NEURAL MECHANISMS FOR STIMULUS-RESPONSE PREPARATION

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NEURAL MECHANISMS FOR STIMULUS-RESPONSE PREPARATION

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TABLE OF CONTENTS

ACKNOWLEDGEMENTS . . . . **iii**

LIST OF TABLES . . . . **vi**

LIST OF FIGURES . . . . **vii**

SUMMARY . . . . **viii**

I INTRODUCTION **1**
- 1.1 Cue-Related Performance Benefits 1
- 1.2 Early Theories of Response Cuing 4
  - 1.2.1 Response Preparation 5
  - 1.2.2 Response Selection 6
- 1.3 Cognitive Control: Beyond Stages 8
  - 1.3.1 The Grouping Model 8
  - 1.3.2 Task Sets 10
- 1.4 Neural Mechanisms 11
  - 1.4.1 Cue-Related Activity 11
  - 1.4.2 The Response Cuing Paradigm 12
- 1.5 Current Study 15

II METHODS **16**
- 2.1 Participants 16
- 2.2 Apparatus 16
- 2.3 Stimuli 17
- 2.4 Procedure 17
  - 2.4.1 Practice Block 18
  - 2.4.2 Functional Localizer 20
  - 2.4.3 Feedback Structure 20
- 2.5 fMRI Procedure 20
- 2.6 Behavioral Analysis 20
- 2.7 fMRI Processing and Analysis 21
  - 2.7.1 Whole-Brain Analysis 21

2.7.2 Regions of Interest and Small-Volume Correction 22

III RESULTS 25

3.1 Behavioral Results 25

3.2 Imaging Results 27

3.2.1 Whole-Brain Analysis 29

3.2.2 Localizer Analysis 31

3.2.3 Regions-of-Interest Analysis 31

IV DISCUSSION 38

REFERENCES 43

LIST OF TABLES

1 Results from Reeve and Proctor's manipulation 8

2 Contrasts of Interest 21

3 Cue related regions of interest 23

4 Regions Active for Stimulus Presentation versus Baseline 29

5 Regions Active for Stimulus Presentation versus Baseline 30

LIST OF FIGURES

1 Rosenbaum's response pad design 2

2 Results of Rosenbaum's response cuing experiment 3

3 Serial response processing model 4

4 Mappings for Miller's response cuing experiment 5

5 Results of Miller's response cuing design 6

6 Mappings for Reeve and Proctor's manipulation 7

7 The Grouping Model 9

8 Visual attention cuing experimental design 12

9 Cue-related activation in Hopfinger and colleagues' visual attention task . . 13

10 Activity for cued versus uncued trials as found by Adam, Backes, et al. . . 14

11 Representative mapping of the current design 17

12 Trial structure of the current design 19

13 Visualization of ROIs from Adam, Backes, et al. 22

14 Left and right motor regions of interest 24

15 Accuracy by Cue Type x CSI 26

16 Comparison of RTs for neutral cue types between block 26

17 RT for cue type by CSI duration 27

18 RT by cue type collapsed across block type and CSI duration 28

19 RT by specific cue 28

20 Images of results for uncued stimuli versus baseline at the stimulus event . 30

21 Images of results for uncued face stimuli versus place stimuli at the stimulus event 31

22 Response processing region biasing by left versus right response cues 34

23 Stimulus processing region biasing by left versus right response cues 35

24 Stimulus processing region biasing by face versus place stimulus cues 36

25 Response processing region biasing by face versus place response cues . . . 37

SUMMARY

Human behavior relies on the accumulation of task-relevant information to narrow the range of possible responses to a single response. How do we utilize advance information that can help us select and prepare responses to a task? How is this performance benefit facilitated in the brain? Previous literature suggests a subset of brain regions involved in cue-specific processing. We investigated how informative cues affect brain processing. Specifically, to what extent is activity modulated for stimulus-related and response-related cues versus neutral cues in control- and processing-related regions? Participants made manual responses to the identity of face or place stimuli in a variation of the response cuing paradigm while fMRI BOLD signal was recorded. Prior to the stimulus, a letter cue indicating the upcoming stimulus type (face or place) or response hand (left or right) or a neutral cue was presented. We proposed three hypotheses: 1) control-related activity (e.g., prefrontal, parietal) would increase for cued vs. uncued trials; 2) activity in face and place processing regions and left and right premotor regions would activate for their respective cues, although all cues were letters; and 3) stimulus processing regions would also be activated by response cues, and vice versa.

CHAPTER I

INTRODUCTION

Human behavior relies on the accumulation of task-relevant information to narrow the range of possible responses to a single response. When we wake up in the morning, for example, we use a plethora of information to decide our next steps before we ever get out of bed. Is it a workday? Do I have plans for the morning? How much time do I have to get ready? How long does it take me to shower? We use this contextual information to tailor our morning. For example, if our alarm goes off an hour before we need to leave the house for work, we may decide to take a shower and put on a business suit before breakfast, since we know we sometimes leave late when we eat first. These decisions require the integration of more information than could be processed in a lifetime if we always had to start the decision-making process once we have everything in front of us. Yet we are able to execute these processes seemingly effortlessly countless times throughout the day. How do we utilize advance information that can help us select and prepare responses to a task especially when such advanced information does not completely specify the necessary behavior? How is this performance benefit facilitated in the brain? These are the questions addressed by the present research.

1.1 Cue-Related Performance Benefits

Rosenbaum (1983) developed the response cuing paradigm to investigate whether people could use partially informative cues presented prior to the stimulus to aid performance. Participants responded to colored circles that appeared on screen using a button box (see Figure 1) and under a procedure that allowed Rosenbaum to independently vary the arm (left or right), direction (forward or backward), and extent (near or far from center) of motion required to respond. The design also allowed for each dimension to be cued independently. Rosenbaum used this design to look at how cues informing each of these dimensions, both individually and in combination, affected accuracy and reaction time (RT).

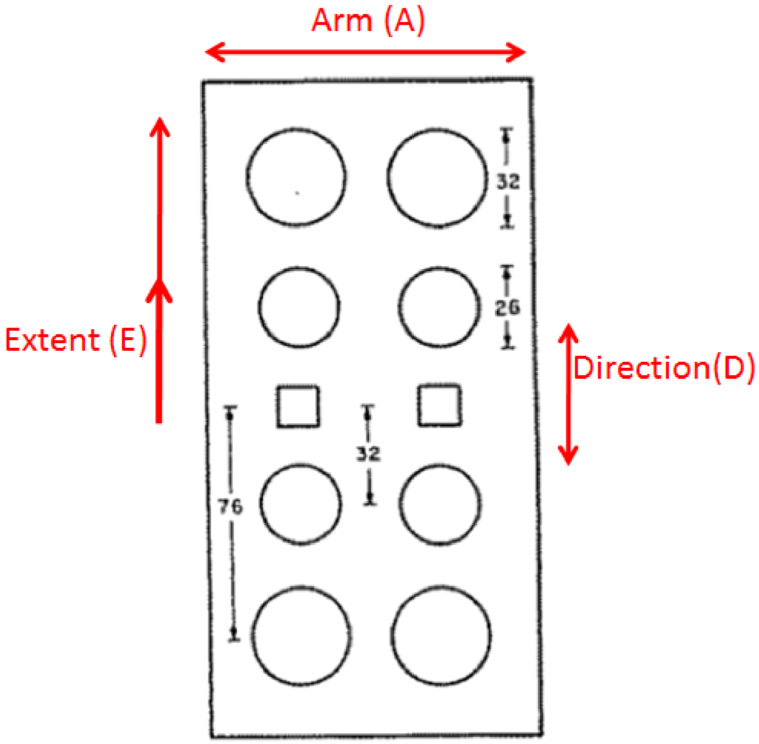

Figure 1: Rosenbaum's (1980) response pad design. Participants placed the index fingers of each hand on the two center buttons. When the colored circle stimulus was presented, they released the center button for the appropriate hand and pressed the button corresponding to the stimulus. The design allowed for independent assignment of the arm, direction, and extent of the movement. It also allowed for independent cues indicating some or all of these dimensions.

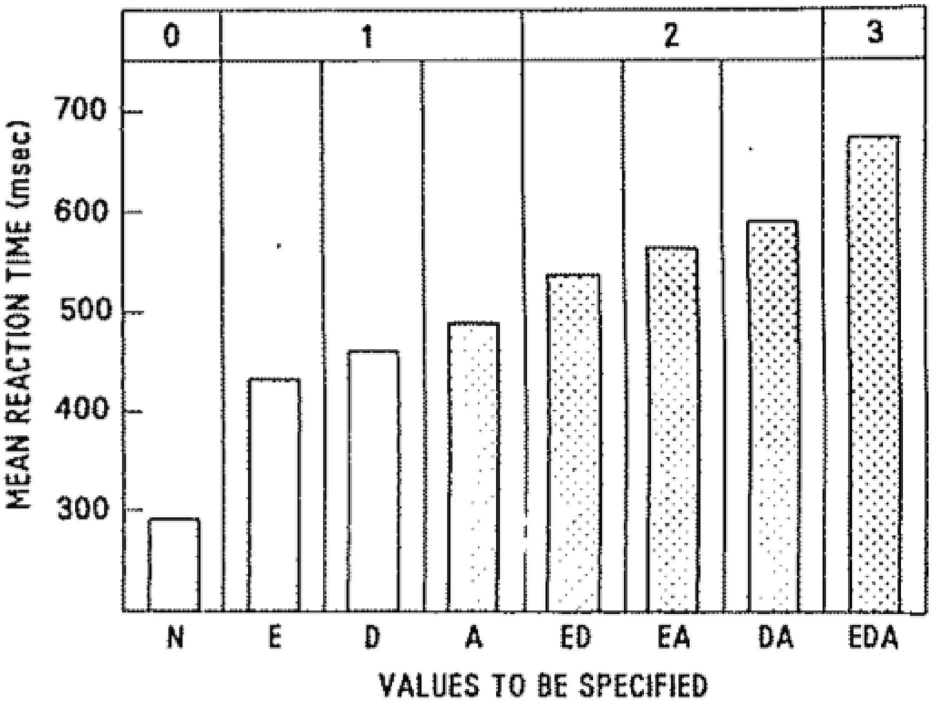

Figure 2: Results of Rosenbaum's (1980) response cuing experiment. The X-axis corresponds to the number of dimensions remaining to be specified; i.e., which dimensions were not cued. Mean reaction time was reported for each set of unspecified dimensions. The fastest reaction time was seen when all dimension values were given in advance. Reaction time increased with the number of unspecified dimensions.

The results of Rosenbaum's (1980) series of studies (shown in Figure 2) showed that humans can use cuing information to speed up their performance. Each of the informative cue types showed decreased RTs in comparison to the uncued condition. Additionally, RTs increased linearly as the number of cued dimensions decreased. That is, giving more information about the upcoming response reduced the time participants took to respond at the stimulus. This result suggested that people can prepare individual subcomponents of a response independently when given partial response information; however, Rosenbaum's results addressed neither what these subcomponents may be, nor which of them may be the locus of a cuing benefit.

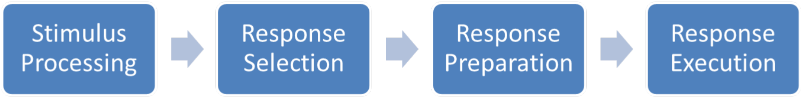

Figure 3: Serial response processing model. Cuing benefits were thought to be instantiated either at the response selection or response preparation stage.

1.2 Early Theories of Response Cuing

From Rosenbaum's (1980) results, the field of perception and action became interested in the mechanism of response processing and to identify the locus of the cue benefit. Theories of perception and action developed just after Rosenbaum's work focused on the then-popular (and still relevant) stage-based processing model, as shown in Figure 3. In this model, information flowed from one stage to the next, and a specific subset of calculations was performed on the information at each stage. Researchers disagreed on whether each stage consisted of discrete (i.e., completing calculations on a full set of information before passing the information forward; see Sternberg, 1969) or continuous (i.e., passing information forward as calculations are completed incrementally on the set; see McClelland, 1979) processing; however, they generally agreed on which stages occurred and in which order (viz., stimulus encoding, response selection, response preparation, movement production). The model began with stimulus encoding, or the input of perceptual information and translation into meaningful mental representations. Next, response selection operated on these stimulus representations to select a representation of the required response from the set of possible responses. After this, response preparation translated this selected response representation into a motor code. Finally, movement production used this motor code to produce the required response.

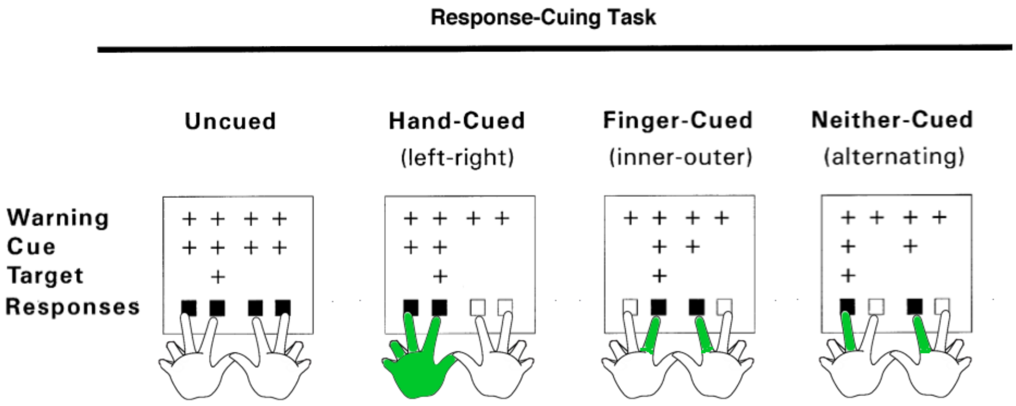

Figure 4: Mappings for Miller's (1982) response cuing experiment. In Miller's design, the hands were placed side by side with the first two fingers mapped two the two keys on each side of the response keyboard. After the warning signal, a cue appeared that spatially cued a subset of the response options. The cued subset in each informative condition is indicated in green.

It was hypothesized that a cue benefit resulted from the interaction of cue-related information with one of these stages; however, researchers disagreed over which stage was responsible for this benefit. Some researchers argued that the benefit was the result of response preparation (e.g., Miller, 1982); others that the benefit occurred in response selection (e.g., Reeve and Proctor, 1984).

1.2.1 Response Preparation

Miller (1982) developed a variant of Rosenbaum's procedure that used spatially compatible cues to cue different subsets of motor responses. In his procedure, participants saw four crosses on the screen that were spatially mapped to four fingers (i.e., leftmost cross mapped to leftmost finger and so on). For each trial, the participants saw a warning signal with all four crosses, followed by a cue signal. The cue could consist of all four crosses (uninformative) or a subset of two. Then, participants saw and responded to a stimulus consisting of a single cross (see Figure 4).

Of particular interest was his variation of the task in which the two left stimuli were mapped to the first and middle finger of the left hand and the two right stimuli to those of the right. In this condition, the cues produced a particular pattern of subsets: two fingers

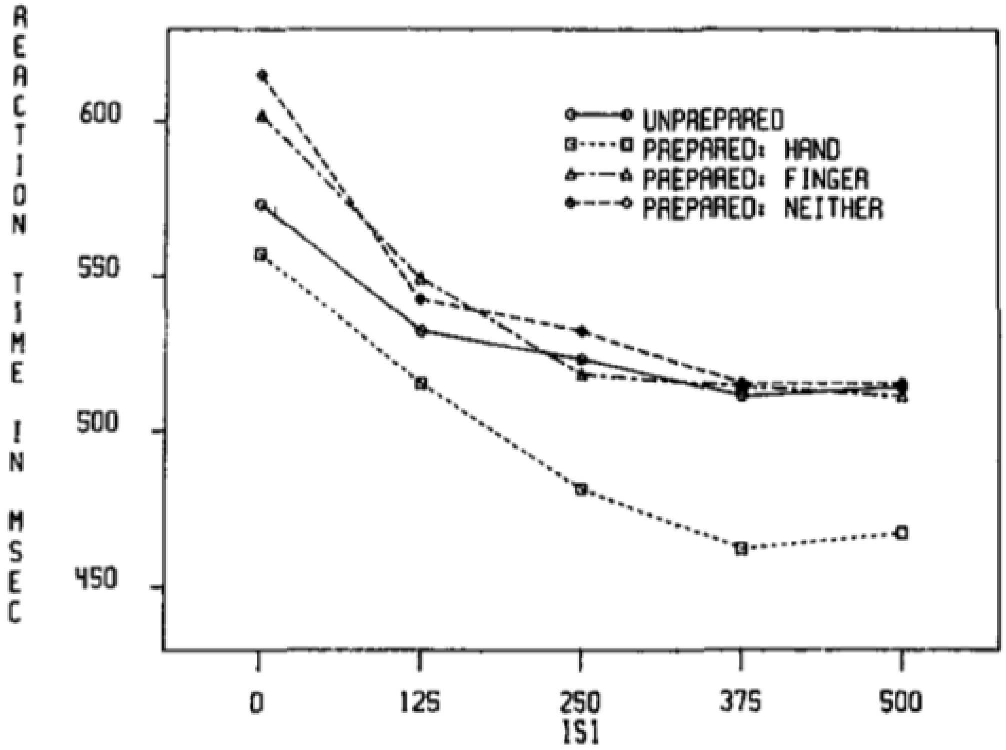

Figure 5: Results of Miller's (1982) response cuing design. Cues that reduced the responses to one hand (i.e., "Prepared-hand" condition) showed a RT benefit over other cue types for all investigated lengths of ITI. This benefit was observed for participants who were not given explicit instructions to utilize the cues.

on one hand, termed the hand condition; first or middle fingers of both hands, termed the inner/outer condition; or the remaining two combinations, termed the neither condition. Miller (1982) reported a pattern of performance in which hand-informative cues produced a RT benefit over other cue types (Figure 5). This suggested a special benefit of reducing the responses to one hand. Miller proposed that this benefit occurred during the response preparation stage because he assumed that the response selection stage depends on discrete information from the stimulus encoding stage, and therefore depends on the presentation of the stimulus rather than the cue.

1.2.2 Response Selection

Reeve and Proctor (1984) proposed a different model than Miller (1982). They suggested instead that the cuing benefit occurred in the response selection stage. To investigate this,

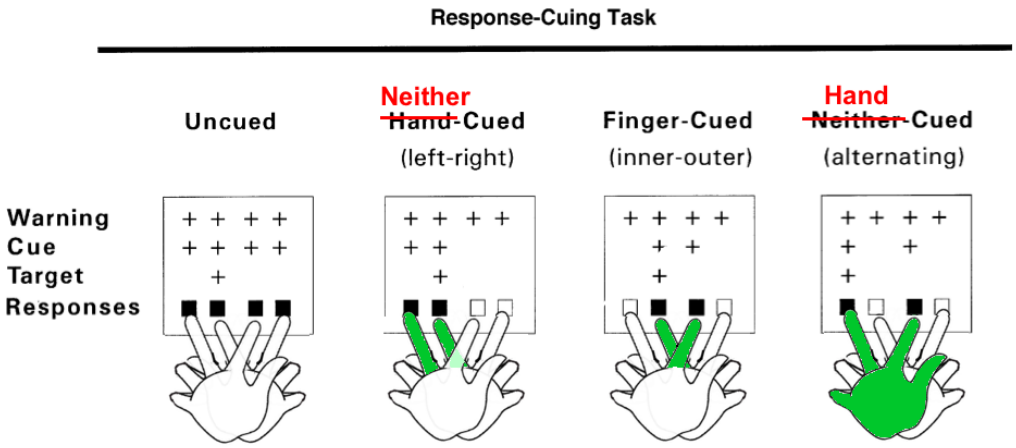

Figure 6: Mappings for Reeve and Proctor's (1984) manipulation. This design resulted in a reversal of the pattern of cues that indicated the hand- and neither-subsets of responses.

they used Miller's task, but crossed the hands as in Figure 6, thus making the stimuli and responses spatially incompatible. In this design, the same cue that corresponded to the hand-condition in Miller's design should therefore correspond to the neither condition here. If, they reasoned, the cue benefit was due to response production, then crossing the hands should not affect the pattern of cue benefits found by Miller (because stimulus-response compatibility is widely held to affect response selection, not response production). On the other hand, if the cue benefit effect occurred in response selection, translation from the stimulus to response should take more time within-hand, as the mapping is no longer directly related to the spatial positioning of the cue.

The results from this design supported Reeve and Proctor's (1984) claim that cue benefits occur in response selection. They found that the neither-cued condition (i.e., two left- or rightmost response positions cued) showed the fastest RTs, rather than the hand-cued condition (Figure 7). Thus, Reeve and Proctor demonstrated a reversal of the effect shown in Miller's (1982) experiment. Rather than the hand condition producing the fastest RTs, as in Miller's design, the neither condition was the fastest. However, this pattern shift was also accompanied by a general increase in RTs for all conditions in comparison to the RTs for hands placed side by side, as in Miller's experiment (by an average of 222 ms across all conditions), which calls into question how comparable the experiments really are. For

Table 1: Results from Reeve and Proctor's (1984) manipulation. The overlapped hand manipulation resulted in a reversal of the cuing benefit such that the Neither condition showed the fastest RTs rather than the Hand condition (as in Miller's, 1982, experiment). This corresponds to a cuing benefit for the same pattern of cues presented on screen (i.e., the two left- or rightmost positions) in both mappings, despite the change in response finger.

	Hand Placement	
Preparation Condition	**Adjacent**	**Overlapped**
Unprepared	551	771
Prepared:Hand	502	765
Prepared:Finger	516	746
Prepared:Neither	547	721

example, the increase in overall RT in Reeve and Proctor's design may indicate a more global, strategic, change in processing that may have affected their cuing effect in unknown ways.

1.3 Cognitive Control: Beyond Stages

After the initial development of the response cuing literature, additional research was conducted in this area largely did not move the field forward until (Adam, Hommel, & Umiltà, 2003) proposed the Grouping Model. This proposal represented a fundamental shift in the way the field conceived of the mechanisms behind response processing.

1.3.1 The Grouping Model

Adam, Hommel, et al. (2003) proposed a cognitive model of response cuing that attempted to explain the conflicting evidence from the early literature. In their Grouping Model, the precuing advantage for specific cue types was driven by subgrouping processes at the stimulus and response levels. That is, automatic, Gestalt-like processes identify a subset of both the stimulus and response sets that help to limit the number of possible responses prior to response selection, resulting in faster RTs. Importantly, the Grouping Model deemphasizes the traditional serial model that was the focus of previous theories; instead, it emphasizes the biasing of attention through both automatic and controlled grouping processes. Some of these grouping principles occur at the stimulus level and are largely

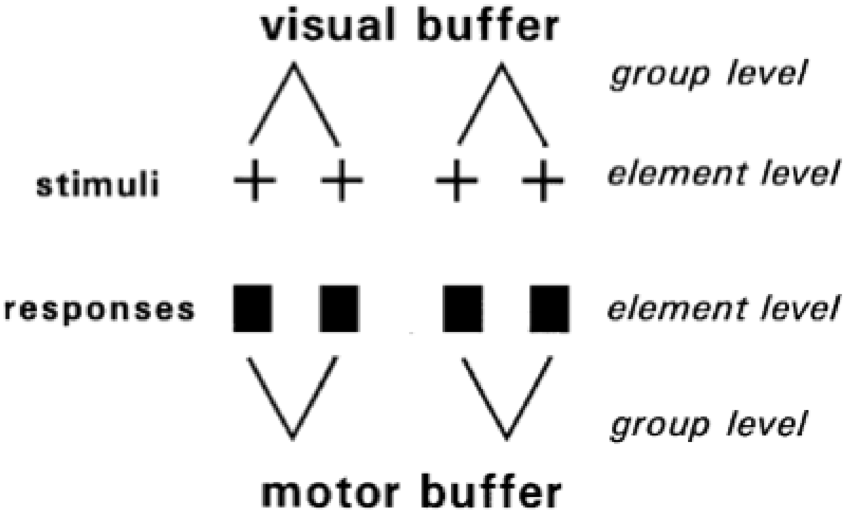

Figure 7: The Grouping Model (Adam, Hommel, et al., 2003). Stimuli and responses form Gestalt-like subgroups that facilitate processing when the subgroup at the stimulus level matches that at the response level. In Millers (1982) paradigm, the hand cue resulted in an overlap of the left- or right-side visual grouping at the stimulus level and the anatomical grouping at the response level.

visually driven; for example, in Miller's (1982) design, stimuli are presented in a row with extra spacing between stimuli in the center of the row; this causes groups to emerge for the left and right sides of the screen. Similar processes can occur at the response level, often based on anatomical position (e.g., separated by hand). These groupings are illustrated in Figure 7.

The overlap between stimulus and response groupings then drives the strength of the grouping effect on RT. In the case of the hand advantage, cuing the two left-most stimulus positions when they are mapped to the left hand results in an easily identified subgroup for half of the original stimulus-response set (viz., left half of the screen and left hand). Conversely, an automatic subgroup is not identified when the outermost responses are cued, as this crosses visual and anatomical groupings (but see Adam, Hommel, and Umiltà (2005) for more detailed explanation on grouping processes[1]). Ultimately, Adam and colleagues concluded that the hand advantage represents a special case of strong, fast grouping processes and is due to a combination of stimulus and response group saliency.

1.3.2 Task Sets

The grouping principles discussed by Adam, Hommel, et al. (2003) may describe a task set, or the related linking of the stimuli, responses, context, goal state, and other factors associated with a task (Hommel, 2004). In fact, response cuing may be a specific example of the implementation of a task set. Task sets are activated by control mechanisms to prepare for and execute a task. In the response cuing procedure, the task set is the set of possible stimuli and responses that can be presented and how they are mapped. In the uncued condition of Miller's (1982) experimental design, then, this task set was the four spatially indicated positions that could be the upcoming target and the four corresponding response movements, along with the mapping that correlated each stimulus to its associated response.

An important aspect of the task set is that it can layer hierarchically; that is, task sets for high-level functions may themselves activate whole task sets that might represent subordinate sets of task-related information. For example, a task set for getting ready in the morning may in turn organize task sets for shower, make coffee, and eat breakfast, each of which contains the required set of behaviors for each individual action, into a coherent morning program that can be tailored according to the context of a given morning's requirements.

Similarly, the Grouping Model allows for hierarchical task setting in response cuing. In this case, the subgroups created by Gestalt grouping processes result in the formation of task sets that represent each of these subgroups individually when the subgroups are salient

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[1] 1A large part of the response cuing literature has historically looked not only at informative versus uninformative cues, but also at differences between different types of informative cues. Specifically, there is evidence for varying benefit for hand- inner/outer- and neither-informative cues. Adam and colleagues discuss this concept in terms of their grouping model in two reports: one that discusses grouping principles (Adam, Hommel, et al., 2003), and one that discusses automatic versus effortful processing (Adam et al., 2005). These more specific discussions, in conjunction with the work described here, clarify the possible mechanisms behind the nuances of the behavioral results from the response cuing literature.

between the stimulus and response levels. An overarching task set for the experiment then controls the activation of one or both task sets according to the current cue information. Therefore, in Miller's (1982) design, when a participant receives an uninformative cue, the overarching task set activates both task sets, and participants must actively prepare the mapping for all four stimulus-response pairs. When the cue is informative for hand, control mechanisms would shift activation to the only relevant subordinate task set, which reduces the number of activated stimulus-response pairs to two. On the other hand, in Reeve and Proctor's (1984) design, the salience between a one-handed response set and the visual stimulus grouping is lost; thus, the experiment cannot be represented as a set of subgrouped tasks. The hand-cue no longer activates a reduced subtask, and the participant must activate the overarching task for the entire SR set. The behavioral benefit of cuing, then, may be a result of decreased working memory load as task set size decreases.

1.4 Neural Mechanisms

Understanding the dynamics of brain activity in cuing situations can help elucidate the organization of task related information and reveal the timecourse of cue- and task-related processing. While response cuing has not been a popular task to investigate with neuroimaging techniques, several studies have investigated how cues affect activity in the brain.

1.4.1 Cue-Related Activity

Hopfinger, Buonocore, and Mangun (2000), for example, conducted a neuroimaging study of visual attention mechanisms that looked specifically at cue-related activity. In their experiment, participants were presented with a cue that indicated one side of the screen and were instructed to attend to the cued side only. They then saw a pair of reversing checkerboard stimuli, one on each side, and were asked to discriminate whether the checkerboard on the attended side had any spaces that were grey rather than black or white (Figure 8). Of key importance in this design was the variation in ISI (17% 1000ms, 83% 8150ms). This jitter served to isolate activity related to the cue and stimulus presentations.

Hopfinger and colleagues (2000) then analyzed which brain regions were active at the cue versus the target. They found a number of areas specific to cue, but not target, presentation,

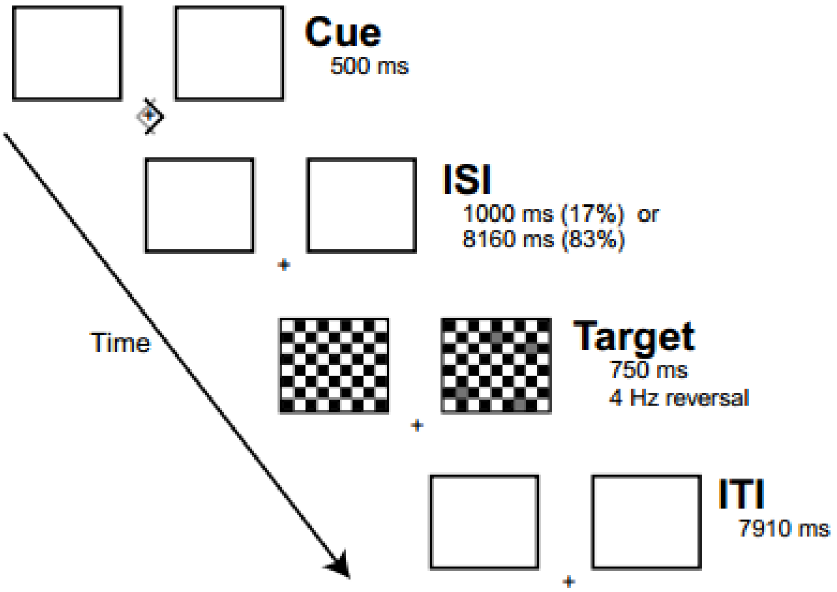


Figure 8: Visual attention cuing experimental design (Hopfinger et al., 2000). Participants fixated on the cross at the start of the trial. An arrow then appeared to one side of the arrow, indicating which side of the screen to attend. After the ISI (17% 1000ms, 83% 8150ms), two checkerboards were presented. Participants indicated if the checkerboard on the cued side had grey squares amid the black and white checks.

including frontal cortex (superior frontal gyrus, SFG; middle frontal gyrus, MFG; frontal eye fields, FEF; intra-parietal sulcus, IPS; superior parietal cortex, SPC; and superior temporal sulcus, STS; see Figure 9 for illustration). They concluded that these areas, in contrast to target-specific regions, were directly related to top-down attentional control implementation.

1.4.2 The Response Cuing Paradigm

Adam, Backes, and colleagues (2003) used fMRI to extend the literature of cue-related activity to the response cuing paradigm. This study used Miller's (1982; see Figure 4) design compare cued activity to uncued activity, which allowed them to separate activity due to informative versus uninformative cues using subtraction. Specifically, they looked at activity on cued versus uncued blocks of trials, reasoning that activation in uncued blocks represented pure execution processes because there was no a priori information to use to prepare the upcoming response. They found activation in a number of regions relating to informative cue-specific activity, including frontal cortex (MFG, dorsal, DPMC;

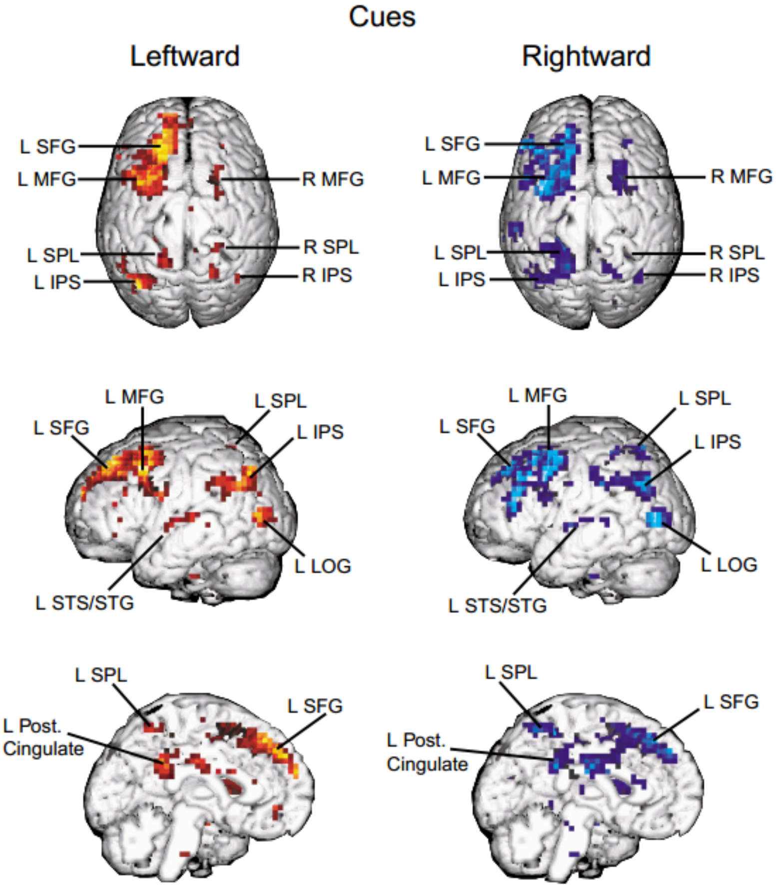


Figure 9: Cue-related activation in Hopfinger and colleagues (2000) visual attention task. Leftward and rightward cues showed largely the same pattern of activation, which included bilateral prefrontal, parietal, and temporal regions, as well as left occipital activation.

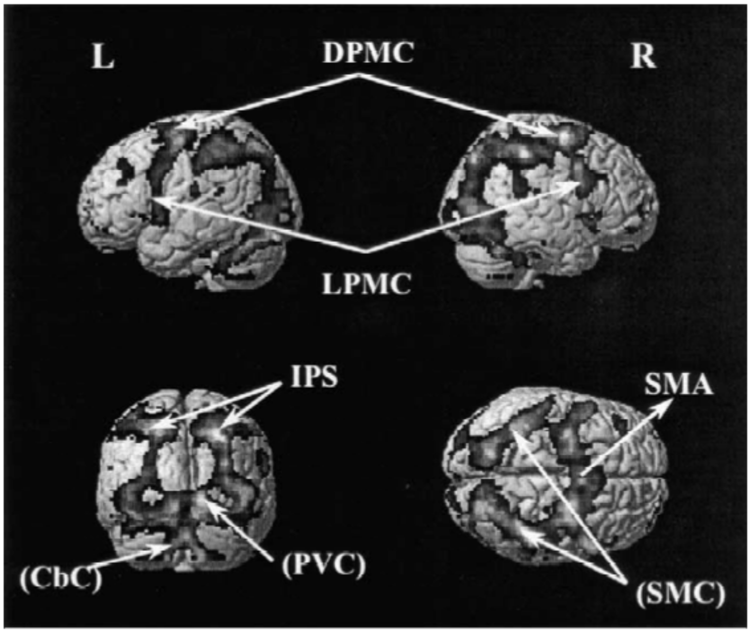


Figure 10: Activity for cued versus uncued trials as found by Adam, Backes, et al. (2003). These regions largely overlap with the results by Hopfinger and colleagues (2000).

and lateral, LPMC, premotor cortex; supplementary motor area, SMA; IPS; SPC; inferior parietal cortex, IPC; and basal ganglia; Figure 10).

These data overlap to some extent with Hopfinger and colleagues' (2000) result, but do show some differences (viz. FEF in Hopfinger and colleagues' results versus D/LPMC, SMA, IPC, and basal ganglia for Adam and colleagues, 2003). This may suggest that a subset of regions are generally involved in cue processing and/or control implementation that are common between the two studies, while the other regions are showing downstream effects of these processes that are task-specific. However, Adam and colleagues' design relies on subtraction methodology to isolate cue-related processes, when it is possible that cue-related processing dynamics are not purely additive with other response processing dynamics. Based on the behavioral literature, it is likely that a number of these subprocesses are occurring during the cue, as well as the cue-stimulus interval, that have yet to be teased apart with neuroimaging data.

1.5 Current Study

The current study proposed the first event-related fMRI investigation of cue-related activity in a variation of the response cuing paradigm. Participants were given a set of stimulus-response mappings in which half of the stimuli were pictures of faces and the other half were places; stimuli were segregated by type to separate hands (See Figure 12). Participants saw a cue that informed the upcoming stimulus type, response hand, or neither. They then saw a picture stimulus corresponding to one of the stimuli in the mapping and responded with the button that corresponded to that picture. The event-related design allowed us to contrast activity for informative versus uninformative cues.

We hypothesized that we would see cue-specific activity in some or all of the regions identified by Adam, Backes, et al. (2003). Furthermore, we predicted that our results would show activity specific to individual informative cue types, specifically in lower-level sensorimotor processing areas (viz., FFA, PPA, and lateralized motor regions) that are thought to be modulated by control mechanisms (c.f., Egner and Hirsch, 2005). This would suggest that the cue allows participants to preemptively perform some response selection and preparation processing beyond the explicit information provided by the cue. The specific patterns of activation in our experiment will help illuminate the exact nature of the time course and processing dynamics of how people make use of partial information to guide and control their behavior.

CHAPTER II

METHODS

2.1 Participants

Participants included 41 volunteers from the Georgia Institute of Technology community between the ages of 18 and 38 years old (15 female, 26 male). 6 participants (3 female, 3 male) withdrew from the study before completion of both sessions; an additional 12 (5 female, 7 male) were not included in the analyses due to performance issues (1 sleeping, 1 not responding to stimuli) or excess motion (repeated translations of greater than 1mm across a single block; position changes were measured in real-time) during the scan. Participants had no prior record of brain injuries, had normal or corrected to normal vision, and were not otherwise contraindicated for the fMRI scanner.

2.2 Apparatus

Session 1 was conducted in the PST MRI simulator available at the Center for Advanced Brain Imaging (CABI) at the Georgia Institute of Technology. In this session, only behavioral data were collected. In Session 2, fMRI data were collected using the Siemens 3T Trio Magnetic Resonance Imaging System with a 12 channel headcoil. Visual stimuli for the experiment were shown using the Avotec Silent Vision 6011 projector. Participants made responses using two hand-specific Current Designs fORP 4-button boxes; fingers of the left hand were mapped to the left box, and fingers of the right hand to the right box. Boxes were positioned on the abdomen in both sessions, with a Velcro foam pad used in session 2 to fix the boxes to the correct sides. The experiment was run on E*Prime 2.0.10 software. Participants lay facing up in the scanner with a mirror adjusted to a comfortable distance from the eyes for viewing the experiment screen. During Session 1, the participants wore over-ear headphones and heard pre-recorded scanner sounds played on a CD player to simulate the experience of being in the scanner as closely as possible. During Session 2,

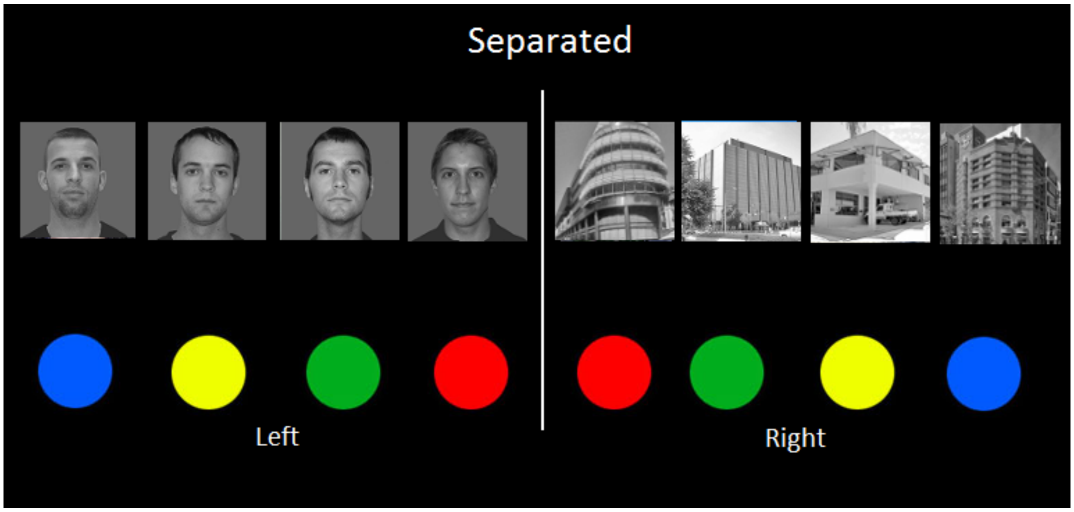


Figure 11: Representative mapping of the current design. The colored circles represent each of the response buttons, using their original colors as viewed on the response box from above.

participants wore earplugs and Avotec Silent Scan 3100 headphones to protect the participants' hearing and allow for communication with the experimenter from the control room. Foam padding and medical tape was used to minimize head motion during the scan.

2.3 Stimuli

Face images were taken from the AR Face Database (Martinez & Benavente, 1998). Face images started at the shoulders and included hair; all images showed people in black t-shirts on a dark grey background with black and white coloration. Place images consisted of 4 black and white pictures of buildings taken from the Hazeltine laboratory (University of Iowa). All participants saw the same 8 images, which are shown in Figure 11.

Cues consisted of the letters F, P, L, R, and O, shown in white on a black background in the center of the screen. F and P corresponded to an upcoming face or place stimulus, respectively; similarly, L and R represented left and right responses. O was used as an uninformative cue. The fixation cross was likewise white and centered.

2.4 Procedure

Data were collected in two sessions. The first session was no less than 1 day and no more than 5 days prior to the second session. In Session 1, participants were given a set of mappings that associated the stimuli to the 8 buttons of the two button boxes and instructed to learn these associations. For all participants, faces were mapped to the buttons on one hand and places to the buttons on the other. This mapping is illustrated in Figure 11. Mappings were counterbalanced between- and within-hand such that faces and places each appeared on the left hand in half of subjects, with the subset of face and place images appearing in 4 different possible orders within their respective hands.

For each trial, participants were shown a cue consisting of a single letter at the center of the screen for 2 seconds. This cue was either informative for the upcoming stimulus (F = face, P = place), the upcoming response hand (R = right hand, L = left hand), or neither (O, neutral cue). Cues were presented with 100% validity to the upcoming stimulus and blocked so that participants only saw one of the two informative cue types in a single block; the cue type presented was alternated by block. The cue was followed by a cue-stimulus interval (CSI), which consisted of a fixation cross presented in the center of the screen. This CSI was presented with a jitter of 2, 4, or 8 seconds, with a 2-second CSI occurring on half of the trials and 4- and 8 second CSIs each occurring on 1/4 of the trials, using the exponential decay design described by Ollinger, Shulman, and Corbetta (2001). The CSI was followed by the presentation of one of the 8 possible stimulus images for 2 seconds. Participants were instructed to respond to the stimulus within the 2-second presentation window. After the stimulus interval, an inter-trial interval (ITI) was presented. This ITI had the same jitter structure as the CSI. In the case of a correct response on the preceding trial, the ITI showed a fixation cross; in the case of an incorrect response, the ITI showed the stimulus-response mappings. This trial structure is illustrated in Figure 12. Each block consisted of 40 trials, with a total of 6 blocks.

Session 2 used the same experimental procedure with adjusted feedback and included a short pre-experiment practice block and functional localizer task.

2.4.1 Practice Block

During the structural scan, participants completed a short practice block of neutral cue-only trials (30 trials, 75% of a full block, random inclusion of trials). This allowed for

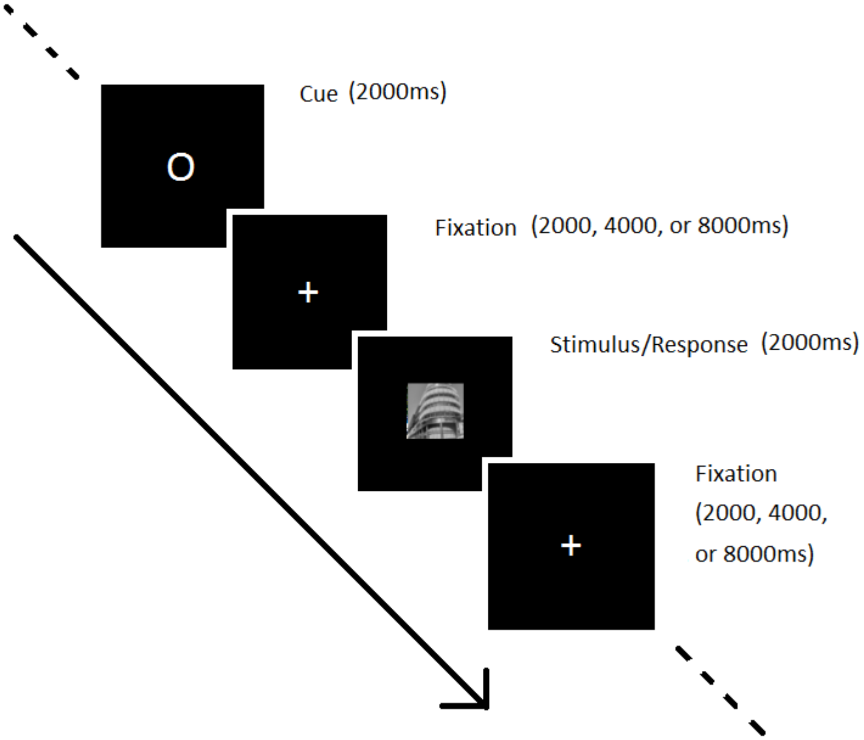


Figure 12: Trial structure of the current design. In each trial, participants saw either a neutral cue or one of the informative cues for the cue type associated with that block. This was followed by the CSI and subsequent stimulus presentation. Cues were 100% valid.

participants to refresh their memories of the mappings from the previous session to avoid learning effects during MRI acquisition.

2.4.2 Functional Localizer

An active FFA/PPA localizer was used to identify face- and place-specific processing regions. Participants viewed pictures of faces or buildings; these were presented in 10 alternating blocks. Blocks consisted of 20 images each, shown for $300ms$ with a $500ms$ inter-stimulus interval. Each block was separated by 8 seconds of fixation. Participants were instructed to press any button on the button boxes when the same image appeared twice in a row (1-back task). On average, there were 0-2 repeats per block.

2.4.3 Feedback Structure

In session 2, the feedback structure was changed such that the ITI always showed a fixation cross, and average accuracy and RT for the current block was shown at the end of the block. The ITI jitter structure remained the same.

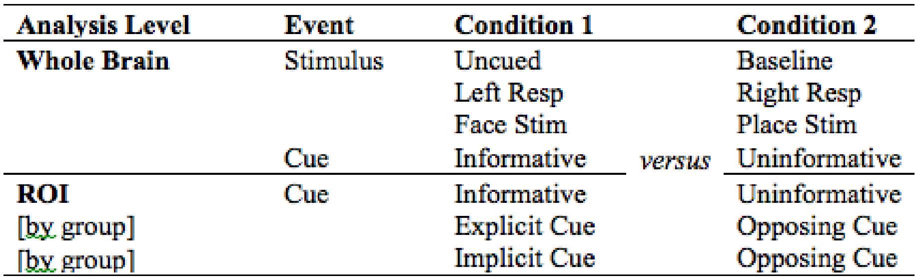
2.5 fMRI Procedure

Images were acquired using a Siemens 3T Trio MR scanner. A standard RF head coil was used, with foam padding inserted between the head and headrest on the sides of the head above the ears to restrict head motion. A three-plane localizer and high-resolution 3D MPRAGE structural scan (1 mm isotropic voxels) were collected at the beginning of the MRI session. An echoplanar sequence ($TR = 2000ms$, $TE = 30ms$) was used to acquire data sensitive to the blood oxygen level dependent signal. Each functional volume contained 37 axial slices of 3 mm isotropic voxels. The functional localizer was run first (about 4:06 min, 123 volumes/run), followed by 6 experimental blocks (about 9:40 min each, 290 volumes/run).

2.6 Behavioral Analysis

Mean RTs and accuracies were calculated for each subject as a function of cue type (stimulus-informative, response-informative, or uninformative) and CSI. Overall accuracy was calculated as well across subjects and conditions. A two-way repeated measures analysis of

Table 2: Contrasts of Interest. Resp = Response, Stim = Stimulus, ROI = Regions of Interest.



Analysis Level	Event	Condition 1		Condition 2
Whole Brain	Stimulus	Uncued		Baseline
		Left Resp		Right Resp
		Face Stim		Place Stim
	Cue	Informative	*versus*	Uninformative
ROI	Cue	Informative		Uninformative
[by group]		Explicit Cue		Opposing Cue
[by group]		Implicit Cue		Opposing Cue

variance (ANOVA) was performed on the RT and accuracy data with cue type and CSI as within-subjects factors. Post-hoc comparisons were conducted on the RT data using Tukey's honestly significant difference (HSD) procedure.

2.7 fMRI Processing and Analysis

Data reconstruction, processing and analyses for each participant were performed using the Analysis of Functional NeuroImages software package (Cox, 1996). After reconstruction, the 3-D+time data were despiked; slice acquisition timing differences were corrected; the structural image was normalized to the Montreal Neurological Institute (MNI) reference brain; head-motion artifacts were corrected to the second sub-brick with a least squares approach using a six- parameter, rigid-body transformation algorithm (Friston et al., 1995); and the data were smoothed with an 8.0mm full-width half-maximum Gaussian kernel.

2.7.1 Whole-Brain Analysis

Data were analyzed using a modified general linear model (Worsley & Friston, 1995). We created design matrices for each participant with covariates for each event (viz., cue, stimulus, and baseline) corresponding to a correct response as a function of cue type (viz, face/place/left/right/neutral). These covariates were convolved with an idealized hemodynamic response function. A high-pass filter removed frequencies below .00345Hz. Contrast images were computed for each participant for each of our hypotheses. Table 2 outlines each of our contrasts of interest in the order they are presented here.

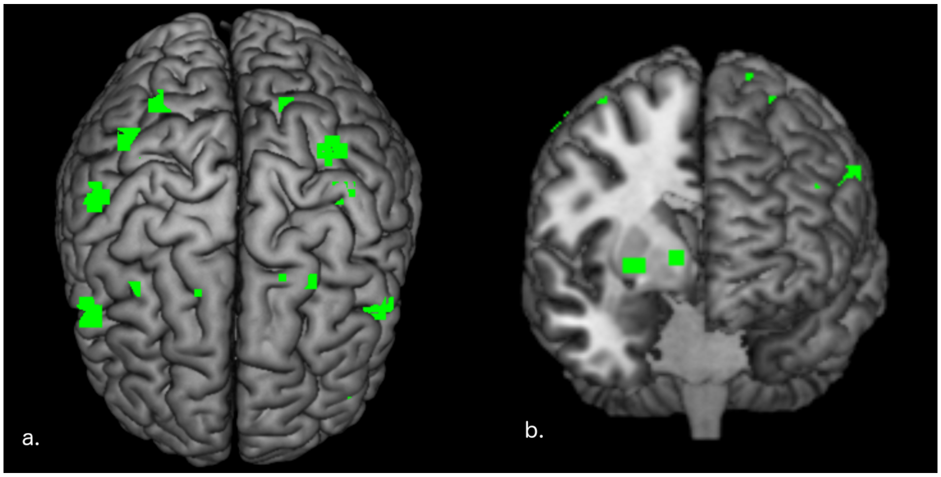


Figure 13: Visualization of ROIs from Adam, Backes, et al. (2003). Figure (a) represents frontoparietal regions identified in the surface cortex, and figure (b) shows a coronal slice revealing the subcortical ROIs for caudate and putamen.

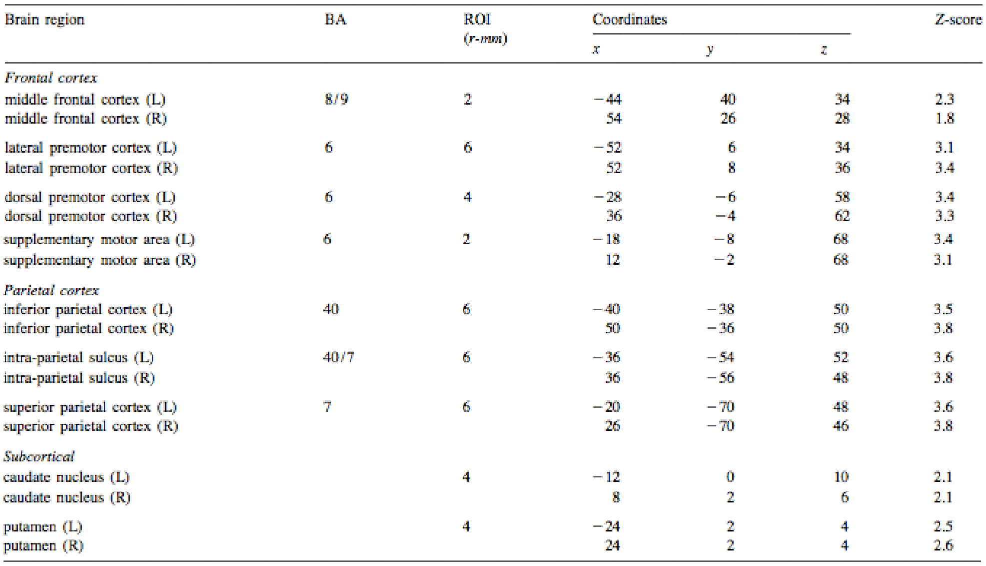
2.7.2 Regions of Interest and Small-Volume Correction

The experimental question addressed here (viz., how does cuing affect downstream processing before the presentation of the stimulus) involves investigating activity during the cue event across our four cues compared by cue type (i.e., face cue versus place and left cue versus right) in brain regions previously implicated in cue and sensorimotor processing. Therefore, we used a small volume correction (Worsley & Friston, 1995) to investigate activity in our contrasts of interest. Our regions of interest included a widespread set of cue processing-related regions, defined previously by Adam, Backes, et al. (2003); functionally defined, lateralized motor processing regions, defined by the stimulus-related event data; and functionally defined face and place processing regions, extracted from the localizer data. -values were extracted from these ROIs for each condition for subsequent analysis.

2.7.2.1 Cue-Related Regions

Cue processing-related ROIs were created using spherical ROIs as defined (peak + radius) by the regions identified in Adam, Backes, et al. (2003). Table 3 and Figure 13 present the regions included in the analysis by dimension definition and spatial layout, respectively.

Table 3: Cue-related regions of interest. Table adapted from Adam, Backes, et al. (2003). Original caption: "Sites of activation from the precuing condition compared to the baseline condition (stereotaxic coordinates are expressed in millimeters). BA = Brodmann area, ROI = region of interest, L = left, R = right. Coordinates are according to the coordinates of Talairach and Tournoux [38]."



Brain region	BA	ROI (*r-mm*)	Coordinates			Z-score
			x	*y*	*z*	
Frontal cortex						
middle frontal cortex (L)	8/9	2	−44	40	34	2.3
middle frontal cortex (R)			54	26	28	1.8
lateral premotor cortex (L)	6	6	−52	6	34	3.1
lateral premotor cortex (R)			52	8	36	3.4
dorsal premotor cortex (L)	6	4	−28	−6	58	3.4
dorsal premotor cortex (R)			36	−4	62	3.3
supplementary motor area (L)	6	2	−18	−8	68	3.4
supplementary motor area (R)			12	−2	68	3.1
Parietal cortex						
inferior parietal cortex (L)	40	6	−40	−38	50	3.5
inferior parietal cortex (R)			50	−36	50	3.8
intra-parietal sulcus (L)	40/7	6	−36	−54	52	3.6
intra-parietal sulcus (R)			36	−56	48	3.8
superior parietal cortex (L)	7	6	−20	−70	48	3.6
superior parietal cortex (R)			26	−70	46	3.8
Subcortical						
caudate nucleus (L)		4	−12	0	10	2.1
caudate nucleus (R)			8	2	6	2.1
putamen (L)		4	−24	2	4	2.5
putamen (R)			24	2	4	2.6

2.7.2.2 *Motor-Related Regions*

Left and right motor regions were defined functionally at the group level by comparing uncued left versus right response activity from the experimental data and extracting the four clusters identified in left and right premotor cortex and cerebellum (Figure 14; see Whole Brain Results: Stimulus-Related Activity below for details of results).

2.7.2.3 *Stimulus-Related Regions*

Face and place processing regions were identified for each subject on an individual basis by assessing the BOLD contrast recorded during the localizer task. First, we created design matrices with covariates for face blocks, place blocks, and baseline blocks. These design matrices were convolved with an idealized hemodynamic response function and subjected to a high-pass filter of .00813 Hz. We then computed the contrast image for face versus place blocks. To define face and place ROIs for each participant, we extracted the activity for faces and places and constrained the clusters to the anatomical locations previously

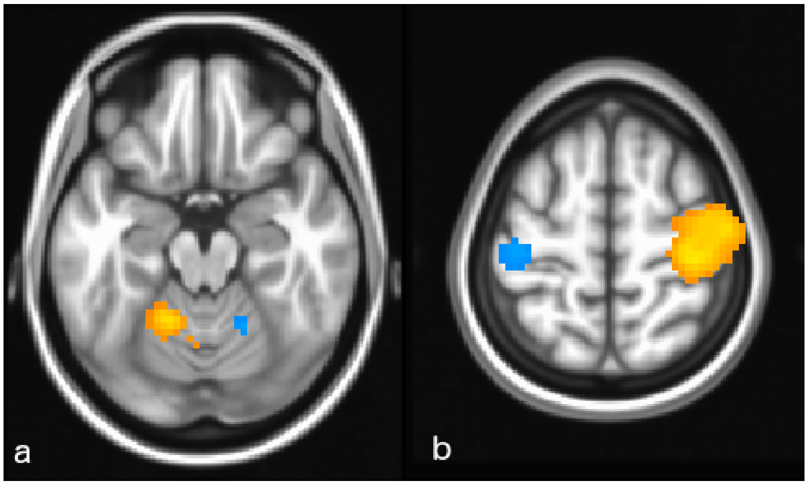


Figure 14: Left and right motor regions of interest. ROIs were identified at the group level. Premotor activity was contralateral to the executed motor movement and cerebellar activity ipsilateral. Clusters were extracted at the $q < .05$ corrected level.

identified as being face/place processing related (viz, FFA and LOC, Kanwisher & Yovel, 2006; PHG and LG, Gorno-Tempini & Price, 2001).

CHAPTER III

RESULTS

3.1 Behavioral Results

First, we investigated accuracies across all trials. Accuracies approached ceiling (Overall average = 95.1%) and were analyzed using an arcsine transformation as shown below.

$$X = sin^{-1}\sqrt(x)$$

A two-factor, repeated measures ANOVA for cue type and CSI duration did not show any main effects for cue type, $F(2,44) = .859$, $p = .431$, but showed a main effect for CSI, $F(2,44) = 3.528$, $p = .038$. Post hoc t-tests revealed that this was due to a significant difference between the mean accuracies for CSIs of 8s versus 2s, $t(22) = 2.41$, $p = .012$ (Figure 15). This result indicates that participants were 1.2% more accurate on 8s CSI trials than 2s CSI trials. Still, this difference accounts for less than 4 fewer errors in that condition over the experiment than the others overall, so we dont expect this difference to have had much effect on the brain activity described below. We focus the rest of the behavioral analyses on the RT effects in correct trials.

A t-test of RTs for neutral cues between blocks of stimulus and response-cue types was not significant, $t(22) = .929$, $p = .363$ (two-tailed; see Figure 16); therefore, we collapsed across block type for subsequent analyses. A two-factor, repeated measures ANOVA compared correct RTs for cue type and CSI. The ANOVA revealed a main effect for cue type, $F(2,44) = 4.979$, $p = .011$. The main effect of CSI was not significant, $F(2,42) = .564$, $p = .573$. There was no significant interaction between cue type and CSI, $F(4,84) = .645$, $p = .632$ (Figure 17). Because there was no main effect of CSI or interaction, we collapsed across CSI for subsequent analyses.

We next ran planned comparisons to characterize the effect of cue type collapsed across block type. The neutral versus response cue comparison ($O - R = 20.07 \pm 8.9ms$) was statistically significant, $t(22) = 2.255$, $p = .017$. Likewise, the neutral versus stimulus

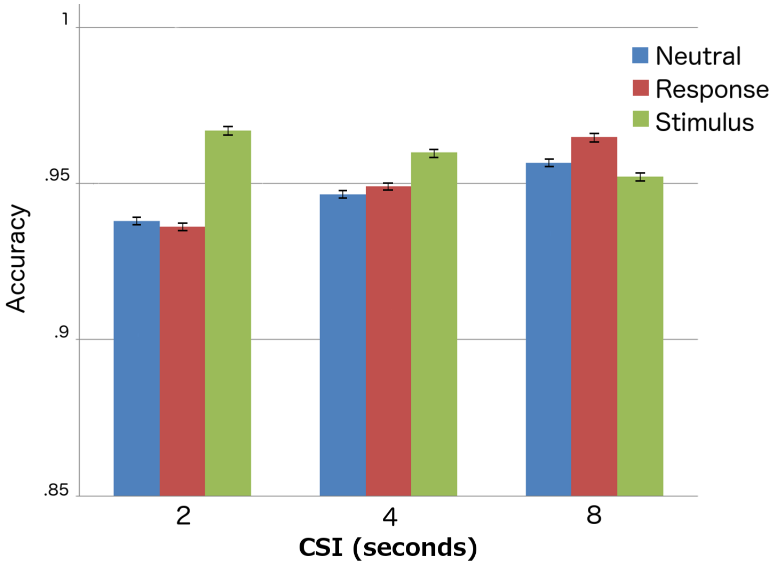


Figure 15: Accuracy by Cue Type x CSI. There was a difference between accuracies for CSIs of $8s$ and $2s$ across cue types, $p = .012$. There were no other significant effects in the accuracy data.

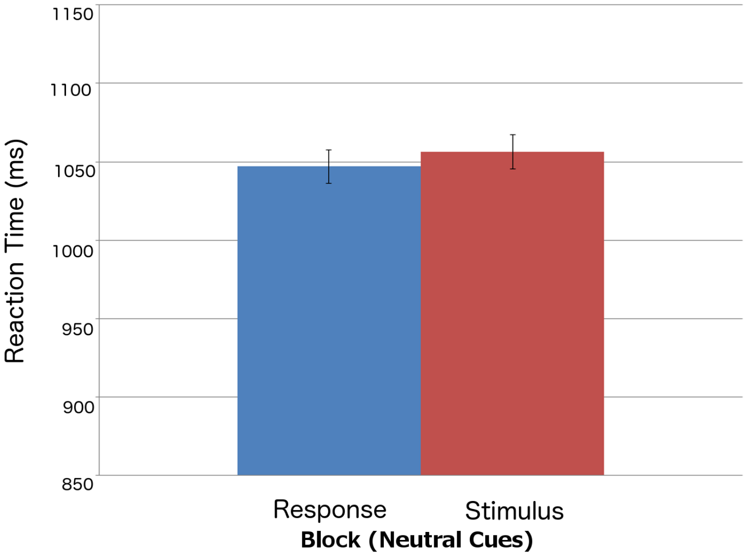


Figure 16: Comparison of RTs for neutral cue types between block. The difference between RTs for neutral cues in the stimulus ($RT = 105910.7ms$) and response blocks ($RT = 104910.7ms$) was not statistically significant ($p = .363$).

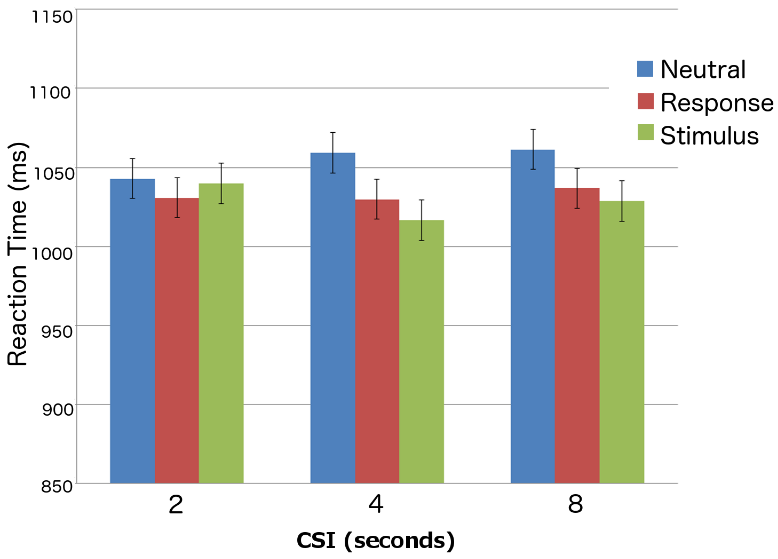


Figure 17: RT for cue type by CSI duration. A repeated measures ANOVA revealed a significant main effect of cue type, $p = .011$. The main effect of CSI duration and the interaction between CSI and cue type were not significant.

cue comparison ($O - S = 21.85 \pm 7.87ms$) was also statistically significant, $t(22) = 2.776$, $p = .006$. Thus, RTs decreased for both informative cue types relative to uninformative cues. The stimulus- versus response-cue comparison ($S - R = -1.78 \pm 9.16ms$) was not significant, $t(22) = -.194$, $p = .424$, indicating that there was no difference in performance for different informative cue types (Figure 17).

Importantly, comparing performance within informative cue types identified a significant difference in RTs for stimulus cues. Post-hoc analyses used Tukeys HSD test to correct for multiple comparisons, $r = 3$. There were significant differences in RT for face versus place ($F - P = 103.1 \pm 20.5ms$) cues, $q(22) = 7.10$; $p < .001$, and place versus neutral ($P - O = -72.6 \pm 11.2ms$) cues, $q(22) = 9.15$; $p < .001$. RTs for face versus neutral cues were not significantly different ($F - O = 30.5 \pm 14.4ms$), but there was a trend for increased RTs for face cues, $q(22) = 2.99$; $p = .110$ (Figure 19).

3.2 Imaging Results

The event-related design of this study allowed us to look at activity produced at the cue and the stimulus independently. First, we conducted whole-brain contrasts at both the stimulus and the cue presentation trial periods. All contrasts were corrected for the false

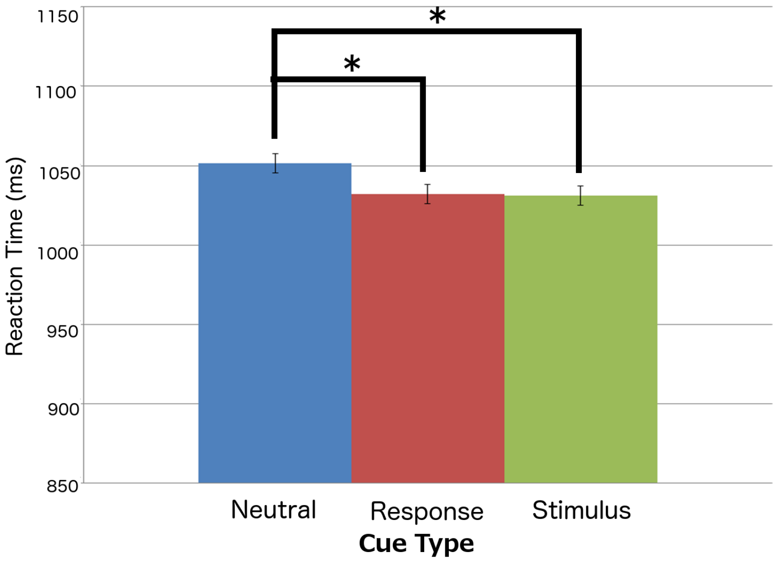


Figure 18: RT by cue type collapsed across block type and CSI duration. Planned comparisons between cue types showed a significant difference in RTs for Neutral versus Response cues and Neutral versus Stimulus cues. The difference between RTs for Response and Stimulus cues was not significant.

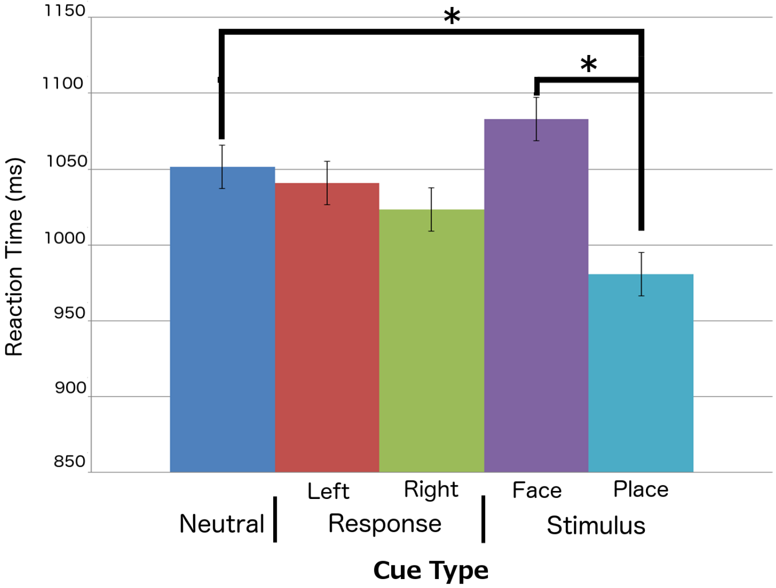


Figure 19: RT by specific cue. There was a significant difference in RT between Face and Place cues, as well as Neutral versus Place cues. This difference indicated greater RTs for faces than places.

Table 4: Regions Active for Stimulus Presentation versus Baseline. Whole-brain analysis revealed six regions with peak activations for the stimulus-versus-baseline comparison. All regions were significant at the $q = .05$ threshold with a cluster size greater than 10 voxels. (AAL = Automated Anatomical Label, BA = Brodmanns Area, SMA = Supplementary Motor Area).

AAL	**BA**	**Cluster Size**	**x**	**y**	**z**
Right Inferior Occipital	19	25	-33	87	-6
Left SMA	6	24	6	-12	54
Left Precentral Gyrus	44	21	45	-9	33
Left Inferior Parietal	7	16	27	48	48
Left Fusiform Gyrus	37	15	39	60	-12
Left Superior Parietal	7	14	24	63	48

discovery rate (FDR), and all significance levels are $q < .05$ unless otherwise noted; reported coordinates are local peak activation values. We then conducted regions-of-interest (ROI) analyses to compare activity in our functionally defined sensorimotor processing regions.

3.2.1 Whole-Brain Analysis

3.2.1.1 Stimulus-Related Activity

We first investigated uncued activity at the stimulus event to identify which regions were activated during task execution. Based on previous response cuing studies (Adam, Backes, et al., 2003; Hopfinger et al., 2000), we hypothesized that sensory- (FFG, PHG, LOC) and motor- (LPMC, DPMC, SMC, SMA) related processing areas would show significant activation when comparing all uncued activity at the stimulus to the baseline condition, as well as association cortex (MFG, IPC, SPC, IPS) and basal ganglia (striatum). When we compared activity for the uncued stimulus events versus baseline, our results showed significant activity in 6 regions with a cluster size above 10 voxels, shown in Table 4 and Figure 20.

We next compared activity for face stimuli versus place stimuli and for left versus right responses at the stimulus. Faces did not show any areas of significantly greater activity than places. Places showed greater activity than faces in 4 regions (shown in Table 5 and Figure 21).

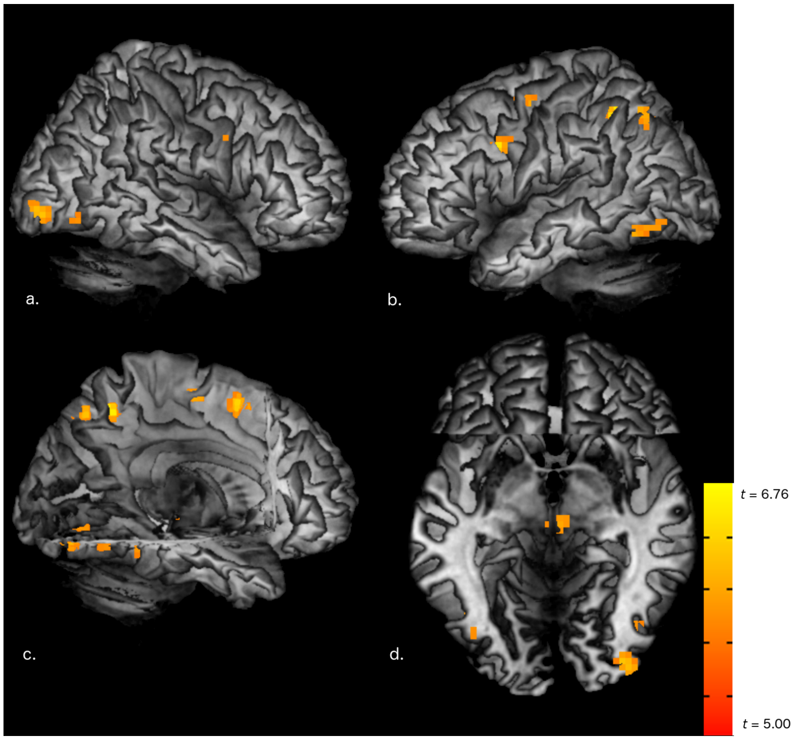


Figure 20: Images of results for uncued stimuli versus baseline at the stimulus event. (a) Right surface cortex; (b) left surface cortex; (c) saggital cutaway revealing right deep frontoparietal cortical activity; (d) axial cutaway revealing deep cortical FFG activation.

Table 5: Regions Active for Stimulus Presentation versus Baseline. Whole-brain analysis revealed six regions with peak activations for the stimulus-versus-baseline comparison. All regions were significant at the $q = .05$ threshold with a cluster size greater than 10 voxels. (AAL = Automated Anatomical Label, BA = Brodmanns Area, SMA = Supplementary Motor Area).

Contrast	**AAL**	**BA**	**Cluster Size**	**x**	**y**	**z**
Face>Place	*No Significant Activity*					
Place>Face	Right Middle Occipital	19	70	-36	81	15
	Left Parahippocampal Gyrus	37	38	33	42	-6
	Right Fusiform Gyrus	37	37	-30	48	-3
	Left Middle Occipital	19	26	33	87	21

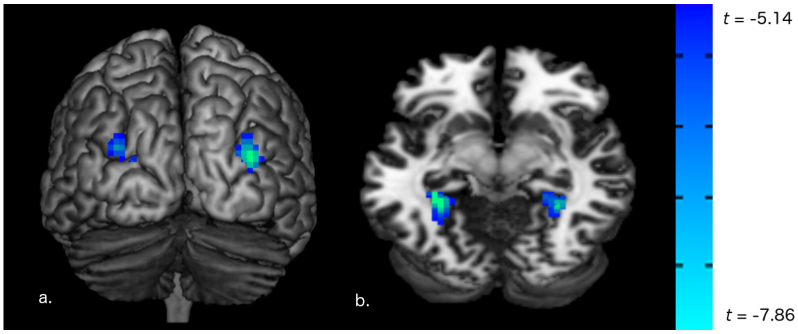


Figure 21: Images of results for uncued face stimuli versus place stimuli at the stimulus event. Figure (a) shows surface activity in the middle occipital gyrus; figure (b) shows an axial cutaway (rotated with a pitch of 45° for visualization) revealing deep cortical and subcortical activation in PHG and FFG.

As discussed previously, left responses showed significantly greater activity than right responses in right PMC and left cerebellum, and the reverse showed activity in left PMC and right cerebellum. These comparisons showed the expected lateralization of motor-related regions (Figure 15).

3.2.1.2 Cue-Related Activity

Activity for cued versus uncued trials at the cue did not survive whole-brain correction. Similarly, neither the face versus place cues nor the left versus right cues showed significant whole-brain activity.

3.2.2 Localizer Analysis

The localizer data showed significant activity in most of the anatomical regions of interest in 22 participants for faces > places and in 22 participants for places > faces. Of the participants that showed significant activity for faces, all participants had clusters in both FFG and LOC. Of the participants that showed significant activity for places, 18 participants had clusters in PHG and 22 had clusters in LG; 18 participants from these two pools had clusters in both regions.

3.2.3 Regions-of-Interest Analysis

We first investigated general cue-related activity across the ROIs by collapsing across trial types and assessing all cued trials versus uncued trials. More specifically, we hypothesized that we would see general cue-related activity in the regions previously defined by Adam, Hommel, et al. (2003). However, no regions showed significant cuing effects.

To investigate the specific effects of individual cues on these regions, we compared activity in our previously defined ROIs for stimulus and response specific cue types (i.e., face versus place stimulus cues and left versus right response cues). To understand how grouping processes affected biasing of processing region activation, we looked at two conditions. The first, referred to here as the explicit cue condition, refers to the stimulus or response that is directly referenced by the cue. For example, consider a subject whose mapping involves making left hand responses to face stimuli and right hand responses to place stimuli. An "F" during the cuing event would explicitly cue an upcoming face stimulus. The second condition, called the implicit cue condition, refers to the stimulus or response that is indirectly indicated by a cue by virtue of the perfectly overlapped nature of our stimulus and response sets. In the previous example, the same "F" cue, while explicitly cuing a face stimulus, would also indirectly indicate that the upcoming response must be executed with the left hand. If subjects are processing the stimuli and responses as S-R pairs, we would expect to see activation of the cue-related regions by both the explicit and implicit cue. In the same example, this would mean that at an "F" cue event, we would expect to see increased activity in FFA/LOC (Face-related; explicit) and right premotor/left cerebellum (Left response-related; implicit). These effects were investigated by block type.

3.2.3.1 Response-Cued Blocks

To investigate explicit cue effects in the response-cued blocks, we looked at activity at "L" versus "R" cues in the left and right motor and cerebellar ROIs. The results showed a significant difference in activity between contralateral and ipsilateral premotor cortex, $t(22) = 8.044$, $p < .001$. The results also showed a significant difference in activity between ipsilateral and contralateral cerebellar regions, $t(22) = 5.940$, $p < .001$ (Figure 22).

Likewise, to investigate implicit cue effects, we looked at the same contrast in the face and place processing-related regions according to the mapping order of each subject. (E.g., for subjects with faces mapped to the left hand, we investigated Face ROI > Place ROI for ”L” versus ”R” cues, and vice versa for subjects with faces mapped to the right hand). This contrast did not show significant effects, $t = -.274$, $p = .393$ (see Figure 23).

3.2.3.2 Stimulus-Cued Blocks

To investigate explicit cue effects in the stimulus-cued blocks, we looked at activity at ”F” versus ”P” cues in the face and place processing-related regions. This contrast did not show significant effects, though there was a trend for increased activity in FFA for faces, $t = 1.317$, $p = .101$ (see Figure 24).

To investigate implicit cue effects, we looked at activity at ”F” versus ”P” cues in contralateral motor regions and ipsilateral cerebellar regions according to the mapping order of each subject, similar to the analysis of the response blocks. The results showed significant differences in activity between contralateral and ipsilateral motor regions, $t(22) = 5.964$, $p < .001$, as well as between ipsilateral and contralateral cerebellar regions, $t(22) = 6.030$, $p < .001$ (Figure 25).

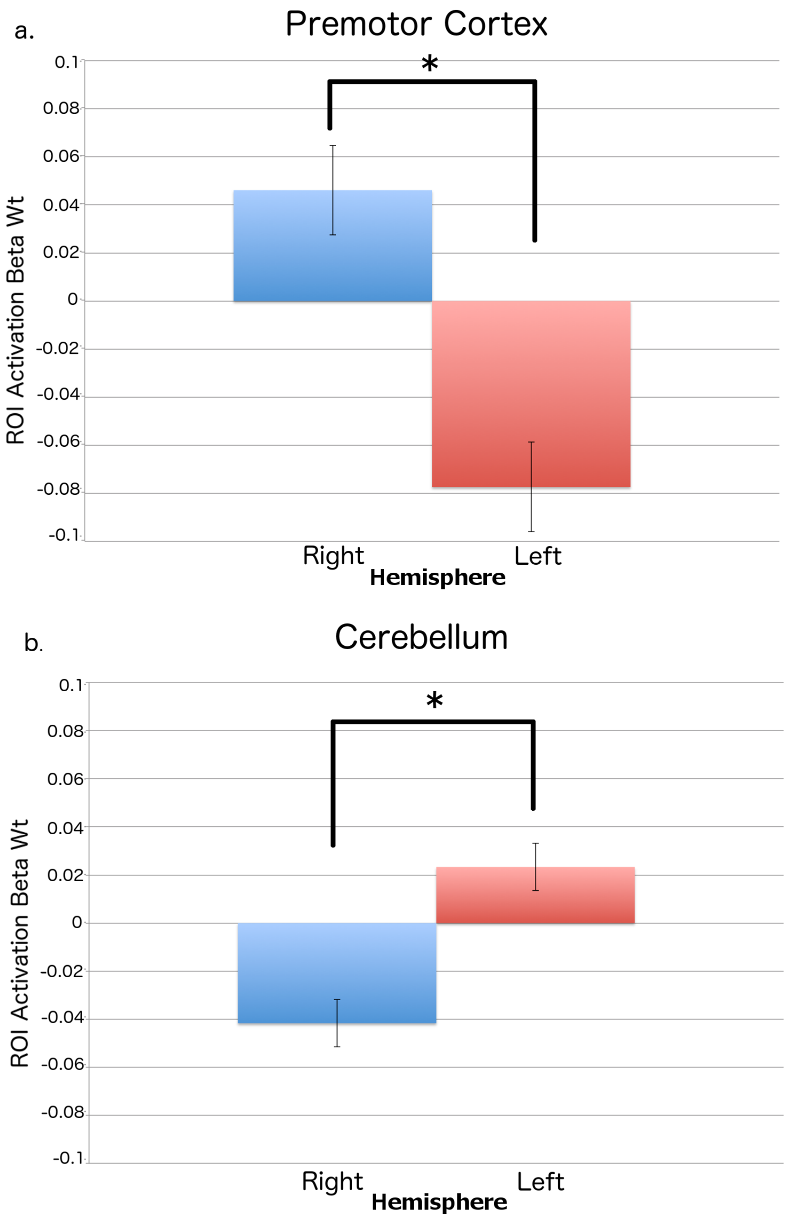


Figure 22: Response processing region biasing by left versus right response cues. Results showed (a) contralateral biasing in premotor cortex and (b) ipsilateral biasing in cerebellar regions.

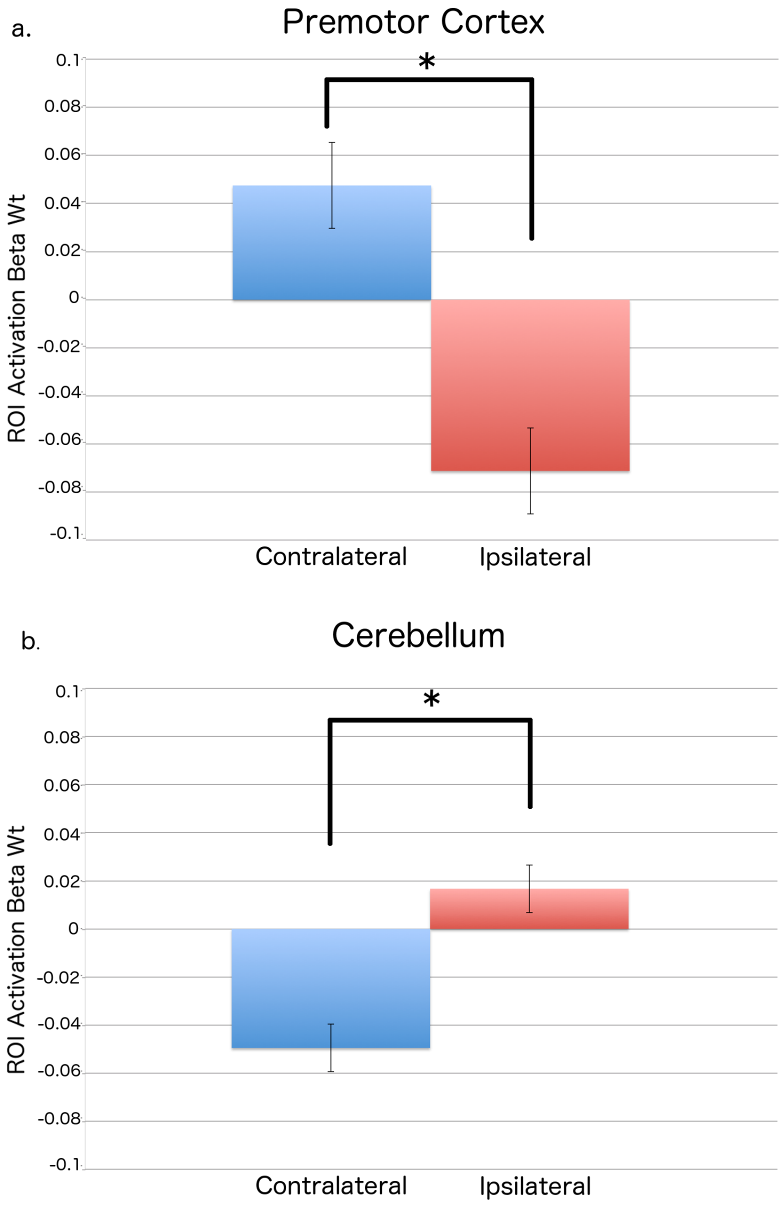


Figure 23: Stimulus processing region biasing by left versus right response cues. Results are shown split by mapping group, i.e., which hand each stimulus was mapped to. Results did not show a significant difference in activity between these regions in either group.

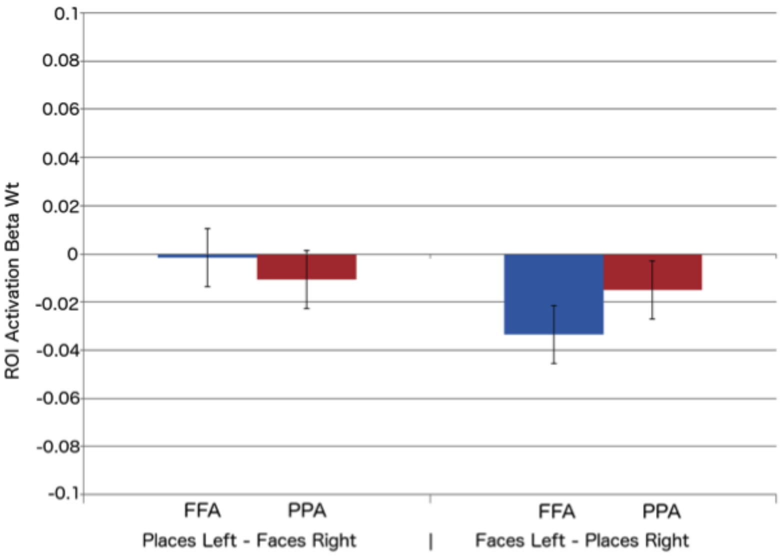


Figure 24: Stimulus processing region biasing by face versus place stimulus cues. Results did not show a significant difference in activity between these regions.

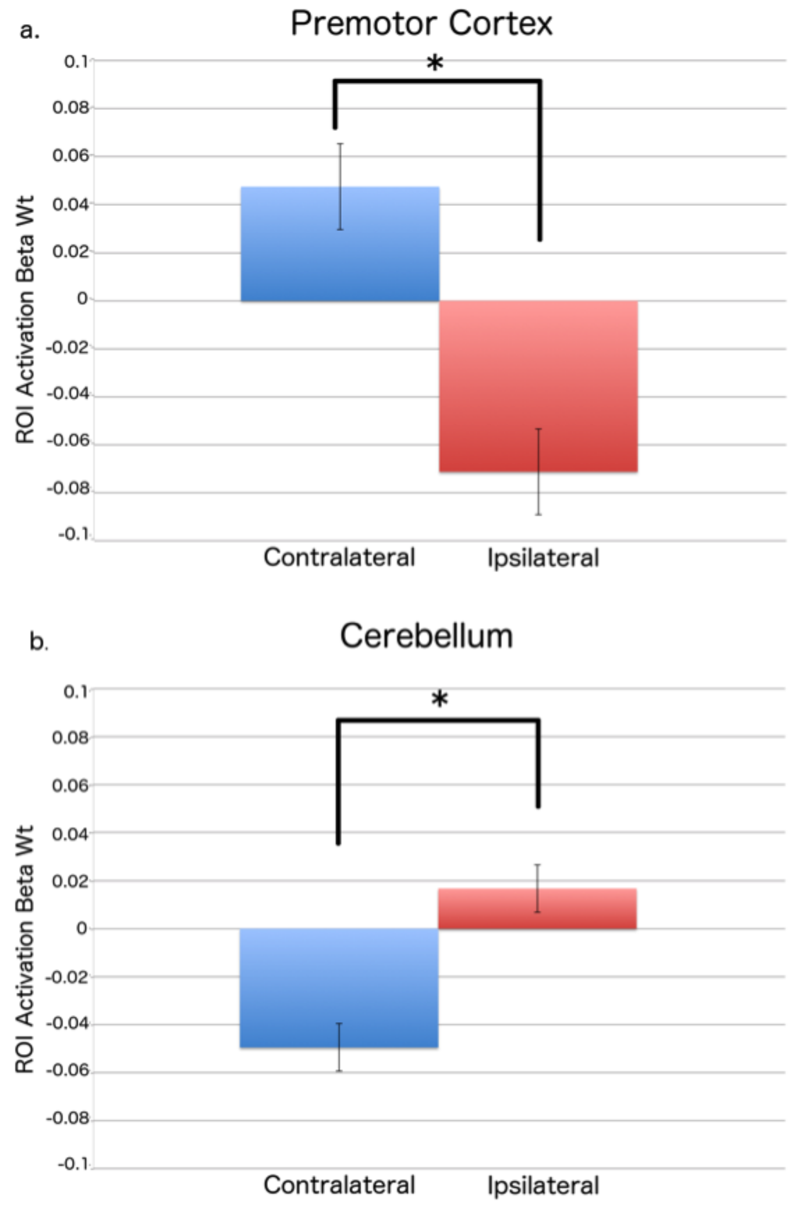


Figure 25: Response processing region biasing by face versus place response cues. Activity is shown collapsed across mapping groups. Results showed (a) contralateral biasing in premotor cortex and (b) ipsilateral biasing in cerebellar regions.

CHAPTER IV

DISCUSSION

The present experimental design allowed us to investigate response cuing at a number of levels. At the highest level, we hypothesized that the activity pattern at the cue for informative versus uninformative cues would reflect much the same regions discussed by Adam, Hommel, et al. (2003) and Hopfinger et al. (2000). However, neither the whole-brain nor the ROI analyses replicated these effects.

At the whole-brain level, no activity for the informative versus uninformative cue contrast survived correction; this likely indicates a lack of power inherent in our design. Each trial in our design had an average duration of 12 seconds, while the cue lasted only 2 seconds. This reduced the data available for cue-related analysis by one-sixth. In contrast, Adam, Hommel, and colleagues (2003) used full trials in their contrast, relying on the differences in trial types to elucidate cue processing-specific activity. While this design allowed them to use a much larger portion of the data, it did not allow for the investigation of the event-specific timecourse of activity. Future research should focus on developing designs that maximize the usable signal in event-related contrasts, especially for investigations of the highly variable association cortices.

We had hoped that the ROI analysis would alleviate the power issues in the whole-brain analysis; however, we failed to see activity in the expected regions for informative versus uninformative cues. It is unclear why we failed to replicate previous work. It is possible that our design is taking advantage of a cuing effect that is separate from those investigated by Adam, Backes, et al. (2003) and Hopfinger et al. (2000). Unlike the preceding literature, our design used endogenous cues to impart information about the upcoming trial. In other words, participants had to translate an otherwise unrelated letter cue into a meaningful piece of information related to the task based on the given instructions. On the other hand, both Adam, Backes, and colleagues and Hopfinger et al used exogenous cues in their experiments. Hopfinger and colleagues used an arrow pointing in the direction of one of the two checkerboards to directly indicate which to attend; similarly, Adam, Backes, and colleagues (2003) used cues that directly mapped to the spatial order of the response buttons to indicate a subset of upcoming responses. Adam, Hommel, et al (2003) suggested in their behavioral experiment that exogenous and endogenous cues may involve different cognitive processes; specifically, whereas exogenous cues use the same dimension for the cue as for the stimulus, endogenous cues require a translation from the cue dimension to the stimulus dimension before the information can be used for response preparation. This may require two unique processing pathways that activate distinct networks of regions, which could have resulted in the failure here to produce activity in the regions identified by Adam and colleagues.

However, this explanation seems unlikely. Rather than two separate pathways processing endogenous and exogenous cues, we would expect to capture additional activity that reflected the additional translational steps found in endogenous cue processing, rather than a loss of activity in regions implicated in other aspects of cue processing more generally. An alternative explanation for our results that would fit this idea is that cue processing unfolds over time and we only captured the first part of it while the cue was onscreen. In our design, we treated the CSI event as noise; however, if cue processing does not occur purely during the presentation of the cue, but unfolds over time during the entire interval between the start of cue presentation and the presentation of the stimulus, then a number of processing steps occurred during this CSI interval and were lost in the analysis. This idea is supported by the visual trend for a larger cue benefit for longer CSIs (Figure 18). At the same time, it may be that the cuing effect produces variable but not sustained activity across the CSI. Repeated analysis of these data (analysis not presented here) including the CSI in the duration of the cue event did not show significant cue-related activity, which suggests the latter hypothesis. Further research will need to develop new ways to assess these data on short time resolutions and tease apart the subtle dynamics associated with the CSI interval.

At our next level of analysis, we investigated the ability of a specific cue to bias processing toward the region(s) that corresponded with the explicitly cued stimulus or response type; e.g., in the face condition, we would expect to see greater activity in FFA, whereas in the place condition we would expect to see PPA activation. Our results demonstrated this pattern in contralateral premotor cortex and ipsilateral cerebellum for left versus right response cues, indicating that participants are able to use response-related cues to prepare the related motor before stimulus presentation. This supports the possibility that the dynamics of cue processing extend beyond the cue presentation event, as this biasing would be the result of downstream effects of these processes.

We did not find the same pattern of results for face versus place cues in face- and place-related processing regions. This may be related to the same power issues discussed for the whole brain results. In this case, the data are even more limited; of the one-sixth of data that consist of cue events, to perform the analysis required limiting the data even further to just one-third of the remaining pool (two-thirds of trials were informative cues; one-half of these were stimulus blocks), such that the final data size was one-eighteenth of the full set of data. However, the fact that response regions showed a robust biasing effect with these same power limitations may suggest a more mechanistic explanation. It is possible that biasing of face and place processing occurs on a different timescale than biasing of response hand; that is, biasing of response regions may occur earlier in processing, or perhaps require fewer mediating steps before biasing can be executed.

Our remaining results may shed more light on these dynamics. In addition to the explicit cuing effects discussed above, we investigated whether these same cues could produce biasing of activity in regions related to the processing of the implicitly cued stimulus or response. Interestingly, we found the same pattern of results for this comparison as we saw in the explicit cue comparison; that is, implicit left/right response cues showed significant biasing of activity in the related contralateral premotor and ipsilateral cerebellar regions, but implicit face/place stimulus cues did not show significant biasing of activity in face and place processing regions. The increased biasing of response processing regions than sensory processing regions in the 2-second cue interval could have two different mechanisms. If cues for responses are processed earlier or faster than cues for stimuli, assuming biasing processes have a consistent duration, then we would not expect to see response region biasing in the implicit cue comparison. In the explicit comparison, we found motor processing region biasing within the two-second cue event, but not stimulus processing region biasing. These results correspond to the presentation of L/R cues and F/P cues, respectively; in the explanation above, this would imply that participants are processing L/R cues faster than F/P cues. In the implicit condition, participants would then have to process this slower F/P cue before being able to translate this into the corresponding response hand, which would predict even slower processing dynamics than the implicit biasing of the L/R cues. Alternatively, it may be that the biasing effect produces a stronger effect in response processing regions than in stimulus processing regions, but that these effects follow the same timecourse. This would produce the results found here; however, it is not clear why this would be the case. Further research is needed to better understand the roles of each of the regions related to cue processing, the networks that connect them, and the activation dynamics that occur on a short timescale.

We can speculate briefly on a mechanistic explanation of our results by going back to our earlier discussion of task sets. If participants are representing their task as two separate subtasks, then the cue may be used to activate one task set over another. This selection process would take the same time regardless of cue type. The task set would include both the stimulus and response subsets related to the cued subtask. Activation of a task set would then produce a cascade that biased both sensory and motor processing regions; however, the biasing pathways for each of these may have varying activation times. If, then, the part of the cascade that biased motor processing regions took less time to develop than that for the sensory processing regions of the same subtask, we would see precisely the results reported here. In either the explicitly or implicitly cued case, we would (and did) see biasing of the corresponding motor processing regions within the timeframe of analysis, whereas we would not see a similar of biasing of sensory processing regions.

Beyond these questions of cue processing dynamics, there remains the strange RT effect between face cues and place cues (Figure 20). It is not clear why face cues produced slower RTs than place cues. Our stimuli consisted of black and white images, and place stimuli were specifically images of buildings. It is possible that the building images used here were simply more easily distinguished from one another than the face images. In any case, this difference may have played a role in the lack of activity seen for stimulus-related cues; especially if the trend for face cues producing slower RTs even than neutral cues indicated a real effect, participants may have been processing face cues on a different timescale than the other cues, or even strategically avoided processing face cues altogether if they felt the cue was not informative enough to benefit performance. The collapsing of face and place cues may then have combined typical cue-related activity present at the place cue events with abnormal or nonexistent cue-related activity for face-cue events, resulting in a loss of signal.

Despite the rich literature behind the response cuing paradigm, these data overall indicate that there is still much to understand about the brain activity and dynamics of processing underlying what on the surface is a simple task. As discussed previously, future research on these neural mechanisms will need to develop new paradigms and techniques for teasing apart the subtle, often short time-scale dynamics that have been implicated by our data. Furthermore, our results suggest a key role of task sets in the cuing effect seen in this and other variations of the response cuing paradigm. It is likely that the processes underlying these two concepts are highly overlapping; collaboration of these two fields would undoubtedly help illuminate the mechanisms behind these phenomena.

REFERENCES

[1] Adam, J. J., Backes, W., Rijcken, J., Hofman, P., Kuipers, H., and Jolles, J., "Rapid visuomotor preparation in the human brain: a functional mri study," *Brain Research. Cognitive Brain Research*, vol. 16, no. 1, pp. 1–10, 2003. 10.1016/S0926-6410(02)00204-5.

[2] Adam, J. J., Hommel, B., and Umiltà, C., "Preparing for perception and action (i): The role of grouping in the response-cuing paradigm," *Cognitive Psychology*, vol. 46, 2003. 10.1016/S0010-0285(02)00516-9.

[3] Adam, J. J., Hommel, B., and Umiltà, C., "Preparing for perception and action (ii): Automatic and effortful processes in response cueing," *Visual Cognition*, vol. 12, 2005. 10.1080/13506280444000779.

[4] Cox, R., "Afni: software for analysis and visualization of functional magnetic resonance neuroimages," *Computers and Biomedical Research, an International Journal*, vol. 29, no. 3, pp. 162–173, 1996. 10.1006/cbmr.1996.0014.

[5] Egner, T. and Hirsch, J., "Cognitive control mechanisms resolve conflict through cortical amplification of task-relevant information," *Nature Neuroscience*, vol. 8, no. 12, pp. 1784–1790, 2005. 10.1038/nn1594.

[6] Friston, K. J., Holmes, A. P., Poline, J. B., Grasby, P. J., Williams, S. C. R., Frackowiak, R. S. J., and Turner, R., "Analysis of fmri time-series revisited," *NeuroImage*, vol. 2, no. 1, pp. 45–53, 1995.

[7] Gorno-Tempini, M. and Price, C., "Identification of famous faces and buildings a functional neuroimaging study of semantically unique items," *Brain*, vol. 124, no. 10, pp. 2087–2097, 2001.

[8] Hommel, B., "Event files: feature binding in and across perception and action," *Trends in Cognitive Sciences*, vol. 8, 2004. 10.1016/j.tics.2004.08.007.

[9] Hopfinger, J., Buonocore, M., and Mangun, G., "The neural mechanisms of top-down attentional control," *Nature Neuroscience*, vol. 3, no. 3, pp. 284–291, 2000. 10.1038/72999.

[10] Kanwisher, N. and Yovel, G., "The fusiform face area: a cortical region specialized for the perception of faces," *Philosophical Transactions of the Royal Society B: Biological Sciences*, vol. 361, no. 1476, pp. 2109–2128, 2006.

[11] Martinez, A. M. and Benavente, R., "The ar face database," *CVC Technical Report*, vol. 24, 1998.

[12] McClelland, J. L., "On the time relations of mental processes: An examination of systems of processes in cascade," *Psychological Review*, vol. 86, no. 4, p. 287, 1979.

[13] Miller, J., "Discrete versus continuous stage models of human information processing: in search of partial output," *Journal of Experimental Psychology. Human Perception and Performance*, vol. 8, no. 2, pp. 273–296, 1982.

[14] Ollinger, J. M., Shulman, G. L., and Corbetta, M., "Separating processes within a trial in event-related functional mri," *NeuroImage*, vol. 13, 2001. 10.1006/nimg.2000.0710.

[15] Reeve, T. and Proctor, R., "On the advance preparation of discrete finger responses," *Journal of Experimental Psychology: Human Perception and Performance*, 1984.

[16] Rosenbaum, D. A., "The movement precuing technique: Assumptions, applications, and extensions," *Advances in Psychology*, vol. 12, pp. 231–274, 1983.

[17] Sternberg, S., "Memory-scanning: mental processes revealed by reaction-time experiments," *American Scientist*, vol. 57, no. 4, pp. 421–457, 1969.

[18] Worsley, K. J. and Friston, K. J., "Analysis of fmri time-series revisited—again," *NeuroImage*, vol. 2, no. 3, pp. 173–181, 1995.