INVESTIGATING THE SUB-REGIONAL ORGANIZATION OF PREFRONTAL CORTEX

A Thesis
Presented to
The Academic Faculty

by

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In Partial Fulfillment
of the Requirements for the Degree
Doctorate of Philosophy in the
School of Psychology

Georgia Institute of Technology
December 2016

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INVESTIGATING THE SUB-REGIONAL ORGANIZATION OF PREFRONTAL CORTEX

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This dissertation is dedicated to:

My fiancé, Craig Campbell,
who, despite enduring five years of 2,500 miles of separation between us,
has still managed to be my biggest anchor and closest support;

My father, Bob Cookson,
who, despite facing challenges in his own PhD program,
has consistently been my biggest cheerleader and inspiration;

My mother, Melody Cookson,
who, despite her jokes that I am the “smart” one,
is probably the smartest of all of us, and will always be my Lorelai;

My brother, Bobby Cookson,
who, despite running away to the circus,
has served as my reminder that we are always close to home if we need it;

Bodhi Verhaeghen,
who, despite being only eight years old,
has made these five years some of the most meaningful and memorable of my life;

And to Dr. Lawrence R. James,
mentor and friend.
ACKNOWLEDGEMENTS

Over the past five years, I have received support and encouragement from many people. Dr. Eric Schumacher has been a fantastic advisor who mentored me and supported my growth as a researcher while respecting me as a peer. His advisement has made me a better writer, investigator, and mentor, which I will carry with me into my future endeavors.

My dissertation committee of Drs. David Badre, Dobromir Rahnev, Paul Verhaeghen, and Mark Wheeler has provided great support over the past two years. Each of my committee members provided invaluable counsel and suggestions that improved my ideas, my methodology, my analysis, and my interpretation of these data.

My lab members have also been a great support during this process. Zoey Morton did the lion’s share of data collection, and stepped up to the task as a new undergraduate in the lab with admirable dedication. Matthew Bezdek, Christine Godwin, and Derek Smith provided useful insights on my progress both in lab meetings and passing counsel.

I would also like to thank my department. Special thanks go to Dr. Paul Verhaeghen, who, in addition to serving on my committee, has also helped me through the administrative side of my PhD as the School of Psychology Graduate Coordinator. Jan Westbrook has also been singularly helpful, providing me with the resources and information I needed to complete the PhD process throughout my time in the department.

Many thanks to Jared Batterman, David Martinez, and John Price, who have been my closest friends in the department. They were there when I first developed my dissertation topic, and always gave me a sounding board for my ideas and good company to go with it. Also thanks to Ty Autry, Alex Burkle, and Mike Glatzer, who helped me stay grounded outside of graduate school.

Finally, I would like to thank all of my friends and family for their unwavering support and encouragement, and Taco Mac for giving all of us the food we want, the beer we need, and the queso we deserve.
3.2.3 Discussion .................................................. 51

IV FMRI EXPERIMENT ......................................... 53

4.1 Specific Methods ............................................. 53
4.1.1 Participants .............................................. 53
4.1.2 Fixation Screen and Stimulus Ranges .................. 53
4.1.3 Experimental Timings and Sessions .................... 53
4.1.4 fMRI Design .............................................. 55
4.1.5 Behavioral Analysis ..................................... 55
4.1.6 fMRI Processing and Analysis ......................... 55

4.2 Results ....................................................... 56
4.2.1 Behavioral Results ..................................... 56

4.3 Imaging Results ............................................. 67
4.3.1 Visualization of Whole Brain Main Effects .......... 67
4.3.2 ROI Analysis ............................................ 71

V DISCUSSION .................................................. 90

5.1 Behavioral Validity ........................................ 90
5.2 The Rostrocaudal Axis ..................................... 91
5.3 The Dorsoventral Axis ..................................... 93
5.4 Hemispheric Lateralization ............................... 95
5.5 Methodology ................................................ 97

VI CONCLUSIONS ............................................... 101

APPENDIX A — POST-EXPERIMENT QUESTIONNAIRE .... 103

APPENDIX B — EYE MOVEMENTS IN PILOT PHASE 1 .... 104

APPENDIX C — OVERLAP BETWEEN CURRENT RESULTS AND PRIOR LITERATURE ROIS ......................... 105

APPENDIX D — ACTIVITY MAP OF CUE VERSUS BASELINE CONTRAST .................................................. 106

REFERENCES ..................................................... 107
## LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pilot Phase 1 Dimension Bounds</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>Pilot Phase 2 Dimension Bounds</td>
<td>43</td>
</tr>
<tr>
<td>3</td>
<td>Final Stimulus Dimension Bounds</td>
<td>54</td>
</tr>
<tr>
<td>4</td>
<td>ROI Coordinates by Factor</td>
<td>57</td>
</tr>
<tr>
<td>5</td>
<td>Pairwise Comparisons of Main Effect of cuetype on Accuracy</td>
<td>60</td>
</tr>
<tr>
<td>6</td>
<td>Pairwise Comparisons of Main Effect of Dimension on Accuracy</td>
<td>60</td>
</tr>
<tr>
<td>7</td>
<td>Pairwise Comparisons of Main Effect of Epoch on Accuracy</td>
<td>61</td>
</tr>
<tr>
<td>8</td>
<td>Pairwise Comparisons of Main Effect of cuetype on RT.</td>
<td>64</td>
</tr>
<tr>
<td>9</td>
<td>Pairwise Comparisons of Main Effect of Dimension on RT.</td>
<td>64</td>
</tr>
<tr>
<td>10</td>
<td>Pairwise Comparisons of Main Effect of Epoch on RT.</td>
<td>65</td>
</tr>
</tbody>
</table>
LIST OF FIGURES

1  Breakdown of judgment types ........................................ 4
2  Example of set reduction by information contained in cue ........ 6
3  Representation of possible cues ..................................... 24
4  Trial structure ....................................................... 30
5  Accuracy by cuetype for pilot phase 1 ............................. 33
6  Accuracy by Epoch for pilot phase 1 ................................ 34
7  Accuracy by Dimension for pilot phase 1 ............................ 34
8  RT by cuetype for pilot phase 1 .................................... 35
9  RT by Epoch for pilot phase 1 ..................................... 36
10 RT by Dimension for pilot phase 1 .................................. 36
11 RT for Cuetype by Dimension Interaction for pilot phase 1 ....... 37
12 Representation of Fixation Screen ................................... 42
13 Accuracy by cuetype for pilot phase 2 .............................. 44
14 Accuracy by Epoch for pilot phase 2 ................................ 45
15 Accuracy by Dimension for pilot phase 2 ............................ 45
16 Cuetype by Dimension Interaction for Accuracy for pilot phase 2 46
17 Congruency by Dimension Interaction for Accuracy for pilot phase 2 47
18 RT by cuetype for pilot phase 2 .................................... 47
19 RT by Dimension for pilot phase 2 .................................. 48
20 RT by Epoch for pilot phase 2 ..................................... 48
21 Cuetype by Dimension Interaction for RT for pilot phase 2 ....... 49
22 Congruency by Dimension Interaction for RT for pilot phase 2 .... 50
23 Representation of Final Stimulus Bounds ............................. 54
24 Representation of ROI Distribution ................................... 57
25 Accuracy by cuetype ................................................. 58
26 Accuracy by Dimension .............................................. 59
27 Accuracy by Epoch .................................................. 59
28 Interaction of Dimension and Congruency on Accuracy ............ 62
29 RT by cuetype ......................................................... 62

viii
<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>RT by Dimension</td>
</tr>
<tr>
<td>31</td>
<td>RT by Epoch</td>
</tr>
<tr>
<td>32</td>
<td>Interaction of cuetype and Dimension on RT</td>
</tr>
<tr>
<td>33</td>
<td>Interaction of cuetype and Congruency on RT</td>
</tr>
<tr>
<td>34</td>
<td>Interaction of Dimension and Congruency on RT</td>
</tr>
<tr>
<td>35</td>
<td>Visual of the Main Effect of Cue at the Cue Timepoint</td>
</tr>
<tr>
<td>36</td>
<td>Visual of the Main Effect of Cue at the Stimulus Timepoint</td>
</tr>
<tr>
<td>37</td>
<td>Visual of the Uncorrected Effect of Cue at the Cue Timepoint</td>
</tr>
<tr>
<td>38</td>
<td>Visual of the Main Effect of Response Hand at the Cue Timepoint</td>
</tr>
<tr>
<td>39</td>
<td>Visual of the Main Effect of Response Hand at the Stimulus Timepoint</td>
</tr>
<tr>
<td>40</td>
<td>Visual of the Main Effect of Judgment Type at the Cue Timepoint</td>
</tr>
<tr>
<td>41</td>
<td>Visual of the Main Effect of Judgment Type at the Stimulus Timepoint</td>
</tr>
<tr>
<td>42</td>
<td>ROI Main Effect of Cuetype at the Cue Timepoint</td>
</tr>
<tr>
<td>43</td>
<td>ROI Main Effect of Rostrocaudal Location at the Cue Timepoint</td>
</tr>
<tr>
<td>44</td>
<td>ROI Main Effect of Hemisphere at the Cue Timepoint</td>
</tr>
<tr>
<td>45</td>
<td>ROI Cuetype x Rostrocaudal Location Interaction at the Cue Timepoint</td>
</tr>
<tr>
<td>46</td>
<td>ROI Cuetype x Hemisphere Interaction at the Cue Timepoint</td>
</tr>
<tr>
<td>47</td>
<td>ROI Response Hand x Hemisphere Interaction at the Cue Timepoint</td>
</tr>
<tr>
<td>48</td>
<td>ROI Rostrocaudal Location x Dorsoventral Location Interaction at the Cue Timepoint, Reduced Model</td>
</tr>
<tr>
<td>49</td>
<td>ROI Main Effect of Cuetype at the Stimulus Timepoint</td>
</tr>
<tr>
<td>50</td>
<td>ROI Main Effect of Judgment Type at the Stimulus Timepoint</td>
</tr>
<tr>
<td>51</td>
<td>ROI Main Effect of Rostrocaudal Location at the Stimulus Timepoint</td>
</tr>
<tr>
<td>52</td>
<td>ROI Main Effect of Dorsoventral Location at the Stimulus Timepoint</td>
</tr>
<tr>
<td>53</td>
<td>ROI Main Effect of Hemisphere at the Stimulus Timepoint</td>
</tr>
<tr>
<td>54</td>
<td>ROI Cuetype x Rostrocaudal Location Interaction at the Stimulus Timepoint</td>
</tr>
<tr>
<td>55</td>
<td>ROI Response Hand x Hemisphere Interaction at the Stimulus Timepoint</td>
</tr>
<tr>
<td>56</td>
<td>ROI Response Hand x Hemisphere x Dorsoventral Location Interaction at the Stimulus Timepoint</td>
</tr>
<tr>
<td>57</td>
<td>ROI Cuetype x Dorsoventral Location Interaction at the Stimulus Timepoint, Reduced Model</td>
</tr>
</tbody>
</table>
SUMMARY

The prefrontal cortex (PFC) is involved in many cognitive processes important for complex, flexible human behavior (e.g., Duncan & Owen, 2000). Recent research has posited at least two axes of functional organization in PFC: a rostrocaudal axis, along which the PFC processes tasks of varying abstractness or complexity (e.g., Badre 2008); and a dorsoventral axis, along which the PFC handles various modes of task-related information (e.g., Goldman-Rakic, 1995; O’Reilly, 2010; Petrides, 1995). However, it remains unclear how these two axes may interact with one another, as well as with other known organizational principles in PFC (viz., lateralization of motor control). The present experiment aimed to address these questions using a novel “hierarchical precuing” task that combined a traditional cuing procedure with a hierarchical mapping structure in an event-related functional magnetic resonance imaging (fMRI) design. Participants made one of four possible judgments about pairs of stimuli based on simple characteristics shared by the pair. Two judgments related to spatial features of the stimuli (viz., left/right or above/below fixation), and two to nonspatial features (viz., color or shape of stimulus). One spatial judgment and one nonspatial judgment are mapped to each hand. Cues presented at the start of each trial allowed participants to prepare response sets based on whether they received information about the upcoming judgment type, response hand, both, or neither. The cues produced a stair-step effect on reaction time as a function of the amount of information presented a priori; that is, as the amount of information contained in the cue increased, reaction time decreased, regardless of the exact information contained in the cue. The fMRI data demonstrated segregation of activity in PFC at the cue time point for the main effects of each factor: a rostrocaudal distribution as a function of cue content; a dorsoventral distribution according to judgment domain; and lateralization of activity as a function of response hand. We then investigated how different combinations of cue content, processing domain, and response hand interact to influence the distribution of activity within these regions of interest.
(ROIs). These results demonstrate how the functional structure of the PFC integrates these different axes across the cortex and validate the hierarchical precuing task as a procedure for integrating multiple cognitive factors into a single event-related task design.
CHAPTER I

BACKGROUND

The prefrontal cortex (PFC) is involved in many types of cognitive processes (e.g., working memory, goal maintenance, action sequencing and planning, language, rule maintenance, and task setting and switching) important for complex flexible human behavior (Damasio, 1995; Dubois et al., 1995; Duncan & Owen, 2000; Miller, 2000; Shimamura, 1995). This wide variety of functions does not immediately suggest a common set of simple underlying neural mechanisms. Yet, the organization of PFC representations is not random: different regions of the PFC appear to have specialized functions (Goldman-Rakic, 1984; Levy & Goldman-Rakic, 2000). Ventrolateral (VL) PFC, for example, has been associated with memory retrieval (Badre & Wagner, 2007); dorsolateral (DL) PFC with response selection and task set instantiation (Sakai et al., 2000; Schumacher & D’Esposito, 2002); and anterior (A) PFC/frontopolar cortex (FPC) with goal states and valuation (Stalnaker, Cooch, & Schoenbaum, 2015). However, there is significant disagreement on the scale, boundaries, and dimensions of these functional divisions. A number of attempts have been made to integrate the various theories of PFC segregation to account for the various findings in the literature.

Miller and Cohen (2001) describe a theory of PFC function in which activity in the PFC represents goal states; these goal states then serve to provide top-down biasing of other regions of the brain (e.g., sensory cortex, motor cortex, the medial temporal lobe, and subcortical structures) necessary to accomplish the goal. In this model, the PFC is more or less completely domain general. That is, Miller and Cohen do not describe major subdivisions of the PFC, nor do they describe how sub-functions of this goal state representation and top-down influence might be apportioned across the cortex. Fuster (2001) describes a similar generalized PFC theory; however, here the PFC serves to organize behavior over time, which is accomplished by the subfunctions of attention, working memory,
and preparatory set. While Fuster describes these separable sub-functions as each being supported by the PFC, he claims that each is distributed across the cortex, rather than each being localized to a single subregion. Duncan’s (2010) proposed multiple-demand (MD) system echoes this sentiment of distributed function. This theory posits a network of brain regions that together create the mental programs that coordinate the processing and execution of complex tasks with highly variable demands. While these demands may recruit different regions and networks outside of this system during execution of the task, the MD system processes the hierarchy of demands and contingencies at an amodal level, providing a highly flexible organizational system across tasks.

On the other hand, some researchers suggest that the PFC is segregated on the basis of the domain of the information being processed for a given task. Levy and Goldman-Rakic (2000) theorize that DLPFC is involved in spatial processing, while VLPFC is involved in nonspatial processing (dorsomedial PFC is not posited to show a differentiation between domains), which they first demonstrated using a delayed-match-to-sample task. Schumacher, Elston, and D’Esposito (2003) also report evidence for a spatial/nonspatial distinction, this time in a response selection task, but not along the dorsal-ventral direction; instead, they show differences in hemispheric involvement by processing domain. Postle, D’Esposito, and Corkin (2005) posit that the dorsal-ventral distinction is instead between verbal (ventral) and nonverbal (dorsal) processing domains, which they demonstrate using variations on the n-back task. They suggest that the spatial/nonspatial distinction above instantiates due to the higher verbalizability of nonspatial information compared to spatial information, and is in fact parsimonious with their account. Braver and colleagues (2001) describe a different distinction in which DLPFC (as well as frontopolar cortex, FPC) is active in the active maintenance and manipulation ascribed to working memory function, while VLPFC is sensitive to stimulus types in both working and long-term memory processes. Thus, they theorize that PFC is segregated by task versus material selectivity, rather than task domain.

Each of these theories focus on a small subset of processes thought to be handled by the PFC. Miller and Cohen (2001), for example, base their theory on evidence from the cognitive control literature; Fuster (2001) from the perspective of temporal processing;
Levy and Goldman-Rakic (2000), Postle, D’Esposito, and Corkin (2003) and Braver and colleagues (2001) from perspectives of working and long-term memory, and Schumacher, Elston, and D’Esposito (2003) from the response selection literature. Interpretations of the tasks used to support these theories in turn typically draw from the literature from which the tasks derive. For example, an investigation of the segregation of PFC processes in cognitive control may interpret findings based on task representation, preparation, conflict resolution, switching, and levels of task complexity (Cooper & Shallice, 2006; Badre, 2008; Sakai, 2008; de Jong, 1995; Kiesel et al, 2010; Matsumoto & Tanaka, 2004); working and long-term memory interpretations distinguish encoding, maintenance, manipulation, and retrieval, as well as concepts of recollection and familiarity (Jonides et al, 2008; Levy & Goldman-Rakic, 2000; Gabrieli, 1998; Braver et al, 2001; Cabeza, Dolcos, Graham, & Nyberg, 2002; Ranganath, Johnson, & D’Esposito, 2003); response selection tasks may instead highlight stimulus-response associations and compatibility (Kornblum, Hasbroucq, & Osman, 1990; Schumacher & D’Esposito, 2002; Schumacher, Elston, & D’Esposito, 2003). These various distinctions have had their fair share of overlap (Schumacher, Cole, & D’Esposito, 2007; Dosenbach et al, 2008; Duncan & Owen, 2000; Kane & Engle, 2002, 2003); however, there is still not a clear picture of how they are organized in the PFC, and what shared processes might underlie them.

The present experiment aims to address this issue by developing a new task that allows for the orthogonal manipulation of information domain and task representation, both of which have been posited as bases for PFC functional distinctions (O’Reilly, 2010). This task, which we call the “hierarchical precuing” procedure, explicitly investigates the interaction between two established axes of organizational structure (i.e., the rostrocaudal and dorsoventral axes), as well as how this interaction is influenced by preparatory motor processes. Participants make judgments on pairs of stimuli based on a shared feature dimension. These dimensions can relate to object/feature judgments or spatial/location judgments, following the spatial/nonspatial distinction of Levy and Goldman-Rakic (2000). There are two possible object/feature judgments (color and convexity) and two possible spatial/location judgments (vertical hemifield location and distance from vertical midline),
Figure 1: Breakdown of judgment types. In the current experiment, participants made judgments of pairs of stimuli according to the dimension along which they shared the same value according to a forced choice decision. These dimensions fell into one of two types: spatial and object/feature judgments.

As outlined in Figure 1. One of each judgment pair is mapped to the left and right hands. Each judgment type requires a forced choice response between two options, which are indicated by an index or middle finger button press on the appropriately mapped response hand. On each trial, participants can be cued on whether the upcoming judgment will be based on a spatial- or object identity-related dimension; whether they will make a response with the left or right hand; both of these; or neither.

As an example of how these factors interact, consider the following example, illustrated in Figure 2. A participant may have color and vertical hemifield judgments mapped to the left hand and convexity and vertical midline distance judgments mapped to the right hand. Cuing for the judgment dimension (spatial/location or object/feature) reduces the
possible decision set by half, but does not reduce the response set to a single hand; cuing for hand (left or right) reduces the response set and simultaneously reduces the decisional set by half; cuing both reduces the decision to a two-choice task where the response hand is known; and cuing neither provides an unprepared condition. The cues, then, should allow for some level of response preparation based on the amount of information provided at the cue. If the PFC is organized according to task set complexity, the information provided by the cues should engage different subdivisions of preparatory processes that are distributed along the rostrocaudal axis (viz., Badre, 2008). If PFC organization is further segregated by processing domain (in this design, spatial versus nonspatial information, viz. Levy & Goldman-Rakic, 2000), the judgment dimension should allow for the distinguishing between dorsal (spatial) and ventral streams (nonspatial) as a function of the judgment type for a given trial. The response hand manipulation should further allow for the investigation of lateralized preparatory processes specifically, lateralization of motor response preparation - and their interaction with the other factors above.

1.1 The Rostrocaudal Hierarchy: A Novel Task

A number of researchers have proposed the existence of a hierarchy in the PFC in which more caudal regions handle more "low-level" control (e.g., linking stimuli and responses), while more rostral areas handle more abstract aspects of a task (e.g., maintaining relationships among stimuli, adjusting performance due to context, etc.). Generally, divisions along this rostrocaudal axis have been found in manipulations of the complexity of a task (Koechlin, Ody, & Kouneiher, 2003; Badre & D'Esposito, 2007; Koechlin & Summerfield, 2007; Badre, 2008; Bahlmann, Aarts, D’Esposito, 2015; Bahlmann, Blumenfield, & D’Esposito, 2015; Nee, Jahn, & Brown, 2014; Nee & D’Esposito, 2016); for example, a task that cues participants to determine the color of a stimulus with one cue and the shape of the same stimulus with another cue requires participants to first determine the stimulus dimension they will use to make their discrimination (processed by rostral PFC) before executing the discrimination task proper (processed by caudal PFC).

However, the exact dimension along which a task is abstracted along the rostrocaudal
Figure 2: Example of set reduction by information contained in cue. (A) Visualization of example mapping. In the example, Color and vertical hemifield judgments are mapped to the left hand (shown anatomically), and convexity and midline distance judgments to the right. (B) Highlighting of cued sets by cuetype. In the neutral condition, all possible sets are indicated. For the single-level cues, two subsets of the overall task are indicated; the cuetype determines if this set reduction limits the response to one hand. Finally, the two-level cue reduces the set to a single, identifiable judgment dimension on one hand.
axis has been debated. Badre and D’Esposito (2007) propose that the rostrocaudal hierarchy is built on the demand for control that a task places on the PFC, driven by the increasingly abstracted relations that must be represented in order to execute the task. In this model, the most caudal regions of PFC represent direct stimulus-response mappings. Complexity, or abstractness, is added as relationships are drawn between these mappings and other features of a task, such as a cue that indicates one of two subsets of mappings to be executed.

To demonstrate this, the authors (Badre & D’Esposito, 2007) devised a task in which task decisions have to take place at varying levels of abstraction, which they term the “relational complexity” task. At the lowest level, participants select responses to presented stimuli (colored squares) based on a learned mapping. This level of control is termed “response control.” The next abstraction level uses cue-dependent responses, in which participants have to respond to one of a number of potential target features based on the cue presented (e.g., responding to the color of a target when the cue color is red or orientation when the cue color is blue). This level is termed “feature control.” At the next level, participants make decisions on relationships between the features of two stimuli (i.e., matching/nonmatching) rather than decisions on the features themselves; for example, participants might decide if the colors of two stimuli are the same when the cue color is red, and if they are at the same orientation angle when the cue color is blue. This level is termed “dimensional control.” Finally, “contextual control” involves the switching between different dimensions at varying frequencies according to the temporal context of the experiment (i.e., the current task block). At each level of abstraction, then, the design adds another layer of contingencies that had to be resolved in order to correctly execute the task. Functional magnetic resonance imaging (fMRI) recordings taken during the execution of this task demonstrated increasingly rostral activation with increased abstraction of the task decisions required. Badre and D’Esposito (2007) argued that this result suggest a demand-based recruitment of PFC; that is, that more rostral PFC is recruited because the task requires resolution of conflict at an abstract level before decisions at the lower levels can be made.

Another theory of the rostrocaudal hierarchy, control-signal theory, is that abstraction takes place temporally and is driven by a top down control signal, rather than bottom-up
task-based demand (reviewed by Koechlin & Summerfield, 2007). Control signal theory derives from information theory, which aims to quantify the information present in a signal. In control signal theory, activity at each of the levels of the rostrocaudal hierarchy are posited to represent some amount of information that is shared between that level and more caudal levels and some additional information that is unique to that level. Whether increasingly abstracted levels of the hierarchical system are engaged during a task depends on the information overlap between the levels. At the most caudal levels of PFC, activation represents “sensory control”, or the direct mapping of stimulus to response (similar to Badre & D’Esposito, 2007). More rostrally, the VLPFC represents “contextual control.” Here, more rostral regions provide contextual information that allows for the selection of a stimulus-response set, which is then used by more caudal regions to select a response. The next level of control, termed “episodic control,” allows for the restructuring of an existing stimulus-response set to code new mappings based on changing instructions (i.e., learning). Finally, at the most rostral areas of the PFC, the control signal theory posits “branching control” over the rest of the system. This level of control allows for the temporary suspension of one representation of context, episode, and/or task set in favor of another that is relevant to the current situation. This control level is the most temporally abstracted because it allows multiple sets to be held in mind over the course of multiple tasks and/or episodes.

To demonstrate this, Koechlin and colleagues (2003) used a set of color and letter tasks that varied in their level of temporal abstraction, similar to the structure of Badre and D’Esposito’s (2007) relational complexity task. In a first experiment, they tested three different levels of temporal abstraction by manipulating difficulty within a given level of control. Sensory control is manipulated by varying the number of possible responses in a block. Contextual control added a cue that determined which judgment participants would make on the letter stimulus to determine their response (vowel/consonant or upper/lowercase). Finally, episodic control is manipulated by varying the relationship between the cues and stimulus-response mapping between blocks. Branching control is investigated in a separate experiment (Koechlin et al, 2000) where participants are required to temporarily suspend an ongoing task to prioritize a second task, in effect maintaining the context of the first
task over a delay period for reinstatement after completion of the intervening task. Taken together, the results of these two experiments show increasingly rostral activity for more abstract actions, similar to the results of Badre and D’Esposito (2007).

Thus, these two theories (Badre, 2008; Koechlin & Summerfield, 2007) describe a PFC organization that follows a rostrocaudal hierarchy (see also, Christoff & Gabrieli, 2000); however, Control Demand theory predicts that this hierarchy processes different levels of relational complexity, while Control Signal theory posits that it mediates the integration of different temporal contexts. It is not clear which of these theories, if either, in fact describes the true underlying organizational structure of the rostrocaudal axis of the PFC, and the similarities between the tasks used to support each theory make distinguishing their predictions difficult. Nevertheless, the evidence supporting both of these theories show very similar patterns, and both theories are consistent in highlighting a hierarchical organization of the PFC along the rostrocaudal axis that operates at different levels of task representations.

The current experiment aims to use a precuing design to engage these different levels of representation in a new task. When participants are given a cue, they are able to prepare some subset of the task space before the stimulus itself is presented. The level of the task abstraction for that prepared set changes with the number of pieces of information that have been provided. At one extreme, being provided a cue for neither the judgment type nor the response hand leaves the participant with the entire task space to prepare (if, in fact, they prepare the task to this noninformative cue). At the other extreme, being provided a cue for both pieces of information allows participants to reduce the task to a forced-choice decision reminiscent of the “response control” levels described in Control Demand theory (Badre, 2008; also “sensory control” in Control Signal theory, Koechlin & Summerfield, 2007). On the other hand, if participants are given only one piece of information or the other, then their decision requires making a judgment of which dimension is shared by both presented stimuli, which fits “dimensional control” from Control Demand theory, before they can resolve the less complex forced-choice decision.

A complete understanding of PFC function also requires that we understand how PFC
interacts with other cortical and subcortical brain regions. The PFC is known to have extensive, systematically organized, and reciprocal connections with the basal ganglia (BG), referred to as corticostriatal loops (Alexander, DeLong, & Strick, 1986; Jeon, Anwander, & Friederici, 2014). These loops are thought to subserve learning and feedback mechanisms in motor programming (Lopez-Paniagua & Seger, 2011) that allow for the integration of information across different timescales. Chatham and Badre (2015) describe a possible mechanism for this interaction in which the corticostriatal loops act as a multi-level gating system for the influx and efflux of information in working memory. More specifically, they hypothesize that the BG provide two types of gates: input gating allows information into working memory when the current context suggests that that information may be useful for processing; output gating limits the output of processed information from working memory for subsequent action selection. These gating mechanisms have been shown to interact with the rostrocaudal hierarchy (Frank & Badre, 2011; Badre & Frank, 2012). To demonstrate, the authors describe a Bayesian model of a hierarchical cognitive control process characterized by a series of nested corticostriatal loops. They then verify this model using fMRI data recorded while participants performed a two-set reinforcement learning task on conjunctions of stimuli mapped to different responses. One of the sets of stimuli, referred to here as the “rule-based” block, follows an abstract rule that can be applied to the stimuli; the other, called the “flat” block, does not follow such a structure. In the flat block, but not the rule-based block, activity in dorsal premotor cortex declined over the course of learning, consistent with predictions of the model for tasks governed by less and more abstract rules, respectively. Thus, connections between the PFC and striatum are involved in the learning of rules governing task execution and operate simultaneously at different levels in the task representation hierarchy. Given the interaction between PFC and BG functions, these and other cortical-subcortical networks may account for some of the variation in results and interpretations of investigations of the rostrocaudal hierarchy.

The cues in the current experiment explicitly provide task context prior to the presentation of the stimulus. Participants are instructed to use the information in the cue to perform the task, and thus it is likely that participants in this experiment will use input
gating mechanisms to update working memory with the relevant task dimensions on each trial. Thus, in addition to the expected manipulation of task complexity described above, this new procedure provides three key features that make it unique in the literature: 1) a single task that is executed across the duration of the experiment, rather than episodic blocks of different conditions encountered only once during the experiment; 2) an event-related design that allows for the investigation of activity by trial, rather than by block; and 3) the ability to separate activity related to the cue and the stimulus timepoints within the trial, allowing for the investigation of the activity unique to preparatory processes occurring at the first stage of the input gating process specifically.

Because of these features, we can investigate the patterns of activity at the cue and stimulus presentations separately as a function of what cue the participant is given. The predictions for this timepoint are unclear, as previous research has collapsed across the duration of the trial for analysis (Koechlin, Ody, & Kouneiher, 2003; Badre & D’Esposito, 2007; Koechlin & Summerfield, 2007; Badre, 2008; Bahlimann, Aarts, D’Esposito, 2015; Bahlimann, Blumenfield, & D’Esposito, 2015; Nee & D’Esposito, 2016). However, a few hypotheses may be made from the theories described above. Where our cue timepoint predictions above draw from control demand theory (Badre, 2008), it is possible that control signal theory (Koechlin & Summerfield, 2007) may lead us to predictions for the stimulus timepoint via the resolution of uncertainty. At the stimulus, the amount of information provided is inverted from that at the cue time point of the same trial; that is, trials in which participants see a neutral cue, which affords no uncertainty resolution at the cue timepoint, allow for the resolution of all uncertainty at the stimulus, which should lead to the most rostral activity at the stimulus timepoint. Likewise, trials in which participants see both dimensions cued will have little remaining uncertainty to resolve at the stimulus, but the forced choice remaining to be specified for the cues specifying both response hand and judgment domain will result in significant caudal activity. On the other hand, the distribution of processes along the rostrocaudal axis may in fact reflect the recruitment of gating mechanisms (Frank & Badre, 2011; Badre & Frank, 2012); in this case, as the current design predicts an input gating strategy such that gating effects take place at the cue, the
activity at the stimulus may not engage the rostrocaudal axis at all, instead reflecting a different pattern of organization that supports task execution rather than task preparation.

1.2 The Dorsoventral Axis: Interacting Theories

The rostrocaudal hierarchy is not the only axis-based theory of PFC organization; there is also evidence for functional segregation in the dorsoventral direction. The dorsal and ventral distinctions are drawn from the equivalently named dorsal and ventral streams originally identified in the visual system (Mishkin & Ungerleider, 1982; Goodale, Milner, Jakobson, & Carey, 1991). In the visual system, the ventral stream is described as the "what" stream, or the branch of processing dedicated to stimulus identification; on the other hand, the dorsal stream is described as the "how" (sometimes "where" due to its heavy spatial component) stream, being dedicated to identifying ways in which one interacts with the identified object.

Goldman-Rakic (1995; see also Levy & Goldman-Rakic, 2000) describes a possible extension of these two branches into the frontal cortex. She suggests that the dorsal-ventral segregation pattern is based on stimulus domain; specifically, that more dorsal regions are involved in processing spatial information, while ventral regions are involved in processing nonspatial information, consistent with the organization seen in the visual system (for review, see Romanski, 2004). Evidence for this organization comes from single-cell recordings in monkeys: cells in dorsal PFC show activity during a spatial working memory task (Kojima & Goldman-Rakic, 1984), while those in ventral PFC are activated by objects presented to the foveal region (Badre & Frank, 2012; Wilson, Scalaidhe, & Goldman-Rakic, 1993). A similar pattern has been seen in humans using transcranial magnetic stimulation (Mottaghy et al, 2002) and neuroimaging methods (for review, see Ungerleider, Courtney, & Haxby, 1998).

In one early study, Courtney and colleagues (1996) use positron emission tomography (PET) to record the regional cerebral blood flow (rCBF) during performance of object and spatial memory tasks. Specifically, participants are shown images of faces presented in one of 24 locations on screen. On any given trial, participants are instructed to either maintain the identity of the faces or the locations they will see, but not both. At the start of the
trial, three images are shown in succession; then, following a blank period, a probe is shown. Participants respond to this probe with whether the face image or the location in which it was shown was also a part of the previous set of three. Both the face and location tasks show increased rCBF frontal regions; however, this increase is localized to superior frontal regions in the location working memory task, and to middle and inferior frontal regions in the face working memory task. This pattern is consistent with a spatial/non-spatial distinction for the dorsoventral axis, as posited by Goldman-Rakic (1995); however, controversy remains surrounding what dimension of segregation actually underlies this axis (reviewed by Wager & Smith, 2003 and O’Reilly, 2010).

Postle, D’Esposito, and Corkin (2005) suggest that the spatial/nonspatial domain distinction in the dorsoventral axis may in fact be an epiphenomenon being driven by a confounding tendency to use verbal coding strategies in object-based but not spatial working memory. To demonstrate, the authors describe two experiments using one spatial and one object-based variant of an n-back task to investigate how interference from verbal and nonverbal domains may differentially disrupt performance on the two tasks. Performance on the object-based task was more sensitive to verbal interference, indicating a verbal coding strategy; on the other hand, the spatial task was more sensitive to motion-based interference, suggesting a nonverbal coding strategy. The authors posit that these coding strategy differences are confounded with most object/spatial working memory tasks, and are the basis for the distinctions previously described by proponents of the stimulus domain distinction.

Rather than segregation by stimulus or coding strategy domain, Petrides (1994, 1995; see also Braver et al, 2001) proposes that the dorsal-ventral distinction represented the segregation of different functions of working memory. In this conception, VLPFC is involved in information maintenance over delay intervals, while DLPFC is involved in manipulation and monitoring functions as it relates to information in working memory. This distinction was first supported with lesion studies in non-human primates, and then later in lesion and neuroimaging studies in humans. One experiment using fMRI in humans is reported by D’Esposito, Postle, Ballard, and Lease (1999). In this study, participants complete a delayed-response task in which they are shown a string of letters, followed by delay, before
they respond to a letter-digit pair probe. In one condition, participants are instructed to maintain the string until the probe is shown, at which point they report whether the probe letter was located in the digit position in the string of letters unaltered. In a second condition, they are instructed to alphabetize the string during the delay in anticipation of the probe, at which point they respond with whether the probe matched the indicated position in the manipulated string. The fMRI results from this analysis show activity in VLPFC in both conditions, but greater activity in DLPFC for the manipulation condition over the maintenance condition, consistent with a process-based account of the dorsoventral axis.

O’Reilly (2010) describes yet another possible conceptual link between the ventral (“what” pathways) and dorsal (“where” or “how” pathways) streams of the visual and control systems. In this theory, the ventral stream is involved in retrieval processes driven by both internal and external context that activate relevant information. In the same way, the dorsal stream is involved in response selection processes; in other words, activating behaviors based on current environmental context. Corroborating this idea, Barredo, Oztekin, and Badre (2015) demonstrate that ventral and dorsal PFC are differentially activated by retrieval and selection processes, respectively. Their study used fMRI in conjunction with a source monitoring task that varied the amount of source repetitions. Low repetition trials resulted in increased ventral PFC and medial temporal activity at retrieval, consistent with an increased demand for control during the retrieval process. These regions are functionally connected and, simultaneously, distinguished from a separate functional network in more dorsal regions that have been implicated in response selection (e.g., Schumacher, Elston, & D’Esposito, 2003).

In addition to the debate surrounding the nature of the dorsoventral axis, there is also the question of how a dorsoventral organization may be integrated with the rostrocaudal organization described above. Bahlmann, Blumenfield, and D’Esposito (2015) recently conducted an experiment investigating the interaction between the rostrocaudal and dorsoventral axes. Their experiment adapts the relational complexity task devised by Badre and
D’Esposito (2007) to use either verbal (words) or spatial (dot location) stimuli while collecting fMRI recordings. They then assess the distance between the loci of peak activity for each stimulus type within a set of regions of interest (ROIs) identified for each level of complexity. If, they reason, the two streams are independent, then the task should show two rostrocaudal progressions—a more dorsal one for spatial stimuli, and a more ventral one for verbal stimuli. If they interact, then one of two patterns is possible. If the highest levels of control are involved in selecting sets irrespective of the specific stimuli involved in their processing, then the most rostral areas of PFC should show one region of activity regardless of stimulus, while more caudal regions should show two streams, one dorsal and one ventral, segregated by stimulus type. On the other hand, if stimulus type serves as the highest level of task differentiation, then the opposite pattern should occur; namely, that only the most rostral regions should show segregation by stimulus type, while caudal regions should be activated uniformly for all types.

Their results support the latter hypothesis; stimulus type produces separable activity only in the ROI associated with the highest level of complexity involved in a given session (i.e., the most rostral ROI found for that session). These results may suggest that the stimulus type is used to code the most abstract level of the task, while more caudal neural regions coded task rules in a stimulus-independent way. In other words, participants may represent the experiment as either a spatial or verbal task, within which different mappings need to be learned for the relational complexity aspect of the task. However, as even the authors note, these results are surprising because they are not intuitive to the relational complexity account, in which low-level control processes should not be affected by the particular task context in which they are executed.

The experiment by Balhman, Blumenfield, and D’Esposito (2015) has a number of limitations that may have led to the surprising result described above. First, like previous versions of the relational complexity task, the factors are manipulated in such a way that each combination of abstraction level and stimulus type is presented in different sessions, where order is the same across participants. This may lead to strategies that force the use of stimulus type as a high-level dimension for implementing control processes; because the
stimulus type remains consistent across entire sessions, it provides the highest-level discrimination for which representational set to use at a given level of complexity. This would lead to the pattern of activity found if participants first select between two sets based on stimulus domain and maintain this set throughout the session. Recently, Schumacher and Hazeltine (in press) have described such a task representation, which they call a "task file". The task file consists of a representation of not only the stimuli and responses associated with a task and the links that connect them, but of the contextual information that influences the selection of the task as well. Importantly, these task files can be linked hierarchically; for example, if a task consists of two subsets of stimuli and responses that are indicated by a cue, it can be represented by a task file consisting of the two cues, which in turn link to two separate task files that link their stimulus-response subgroups with their appropriate contextual cue. Similarly, participants in Bahlmann, Blumenfield, and D’Esposito’s experiment may have represented the task hierarchically, where the contextual links at the highest level of the task are the two stimulus dimensions.

In addition to this representational issue, the use of verbal and spatial stimuli for the dorsal-ventral axis manipulation likely results in different task strategies between sessions as well. Verbal, but not spatial, stimuli may afford the use of semantic rather than perceptual coding of the task, which may allow for the use of imagery or similar strategies for executing the verbal task, such as imagining ways to interact with the concepts represented by the verbal stimuli. In accordance with the theory posited by O’Reilly (2010) above, this would result in more dorsal processing, which may have led to the overlap found in this experiment.

A second experiment by Nee and D’Esposito (in press), in fact, describes results that conflict with those reported by Bahlmann, Blumenfield, and D’Esposito (2015). They combine verbal (letters) and spatial (location of letters on screen) stimuli into a single set, such that in all conditions the targets are letters that appeared in different locations on the screen. Participants initially perform a 1-back task in all versions of the task; in the verbal condition, they report if the letters follow a sequence that spells a word (‘TABLET’), and in the spatial condition, they report if the locations followed a sequence that trace an expected pattern. The authors then manipulate this by introducing a delay period in which
participants maintain the previously viewed stimulus over a period of fixation; a task switch in which participants start a new 1-back sequence; or both, in which participants maintain the last stimulus from the first set over a delay while performing a second 1-back set during the intervening time period. They report results that suggest domain segregation in caudal PFC regions (i.e., for lower control demand), but not in the most rostral regions (i.e., for increased control demand), in contrast with the findings of Bahlmann, Blumenfield, and D’Esposito.

Thus, it is not clear how the rostrocaudal and dorsoventral axes might interact. The current experiment aims to provide a novel task that allows for an event-related investigation of the dorsoventral axis and its interactions. In fact, the current experiment contains two manipulations hypothesized to influence activity along the dorsoventral axis. Following Levy and Goldman-Rakic’s (1995) hypothesis, our judgment domains can be categorized as spatial and nonspatial. In this vein, activity should vary along the dorsoventral axis as a function of whether participants are cued for one judgment type or the other. On the other hand, the fact that this design allows for the cuing of two different pieces of information - namely, stimulus-related or response-related information - gives us a manipulation in the spirit of O’Reilly (2010). The cue in this experiment has the capacity to provide information about different aspects of the task on different trials to probe preparatory processes for different parts of the information processing stream. If this is the case, regardless of the judgment domain, cues indicating information at the stimulus level should be processed more ventrally, while cues indicating information at the response level should be processed more dorsally. There is yet disagreement over which conception reflects the true nature of the dorsoventral axis, but the current design allows for a direct comparison of the two. In addition, the event-related design of the current task will allow us to separate these processes at the cue and stimulus timepoints. In combination with the cue effects described in the previous section, it will also investigate the interaction of this dorsoventral axis with the rostrocaudal axis, and help resolve the previously equivocal literature.
1.3 Motor Preparation: Other Influences on PFC Activity

The motor homunculus (MH) was first described by Wilder Penfield from his neural stimulation experiments during surgeries on epileptic patients. He describes an organization of the motor cortex (as well as sensory cortex) in which different regions of the body are mapped to the primary motor strip (M1). In particular, the hands are mapped to the dorsal to middle lateral surface. These mappings are contralateral to their effectors on each side. The use of left and right hand responses allows us to take advantage of this hemispherization to add a third leg of investigation to the current experiment.

Previous research in our lab (Cookson, Hazeltine, & Schumacher, in press) demonstrates motor region activity biasing during the presentation of a partially informative cue. In this experiment, participants learn stimulus-response pairings of face and scene stimuli mapped to the two hands; in the mapping structure, faces and scenes are separated such that all face stimuli are mapped to one hand and all scene stimuli to the other. Thus, when participants are presented with a cue for either A) which type of stimulus would be presented or B) which hand would make the response, it implicitly gives the participant information at both the stimulus and response levels. Crucially, preparatory motor activity lateralization is induced in premotor cortex (and cerebellum) by both types of cues, suggesting that the cue prompts motor preparation as soon as the information is made available. Thus, this past experiment demonstrates that at least the PMC shows lateralized biasing during motor preparation. However, in this experiment, we did not see significant cue-related activity in any more rostral prefrontal regions; this may be because the simple stimulus-response associations learned in that design did not require higher order control.

The current design aims to extend these results and to understand how this motor preparation may interact with other levels of control; that is, whether lateralization of motor activity during preparation interacts with the organization of representation processing along rostrocaudal axis. In this experiment, each presented stimulus pair requires a response on either the left or right hand, as in the previous experiment. Both the single response hand cue and cuing for both dimensions allows for the reduction of the set to a single hand; however, as outlined above, they predict different loci of activity along the rostrocaudal
axis. If lateralization biasing occurs independent of representation preparation, then biasing should occur in both conditions, regardless of complexity level. On the other hand, if they interact, then lateralization biasing should only occur in more caudal regions, while activity in more rostral regions represents motor-general task processing.

1.4 Current Study

The current study, as described above, aims to use a single task to investigate the organizational structure of, and interaction between, three proposed gradients of PFC function: the rostrocaudal axis, representing task abstraction; the dorsoventral axis, representing stimulus domain; and the two hemispheres, representing motor lateralization. Importantly, on each trial, the task is the same: to identify a shared feature dimension and make a forced choice response. Furthermore, the stimuli are similar across factor levels: however, the factors can be manipulated in an event-related manner. As such, our factors can be counterbalanced between participants and directly compared within participants. fMRI recordings have been recorded during execution of the task. ROIs are then defined across the surface of the PFC and used to investigate motor biasing effects as a function of the task factors and ROI location.

This design may produce a number of different results. One hypothesis, in the spirit of Fuster (2001), is that PFC function is indeed distributed across the cortex. In this case, even if a subset of PFC is involved in executing the task, there will be no difference in the activation patterns within this area as a function of the various factors being manipulated on each trial. Such a result would suggest that previous reports of task-related organizational principles are epiphenomenal as a function of the task, perhaps in the structure of the task or the strategies employed by the participant to execute it. On the other hand, if the previously identified organizational principles are in fact task-general properties of PFC organization, we would expect the activity patterns elicited by the cues to differ systematically as a function of their factor combinations. In this case, the question remains: What pattern will this systematic difference follow? These data should reveal what subset of factors (viz., cue content, judgment domain, and/or response hand) show differences across which
organizational axes, as well as which, if any, of these axes interact to produce different patterns for different combinations of those factors.
CHAPTER II

DESIGN

This hierarchical cuing procedure uses a 4x2x2 design, with factors for cue level, stimulus category, and response hand. Participants are shown pairs of stimuli that are defined along four dimensions: color temperature, shape convexity, vertical location, and horizontal location. Each dimension is associated with a two-choice judgment. That is, participants can judge the color of each stimulus as “warm” or “cool”; the shape convexity as “concave” or “convex”; the vertical location as “above” or “below” the horizontal center line of the screen; and the horizontal location as toward the “inside” center column of the screen or toward the “outside” side edges.

The stimulus dimensions can be categorized as “object” or “spatial” judgment types, with two dimensions (object dimensions: color and convexity; spatial dimensions: vertical hemifield and vertical midline distance) assigned to each judgment type. Within each judgment type, one of the two dimensions is assigned to each response hand, with the two possible judgment results being mapped to the index and middle finger of that hand. For each pair of stimuli, participants are asked to identify the dimension along which the pair of stimuli shared the same judgment (e.g., both stimuli were a “cool” color), and to indicate their judgment decision using their learned mapping structure.

Before the presentation of each stimulus pair, a cue is shown that contains a variable amount of information about the upcoming trial. Specifically, participants can be given no information; information about the hand with which they will make their response; information about the type (object or spatial) of judgment they will be making; or information for both the hand and judgment type at once. Three levels of decisional abstraction are therefore possible by cuing for both, one, or none of the upcoming judgment type and response hand.

Participants complete a training session that brings them to criterion level performance.
and assesses their eye and body motion in a scanner-like environment during task performance to ensure the fidelity of the data in the second session. They then return within 7 days (minimum separation 1 day) to complete the experimental session of the study.

2.1 Stimulus Dimensions and Judgments

2.1.1 Object/Feature-Based Dimensions

2.1.1.1 Color Temperature

The color of each stimulus is defined along Derrington-Krauskopf-Lennie (DKL; Derrington, Krauskopf, & Lennie, 1984) color space. This color space has been defined according to observations of opponent-color cells in the lateral geniculate nucleus (LGN), which represent the information conveyed by photoreceptors coding for “opposing” values (i.e., blue-yellow, red-green, and black-white). In this space, the range of observable colors are plotted as a color wheel oriented orthogonally to the luminance of the observed color, allowing for the presentation of isoluminant colors defined as the angle along the color wheel at a given luminance value (here, luminance is held constant at 0°). Degree ranges along the isoluminant plane are set for “warm” and “cool” colors such that “warm” colors include reds, oranges, yellows, and a limited range of lime greens; “cool” colors, likewise, include a subset of dark greens, blues, and purples. The precise degree ranges for these judgments are indicated in the specific methods for each experiment.

2.1.1.2 Shape Convexity

Each stimulus is derived from a square of 200 pixels (px) on each side. The sides of the template square are then warped so that the center of each line is deflected toward the center to form a “concave” shape, or away to form a “convex” shape. The sides of the shape are redrawn as a result of this deflection to form a quadratic parametric curve with the corners of the square maintained in their original positions. The deflection range in each direction varies from 25 to 75px away from center with a resolution of 1px. These stimulus images are then resampled to a size of 70px for experiment presentation.
2.1.2 Spatial Dimensions

2.1.2.1 Vertical Location

The vertical location dimension establishes the y-coordinate of the presentation location for each stimulus, independent of the horizontal location (x-coordinate). Vertical location is defined as a function of the height of the presentation window (1024px in all subsequently presented experiments). Stimuli can be presented “above” or “below” the horizontal midline of the screen at a range of heights with resolution of 1px, where the position of the center of the stimulus determines its categorization. Ranges for the upper and lower presentation ranges are indicated in the specific methods for each experiment.

2.1.2.2 Horizontal Location

The horizontal location dimension establishes the x-coordinate of the presentation location for each stimulus, independent of the vertical location (y-coordinate). Horizontal location is defined as a function of the width of the presentation window (1280px in all subsequently presented experiments). Stimuli can either appear toward the vertical midline of the screen or toward the side edges, allowing for a judgment that the stimulus is toward the “inside” or “outside” of the screen. Stimuli can be presented at a range of horizontal locations with a resolution of 1px, where the position of the center of the stimulus determines its categorization. Ranges for the upper and lower presentation ranges are indicated in the specific methods for each experiment.

2.2 Cues

Cues consist of two words or letter blocks presented in capital letters, with one presented above and one below the central fixation. Cues for judgment type (“SPATIAL” or “OBJECT”) appear above the center fixation, and cues for response hand (“LEFT” or “RIGHT”) below. When information is not to be given for a particular cuetype, “XXXXX” serves as the placeholder in the relevant cue position. Representative images of these cues are illustrated in Figure 3.
Figure 3: Representation of possible cues. Each pair of cues is presented in the positions immediately above and below a center fixation point. Cues for Judgment Type ("SPATIAL" or "OBJECT") appear above, and cues for Response Hand ("LEFT" or "RIGHT") below. Positions in which an informative cue is not to be given are filled with “XXXXX”.
2.3 **Apparatus**

Stimuli are presented using PsychoPy software (Peirce, 2007) presented through a personal computer (PC) (pre-experiment training) or an Avotec Projector (mock and MRI scanners). Responses are collected using two PST button boxes; all devices are scanner-compatible. Participants wear covered protective earphones in both sessions, with earplugs in the MRI for additional protection from the MRI noise. In the MRI, head movement is restricted with soft padding. In the mock scanner, scanner noises are simulated using a standard CD player with sounds recorded from MRI sessions. Eye motion is tracked in the mock scanner using a Logitech HD Webcam C270, and in the MRI scanner using an Avotec Real Eye 5701 MRI-compatible eye tracker. Head motion is tracked in the mock scanner using a PST MoTrak system, and in the mock scanner using the real-time motion tracking software provided in-house at CABI. All presentation, scanning, and response collection apparatus are available through the Georgia State University/Georgia Institute of Technology Center for Advanced Brain Imaging CABI.

2.4 **Screen Setup**

The screen in these experiments is always presented at a resolution of 1024x768px. The screen background is black. Text, including the instructions, cues, feedback, and fixation screens, is presented in white font. The exact structure of the fixation screen is described in the specific methods for each experiment; however, in each case, a marker is placed at the center of the screen.

2.5 **Participants**

Participants have been recruited from the Georgia Institute of Technology student body and surrounding community. To minimize variability in the PFC due to development and handedness, participants are over the age of 18 years old and are right-handed. They also have normal or corrected-to-normal vision, and are not otherwise contra-indicated for an MRI protocol. Participants gave written informed consent under the Georgia Institute of Technology Institutional Review Board and were compensated with course credit.
2.6 Training Procedure

During the first session of the experiment, participants are trained extensively on the procedure to ensure adequate learning of the task. First, participants familiarize themselves to the four possible responses in the task (index or middle finger press; the left or right hand) by responding to explicit instructions, e.g., “Press the RIGHT MIDDLE finger.” This practice block contains 8 trials, counterbalanced across the four possible response options.

Next, participants complete a set of mapping training blocks, one per judgment dimension. These blocks instruct participants on the responses required for each of the four judgment dimensions based on their assigned mapping. At the start of each block, participants are presented with instructions that indicate: 1) what judgment is to be made for that particular dimension; 2) the hand that will be used to respond to that dimension; and 3) what responses correspond to each of the two possible judgment decisions. Following the instructions for a given dimension, participants complete 16 practice trials for that dimension, in which they performed the instructed judgments on a single stimulus. In all participants, the mapping blocks introduce the dimensions in the following order: color temperature, shape convexity, vertical location, and lastly horizontal location. Stimuli start as squares presented in the center of the screen bearing a particular color. As participants progress through the mapping training phase, the stimuli gain values along each of the new dimensions, and are given random values along the previously learned dimensions. This allows participants to incrementally familiarize themselves with the nature of the stimuli they will see on-screen. When the vertical location dimension is introduced, participants are further instructed to maintain fixation on the center of the screen at all times during the task. At this time, the experimenter begins monitoring the participant’s eye movements during the course of the session, and provides feedback on the participant’s success in inhibiting their eye movements at the end of each block. The instruction to maintain fixation on the center of the screen is emphasized at the beginning of each subsequent block and run.

Once the mapping training is complete, participants are introduced to the experimental task proper, without cues. They are instructed that they will now see stimuli appear in pairs, and that these pairs of stimuli will share a judgment decision value along exactly one
of the four possible dimensions. They are then instructed to identify the shared dimension and respond with the appropriate response for the judgment decision value shared by the pair, according to their previously learned mapping. They then complete a practice block consisting of 32 trials in which they respond to pairs of stimuli as they were presented onscreen. This practice block is counterbalanced across judgment types, response hands, and judgment decision values.

Finally, participants are introduced to the cuing aspect of the task. They are instructed that each trial will be preceded by a cue that may give some information about the upcoming trial. The instructions explain the information that could be contained in the two parts of the cue and describe how these two parts can combine into the different cue levels (no information, hand-only, judgment-only, or both). Participants are instructed to use the cues to the best of their ability to help their performance during the task. Following these instructions, participants complete a full practice run of the experimental procedure, as described below.

2.7 Experimental Procedure

The experiment proceeds in two sessions. When participants arrive for the first session of the experiment, they are oriented to the experimental procedure and consent documents, and the experimenter confirms the participant’s qualification to participate. At this time, participants are assigned their mapping group. In each mapping, one dimension from each judgment type (object, spatial) is mapped to each hand, so that, on each side, one object-based and one spatial judgment is mapped to the same hand. Index and middle finger mappings for judgments are assigned for each of the two decisional options of the mapped dimension. These mappings are partially counterbalanced between participants for a total of 8 counterbalancing groups. Participants are trained on their assigned mapping at the start of session 1, as described above, and complete session 2 using the same mapping.

Once the consent process is complete, the participant is oriented to and assisted into the mock scanner. The mock scanner is set up to collect eye tracking and motion tracking data at the start of the session. They next go through the training procedure described
above; the full training procedure takes approximately 30 minutes, with eye motion tracking proceeding as described in the training procedure. Next, the participant completes a set of additional full experimental runs to reach criterion performance on the task. At the start of the first of these runs, the participant is informed that the experimenter will start playing the MRI sounds, and that they should remain as still as possible. The experimenter starts the MoTrak tracking system at the start of the first run. Experimental runs in both sessions consist of 32 trials. Runs present all possible combinations of cuetypes, judgment types, response hands, and decision values. The exact number of runs presented in the first session is described in the specific methods for each experiment in the following chapters.

Feedback is given at the end of each trial: if participants gave the correct response, they are shown the fixation screen; and if they gave an incorrect response, they are told what the correct response should have been. At the end of each run, they are given overall feedback for their accuracy and RT across the run. The experimenter also gives them feedback on whether they are successfully inhibiting eye and head motion.

The second session takes place 1-7 days after the first. This session takes place either in the mock scanner (Pilots) or in the MRI scanner (Experiment). Once the participants are ready to begin, they complete a shortened version of the training procedure described above; this takes approximately 15 minutes. Finally, they complete 16 experimental runs. In the MRI scanner, the Avotec eye tracker is fixed to the head coil when the participant is placed in the MRI scanner, and is connected to a live feed screen. The experimenter adjusts the eye tracker so that the live feed shows at least one of the participant’s eyes clearly on the screen, such that movements of the eye can easily be distinguished. Otherwise, eye and head motion tracking proceed as before. Upon completion of the task, participants are extracted from the mock scanner and brought back to the lab, where they complete a debriefing questionnaire (see Appendix A for questions) and are allowed to ask any questions they have about the experiment. During the second session, feedback on the experimental runs is presented only at the end of each run.

On each trial, participants make judgments of pairs of stimuli based on the feature that the two stimuli share. First, they see a cue that indicates the judgment type (object or
spatial), response hand (left or right), both, or neither for the upcoming trial. This is followed by a fixation screen for a CSI that is jittered (see specific experiment methods in the following chapters for timing and fixation information in each experiment). Following this interval, two stimuli are presented simultaneously on the screen, one in the left half and one in the right. The stimuli have different judgment values for each of the four dimensions described above except for one; participants are instructed to make a judgment about this shared dimension and to make the appropriate index or middle finger response on the hand associated with that judgment decision value. Participants are able to make their response for the interval that the stimuli are on-screen; this is followed by a fixation screen with a jittered ITI duration like that in the CSI presentation. Participants are instructed to respond as quickly and accurately as possible on each trial, and to use the cues presented at the beginning of each trial to prepare the possible upcoming responses to the best of their ability. An illustration of the trial structure is found in Figure 4.
Figure 4: Trial structure. In each trial, participants received a cue for the upcoming judgment type, response hand, both, or neither. Next, the participants saw a fixation cross for a jittered CSI. Following this was the stimulus presentation, at which point participants were instructed to respond. The ITI, like the CSI, presented a fixation cross for a jittered interval.
CHAPTER III

PILOT EXPERIMENTS

To validate and refine the experiment design, we have completed a two-phase pilot that iterates on the parameters of the design based on the behavioral results and participant feedback via survey. The pilot has been conducted in two phases, where each phase has allowed us to identify issues and iterate on the design to improve those issues. We have found a consistent effect of cues that seems to be dependent primarily on the amount of information being provided rather than the nature of that information. There is an effect of the judgment dimension on RT; changes have therefore been made to the design to minimize those differences. Likewise, there is an interaction between cuetype and dimension, but design changes have aimed to minimize any existing differences, and differences in the cue effect due to this interaction seem to be on effect magnitude rather than the actual pattern of the cuetype effect for different judgment dimensions.

3.1 Phase 1

3.1.1 Specific Methods

3.1.1.1 Participants

Phase 1 includes 7 participants. Participants range from 18-23 years of age.

3.1.1.2 Fixation Screen and Stimulus Ranges

The fixation screen in Phase 1 consists of a single cross presented in the center of the screen in white font. Ranges for the four dimension boundaries are shown in Table 1. Screen center is defined as point (0,0) for the pixel ranges that follow.

3.1.1.3 Experimental Timings and Sessions

Cue and stimulus events are presented for 2 seconds each. The CSI and ITI are jittered according to the exponential method described by Ollinger and colleagues (50% of trials:}
Table 1: Pilot Phase 1 Dimension Bounds.

<table>
<thead>
<tr>
<th>Judgment Type</th>
<th>Dimension</th>
<th>Value</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Object-Based</td>
<td>Color Temperature</td>
<td>Warm</td>
<td>0</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>(Degrees)</td>
<td>Cool</td>
<td>180</td>
<td>270</td>
</tr>
<tr>
<td>Shape Convexity</td>
<td>Concave</td>
<td>-75</td>
<td>-25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Convex</td>
<td>25</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Spatial</td>
<td>Vertical Location</td>
<td>Above</td>
<td>35</td>
<td>349</td>
</tr>
<tr>
<td></td>
<td>(Vertical Pos., px)</td>
<td>Below</td>
<td>-349</td>
<td>-35</td>
</tr>
<tr>
<td></td>
<td>Inside (Left)</td>
<td>-221</td>
<td>-35</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Horizontal Pos., px)</td>
<td>Right</td>
<td>221</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Outside (Left)</td>
<td>-477</td>
<td>-291</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Right)</td>
<td>291</td>
<td>477</td>
<td></td>
</tr>
</tbody>
</table>

2s; 25% of trials: 4s; 25% of trials: 8s; Ollinger, Corbetta, & Shulman, 2001; Ollinger, Shulman, & Corbetta, 2001).

Both sessions of the first phase pilot take place in the mock scanner. In the first session, the participant completes 8 additional full experimental runs to reach peak performance on the task, regardless of the rate of progress. During the first session, feedback is given trial-by-trial as well as at the end of each run. Experimental runs have an average duration of 12s/trial, 6:24/run.

3.1.1.4 Behavioral Analysis

Mean RTs and accuracies on session 2 are calculated for each subject as a function of cue-type, the four judgment dimensions, and time. The time comparison bins the experimental runs into three bins of four runs each; these bins will be referred to here as “epochs”. Overall accuracy is calculated as well across subjects and conditions. A three-way repeated measures analysis of variance (ANOVA) has been performed on the RT and accuracy data for the three factors. Post-hoc comparisons are conducted as needed using Tukey’s honestly significant difference (HSD) procedure.

3.1.1.5 Quality Control Analysis

As it is unclear whether participants would be able to successfully learn to complete the task while maintaining fixation, the first pilot phase includes quantification of eye movements.
Figure 5: Accuracy by cuetype for pilot phase 1. Bars show accuracy for each factor arranged left to right in order of decreasing information content. Differences in accuracy were not significant. Legend: 2 = “both” cues; 1H = “hand-only” cues; 1J = “judgment-only” cues; 0 = “no information” cues.

On a given trial, if participants move their eyes upon presentation of the stimulus, the experimenter is instructed to press the ”M” key on the mock scanner experimenter keyboard, which logs an eye movement for that trial. The frequency of these movements was then graphically assessed as a function of the session and block.

3.1.2 Results

3.1.2.1 Accuracy

Accuracies approached ceiling (Overall average = 94.4%) and were analyzed using an arcsine transformation: \( X = \sin^{-1}\sqrt{x} \). The ANOVA revealed no significant main effects or interactions for any factors. The results for the main effect of each factor are illustrated separately in Figures 5 (Cuetype), 6 (Epoch), and 7 (Dimension).

3.1.2.2 Reaction Time

RTs were analyzed for correct trials only. The ANOVA revealed a main effect of cuetype (Figure 8), \( F(1.401, 8.404) = 29.797, p < .001, \eta^2_p = .832 \), and for epoch (Figure 9), \( F(3, 8) = 3.364, p = .042, \eta^2_p = .359 \), as well as a trending main effect of dimension (Figure 10),
Figure 6: Accuracy by Epoch for pilot phase 1. Each epoch averaged across 4 runs. Differences in accuracy were not significant.

Figure 7: Accuracy by Dimension for pilot phase 1. Differences in accuracy were not significant.
Figure 8: RT by cuetype for pilot phase 1. Bars show RT for each factor arranged left to right in order of decreasing information content for correct trials only. There was a main effect of cuetype on RT, $F(1.401, 8.404) = 29.797, p < .001, \eta^2_p = .832$. Legend: 2 = “both” cues; 1H = “hand-only” cues; 1J = “judgment-only” cues; 0 = “no information” cues.

$F(3, 8) = 3.031, p = .056, \eta^2_p = .336)$. That is, participants’ performance depended on how far into the session they are and which cuetype they received on a given trial. Performance may also have been slightly influenced by the stimulus dimension being judged on a given trial.

To further investigate these main effects, we conducted post-hoc comparisons for each factor. In each case, the corrected $\alpha = .0083$. For cuetype, post-hoc comparisons revealed significant differences between cues for both hand and judgment versus all other cuetypes, as well as cues for hand only versus cues for no information. The remaining comparisons were significant at $\alpha = .05$, but do not survive correction. For epoch, post hoc comparisons revealed no significant differences between conditions after correction. The difference between epochs 1 and 2 (i.e., blocks 1-4 and 5-8) was significant before correction.

There was a significant interaction between cuetype and dimension ($F(6.340, 38.043) = 2.697, p = .026, \eta^2_p = .310$); that is, the effect of cuetype depended on the stimulus dimension being judged on a given trial. This interaction is shown in Figure 11. No other interaction terms were significant.
Figure 9: RT by Epoch for pilot phase 1. Each epoch averaged across 4 runs. RTs for correct trials only. There was a main effect of epoch on RT, $F(3, 8) = 3.364, p = .042, \eta_p^2 = .359$.

Figure 10: RT by Dimension for pilot phase 1. RTs for correct trials only. The effect of dimension on RT was near significance, $F(3, 8) = 3.031, p = .056, \eta_p^2 = .336$. 
Figure 11: RT for Cuetype by Dimension Interaction for pilot phase 1. Cuetype effect is shown individually for each dimension. RTs shown for correct trials only. The interaction effect was significant, $F(6.340, 38.043) = 2.697, p = .026, \eta^2_p = .310$.

3.1.2.3 Quality Control Results

Eye motion tracking results were assessed graphically to ensure that movements were minimized during the second session. The results are shown in Appendix B. Session 1 showed a steep decline in eye movements from the beginning of collection through the third block. Following this, eye movements remained close to zero for the duration of the session. Session 2 showed low eye movements across the session, with a small decline in movements from the training to the experimental runs.

3.1.2.4 Post-Experiment Questionnaires

The questionnaires revealed a number of factors in this experiment that were relevant to performance. In general, participants found the task to be neutral to somewhat easy (5 point Likert scale, 1 = Very Difficult, 5 = Very Easy: Average response = 3.4). A common issue for participants’ performance was fatigue. Six participants noted that they became fatigued or bored or mind-wandered over the course of the experiment. Four participants specifically noted that they felt that the long CSI and ITI time influenced their ability to successfully perform the task over time, and two noted that the total duration or number
of blocks in the experiment was a factor in their fatigue (Overlap = 0 participants).

Another issue identified by examination of the questionnaire that may have influenced performance was the possibility of overlearning. Four participants suggested that they felt like they had automatized the task before the end of the second session. Furthermore, one participant specifically noted that they had stopped trying to use the cues, and two participants suggested that they had internalized patterns in the relations of the locations of the stimuli that belied the judgment dimension for that trial without needing to see the cue or assess the stimuli themselves (overlap = 1 participant).

The responses to the questionnaire also suggested reasons why performance differed between judgment dimensions. Six participants noted the presence of a lime-green color for the stimuli that was counter-intuitively categorized as a warm color due to the yellow content in the color. This may have resulted in a particularly difficult trial condition that required the inhibition of a prepotent "cool" response on these trials, which would cause the slow RTs found here. Individual participants also note difficulty with each of the dimensions for various reasons, but in particular 1 participant noted a counterintuitive mapping for the horizontal location condition. Specifically, this condition required an inner-outer judgment; when participants have the "inside" response mapped to the index finger, this is congruent to egocentric mappings in which the index finger is closer to the "inside" of the body; however, mapping the same judgment to the middle finger becomes counterintuitive and can result in more difficult or slower responding. This is formally known as the Kornblum effect.

Finally, a number of participants verbally noted that they had problems seeing stimuli presented near the outer edges of the screen.

3.1.3 Discussion

The results of the phase 1 pilot demonstrated a few key points. First, the RT data showed a significant effect of cuetype (Figure 8), and the accuracy data show a similar visual trend (Figure 5). For RT, post-hoc comparisons between conditions generally demonstrated a decrease in RT from non-informative to partially to fully informative cues; in other words,
participants showed better performance as a function of how much information was con-
tained in the cue. This effect did not depend on the type of information contained in the cue, as there was no difference in performance for both cues that reduced the set by half (viz., hand and judgment only cues). These results demonstrate that participants were using the cues as instructed, and that this information was, in fact, able to facilitate performance. Interestingly, there was not a significant difference between the judgment information cue and the no information cue; however, this may have been due to the small sample size.

While it is only marginally significant, the phase 1 pilot also demonstrated a main effect of dimension (Figure 10). More specifically, performance for color and vertical location dimensions significantly differed; that is, people were significantly slower for the color dimension than the vertical location dimension. Furthermore, performance on vertical and horizontal location dimensions was significantly different before correction for multiple comparisons, and visual inspection of the data suggested that vertical location judgments were marginally faster than the other dimensions. Overall, these data suggest that there may have been additional inequities in the data not revealed by this particular sample. Responses to the post-experiment questionnaire may suggest potential solutions to these inequities. A majority of participants noted particular difficulty on a specific value for the color dimension; removal of this value may equate performance on this dimension. Additionally, the two location-based judgments appeared to be differentially difficult. This may have been due to the layout of our experiment screen; in this pilot, the fixation cross was shown in the center of the screen, effectively providing a boundary line for the vertical location condition. Conversely, participants did not see any markers at the inner-outer boundary, and therefore had to intuit this boundary themselves. This is in contrast to each of the other dimensions, which had clear boundaries that did not have to be interpreted from the task itself. Pilot 2 attempted to correct these inequities.

There was also a significant interaction between cuetype and dimension (Figure 11). Post-hoc comparisons of the effect of cue within each dimension condition (not shown), especially after correction for multiple comparisons, showed inconsistent patterns that were not easily interpreted. This may be a result of the small sample size, but may less trivially
suggest that participants were employing different strategies for using the cues as a function of the dimension, or were simply not using the cues on a subset of the dimensions despite the finding of the expected cuing effect in the overall data. The second pilot aimed to clarify these patterns and reduce this interaction effect as much as possible with the changes to the dimensions described above.

A comparison of performance over time, as binned into epochs of four blocks each, revealed that participants were performing differently as the session progressed (Figure 9). None of the post-hoc comparisons survived correction for multiple comparisons. However, there was a trend for RTs on the first epoch to be longer than those in the second. This may suggest that participants took slightly longer to completely learn or re-learn the task to ceiling than the practice duration allowed. It is also possible that some participants took longer to learn the task than others and/or reach a lower ultimate level of performance. However, at the same time, the difference in RT did not persist for epoch 1 versus epochs 3 or 4, which would be true for a pure learning effect. Furthermore, responses to the post-experiment questionnaire suggested that the quantity of practice may have been more than was necessary to reach peak performance on the task, and that, in some cases, may even have led to a reduced engagement with the cues. The survey responses also suggested specifically that some fatigue may have been directly related to the wait time between events, rather than just the duration of the session as a whole. Thus, fatigue and overlearning due to the length of the sessions, and specifically the lengths of the CSI and ITI, may have had impacts on performance later in the session. Phase 2 attempted to: 1) reduce the task time by reducing CSI and ITI durations; 2) improve the rate of learning through improved instruction; and 3) develop a method to screen out participants that may have been learning the task remarkably slowly or to a particularly low peak performance level.

Finally, the quantitative assessment of eye movements strongly suggested that participants were able to learn to restrict their eye movements very early during the course of learning, despite the complexity of the task and the potentially large distances between the stimuli on screen. Experimenters in future iterations of the study were instructed to monitor eye movements and give feedback as before; however, because the occurrence of
eye movements was so low so early in the first session, quantitative logging was decided to be unnecessary.

3.2 Phase 2

The first phase of the pilot demonstrated that participants are able to learn the task to ceiling and that the cues produce the expected pattern of results. However, it also revealed unexpected differences in performance between the different dimensions of the task. It also suggested that the timing and duration of the task may lead to fatigue and/or over-learning. A number of adjustments were made to the procedure to address these issues, and a second pilot has been run to quantify the effects of these changes.

3.2.1 Specific Methods

3.2.1.1 Participants

The phase 2 pilot includes 10 participants, collected and analyzed separately from the phase 1 data. One participant was excluded from the second session, and therefore from analysis, due to failure to reach criterion performance as defined below.

3.2.1.2 Fixation Screen and Stimulus Ranges

To more clearly delineate the boundaries of the horizontal location dimension, the fixation screen has been changed as shown in Figure 12. A square fixation point (80px) is shown in the center of the screen, surrounded by four smaller (40px) square points arranged in a rectangle centered around the fixation point such that each of the four points marks a corner of the rectangle. These four corner points represent the boundary line between the “inside” and “outside” decision conditions. Furthermore, grey edges have been added to the left and right edges of the screen to better delineate the outer bounds of the horizontal aspect of the screen.

Ranges for the four dimension boundaries for this phase are shown in Table 2. Screen center is defined as point (0,0) for pixel ranges. The color temperature dimension has been adjusted to reduce the range such that the occurrence of counterintuitive lime green colors is more limited in the “warm” color condition. The boundary zone between the “above”
Figure 12: Representation of fixation screen. This fixation screen is used for the CSI and ITI frames of the experiment in both the second phase pilot and the fMRI experiment.

and “below” conditions is reduced in size (i.e., the lower boundary of the “above” condition and upper boundary of the “below” condition were made closer to the midline) and the range of possible presentation locations extended outward to increase the difficulty of this decision to more closely resemble that of the other dimensions. Likewise, the boundaries of the horizontal location condition have been adjusted slightly. The vertical and horizontal location conditions have also been scaled to add a boundary edge of 1 stimulus size around the entire outer edge of the screen to ensure stimulus visibility. No changes have been made to shape convexity.

3.2.1.3 Experimental Timings and Sessions

Cue and stimulus events are presented for 2s (5 participants) or 1.9s (4 participants) each, the latter change made to reduce the overall duration of the experiment as a result of separate observations in pilot scanning sessions. The CSI and ITI are jittered using the Analysis of Functional NeuroImages (AFNI) software package (Cox, 1996) using an optimization algorithm with parameters specifying minimum duration of .25s and a step of
Table 2: Pilot Phase 2 Dimension Bounds.

<table>
<thead>
<tr>
<th>Judgment Type</th>
<th>Dimension</th>
<th>Value</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Object-Based</td>
<td>Color Temperature</td>
<td>Warm</td>
<td>0</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cool</td>
<td>180</td>
<td>255</td>
</tr>
<tr>
<td>Shape Convexity</td>
<td>Concave</td>
<td>-75</td>
<td>-25</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Convex</td>
<td>25</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Spatial</td>
<td>Vertical Location</td>
<td>Above</td>
<td>35</td>
<td>279</td>
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<tr>
<td></td>
<td></td>
<td>Below</td>
<td>-279</td>
<td>-35</td>
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<td>Inside (Left)</td>
<td>-186</td>
<td>-35</td>
<td></td>
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<td>Outside (Left)</td>
<td>-407</td>
<td>-256</td>
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<td></td>
<td>(Right)</td>
<td>35</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>(Horizontal Pos., px)</td>
<td>256</td>
<td>407</td>
<td></td>
</tr>
</tbody>
</table>

.25s. The algorithm produces a random experimental timing given the desired events (i.e., the factor combinations for the cue and stimulus timepoints) and a desired run duration as calculated from a desired average duration of the CSI and ITI events (1.9s vs 2s each, same distribution of participants; total run duration = 246s or 260s). An estimate of the unexplained variance for this design is then calculated. For the experimental runs in each session, this process is iterated 1000 times, comparing the unexplained variance for each design and keeping the design that minimizes this value. The same process is completed over 100 iterations to produce the timings for the cue practice block for each session.

Both sessions of the second phase pilot take place in the mock scanner. In the first session, participants complete between 6 and 12 experimental runs after completing the training. The number of runs completed by each participant is determined by the how quickly the participant reaches a criterion performance; specifically, an average accuracy of 90% over the three most recent blocks. This allows us to dynamically adjust the amount of practice each subject receives as a function of how quickly they learn the task. In session 2, all participants complete 16 experimental runs. Each run is approximately 4:12 min or 4:33 min (1.9s vs 2.0s events; same distribution of participants).
3.2.1.4 Behavioral Analysis

Mean RTs and accuracies on session 2 have been calculated for each subject as a function of the three previous within-subjects factors (cuetype, the four judgment dimensions, time) as well as a between-subjects factor for the inner-outer mapping congruency for each participant to investigate potential influences of the Kornblum effect on our results. A four-way repeated measures ANOVA has been performed on the RT and accuracy data for the four factors. Post-hoc comparisons are conducted as needed using Tukey’s HSD procedure.

3.2.2 Results

3.2.2.1 Accuracy

Accuracies approached ceiling (Overall average = 95.5%) and were analyzed using an arcsine transformation. The ANOVA revealed a main effect of cuetype, $F(3, 21) = 5.654, p = .005, \eta^2_p = .447$; that is, performance differed as a function of which cue participants received on a given trial. These results are illustrated in Figure 13. The main effects of time (Figure 14), dimension (Figure 15), and mapping congruency were not significant.

There was also a significant interaction between cuetype and dimension, $F(9, 72) =$
Figure 14: Accuracy by Epoch for pilot phase 2. Each epoch averaged across 4 runs. Differences in accuracy were not significant.

Figure 15: Accuracy by Dimension for pilot phase 2. Differences in accuracy were not significant.
Figure 16: Cuetype by Dimension Interaction for Accuracy for pilot phase 2. Cuetype effect is shown individually for each dimension. This interaction was significant, $F(9,72) = 2.573, p = .013, \eta^2_p = .243$.

2.573, $p = .013, \eta^2_p = .243$, shown in figure 16. That is, the effect of cuetype on accuracy depended on the stimulus dimension being judged on a given trial. No other interaction terms, including the dimension by congruency interaction (Figure 17), were significant; that is, the congruency between the horizontal location judgment and the response mapping to the index and middle (inner/outer) fingers did not significantly influence the accuracy of responding for the horizontal judgment versus other judgments.

3.2.2.2 Reaction Time

RTs were analyzed for correct trials only. The ANOVA revealed a main effect of cuetype (Figure 18), $F(3,24) = 76.438, p < .001, \eta^2_p = .905$, and dimension (Figure 19), $F(2.023,14.163) = 5.878, p = .014, \eta^2_p = .456$. That is, performance differed as a function of which cue participants received on a given trial, as well as which stimulus dimension was being judged on that trial. The main effects of time (Figure 20) and congruency were not significant.

To further investigate these main effects, we conducted post-hoc comparisons for each factor. In each case, the corrected $\alpha = .0083$. For cuetype, post-hoc comparisons revealed
**Figure 17:** Congruency by Dimension Interaction for Accuracy for pilot phase 2. This interaction was not significant. Legend: C = “Congruent”, I = “Incongruent”.

**Figure 18:** RT by cuetype for pilot phase 2. Bars show RT for each factor arranged left to right in order of decreasing information content for correct trials only. There was a main effect of cuetype for RT, $F(3, 24) = 76.438, p < .001, \eta_p^2 = .905$. Legend: 2 = “both” cues; 1H = “hand-only” cues; 1J = “judgment-only” cues; 0 = “no information” cues.
Figure 19: RT by Dimension for pilot phase 2. RTs for correct trials only. There was a main effect of dimension for RT, $F(2.023, 14.163) = 5.878, p = .014, \eta^2_p = .456$.

Figure 20: RT by Epoch for pilot phase 2. Each epoch averaged across 4 runs. RTs for correct trials only. The effect of Epoch on RT was not significant.
significant differences between cues for both hand and judgment versus all other cuetypes, as well as cues for hand only and judgment only each versus cues for no information. The difference between hand only and judgment only cues was not significant. For dimension, post-hoc comparisons revealed significant differences only between color versus convexity judgments after correction. Before correction, additional significant differences were seen between horizontal location versus both convexity and vertical location judgments and color versus vertical location judgments.

There was a trending interaction between cuetype and dimension, $F(9.000, 63.000) = 2.016, p = .052, \eta^2_p = .224$, shown in Figure 21. That is, the effect of cuetype on RT depended on the stimulus dimension being judged on a given trial. No other two-way interaction terms were significant, including the congruency by dimension interaction (Figure 22). There was also a significant 3-way interaction between epoch, cuetype, and dimension, $F(27.000, 189.000) = 1.638, p = .031, \eta^2_p = .190$. 

**Figure 21:** Cuetype by Dimension Interaction for RT for pilot phase 2. Cuetype effect is shown individually for each dimension. This interaction was near-significant, $F(9.000, 63.000) = 2.016, p = .052, \eta^2_p = .224$. 


Figure 22: Congruency by Dimension Interaction for RT for pilot phase 2. This interaction was not significant. Legend: C = “Congruent”, I = “Incongruent”.

3.2.2.3 Post-Experiment Questionnaires

In general, participants found the task to be neutral to somewhat easy (5 point Likert scale, 1 = Very Difficult, 5 = Very Easy: Average response = 3.4), confirming the result from the phase 1 pilot. 4 participants noted that they became fatigued or bored or mind-wandered over the course of the experiment. 1 participant specifically noted that they felt that the long CSI and ITI time influenced their ability to successfully perform the task, and none note that the total duration or number of blocks in the experiment was a factor in their fatigue. Conversely, 2 participants noted that they felt restless toward the end of the sessions.

In phase 2, no participants suggested that they felt like they had automatized the task before the end of the second session. No participant specifically noted that they had stopped trying to use the cues, nor did any participants suggest that they had internalized patterns in the relations of the locations of the stimuli that belied the judgment dimension for that trial without needing to see the cue or assess the stimuli themselves.

Only 3 participants noted a lime-green color for the stimuli that they found more difficult to categorize. 2 participants noted the counterintuitive Kornblum effect for the horizontal
location condition. In the case of both accuracy and RT, however, despite a main effect of dimension, the ANOVA found no between group differences in performance, nor an interaction between group and dimension condition. In other words, the participants’ performance across different dimensions did not depend on whether that participant had a congruent or incongruent mapping structure, suggesting that the Kornblum effect was minimal in this case.

3.2.3 Discussion

The results of the phase 2 pilot demonstrated a number of improvements over the phase 1 design. First, both the accuracy and RT data showed a significant effect of cuetype (Figures 13 and 18). The effect of cuetype on RT was particularly strong at $\eta_p^2 = .905$, and post-hoc comparisons very clearly demonstrated a decrease in RT from non-informative to partially to fully informative cues; in other words, participants showed better performance as a function of how much information was contained in the cue. In this second phase, this effect did not depend on the type of information contained in the cue, as there was no difference in performance for both cues that reduce the set by half (viz., hand and judgment only cues). These results demonstrate that participants use the cues as instructed, that this information is, in fact, able to facilitate performance, and that this facilitation does not depend on the type of information contained in the cue.

The phase 2 pilot also demonstrated a main effect of dimension on RT (Figure 19). More specifically, performance for color and convexity dimensions significantly differed; that is, people were significantly slower for the color dimension than the convexity dimension. Furthermore, performance on the horizontal location dimension was significantly slower than both the convexity and vertical location dimensions before correction for multiple comparisons, and visual inspection of the data suggested that vertical location judgments were again marginally faster than the other dimensions.

There was once again a significant interaction between cuetype and dimension (Figures 16 and 21). Unlike the phase 1 pilot, however, for the phase 2 pilot, post-hoc comparisons of the effect of cue on RT within each dimension condition demonstrated a consistent difference
between cues for both hand and judgment versus all other cuetypes in all four conditions, and significant or pre-correction significant differences between cues for no information and all other cues in 3 out of the 4 dimensions (excluding color). This suggests a pattern in which the conceptual effect of cue was the same across conditions, but at different scales. In other words, the data suggest that participants were using the cue in the same way for all dimension conditions, rather than approaching the cue in different ways as a function of the other conditions of the trial.

Finally, a comparison of performance over time, as binned into epochs of four blocks each, did not reveal significant differences in performance across time (Figures 14 and 20). In other words, participants appeared to have reached peak performance by session 2. Furthermore, only one participant did not reach the performance cutoff by the end of session 1 as noted above, demonstrating that the majority of participants were able to successfully learn the task to criterion. This suggests that the training and practice sessions are generally sufficient for learning the task, and that the criterion employed in session one is generally indicative of successful performance in session 2.

Overall, the two phases of the pilot demonstrated the behavioral validity of the proposed experimental design and allowed for fine-tuning of the design to improve the timings and dimension ranges. Participants were fully capable of learning the task to a criterion level in session 1, which generally translated to consistent peak performance across the duration of session 2, minimizing the influence of learning (or overlearning) on these data. The design produced a strong, consistent cuing effect, especially in the RT data, which remained consistent across the duration of the second session. The differences in performance for different cuetypes across dimension conditions appeared to be due primarily to differences in the scale of the effect size for each dimension, rather than the result of differential strategies, and therefore would not appear to have had a direct influence on the manner in which participants were actually executing the task at a high level.
CHAPTER IV

FMRI EXPERIMENT

4.1 Specific Methods

4.1.1 Participants

20 participants (10 female) have been recruited from the student population at the Georgia Institute of Technology. One participant was removed from analysis due to a technical issue with data collection, and one participant was removed due to sub-criterion performance on session 2.

4.1.2 Fixation Screen and Stimulus Ranges

The fMRI experiment uses the same fixation screen as the second phase pilot experiment. Ranges for the four dimension boundaries for this experiment are shown in Table 3. Screen center is defined as point (0,0) for pixel ranges. The boundary zone between the “above” and “below” conditions has been reduced in size again to increase the difficulty of this decision. The boundaries of the horizontal location condition are adjusted to further improve visibility at the edges of the screen. No further changes have been made to color temperature or shape convexity. Representative images of these stimulus ranges are illustrated in Figure 23.

4.1.3 Experimental Timings and Sessions

Stimulus timings follow the procedure from the phase 2 pilot experiment with 1.9s fixed events for all participants. The first session of the experiment takes place in the mock scanner. In this session, participants follow the same procedures as in the second phase pilot.

In the second session, participants arrive to the lab and are asked to review their MRI screening forms for any possible changes since their previous session. Once the participants are cleared for scanning, they are prepared for and assisted into the MRI scanner. Once the participants are ready to begin, they complete their practice blocks during the T1
Table 3: Final Stimulus Dimension Bounds.

<table>
<thead>
<tr>
<th>Judgment Type</th>
<th>Dimension</th>
<th>Value</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Object-Based</td>
<td>Color Temperature</td>
<td>Warm</td>
<td>0</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>(Degrees)</td>
<td>Cool</td>
<td>180</td>
<td>255</td>
</tr>
<tr>
<td>Shape Convexity</td>
<td>Concave</td>
<td>-75</td>
<td>-25</td>
<td></td>
</tr>
<tr>
<td>(Deflection Radius, px)</td>
<td>Convex</td>
<td>25</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Spatial</td>
<td>Vertical Location</td>
<td>Above</td>
<td>18</td>
<td>279</td>
</tr>
<tr>
<td>(Vertical Pos., px)</td>
<td>Below</td>
<td>-279</td>
<td>-17</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Horizontal Location</td>
<td>Inside (Left)</td>
<td>-168</td>
<td>-35</td>
</tr>
<tr>
<td>(Horizontal Pos., px)</td>
<td>(Right)</td>
<td>35</td>
<td>169</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Outside (Left)</td>
<td>-407</td>
<td>-274</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Right)</td>
<td>274</td>
<td>407</td>
<td></td>
</tr>
</tbody>
</table>

Figure 23: Representation of final stimulus bounds. (A) Boundaries for color temperature shown on a DKL isoluminant color wheel. Non-greyed areas represent the range of possible colors. (B) Boundaries for the convex (left) and concave (right) conditions of shape convexity. Grey regions show the range of possible distortions. (C) Boundaries for the vertical location condition. Grey regions show the range of possible positions. (D) Boundaries for the horizontal location condition. Stimuli were presented to both the left and right sides of the screen; judgment was made relative to the center line, marked in white. Grey regions show the range of possible positions.
acquisition and functional localizer sequences. They then complete their experimental runs. After the session, participants are escorted back to the lab to complete the post-experiment questionnaire.

4.1.4 fMRI Design

This experiment uses a fast event-related design. Image collection used a standard radio-frequency head coil. At the beginning of the session, a 3D MPRAGE structural scan (1mm isotropic voxels) is collected, followed by a three-plane localizer. The blood-oxygen level-dependent (BOLD) signal is recorded using an interleaved echoplanar T2* sequence (TR=2000ms, TE=30ms, 3mm isotropic voxels). Each functional volume contains 37 axial slices, with 130 volumes/run.

4.1.5 Behavioral Analysis

Behavioral data for session 2 have been analyzed in the same manner as the second phase pilot experiment.

4.1.6 fMRI Processing and Analysis

4.1.6.1 Whole Brain Processing and Visualization

Data preprocessing and analysis have been conducted using AFNI (Cox, 1996). Preprocessing procedures include volume reconstruction and despiking, followed by slice timing and 6-parameter rigid-body motion correction. Finally, data undergo structural-functional alignment and registration to standard MNI space. The individual data are analyzed using typical general linear modeling techniques. Nuisance regressors are included for constant, linear, and quadratic trends, as well as the 6 motion parameters extracted from preprocessing. Then, events are defined for the cue and stimulus timepoints of each trial, labeled for the cuetype, judgment type, and response hand. Additional contrasts are defined for all cues versus baseline and for additional effects of interest (described in the Results section as applicable). The results of these individual contrasts (beta weights) are then scaled to a mean of 100 such that the weight values reflect the percent signal change for the contrast.

A group-level mask for the brain space has been created by averaging each participant’s
anatomical mask together and thresholding the mask to include voxels only represented in 80% or more of participants. A second mask has also been created that covers the PFC, limited to those voxels also included in the group brain mask; the group-level statistics are restricted to this area to maximize the power of the analysis. To extract group-level statistics for our contrasts, the individual beta weights for each contrast are subjected to a one-sample $t$-test within the voxels contained in the PFC mask.

### 4.1.6.2 ROI Definition and Analysis

To define ROIs for this experiment, we adapt a method used in previous investigations of the rostrocaudal axis (e.g., Badre & D’Esposito, 2007) to our precuing design. In detail, peaks are extracted from the cue versus baseline contrast (positive contrast only) at the group level using an FDR-corrected threshold of $q=.05$. A total of 12 peaks have been identified from this process here. Spherical ROIs with a radius of 6mm are next defined around each of these points, masked with the group brain mask to remove portions of the volumes that are located outside of the defined brain space. The points are then ordered separately according to their positions relative to one another, first anteriorly to posteriorly, then dorsally to ventrally. Their hemispheric location (left or right) is noted as well. 3 pairs of these ROIs have been identified that represent approximately the same location in both axis directions in each hemisphere; the remaining 6 ROIs are mirrored in the opposite hemisphere to provide an equivalent point in both hemispheres for all identified locations. The 18 resultant ROIs represent a full factorial combination of 3 bins of locations along the anterior-posterior direction, 3 bins of locations along the dorsal-ventral direction, and the two hemispheres. These ROIs are described in Table 4 and visualized in Figure 24. Average beta values for each condition are extracted for each ROI by participant.

### 4.2 Results

#### 4.2.1 Behavioral Results

##### 4.2.1.1 Accuracy

Accuracies approached ceiling (Overall average = 95.1%) and were analyzed using an arcsine transformation. The ANOVA revealed a main effect of cuetype, $F(3,48) = 19.564, p <$
Table 4: ROI Coordinates by Factor. Coordinates are shown in MNI space. Table is laid out with the rostrocaudal location in the first column, dorsoventral location in the second, and hemisphere in the third. A: Anterior; M: Middle; P: Posterior; D: Dorsal; V: Ventral; L: Left Hemisphere; R: Right Hemisphere.

<table>
<thead>
<tr>
<th>AP</th>
<th>DV</th>
<th>LR</th>
<th>L</th>
<th>P</th>
<th>I</th>
<th>Mirror?</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>D</td>
<td>L</td>
<td>-51</td>
<td>33</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>51</td>
<td>36</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>L</td>
<td>-42</td>
<td>27</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>42</td>
<td>27</td>
<td>27</td>
<td>*</td>
</tr>
<tr>
<td>V</td>
<td>L</td>
<td>-33</td>
<td>39</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>33</td>
<td>39</td>
<td>9</td>
<td>*</td>
</tr>
<tr>
<td>M</td>
<td>D</td>
<td>L</td>
<td>-6</td>
<td>9</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>6</td>
<td>9</td>
<td>54</td>
<td>*</td>
</tr>
<tr>
<td>M</td>
<td>L</td>
<td>-21</td>
<td>6</td>
<td>45</td>
<td></td>
<td>*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>21</td>
<td>6</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>L</td>
<td>-57</td>
<td>12</td>
<td>39</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>57</td>
<td>12</td>
<td>39</td>
<td>*</td>
</tr>
<tr>
<td>P</td>
<td>D</td>
<td>L</td>
<td>-39</td>
<td>3</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>39</td>
<td>3</td>
<td>69</td>
<td>*</td>
</tr>
<tr>
<td>M</td>
<td>L</td>
<td>-33</td>
<td>-6</td>
<td>54</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>33</td>
<td>0</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>L</td>
<td>-42</td>
<td>3</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
<td>42</td>
<td>6</td>
<td>33</td>
<td></td>
</tr>
</tbody>
</table>

Figure 24: Representation of ROI Distribution. ROIs are shown on axial slices starting inferiorly and proceeding superiorly from left to right, top to bottom. Slice distribution image included for reference. Legend: A = Anterior, M = Middle, P = Posterior; D = Dorsal, M = Middle, V = Ventral.
Figure 25: Accuracy by cuetype. Bars show accuracy for each factor arranged left to right in order of decreasing information content. There was a main effect of cuetype for accuracy, $F(3, 48) = 19.564, p < .001, \eta^2_p = .550$. Legend: 2 = “both” cues; 1H = “hand-only” cues; 1J = “judgment-only” cues; 0 = “no information” cues.

.001, $\eta^2_p = .550$; that is, performance differed as a function of which cue participants received on a given trial. These results are illustrated in Figure 25. There was also a significant effect of dimension, $F(3, 48) = 5.109, p = .004, \eta^2_p = .242$; that is, performance differed as a function of the specific dimension participants were responding to each trial. These results are illustrated in Figure 26. There was furthermore an effect of epoch, $F(3, 48) = 4.803, p = .005, \eta^2_p = .231$; that is, performance changed over time. These results are illustrated in Figure 27. The main effect of congruency was not significant, $F(1, 16) = .184, p = .673, \eta^2_p = .011$.

To better understand the differences in performance underlying these main effects, we performed post-hoc pairwise comparisons separately within each effect. All post-hoc comparisons were corrected using the Bonferroni procedure. For the effect of cuetype, cues that indicated both the response hand and the judgment type (henceforth referred to as “Both” cues) were more accurate than all other cuetypes, and cues that indicated no information (henceforth referred to as “noninformative” cues) were less accurate than all other cuetypes except cues for the judgment type only (“Judgment” cues). Cues for the response hand
**Figure 26:** Accuracy by Epoch. Each epoch averaged across 4 runs. There was a main effect of epoch for accuracy, $F(3, 48) = 4.803, p = .005, \eta^2_p = .231$.

**Figure 27:** Accuracy by Dimension. There was a main effect of dimension for accuracy, $F(3, 48) = 5.109, p = .004, \eta^2_p = .242$. 
Table 5: Pairwise Comparisons of Main Effect of cuetype on Accuracy. Mean values shown are % correct. **: Significant after correction; *: Significant.

<table>
<thead>
<tr>
<th>Pair</th>
<th>Mean</th>
<th>S.E.</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Hand</td>
<td>0.039</td>
<td>± 0.012</td>
<td>.028*</td>
</tr>
<tr>
<td>– Judgment</td>
<td>0.073</td>
<td>± 0.016</td>
<td>.002*</td>
</tr>
<tr>
<td>– Neither</td>
<td>0.120</td>
<td>± 0.017</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Hand</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Judgment</td>
<td>0.034</td>
<td>± 0.014</td>
<td>.185</td>
</tr>
<tr>
<td>– Neither</td>
<td>0.080</td>
<td>± 0.015</td>
<td>.001*</td>
</tr>
<tr>
<td>Judgment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Neither</td>
<td>0.046</td>
<td>± 0.021</td>
<td>.266</td>
</tr>
</tbody>
</table>

Table 6: Pairwise Comparisons of Main Effect of Dimension on Accuracy. Mean values shown are % correct. *: Significant.

<table>
<thead>
<tr>
<th>Pair</th>
<th>Mean</th>
<th>S.E.</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Convexity</td>
<td>-0.024</td>
<td>± 0.020</td>
<td>1.000</td>
</tr>
<tr>
<td>– Horizontal</td>
<td>0.041</td>
<td>± 0.022</td>
<td>.502</td>
</tr>
<tr>
<td>– Vertical</td>
<td>-0.028</td>
<td>± 0.017</td>
<td>.717</td>
</tr>
<tr>
<td>Convexity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Horizontal</td>
<td>0.065</td>
<td>± 0.022</td>
<td>.058</td>
</tr>
<tr>
<td>– Vertical</td>
<td>-0.003</td>
<td>± 0.017</td>
<td>1.000</td>
</tr>
<tr>
<td>Horizontal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Vertical</td>
<td>-0.068</td>
<td>± 0.019</td>
<td>.017*</td>
</tr>
</tbody>
</table>

(“Hand” cues) and Judgment cues were not different from each other. These results are summarized in Table 5. For the effect of dimension, trials in which participants responded to horizontal location were significantly less accurate than those in which they respond to vertical location; no other pairwise comparisons were significant for this effect. These results are summarized in Table 6. Finally, for the effect of epoch, epoch 1 was significantly less accurate than epoch 2; no other pairwise comparisons were significant for this effect. These results are summarized in Table 7.

In addition to these main effects, there was also a significant interaction between dimension and congruency, $F(3, 48) = 4.506, p = .007, \eta^2_p = .220$. This interaction is illustrated in Figure 28. In other words, the difference in accuracy on each dimension depended on whether participants learned a congruent (i.e., “inside” responses mapped to the index fingers) or incongruent (i.e., “inside” responses mapped to the middle fingers) mapping for the horizontal location dimension. No other interactions were significant. Post-hoc comparisons
Table 7: Pairwise Comparisons of Main Effect of Epoch on Accuracy. Mean values shown are % correct. *: Significant.

<table>
<thead>
<tr>
<th>Pair</th>
<th>Mean</th>
<th>S.E.</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epoch 1 – Epoch 2</td>
<td>-0.058</td>
<td>± 0.016</td>
<td>.016*</td>
</tr>
<tr>
<td>Epoch 2 – Epoch 3</td>
<td>-0.037</td>
<td>± 0.016</td>
<td>.199</td>
</tr>
<tr>
<td>Epoch 2 – Epoch 4</td>
<td>0.021</td>
<td>± 0.015</td>
<td>1.000</td>
</tr>
<tr>
<td>Epoch 3 – Epoch 4</td>
<td>0.019</td>
<td>± 0.011</td>
<td>.743</td>
</tr>
</tbody>
</table>

of all interaction effects did not reveal significant pairwise differences between conditions (Table 10).

4.2.1.2 Reaction Time

RTs were analyzed for correct trials only. The ANOVA revealed a main effect of cuetype, $F(3, 48) = 308.208, p < .001, \eta_p^2 = .951$; that is, performance differed as a function of which cue participants received on a given trial. These results are illustrated in Figure 29. There was also a significant effect of dimension, $F(3, 48) = 9.475, p < .001, \eta_p^2 = .372$; that is, performance differed as a function of the specific dimension participants are responding to each trial. These results are illustrated in Figure 30. There was furthermore an effect of epoch, $F(3, 48) = 3.561, p = .021, \eta_p^2 = .182$; that is, performance changed over time. These results are illustrated in Figure 31. The main effect of congruency was not significant, $F(1, 16) = .335, p = .571, \eta_p^2 = .020$.

To better understand the differences in performance underlying these main effects, we performed planned pairwise comparisons separately within each effect. All comparisons were corrected using the Bonferroni procedure. For the effect of cuetype, Both cues were faster than all other cuetypes, and noninformative cues were slower than all other cuetypes. Hand cues and Judgment cues were not different from each other. These results are summarized in Table 8. For the effect of dimension, trials in which participants responded to horizontal location were significantly slower than those in which they responded to either color or vertical location; no other pairwise comparisons were significant for this effect. These results
Figure 28: Interaction of Dimension and Congruency on Accuracy. Accuracy differed by dimension as a function of whether participants’ mapping was congruent or incongruent for the horizontal location dimension. $F(3, 48) = 4.506, p = .007, \eta^2_p = .220$.

Figure 29: RT by cuetype. Bars show accuracy for each factor arranged left to right in order of decreasing information content. There was a main effect of cuetype for accuracy, $F(3, 48) = 308.208, p < .001, \eta^2_p = .951$. Legend: 2 = “both” cues; 1H = “hand-only” cues; 1J = “judgment-only” cues; 0 = “no information” cues. Results shown for correct trials only.
Figure 30: RT by Dimension. There was a main effect of dimension for accuracy, $F(3, 48) = 9.475, p < .001, \eta^2_p = .372$. Results shown for correct trials only.

Figure 31: RT by Epoch. Each epoch averaged across 4 runs. There was a main effect of epoch for accuracy, $F(3, 48) = 3.561, p = .021, \eta^2_p = .182$. Results shown for correct trials only.
Table 8: Pairwise Comparisons of Main Effect of cuetype on RT. Mean values shown are in seconds. **: Significant after correction; *: Significant.

<table>
<thead>
<tr>
<th>Pair</th>
<th>Mean</th>
<th>S.E.</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both</td>
<td>-0.141</td>
<td>± 0.006</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>- Hand</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Judgment</td>
<td>-0.157</td>
<td>± 0.006</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>- Neither</td>
<td>-0.215</td>
<td>± 0.010</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Hand</td>
<td>-0.016</td>
<td>± 0.007</td>
<td>.148</td>
</tr>
<tr>
<td>- Judgment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Neither</td>
<td>-0.074</td>
<td>± 0.008</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Judgment</td>
<td>-0.057</td>
<td>± 0.007</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>- Neither</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 9: Pairwise Comparisons of Main Effect of Dimension on RT. Mean values shown are in seconds. *: Significant.

<table>
<thead>
<tr>
<th>Pair</th>
<th>Mean</th>
<th>S.E.</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>-0.040</td>
<td>± 0.023</td>
<td>.599</td>
</tr>
<tr>
<td>- Convexity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Horizontal</td>
<td>-0.106</td>
<td>± 0.023</td>
<td>.002*</td>
</tr>
<tr>
<td>- Vertical</td>
<td>0.025</td>
<td>± 0.025</td>
<td>1.000</td>
</tr>
<tr>
<td>Convexity</td>
<td>-0.066</td>
<td>± 0.029</td>
<td>.228</td>
</tr>
<tr>
<td>- Horizontal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Vertical</td>
<td>0.065</td>
<td>± 0.032</td>
<td>.341</td>
</tr>
<tr>
<td>Horizontal</td>
<td>0.131</td>
<td>± 0.024</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>- Vertical</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

are summarized in Table 9. Finally, for the effect of epoch, epoch 3 was significantly faster than epoch 1; no other pairwise comparisons were significant for this effect (not shown).

In addition to these main effects, there were also a number of significant interactions. cuetype interacted with dimension as illustrated in Figure 32, $F(9,144) = 3.269, p = .001, \eta^2_p = .170$. That is, the RT benefit of the amount of information contained in the cue was influenced by the dimension the participant responded to on each trial. There were also interactions between congruency and both cuetype, $F(3,48) = 5.239, p = .003, \eta^2_p = .247$ (Figure 33) and dimension, $F(3,48) = 4.464, p = .008, \eta^2_p = .218$ (Figure 34). That is, the effects of cuetype and dimension both depended on the congruency of the participant’s mapping for the horizontal location condition. No other interactions were significant. Planned comparisons of all interaction effects did not reveal significant pairwise differences between conditions.
Table 10: Pairwise Comparisons of Main Effect of Epoch on RT. Mean values shown are in seconds. *: Significant.

<table>
<thead>
<tr>
<th>Pair</th>
<th>Mean</th>
<th>S.E.</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epoch 1 − Epoch 2</td>
<td>0.019</td>
<td>± 0.012</td>
<td>.748</td>
</tr>
<tr>
<td>− Epoch 3</td>
<td>0.037</td>
<td>± 0.011</td>
<td>.027*</td>
</tr>
<tr>
<td>− Epoch 4</td>
<td>0.022</td>
<td>± 0.011</td>
<td>.756</td>
</tr>
<tr>
<td>Epoch 2 − Epoch 3</td>
<td>0.018</td>
<td>± 0.010</td>
<td>.558</td>
</tr>
<tr>
<td>− Epoch 4</td>
<td>0.003</td>
<td>± 0.012</td>
<td>1.000</td>
</tr>
<tr>
<td>Epoch 3 − Epoch 4</td>
<td>-0.015</td>
<td>± 0.009</td>
<td>.787</td>
</tr>
</tbody>
</table>

Figure 32: Interaction of cuetype and Dimension on RT. The influence of the cuetype on RT differed as a function of the dimension being responded to on a given trial. $F(9, 144) = 3.269, p = .001, \eta_p^2 = .170$. 
Figure 33: Interaction of cuetype and Congruency on RT. The influence of the cuetype on RT differed as a function of whether participants’ mapping was congruent or incongruent for the horizontal location dimension. $F(3, 48) = 5.239, p = .003, \eta^2_p = .247$.

Figure 34: Interaction of Dimension and Congruency on RT. The influence of the judgment dimension on RT differed as a function of whether participants’ mapping was congruent or incongruent for the horizontal location dimension. $F(3, 48) = 4.464, p = .008, \eta^2_p = .218$. 
4.3 Imaging Results

We conducted a whole-brain GLM for each of our combinations of factors (viz., cuetype, judgment type, and response hand) with the cue and stimulus event timepoints defined separately for each. We next masked the whole brain results to the PFC and performed group contrasts on a number of contrasts of interest, as described in the following sections. All contrasts are corrected for the false discovery rate (FDR) to a level of \((q < .05)\) and show results in the positive direction only unless otherwise noted.

4.3.1 Visualization of Whole Brain Main Effects

We first visualized the patterns of activity for the main effects of each of our factors of interest at the cue and stimulus timepoints by mapping each contrast onto the same brain space to identify regions of overlap versus those unique to individual contrasts.

For the main effect of cuetype, we combined covariates across judgment types and response hands for each cuetype and compared them to baseline. The results of these contrasts are shown in Figure 35 for the cue timepoint and Figure 36 for the stimulus timepoint. In brief, at the cue, the main effect of cuetype manifested as a pattern of activity in which cues with more information (Both cues) were processed in more caudal regions, while cues with less information were processed more rostrally. More specifically, Hand and Judgment cues, both of which specify one of two possible pieces of information, showed activity in largely the same areas, slightly more rostral than the areas activated by Both cues. Noninformative cues demonstrated generally less activity than the other cuetypes, with peaks surviving correction only in a few locations in medial PFC and in the frontal pole, which was the most rostral peak located for any of our four cuetypes. Furthermore, when our contrasts were left uncorrected (all positive activity only), noninformative cues uniquely showed activity in bilateral frontal pole; the latter is additionally shown in Figure 37. It is also noted that, across the Both, Hand, and Judgment cuetypes (and noninformative cues as well, when uncorrected), there was a large area of common activation that spanned most of the length of the middle frontal gyrus and deflected dorsally at the caudal end, lateralized to the left side of the brain. A similar pattern of common activation was observed at the stimulus
Figure 35: Main Effect of Cue at the Cue Timepoint. Cues imparting different amounts of information showed segregation of activity along a rostrocaudal gradient, irrespective of the exact type of information contained in the cue. A) Hand and Judgment cues mapped additively to the same brain space. B) Both cues mapped additively to the results in (A). C) Noninformative cues mapped additively to the results in (B). D) Multislice view of noninformative cue effect in FPC. E) Multislice view of noninformative cue effect in SFG. Legend applies to all subfigures and shows the range of mapped t-values.

timepoint as well, this time bilaterally; however, the rostrocaudal pattern as a function of cue information described above for the cue timepoint was not readily apparent visually at the stimulus.

For the main effect of response hand, we included only covariates that would indicate one response hand at the cue (i.e., Both cues and Hand cues). We combined across the two possible cuetypes and both judgment types for left and right hand responses and compared them to baseline. The results of these contrasts are shown in Figure 38 for the cue timepoint and Figure 39 for the stimulus timepoint. At the cue, both contrasts revealed a pattern of lateralized activity along the left MFG similar to that common across the cue conditions. In addition to this common activity, left hand cues showed unique activity in right PMC, while right hand cues showed activity in left PMC. In other words, hand cues uniquely activated the PMC in the hemisphere responsible for preparing movements on the indicated side. At the stimulus, much like in the cuetype effect, there was a common region of activation in
Figure 36: Main Effect of Cue at the Stimulus Timepoint. A) Hand and Judgment cues mapped additively to the same brain space. B) Both cues mapped additively to the results in (A). C) Noninformative cues mapped additively to the results in (B). D) Separate mappings of the four cue effects. The stimulus timepoint did not show rostrocaudal segregation by cuetype.

Figure 37: Uncorrected Effect of Cue at the Cue Timepoint. Additive map of all four cuetypes, uncorrected. When left uncorrected, the noninformative cues elicit a strong rostral activation.
Figure 38: Main Effect of Response Hand at the Cue Timepoint. Left and right cues showed lateralized activation in the PMC and M1 according to the region involved in processing movements for the indicated hand at the cue timepoint.

bilateral MFG extending along the entire rostrocaudal axis; in addition, this contrast also showed the lateralized activity in motor regions that was found at the cue timepoint.

Likewise, for the main effect of judgment type, we included only covariates that would indicate one judgment type at the cue (i.e., Both cues and Judgment cues). We combined across the two possible cuetypes and the response hand for spatial and nonspatial judgments and compared them to baseline. At the cue, both contrasts revealed a pattern of lateralized activity along the MFG similar to that common across the cue conditions. The corrected contrasts did not reveal any unique activity for either contrast; however, in the uncorrected contrasts, an additional, unique locus of activity was observed for each contrast in the right hemisphere. More specifically, spatial judgment cues elicited activity in right caudal SFG; on the other hand, object/feature-based judgments elicited activity in IFG/MFG slightly more rostral to the locus of spatial judgment-related activity. This pattern follows the expected separation of spatial and nonspatial processing along the dorsoventral axis. The corrected and uncorrected results are both shown in Figure 40 for the cue timepoint. At the
stimulus timepoint, the same common bilateral activity as the other two main effects was found in both contrasts; however, neither the corrected nor the uncorrected contrasts showed any unique activity patterns. An additive map of the corrected contrasts at the stimulus timepoint is shown on both the 3-D surface and in multislice format (axial orientation) in Figure 41.

4.3.2 ROI Analysis

4.3.2.1 Cue Timepoint

Beta values extracted for each ROI were first subjected to a six-way repeated measures ANOVA, where factors were defined for cuetype (4 levels), judgment (2), and response hand (2), as well as each of 3 location directions, anterior-posterior (3), dorsal-ventral (3), and hemisphere (2). This analysis revealed a main effect for cuetype, $F(3, 51) = 6.119, p = .001, \eta_p^2 = .265$, illustrated in Figure 42, indicating that activity was different based on the amount of information presented at the cue. There was also a main effect of rostrocaudal location, $F(2, 34) = 3.992, p = .028, \eta_p^2 = .190$ (Figure 43), indicating that

Figure 39: Main Effect of Response Hand at the Stimulus Timepoint. Left and right cues showed lateralized activation in the PMC and M1 according to the region involved in processing movements for the indicated hand at the stimulus timepoint.
**Figure 40:** Main Effect of Judgment Type at the Cue Timepoint. A) Judgment cues did not show unique activity after correction. B) Uncorrected results showed separate activity in right hemisphere for spatial and nonspatial processing along a dorsoventral axis.
Figure 41: Main Effect of Judgment Type at the Stimulus Timepoint. A) Additive rendering of contrasts on prefrontal surface. Judgment cues did not show unique activity after correction. B) Multislice axial rendering of contrasts throughout prefrontal cortex. Slices are ordered starting at the lowest slice in the bottom left and proceeding left to right, bottom to top.
Figure 42: ROI Main Effect of Cuetype at the Cue Timepoint. Activity differed by cue type. This interaction was driven by the difference between the noninformative cue and the other informative cues. $F(3, 51) = 6.119, p = .001, \eta^2_p = .265$. Legend: B = Both, H = Hand, J = Judgment, N = Noninformative.

preparatory activity varied intrinsically with location along this axis, and a main effect of hemisphere, $F(1, 17) = 44.153, p < .001, \eta^2_p = .722$ (Figure 44), indicating that the magnitude of preparatory activity differs between hemispheres.

The interaction terms in this analysis consisted of three types. Experimental factors could interact with other experimental factors, indicating differences in activity to experimental factors that depended on the level of another experimental factor, consistent across ROIs. Location factors could interact with other location factors, indicating intrinsic differences in activity across the ROIs independent of the experimental manipulations. Finally, experimental factors could interact with location factors, indicating that experimental manipulations engaged processes that were localized to different subregions of the PFC. There were no significant interactions purely between experimental factors.

In terms of significant location-location interactions, dorsoventral location interacted with hemisphere, $F(1.284, 21.830) = 5.569, p = .021, \eta^2_p = .247$. Furthermore, there was a significant three-way interaction for all location terms (rostrocaudal location, dorsoventral
Figure 43: ROI Main Effect of Rostrocaudal Location at the Cue Timepoint. Activity intrinsically varied along the rostrocaudal axis. $F(2, 34) = 3.992, p = .028, \eta^2_p = .190$. Legend: A = Anterior, M = Middle, P = Posterior.

Figure 44: ROI Main Effect of Hemisphere at the Cue Timepoint. Activity in the left hemisphere was greater than in the right hemisphere. $F(1, 17) = 44.153, p < .001, \eta^2_p = .722$. Legend: L = Left, R = Right.
activity to the cues depended on location along the rostrocaudal axis. This interaction was still significant when noninformative cues were removed. $F(5.694, 96.799) = 4.703, p < .001, \eta^2_p = .217$. Legend: B = Both, H = Hand, J = Judgment, N = Noninformative; A = Anterior, M = Middle, P = Posterior.

Finally, a number of significant interactions involved both experimental and location factors. Cuetype interacted with rostrocaudal location, $F(5.694, 96.799) = 4.703, p < .001, \eta^2_p = .217$, indicating that different cues were engaging each location along the axis in different proportions. This interaction is shown in Figure 45. Cuetype and rostrocaudal location further interacted with dorsoventral location, $F(8.866, 150.726) = 3.204, p = .001, \eta^2_p = .159$, indicating that the different rostrocaudal activity patterns further depended on dorsoventral location. Cuetype also interacted with hemisphere, $F(3, 51) = 20.881, p < .001, \eta^2_p = .551$, indicating that the cues showed different levels of lateralization. This interaction is shown in Figure 46. Furthermore, cuetype interacted with all three location factors, $F(8.925, 151.720) = 5.649, p < .001, \eta^2_p = .249$, indicating that these patterns further depended on hemisphere.

Response hand interacted with hemisphere as well, $F(1, 17) = 5.666, p = .029, \eta^2_p = .250,$ Figure 45: ROI Cuetype x Rostrocaudal Location Interaction at the Cue Timepoint. Activity to the cues depended on location along the rostrocaudal axis. This interaction was still significant when noninformative cues were removed. $F(5.694, 96.799) = 4.703, p < .001, \eta^2_p = .217$. Legend: B = Both, H = Hand, J = Judgment, N = Noninformative; A = Anterior, M = Middle, P = Posterior.
Figure 46: ROI Cuetype x Hemisphere Interaction at the Cue Timepoint. Activity to the cues depended on hemisphere. This was likely driven by the noninformative cue. $F(3,51) = 20.881, p < .001, \eta_p^2 = .551$. Legend: B = Both, H = Hand, J = Judgment, N = Noninformative; L = Left, R = Right.

indicating that activity was biased to different hemispheres based on the hand being prepared to make the response. Planned comparisons showed significant differences only for Left greater than Right hemisphere for each response hand (Left hand: $t(17) = 6.749, p < .001$; Right hand: $t(17) = 7.946, p < .001$); however, Figure 47 visually shows a pattern that suggests biasing according to the hemisphere that would process the response hand. These two factors further interacted with rostrocaudal location, $F(1.511,25.684) = 3.714, p = .049, \eta_p^2 = .179$, indicating that the response hand biasing occurred in different locations rostrocaudally as a function of hemisphere. Like the cuetype factor, response hand interacted with all three location factors as well, $F(4,68) = 6.631, p < .001, \eta_p^2 = .281$, indicating that these patterns further depended on dorsoventral location. Additionally, there was a four-way interaction between cuetype, hand, rostrocaudal location, and hemisphere, $F(6,102) = 3.185, p = .007, \eta_p^2 = .158$, indicating that the pattern of biasing by response hand was cue-dependent as well.

The only significant interaction involving judgment domain was a three-way interaction
Figure 47: ROI Response Hand x Hemisphere Interaction at the Cue Timepoint. Activity for left versus right hand responses depended on hemisphere. \( F(1,17) = 5.666, p = .029, \eta^2_p = .250 \). Legend: L = Left, R = Right.

with response hand and rostrocaudal location, \( F(2,34) = 4.820, p = .014, \eta^2_p = .221 \).

Planned pairwise comparisons revealed that the main effect of cuetype was driven by a difference between the noninformative cue and the other cuetypes, where all three informative cuetypes produced significantly greater activity than the noninformative cue (not shown). In fact, the noninformative cue elicited little to no activity, indicating that participants were not engaging in preparatory processes when presented with a noninformative cue. Because of this, it is possible that some or all of the interactions involving cuetype simply reflected this difference, rather than differences in preparatory processes to different informative cues. Likewise, the main effect of hemisphere was due to significantly higher activity in the left hemisphere than the right across conditions; in other words, preparatory processing in this task appears to be lateralized to the left hemisphere. In fact, average activity in the right hemisphere was close to zero, implying that preparatory activity was largely confined to the left hemisphere. Again, this may mean that interaction terms involving hemisphere simply be reflected this disparity. Furthermore, except for one interaction, judgment domain was not involved in any other effects, suggesting that the preparatory
processes being engaged in this task may not be sensitive to spatial/nonspatial domain.

In order to identify which of the effects from this analysis were theoretically meaningful, we repeated the analysis of the cue timepoint using activity just to informative cues in ROIs located only in the left hemisphere, collapsed across judgment domains (3x2x3x3 design). The reduced model identified main effects for rostrocaudal location, $F(2, 34) = 4.652, p = .016, \eta^2_p = .215$, and dorsoventral location, $F(1.422, 24.167) = 4.045, p = .043, \eta^2_p = .192$. There was also a significant interaction between these two factors, $F(2.753, 46.797) = 4.631, p = .008, \eta^2_p = .214$, shown in Figure 48. Additionally, there is a significant interaction between cuetype and rostrocaudal location, $F(3.329, 56.587) = 2.749, p = .046, \eta^2_p = .139$. No other terms are significant in this reduced model, suggesting that the effects identified only in the full model were due to one of the three factors showing minimal influence on processing in this experiment.

To understand the nature of the interaction between cuetype and rostrocaudal axis, we have conducted planned comparisons between cuetypes at each rostrocaudal location,
as well as comparisons between locations for each cuetype (left hemisphere only) using two-tailed tests. When comparing between cuetypes at a given location, no comparisons were significant. On the other hand, comparisons for different locations for a given cuetype showed a number of effects. For Both cues, Posterior regions showed significantly higher activity than both Anterior, \( t(17) = 3.491, p = .003 \), and Middle regions, \( t(17) = 2.608, p = .018 \). Posterior regions showed significantly higher activity than Anterior regions for Hand, \( t(17) = 2.169, p = .045 \), and Judgment, \( t(17) = 2.550, p = .021 \) cues as well. While comparisons between Middle and Posterior regions for these latter cuetypes were not significant, they did show a similar trend to the effect seen in Both cues. Anterior and Middle regions did not show significant differences in any cuetypes.

4.3.2.2 Stimulus Timepoint

As in the cue timepoint, beta values extracted for each ROI were subjected to a six-way repeated measures ANOVA, where factors were defined for cuetype (4 levels), judgment (2), and response hand (2), as well as each of 3 location directions, anterior-posterior (3), dorsal-ventral (3), and hemisphere (2). This analysis likewise revealed a main effect for cuetype, \( F(3, 51) = 11.968, p < .001, \eta_p^2 = .413 \), illustrated in Figure 49, again indicating that activity generally depended on the amount of information presented at the cue. There was also a main effect of judgment, \( F(1, 17) = 7.594, p = .014, \eta_p^2 = .309 \), shown in Figure 50, indicating that activity also generally differed by the specific judgment being made on a given trial. There were main effects for all three location factors as well: rostrocaudal location, \( F(2, 34) = 11.357, p < .001, \eta_p^2 = .401 \) (Figure 51); dorsoventral location, \( F(1.472, 25.018) = 17.927, p < .001, \eta_p^2 = .401 \) (Figure 52); and hemisphere, \( F(1, 17) = 4.518, p = .048, \eta_p^2 = .210 \) (Figure 53). As in the cue timepoint, these effects indicate underlying inherent differences in activity across our ROIs.

There were no significant interactions purely between experimental factors. In terms of significant location-location interactions, rostrocaudal location interacted with dorsoventral location, \( F(2.165, 36.799) = 15.222, p < .001, \eta_p^2 = .472 \). Furthermore, there was a significant three-way interaction for all three location terms, \( F(3.200, 54.406) = 4.023, p = \)
Figure 49: ROI Main Effect of Cuetype at the Stimulus Timepoint. Activity across ROIs depended on the cue. This effect was driven by the Both cue condition. $F(3, 51) = 11.968, p < .001, \eta_p^2 = .413$. Legend: B = Both, H = Hand, J = Judgment, N = Noninformative.

Figure 50: ROI Main Effect of Judgment Type at the Stimulus Timepoint. Activity was greater for the spatial domain than for the object/feature domain. $F(1, 17) = 7.594, p = .014, \eta_p^2 = .309$. Legend: S = Spatial; O = Object.
Figure 51: ROI Main Effect of Rostrocaudal Location at the Stimulus Timepoint. Activity intrinsically varied along the rostrocaudal axis. $F(2, 34) = 11.357, p < .001, \eta^2_p = .401$. Legend: A = Anterior, M = Middle, P = Posterior.

Figure 52: ROI Main Effect of Dorsoventral Location at the Stimulus Timepoint. Activity intrinsically varied along the dorsoventral axis. $F(1.472, 25.018) = 17.927, p < .001, \eta^2_p = .401$. Legend: D = Dorsal, M = Middle, V = Ventral.
Figure 53: ROI Main Effect of Hemisphere at the Stimulus Timepoint. Activity in the left hemisphere was greater than in the right hemisphere. $F(1, 17) = 4.518, p = .048, \eta^2_p = .210$. Legend: L = Left, R = Right.

$.010, \eta^2_p = .191$; these terms again indicated intrinsic activity differences in our ROIs.

Again, the majority of interactions involved both experimental and location factors. Cuetype interacted with each location factor: rostrocaudal location, $F(6, 102) = 2.779, p = .015, \eta^2_p = .141$, shown in Figure 54; dorsoventral location, $F(6, 102) = 3.870, p = .002, \eta^2_p = .185$; and hemisphere, $F(2.391, 40.650) = 5.659, p = .004, \eta^2_p = .250$. Cuetype also interacts with all three location factors, $F(8.819, 149.919) = 2.538, p = .010, \eta^2_p = .130$. These terms indicate that activity to different cues depended on location along all three axes.

Response hand interacted with hemisphere, $F(1, 17) = 4.783, p = .043, \eta^2_p = .220$, as in the cue time period. This interaction is shown in Figure 55. These two factors further interacted with dorsoventral location, $F(1.241, 21.099) = 14.974, p < .001, \eta^2_p = .468$, shown in Figure 56, indicating that the response hand biasing occurred in different locations dorsoventrally as a function of hemisphere. Like the cuetype factor and as in the cue timepoint, response hand further interacted with all three location factors, $F(2.555, 43.435) = 5.426, p = .004, \eta^2_p = .242$, indicating that these patterns further depended on rostrocaudal
Location. Additionally, there was a four-way interaction between cuetype, hand, dorsoventral location, and hemisphere, $F(4.894, 83.201) = 2.650, p = .029, \eta^2_p = .135$, indicating that the pattern of biasing by response hand was cue dependent as well.

The only significant interaction involving judgment domain was a three-way interaction with rostrocaudal and dorsoventral location, $F(3.223, 54.790) = 3.503, p = .019, \eta^2_p = .171$.

Planned pairwise comparisons revealed that the main effect of cuetype was driven by a difference between the Both cue and the other cuetypes, where all three other cuetypes produced significantly greater activity than the Both cue (not shown). However, unlike the cue timepoint, in which noninformative cues elicited no activity, Both cues did produce positive activity to the stimulus. At this timepoint, the effect of cuetype was likely due to the difference in preparation between both cues and other cuetypes during the cue time period; in other words, the lower activity for Both cues at the stimulus timepoint was likely due to the additional preparation the extra piece of information afforded participants at the cue timepoint. The main effect of hemisphere was due to significantly higher activity in
the left hemisphere than the right across conditions, as seen at the cue timepoint; however, in this case, there was positive activity in both hemispheres, suggesting that task execution activity is bilateral, with some additional processes being left-lateralized. Again as in the cue timepoint, the judgment factor was only involved in one interaction; however, unlike the cue timepoint, this interaction involved the dorsoventral axis, suggesting that domain sensitivity may be a feature of task execution, rather than preparation.

While the reduced model used in the cue timepoint did not appear to be an appropriate fit for the stimulus timepoint, we used a reduced model that assessed ROIs in the left hemisphere only to understand how the preparatory effects identified for the cue timepoint may remain consistent or change at the cue timepoint. The reduced model identified main effects for: cuetype, $F(3,51) = 14.109, p < .001, \eta^2_p = .454$; judgment domain, $F(1,17) = 4.667, p = .045, \eta^2_p = .215$; rostrocaudal location, $F(2,34) = 9.592, p < .001, \eta^2_p = .361$; and dorsoventral location, $F(2,34) = 11.497, p < .001, \eta^2_p = .403$. There were significant two-way interactions between dorsoventral location and a number of factors: cuetype, $F(4.287,72.874) = 3.001, p = .021, \eta^2_p = .150$, shown in Figure 57; hand,
Figure 56: ROI Response Hand x Hemisphere x Dorsoventral Location Interaction at the Stimulus Timepoint. $F(1.241, 21.099) = 14.974, p < .001, \eta^2_p = .468$. (Top) Hemisphere x response hand interaction in dorsal ROIs. There is a visual pattern of hemispheric biasing in these regions. (Middle) Hemisphere x response hand interaction in middle ROIs. (Bottom) Hemisphere x response hand interaction in ventral ROIs. Legend: L = Left, R = Right; D = Dorsal, M = Middle, V = Ventral.
Figure 57: ROI Cuetype x Dorsoventral Location Interaction at the Stimulus Timepoint, Reduced Model. Activity to the cues depended on location dorsoventrally. This effect was likely driven by the Both cue condition. \( F(4.287,72.874) = 3.001, p = .021, \eta_p^2 = .150 \). Legend: B = Both, H = Hand, J = Judgment, N = Noninformative; D = Dorsal, M = Middle, V = Ventral.

\( F(1.408, 23.936) = 7.068, p = .008, \eta_p^2 = .294 \); and rostrocaudal location, \( F(1.890, 32.133) = 17.264, p < .001, \eta_p^2 = .504 \). Finally, the model identified a three-way interaction between judgment domain, rostrocaudal location, and dorsoventral location, \( F(3.686, 62.667) = 2.955, p = .030, \eta_p^2 = .148 \), shown in Figure 58. Further reducing the model by removing Both cues from the analysis to mirror the cue timepoint analysis only removed the main effect of cuetype and the interaction between cuetype and dorsoventral location, indicating that these effects were driven by the uniquely low activity exhibited by the Both cuetype.

To understand the nature of the interactions between response hand and the dorsoventral axis and hemisphere factors, we conducted planned comparisons using two-tailed t-tests. Activity was greater in the left hemisphere than the right for right handed responses, \( t(17) = 3.520, p = .003 \). No other comparisons were significant for this the response hand by hemisphere interaction. Analyses for the dorsoventral location interaction were conducted in the left hemisphere only. For comparisons between response hands at a given dorsoventral location, no comparisons were significant. For comparisons within response
Figure 58: ROI Judgment Type x Dorsoventral Location x Rostrocaudal Location Interaction at the Stimulus Timepoint, Reduced Model. $F(3.686, 62.667) = 2.955, p = .030, \eta^2_p = .148$. (Top) Hemisphere x response hand interaction in dorsal ROIs. There is a visual pattern of hemispheric biasing in these regions. (Middle) Hemisphere x response hand interaction in middle ROIs. (Bottom) Hemisphere x response hand interaction in ventral ROIs. Legend: S = Spatial; O = Object; A = Anterior, M = Middle, P = Posterior; D = Dorsal, M = Middle, V = Ventral.
hand between different locations, dorsal regions were greater than middle regions for both
hands (Left: \( t(17) = 3.435, p = .003 \); Right: \( t(17) = 3.915, p = .001 \)) and ventral regions
were greater than middle regions for both hands (Left: \( t(17) = 6.113, p < .001 \); Right:
\( t(17) = 5.057, p < .001 \)).
The current experiment aimed to investigate the subregional functional structure of the PFC using a novel task, the hierarchical precuing task, that incorporates manipulations of task complexity, decision domain, and response hand. The current analyses adapted the univariate methods from previous investigations of PFC organization (Badre & D'Esposito, 2007; Nee & D'Esposito, 2016) to the current task. The results demonstrate that the hierarchical precuing task is a behaviorally valid variation on the traditional precuing paradigm, and that it can be used to engage processes that are distributed along multiple axes of organization in the brain.

5.1 Behavioral Validity

Despite the complexity of the task, participants were able to learn and execute the task within the practice session, and were able to perform at criterion for the duration of the fMRI session. The behavioral results showed that participants did, in fact, benefit from informative cues, consistent with previous literature (Miller, 1982; Reeve & Proctor, 1984). More specifically, the results showed a stair-step benefit to informative cues such that participants responded faster and more accurately when provided more information at the cue, regardless of what that information was (see Figure 28). Previous cuing experiments using multi-level cues, such as Rosenbaum (1980, 1983), have also shown incremental benefits to the cue as the amount of imparted information increases, suggesting that the current design may be engaging the same processes as standard cuing paradigms. There were small differences in performance as a function of the relevant judgment dimension for a given trial (see Figure 29); however, the pilot experiments allowed us to adjust the dimensions to minimize these differences, and they did not appear to substantially influence participants’ ability to use the cue (Figure 31). Likewise, there were small changes in performance as a function of time across the experimental session (Figure 30), but participants performed at ceiling
across the experimental session (Figure 26), and the small differences over time did not appear to significantly impact the way participants interacted with the cue itself. Future implementations of this design should likewise be sure to check that the manipulations used have equated performance as much as possible, and that participants are given adequate time to reach performance criterion on the first session.

5.2 The Rostrocaudal Axis

The cues in the hierarchical precuing design provided participants with three different levels of information. It was hypothesized that these different levels of information would allow for the preparation of sets of various sizes and complexities, and that this preparatory process would engage different locations along the rostrocaudal axis according to the amount, and possibly the type, of information contained within the cue. The primary effect of interest from the ROI analysis was the interaction between cuetype and rostrocaudal location (See Figure 44). This interaction term supports the hypothesis that the cues are engaging processes that are supported by different subregions along the rostrocaudal axis. There was also main effect of cuetype that was driven by a pattern of generally low activity to noninformative cuetypes (Figure 41); however, the interaction effect was identified in both the full and reduced models, indicating that the differences in activity rostrocaudally were not simply due to this lack of activity, but rather a real effect due to differences in processing of informative cues giving different information. Planned comparisons did not clearly identify the driving force of this interaction; however, both the whole brain illustration (Figure 34) and the graph of the ROI results suggested that the effect was driven by a difference between the Both cue and the other informative cues. More specifically, processing of Both appeared to be seated more caudally than that that processes Hand and Judgment cues. Hand and Judgment cues appeared to have a similar pattern of activity across rostrocaudal locations, consistent with the behavioral results, which did not show a difference in performance between these two conditions.

Taken together, these results support the hypothesis that the cues allow participants to reduce the task set on a given trial to different levels of relational complexity, in keeping
with the control demand theory (Badre, 2008). More specifically, Both cues appear to reduce the set to a level of feature control, which is processed in caudal PFC; Hand and Judgment cues reduce the set to a level of relational control, which is processed more rostrally; and noninformative cues appear not to engage preparatory processes during the cue timepoint. This latter result explains the limited activity in the most rostral regions of PFC (notably, this limited rostral progression is similar to the results of Cookson, Hazeltine, and Schumacher, in press, which showed no rostral activity). If participants were preparing the full task contingency to the noninformative cue, perhaps at a demand requiring episodic control, we would expect this cue to show a similar left-lateralized activity pattern that was seated more rostrally than the informative cuetyp. However, because participants were not engaging preparatory processes for trials that would require the most complex representation of the task, cue-related activity was generally limited to regions between mid lateral PFC and PMC in this task. Future iterations of this design could further manipulate the engagement of processes along the rostrocaudal axis by introducing a third level to the precuing hierarchy that requires the specification of a third task feature to execute the task, perhaps by introducing a temporal component of the task as in previous manipulations of control demand engaging episodic control (Badre, 2008; branching control in control signal theory, Koechlin & Summerfield, 2007). In this case, we would predict that overall activity to the cue would extent further rostrally, and that processing of the informative cues would again be arranged along the rostrocaudal axis in order of the amount of information imparted by the cue, where this newest level activates even more rostral regions than the current task.

The segregation of the cue and stimulus timepoints in this design allowed us to further investigate how this pattern of engagement of processes organized along the rostrocaudal axis differed from the cue to the stimulus timepoint. Previous research on the rostrocaudal axis has relied on block designs (e.g., Koechlin, Ody, & Kouneiher, 2003; Badre & D’Esposito, 2007), which are confounded by processes not directly related to the resolution of task complexity (e.g., motor execution) and cannot speak to whether these processes
are consistent across a trial or occur only at certain stages of processing. The current experiment, in fact, showed different effects at the cue and stimulus timepoints; only at the cue timepoint was there an interaction between cuetype and rostrocaudal location. These results suggest that the processes that are organized by the rostrocaudal axis are being engaged by a cue-specific mechanism specifically, the gating mechanisms being controlled by the PFC’s connections with the striatum. As the current experiment specifically promotes an input gating strategy, it is reasonable to assume that participants are engaging these corticostriatal mechanisms as soon as the cue information is made available. The model proposed by Frank and Badre (2011) posits that these circuits are the underlying mechanism driving recruitment of PFC processes that are arranged rostrocaudally, due to the hierarchical architecture of the connections themselves; therefore, because the cuetypes are engaging rostrocaudally organized processes only at the cue timepoint, it is likely that these circuits are the mechanism underlying cue engagement, and that they occur over a very specific and limited time period over the course of a trial. Thus, the event related design used in the current experiment has allowed us to expand on the theories of rostrocaudal organization by identifying the potential underlying mechanism of these processes and allowing us to understand the dynamics of these processes across a trial.

5.3 The Dorsoventral Axis

The lack of interaction between the DMV axis and the judgment manipulation at the cue timepoint in this task did not support a conception of the dorsoventral axis in which preparatory processing is segregated by spatial versus nonspatial domain. This result may not be surprising, as the organization of the dorsoventral axis is already contentious in the literature. The lack of effect here may have been the result of differences between the current task and previous tasks used to investigate such an effect. Previous literature supporting such a segregation has emerged almost exclusively from working memory tasks (e.g., Levy & Goldman Rakic, 2000), while the current task more closely related to a response selection paradigm. In fact, Schumacher, Elston, and D’Esposito (2003) similarly failed to replicate the dorsoventral spatial/nonspatial segregation effect in a response selection paradigm,
instead identifying a hemispheric segregation for the two domains.

In addition to potential differences in processing demands, the current task may have differed from previous tasks in terms of verbalizability. As described in the introduction, Postle, D’Esposito, and Corkin (2005) posit that different uses of verbal and nonverbal coding strategies may underlie the differences in processing in traditional working memory tasks in the spatial and nonspatial domains. In their study, the spatial working memory task required the encoding and maintenance of a set of three stimulus locations from a 4x6 grid, where the exact point of each stimulus position is varied slightly across the grid structure. This results in a structure that is difficult to assign verbal codes to at the pace of the experiment. On the other hand, the spatial judgments being made here were easily verbalizable, e.g., “ABOVE” versus “BELOW” in the vertical location judgment. While the precise location of the stimulus on screen was varied continuously within the potential presentation windows, the participant may ultimately have translated the spatial information into these verbal codes for subsequent judgment, response selection, and preparation. If indeed the spatial/nonspatial dorsoventral distinction is an epiphenomenon of these verbal versus nonverbal coding strategies, then the current experiment may simply have been only engaging one (verbal) of the two strategies, and thus processing of the two judgment types occurred in approximately the same area of the brain. Notably, the ROIs identified in the current experiment are located more dorsally than the ROIs typically identified in dorsoventral axis investigations (see, for example, Nee & D’Esposito, 2016). Future versions of this design should incorporate different manipulations of the task that allow for the comparison of the different hypotheses of dorsoventral organization.

Rather than a simple epiphenomenon, the event-related design may instead allow us to draw a different, more interesting conclusion. Where the rostrocaudal axis showed interactions at the cue timepoint, but not the stimulus timepoint, the dorsoventral axis showed the reverse. Specifically, the judgment manipulation showed a three-way interaction with rostrocaudal and dorsoventral location at the stimulus timepoint, but not at the cue (Figure 57). This interaction suggests that the judgment manipulation did, in fact, engage processes that are distributed along the dorsoventral axis and, interestingly, that these
patterns differed along the rostrocaudal axis, as has been posited previously (Bahlmann, Blumenfield, & D’Esposito, 2015; Nee & D’Esposito, 2016). However, it also suggests that these execution processes were separate from preparatory processes, which only influenced activity at the cue, and that the interactions reported in those experiments were actually confounds of two separate aspects of task processing that occur at different timepoints in the trial. Notably, the two other investigations of the interactions between the dorsoventral and rostrocaudal axes described here both failed to find an effect of domain using traditional univariate methods; instead, in both cases, pattern classification methods were used to tease apart subthreshold differences in activity to domain manipulations. Future investigations should apply these methods to activity at the cue timepoint to determine if these subthreshold patterns are likewise present here, or if in fact the influences of cuetype and judgment domain are engaging different processes over time.

5.4 Hemispheric Lateralization

Unlike the cuetype and judgment domain effects described above, the response hand manipulation showed effects at both timepoints in these results (see Figures 46 and 54). At both times, specifically, there was an interaction between response hand and hemisphere. The planned comparisons further showed that there was a biasing of processing right-handed responses toward the left hemisphere at both the cue and stimulus timepoints. Activity at both timepoints was strongly left-lateralized, regardless of experimental factors; as such, it is in some ways not surprising that comparisons at this timepoint for the left hand did not show significant differences in the expected direction, instead showing significantly greater activity in the left hemisphere. At the same time, the graphs of the results do suggest a trend for the reverse pattern for left-hand responses.

The current results showed a much weaker biasing than previous work in our lab (Cookson, Hazeltine, & Schumacher, in press). This is likely due to the difference in how the current task nested its factors compared to that experiment. More specifically, Cookson, Hazeltine, and Schumacher employed a task in which each hand was associated with only one of the two stimulus types. On the other hand, in the current experiment, both response
hands were associated with one judgment of each domain. The importance of subset salience in the precuing task is discussed by Adam, Hommel, and Umiltà (2003) and expanded to a general theory of task setting by Hazeltine and Schumacher (2016) in their discussion of task files. Because the hierarchy of the current design overlapped different response hands and judgment domains, there was potential interference, or crosstalk, between the representations of subsets of the task that were activated by the informative cues, which may have resulted in weaker or more distributed recruitment of preparatory processes in the brain that supported this activation. To confirm this, the current design could be simplified so that instead of making decisions on pairs of stimuli, participants could make decisions on single stimuli with two feature sets that have four potential responses, with two mapped to each hand. This manipulation would reduce the relational complexity of the experiment to the same level as that in Cookson, Hazeltine, and Schumacher, while maintaining the uncertainty in the task subsets. Comparing the biasing of response hand in this design versus a design in which all stimuli of a single type were mapped to the same hand would support the necessity of task salience for this preparatory process to occur.

Response hand also interacted with the dorsoventral axis at the stimulus, but not at the cue (Figure 55). The comparisons for this interaction did not identify the source of a difference in activity patterns along this axis; however, it is possible that this interaction reflects the fact that hand movements are processed in dorsal motor cortex. The fact that response hand and judgment type both engaged the dorsoventral axis at the stimulus timepoint may further suggest that these factors are engaging similar processes. At the stimulus, participants are actively making their response, so it is likely that some or all of this activity is related to motor execution; similarly, they are actively processing the stimulus pair, so it is possible that the difference in dorsoventral activity by judgment type represents separable response selection processes in these two domains. Interestingly, at the cue, response hand was involved in a number of interactions with cuetype and the rostrocaudal axis, which may suggest that preparatory processes are operating on this information as well, for example, that activating the relevant task file for a given cue recruits response preparation regions in anticipation of information that will allow the selection of
a response. However, these effects were not significant in the reduced model, so it is as yet unclear whether these were spurious effects due to our irrelevant factors, or if the effects were simply washed out due to the salience effect discussed above. To investigate, the current design could be reimagined in more or less the opposite fashion of the variation suggested previously. Specifically, participants could make decisions on stimulus pairs, but the judgments could be mapped to the response hands so that judgments of the same domain are mapped to the same hand. To further maximize the set salience, the responses could be mapped to different pairs of fingers, so that participants respond with the index and middle fingers for one judgment, and the ring and pinky fingers for the other judgment. If the equivocal results here were due to crosstalk between the nested task files build into this design, then this variation should demonstrate the strong response hand biasing seen in Cookson, Hazeltine, and Schumacher.

5.5 Methodology

The ROIs used in this analysis were functionally defined by extracting peaks from the group-level “Cue versus Baseline” contrast and mirroring unmatched ROIs into the opposing hemisphere. We then defined each ROI’s relative positions anterior-posteriorly and superior-inferiorly to result in a 3x3 “grid” along these axes in each hemisphere. As the definition of the ROIs is critical to interpreting the current findings, it is worth an in-depth discussion of the selection and implementation of the analysis, its limitations, and the alternatives explored in the course of exploring the results.

This methodology was adapted from those of previous studies (Badre & D’Esposito, 2007; Nee & D’Esposito, 2016); however, some changes were made to the method to account for some of the differences between those studies and the current design. First, the previous studies extracted their peaks from a general Task versus Baseline contrast, whereas the current experiment contrasted activity at the Cue timepoint only. This may limit the extent to which the current design can inform the results of previous investigations. In fact, for the current experiment, peaks were extracted from three different contrasts versus Baseline: Cue timepoint, Stimulus timepoint, and Task (i.e., Cue and Stimulus timepoints).
Activity at the stimulus was found bilaterally and extended completely from the most caudal to the most rostral regions; however, it was dominated by peaks in the most posterior regions, in or near the motor strip. This pattern is consistent with activity related primarily to task execution. Furthermore, the space activated at the Stimulus timepoint was more extensive than that for either the Cue or the Task contrasts, which raised concerns about whether the ROIs identified for this contrast would be located outside of the areas that were activated during the cue. As such, it was not clear that this timepoint would provide a distribution of ROIs that would adequately cover both the task preparation and execution spaces.

Activity for the Cue and Task versus Baseline contrasts was largely confined to the same space. In fact, only two of the peaks identified for the Cue timepoint alone differed from those identified from general Task-related activity; furthermore, one of these two peaks at the Cue timepoint was a homologous region for a different peak identified for the general Task, and the other peak simply did not appear at all in the Task-related contrast. Therefore, the results from these two contrasts would likely have yielded the same or similar results. Ultimately, the Cue contrast was used because it produced a set of ROIs that allowed for full coverage of the both anterior-posterior and superior-inferior axes.

While the method of defining ROI location relatively is taken from existing literature, the current design is, to our knowledge, the most ambitious implementation to date; where previous experiments have defined between 2 and 6 peaks confined to one hemisphere, the current design defined 12 peaks experimentally and expanded the analysis set to 18 with mirroring, with ROIs in both hemispheres. These differences allowed us to conduct a more fine-grained investigation of any location-based effects in our data, but may have resulted in limitations in the results or their interpretation.

First, the use of ROIs in both hemispheres is a significant departure from the previous literature. As noted above, previous experiments have limited their ROIs to the left hemisphere because activity in PFC has been shown to be left-lateralized in a wide variety of paradigms, including the relational complexity task (Bahlmann, Blumenfield, & D’Esposito,
N-back task (as adapted by Nee & D’Esposito, 2016), and the A-X continuous performance task (Nee & Brown, 2012). Verbal processing is also generally found to be left lateralized, regardless of the task (Ojemann & Dodrill, 1985). Indeed, the results here likewise showed left lateralization at the cue timepoint, and the overall task-related activity was lateralized as well. There was also a main effect of hemisphere at both the Cue and Stimulus timepoints in the ROI analysis. However, at the stimulus, there was significant activity in both hemispheres, despite a left hemisphere bias. Additionally, we included specific hypotheses about the lateralization of motor responses, which should recruit bilateral premotor cortex at a minimum. Therefore, for at least the initial model, having ROIs in both hemispheres allowed us the maximum opportunity to understand our data.

Second, the current design uses a much larger number of regions of interest, and yet the area of activation from which these regions are extracted is smaller than those used in previous studies. This means that the regions we have identified here are closer together than those in previous studies. The larger distance between regions in previous studies maximized their ability to distinguish differences in activation to different factors. The current study lacks this resolution advantage, and this is likely reflected in our general failure to identify effects in our planned comparisons for our interactions of interest. However, the results presented here nonetheless show a number of interesting effects.

To investigate how the choice in ROIs might influence these results, we conducted additional analyses using the ROIs identified in two different studies: one that investigated ROIs only along the rostrocaudal axis (3 ROIs, Badre & D’Esposito, 2007), and one that investigated ROIs along both the rostrocaudal and dorsoventral axes (3x2 ROIs, Nee & D’Esposito, 2016). In both cases, there was little overlap between the area activated by our task and the location of the ROIs (in the case of The ROIs from Badre & D’Esposito, 2007, this was due to slight offsets between the ROIs and the task-related activity, while in the case of Nee & D’Esposito (2016) the ROIs were localized in markedly different regions; illustrated in Appendix C). Interestingly, where the ROIs did not overlap with task-related activity, there was consistent significant negative activity (see Appendix D). In other words, ROIs outside of the area explicitly more active during the task were instead more active.
during periods included in the baseline term.

This strange pattern may be a result of how we defined the baseline term for this analysis. Here, the baseline term included both the cue-stimulus and intertrial intervals. This method was adapted from our previous event-related precuing study (Cookson, Hazel-tine, & Schumacher, in press), in order to claim the independence of the cue and stimulus timepoints; however, it is likely that some task-related processing is occurring during the cue-stimulus interval, as it essentially serves as a working memory delay period. To understand how this activity may contribute to the baseline pattern, follow-up analyses of these data should compare the current analysis to one in which the baseline includes only the intertrial intervals. Future experiments may also be designed to specifically investigate the pattern of cue-stimulus interval activity and its dynamics to better understand how preparatory activity progresses prior to task execution.
CHAPTER VI

CONCLUSIONS

Because of the event-related, hierarchically nested design employed in this experiment, the results allow us to separate activity due to preparatory processes, which may represent the recruitment of corticostriatal gating mechanisms, from that of task execution processes, which represent the actual response selection and execution, and investigate the effect of a number of factors on each as a separate timepoint. This separation has revealed that the processes underlying the rostrocaudal axis of organization may operate, at least partially, independently of those underlying the dorsoventral axis, and at a completely different timepoint during the course of the trial, despite previous accounts from block designs that suggest an interaction between processes distributed along these axes. More specifically, for the rostrocaudal axis, the results suggest that cues giving different information recruit processes that are distributed along the rostrocaudal axis according to the way the information at the cue reduces the complexity of the prepared set, and that this represents an underlying input gating mechanism driven by the PFC’s corticostriatal connections. This effect is specific to the time period immediately following the presentation of the cue, and does not persist into the time period in which the stimulus is processed and the response is selected and executed.

On the other hand, manipulations of judgment domain do not appear to influence processing at the cue; instead, domain manipulations recruit processes that are distributed dorsoventrally at the stimulus timepoint, when stimuli are actively being processed for response selection and execution. In effect, the rostrocaudal axis appears to organize processes that handle amodal processes that represent the rule structure supporting the task, while the dorsoventral axis organizes the modally segregated processes that assess the stimulus and response features of the task within the structure outlined by rostrocaudal processes. Because the current experiment temporally separates information that can be processed by
these two axes, we see each axis being engaged uniquely at the timepoint at which the presented information would recruit them. These results together suggest that the interactions previously described between the rostrocaudal and dorsoventral axes may have been products of the block designs used to investigate them (Bahlmann, Blumenfield, & D’Esposito, 2015; Nee & D’Esposito, 2016), and emphasize the need to investigate the neural mechanisms of information processing as dynamic activations of network nodes over time, rather than a single static network that is activated across the trial.

The results also provide some preliminary evidence that response hand preparation is a highly specific effect confined to the premotor regions located most proximal to the portion of motor cortex involved in executing hand movements. This conclusion suggests that the regions involved in response hand preparation are spatially specific, and are activated as one of the many nodes in the dynamic information processing network. Interestingly, this was the only factor that showed an effect at both timepoints in the trial; however, at the cue timepoint, the effect depended on the rostrocaudal axis, while at the stimulus, it depended on the dorsoventral axis. This may suggest that these regions may be recruited as a part of the activation of a task file as a function of the information contained in the cue, and kept online to guide the activation of the appropriate motor regions for the stimulus portion of the trial.

The current experiment has provided a number of interesting new observations that inform questions about the subregional functional organization of the PFC. It validates the hierarchical precuing design both behaviorally and with fMRI results as a novel task that can be used to investigate the influence of multiple factors, manipulated independently, on the processes being recruited in the PFC at two different time points in the task. The design described here presents a number of interesting first results and provides an exciting new method for teasing apart the complex web of processes located in the PFC along a number of dimensions simultaneously.
APPENDIX A

POST-EXPERIMENT QUESTIONNAIRE

A.1 How difficult did you find this task? (5-point Likert scale)
A.1.1 Did you use any strategies to help you perform the task? What, if any?
A.1.2 Did you find that the cues helped you with the task? Describe:
A.1.3 Did you find it difficult to pay attention to the task? When and why?
A.2 Did you feel like any aspects of the stimuli affected your ability to successfully complete the tasks either positively or negatively? How?
A.3 Did you observe anything else about the task that you want to tell us? Your comments on the tasks help us to improve them for future experiments.
EYE MOVEMENTS IN PILOT PHASE 1

Figure 59: Eye Movements in Pilot Phase 1. The blue line represents session 1, and the red line represents session 2. T = training block.
Figure 60: Overlap between Current Results and Prior Literature ROIs. A) Comparison of Cue-related task activity with ROIs from Badre & D’Esposito (2007). Cue activity is shown in warm colors, ROIs in cool colors. B) Comparison of Cue-related task activity with ROIs from Nee & D’Esposito (2016). Cue activity is shown in warm colors, ROIs in cool colors. C) Representative image of ROIs from Nee & D’Esposito (2016; shown in warm colors) and Badre & D’Esposito (2007; shown in cool colors).
Figure 61: Activity Map of Cue versus Baseline Contrast. Positive contrast is shown in warm colors; negative contrast is shown in cool colors. Contrast was thresholded to a FDR-corrected level of $q = .05$. 
REFERENCES


