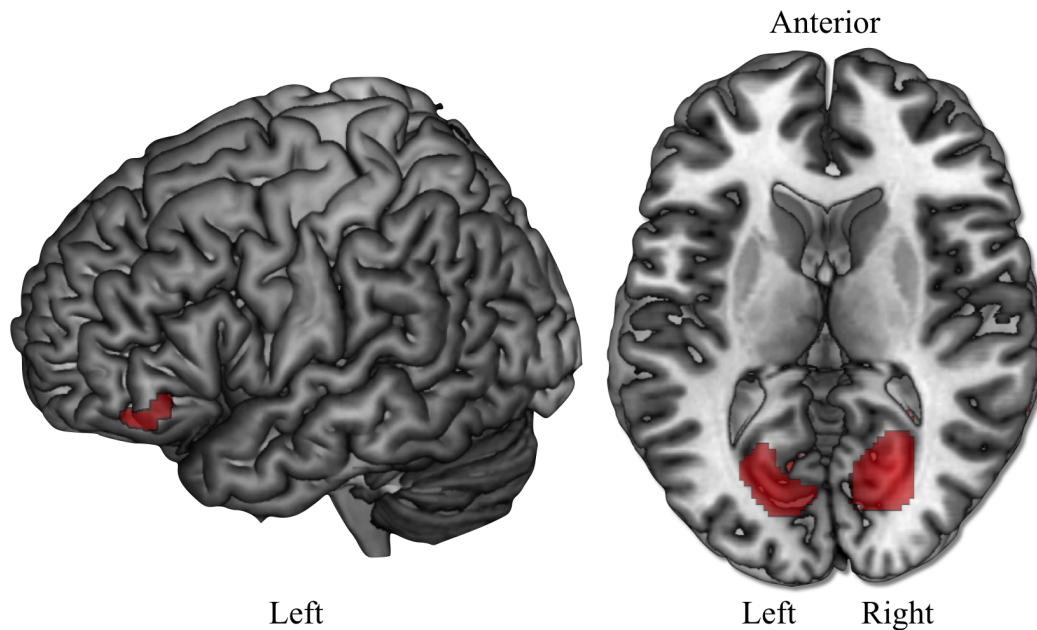
cue processing, in red) are depicted in Figure 3 (overlap in purple), and are listed along with their MNI coordinates in Table 1.

*Figure 3.* Contrast A or “all informative cue processing” in blue, overlaid with contrast B or “controlled” preparation (incongruent cues) in red. Purple voxels indicate regions that were significantly involved both contrasts. Figure shown at an uncorrected height of  $p < 0.001$  with a cluster threshold of 20 contiguous voxels.

**3.2.1.3 Contrast C: Effects of all preparation on task execution.** The effects of preparation on subsequent task execution were examined by comparing brain activity during the response phase for trials following informative cues to those that followed noninformative cues. Interestingly, execution of trials following informative cues resulted in significantly *greater* activity bilaterally in the primary visual cortex than did execution of trials following noninformative cues, along with the orbital portion of the left inferior frontal gyrus (IFG). There were no voxels in which execution following noninformative cues elicited greater activation than



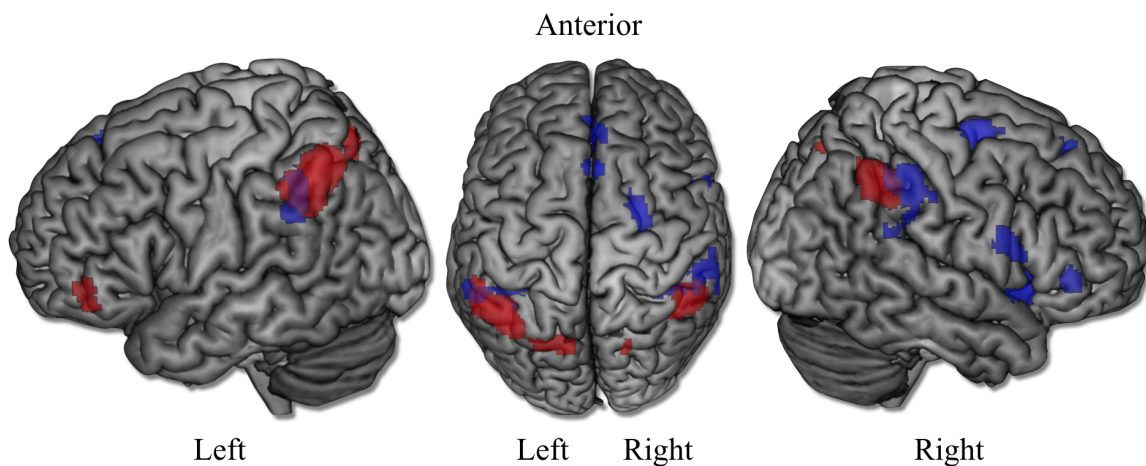
execution following informative cues. The results of this contrast are depicted in Figure 4, and are listed along with their MNI coordinates in Table 1.



*Figure 4.* The effects of trial informative preparation on execution (arrows following congruent and incongruent cues > arrows (congruent and incongruent) following noninformative cues). Figure shown at an uncorrected height of  $p < 0.001$  with a cluster threshold of 20 contiguous voxels.

**3.2.1.4 Contrast D & E: Response conflict resolution with (D) and without (E) informative cued preparation.** To understand the impact of preparatory cue processing on the resolution of conflict arising from overriding a dominant response, we compared the conflict resolution activation (indexed by greater activation when executing an incongruent trial than when executing a congruent trial) in the noninformative cue condition and in the informative cue condition. Conflict resolution following noninformative cues (incongruent > congruent trial execution) elicited patterns of activation in networks typically associated with response

inhibition (Aron, 2007; 2011) as well as in regions previously associated with cue processing (right insula, anterior cingulate, and parietal regions). In contrast, conflict resolution following informative preparatory cues resulted in more focal patterns of activation, including bilateral parietal regions and a left frontal area corresponding to BA10, widely associated with execution of goal-directed behavior (Burgess, Gilbert, & Dumontheil, 2007). The results from these two contrasts reflecting response conflict resolution with (in red) and without (in blue) preparatory cuing are depicted in Figure 5, and are listed along with their MNI coordinates in Table 1.



*Figure 5.* Contrast D, or conflict resolution following informative preparation, shown in red. Contrast E, or conflict resolution following noninformative preparation (“on the fly”), in blue. Notice reduced activity during execution following informative preparation. Purple voxels represent overlap. Figure shown at an uncorrected height of  $p < 0.001$  with a cluster threshold of 20 contiguous voxels.

**Table 1***Significant grey matter activation across contrasts of interest in POP task*

| Cortical region   | Brodmann's Area | Cluster size | Peak t-value | Cluster peak MNI coordinates |          |          |
|---|-----------------|--------------|--------------|------------------------------|----------|----------|
|   |                 |              |              | <i>x</i>                     | <i>y</i> | <i>z</i> |
| <b>Contrast A: Informative cue processing</b>   |                 |              |              |                              |          |          |
| Bilateral middle cingulate, superior frontal medial                                       |                 | 1409         | 5.18         | -8                           | 14       | 48       |
| LH inferior frontal, middle frontal, superior temporal, insula                            | 6, 13           | 1518         | 5.09         | -52                          | -4       | 46       |
| LH inferior parietal, middle temporal   | 40              | 1187         | 4.69         | -52                          | -46      | 52       |
| LH precuneus  | 7               | 71           | 3.72         | -8                           | -66      | 42       |
| RH middle temporal  | 21              | 25           | 3.67         | 50                           | -32      | 0        |
| RH inferior frontal, insula   | 45              | 134          | 3.94         | 36                           | 26       | 6        |
| <b>Contrast B: Override cue processing</b>  |                 |              |              |                              |          |          |
| Bilateral thalamus, RH caudate, RH insula, RH hippocampus                                 |                 | 3937         | 5.4          | -24                          | -24      | 4        |
| Bilateral anterior cingulate, middle cingulate  | 24              | 2819         | 5.67         | -8                           | 28       | 30       |
| LH inferior frontal, middle frontal, superior temporal, superior frontal, insula, putamen | 10, 44, 47      | 1855         | 4.77         | -58                          | 10       | 30       |
| LH inferior parietal, superior parietal, middle occipital, middle temporal, precuneus     | 40              | 3231         | 5.49         | -42                          | -48      | 48       |
| LH precentral   | 4               | 108          | 4            | -50                          | -14      | 44       |
| LH middle frontal   | 6               | 330          | 4.61         | -24                          | -6       | 50       |
| LH paracentral, middle cingulate  | 5               | 209          | 4.21         | -2                           | -42      | 56       |
| RH superior temporal, middle temporal, inferior parietal                                  |                 | 676          | 4.89         | 64                           | -44      | 14       |
| RH middle temporal, cuneus, precuneus   |                 | 811          | 5.37         | 22                           | -92      | 14       |

|                             |    |     |      |    |     |    |
|-----------------------------|----|-----|------|----|-----|----|
| RH inferior frontal         | 46 | 102 | 4.28 | 44 | 10  | 24 |
| RH inferior parietal lobule | 7  | 326 | 4.04 | 26 | -52 | 46 |

**Contrast C: Effects of all preparation on task execution**

|  |        |      |      |     |     |     |
|--|--------|------|------|-----|-----|-----|
| Bilateral primary visual cortex (calcarine sulcus) | 17, 18 | 2209 | 5.47 | 22  | -62 | 6   |
| Left inferior frontal orbital gyrus                | 47     | 53   | 4.33 | -38 | 44  | -12 |
| Right middle temporal gyrus                        | 21     | 26   | 3.95 | 58  | -46 | -6  |
| RH precentral gyrus                                | 6      | 85   | 4.04 | 42  | -6  | 36  |

**Contrast D: Response conflict resolution with preparation**

|                                 |    |      |      |     |     |     |
|---------------------------------|----|------|------|-----|-----|-----|
| LH inferior frontal             | 10 | 69   | 4.3  | -42 | 46  | -10 |
| RH inferior parietal lobule     |    | 640  | 4.78 | 44  | -46 | 46  |
| LH inferior parietal            |    | 1099 | 5.34 | -54 | -48 | 48  |
| LH superior parietal, precuneus | 7  | 146  | 4.29 | -12 | -72 | 58  |
| RH superior parietal            | 7  | 21   | 3.53 | 18  | -72 | 54  |

**Contrast E: Response conflict resolution without preparation**

|  |    |     |      |     |     |    |
|--|----|-----|------|-----|-----|----|
| RH inferior frontal, superior temporal, insula | 47 | 591 | 5.18 | 40  | 18  | -4 |
| RH inferior frontal, middle frontal            |    | 67  | 3.92 | 44  | 38  | 0  |
| RH putamen, caudate                            |    | 59  | 4.13 | 14  | 0   | 10 |
| Bilateral anterior cingulate                   | 32 | 56  | 3.62 | -4  | 36  | 14 |
| RH inferior frontal, precentral                |    | 143 | 4.16 | 58  | 10  | 22 |
| RH inferior parietal lobule                    |    | 449 | 4.62 | 36  | -42 | 44 |
| LH inferior parietal lobule                    |    | 296 | 4.58 | -38 | -44 | 44 |
| Bilateral middle cingulate                     |    | 122 | 3.93 | 4   | 38  | 36 |
| RH superior frontal, medial frontal            |    | 45  | 4.07 | 6   | 34  | 50 |
| RH superior frontal, middle frontal            | 6  | 240 | 4.89 | 24  | -4  | 62 |
| Bilateral supplemental motor                   | 8  | 89  | 4.9  | 4   | 18  | 58 |

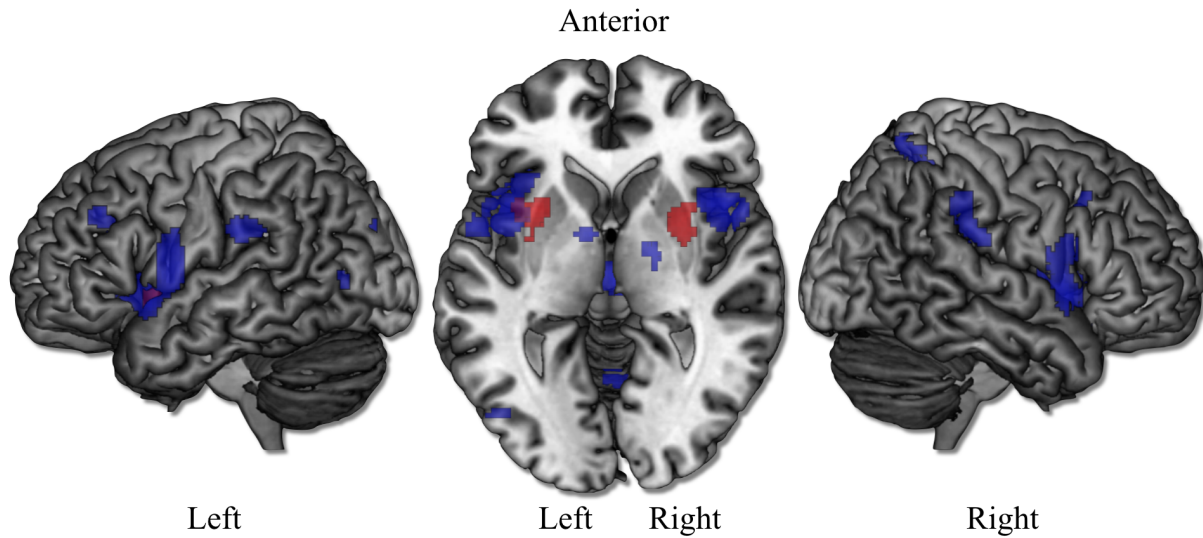
To directly compare the contrasts reflecting conflict resolution following informative and noninformative cues, an F-test of congruency by cuing condition conducted was conducted on

the neuroimaging data, however no significant results were revealed. Given the relatively large differences in patterns of activation at the group level, and the significant behavioral interaction, we hypothesized that this lack of significance may reflect variability across participants. As such variability can provide additional information about the nature of preparatory processes, we followed up by conducting individual differences analyses, relating patterns of behavior to patterns of brain activation during conflict resolution with and without preparation.

**3.2.2 Individual differences analyses.** Individual differences analyses were conducted to determine whether better conflict resolution (as indexed by faster reaction times to override trials) was associated with the same neural mechanisms with or without informative cue preparation. To do so, first, brain activation for execution following noninformative cuing was correlated with response times for those trials. This analysis revealed individual patterns of activation during override execution following noninformative cues (“on the fly” execution) in broadly distributed bilateral frontal, parietal and temporal regions including those widely associated with inhibitory control and response inhibition (right inferior frontal and subcortical globus pallidus). There were no positive correlations observed, suggesting that no regions reliably predicted slower performance

In contrast, faster response conflict resolution following informative cue preparation (“controlled”) resulted from more focal patterns of activation, namely those of the bilateral putamen and right middle cingulate gyrus. This pattern of results suggests that the more these regions were activated, the better an individual was able to override response conflict following an informative, preparatory cue. Again no regions were positively correlated with reaction time. The juxtaposition of regions of activation associated with better performance in cued (in red)

versus on the fly (in blue) is depicted in Figure 6, and are listed along with their MNI coordinates in Table 2.



*Figure 6.* In red, brain regions that negatively correlate with incongruent response times during execution following informative cues. In blue, brain regions that negatively correlate with incongruent response times during execution following noninformative cues. Purple voxels represent overlap. Figure shown at an uncorrected height of  $p < 0.001$  with a cluster threshold of 20 contiguous voxels.

**Table 2**

*Significant grey matter activation for individual differences analyses*

| Cortical region   | Brodmann's Area | Cluster size | Peak t-value | Cluster peak MNI coordinates |     |    |
|---|-----------------|--------------|--------------|------------------------------|-----|----|
|   |                 |              |              | x                            | y   | z  |
| <b>Negative correlation between informative cued execution activation &amp; informative cued execution response times</b> |                 |              |              |                              |     |    |
| Bilateral middle cingulate gyrus  | 23              | 118          | 4.34         | 6                            | -28 | 28 |

|                    |  |     |      |     |    |    |
|--------------------|--|-----|------|-----|----|----|
| LH putamen, insula |  | 214 | 4.55 | -30 | 10 | -2 |
| RH putamen         |  | 115 | 4.02 | 30  | 6  | 2  |

**Negative correlation between noninformative cued execution activation & noninformative cued execution response times**

|  |            |      |      |     |     |     |
|--|------------|------|------|-----|-----|-----|
| LH insula, inferior frontal gyrus, superior temporal gyrus | 13, 44, 47 | 1076 | 5.06 | -40 | 12  | 2   |
| LH medial globus pallidus, lentiform nucleus               |            | 23   | 3.95 | -8  | 0   | 0   |
| LH middle occipital gyrus, middle temporal gyrus           | 19         | 67   | 4.01 | -34 | -66 | 6   |
| LH inferior parietal lobule, postcentral gyrus             | 40         | 151  | 4.27 | -62 | -26 | 26  |
| LH superior frontal gyrus, middle frontal gyrus            | 9          | 77   | 4.29 | -40 | 34  | 34  |
| RH inferior frontal gyrus, insula                          | 13, 47     | 98   | 4.61 | 30  | 20  | -12 |
| RH substantia nigra, pallidum, subthalamic nucleus         |            | 330  | 5.03 | 4   | -16 | -12 |
| RH insula, inferior frontal gyrus, superior temporal gyrus | 13, 44, 47 | 698  | 5.26 | 46  | 12  | -2  |
| RH cerebellum anterior lobe, culmen, vermis 4,5            |            | 57   | 4.12 | 2   | -60 | -4  |
| RH thalamus  |            | 33   | 3.78 | 10  | -4  | 16  |
| RH inferior parietal lobule, postcentral gyrus             | 40         | 196  | 4.12 | 58  | -30 | 26  |
| RH middle frontal gyrus, inferior frontal gyrus            | 9          | 30   | 3.81 | 48  | 20  | 40  |
| RH superior parietal lobule, inferior parietal lobule      | 7          | 213  | 4.15 | 20  | -60 | 66  |

#### 4. Discussion

Taken together, the results from this experiment provide converging evidence that the neurocognitive mechanisms deployed to override a dominant behavioral response differ when the opportunity to prepare ahead of time is presented. Specifically, we showed that preparatory “override” cues resulted in the amelioration of behavioral effects associated with response

conflict resolution (Figure 2), and that these reduced cognitive costs were reflected by reduced involvement of cortical processing centers such as the right inferior frontal gyrus, known to be involved in inhibitory control (Figure 4). Importantly, individual differences analyses showed that “good” response conflict inhibition was associated with recruitment of largely non-overlapping brain regions when preparatory cues were given as compared to executing conflict resolution “on the fly” (Figure 6). Below we discuss these results in light of the broader literature on cognitive control and preparatory processes.

#### **4.1 Preparation for congruent and incongruent responding**

To better understand how preparatory cues specifically influenced the overriding of a dominant motor response, which is the primary focus of this paper, it is important to first consider the neural underpinnings of preparatory processes more broadly across congruent and incongruent informative trials. In this experiment, it was possible to observe the processes related to this preparation by contrasting brain activity for all informative cues against all noninformative cues. Our results indicate that preparation using the more specific informative cues, irrespective of trial type (congruent or incongruent) recruited a network of regions broadly associated with goal-directed behavior. For example, the frontal, parietal and anterior insular regions associated with processing all informative cues (Figure 3, blue) overlap highly with the network described with the regions described by Duncan (2010) as a general “multiple demand” system used by all primate brains to accomplish complex tasks in a goal directed manner (Duncan, 2010). These regions are also highly overlapping with those previously associated with cue processing in task switching paradigms (Ruge et al., 2005; 2013; Shi et al., 2010). When viewed in light of the main effect of cuing observed in our behavioral data, these results suggest that preparation with informative cues (even for congruent trials) facilitates execution by some

degree. The involvement of the multiple demand network in both this and more equibiased task-switching paradigms suggests that one mechanism by which preparation can facilitate responding is by the early biasing of the specific stimulus-response (S-R) set for a particular trial, something that cannot occur from noninformative cues that are not specific to trial type.

One novel piece of information provided by the current experiment is the result suggesting that early biasing of task-relevant information resulted in increased activation of primary visual areas during task execution (Figure 4). Such increased activation in primary visual areas has previously been associated with top-down attentional control mechanisms (Yamagishi, Goda, Callan, Anderson, & Kawato, 2005), and is in line with previous research that has found cortical amplification of task-relevant information as means for improving conflict resolution (Egner & Hirsch, 2005; Egner, Etkin, Gale, & Hirsch, 2008). We propose that the parietal cortex may link our observed patterns of activation during informative cues with those observed during cued task execution. Specifically, the parietal cortex has been implicated in top-down changes in attention with dynamic task demands (Dosenbach et al., 2008), and it is known to connect directly to the primary visual areas over which our increased activation was observed (Rockland & Ojima, 2003). Thus, we propose that the biasing of specific S-R mappings during informative cue processing allows an individual to narrow attention to a particular feature of the stimulus (i.e., arrow direction), and that this knowledge combined with enhanced activation in primary visual areas contributes to more efficient response execution following any cued trial.

#### **4.2 Preparing to Override Response Conflict**

The primary goal of this experiment was to examine the extent to which processes specifically associated with response conflict resolution could be deployed during a preparatory cue. Thus we turn our discussion to the regions that were more active when processing cues that

conflict trials were approaching than when processing cues that congruent trials were approaching. Our contrast of incongruent preparatory cues (e.g., red circle) versus congruent preparatory cues (e.g., green circle) revealed activation in the left dorsolateral prefrontal cortex that was *unique* to processing incongruent cues, as well as *greater* activation in bilateral insula, anterior and cingulate, and left parietal cortex (Figure 3, red). This increased activation in the cingulate cortex is consistent with previous research highlighting its role in conflict monitoring (Barber & Carter, 2005; Botvinick, Cohen, & Carter, 2004; Carter et al., 1998), and activation in bilateral insula has been widely associated with salience detection (Botvinick et al., 2004; Botvinick, Carter, Nystrom, Fissell, & Cohen, 1999). Thus, increased activation in these regions specifically for conflict cues may suggest the deployment of regions typically associated with response conflict *in advance* of the response execution.

Consistent with this view, no cingulate or insula activation was observed during execution of response override trials *following* preparatory cues (Figure 5, red). In contrast, when no preparation was possible (in the non-informative cued condition), overriding dominant responses “on the fly” recruited both anterior and middle cingulate regions and right insula. Taken together, these results suggest that this network of control regions becomes activated at the earliest point at which the need for controlled responding becomes detected.

But how might activation during the cue for conflict support facilitated responding? It is important to note that while the cues provide information that non-dominant responding will be needed, they do not provide information about the *specific direction* of response (e.g., left versus right). Thus, the most likely explanation for how activation at the cue supports responding is that it provides enhanced access to both non-dominant S-R mappings (i.e., left arrow = right response; right arrow = left response). Evidence for this type of processing can be inferred by the

recruitment of subcortical structures known to be involved in dynamic prioritization of signals to the prefrontal cortex (Cohen & Frank, 2009; Hazy, Frank, & O'Reilly, 2007; Stocco, Lebiere, & Anderson, 2010). Further evidence for the role of the striatum in preparation and execution of controlled responses is discussed in the individual differences section below. Taken together, these results in combination with the observed behavioral interaction between task congruency and cuing, suggest that some portion of the neurocognitive responses typically associated with response conflict resolution “on the fly” can be deployed in advance of actually responding to the conflict.

### **4.3 Individual Differences in Conflict Resolution with and without Preparation**

The results from our individual differences analyses provide extended evidence that overcoming response conflict with and without preparation is fundamentally different. Interestingly, following cues allowing one to prepare for conflict in advance, efficient conflict resolution (as correlated with faster response times) was primarily associated with recruitment of the putamen, bilaterally (Figure 6, red). As the putamen is known to more heavily affect motor signaling (in comparison to the caudate; Ali, Green, Kherif, Devlin, & Price, 2010; Gil Robles, Gatignol, Capelle, Mitchell, & Duffau, 2005), this result is consistent with the proposal that striatal activation during incongruent cues reflects a biasing of non-dominant S-R mappings. In striking contrast, when no opportunity to prepare for conflict was provided, efficient conflict resolution was associated with recruitment of distributed cortical and subcortical regions related to response inhibition and cognitive control more broadly (Figure 6, blue). This is consistent with the proposal that without preparatory cues, response conflict mechanisms must be executed “on the fly,” and the ability to recruit these networks results in improved performance. It is important to note here that with the exception of a small region in the left anterior insula, the network of

regions associated with efficient conflict resolution with and without preparation were almost entirely non-overlapping. Thus, the individual differences results provide supporting evidence that the ability to prepare for conflict in advance results in both qualitative and quantitatively separate mechanisms for addressing the conflict when it arises.

These results are not without limitations, however, which should be mentioned when considering the interpretations proposed. First, although the group contrasts for overriding conflict with and without informative cue preparation suggested differential patterns of neural recruitment (Figure 5), the direct comparison of these results using F-tests were not significant. Second, although we make inferences about how activation in particular regions during cue processing may result in different patterns of activation during execution, no direct measure of such influence is described herein. For instance, dynamic causal modeling can be used to directly test the extent to which activation in one region across time drives activation in another region, and the extent to which these drives are modulated by specific task conditions (for instance the presence of preparatory cues). Of particular relevance to the current study, recent research using dynamic causal modeling during a cognitive control task revealed that in high-demand conditions, the anterior cingulate cortex influenced activation in both the dorsolateral prefrontal cortex and in the basal ganglia (Becker, Prat, & Stocco, 2016). We see this as an exciting and important area for future research.

## **5. Conclusion**

The results reported herein extend previous research on the neural basis of preparatory cue processing by providing evidence about how biased response overriding is influenced by the presence of preparatory conflict cues. Our results provide converging evidence that the neural mechanisms being utilized to exert control during planned conflict resolution are at least partly

different from those used to exert control on the fly. Specifically, we have shown that some of the neural mechanisms typically associated with response conflict resolution, such as conflict monitoring in the cingulate cortex and salience detection in insular regions, can be deployed at the earliest point at which conflict is detected or anticipated. This early deployment may likely involve the biasing of non-dominant S-R patterns through fronto-striatal signaling mechanisms that affect frontal neural representations. Such early preparation effectively distributes the processes typically associated with response conflict resolution across preparation and execution, resulting in reduced neural and behavioral costs during response execution.

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