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## Research Report

# Preparatory neural activity predicts performance on a conflict task

Emily R. Stern<sup>a,\*</sup>, Tor D. Wager<sup>a</sup>, Tobias Egner<sup>b</sup>, Joy Hirsch<sup>b</sup>, Jennifer A. Mangels<sup>a</sup>

<sup>a</sup>Department of Psychology, Columbia University, New York, NY 10027, USA

<sup>b</sup>Functional MRI Research Center, Columbia University, New York, NY 10027, USA

### ARTICLE INFO

#### Article history:

Accepted 23 July 2007

Available online 9 August 2007

#### Keywords:

Attention

Cognitive control

Advance preparation

Feature biasing

Conflict

Stroop

### ABSTRACT

Advance preparation has been shown to improve the efficiency of conflict resolution. Yet, with little empirical work directly linking preparatory neural activity to the performance benefits of advance cueing, it is not clear whether this relationship results from preparatory activation of task-specific networks, or from activity associated with general alerting processes. Here, fMRI data were acquired during a spatial Stroop task in which advance cues either informed subjects of the upcoming relevant feature of conflict stimuli (spatial or semantic) or were neutral. Informative cues decreased reaction time (RT) relative to neutral cues, and cues indicating that spatial information would be task-relevant elicited greater activity than neutral cues in multiple areas, including right anterior prefrontal and bilateral parietal cortex. Additionally, preparatory activation in bilateral parietal cortex and right dorsolateral prefrontal cortex predicted faster RT when subjects responded to spatial location. No regions were found to be specific to semantic cues at conventional thresholds, and lowering the threshold further revealed little overlap between activity associated with spatial and semantic cueing effects, thereby demonstrating a single dissociation between activations related to preparing a spatial versus semantic task-set. This relationship between preparatory activation of spatial processing networks and efficient conflict resolution suggests that advance information can benefit performance by leading to domain-specific biasing of task-relevant information.

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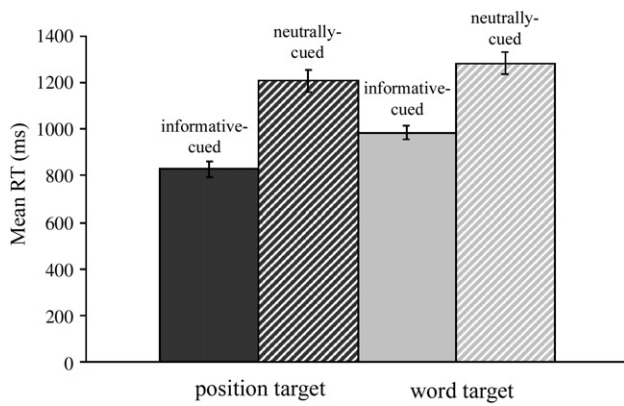
## 1. Introduction

The ability to selectively tune attention toward relevant information in the environment is at the heart of cognitive flexibility. The behavioral benefits of selective attention are clearly evident in cued attention studies, which find that advance information can decrease reaction time (RT) across a variety of tasks (e.g., Meiran, 1996; Posner et al., 1980; Sudevan and Taylor, 1987). Neuroimaging studies suggest that advance cueing of task-relevant information involves the activation of

feature-specific sensory or association areas (sites of control) via top-down biasing signals from executive regions (sources of control) located in frontal and parietal cortices (e.g., Corbetta and Shulman, 2002; Desimone and Duncan, 1995; Driver and Frackowiak, 2001; Giesbrecht et al., 2006; Hopfinger et al., 2000; Kastner et al., 1999; Luks and Simpson, 2004). Increasingly, evidence suggests that neural regions involved in attentional control demonstrate domain or feature-specificity (Goldman-Rakic, 1995; Smith and Jonides, 1999; Sakai and Passingham, 2003; Thompson-Schill et al., 2005), although some may be part

\* Corresponding author. E.R. Stern is now at the University of Michigan, Department of Psychiatry, 4250 Plymouth Road, 2701 Rachel Upjohn Building, Ann Arbor, MI 48105, USA. Fax: +1 734 936 7868.

E-mail address: [emistern@med.umich.edu](mailto:emistern@med.umich.edu) (E.R. Stern).



**Fig. 1 – Behavioral data. Mean reaction time for targets based on relevant feature (position vs. word) and cue specificity (informative vs. neutral).**

of a more general core control network (Cristescu et al., 2006; Dosenbach et al., 2006). For example, we have found that response times associated with cue-based preparation are correlated across different types of switches between stimulus materials and tasks, indicative of a domain-general anticipatory process (Wager et al., 2006).

Preparatory attention may be particularly important when task-irrelevant information has the potential to interfere directly with performance, such as in the Stroop conflict task (Stroop, 1935). In the classic Stroop task, a dominant stimulus feature (e.g., word meaning) interferes with a task-relevant, non-dominant feature (e.g., color), both at the level of response output and stimulus representation (De Houwer, 2003; Zhang and Kornblum, 1998). Conflict engendered by these competing stimulus representations may be reduced if preparatory information regarding the task-relevant feature is provided, yet the relationship between decreased RT associated with advance cueing and preparatory feature biasing has not been extensively investigated. In one of the few previous studies addressing this issue, MacDonald et al. (2000) found that dorsolateral prefrontal cortex (DLPFC) activity during a preparatory cue period was related to reduced RT on incongruent trials. However, in this study there were no trials in which subjects were not cued with the relevant task set. Thus, the relationship between preparatory activity and reduced conflict directly attributable to feature-specific cueing, as compared to a less selective process such as vigilance or general anticipatory attention, could not be examined. Considering that multiple studies have found prefrontal and parietal activation in vigilance or general anticipatory attention tasks that do not require selection of one stimulus feature over another (Brunia and van Boxtel, 2001; Cabeza and Nyberg, 2000; Pardo et al., 1991; Roshal and Knight, 1995), it is important to control for the influence of these general processes when seeking to identify neural activity unique to preparatory feature-biasing.

The current event-related fMRI study was designed to clarify these important questions. In the task, subjects were required to make a response according to the spatial location or meaning of target words in which these two potentially relevant features were in conflict (e.g., the word “LEFT” located to the right of central fixation). Prior to receiving these stimuli,

subjects sometimes received feature-specific, informative cues indicating whether location or meaning would be the relevant feature. These cues designated the task-relevant “set”, without indicating the actual spatial location or word meaning of the target stimulus. Importantly, we also included trials in which target stimuli were preceded by neutral, uninformative cues that simply signaled the beginning of the preparatory period. As these neutral cues did not designate the task-relevant feature ahead of time, contrasting neural activity elicited by informative and neutral cues served as a control for the influence of general anticipatory attention.

Furthermore, in addition to examining group-averaged data, we expected that the extent to which preparatory activity directly influenced performance on a conflict task would be most apparent in brain-behavior relationships across subjects. Specifically, if subjects with greater preparatory activity in response to informative cues exhibited improved conflict resolution, this would provide evidence that the ability to quickly ignore or override incompatible information is not just a result of processes occurring at the time of target presentation, but may also be influenced by the generation of a task-set prior to conflicting stimuli (MacDonald et al., 2000). To this end, we examined correlations between preparatory neural activity and reaction times benefits associated with informative as compared to neutral cues. To the extent that there is domain-specificity in frontal and parietal sources (Goldman-Rakic, 1995; Smith and Jonides, 1999) and posterior sites of control (Heil et al., 1997; Nobre et al., 1994; Stephan et al., 2003; Ungerleider and Haxby, 1994), we might expect to find activity involved in preparatory feature biasing to be distinguished

**Table 1 – Whole-brain activations for position minus neutral (P-N) and position minus word (P-W) cue contrasts**

Contrast/Region	BA	Voxels	x	y	z	Max t
<b>P-N</b>						
Superior frontal gyrus/ orbitofrontal	11	27	32	46	-20	6.32
<b>Superior frontal gyrus (aPFC)</b>	<b>10</b>	<b>23</b>	<b>22</b>	<b>54</b>	<b>20</b>	<b>5.91</b>
Dorsal anterior cingulate	32	28	-2	6	48	5.05
<b>Superior/inferior parietal lobule</b>	<b>40</b>	<b>386</b>	<b>38</b>	<b>-54</b>	<b>48</b>	<b>6.62</b>
Precuneus	7	111	12	-72	48	6.79
Inferior parietal lobule	40	56	-42	-40	48	5.17
Superior parietal lobule/ precuneus	7	53	12	-60	66	6.47
Superior parietal lobule	7	36	-32	-54	66	7.69
Cerebellum (declive)	-	25	-36	-60	-30	5.65
Cerebellum (declive)	-	22	26	-56	-26	6.73
Cerebellum (declive)	-	34	-12	-62	-28	5.58
Thalamus (ventral lateral nucleus)	-	47	16	-12	16	6.53
<b>P-W</b>						
Precuneus	7	43	16	-68	42	5.88
Inferior parietal lobule	7	20	-54	-44	44	6.01
Inferior parietal lobule	40	56	34	-50	42	5.39
Middle occipital gyrus	19	63	52	-66	-10	6.34

MNI coordinates represent center of mass. Clusters thresholded at  $p < .001$  with 20 contiguous voxels; those shown in bold font are represented in accompanying figures.

based on the type of informative cue received. By contrast, regions serving a domain-general function should be activated for both informative cue types and may be part of a broader executive control network.

## 2. Results

### 2.1. Behavioral data

For correct trials, a 2-way analysis of variance (ANOVA) with task-relevant feature (location of word vs. meaning of word) and cue specificity (informative vs. neutral) revealed significant main effects as well as an interaction between factors. Regardless of cue specificity, subjects were faster when responding according to the location of the word (henceforth referred to as “position” trials) than when responding according to the meaning of the word (henceforth referred to as “word” trials) [ $F(1, 13) = 30.49, p < .001$ ]. Additionally, RTs were faster on trials in which subjects received an informative cue as compared to a neutral cue [ $F(1, 13) = 133.4, p < .001$ ], revealing the expected benefit from informative cueing. An interaction between factors revealed that the difference in RT between informative and neutral cues was greater for position trials than for word trials [ $F(1, 13) = 5.69, p < .05$ ], such that the mean behavioral cueing effect (calculated as neutrally-cued target RT minus informative-cued target RT) was 377.4 ms for position trials and 297.7 ms for word trials (Fig. 1). The overall slower RT

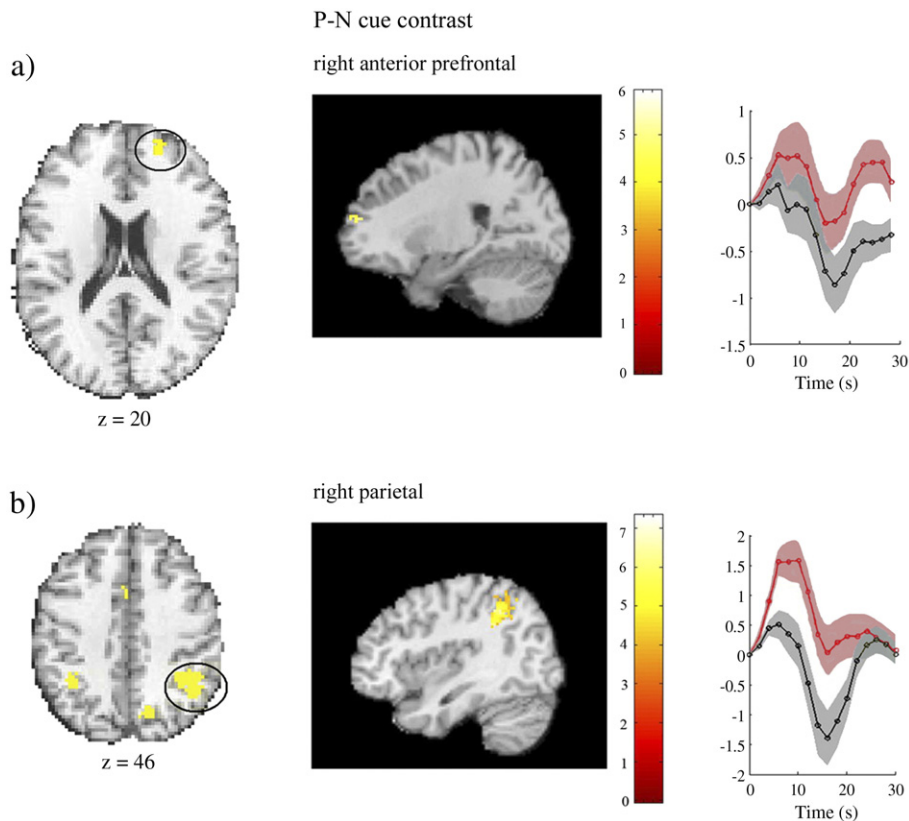
and the smaller benefit received from informative cueing on word trials may indicate that preparatory verbal processing was more difficult to implement than preparatory spatial processing, consistent with data indicating that responding according to word meaning is less “automatic” than responding according to spatial location in the spatial Stroop task, particularly when manual (rather than verbal) responses are made (Baldo et al., 1998; Lu and Proctor, 1995).

The average number of errors made on neutrally-cued trials was 7.3 (out of 52 trials, 14%). Proportionately fewer errors were made on informative cueing trials: the average number of errors made on word- and position-cued trials, respectively, was 2.57 and 2.64 (each out of 25 trials, 10.28 and 10.56%). Thus, as expected, paired samples t-tests indicated a greater percentage of errors for neutrally-cued as compared to either position- or word-cued trials ( $p < .05$  for both), which were not different from each other. These results indicate that informative cueing decreased both RT and error rates, excluding the possibility that these cues altered speed–accuracy trade-offs.

### 2.2. Neuroimaging data

#### 2.2.1. Group-averaged contrasts

Regions that were active during the cue period independent of individual performance variability were identified in group-averaged contrasts and are presented in Table 1. Several frontal and parietal regions were more active in response to position cues than to neutral cues, including right lateral



**Fig. 2** – Selected regions demonstrating greater activation in position-cued than neutrally-cued trials: a) Right aPFC and b) right parietal cortex. Scales correspond to t values of clusters. Time-courses of BOLD signals are shown next to activated regions (position cue period HRF in red and neutral cue period HRF in black).

anterior prefrontal cortex (aPFC) (Fig. 2a), bilateral posterior parietal cortex (Fig. 2b), right lateral orbitofrontal cortex, and left dorsal anterior cingulate cortex (ACC). Outside of the cortex, activation of bilateral regions of the cerebellum and right thalamus were greater in response to position as compared to neutral cues.

No regions exhibited greater activation for the word cue as compared to the neutral cue at the current threshold. In order to determine whether similar regions active during the position cue period could be found during the word cue period, we lowered the threshold to  $p < .005$  with 20 contiguous voxels. At this lenient threshold, activation was found in right lateral aPFC (peak of activation in MNI coordinates: 22, 52, 22), in a region closely overlapping with that identified in the position vs. neutral cue contrast, as well as in two areas of the right anterior paracentral lobule (6, -32, 60; 8, -26, 72) possibly related to motor processes.

In a direct contrast between the position and word cue periods, regions of bilateral parietal cortex and right occipital cortex were more active during the position cue period (P–W). The converse contrast (W–P) found no activation at the current threshold, but revealed a region of rostral anterior cingulate cortex (-4, 42, 12) at the lowered threshold.

### 2.2.2. Relationship between preparatory activity and behavioral cueing effects

We additionally performed a regression analysis examining the relationship between neural and behavioral differences

associated with the informative vs. neutral cue contrasts, thereby providing a sensitive measure of preparatory control regions that might not be detected in the group-averaged analysis. Table 2 shows those regions where increased activity in the position–neutral cue contrast predicted a greater behavioral cueing effect (positive correlation) or a smaller behavioral cueing effect (negative correlation).

Subjects who had greater activity during the position cue period as compared to the neutral cue period in right superior frontal gyrus/DLPFC (BA 9) (Fig. 3a) exhibited a greater RT benefit from the position cue. In addition, activity in multiple regions outside of frontal cortex, including large areas of bilateral posterior parietal cortex (Fig. 3b), right posterior middle temporal gyrus, left temporo-parietal junction (TPJ), and bilateral occipital cortex, were also positively correlated with the behavioral cueing effect (see Table 2). Thus, bilateral posterior parietal cortex was found to be differentially active for position as compared to either neutral cues (Fig. 2b) or word cues, and also predicted the degree of behavioral cue benefit observed on position-cued trials (Fig. 3b).

A negative correlation was found between activation in a region of right precentral gyrus (BA 4/6) and the behavioral cueing effect on position trials (see Table 2). One possible explanation is that this activation represents sensory-motor processing engaged by subjects attempting to anticipate the actual response direction prior to stimulus onset. It is likely that such a strategy would be negatively correlated with performance, as the correct movement cannot be accurately estimated until target presentation.

Variability in neural activity for the word vs. neutral cue contrast did not predict differences in the word behavioral cueing effect at the  $p < .001/20$  voxel threshold. Nonetheless, as with results from group-averaged data on word trials, we sought to explore whether there would be any overlap between regions showing a positive correlation for position trials and those found for word trials at a lowered threshold. At the  $p < .005/20$  voxel threshold, preparatory neural activity in response to word cues that was positively correlated with cueing benefit was found in regions putatively related to semantic processing. Specifically, subjects who had greater activity in multiple regions of left inferior frontal gyrus (-52, 22, 16; -30, 24, -20) and bilateral temporal cortex (60, -58, -4; -52, -40, -16; -60, 10, 2) exhibited relatively faster RTs to word-cued targets. In further contrast to the position cue period, the only parietal activations found were in postcentral gyrus and posterior cingulate gyrus. Regions of bilateral occipital cortex, bilateral hypothalamus, and right medial orbital gyrus also showed a positive relationship between word cue period activity and the behavioral cueing effect. Importantly, the vast majority of frontal, parietal, and temporal regions associated with word cue benefits at this low threshold did not overlap with those predicting position cue benefits.

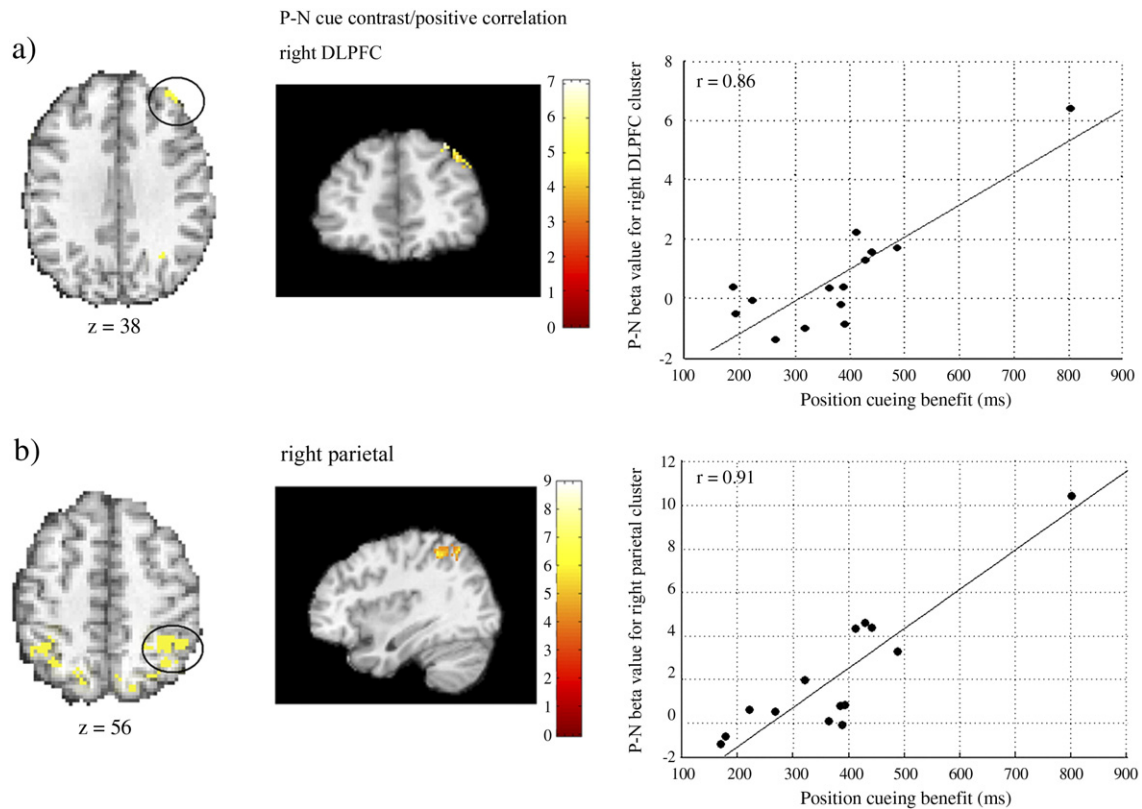
**Table 2 – Whole-brain activations for correlations between position minus neutral (P–N) cue contrast and behavioral cueing effects**

Contrast/Region	BA	Voxels	x	y	z	Max t
P–N/behavioral cueing effect						
<i>Positive correlation</i>						
<b>Superior frontal gyrus (DLPFC)</b>	<b>9</b>	<b>36</b>	<b>36</b>	<b>46</b>	<b>40</b>	<b>7.06</b>
Temporo-parietal junction (TPJ)	39	34	-56	-64	22	5.93
Middle/inferior temporal gyrus	21/37	33	64	-52	-4	7.87
Precuneus	7	41	12	-78	52	6.60
Precuneus	7	43	-22	-74	60	7.92
Precuneus/superior parietal lobule	7	28	16	-62	70	5.29
<b>Inferior/superior parietal lobule</b>	<b>40/7</b>	<b>243</b>	<b>36</b>	<b>-56</b>	<b>58</b>	<b>8.91</b>
Inferior/superior parietal lobule	40/7	183	-42	-56	54	8.34
Inferior parietal lobule	39	30	32	-64	32	7.68
Middle occipital gyrus	19	46	28	-80	16	5.67
Inferior occipital gyrus	18	21	38	-92	-14	7.52
Cuneus/middle occipital gyrus	18	30	-22	-96	20	5.94
<i>Negative correlation</i>						
Precentral gyrus	4/6	40	50	-8	34	-12.91

MNI coordinates represent center of mass. Clusters thresholded at  $p < .001$  with 20 contiguous voxels; those shown in bold font are represented in accompanying figures.

### 3. Discussion

In an effort to investigate the role of preparatory feature-specific biasing in improving the efficiency of conflict resolution, we examined the relationship between neural activity associated with advance cueing of task-relevant features and



**Fig. 3** – Areas in which increased preparatory activity in the position minus neutral (P-N) cue contrast is related to greater behavioral cueing effect for position trials. a) Right DLPFC and b) right parietal cortex. Scales correspond to *t* values of clusters. Robust regression scatterplots show the relationship between position cueing benefit on x-axis and preparatory activity for P-N cue contrast on y-axis.

RT to incongruent stimuli in a spatial Stroop task. Informative cues that could be used to bias attention toward the task-relevant domain were contrasted with neutral cues that served to engage general anticipatory processes. As expected, subjects responded significantly faster to incongruent targets when they were preceded by informative cues as compared to neutral cues, and preparatory activity in bilateral parietal cortex was found when subjects prepared to respond to spatial information as compared to semantic information. Individual differences in the magnitude of the informative cueing benefit were positively correlated with activity within distributed regions of frontal and parietal cortex when subjects prepared to respond to the spatial information. By contrast, when preparing to respond to word meaning, no activity was found to reach statistical significance, although regions associated with verbal processing such as inferior frontal gyrus and temporal cortex (Nobre et al., 1994; Thompson-Schill et al., 2005) were related to cueing benefits when the threshold was lowered. Overall, there was little overlap between effects associated with spatial and semantic cueing, supporting the view that conflict resolution is subserved by activity within feature-specific control networks, at least when attending to spatial information.

### 3.1. Preparatory activity in frontal cortex

Previous studies have identified preparatory activity in frontal cortex in response to cues designating a relevant feature or

task-set (Brass and von Cramon, 2002, 2004; Giesbrecht et al., 2003; MacDonald et al., 2000; Sakai and Passingham, 2003; Wager et al., 2005a). Our results extend these findings in many important ways. First, we have identified activity associated with preparatory attention to spatial properties when controlling for the influence of general anticipatory attention. Secondly, we have directly linked neural activity associated with preparatory feature-biasing to behavioral improvement associated with advance cueing. Compared with the neutral cue period, increased activity during the position cue period in a relatively anterior region of right dorsolateral PFC was related to a larger cueing benefit (i.e., decreased RT on position-cued trials). This DLPFC activity may represent a “source” of top-down biasing of spatial representations located in more posterior regions, consistent with reports of right-hemisphere dorsal frontal activity associated with spatial working memory (Goldman-Rakic, 1995; Smith and Jonides, 1999). Although no activity was found to reach statistical significance in response to word cues, we examined preparatory activity on word trials at a lowered threshold in attempts to determine whether any overlap between position and word cue periods would be found. Whereas word cues activated a region of right anterior prefrontal cortex that overlapped with that identified in the position cue period, this activity did not relate to RT benefits associated with informative cueing for either position or word trials. Indeed, in the correlational analyses, this lenient criterion failed to demonstrate similarity between position

and word cue activity, and instead revealed a relationship between the cueing benefit on word trials and preparatory activity in a large region of left inferior frontal gyrus. Although below our primary reporting threshold in this task, it is possible that this effect reflects the generation of top-down signals involved in preparatory biasing of verbal information, consistent with previous studies showing activity in left inferior frontal gyrus involved in the selection of semantic information (Cristescu et al., 2006; Moss et al., 2005; Thompson-Schill et al., 2005, 1997).

Previous studies of preparatory attention to specific colors or spatial locations (Corbetta and Shulman, 2002; Giesbrecht et al., 2003; Hopfinger et al., 2000) or to task-sets of non-conflict stimuli (Brass and von Cramon, 2002, 2004) have generally noted activity in more posterior frontal regions including the inferior frontal junction, human frontal eye fields, and precentral gyrus. The more anterior locus of DLPFC activation we found during preparation to attend to spatial information may be due in part to the complexity of the paradigm employed. Subjects in our study were informed about the relevant feature of upcoming stimuli without knowing which particular location or word meaning would require a response, perhaps engaging more abstract control processes than previous cued attention tasks. Indeed, it has been suggested that the frontal lobes are organized hierarchically, with more anterior regions involved in performing tasks of increasing complexity (Koechlin et al., 2003) or uncertainty (Pollmann, 2004). Arguably, even non-cued Stroop tasks contain a higher degree of complexity than many tasks examining attentional selection of non-conflicting stimuli. Consistent with this, many studies using the classic Stroop task report that incongruent targets elicit activity primarily in DLPFC and anterior PFC regions (e.g., Banich et al., 2000; Carter et al., 1995; Liu et al., 2004; Milham et al., 2001, 2003; Kerns et al., 2004). Further, these results are congruent with our previous findings that preparatory DLPFC activity in task-switching aids subsequent performance, in which participants with greater activity took longer to process a cue to switch, which may represent the time needed to fully complete advance preparation (Wager et al., 2005a).

As mentioned above, a region of right anterior PFC (BA 10) was found to be more active during the position cue period and during the word cue period at a lowered threshold— as compared to the neutral cue period, yet was not related to performance variability in behavioral cueing effects. This area has been shown to be involved in episodic memory retrieval (for review see Rugg and Wilding, 2000). Different rule retrieval demands between informative and neutral cues may be driving this aPFC response. Specifically, informative cues consistently require retrieval of a task rule, resulting in a constant demand on episodic retrieval processes that may operate independently of processes directly associated with between-subject RT variability. In contrast, because no task rule is specified for the neutral cue, subjects may only retrieve rule information after targets are presented and the relevant set is clearly designated. In a similar paradigm using event-related potentials, we identified sustained preparatory activity at right prefrontal electrodes in response cues designating a spatial or verbal task-set (Stern and Mangels, 2006). As with the current fMRI data, results from that study indicated that this

pre-stimulus activity was not feature-specific, although greater activity at these electrodes was related to faster RT on a within-subjects basis. Given the different methodologies employed, it is difficult to know whether these findings represent the same cognitive processes. However, a possible alternative explanation is that right aPFC instantiates control in a domain-general way (Sakai and Passingham, 2003), but was not activated with sufficient between-subject variability to be related to differences in behavioral cueing effects in the current study.

Indeed, it is surprising that we did not find many common frontal regions that related performance to activity in the position and verbal cue periods, as other researchers have provided evidence of a domain-general frontal network for allocating attention (Cristescu et al., 2006; Dosenbach et al., 2006). Although it is presently unclear why there was little overlap between these conditions, it is possible that domain-general control is more likely to be elicited by tasks that do not require resolution of conflicting stimulus or response representations. It is also possible that, in the case of the correlational results, domain-general sources of control set up processing “states” that are less sensitive to individual performance variability. Clearly, further research is needed to characterize the different conditions where domain-general or domain-specific sources of top-down control are preferentially engaged.

### 3.2. Preparatory activity in posterior regions related to behavior

Robust parietal activation was found for the position cue period but not for the word or neutral cue periods, and was positively related to the behavioral cueing effect on position trials. Parietal activity has been widely noted when subjects are cued to attend to a specific location where a target stimulus will arrive (Corbetta and Shulman, 2002; Giesbrecht et al., 2003; Hopfinger et al., 2000). Here we show that preparing to attend to the spatial properties of stimuli (i.e., spatial task-set) involves activation of a similar set of parietal regions as those involved in preparing to attend to a specific location (see also Sakai and Passingham, 2003). Further, to our knowledge this is the first investigation to show a direct relationship between preparation for spatial processing and the ability to respond quickly and accurately to spatial information in the face of conflict with verbal information. It is unclear whether parietal involvement in the current paradigm reflects activation of the source or sites of top-down control, although our results suggest that it does not operate in a domain-general way, but is instead specific to spatial processing. It is of course possible that parietal cortex serves as both a target of control processes originating in prefrontal cortex and as a source of top-down biasing signals to visual cortices (e.g., Kastner and Ungerleider, 2000; Giesbrecht et al., 2006), particularly for spatial information (e.g., Mesulam, 1999).

Unlike position trials, no posterior cortical regions were activated at the current threshold during the word cue period activity, either in group-averaged contrasts or in regression analyses. However, at a lowered threshold, activation of multiple foci in temporal cortex were uniquely associated with a larger behavioral cueing effect on word trials. These

findings are consistent with previous studies identifying a wide variety of temporal areas involved in the conceptual processing of words (Chan et al., 2004; Demonet et al., 1992; Marinkovic, 2004; Nobre et al., 1994; Price, 1998; Scott et al., 2003). We did, however, also find a right posterior temporal region commonly related to cueing benefits on position trials, and on word trials at the lowered threshold. Given previous research showing that this region is involved in processing global features of stimuli (Martinez et al., 1997; Fink et al., 1996), we suggest that this activity is related to attending to or imagining the possible spatial configurations of upcoming targets rather than to the implementation of domain-general preparatory control. It is plausible that global processing would facilitate performance on word trials as well as position trials, given that the spatial location of target words must be detected prior to analysis of semantic content.

### 3.3. Differences between position and word trials in overall amount of activation

Activations found during the word cue period were consistently less powerful than those found during the position cue period. This was unexpected, as responding according to word meaning has been shown to be less “automatic” than responding according to spatial location in the spatial Stroop (Baldo et al., 1998; Lu and Proctor, 1995), and one might expect to find *more* activation when the subject is preparing to engage in the more effortful task (MacDonald et al., 2000). One interpretation is that the relatively complicated nature of our paradigm further increased the difficulty of responding to word meaning, rendering preparatory verbal processing very difficult or even impossible for some subjects. These subjects may have instead waited until target presentation to engage verbal biasing mechanisms, leading to considerable intersubject variability but reduced overall group activation during the word cue period. Such an interpretation is supported by our behavioral data, which indicate that the RT benefit subjects experienced from informative cues was actually smaller for word trials as compared to position trials.

### 3.4. Conclusions

We have demonstrated that preparatory neural activation at multiple cortical regions related to RT benefits in response to conflict stimuli, even when the influence of general anticipatory processes is minimized, supporting the notion that benefits of advance preparation are due in part to task-/feature-specific top-down biasing processes. Although factors potentially independent of preparatory activity can influence response time, such as speed of orienting or response selection occurring after the target has been presented, this study demonstrates that a significant portion of the RT variance found when processing spatial information in the presence of conflict can be attributed to preparatory activation of domain-specific regions.

Although the regions we report in the current study did not pass correction for multiple comparisons across the whole brain, the use of a stringent criterion for cluster extent (20 voxels) allowed us to examine activity at uncorrected significance thresholds while still limiting the possibility of Type I

error, due to the fact that true signal will activate multiple contiguous voxels more frequently than noise (Forman et al., 1995; Xiong et al., 1996). Future work would clearly benefit from increasing sample size as well as trial count in order to enhance the power of resultant activations. Nevertheless, we feel these results emphasize the importance of preparatory neural activity in predicting performance variability among subjects. The fact that many of our results demonstrating feature-specific activations emerged in correlational analyses suggests that subjects varied in their ability to bias information during the preparatory period. As such, this type of inter-subject analysis may be highly valuable for research examining cognitive processes that have varying performance outcomes. Of interest, feature-specific activity was found only in the analysis of positive correlations with behavioral cueing effects, lending further support for the notion that control is implemented by activating task-relevant information rather than suppressing task-irrelevant information (Egner and Hirsch, 2005; for an alternative finding, see Nobre et al., 2006). In addition to investigating variability between subjects, additional studies would benefit from examining variability within subjects on a trial-to-trial basis (see Stern and Mangels, 2006). This complementary approach may provide a particularly sensitive measure of the ways in which preparatory control impacts behavior.

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## 4. Experimental procedures

### 4.1. Subjects

Sixteen right-handed native English speaking volunteers (mean age: 24.3 years, range: 18–32, 7 females) participated in the experiment. All participants had normal or corrected-to-normal vision and were free of neurological or psychiatric illness. MRI safety screening and written informed consent were given according to institutional review board (IRB) guidelines. Data from two subjects were excluded due to excessive head movement during scanning, leaving 14 subjects for all subsequent analyses.

### 4.2. Design and procedure

Subjects responded according to the spatial or semantic properties of the target stimulus, which consisted of a direction word (“up”, “down”, “left”, or “right”) presented in a location relative to center that was different from word meaning (incongruent trials). We used only incongruent trials in order to heighten the need for preparatory control on each trial.

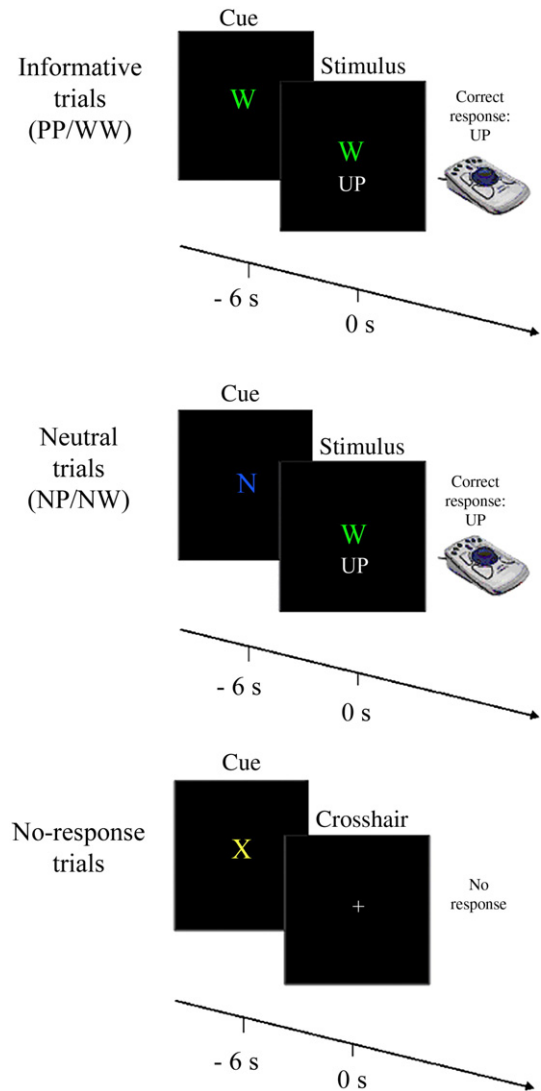
The spatial Stroop holds some advantages over the color-word Stroop when examining the neural basis of top-down biasing. There is considerable evidence that verbal and spatial information is processed in distinct lobes (temporal vs. parietal) and possibly hemispheres (left vs. right) (Heil et al., 1997; Nobre et al., 1994; Stephan et al., 2003; Ungerleider and Haxby, 1994), thus allowing us to more easily distinguish between domain-specific regions functioning as the sites of control. Additionally, in order to avoid movement artifacts

associated with vocal responses, neuroimaging studies using the color–word Stroop often have to train subjects on arbitrary color–finger mappings, thereby increasing the working memory demands of the task. The compatibility between spatial processing and manual responding in the spatial Stroop (Baldo et al., 1998; Lu and Proctor, 1995) avoids the difficulty involved in separating activity related to attentional control from that involved in remembering color–finger mappings.

Stimuli were projected on a screen while subjects were positioned in the fMRI scanner. The distance between central fixation and targets subtended approximately 2° of visual angle in all positions. Each trial began with a 6 s centrally-presented letter cue that was one of three different types: 1) an *informative cue*, designating whether subjects should respond to upcoming incongruent targets based on spatial position or meaning of word (40% of trials), 2) a *neutral cue*, informing subjects that they would need to respond to an upcoming target without providing advance information about how they would have to respond (40% of trials), and 3) a *no-response cue*, informing subjects that they would not receive a target and thus would not need to make a response on the current trial (20% of trials). As our goal was to isolate feature-specific activity from that related to general anticipatory attention, we needed to ensure that neutral cues were successful in eliciting general preparatory processes. Thus, no-response cues were included to highlight the fact that neutral cues should be used to engage general preparatory strategies even if no specific feature processing could be accomplished. However, as it was not our aim to investigate general preparatory attention on its own, contrasts between neutral and no-response cues were not pursued.

Examples of trial types can be seen in Fig. 4. Informative cues were either an orange letter “P” or a green letter “W”, indicating that subjects should respond according to the spatial position or word meaning of the upcoming target word, respectively, and were followed by presentation of the target while the cue remained in the center of the screen (referred to as position-cued and word-cued trials). The neutral cue was a blue letter “N”, which was followed by either a “P” or “W” in the center of the screen when the target word was presented (referred to as neutrally-cued position or neutrally-cued word trials). The no-response cue was a yellow letter “X”, which was followed by a crosshair that remained on-screen for 1 s. Cues were presented in color in order to increase their overall salience and differentiation from each other. Subjects were instructed to respond to the target by moving an MRI-compatible trackball with their right index finger as quickly and as accurately as possible. Reaction time was recorded as the time between target presentation and the onset of trackball movement. All targets remained on-screen until a response was made. The inter-trial interval was varied between 4 and 8 s using an approximately exponential distribution.

Subjects completed 6 runs containing 30 trials each. Each run was 6 min long, and consisted of 8 informative cue trials (4 position-cued and 4 word-cued trials), 8 neutral cue trials (4 neutrally-cued position and 4 were neutrally-cued word trials), and 6 no-response cue trials. Eight partial trials (“catch trials”), in which the informative or neutral cue was followed by a crosshair instead of a target (4 neutrally-cued partial, 2 position-cued partial, 2 word-cued partial), were



**Fig. 4 – Paradigm. Examples of informative, neutral, and no-response trial types. During the experiment, stimuli were presented on a black background with cues in orange (“P”), green (“W”), blue (“N”), or yellow (“X”) font and target words in white font. (To view colored versions of stimuli, the reader is referred to the web version of this article.)**

included in each run in order to model the cue period without influence of target period activity (Ollinger et al., 2001). Two different randomizations were used in which the ordering of trials was pseudo-random and generated by a genetic algorithm (Wager and Nichols, 2003) in order to optimize the detection of differences between conditions. The majority of trials involved a switch of cue (74–77% depending on randomization), further enhancing the need for control implementation on each trial. At the end of each run, subjects received feedback in the form of a tallied score based on accuracy and speed of RT for each trial during the run. Each correct response increased the tally by between 0 and 5 points (with faster RTs yielding higher scores) and each incorrect response reduced the tally by 3 points. Subjects were informed that they would receive extra monetary compensation based

on their final score; however, everyone received the same amount of compensation (the greatest monetary value that could be accumulated) at the end of the experiment.

All subjects completed several practice trials and received verbal instructions prior to being scanned in the fMRI session. Stimuli were created and presented using Presentation software (Neurobehavioral systems, Inc., Albany, CA). In the scanner, stimuli were projected onto a screen that could be viewed through a mirror attached to the head-coil.

#### 4.3. FMRI data acquisition

Images were acquired with a GE Signa 1.5-T scanner. Functional data were acquired parallel to the AC–PC line with a T2\*-weighted EPI sequence of 24 contiguous axial slices (TR=2000, TE=40, flip angle=60, foV=190\*190, array size 64\*64) of 4.5-mm thickness and 3×3 mm in-plane resolution, providing whole-brain coverage. Each run acquired 193 whole brain volumes, the first 5 of which were discarded in order to allow the scanner to stabilize. Structural images were acquired with a T1-weighted SPGR sequence (TR=19, TE=5, flip angle=20, FoV=220) recording 124 slices at thickness of 1.5 mm and in-plane resolution of 0.86×0.86 mm.

#### 4.4. FMRI data analysis

SPM2 software (Wellcome Department of Cognitive Neurology, University College London, UK) was used for data preprocessing. Functional T2\* images were first corrected for differences in slice-timing and then spatially realigned to the first volume scanned in the first run for each subject. The structural T1 image was co-registered to a mean image of the realigned functional scans. Each subject's T1 image was warped to the Montreal Neurological Institute (MNI) template T1 brain, and parameters from this normalization were applied to functional images. Functional images were spatially smoothed using a Gaussian kernel of 8 mm<sup>3</sup> full-width at half maximum (voxel size after preprocessing was 2×2×2 mm).

Functional data were analyzed by deconvolving the hemodynamic response function (HRF) from each voxel in the times series using iteratively reweighted least squares (IRLS) procedure with a finite impulse response (FIR) model estimating the BOLD response for events of interest (position cue, word cue, neutral cue, and no-response cue for preparatory period; 4 regressors for target period activity and 1 regressor for error trials). The IRLS is contained in the Matlab R2006a function `robustfit.m`, and was tested and validated using simulations and on neuroimaging data (Wager et al., 2005b). The Robust Regression Toolbox (written by TDW), freely available at <http://www.columbia.edu/cu/psychology/tor/>, contains the code used to run the analyses described in this paper. Such a method is particularly useful when examining potentially sustained cue period activity because it does not assume that the HRF for all conditions conforms to the shape of the canonical HRF. In particular, it has been suggested that the response in anterior prefrontal cortex may be delayed relative to that in more posterior regions (Buckner et al., 1996; Schacter et al., 1997). The activation measure of interest was the maximum deviation of the fitted FIR response within 20 s from the start of the event. Position, word, and neutral cues

followed unexpectedly by crosshairs (catch trials) were included in all analyses in order to model cue period activity without contamination of target-related activity (Ollinger et al., 2001). A 128-s temporal highpass filter was applied to the data to exclude low-frequency artifacts such as scanner drift. Time-series autocorrelation was not modeled. In order to minimize the influence of outliers, data at each voxel was winsorized at 3 standard deviations. Further, robust regression procedures minimize the impact of local mis-alignment of one or a few participants' brains and other artifacts that result in outliers.

The primary contrasts of interest were informative position cues minus neutral cues (P–N), informative word cues minus neutral cues (W–N), and the direct contrast between informative position and informative word cues (P–W, W–P). Trials in which subjects made an incorrect response were counted as errors and were not included in the contrasts. For each contrast, a voxel-wise contrast map of differences in activation was calculated for each subject and entered into random-effects analyses at the group level. The analysis was restricted to a mask that included gray matter in the normalized template and white matter within an approximately 10 mm border. In order to correct for the increase in Type I error associated with comparing all voxels in the brain, a combined voxel intensity and extent threshold was applied such that only activations containing 20 contiguous voxels surpassing a threshold of  $p < .001$  were examined. This method is less susceptible to Type II error than Bonferroni correction, and is based upon the observation that true signal will activate multiple contiguous voxels more frequently than noise (Forman et al., 1995; Xiong et al., 1996). Whole-brain rather than region-of-interest (ROI) analyses were chosen based on previous results implicating a wide variety of frontal, parietal, and temporal regions in attentional control (Corbetta and Shulman, 2002; Coull, 1998; Wager et al., 2004).

In addition to identifying regions activated in the group-averaged contrasts, correlations between preparatory neural activity and performance benefits associated with receiving an informative versus neutral cue were examined separately for position and word trials. For each subject, RTs for position-cued targets (PP) were subtracted from neutrally-cued position targets (NP), and RTs for word-cued targets (WW) were subtracted from neutrally-cued word targets (NW), with larger values corresponding to a greater benefit from receiving the feature-specific cue (*behavioral cueing effect*). Each behavioral cueing effect (position or word) was entered into a multiple regression analyses with its respective cue period contrast (P–N or W–N). Those regions where increased activity in the cue period contrast predicted a greater behavioral cueing effect (across subjects) yielded positive correlations, while those regions where increased activity in the cue period contrast predicted a smaller behavioral cueing effect yielded negative correlations.

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#### Acknowledgments

This research was supported by NIH grant R21 066129 awarded to J.A. Mangels and the Columbia University Provosts Academic Quality Fund. We would like to thank Matthew Greene

and Heather Dey for their help with programming and data analysis.

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