THE COORDINATION AND CONTROL OF ATTENTION IN LATERAL PREFRONTAL CORTEX

By

Christopher L. Asplund

Dissertation

Submitted to the Faculty of the

Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

in

Neuroscience

December 2010

Nashville, Tennessee

Approved:

Professor Mark Wallace

Professor René Marois

Professor Frank Tong

Professor John Rieser

ACKNOWLEDGEMENTS

I have had the good fortune of receiving assistance, guidance, criticism, and support from a multitude of people. Let me start by thanking René, my advisor. He provided the right mix of patience, understanding, and ass-kicking to ensure that this dissertation was the best we could make it. Even when my enthusiasm for the work flagged, René was always there to convince me that I should take a step back and become excited again about what I was doing. The rest of my committee also displayed consistent enthusiasm for the project, offering useful criticisms as the dissertation aims changed and developed over the past several years. I have also had the priviledge of knowing each of my committee members on a more personal level, and I have benefited greatly from their perspectives and advice.

A few people in the Marois lab directly contributed to the experiments in this dissertation--specifically Jay Todd, Andy Snyder, and Paul Dux--, but simply stating that would grossly underrepresent their importance to my development as a graduate student. Other lab members--Daryl Fougnie, Suk Won Han, Joshua Buckholtz, Michael Treadway--were also important for this development, and their indirect contributions to the dissertation were invaluable. Three outstanding undergraduates assisted in collecting and analyzing data for various experiments and in proofreading the dissertation itself. All three have my thanks: Ellie Conser, Justin Martin, and Janice Louie.

Vanderbilt is a highly collaborative place, and many people and institutions outside my dissertation committee and lab were crucial to this dissertation. Three individuals deserve special thanks: Baxter Rogers, Jascha Swisher, and Jeremiah Cohen. I would also like to thank the Vanderbilt Brain Institute, Neuroscience Graduate Program, Department of Psychological Sciences, and Vanderbilt University Institute of Imaging Sciences. Colleagues and friends in these various organizations--too many to name--left their mark on my work and me. Naturally, none of my research would have happened without funding, much of which came from National Science Foundation grant 0094992 and National Institute of Mental Health grant R01 MH70776 (both to René); a T32 training grant to the Vanderbilt Brain Institute supported me during my first two years at Vanderbilt.

Of course, this dissertation was started long before my time at Vanderbilt. For my formative years and the present, I am grateful to my parents and the rest of my family, who have supported, loved, nutured, and taught at every step. I have also been lucky to count many mentors and teachers during my formal education, namely Jane Wolfe, Al Spens, F. Lee St. John, Philip Johnson-Laird, Jack Gelfand, Bennett Givens, and Dave Noelle. Finally, I thank my muse Peiyan for her unwavering support--whether through lending a friendly ear or providing a template for my table of contents--and love.

ABSTRACT

Our world constantly bombards us with more information than we can process. To ensure that we can act in accordance with our goals and relevant events, we use attention to select and enhance aspects of our environment. Attention is not unitary, able to be captured by salient events (stimulus-driven) or deployed under voluntary control (goal-directed). These two forms of attention rely on largely distinct ventral and dorsal fronto-parietal networks. While these networks have been extensively studied, their control and coordination is poorly understood. Using functional neuroimaging and a variety of behavioral tasks, this dissertation shows that the inferior frontal junction (IFJ) of the prefrontal cortex may be a key region in the control and coordination of attention. I employ a novel ‘Surprise-induced Blindness’ paradigm to show that the IFJ and temporo-parietal junction (TPJ), core members of the ventral attention network, support stimulus-driven attention. I then demonstrate that the IFJ co-activates with the dorsal attention network--including the frontal eye field (FEF) and intra-parietal sulcus (IPS)--for goal-directed attention. This result suggests that the IFJ may coordinate stimulus-driven and goal-directed attention. The remainder of the dissertation functionally distinguishes the IFJ from other regions within the ventral and dorsal attention networks. I first dissociate the function of the IFJ from the ventral attention network’s TPJ by demonstrating that only the latter is activated during a task in which participants reason about others' mental states (Theory of Mind) and while resting between the attention-demanding periods of a search task (Default Mode of Processing). Using an endogenous Posner cueing task, I next show that the IFJ is involved in cue interpretation for setting goal-directed attentional weights, but not in the maintenance of these weights. The FEF and IPS, by contrast, are involved in both processes. I conclude that the IFJ’s primary function may be to connect incoming sensory information with appropriate behavioral or dispositional responses, coordinating the activity of widespread brain regions to do so. Consequently, the IFJ influences central aspects of human information processing and even the contents of consciousness.

TABLE OF CONTENTS

LIST OF TABLES

Chapter

II. THE CENTRAL ROLE OF THE INFERIOR FRONTAL JUNCTION IN STIMULUS-DRIVEN AND GOAL-DIRECTED ATTENTION

III. THE FUNCTIONAL SEGREGATION OF THE VENTRAL ATTENTION NETWORK: SEPARATING THE INFERIOR FRONTAL JUNCTION FROM THE TEMPORO-PARIETAL JUNCTION

IV. THE FUNCTIONAL SEGREGATION OF THE INFERIOR FRONTAL JUNCTION FROM THE DORSAL ATTENTION NETWORK

V. SUMMARY AND CONCLUSION

LIST OF FIGURES

Chapter

I. INTRODUCTION

II. THE CENTRAL ROLE OF THE INFERIOR FRONTAL JUNCTION IN STIMULUS-DRIVEN AND GOAL-DIRECTED ATTENTION

III. THE FUNCTIONAL SEGREGATION OF THE VENTRAL ATTENTION NETWORK: SEPARATING THE INFERIOR FRONTAL JUNCTION FROM THE TEMPORO-PARIETAL JUNCTION

IV. THE FUNCTIONAL SEGREGATION OF THE INFERIOR FRONTAL JUNCTION FROM THE DORSAL ATTENTION NETWORK

V. SUMMARY AND CONCLUSION

CHAPTER I

INTRODUCTION

For many animals, the connection between an environmental event and its behavioral response is often a direct one. Consider a common kitchen inhabitant, the cockroach. Most of its behaviors are automatic responses to simple triggering events. If one flips on the lights or touches its leg, the insect runs, regardless of the appropriateness of the behavior at that moment. While such simple, quick, and hard-wired transformations generally work very well for the cockroach, other animals have developed a different approach. These animals, including humans, instead rely on large and complex brains to adapt flexibly as the environment changes around them. Such flexibility includes choosing to attend to a single item in a crowded scene, selecting an appropriate response to an event, or even completely changing internal goals in light of new information. Highly developed brains allow for the formulation of internal goals and the coordination of thoughts and actions in accordance with them.

The neural underpinnings of this cognitive adaptability have been a topic of intense study in recent years, with many investigations indicating the prefrontal cortex (PFC) as the site of control and coordination of a wide range of mental processes (Miller & Cohen, 2001; Duncan, 2001; Koechlin & Summerfield, 2007; Marois & Ivanoff, 2005). The PFC influences disparate parts of the brain, thereby orchestrating the proper mappings between sensory information, dispositions, and responses (Miller & Cohen, 2001). To support these ever-changing mappings, the neurons within the PFC are themselves flexible in what they represent, demonstrating different neural firing profiles as task demands change (Duncan, 2001). This neural and cognitive flexibility associated with the PFC is relatively new from an evolutionary standpoint, so it is unsurprising that this brain region is among the latest to evolve and be elaborated upon in the primate lineage; it is also one of the last regions to mature in developing humans (Hill et al., 2010; Badre & D'Esposito, 2009; Diamond, 2006).

Despite the general flexibility of the PFC, it can be divided functionally and anatomically into a number of distinct regions (Petrides & Pandya, 2001; Brodmann, 1909; Miller & Cohen, 2001; Koechlin et al., 2003; Koechlin & Summerfield, 2007; Badre et al., 2009; Badre & D'Esposito, 2009; Marois & Ivanoff, 2005). One proposed functional arrangement runs anterior to posterior, with abstract plans formed in the anterior portions and concrete ones more posterior (Koechlin et al., 2003; Koechlin & Summerfield, 2007; Badre, 2008; Badre et al., 2009; Badre & D'Esposito, 2009). These posterior sections of PFC are thought to support processing that is immediately relevant to the environment and our actions in it. In particular, posterior PFC supports the control of visuospatial attention (Corbetta et al., 2008; Corbetta & Shulman, 2002), which allows us to select and enhance certain stimuli in the environment for further processing. It is also associated with "attention to action", which includes monitoring and instructing the premotor regions that plan specific actions (Passingham, 1993).

A general function that has been associated with the posterior PFC is attentional selection of behaviorally relevant percepts and actions. The posterior PFC allows us to select items in our environment visually (perceptual selection; Marois et al., 2000; Marois et al., 2004) and to select rules or mappings related to making responses (Dux et al., 2006; Brass et al., 2005; Bunge, 2004; Crone et al., 2006). Although numerous brain regions support attention and selection, these functions appear to converge in a specific part of posterior PFC, the inferior frontal junction (IFJ; Marois & Ivanoff, 2005; Derrfuss et al., 2005; Brass et al., 2005), placing this brain region at a strategic position to exert control over fundamental functions in human information processing. The overarching goal of the present dissertation is to explore the roles of the IFJ in the control of attention and selection by distinguishing them from the functions of other core members of the attentional networks of the human brain.

Anatomy of the IFJ

By definition, the IFJ sits at the junction of the inferior frontal sulcus and the precentral sulcus. This location is a transition zone between premotor cortex (BA 6) and the anterior regions of prefrontal cortex (e.g., BA 9 and 46). In Brodmann's original parcellation of the human cortex, the IFJ included parts of areas 6, 44, and 9 (see Figure 1; Brodmann, 1909), but more recent parcellations (Petrides & Pandya, 2001; Diamond, 2006) extend BA 8 to the inferior frontal sulcus because the cortex there tends to have a dysgranular layer IV (transitional between agranular and granular) instead of the robustly granular layer IV associated with the rest of BA 9. BA 44 is also dysgranular, so areas 8 and 44 constitute a strip of cortex that is both distinct from and transitional between the agranular premotor and granular anterior prefrontal regions that surround it; indeed, some have consequently suggested that this strip should be considered functionally distinct (Badre, 2008). In addition, Amunts & von Cramon (2006) claim that the cytoarchitecture at the junction of BA 8 and BA 44 is different from that of the surrounding tissue, perhaps indicating that the IFJ is a distinct neuroanatomical region (Amunts et al., 2004).

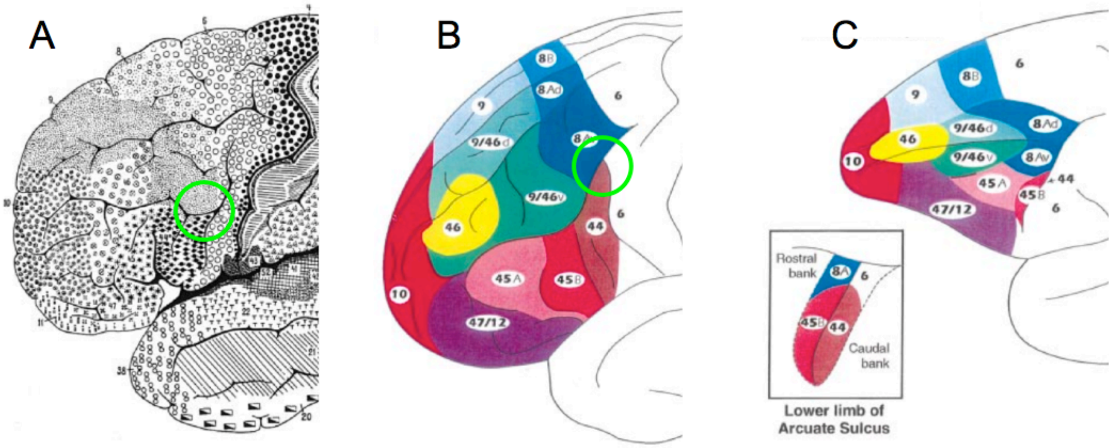

Figure 1. Cytoarchitectonic divisions of the human frontal lobe and macaque frontal lobe. The green circle indicates the approximate position of the IFJ in humans. A) In Brodmann's original maps of human cortex (Brodmann, 1909), the IFJ included areas 9, 44, and 6. B) In Petrides & Pandya's update of human cortical maps (2001), the IFJ includes areas 8, 44, and 6. C) IFJ is likely homologous to the ventral arcuate sulcus (see inset) in the macaque frontal lobe.

The primate literature provides little support for a specialized region homologous to human IFJ, and even a general homology has been difficult to discern. Based on updated parcellations of cortex in humans and macaques

(Petrides & Pandya, 2001), Diamond (2006) has argued that the IFJ is homologous with the ventral branch of the arcuate sulcus. This region includes parts of macaque areas 6, 8, 44, and 45 (Petrides & Pandya, 2001; Walker, 1940), which are in turn thought to be homologous with their similarly-labeled human counterparts. The arrangement of these regions is slightly different in macaques (Figure 1), and the border of areas 8 and 45 has also been identified as a ventral portion of the frontal eye field (FEF). Although the primary portion of FEF is located more dorsally in area 8 (Schall et al., 1995), electrical microstimulation in the putative macaque IFJ elicits small saccades (Bruce et al., 1985). Although in humans the putative FEF (at the intersection of the superior frontal sulcus and precentral sulcus) appears to be distinct from the IFJ, the latter has been observed to be activated during visually-guided (Luna et al., 1998) and memory-guided saccades (Kastner et al., 2007).

Despite the unclear location of the monkey IFJ homologue, the anatomical connections from the ventral arcuate sulcus and its surrounding cortex are potentially relevant to human IFJ connections. In humans, long-distance anatomical connections from the IFJ join the superior longitudinal fasciculus (SLF), whose "constituent fibers are so intermingled that it is quite impossible to determine their precise connexions by gross methods and for this purpose the dissecting microscope is of no real help" (Williams & Warwick, 1975, pg. 971). In macaques, diffusion spectrum imaging (DSI) and autoradiography have found that one division of the SLF connects inferior parietal regions with areas 6 and 44, whereas another division connects superior parietal regions with FEF and prefrontal cortex (Schmahmann et al., 2007). Injected tracers in both the macaque and baboon find that the ventral arcuate sulcus has strong connections with many prefrontal (9/46) and premotor (6) regions (Watanabe-Sawaguchi et al., 1991; Petrides & Pandya, 2001). DTI in humans largely confirms these connectivity results, with one SLF division connecting postero-lateral PFC to the inferior parietal and superior temporal cortex (Doricchi et al., 2008; Umarova et al., 2010; Bernal & Altman, 2010), and another linking more dorsal regions of PFC (likely including the FEF) with the superior parietal cortex and IPS (Umarova et al., 2010; Doricchi et al., 2008). The combination of short-range and long-distance connections gives the IFJ (and its putative homologue, the ventral arcuate sulcus) a reach to both neighboring areas and to more distant regions including the inferior parietal cortex and even the superior parietal cortex by way of the FEF. Thus, the IFJ has the anatomical connections to influence and coordinate disparate cortical areas.

Function of the IFJ

With strong connections between the IFJ and adjacent regions, the functional properties of the regions proximal to the IFJ are also potentially relevant to understanding IFJ function. Ventral to the IFJ is the inferior frontal gyrus (IFG). In the left hemisphere this region contains Broca's area, which underlies some aspects of language processing, while on the right the IFG supports response inhibition (Aron et al., 2004; Chikazoe et al., 2009). Dorsal to the IFJ is the FEF, which directs visuospatial attention and eye movements

(Corbetta et al., 1998; Corbetta & Shulman, 2002). Premotor cortex, which supports motor planning, and dorsolateral PFC (BA 46 and 9), associated with higher-order and more abstract cognitive control, lie posterior and anterior to IFJ, respectively. Although the proximity of these regions does not imply that the IFJ simply performs a blend of the functions ascribed to them, it seems likely that the type of processing--namely control and coordination of attention and actions--is similar across these prefrontal and frontal regions (Brass et al., 2005).

Consistent with its anatomical location and connections to both adjacent and distant brain regions, the IFJ has been found to participate in many different control and coordination processes. One prominent function both in the literature and in this dissertation is the control of visuospatial attention. Attention is not a unitary process, as a fundamental division has been proposed between stimulus-driven attention and goal-directed attention. The former is evidenced when attention is captured by an unexpected event, whereas the latter is the deployment of attention under voluntary control in accordance with ongoing behavioral goals (Egeth & Yantis, 1997; Corbetta & Shulman, 2002). These two forms of attention rely on two largely distinct brain networks, with a ventral one consisting of ventral prefrontal cortex, the IFJ, and the temporo-parietal junction (TPJ) underlying stimulus-driven attention; and a dorsal one including FEF, the intra-parietal sulcus (IPS), and the neighboring superior parietal lobule (SPL) supporting goal-directed attention (see Figure 2; Corbetta & Shulman, 2002).

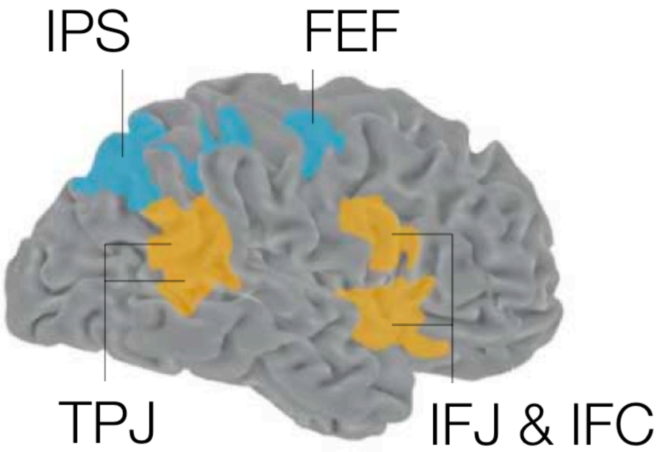

Figure 2. Human brain showing key regions underlying stimulus-driven and goal-directed attention. Regions associated with the former are shown in orange, and regions with the latter in blue. IPS = intra-parietal sulcus, FEF = frontal eye field, TPJ = temporo-parietal junction, IFJ = inferior frontal junction, IFC = inferior frontal cortex. Adapted from Corbetta & Shulman (2002).

Recent studies using resting-state connectivity, however, have suggested that the IFJ may be not be solely devoted to the ventral attention network, as it appears to also connect to the dorsal attention network (He et al., 2007; Corbetta et al., 2008). Indeed, a goal-directed attention function for the IFJ finds other support in the literature: This region (or at least nearby regions of postero-lateral PFC) activates during conditions of high perceptual difficulty due to temporal or spatial crowding, presumably to aid the selection of the relevant target (Marois et al., 2000b, 2004a). It also shows activity that correlates with conscious report during attentional blink paradigms (Marois et al., 2004b).

The selection of a stimulus in the environment (visuospatial attentional selection) is not the only selection function that the IFJ performs. The IFJ is also involved in the selection of appropriate responses to stimuli (Dux et al., 2006; Dux et al., 2009; Sigman & Dehaene, 2008; Marois et al., 2006). For example, the IFJ shows increased activity when participants have to select from one of four possible manual responses to a presented stimulus (4 choices) instead of one of two (2 choices; see Figure 3 and Marois et al., 2006), a manipulation to which I return in Chapter IV of this dissertation. The selection of an appropriate response may involve several component processes ranging from retrieval of the correct stimulus-response mappings from memory to instructing premotor cortex about which response to prepare. Even the selection of a specific set of stimulus-response mappings (rule selection) appears to involve the IFJ (Bunge, 2004; Crone et al., 2006).

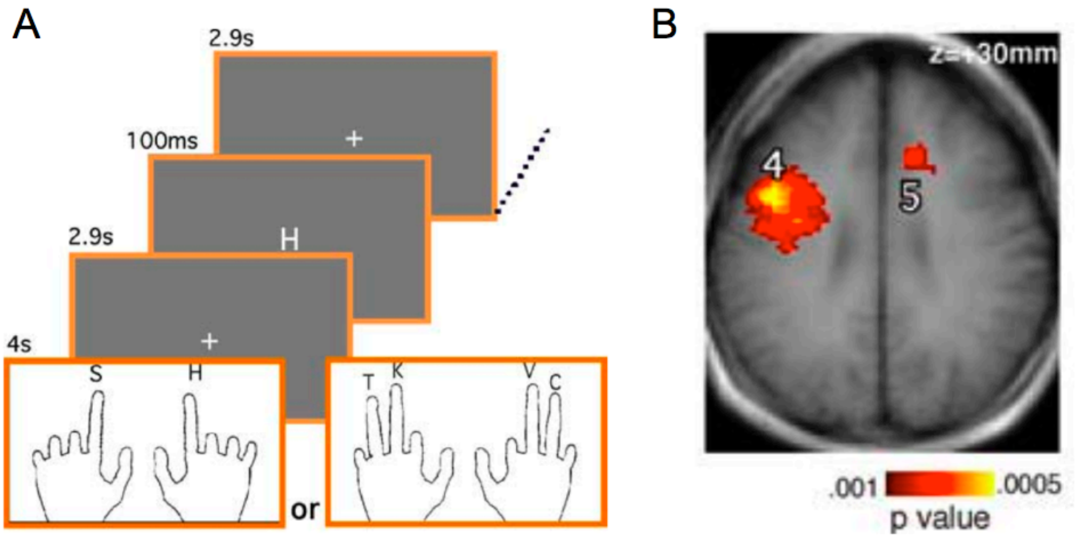

Figure 3. IFJ activation in a response selection load task. A) The task design, in which subjects had to respond to a presented letter with either one of two (2AD) or one of four (4AD) pre-learned manual responses. B) SPM of the comparison of 4AD blocks to 2AD blocks. Adapted from Marois et al. (2006).

The presence of higher-order selection, such as rule selection, in the IFJ resonates with the suggestion that this brain region supports low-level forms of cognitive control, which refers to the ability to coordinate behavior in accordance with internal goals (Derrfuss et al., 2005; Brass et al., 2005). Cognitive control includes the application of rules to guide behavior and the reorganization of stimulus-response mappings according to task demands. Preparing for a task, switching between tasks, or overcoming a prepotent (e.g. overlearned) stimulus-response mapping are all examples of cognitive control--and all recruit the IFJ (Derrfuss et al., 2005; Brass et al., 2005; Derrfuss et al., 2004; Brass & von Cramon, 2002). Overall, the IFJ appears to route information from stimulus to response, whether an overt behavior such as a finger movement or a covert adjustment such as a change in attentional priorities. In this way, the IFJ acts rather like a telephone operator routing calls through a switchboard. This routing need not be obvious; Diamond (2006) argues that the signature function of the IFJ is "being able to grasp how physically separate things might be related (i.e. conceptually connected despite their physical independence)." Learning and deciding upon associations between representations of stimuli and actions, even those that would normally appear unrelated, is thought to be the function of the IFJ.

While the role of the IFJ in cognitive control has been extensively explored (Derrfuss et al., 2004; Derrfuss et al., 2005; Brass & von Cramon, 2002; Brass et al., 2005), as has its relationship to cognitive control performed in other regions of the PFC (Koechlin et al., 2003; Koechlin & Summerfield, 2007; Badre et al., 2009; Badre, 2008; Badre & D'Esposito, 2009; MacDonald et al., 2000; Aron, 2007; Yeung et al., 2006), an understanding of the IFJ's role in attentional control and coordination has lagged behind. This is surprising considering the extensive amount of research that has been devoted to the neural basis of attention and its control in the last few decades (Miller & Cohen, 2001; Desimone & Duncan, 1995; Corbetta et al., 2008; Corbetta & Shulman, 2002; Serences et al., 2005; Yantis et al., 2002). Nevertheless, it remains unclear whether the different regions of the ventral and dorsal attention networks have different roles in attention and how these regions interact across networks. A central goal of this dissertation is to demonstrate that the IFJ participates in both networks, with a unique function that includes the coordination and control of them. To do so I contrast the role of the IFJ and other attentional control regions in a variety of experimental tasks.

Specific aims

The purpose of the experiments contained in this dissertation is to understand the role of the IFJ in attentional control and selection. Given its anatomical connections, the IFJ often co-activates with the two attention networks of the brain. Consequently, many of the experiments aim to dissociate the function of the IFJ from the key brain regions that make up the ventral (TPJ) and dorsal (FEF, IPS) attention networks.

Aim 1: Identify the functional contribution of the IFJ to stimulus-driven and goal-directed attention.

Although the brain networks associated with these two forms of attention are largely distinct, they must ultimately be coordinated for coherent behavior to emerge. Chapter II of this dissertation presents a paradigm (Surprise-induced Blindness (SiB); Asplund et al., in press) that identifies each network separately and then explores the interaction of these two networks.

Aim 2: Functionally segregate the core components of the stimulus-driven attention network (IFJ and TPJ) by examining that network's overlap with Theory of Mind, Task Positive, and Task Negative (Default) networks.

Chapter III further investigates the distinctions between the IFJ and TPJ response patterns by employing a functional overlap approach. The activation patterns from two other tasks known to activate the TPJ (Theory of Mind, in which subjects reason about others' mental states, and fixation, a way to elicit the Default Mode of processing when contrasted with a cognitively-demanding task) were compared with the activation from the SiB experiment.

Aim 3: Temporally segregate the IFJ's attentional roles occurring between stimulus presentation and response execution.

Chapter IV distinguishes the functions that the IFJ may play in goal-directed attention from those of the dorsal attention network (FEF and IPS). I first test whether the IFJ and dorsal regions have different roles in establishing and maintaining attentional control. Second, I characterize these brain regions' functions in the attention-demanding tasks of perceptual selection, response selection, and response execution.

At the conclusion of this thesis, I discuss what the experiments therein have contributed to our understanding of attention and control. In addition, I explore directions for future research. For example, it has yet to be established precisely how the IFJ interacts with other regions; while co-activation patterns and anatomical connections have been established, causal relationships have yet to be determined. Furthermore, it remains unclear whether all of the functions attributed to the IFJ draw on the same small region of tissue or whether the IFJ has functional topography. While additional research is required to elucidate the functional connections and topography of the IFJ, I discuss how understanding the IFJ is relevant to the broader topics of the relationship between brain structure and function as well as the functional architecture of the brain itself.

References

Amunts, K. & von Cramon, D. Y. (2006). The anatomical segregation of the frontal cortex: What does it mean for function? Cortex, 42, 525-528.

Amunts, K., Palomero-Gallagher, N., Brass, M., Derrfuss, J., Zilles, K., & von Cramon, D. Y. (2004). A receptor- and cytoarchitectonic correlate of the functionally defined inferior-frontal junction area. Neuroimage, 22 (Supplemental), 50.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. Trends in Cognitive Sciences, 8(4), 170-177.

Aron, A. R. (2007). The neural basis of inhibition in cognitive control. The Neuroscientist, 13(3), 214-228.

Asplund, C. L., Todd, J. J., Snyder, A. P., Gilbert, C. M. & Marois, R. (In Press). Surprise-induced Blindness: A stimulus-driven attentional limit to conscious perception. Journal of Experimental Psychology: Human Perception & Performance.

Asplund, C. L., Todd, J. J., Snyder, A. P., & Marois, R. (2010). A central role for the lateral prefrontal cortex in goal-directed and stimulus-driven attention. Nature Neuroscience, 13(4), 507-512.

Badre, D. (2008). Cognitive control, hierarchy, and the rostro-caudal axis of the prefrontal cortex. Trends in Cognitive Science, 12(5), 193-200.

Badre, D., Hoffman, J., Cooney, J. W., & D'Esposito, M. (2009). Hierarchical cognitive control deficits following damage to the human frontal lobe. Nature Neuroscience, 12(4), 515-522.

Badre, D. & D'Esposito, M. (2009). Is the rostro-caudal axis of the frontal lobe hierarchical? Nature Reviews Neuroscience, 10, 659-669.

Bernal, B. & Altman, N. (2010). The connectivity of the superior longitudinal fasciculus: A tractography DTI study. Magnetic Resonance Imaging, 28, 217-225.

Brass, M., Derrfuss, J., Forstmann, B., & von Cramon, D. Y. (2005). The role of the inferior frontal junction area in cognitive control. Trends in Cognitive Sciences, 9(7), 314-316.

Brass, M. & von Cramon, D. Y. (2002). The role of the frontal cortex in task preparation. Cerebral Cortex, 12(9), 908-914.

Brodmann, K. (1909). Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipin Dargestellt auf Grund des Zellenbaues. Barth, Leipzig.

Bruce, C. J., Goldberg, M. E., Bushnell, M. C., & Stanton, G. B. (1985). Primate frontal eye fields II: Physiological and anatomical correlates of electrically evoked eye movements. Journal of Neurophysiology, 54(3), 714-734.

Bunge, S. A. (2004). How we use rules to select actions: A review of evidence from cognitive neuroscience. Cognitive, Affective, & Behavioral Neuroscience, 4(4), 564-579.

Chikazoe, J., Jimura, K., Asari, T., Yamashita, K., Morimoto, H., Hirose, S., Miyashita, Y., & Konishi, S. (2009). Functional dissociation in right inferior frontal cortex during performance of Go/No-Go task. Cerebral Cortex, 19(1), 146-152.

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: From environment to theory of mind. Neuron, 58, 306-324.

Corbetta, M. & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews Neuroscience, 3, 201-215.

Corbetta, M., Akbudak, E., Conturo, T. E., Snyder, A. Z., Ollinger, J. M., Drury, H. A., Linenweber, M. R., Petersen, S. E., Raichle, M. E., Van Essen, D. C., & Shulman, G. L. (1998). A common network of functional areas for attention and eye movements. Neuron, 21, 761-773.

Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. Science, 279, 1347-1351.

Courtney, S. M, Ungerleider, L. G., Keil, K., & Haxby, J. V. (1997). Transient and sustained activity in a distributed neural system for human working memory. Nature, 386, 608-611.

Crone, E. A., Wendelken, C., Donohue, S. E., & Bunge, S. A. (2006). Neural evidence for dissociable components of task-switching. Cerebral Cortex, 16, 475-486.

Derrfuss, J., Brass, M., von Cramon, D. Y., Lohmann, G., & Amunts, K. (2009). Neural activations at the junction of the inferior frontal sulcus and the inferior precentral sulcus: Interindividual variability, reliability, and association with sulcal morphology. Human Brain Mapping, 30(1), 299-311.

Derrfuss, J., Brass, M., Neumann, J., & von Cramon, D. Y. (2005). Involvement of the inferior frontal junction in cognitive control: Meta-analyses of switching and Stroop studies. Human Brain Mapping, 25(1), 22-34.

Derrfuss, J., Brass, M., & von Cramon, D. Y. (2004). Cognitive control in the posterior frontolateral cortex: evidence from common activations in task coordination, interference control, and working memory. Neuroimage, 23(2), 604-612.

Desimone, R. & Duncan, J. (1995). Neural mechanisms of selective visual attention. Annual Review of Neuroscience, 18, 193-222.

Diamond, A. (2006). Bootstrapping conceptual deduction using physical connection: Rethinking frontal cortex. Trends in Cognitive Sciences, 10(5), 212-218.

Duncan, J. (2001). An adaptive coding model of neural function in prefrontal cortex. Nature Reviews Neuroscience, 2, 820-829.

Dux, P. E., Ivanoff, J., Asplund, C. L., & Marois, R. (2006). Isolation of a central bottleneck of information processing with time-resolved fMRI. Neuron, 52, 1109-1120.

Dux, P. E., Tombu, M. N., Harrison, S., Rogers, B. P., Tong, F., & Marois, R. (2009). Training improves multitasking performance by increasing the speed of information processing in human prefrontal cortex. Neuron, 63, 127-138.

Egeth, H. E. & Yantis, S. (1997). Visual attention: Control, representation, and time course. Annual Review of Psychology, 48, 269-297.

He, B. J., Snyder, A. Z., Vincent, J. L., Epstein, A., Shulman, G. L., & Corbetta, M. (2007). Breakdown of functional connectivity in frontoparietal networks underlies behavioral deficits in spatial neglect. Neuron, 53, 905-918.

Hill, J., Inder, T., Neil, J., Dierker, D., Harwell, J., & Van Essen, D. (2010). Similar patterns of cortical expansion during human development and evolution. Proceedings of the National Academy of Sciences, 107(29), 13135-13140.

Kastner, S., DeSimone, K., Konen, C. S., Szczepanski, S. M., Weiner, K. S., & Schneider, K. A. (2007). Topographic maps in human frontal cortex revealed in memory-guided saccade and spatial working-memory tasks. Journal of Neuophysiology, 97, 3494-3507.

Koechlin, E., Ody, C., & Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. Science, 302, 1181-1185.

Koechlin, E. & Summerfield, C. (2007). An information theoretical approach to prefrontal executive function. Trends in Cognitive Science, 11(6), 229-235.

Luna, B., Thulborn, K. R., Strojwas, M. H., McCurtain, B. J., Berman, R. A., Genovese, C. R., & Sweeney, J. A. (1998). Dorsal cortical regions subserving visually guided saccades in humans: An fMRI study. Cerebral Cortex, 8(1), 40-47.

MacDonald, A. W., Cohen, J. D., Stenger, V. A., & Carter, C. S. (2000). Dissociating the role of dorsolateral prefrontal cortex and anterior cingulate cortex in cognitive control. Science, 288, 1835-1837.

Marois, R., Leung, H.-C., & Gore, J. C. (2000a). A stimulus-driven approach to object identity and location processing in the human brain. Neuron, 25, 717-728.

Marois, R., Chun, M. M., & Gore, J. C. (2000b). Neural correlates of the attentional blink. Neuron, 28, 299-308.

Marois, R., Chun, M. M., & Gore, J. C. (2004a). A common parieto-frontal network is recruited under both low visibility and high perceptual interference conditions. Journal of Neurophysiology, 92, 2985-2992.

Marois, R., Yi, D.-J., & Chun, M. M. (2004b). The neural fate of consciously perceived and missed events in the attentional blink. Neuron, 41, 465-472.

Marois, R. & Ivanoff, J. (2005). Capacity limits of information processing in the brain. Trends in Cognitive Sciences, 9(6), 296-305.

Marois, R., Larson, J. M., Chun, M. M. & Shima, D. (2006). Response-specific sources of dual-task interference in human pre-motor cortex. Psychological Research, 70(6), 436-447.

Miller, E. K. & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. Annual Review of Neuroscience, 24, 167-202.

Passingham, R. E. (1993). The Frontal Lobes and Voluntary Action. Oxford University Press.

Petrides, M. & Pandya, D. N. (2001). Comparative cytoarchitectonic analysis of the human and macaque ventrolateral prefrontal cortex and coritocortical connection patterns in the monkey. European Journal of Neuroscience, 16, 291-310.

Schall, J. D., Morel, A., King, D. J., & Bullier, J. (1995). Topography of visual cortex connections with frontal eye field in macaque: Convergence and segregation of processing streams. Journal of Neuroscience, 15, 4464-4487.

Schmahmann, J. D., Pandya, D. N., Wang, R., Dai, G., D'Arceuil, H. E., de Crespigny, A. J., & Wedeen, V. J. (2007). Association fibre pathways of the brain: Parallel observations from diffusion spectrum imaging and autoradiography. Brain, 130, 630-653.

Serences, J. T., Shomstein, S., Leber, A. B., Golay, X., Egeth, H. E., & Yantis, S. (2005). Coordination of voluntary and stimulus-driven attentional control in human cortex. Psychological Science, 16(2), 114-122.

Sigman, M. & Dehaene, S. (2008). Brain mechanisms of serial and parallel processing during dual-task performance. The Journal of Neuroscience, 28(30), 7585-7598.

Umarova, R. M., Saur, D., Schnell, S., Kaller, C. P., Vry, M.-S., Glauche, V., Rijintes, M., Hennig, J., Kiseley, V., & Weiller, C. (2010). Structural connectivity for visuospatial attention: Significance of the ventral pathways. Cerebral Cortex, 20, 121-129.

Walker, A. E. (1940). A cytoarchitectural study of the prefrontal area of the macaque monkey. Journal of Comparative Neurology, 73, 59-86.

Watanabe-Sawaguchi, K., Kubota, K., & Arikuni, T. (1991). Cytoarchitecture and intrafrontal connections of the frontal cortex of the brain of the Hamadryas Baboon (Papio hamadryas). The Journal of Comparative Neurology, 311, 108-133.

Williams, P. & Warwick, R. (1975). Functional neuroanatomy of man (Neurology section of Gray's Anatomy). W. B. Saunders Co., Philadelphia.

Yantis, S., Schwarzbach, J., Serences, J. T., Carlson, R. L., Steinmetz, M. A., Pekar, J. J., & Courtney, S. M. (2002). Transient neural activity in human parietal cortex during spatial attention shifts. Nature Neuroscience, 5, 995-1002.

Yeung, N., Nystrom, L. E., Aronson, J. A., & Cohen, J. D. (2006). Between-task competition and cognitive control in task switching. Journal of Neuroscience, 26(5), 1429-1438.

CHAPTER II

THE CENTRAL ROLE OF THE INFERIOR FRONTAL JUNCTION IN STIMULUS-DRIVEN AND GOAL-DIRECTED ATTENTION

This chapter is based on Asplund et al. (2010).

Reading this manuscript requires attention to be voluntarily deployed, in a ‘top-down’ fashion, to this task. As a consequence of selectively attending to the page, one may become oblivious to surrounding sounds and sights. If a fire alarm suddenly blares, however, this salient stimulus will likely capture attention in a ‘bottom-up’ manner and interrupt the ongoing task so that an appropriate course of action can be initiated. This simple example illustrates a fundamental aspect of attention: What ultimately reaches our awareness and guides our behavior depends on the interaction between the two principal forms of attention, goal-directed and stimulus-driven (Corbetta & Shulman, 2002; Egeth & Yantis, 2002).

While much is known about the neural mechanisms supporting goal-directed (Corbetta & Shulman, 2002; Corbetta et al., 2000; Kastner et al., 1999; Serences et al., 2005; Yantis et al., 2002; Chiu & Yantis, 2009) and stimulus-driven attention (Corbetta & Shulman, 2002; Serences et al., 2005; Downar et al., 2000; Downar et al., 2002; Horovitz et al., 2002; Linden et al., 1999; Marois et al., 2000), how these two forms of attention are ultimately coordinated is not yet understood. The finding that these attentional forms are supported by largely distinct neural networks – with a dorsal network that includes the frontal eye field (FEF) and superior parietal cortex (Corbetta & Shulman, 2002; Kastner et al., 1999; Serences et al., 2005; Yantis et al., 2002; Chiu & Yantis, 2009; Corbetta et al., 2008) supporting goal-directed attention, and a ventral one that consists of the lateral and inferior frontal/prefrontal cortex and the temporo-parietal junction (TPJ) underlying stimulus-driven attention (Corbetta & Shulman, 2002; Corbetta et al., 2000; Downar et al., 2000; Downar et al., 2002; Marois et al., 2000; Corbetta et al., 2008) – has further complicated the issue. As a result, several hypotheses have been proposed to explain how these two forms of attention may be coordinated: through an interaction between the ventral and dorsal networks (Corbetta & Shulman, 2002), across the dorsal (Buschman & Miller, 2007; Gottlieb, 2007) or ventral (Serences et al., 2005) attention network, or in the anterior component of the ventral network (He et al., 2007). Many of these proposals, however, are based on studies employing tasks that conflate stimulus-driven and goal-directed attention, thereby making it difficult to determine the relative contribution of bottom-up and top-down neural processes to task performance. For example, the brain mechanisms of stimulus-driven attention cannot easily be dissociated from those supporting goal-directed behavior if the stimulus-driven attention task involves spatial shifts of attention, goal-oriented processes, or motor responses, as none of these cognitive processes is necessary to capture attention exogenously but all are known to engage the dorsal attention network (Corbetta & Shulman, 2002; Corbetta et al., 2000; Kastner et al., 1999; Serences et al., 2005; Yantis et al., 2002).

The same concern also applies to our current understanding of how attention controls awareness. Both the ventral and dorsal attention networks have been associated with conscious perception (Serences et al., 2005; Beck et al., 2001; Rees et al., 1999; Marois et al., 2000; Marois et al., 2004; Rees et al., 2002; Husain & Nachev, 2007), lending support to theories of awareness that posit widespread changes in brain activity accompanying conscious perception (Dehaene et al., 2006; Baars, 1997). To date, however, there has not been a specific attempt to assess the relative contribution of the dorsal and ventral networks to the neural basis of attentional limits to conscious perception by using tasks that dissociate between stimulus-driven and goal-directed attentional processes. Hence, the extent to which each of these attention networks may be necessary for awareness is currently unclear (Rees et al., 2002; Husain & Nachev, 2007; Milner & Goodale, 1992).

We have recently developed an experimental procedure that reveals a profound but fleeting deficit in visual awareness resulting from the foveal presentation of an unexpected, task-irrelevant stimulus that involves neither an overt response nor a shift in spatial attention. The deficit, termed Surprise-induced Blindess (SiB), is triggered by an event absent from the observer's goal-directed attentional set and is not under the observer's initial control (Asplund et al., In Press). As such, the procedure represents a powerful way to assess whether stimulus-driven attentional limits to conscious perception can arise within the ventral attention network in the absence of dorsal network involvement. Moreover, because the unexpected event ultimately affects the goal-directed task of detecting a target, SiB experiments are also well suited to reveal the neural mechanisms by which stimulus-driven attention affects goal-directed behavior.

Experiment 1: Surprise-induced Blindness

Thirty-one right-handed individuals (12 females) participated in the experiment. One individual's data were excluded due to technical problems. Participants in this experiment and all others in this chapter had normal or corrected-to-normal vision and received monetary compensation. In addition, the Vanderbilt University Institutional Review Board approved the experimental protocol and written informed consent was obtained from each participant.

Methods

Participants searched for a target letter ('X') in a rapid serial visual presentation (RSVP) stream of distractor letters (white Helvetica font, 1.8° x 1.8°, presented on a dark gray background). Each 8 s trial began with a 3.4 s RSVP of 31 letters randomly chosen from a set of 20 (vowels were excluded), with no letter presented twice in a row. Each stimulus was presented at fixation for 100 ms followed by a 10 ms inter-stimulus interval (ISI). Following the RSVP, a screen appeared for 2 s prompting the participants to respond with an appropriate key press (right index finger for 'target present' and right middle finger for ‘target absent’). The response period was followed by a 2.6 s inter-trial interval (ITI) consisting of a white fixation cross (see Figure 1).

Each participant completed a single fMRI run of 40 trials. The target (present on 77.5% of trials) appeared between frames 25–29. In six of the trials, a Surprise stimulus (grayscale face, 1.8° x 1.8°, distinct for each trial) appeared between frames 22–26 of the RSVP, 330 ms before the target (5 trials) or in a trial with no target (1 trial). Surprise trials occurred between trials 2 and 38 and were separated by a minimum of two Search trials (trials with a target but no Surprise stimulus). Participants practiced Search trials exclusively prior to the fMRI session. Feedback was given only during practice, and participants were required to reach target accuracy above 80% before scanning. At no time were participants informed about the Surprise stimuli.

Behavioral analysis

To assess the effect of repeated Surprise stimulus presentations, we used Cochran Q tests for categorical data of dependent samples (Sheskin, 2000). We then applied Sign tests to determine the significance of the relevant pair-wise comparisons. These and all subsequently described tests were two-tailed with alpha at 0.05 unless otherwise noted.

fMRI procedure

Anatomical 3D high-resolution images were acquired using conventional parameters on a 3T GE MRI system (Milwaukee, WI). Nineteen 7 mm thick axial slices (0 mm skip; 3.75 x 3.75 mm in-plane) were taken parallel to the AC-PC line. T2*-weighted image parameters: 25 ms echo time, 70° flip angle, 240 mm FOV, 64 x 64 matrix, 2000 ms repetition time. The functional scan included 166 brain volumes, with the first 6 volumes discarded for signal stabilization. Trials were presented using Psychophysics ToolBox (Brainard, 1997; Pelli, 1997) for Matlab on an Apple G4 Macintosh. Stimuli were back-projected from an LCD projector onto a screen viewed through a prism mirror by the supine participant.

Data analysis

Data analysis was performed using BrainVoyager 4.9.1, BrainVoyager QX 1.7.9 (Brain Innovation, Maastricht, The Netherlands), and custom Matlab software. Data preprocessing included image realignment, 3D motion correction, linear trend removal, and correction for slice acquisition timing. Statistical Parametric Maps (SPMs) of BOLD activation were created using a multiple regression analysis, with regressors defined for the six Surprise stimuli, Search trials, and No-target trials; boxcar functions for each trial type were convolved with a canonical double γ hemodynamic function (SPM2, http://www.fil.ion.ucl.ac.uk/spm) to generate each regressor. The resulting maps from all participants were spatially smoothed with a 6 mm Gaussian kernel (FWHM), standardized to Talairach space (Talairach & Tournox, 1988), and superimposed to create composite maps. The model fit was assessed using t statistics, with significance determined by the false discovery rate (FDR) threshold at $q < 0.05$ (random-effects analysis).

For group region of interest (ROI) analysis, the center of mass and surrounding activated voxels for each activated focus were selected, up to 1 cm^3. The time-course for each Surprise trial was extracted from each ROI for each participant and then converted to percent signal change (baseline from the time point of Surprise stimulus (SS) onset and two preceding points). The average time courses for pairs of SS (SS1+SS2, SS3+SS4, SS5+SS6) were next computed for each participant. For statistical tests of amplitude, we identified the time point with the largest percent signal change between 6 and 8 seconds following Surprise stimulus presentation for each SS pair for each participant, and then used paired t-tests for the appropriate comparisons.

For the individually-defined ROI analyses, we identified ROIs whose activity correlated with performing the primary target-detection task (SPM of open contrast of the predictor for Search trials). Positive β weights for the predictor were associated with FEF, IPS, and IFJ, whereas negative ones were associated with TPJ. Each ROI in each participant was defined as the peak voxel and significantly activated surrounding area up to 1 cm^3. Anatomical landmarks (FEF at the junction of the superior frontal sulcus and precentral sulcus; IPS in the intraparietal sulcus between $y = –50$ and $y = –70$; IFJ at the junction of the inferior frontal sulcus and precentral sulcus; TPJ around the posterior Sylvian fissure) were used to identify each region, consistent with earlier work (Corbetta et al., 2000; Serences et al., 2005; Corbetta et al., 2008; Marois & Ivanoff, 2005). We next extracted time courses for the Surprise and Search trials, creating baselines and averages as above. For statistical tests of amplitude, we compared the corresponding time points across a given pair of time courses using paired t-tests.

For statistical tests of activity onset timing, we first subtracted each participant's Search trial activity from their Surprise stimulus trial activity for the first pair (SS1+SS2), leaving activation specific to deficit-causing Surprise stimuli. To estimate the hemodynamic response's onset time for these subtracted time courses, we employed a bootstrap approach (Davidson & Hinkley, 1998) owing to the difficulty of acquiring reliable onset measures from each participant's pairs of Surprise stimulus trials. Using linear interpolation, each participant's time courses—for both Search-related (Search trials) and Surprise-related (Surprise trials – Search trials) activity—from each ROI were upsampled to 1 ms resolution and then smoothed with a Gaussian kernel (FWHM = 2 seconds). Thirty samples for each ROI were selected with replacement and averaged, a process that was repeated 10,000 times. For each of the resulting averaged samples, we computed the onset as the time when the time course had achieved 20% of its peak amplitude (results were similar for 10%). Finally, these onset values (10,000 per ROI) were compared across ROIs. For example, right IFJ onsets occurred before right IPS onsets for 9,977 of the samples. From this count, we computed a p-value, which in the example would be 0.0066, two-tailed. Interactions were computed by first subtracting the onset values for Surprise-related activity from those for Search-related activity and then comparing these differences across regions.

As no hemispheric differences were found in any of the above analyses and to increase statistical power, we collapsed the data across hemispheres for all subsequent analyses.

The correlation analyses were performed on the data derived from the GLM analyses after further processing steps had been applied. Global signal fluctuations in this data set were removed by regressing out the time courses from a ventricular region of interest, a white matter region of interest, and the average signal across the entire brain. Second, the data were filtered using a zero-phase forward and reverse band-pass filter ($0.01 < f < 0.2$ Hz). Next, we segmented the data from each individually-defined ROI by trial, performing a percent signal change transform on each trial as described above. Trials were then concatenated by condition, yielding 28 points associated with Surprise trials (SS1+2) and 28 points with Search trials (two randomly selected trials from about 10 that were at least three trials away from any Surprise trials). Time courses for each ROI (collapsed across hemispheres) pair of interest in each participant were then correlated by condition and the resulting values converted using Fisher's z transformation. The correlations between regions were then tested for significance across participants with one-sample t-tests, and the change in correlations between Search and Surprise trials compared across participants with paired t-tests.

Results and Discussion

The experimental manipulation was successful in causing Surprise-induced Blindness (Fig. 1b). Specifically, group target detection performance differed across the Surprise stimuli presentations (Cochran's Q(4) = 30.3, $p < 0.0001$; See Methods), with target detection worse following the first Surprise trial (SS1) than SS3-SS6 (Sign tests, p's < 0.040; See Methods), and worse following SS2 compared to SS5 and SS6 (p's < 0.027). In the third through sixth Surprise trials, performance was comparable to Search trials (trials without Surprise stimuli, for which the target detection rate was 90.4%; Fig. 1b). Target-detection performance in the trials immediately preceding the first two Surprise trials was far better than for their respective Surprise trials (Fig. 1b, Sign tests, p's < 0.0001), indicating that SiB does not result from an initial difficulty with the target detection task. Rather, the finding that unexpected, task-irrelevant stimuli triggered a profound but short-lived impairment in target detection that was essentially dissipated by the third Surprise stimulus presentation is consistent with a stimulus-driven, attention-based origin for this deficit (Asplund et al., In Press).

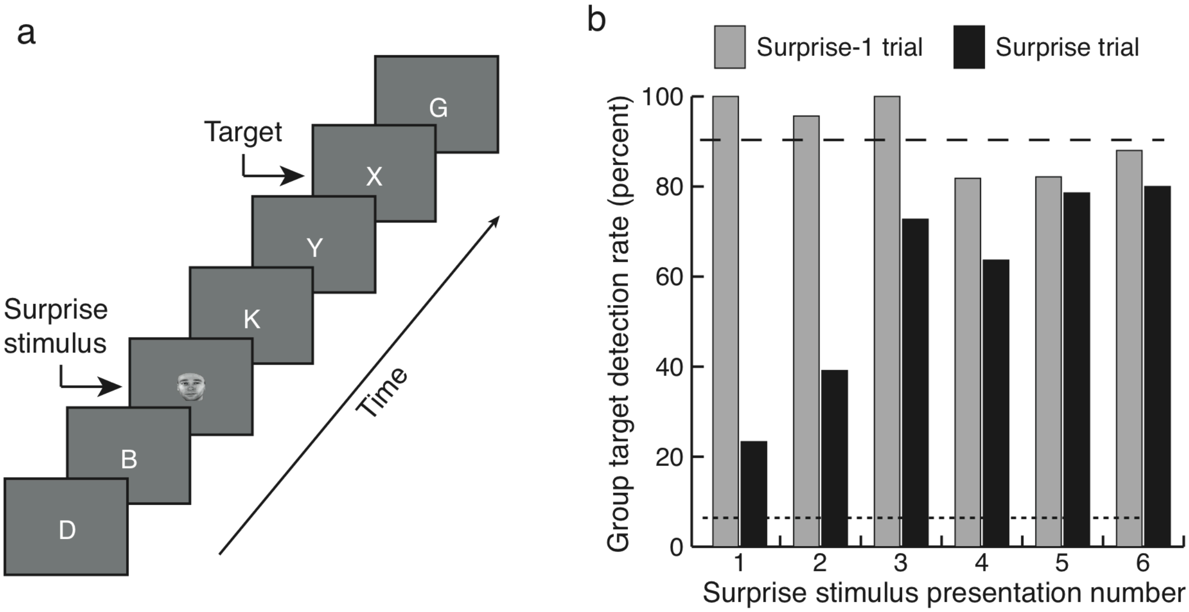

Figure 1. SiB experiment (Experiment 1). A) Trial design. Participants searched for a target letter in a rapid serial visual presentation (RSVP) stream of distractor letters. In a small proportion of trials (Surprise trials), a Surprise face stimulus was shown before the target. B) Group target detection performance. Black bars represent accuracy in Surprise trials, and gray bars represent accuracy in trials immediately preceding the Surprise trials. Dashed line corresponds to the average target hit rate for Search trials (target only). Dotted line corresponds to the false alarm rate.

Neural correlates of SiB

To identify the neural substrates that underlie stimulus-driven attentional limits to conscious perception, we first isolated the brain regions sensitive to the Surprise stimuli, irrespective of presentation number (See Methods). We then examined the BOLD (blood-oxygen-level dependent) signal from these brain regions, testing whether the response pattern mirrored the behavioral performance. Specifically, because the presentations of rare, task-irrelevant stimuli are known to increase neural activity (Downar et al., 2000; Downar et al., 2002; Horovitz et al., 2002; Yamaguchi et al., 2004) and because SiB was only observed for the first pair of Surprise stimuli (SS1+2), we predicted that this pair would cause a greater BOLD response than the two subsequent pairs (SS3+4 and SS5+6) of Surprise stimuli.

A statistical parametric map (SPM) revealed several areas that were recruited more during Surprise than during Search trials (Table 1; Figs. 2 and 3). Several of these areas showed invariant BOLD responses across the six Surprise stimuli presentations, most notably the fusiform gyrus in visual cortex, suggesting that SiB may be a primarily central phenomemon that occurs at later stages than visual information processing (Fig. 3). Correspondingly, the only two regions that demonstrated a BOLD response that quickly habituated after the first two Surprise stimulus presentations were in association cortex (Fig. 2): the inferior frontal junction (IFJ), located in the posterior aspect of the inferior frontal sulcus (parts of Brodmann areas 9, 44, 6), and the temporo-parietal junction (TPJ), at the intersection of the superior temporal gyrus, supramarginal gyrus, and superior temporal sulcus (parts of Brodmann areas 40, 22, 39).

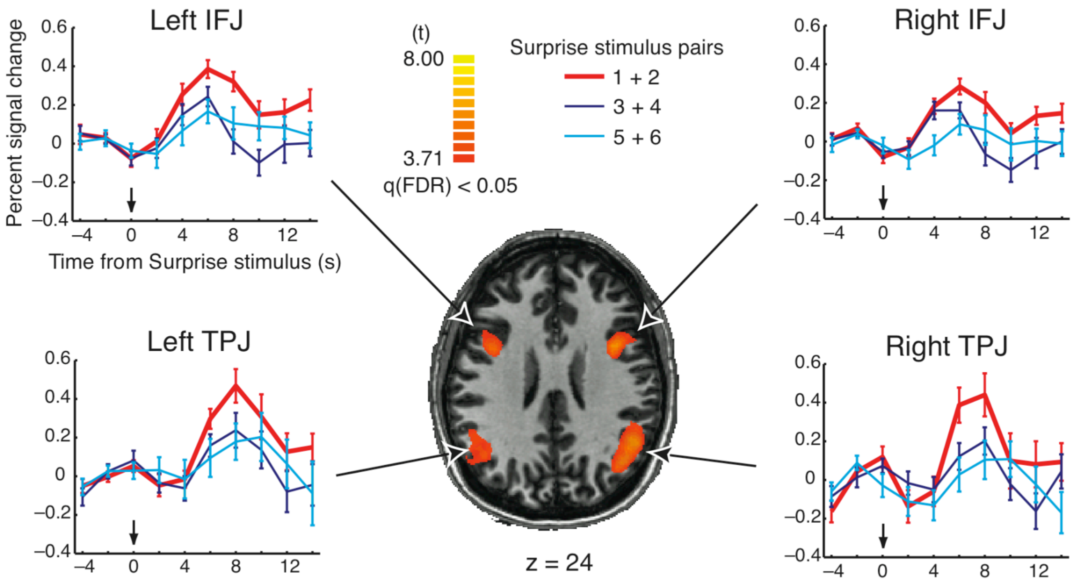

Figure 2. SiB experiment (Experiment 1) SPM. Brain regions showing rapid attenuation of Surprise stimulus-related activation. The SPM highlights brain regions that responded to all six Surprise trials (See Methods), specifically the IFJs (Talairach coordinates (Talairach & Tournoux, 1988) 37, 5, 29 and –40, 8, 25) and TPJs (Talairach coordinates 46, –56, 27 and –49, –56, 23). The time courses illustrate the brain regions from the SPM that showed greater activity in the first pair of Surprise trials compared to the two other pairs of Surprise trials. The Surprise stimulus appears at approximately time zero. Error bars represent standard errors of the mean.

Table 1. Anatomical location and statistical assessment of activation for the ROIs isolated from Surprise trials in Experiment 1 (Surprise trial – Search trial contrast).

Region	Hemi	Tal co-ords (x, y, z)	SS1+2 vs. SS3+4 (t)	SS3+4 vs. SS5+6 (t)	SS1+2 vs. SS5+6 (t)
TPJ	Right	46, –56, 27	2.11*	1.07	2.76*
TPJ	Left	–49, –56, 23	2.35*	1.30	2.86*
IFJ	Right	37, 5, 29	2.72*	–0.37	2.05*
IFJ	Left	–40, 8, 25	2.46*	0.05	2.18*
FG	Right	30, –44, –11	0.42	–0.92	–0.53
FG	Left	–32, –51, –10	1.05	–0.70	0.05
IFG	Right	40, 19, 13	0.75	0.30	1.09
IFG	Left	–48, 19, 7	–0.57	0.77	0.19
OFC	Right	34, 27, –10	–0.22	–0.19	–0.53
OFC	Left	–37, 26, –8	0.27	0.15	0.40
Pulvinar	Bilateral	–7/9, –27, 1	1.46	0.71	1.83
PG	Right	32, –3, –13	–0.09	–0.70	–0.80
STG	Right	33, 12, –27	0.95	0.07	1.26
MTS	Left	–51, 2, –12	–0.17	–0.28	–0.36
SFG	Right	13, 24, 49	0.49	0.74	0.90
Amygdala / SLEA	Right	16, –9, –8	1.58	–0.17	1.26

The three rightmost columns list the t-values resulting from paired t-tests of the given Surprise Stimulus pairs. An asterisk (*) marks comparisons significant at $p < 0.05$. Tal co-ords = Talairach coordinates (Talairach & Tournoux, 1988). TPJ = Temporo-Parietal Junction (Brodmann areas 39, 40, 22), IFJ = Inferior Frontal Junction (Brodmann areas 9, 44, 6), FG = Fusiform Gyrus (Brodmann area 37), IFG = Inferior Frontal Gyrus (Brodmann areas 44, 45), OFC = Orbitofrontal Cortex (Brodmann area 47), PG = Parahippocampal Gyrus, STG = Superior Temporal Gyrus (Brodmann area 38), MTS = Middle Temporal Sulcus (Brodmann area 21), SFG = Superior Frontal Gyrus (Brodmann area 8), Amygdala / SLEA = Amgydala and Sub-Lenticular Extended Amygdala. With the exception of the IFJ and TPJ, none of these brain regions showed activation differences between any of the three Surprise stimulus pairs (all p’s > 0.1). Note that the TPJ foci are anatomically distinct from, and superior to, regions of the superior temporal sulcus involved in processing facial expressions and eye gaze (Hoffman & Haxby, 2000).

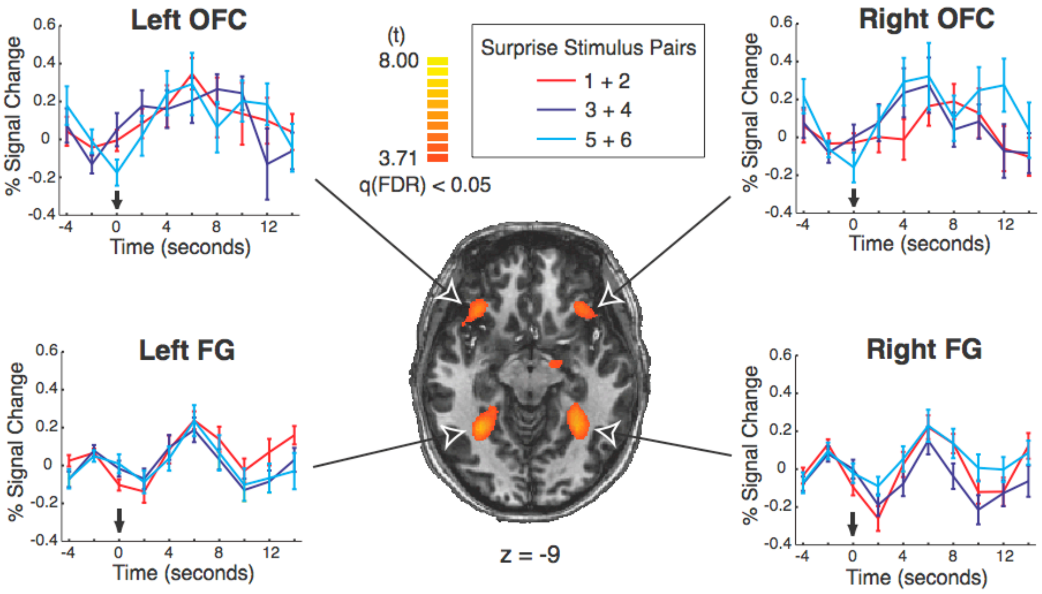

Figure 3. Brain regions showing no adaptation of Surprise stimulus-related activity in Experiment 1 (SiB experiment). The SPM highlights selected brain regions that responded to the six Surprise trials, and the time courses illustrate that these brain regions showed similar activity levels across the three pairs of Surprise trials. The Surprise stimulus appears at approximately time zero. Error bars represent standard errors of the mean. OFC = Orbitofrontal Cortex, FG = Fusiform Gyrus. The orbitofrontal cortex and inferior frontal gyrus (see Table 1) have been associated with the ventral attention network (Corbetta & Shulman, 2002; Egeth & Yantis, 1997). Their non-habituating response to the Surprise stimulus suggests that they represent different information that the information encoded in the more dorsally located IFJ (e.g. whether an event occurs with a low frequency, regardless of that precise frequency or the event's novelty).

For these two brain regions (IFJ and TPJ), in both hemispheres, the peak response to SS1+2 was higher than the response to the two other SS pairs (two-tailed paired t-tests, t(29)'s > 2.05, p's < 0.049), while the peak responses to SS3+4 and SS5+6 were indistinguishable (t(29)'s < 1.30, p's > 0.20; Fig. 2). Thus, the IFJ and TPJ exhibited an activity pattern that mirrored the magnitude of SiB. This activity modulation was caused by the Surprise stimuli, not the perceived absence of a target—which co-varies with SiB—because the peak responses in target-absent trials and Search trials (See Methods) were indistinguishable (two-tailed paired t-tests, t(29)'s < 1.17, p's > 0.25). No other brain regions appeared to show an SiB-like pattern of activation, as an additional SPM that directly contrasted SS1+2 with SS3+4 and SS5+6 demonstrated.

Taken together, these results indicate that the presentation of unexpected, task-irrelevant stimuli activates a large network of cortical and subcortical regions, yet only a subset of this network in the frontal/prefrontal and temporo-parietal cortex show a rapid BOLD response adaptation commensurate with the behavioral performance. This subset of brain regions is anatomically consistent with areas previously implicated in novelty processing (Downar et al., 2000; Downar et al., 2002; Linden et al, 1999; Yamaguchi et al., 2004; Knight, 1984; Opitz et al., 1999; Courchesne et al., 1975), attentional orienting to sensory events (Heilman & Watson et al., 1977; Karnath et al., 2002) and, most strikingly, to the core components of the ventral attention network (Corbetta & Shulman, 2002; Corbetta et al., 2008).

Late dorsal network activation

In contrast to the ventral network, the SPMs (even with a liberal threshold of $p < 0.001$, uncorrected) provided no evidence for Surprise stimulus-related activation in the core brain regions associated of the goal-directed attention network (Corbetta & Shulman, 2002; Corbetta et al., 2008), namely the frontal eye field (FEF) and the intraparietal sulcus (IPS). To analyze the dorsal network's association with SiB with greater sensitivity, for each participant we functionally defined regions of interest (ROIs) for the putative FEF and IPS based on their activation in Search trials, as these regions were strongly activated by the task of searching for and responding to targets (See Methods, Fig. 4a, Table 2).

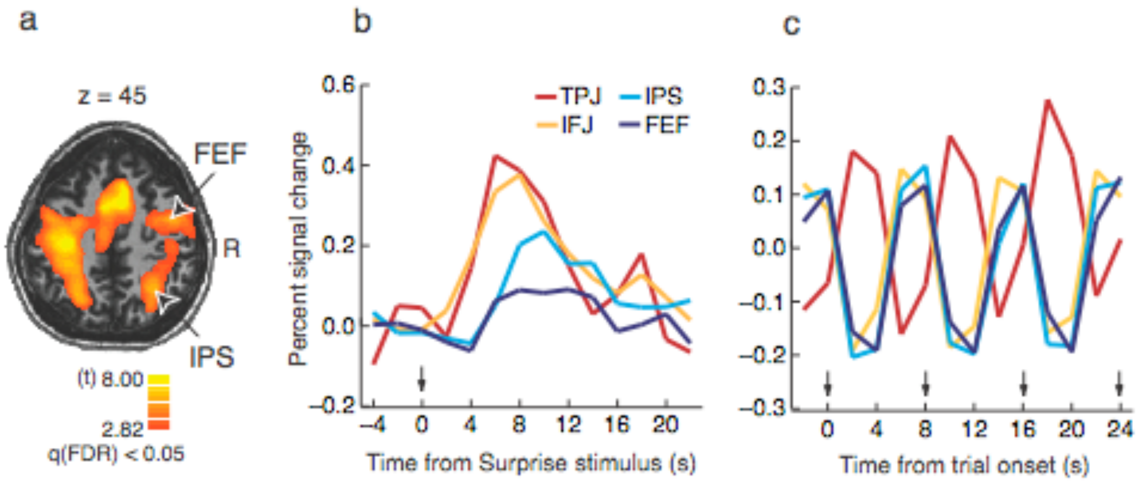

Figure 4. Stimulus-driven and goal-directed attention activity in Experiment 1. A) Dorsal brain regions active during Search trials. B) Surprise stimulus-specific waveform in dorsal (FEF, IPS) and ventral (IFJ, TPJ) regions of interest (ROIs) defined in individual participants (See Methods). Each time course was constructed by subtracting the Search trial time course from the time course for the first two Surprise Stimulus trials. The Surprise stimulus appears at approximately time zero. C) Search trial time course over the same period of time for the same ROIs. Arrows mark each trial's onset. Note that the activation pattern is cyclical, mirroring the trial structure (one trial every eight seconds). The observed hemodynamic responses match the predicted responses for the hypothesized neural activity in each region (see Fig. 5).

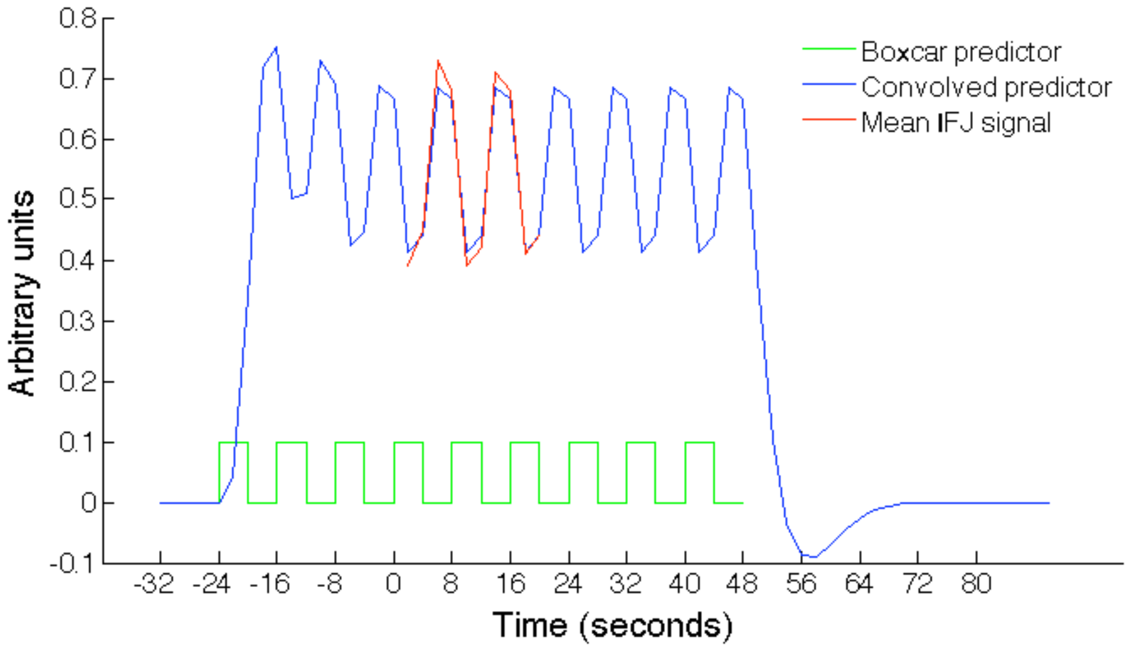

Figure 5. Convolution model of Search trial activity in Experiment 1. The figure demonstrates that the Search trial hemodynamic activity pattern observed in Experiment 1 (SiB experiment; see Fig. 3c) is predicted by linear convolution. To generate such a prediction, we first created a boxcar function (Boxcar predictor) representing the hypothesized neural activity associated with a sequence of Search trials. We next convolved the boxcar with a standard double gamma variate impulse function (as implemented in BrainVoyager QX). The resulting convolved predictor (Convolved predictor) matches well with the signal observed in the goal-directed attention regions (IFJ signal shown). This concordance should come as no surprise, as predictors similar to the convolved one shown in the figure were used to identify goal-directed attention regions.

Table 2. Average anatomical location and statistical assessment of activation for the individually-defined ROIs from Search trials in Experiment 1 (open contrast SPM).

Region	Hemi	Tal co-ords (x, y, z) ± SD	SS1+2 vs. Search (t)	SS3+4 vs. Search (t)	SS5+6 vs. Search (t)
IPS	Right	26 ± 4, –65 ± 6, 36 ± 5	2.81*	0.46	0.28
IPS	Left	–22 ± 4, –66 ± 6, 39 ± 6	3.45*	0.44	1.38
FEF	Right	34 ± 4, –7 ± 3, 51 ± 5	1.79	0.51	0.63
FEF	Left	–32 ± 5, –8 ± 3, 51 ± 5	2.50*	1.95	0.96
TPJ	Right	47 ± 5, –55 ± 5, 28 ± 5	4.52*	3.21*	1.65
TPJ	Left	–49 ± 2, –58 ± 5, 24 ± 4	5.33*	2.37*	1.73
IFJ	Right	40 ± 4, 6 ± 3, 27 ± 3	4.99*	1.67	1.06
IFJ	Left	–42 ± 3, 8 ± 3, 25 ± 2	5.92*	2.51*	1.12

The three rightmost columns list the t-values resulting from paired t-tests of the given Surprise Stimulus pairs versus Target Only activity. See Table 1 for abbreviation key. An asterisk (*) marks those comparisons that are significant at $p < 0.05$. These ROI coordinates closely matched those isolated from the Surprise trials (see Table 1).

The anatomical locations of the resulting ROIs corresponded very well to the conventional positions of the FEF and IPS in goal-directed attention tasks (Corbetta & Shulman, 2002; Corbetta et al., 2000; Kastner et al., 1999; Serences et al., 2005; Yantis et al., 2002; Marois et al., 2000; Corbetta et al., 2008; He et al., 2007). When probed during the Surprise trials, activity in these dorsal regions was greater during SS1+2 compared to Search trials ($t(29)$'s > 2.50, p's < 0.018 save right FEF's marginal effect at $t(29) = 1.79$, $p = 0.084$), but not during subsequent pairs (Table 2). Thus, the more sensitive ROI analysis revealed that the FEF and IPS are also activated by the first two Surprise stimulus presentations. Strikingly, however, the time courses of activation specific to the first pair of Surprise stimuli, revealed by subtracting the underlying Search-related activity from the first two Surprise stimulus trials (See Methods), showed that the IPS and FEF responded significantly later than did the IFJ and TPJ (Fig. 4b; all pair-wise comparisons $p < 0.048$; See Methods), while activity within each of these two pairs did not differ (all p's > 0.55). These results were obtained regardless of whether the IFJ and TPJ ROIs were defined exactly as the IPS and FEF ROIs or defined based on the group-level Surprise trial ROIs (see Tables 1 and 2).

Thus, the ROI analysis revealed that the dorsal network is activated by the Surprise stimuli, but unlike the swift activation pattern in the ventral network following presentations of the first two Surprise stimuli, the dorsal network appears to respond too late (by about 3 seconds) for it to play a causal role in SiB. This conclusion, however, critically depends on the dorsal activation delay reflecting a genuine late neural response rather than inherent differences in the hemodynamic properties of the ventral and dorsal parieto-frontal networks. We therefore performed a follow-up 'spatial SiB' experiment (Experiment 2) to distinguish between these two possibilities.

Experiment 2: Spatial Surprise-induced Blindness

Given the role of the dorsal network in the control of visuo-spatial attention (Corbetta & Shulman, 2002; Kastner et al., 1999; Yantis et al., 2002), we predicted that the sporadic presentations of highly salient, categorically distinct task-irrelevant stimuli in the periphery instead of in the center of the RSVP stream (Fig. 6a) would not only persist in capturing attention (Asplund et al., In

Press), but also lead to shifts of visual-spatial attention or eye movements, thereby promptly recruiting the FEF and IPS in addition to the ventral network.

Methods

Six right-handed individuals (3 females) participated. The timing of each trial was as in Experiment 1 except that 29 stimuli were shown on each trial and the ISI was 17 ms. There were 40 trials during each of six fMRI runs. The target (present on 80% of trials) appeared between frames 23–27. In four of the trials per run (3 target-present and 1 target-absent), a Surprise stimulus appeared 350 ms before the target at one of four spatial locations centered 4.2° from fixation. The Surprise stimuli consisted of distinct, large (6.5° x 6.5°), colorful items, each shown only once. Surprise trials occurred between trials 2 and 38, and were separated by a minimum of three Search trials. Participants practiced the Search task prior to the fMRI session. Participants were not informed about the Surprise stimuli.

fMRI procedure

Anatomical 3D high-resolution images were acquired using conventional parameters on a 3T Philips MRI system. Thirty-three 3.5 mm thick axial slices (0.5 mm skip; 1.875 x 1.875 mm in-plane) were taken parallel to the AC-PC line. T2*-weighted image parameters: 35 ms echo time, 79° flip angle, 240 mm FOV, 128 x 128 matrix, 2000 ms repetition time. There were 161 brain volumes per functional scan. Trials were presented using Psychophysics ToolBox (Brainard, 1997; Pelli, 1997) for Matlab on an Apple MacBook Pro, and stimuli back-projected to the participant as explained for Experiment 1.

Data analysis

Data analysis was performed using BrainVoyager QX 1.11.4 (Brain Innovation, Maastricht, The Netherlands), and custom Matlab software. Data preprocessing, SPM generation, ROI definition, and event-related average construction were identical to the methods in Experiment 1.

We employed a bootstrap analysis to test the hypothesis that the delay in dorsal network activity (relative to the ventral network) was significantly greater in Experiment 1 than in Experiment 2. After constructing bootstrap samples, we obtained the onset measures for the Search-related and Surprise-related activity for each ROI in each experiment. To increase power, we collapsed these measures across hemispheres and network nodes (dorsal or ventral). We then compared the onset measures for Experiment 1 ($(\text{Search} - \text{Surprise})_{\text{Dorsal}} - (\text{Search} - \text{Surprise})_{\text{Ventral}}$) with those for Experiment 2 (same subtractions). As the 90% confidence intervals for the resulting metrics did not overlap, the comparison was significant one-tailed at $p < 0.05$.

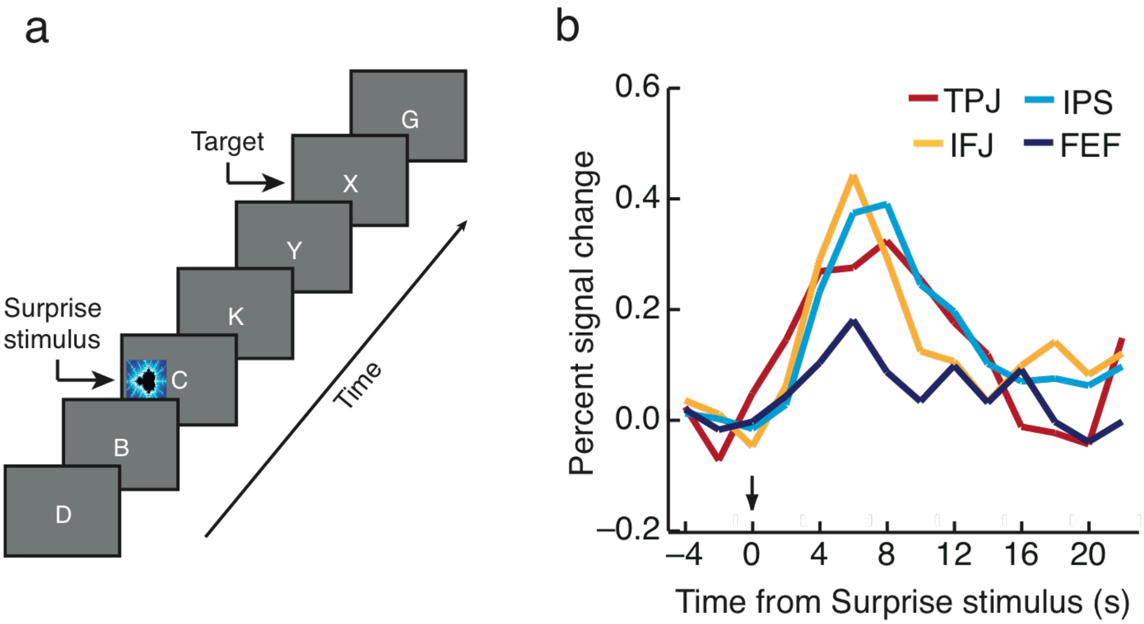

Figure 6. Spatial SiB Experiment (Experiment 2). A) Trial design. The procedure was identical to that in Experiment 1 save that in a small proportion of trials, a colorful Surprise stimulus was shown before the target away from fixation (see Fig. 1a). B) Surprise stimulus-specific waveforms in dorsal and ventral attention network ROIs defined in individual participants. Time courses were constructed in the same fashion as those in Experiment 1 (see Fig. 4b, main text). Note that all four regions show an immediate response to the Surprise stimulus presentations.

Results and Discussion

Consistent with our hypotheses that a varying spatial surprise stimulus would cause a shift of spatial attention that did not readily attenuate across trials, we found a persistent SiB effect and robust activations in both the dorsal and ventral networks (Fig. 6b). Most importantly, there was no longer a delay in activation between the dorsal and ventral networks (p's > 0.36), in marked contrast with Experiment 1 (timing delay difference across experiments: one-tailed p = 0.038; See Methods). Taken together, these results suggest that the delay in activation of the dorsal brain regions during the Surprise trials of Experiment 1 has a neural—not hemodynamic—origin. Consequently, the delayed dorsal response appears to play no part in Surprise-induced Blindness, for the FEF and IPS are likely activated after the events that trigger the perceptual deficit.

Experiment 3: Speeded Surprise-induced Blindness

Because the FEF and IPS activations during Surprise trials in Experiment 1 occurred too late to account for SiB, we considered the possibility that these activations may instead reflect changes in attentional settings in anticipation of trials subsequent to the Surprise stimulus trials (Surprise+1 trials). It is possible, for instance, that subjects enhanced their attentional focus on the primary task in post-Surprise stimuli trials in order to prevent further potential Surprise stimulus presentations from interfering with the goal of target detection. Alternatively, the presentation of a Surprise stimulus (SS) may have caused subjects to divide attention between the primary target detection task and the expectation of further SS presentations. These two accounts make opposite predictions on target detection performance, with the former suggesting an improvement and the latter an impairment. We found that target detection performance for the first two post-surprise stimuli trials in Experiment 1 were not different from those in their pre-SS counterparts (Sign test, $p = 1$), a result that does not distinguish between the two presented accounts. However, because the target detection task may have been too easy to detect subtle differences between pre-SS and post-SS trial performance (accuracy was at or near ceiling), we repeated the SiB experiment with a new group of subjects but using the sensitive measure of target response time to test for performance changes in Surprise+1 trials.

Methods

Twenty-four Vanderbilt University undergraduates (10 males) with normal or corrected-to-normal vision participated for course credit. Two subjects failed to follow task instructions, and their data were removed from the sample. Stimuli (letters and Surprise faces) were identical to those used in Experiment 1. Each trial contained an RSVP of 40 items, with each stimulus presented at fixation for 100 ms with a 17 ms inter-stimulus interval. Subjects' task was to respond to the presence of a target letter 'X' as quickly as possible with a key press. Of the 75 trials in the experiment block, 68 (91%) contained the target as one of the items between 15 and 30 inclusive. Six trials included a Surprise face, which was presented 350 ms before the target (5 trials) or in the absence of a target (always the fifth Surprise stimulus presentation). Six additional trials contained neither a target nor a face (target-absent trials). After 25 practice trials, during which no Surprise faces were presented, subjects completed the experiment trials. Surprise trials and target-absent trials occurred randomly during these trials with the restriction that the trial preceding and the three trials following these key trials contained a target and no Surprise face.

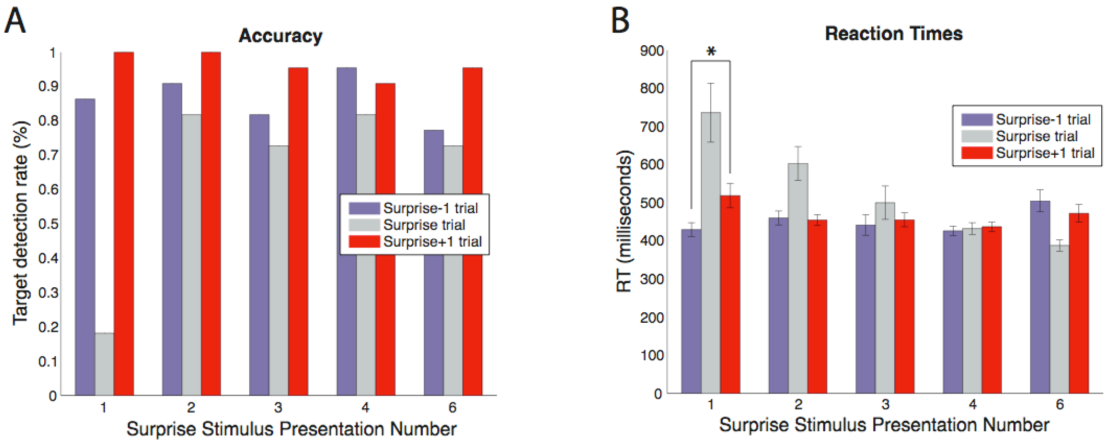

Figure 7. Performance on Speeded SiB Experiment. A) Accuracy results. B) Reaction time results. The asterisk identifies the significant difference ($p < 0.05$) in RT between the Surprise+1 and Surprise-1 trial for the first Surprise stimulus presentation. Error bars represent standard deviations.

Results and Discussion

The accuracy results show SiB, with target detection performance varying across successive Surprise stimulus presentations (Cochran's Q(4) = 29.6, $p < 0.0001$; see Fig. 7a). In the present experiment, target detection was worse for the first Surprise stimulus presentation (SS1) only (Sign tests, p's < 0.0034). As in Experiment 1, there was no target detection accuracy difference between these two groups of trials (Sign test, p = 0.25). However, the key comparison for this experiment is the RT difference between the trial immediately preceding (Surprise-1 trial) and the trial immediately following (Surprise+1 trial) the first Surprise trial. The Surprise+1 trial had a significantly longer mean RT than the Surprise-1 trial (*RT* ± *SD*: 519 ± 32 versus 430 ± 18 ms; t(18) = 2.19, p = 0.042; 19 subjects were included in this comparison, as both the Surprise+1 and Surprise-1 trials had to be hits; see Fig. 7b). Crucially, this pattern was not observed for target-absent trials (423 ± 12 versus 421 ± 15 ms; t(21) = 0.37, p = 0.72) or Miss trials (455 ± 9 versus 451 ± 10 ms; t(20) = 0.72, p = 0.48), indicating that the increased RT in the Surprise+1 trial is due to the presentation of the Surprise stimulus in the preceding trial rather than the failure to detect the presence of the target in that trial.

This speeded SiB task showed that the first presentation of a Surprise stimulus slows target detection in the subsequent trial. This result is consistent with the hypothesis that presentation of a Surprise stimulus modifies attentional settings for the subsequent trial by dividing attentional resources between performance of the primary task and vigilance for the potential presentation of another Surprise stimulus. Though speculative, this hypothesis may account for the late activation of the dorsal, goal-directed attention network following Surprise stimulus presentations that cause SiB.

Interaction of goal-directed and stimulus-driven attention

If the core components of the dorsal attentional network (the FEF and IPS) are not responsible for SiB, then how do the Surprise stimuli ultimately impair the goal-directed task of searching for and responding to a target? That is, how does stimulus-driven attention disrupt goal-directed behavior? The answer is provided by an examination of the temporal dynamics of activation in the two attention networks during the Search trials of Experiment 1. In these trials, the FEF and IPS showed the pattern expected of brain regions associated with goal-directed behavior, namely an activation profile that tightly correlated with performing the primary search task (Fig. 4c). By contrast, TPJ activity was out of phase with the dorsal brain regions, showing deactivation when the others were activated (Fig. 4c, onset shifts of approximately 4 seconds: p's < 0.0001), consistent with the finding that attention-demanding cognitive tasks are often accompanied by suppression of TPJ activity (Corbetta et al., 2008; Marois et al., 2004; Todd et al., 2005; Shulman et al., 2007; Fox et al., 2005). Strikingly, the time course of IFJ activity no longer closely followed that of its ventral network cohort, the TPJ (onset shifts of approximately 4 seconds: p's < 0.0001), but instead closely tracked the activation time course of the dorsal brain regions (Fig. 4c). This IFJ activity in the Search trials does not simply reflect target detection, for the same activity pattern was found in target-absent trials. These findings suggest that the IFJ may be not only a core member of the ventral attention network supporting stimulus-driven attention, but also functionally integrated with the dorsal network during goal-directed behavior.

To test the hypothesis that the same IFJ ROIs identified in Experiment 2 play a key function in goal-directed behavior, we carried out an additional experiment (Experiment 4) that assessed whether the IFJ is activated, along with the FEF and IPS, in a prototypical goal-directed attention task, an endogenous Posner cueing task (Corbetta et al., 2000; Posner et al., 1980) (see Fig. 8a, Methods).

Experiment 4: Endogenous Cueing Task

After completing Experiment 2, the same six individuals participated in Experiment 4 during the same scan session.

Methods

Each trial began with a central dot (0.25° in diameter) changing from white to either green or blue for 2000 ms, which indicated in which of two squares (1.0° across, located 3.4° right or left of fixation) an upcoming target was likely to appear (81% validity). The cue's color-location mapping was counterbalanced across participants. The target, a white dot (0.25°) that appeared inside one of the boxes for 100 ms, was presented 4, 6, 8, or 10 seconds after the cue onset (see Fig. 8a). The frequency of each delay period was exponentially distributed to maximize deconvolution efficiency. Participants responded to the target with a speeded button press. The next trial commenced after an ITI of 4–10 seconds (exponentially distributed). Participants completed 32 trials during each of 3 runs.

One participant's behavioral responses were not collected due to a technical error, and another participant performed the task incorrectly by withholding responses to invalidly-cued targets. Behavioral data for these two individuals were collected during a separate session outside the scanner.

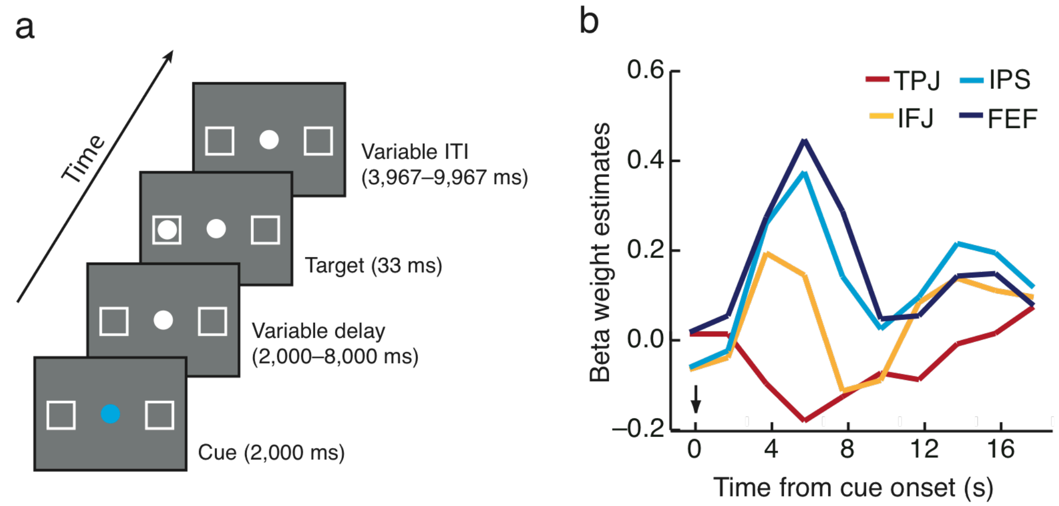

Figure 8. Endogenous Cueing Task (Experiment 4). A) Trial design. A color cue predicted the location of an upcoming target, to which the participant then responded in a speeded manner. B) Cue-related activity in dorsal and ventral attention network ROIs isolated from Experiment 2 (See Methods). The arrow marks cue onset.

fMRI procedure

The imaging procedure was identical to that used for Experiment 2.

Data analysis

After employing the same preprocessing steps used for Experiment 2, time courses from Experiment 2's Search task ROIs were constructed using a deconvolution analysis. Z-transformed β estimates, corrected for serial auto-correlations, were derived for the 10 volumes following the cue onset and for the 10 volumes following target onset, and individual time courses were averaged across participants and hemispheres (Fig. 8b). To test for significant activation in each region, one-sample t-tests were performed on the average of the 3rd and 4th volumes after cue onset.

Results and Discussion

In this task, participants made a speeded response to a target presented at a location that was cued by the color of a central fixation point, with the cue validly predicting the location of the target on 80% of the trials. The task was successful in engaging goal-directed attention, evidenced by the fact that participants were faster at detecting the target at validly cued than at invalidly cued positions (*RT* ± *SD*: 317 ± 36 ms versus 396 ± 64 ms, $t(5) = 4.53$, $p = 0.0062$). Furthermore, the dorsal brain regions were activated during the cue-related period ($t(5)$'s > 3.53, p's < 0.017; See Methods), as expected of brain regions involved in goal-directed attention (Corbetta & Shulman, 2002; Corbetta et al., 2000; Yantis et al., 2002) (Fig. 8b). Most importantly, the IFJ was also activated by the cue ($t(5) = 2.74$, $p = 0.041$), and at the same time as the FEF and IPS. These results were obtained regardless of whether the ROIs were defined in the cueing task or in the Search trials of the RSVP task, attesting to the fact that the brain regions exhibiting goal-directed activity in the Search trials are also involved in visuo-spatial shifts of attention. We therefore conclude that IFJ supports goal-directed behavior, as it is activated along with core members of the dorsal network during the cue period of a classic goal-directed attention task. These conclusions are consistent with previous reports suggesting that similar brain regions are activated in other cued attention shift tasks (Corbetta et al., 1998; Kastner et al., 2007).

Taken together, the results of our experiments indicate that the IFJ participates in both stimulus-driven and goal-directed attention. While the pattern of IFJ activity is consistent with brain regions involved in stimulus-driven attention during the presentation of a Surprise stimulus, its activity profile is instead more consistent with those of goal-directed brain regions during the Search task. It follows from these results that the IFJ should be more functionally integrated with core members of the dorsal network during goal-directed attention, but with core members of the ventral network during stimulus-driven attention. These predictions are borne out by a functional connectivity analysis of Experiment 1 (See Methods), which showed that IFJ activity was correlated positively with FEF and IPS (IFJ-FEF: $t(29) = 9.13$, $p < 0.0001$; IFJ-IPS: $t(29) = 12.19$, $p < 0.0001$; FEF-IPS: $t(29) = 6.87$, $p < 0.0001$)—but negatively with TPJ ($t(29) = -4.27$, $p = 0.00019$)—during the Search trials. Conversely, following the presentation of a Surprise stimulus, the IFJ-FEF and IFJ-IPS correlations decreased (paired t-test of the changes: $t(29) = -2.12$, $p = 0.043$; $t(29) = -2.36$, $p = 0.025$), while those between IFJ and TPJ increased ($t(29) = 2.07$, $p = 0.047$) and those between FEF and IPS did not change ($t(29) = -1.07$, $p = 0.29$). These connectivity results provide additional evidence that the IFJ acts as a neural site underlying stimulus-driven and goal-directed attention, with its response profile and network allegiance dependent on task demands. In that context, SiB would result from the 'bottom-up' engagement of IFJ by the presentation of a Surprise stimulus, thereby transiently disrupting or altering this brain region's control of the target detection task. With behavioral and neuronal habituation to the repeated Surprise stimulus presentations, the IFJ may be able to maintain its goal-oriented activity even in the face of task-irrelevant stimulus presentations.

General Discussion

Our study reveals that both functional divergence and convergence of the dorsal and ventral attentional networks underlie attention and awareness.

Divergence of function between these two networks is clearly evidenced by the SiB procedure, as it shows that stimulus-driven attentional limits to conscious perception can arise from the ventral attention network in the absence of dorsal network or visual cortex modulation. In contrast to these results, previous neurobiological investigations (Dehaene et al., 2006; Beck et al., 2001; Rees et al., 1999; Marois et al., 2000; Marois et al., 2004; Rees et al., 2002; Huettel et al., 2001; Lumer et al., 1998) have frequently implicated regions of both the ventral and dorsal networks in awareness. Such large-scale activation patterns are consistent with ‘global workspace’ models that posit that awareness emerges from the reverberating activity of a widely distributed cortical network (Dehaene et al., 2006; Rees et al., 2002; Baars, 1997). The difference in activation patterns between these previous studies and the present one are likely a result of differences in task design. Whereas previous tasks have included spatial shifts of attention (Corbetta et al., 2000; Serences et al., 2005; Buschman & Miller, 2007; Gottlieb, 2007; Beck et al., 2001; Huettel et al., 2001) or covert or overt responses (Corbetta et al., 2000; Serences et al., 2005; Linden et al., 1999; Marois et al., 2000; Beck et al., 2001; Rees et al., 1999; Marois et al., 2000; Marois et al., 2004; Huettel et al., 2001; Konen & Kastner, 2008) to the critical attention-capturing stimulus, our task was specifically designed to exclude these components as they are unnecessary for exogenous attentional capture but can activate the dorsal attention network (Corbetta & Shulman, 2002; Corbetta et al., 2000; Kastner et al., 1999; Serences et al., 2005; Yantis et al., 2002). As such, our task demonstrates that the dorsal network's contribution to conscious perception may be negligible under these controlled circumstances. This conclusion is consistent with the suggestion that awareness is not necessarily an emergent property of the dorsal network (Milner & Goodale, 1992) but poses a challenge to global network theories of awareness.

These conclusions, however, do not imply that the dorsal network never plays a role in attentional limits to explicit perception. Dorsal structures may contribute to, and be essential for, conscious perception during tasks that involve top-down or goal-oriented processing, such as change detection or binocular rivalry (Dehaene et al., 2006; Beck et al., 2001; Rees et al., 2002; Lumer et al., 1998). Indeed, just as deficits of awareness in different visual domains often have dissociable neural origins (e.g. prosopagnosia versus achromatopsia) (Rees et al., 2002), awareness may also be fractionated at central, attentional stages of information processing. Additional research, aided by better delineation of the topographically distinct sub-regions of the IPS, will be necessary to assess the specific contributions that the dorsal network may play in attentional limits to conscious perception and awareness in general.

In addition to revealing a functional dissociation between the ventral and dorsal attentional networks in awareness, the very nature of SiB—a profound deficit in the detection of a goal-relevant target as a result of the presentation of an unexpected and task-irrelevant stimulus—underscores that stimulus-driven and goal-directed attention must ultimately interact (Corbetta & Shulman, 2002; Egeth & Yantis, 1997; Serences et al., 2005; Corbetta et al., 2008; Buschman & Miller, 2007; Gottlieb, 2007; He et al., 2007). The present study suggests that the ventral attention network's lateral prefrontal component, the inferior frontal junction, is the site of convergence for stimulus-driven and goal-directed attention, a finding that is consistent with recent resting state functional connectivity data suggesting that this brain region functionally interacts with both ventral and dorsal brain structures (He et al., 2007). The IFJ has also been implicated in task-switching and cognitive control (Brass et al., 2005; Koechlin et al., 2003) more generally. This brain region is therefore ideally suited to act as the neural site of coordination for stimulus-driven and goal-directed attention. Moreover, the IFJ's involvement in both the non-spatial and spatial SiB tasks (see Experiments 1 and 2) indicates that this brain region's function generalizes across both spatial and non-spatial forms of attention. While it remains to be seen whether all these attentional processes are mediated by the same or different sub-populations of IFJ neurons, a central role for this brain region in the co-ordination of stimulus-driven and goal-directed attention across both spatial and non-spatial domains resonates very well with the proposal that the IFJ is a critical neural substrate underlying our severely limited attentional capacities (Marois & Ivanoff, 2005).

References

Asplund, C. L., Todd, J. J., Snyder, A. P., Gilbert, C. M., & Marois, R. (In Press). Surprise-induced Blindness: A stimulus-driven attentional limit to conscious perception. Journal of Experimental Psychology: Human Perception and Performance.

Baars, B. J. (1997). In the Theatre of Consciousness: Global Workspace Theory, A Rigorous Scientific Theory of Consciousness. Journal of Consciousness Studies 292–309.

Beck, D. M., Rees, G., Frith, C. D. & Lavie, N. (2001). Neural correlates of change detection and change blindness. Nature Neuroscience 4, 645–650.

Brainard, D. H. (1997). The Psychophysics Toolbox. Spatial Vision 10, 433–436.

Brass, M., Derrfuss, J., Forstmann, B., & von Cramon, D. Y. (2005). The role of the inferior frontal junction in cognitive control. Trends in Cognitive Sciences 9, 314–316.

Buschman, T. J. & Miller, E. K. (2007). Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. Science 315, 1860–1862.

Chiu, Y. -. C. & Yantis, S. (2009). A domain-independent source of cognitive control for task sets: Shifting spatial attention and switching categorization rules. Journal of Neuroscience 29, 3930–3938.

Corbetta, M., Akbudak, E., Conturo, T. E., Snyder, A. Z., Ollinger, J. M., Drury, H. A., Linenweber, M. R., Petersen, S. E., Raichle, M. E., Van Essen, D. C., & Shulman, G. L. (1998). A common network of functional areas for attention and eye movements. Neuron 21, 761–773.

Corbetta, M., Kincade, J. M., Ollinger, J. M., McAvoy, M. P. & Shulman, G. L. (2000). Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nature Neuroscience 3, 292–297.

Corbetta, M. & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews Neuroscience 3, 201–215.

Corbetta, M., Patel, G. & Shulman, G. L. (2008). The reorienting system of the human brain: from environment to theory of mind. Neuron 58, 306–324.

Courchesne, E., Hillyard, S. A. & Galambos, R. (1975). Stimulus novelty, task relevance and the visual evoked potential in man. Electroencephalography and Clinical Neurophysiology 39, 131–143.

Davison, A. C. & Hinkley, D. V. (1998). Bootstrap methods and their application (Cambridge University Press).

Dehaene, S., Changeux, J. P., Naccache, L., Sackur, J. & Sergent, C. (2006). Conscious, preconscious, and subliminal processing: A testable taxonomy. Trends in Cognitive Sciences 10, 204–211.

Downar, J., Crawley, A. P., Mikulis, D. J. & Davis, K. D. (2002). A cortical network sensitive to stimulus salience in a neutral behavioral context across multiple sensory modalities. Journal of Neurophysiology 87, 615–620.

Downar, J., Crawley, A. P., Mikulis, D. J. & Davis, K. D. (2000). A multimodal cortical network for the detection of changes in the sensory environment. Nature Neuroscience 3, 277–283.

Egeth, H. E. & Yantis, S. (1997). Visual attention: control, representation, and time course. Annual Review of Psychology 48, 269–297.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., et al. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. Proceedings of the National Academy of Sciences of the United States of America 102, 9673–9678.

Gottlieb, J. (2007). From thought to action: The parietal cortex as a bridge between perception, action, and cognition. Neuron 53, 9–16.

He, B. J., Snyder, A. Z., Vincent, J. L., Epstein, A., et al. (2007). Breakdown of functional connectivity in frontoparietal networks underlies behavioral deficits in spatial neglect. Neuron 53, 905–918.

Heilman, K. M. & Watson, R. T. (1977). Mechanisms underlying the unilateral neglect syndrome. Advances in Neurology 18, 93–106.

Hoffman, E. A. & Haxby, J. V. (2000). Distinct representations of eye gaze and identity in the distributed human neural system for face perception. Nature Neuroscience 3, 80-84.

Horovitz, S. G., Skudlarski, P. & Gore, J. C. (2002). Correlations and dissociations between BOLD signal and P300 amplitude in an auditory oddball task: a parametric approach to combining fMRI and ERP. Magnetic Resonance Imaging 20, 319-325.

Huettel, S. A., Güzeldere, G. & McCarthy, G. (2001). Dissociating the neural mechanisms of visual attention in change detection using functional MRI. Journal of Cognitive Neuroscience 13, 1006–1018.

Husain, M. & Nachev, P. Space and the parietal cortex. (2007). Trends in Cognitive Sciences 11, 30–36.

Karnath, H. O., Milner, A. D. & Vallar, G. (2002). The cognitive and neural bases of spatial neglect (Oxford University Press).

Kastner, S., Pinsk, M. A., De Weerd, P., Desimone, R. & Ungerleider, L. G. (1999). Increased activity in human visual cortex during directed attention in the absence of visual stimulation. Neuron 22, 751–761.

Kastner, S., DeSimone, K., Konen, C. S., Szczepanski, S. M., Weiner, K. S., & Schneider, K. A. (2007). Topographic maps in human frontal cortex revealed in memory-guided saccade and spatial working-memory tasks. Journal of Neurophysiology 97, 3494–3507.

Koechlin, E., Ody, C. & Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. Science 302, 1181–1185.

Konen, C. S. & Kastner, S. (2008). Representation of eye movements and stimulus motion in topographically organized areas of human PPC. Journal of Neuroscience 28, 8361–8375.

Knight, R. T. (1984). Decreased response to novel stimuli after prefrontal lesions in man. Electroencephalography and Clinical Neurophysiology 59, 9–20.

Linden, D. E., Prvulovic, D., Formisano, E., Völlinger, M., et al. (1999). The functional neuroanatomy of target detection: an fMRI study of visual and auditory oddball tasks. Cerebral Cortex 9, 815–823.

Lumer, E. D., Friston, K. J., & Rees, G. (1998). Neural correlates of perceptual rivalry in the human brain. Science 280, 1930–1934.

Marois, R., Leung, H. C. & Gore, J. C. (2000). A stimulus-driven approach to object identity and location processing in the human brain. Neuron 25, 717–728.

Marois, R., Chun, M. M. & Gore, J. C. (2000). Neural Correlates of the Attentional Blink. Neuron 28, 299–308.

Marois, R., Yi, D. J. & Chun, M. M. (2004). The neural fate of consciously perceived and missed events in the attentional blink. Neuron 41, 465–472.

Marois, R. & Ivanoff, J. Capacity limits of information processing in the brain. (2005). Trends in Cognitive Sciences 9, 296–305.

Milner, A. D. & Goodale, M. A. (1992). Separate visual pathways for perception and action. Trends in Neuroscience 15, 20–25.

Opitz, B., Mecklinger, A., Friederici, A. D. & von Cramon, D. Y. (1999). The functional neuroanatomy of novelty processing: integrating ERP and fMRI results. Cerebral Cortex 9, 379–391.

Pelli, D. G. (1997). The VideoToolbox software for visual psychophysics: Transforming numbers into movies. Spatial Vision 10, 437–442.

Posner, M. I., Snyder, C. R. R. & Davidson, B. J. (1980). Attention and the detection of signals. Journal of Experimental Psychology: General 109, 160–174.

Rees, G., Russell, C., Frith, C. D. & Driver, J. (1999). Inattentional blindness versus inattentional amnesia for fixated but ignored words. Science 286, 2504–2507.

Rees, G., Kreiman, G., & Koch, C. (2002). Neural correlates of consciousness in humans. Nature Reviews Neuroscience 3, 261–270.

Serences, J. T., Shomstein, S., Leber, A. B., Golay, X., et al. (2005). Coordination of voluntary and stimulus-driven attentional control in human cortex. Psychological Science 16, 114–122.

Sheskin, D. J. (2000). Handbook of Parametric and Nonparametric statistical procedures (2nd Ed.) (CRC Press, Boca Raton, FL).

Shulman, G. L., Astafiev, S. V., McAvoy, M. P., d'Avossa, G. & Corbetta, M. (2007). Right TPJ deactivation during visual search: functional significance and support for a filter hypothesis. Cerebral Cortex 17, 2625–2633.

Talairach, J. & Tournoux, P. (1988). Co-planar stereotaxic atlas of the human brain (Thieme Medical Publishers New York).

Todd, J. J., Fougnie, D. & Marois, R. (2005). Visual short-term memory load suppresses temporo-parietal junction activity and induces inattentional blindness. Psychological Science 16, 965–972.

Yamaguchi, S., Hale, L. A., D'Esposito, M. & Knight, R. T. (2004). Rapid prefrontal-hippocampal habituation to novel events. Journal of Neuroscience 24, 5356–5363.

Yantis, S., Schwarzbach, J., Serences, J. T., Carlson, R. L., et al. (2002). Transient neural activity in human parietal cortex during spatial attention shifts. Nature Neuroscience 5, 995–1002.

CHAPTER III

THE FUNCTIONAL SEGREGATION OF THE VENTRAL ATTENTION NETWORK: SEPARATING THE INFERIOR FRONTAL JUNCTION FROM THE TEMPORO-PARIETAL JUNCTION

Functional neuroimaging techniques reveal which brain regions are involved in a given behavioral task. Since the brain enables and constrains the mind, such neurobiological information can shape and test theories of cognitive processing. Two different types of inference allow neuroimaging data to inform psychological theories. In “forward inference”, one uses patterns of brain activity to distinguish between different cognitive hypotheses (Henson, 2006). Conversely, one can “reverse infer” the engagement of a particular cognitive process from activation of a brain region (Poldrack, 2006). This latter inference can be problematic, especially if the function of an activated region is poorly understood. This problem, however, also presents an opportunity: A brain region that is activated in multiple different contexts is likely performing a common function across the eliciting tasks. This function can then be inferred from consideration of these tasks. In this chapter, I use forward and reverse inferences to understand better the nature of the cognitive processes involved in stimulus-driven attention, specifically those processes performed in the inferior frontal junction (IFJ) and temporo-parietal junction (TPJ).

The Surprise-induced Blindness experiments in Chapter II demonstrated that the IFJ and TPJ co-activate when an unexpected stimulus is presented. Such co-activation is expected because both regions are key members of the ventral attention network underlying stimulus-driven attention, which is activated by surprising events (Corbetta & Shulman, 2002; Corbetta et al., 2008). Although often recruited with the dorsal attention network--frontal eye fields (FEF) and superior parietal cortex (including the intra-parietal sulcus, IPS)--the ventral attention network can be isolated using surprising events that demand neither overt responses nor spatial shifts of attention (Asplund et al., 2010). This network can also be specifically identified from intrinsic correlations between brain regions when subjects are performing no task (Fox et al, 2006).

Nevertheless, the IFJ and TPJ do not appear to co-activate in most cognitive or attention tasks (Toro et al., 2008). For example, reasoning about the mental states of others (Theory of Mind, ToM) consistently recruits the TPJ but not the IFJ (Aichhorn et al., 2009; Buckner & Carroll, 2007; Saxe & Kanwisher, 2003; Vogeley et al., 2001; Young et al., 2010; Spreng et al., 2009). Stimulus-driven attention (SDA) and ToM reasoning appear to draw on partially overlapping portions of the TPJ in the right hemisphere (Mitchell, 2008; Decety & Lamm, 2007; Scholz et al., 2009).

Another functional context in which the IFJ and the TPJ may be dissociated is during attention-demanding tasks. Such tasks, including visual search, are often accompanied by suppression of TPJ activity (Shulman et al., 2007; see also Todd et al., 2005; Fox et al., 2005). This activity appears to be in a similar TPJ area to that activated with SDA. Such task-related deactivation is not limited to the right TPJ; a widespread network shows this same pattern. This network is comprised of the TPJs, precuneus, medial frontal cortex (MFC), middle temporal gyri (MTGs), and hippocampus. Because this network is relatively more active during periods of rest (as compared to attention-demanding tasks), it has been associated with a "default mode of processing" (Default). First identified with PET (Raichle et. Al, 2001; Vogt et al., 2006), it is commonly observed using fMRI, both with block designs and even fast event-related approaches (Buckner et al., 2008). The network is also activated by tasks that require internal focus, such as recalling autobiographical memories, thinking of one's future self (prospection), and imagining routes to be navigated (Buckner & Carroll, 2007; Spreng et al., 2009; Spreng & Grady, 2009). Projecting oneself into another person's situation, a key component of ToM reasoning, also draws on the same network (Buckner & Carroll, 2007; Spreng et al., 2009; Spreng & Grady, 2009, but see Saxe et al., 2006; Saxe & Kanwisher, 2003).

It is unclear to what degree the SDA network overlaps with the Default and ToM networks, but there is reason to believe that the overlap goes beyond right TPJ alone. Foremost, the left TPJ is often activated in stimulus-driven attention paradigms (Asplund et al., 2010; Corbetta & Shulman, 2002; Marois et al., 2000; Downar et al., 2000; Linden et al, 1999; Serences et al., 2005). Moreover, both the precuneus and medial prefrontal cortex, which are members of the default network, are known to have attentional roles (Cavanna & Trimble, 2006; Amodio & Frith, 2006; Kastner et al., 1999), and the latter has also been observed in stimulus-driven attention paradigms (Downar et al., 2002; Downar et al., 2000; Linden et al., 1999).

In contrast, the IFJ, a key SDA region (Corbetta & Shulman, 2002; Asplund et al., 2010), has not been associated with either the Default or ToM networks. In fact, resting state functional connectivity suggests that it or proximal regions may be part of a task-positive (TP) network (Fox et al., 2005; Fox et al., 2006; He et al., 2007; Laufs et al., 2003). This network is generally active during attention-demanding tasks; as such, it is the inverse of the Default network, which is also termed "task-negative" (Fox et al., 2005). The TP network also includes, but is not limited to, the dorsal attention network, notably the FEF and IPS (Fox et al., 2005; Fox et al., 2006). Recent studies with attentional tasks (Asplund et al., 2010; Toro et al., 2008) confirm the IFJ’s participation with the dorsal attention network under some circumstances (e.g. the interpretation of an endogenous cue; see Chapter II, Expt. 4).

Nevertheless, a direct comparison of IFJ participation in the four networks described above has not yet been made. In addition, overlap of SDA with ToM and Default has only been examined at the right TPJ. The first purpose of this study is to compare the activation of these two core members of the ventral attention network (the IFJ and TPJ) to determine whether their function can be dissociated directly. The second purpose of the present study is to compare the SDA network with the ToM, Default, and TP networks. By doing so, we can better characterize of the roles of different regions as well as assess the general similarity of the networks. The functional overlaps and dissociations in each region and across the networks as a whole will give us a better understanding of the cognitive processes involved in the tasks associated with each network.

Methods

A reanalysis of the data from Asplund et al. (2010) (Chapter II) provides the SDA, Default, and TP networks; the ToM network is identified in a separate experiment in which participants made judgments about what a friend would do in various hypothetical situations. This ToM experiment involved many of the same participants from Asplund et al. (2010), allowing for more within-subject comparisons of the results.

Surprise-induced Blindness (SiB), Default, and Task-Positive (TP) paradigms.

The full behavioral and imaging details of the SiB experiment can be found in Asplund et al., 2010. Briefly, participants (n=30) searched for a target letter (X) in an RSVP stream of distractor letters (110 ms per frame), indicating whether they detected the letter by key press at the conclusion of each trial (Figure 1a). Each participant completed a single run of 40 trials, with a trial onset asynchrony (TOA) of 8 s. During six of the trials, and unbeknownst to the subjects, a surprise stimulus (grayscale face) occurred 330 ms before the target (5 trials) or in the absence of a target (1 trial).

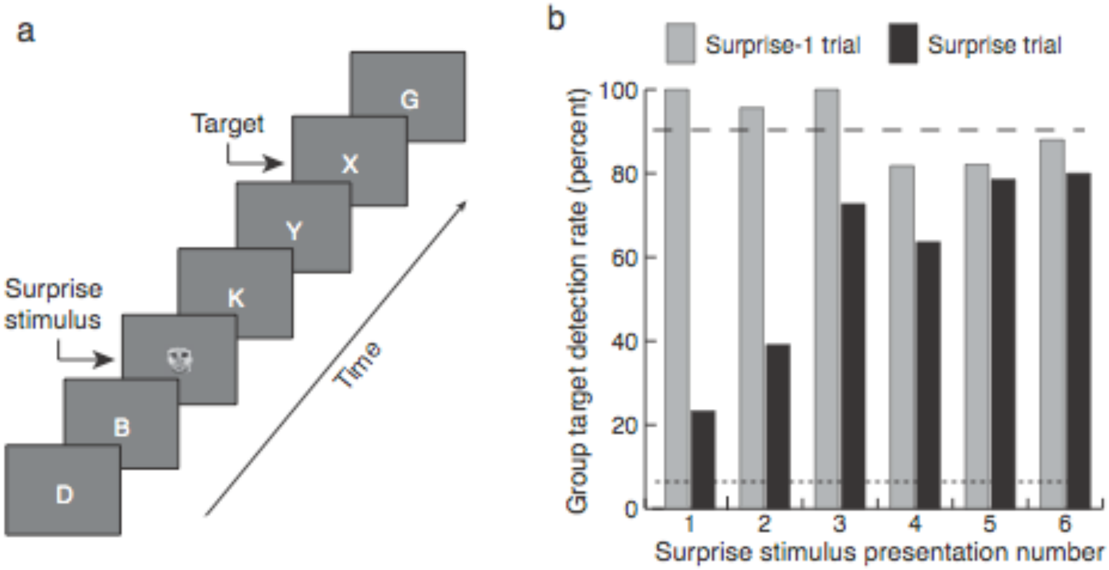

Figure 1. SiB experiment (Experiment 1) from Asplund et al. (2010). (a) Trial design. Participants searched for a target letter in a rapid serial visual presentation (RSVP) stream of distractor letters. In a small proportion of trials (surprise trials), a surprise face stimulus was shown before the target. (b) Group target detection performance. Black bars represent accuracy in surprise trials, and gray bars represent accuracy in trials immediately preceding the surprise trials (surprise-1). Dashed line corresponds to the average target hit rate for search trials (target only). Dotted line corresponds to the false alarm rate.

Data analysis was performed using BrainVoyager 4.9.1, BrainVoyager QX 1.7.9 and 1.10.2, and custom Matlab software. Preprocessing steps for the functional images included image realignment, 3D motion correction, linear trend removal, correction for slice acquisition timing, and spatial smoothing with a 6-mm Gaussian kernel (full width at half maximum). The data were then transformed to Talairach space (Talairach & Tournoux, 1988) for comparison across subjects. Statistical parametric maps (SPMs) of BOLD activation were created using a general linear model (GLM) with multiple regression. To ensure that the SDA and Default analyses were statistically independent, the SDA network was defined using the first half of the single fMRI run we acquired for each subject, while the Default network was identified from the second half. Regressors were created for search trials (trials with a target but no surprise stimulus) and no-target trials in the first and second halves of the fMRI run separately (Search1, Search2, NoTarget1, and NoTarget2). Separate regressors were also created for the first two and final four surprise trials (Surprise1, Surprise2), with only the Surprise1 regressor used for network-identifying contrasts. The first two surprise trials were examined separately because they always occurred during the first half of the run and were the only two trials to evidence Surprise-induced Blindness (see Chapter II). Boxcar functions of hypothesized neural activity timing in each condition were convolved with a canonical double gamma hemodynamic function (SPM2, http://www.fil.ion.ucl.ac.uk/spm) to create each regressor. SDA activity was defined by the contrast [+Surprise1 –Search1], Default activity by the open contrast [–Search2], and TP activity by the open contrast [+Search2].

Theory of Mind (TOM)

Fourteen subjects (6 females, ages 19-27) from the Vanderbilt community participated in the Theory of Mind (TOM) experiment for monetary compensation. The Vanderbilt University Institutional Review Board approved the experimental protocol and subjects gave their informed consent after the nature of the study was explained. The data from two subjects was not used due to image acquisition errors.

The experiment consisted of four tasks: SELF, FRIEND, CONTROL, and MATH. Neither the SELF nor MATH conditions were analyzed for this study, so their descriptions are brief. In both the SELF and FRIEND condition, subjects answered questions about what they or their friend would do in a hypothetical, but probable, moral or social dilemma. Questions were similar to those used in other studies of ToM (Vogeley et al, 2001; Fletcher et al., 1995), and were designed to evoke little humor or emotion. All questions required ‘yes’, ‘no’, or ‘maybe’ responses, each mapped to a finger of the right hand.

Before the experiment, subjects were asked for the name of a friend who they knew very well, with the only restriction that it should be someone with whom they had not had a romantic relationship. Their friend’s first name was used as the protagonist in all the FRIEND questions, which consisted of the same 72 questions used for the SELF condition. Each subject was exposed to 36 SELF and FRIEND questions each, with no overlap of questions between the two conditions. Two sample scenarios and questions follow below.

"Stephanie sees a stray dog run down the street. The dogcatcher comes and asks Stephanie where the dog went. Does Stephanie tell?"

"Stephanie will be out of town for a month and won’t be using her brand new car. Does Stephanie offer it to a friend who needs one?"

The CONTROL task had similar demands for reading, general reasoning, and motoric response. We constructed 36 reasoning questions in which there was no requirement to consider a person's point of view. They included syllogisms, simple physics and science problems, and other general reasoning problems. The questions were matched in phrase length to the SELF and FRIEND questions, and they also required ‘yes’, ‘no’, or ‘maybe’ responses. Examples follow below.

"An army cargo plane releases a package of food from the air. Will the package fall straight down to the ground, perpendicular to the drop point?"

"All zweebles are mammals. The creature being examined by the scientist has been determined to be a zweeble. Is it a mammal?"

In the fourth condition, MATH, subjects determined whether a presented equation was true or false.

The timing of each trial was the same for all tasks, with the scenario present on the screen until subjects responded, up to a maximum of 10 s. The next trial began one second later. Scenario order was randomized across subjects. The SELF, FRIEND, and CONTROL blocks were cued by a four-second panel with instructions (“you”, “friend”, “logical”) indicating what type of block would follow. Subjects completed three fMRI runs. Each run began and ended with 12 s of fixation and contained three blocks of each task presented in counterbalanced order across subjects. The SELF, FRIEND, and CONTROL tasks had four trials per block, while MATH blocks had only three trials each; pilot studies showed that MATH questions took approximately 30% longer to answer than questions in the other conditions.

Anatomical 3D high-resolution images were acquired using conventional parameters on a 3T GE MRI system. Twenty-six 4 mm thick axial slices (0 mm skip; 3.75 x 3.75 mm in-plane) were acquired parallel to the anterior commissure-posterior commissure (AC-PC) line. T2*-weighted image parameters were: 25 ms echo time, 70 degree flip angle, 240 mm FOV, 64 x 64 matrix, 2000 ms repetition time. The functional scan included between 150 and 196 brain volumes (depending on speed of response), with the first six volumes discarded for signal stabilization. Trials were presented using Psychophysics Toolbox (Brainard, 1997; Pelli, 1997) for Matlab on an Apple G4 Macintosh. Stimuli were back-projected from an LCD projector onto a screen viewed through a prism mirror by the supine participant.

Preprocessing steps were identical to those in the SiB Experiment described above. For multiple regression analysis, regressors were created for each condition and separate regressors created for the instruction screens. ToM activity was defined by the contrast [+FRIEND -CONTROL], similar to what others studies have employed (Fletcher et al., 1995; Vogeley, 2001).

Overlap analyses

To assess functional overlaps at the network level, we first found the volume of overlap between the networks in question thresholded at $q(FDR) < 0.05$. The percentage of overlap was then calculated relative to each network's volume; these percentage values were then averaged together (Kung et al., 2007). For example, TOM ∩ Default contained 39% of the TOM network's volume and 23% of the Default network's. For triple overlaps, all three percentages were calculated and then averaged. A similar procedure was used for comparing the overlaps at the TPJ and IFJ. In both cases, overlap regions of interest (o-ROIs) were defined as all contiguous activated voxels in a given region, starting from that region's peak voxel for each SPM. The TPJ o-ROIs were confined relatively well to the TPJ, but the TP network's IFJ o-ROI was contiguous with the anterior insula, posterior superior frontal sulcus (SFS), and MFC. Consequently, overlap percentages with this o-ROI in the denominator were not calculated. Similarly, MFC and precuneus/posterior cingulate activations were contiguous with many other regions (e.g. superior frontal sulcus, middle temporal gyrus, and hippocampus) in the TOM and Default SPMs, rendering overlap percentages for these areas specifically difficult to obtain or interpret.

Overlap percentages can be less than 100% for many reasons other than real functional dissociations between adjoining or partially overlapping regions. One task may cause more spatially extensive activation than another, there may be anatomical variations that render comparisons across subjects problematic, and physiological or random noise may affect the significance levels of different voxels. To generate a rough estimate of what degree of overlap could be expected from o-ROIs defined from the same task (which would be affected by the above factors but presumably not by real functional dissociations), we split the SiB data in two ways, within subjects and across subjects. For the first split, we defined TPJ o-ROIs from the [-Search2] contrast (the Default contrast used elsewhere) with those defined from the [-Search1] contrast (which also acts as a Default contrast). For the second split, we defined TPJ o-ROIs from the first 15 subjects with the [-Search2] contrast and then from the second 15 subjects with the same contrast. These TPJ o-ROIs allowed us to compare the functional overlaps for ROIs from the same task (Default).

Region-of-interest (ROI) analyses

For the group region of interest (ROI) analyses, we first defined ROIs from SPMs identifying each network, with each SPM's threshold set to q(FDR) < 0.05. The peak voxel and surrounding activated voxels for each activated focus were then selected, up to 1 cm^3. The time-course for each trial or block was then extracted from each ROI for each participant and then converted to percent signal change; the baseline was calculated from the trial or block onset time point and the two preceding time points. All trials or blocks in a given condition (Surprise1, Search1, Search2, FRIEND, and CONTROL) were then averaged together within each subject. These event-related averages (ERAs) were the basis for statistical tests of amplitude. For SDA analyses, we first identified the time point with the largest percent signal change between 8 and 10 s after trial onset (which is equivalent to 6 to 8 s after surprise stimulus presentation for Surprise1 trials) for each condition for each participant. Paired t-tests were next employed to compare Surprise1 and Search1 amplitude. For Default, we compared the average of four timepoints corresponding to expected inter-trial activity (0, 2, 8, and 10 s after trial onset; see Figure 5 of Chapter II) to two timepoints corresponding to expected activity during the RSVP (4 and 6 s after trial onset) using paired t-tests. The activity expectations were based on the results of linearly convolving a standard hemodynamic function (double-gamma from SPM2; http://www.fil.ion.ucl.ac.uk/spm) with boxcar functions representing the hypothesized neural activity during the RSVP task (see Supplementary Figure 3 from Asplund et al., 2010). Note that TP (task-positive) is merely the inverse of the Default results for these ROI analyses. Finally, for ToM we compared the average of seven timepoints (6-18 seconds after block onset, since virtually all blocks showed stable signal during this time interval) from each condition with paired t-tests. In the results tables for the ROI analyses (Tables 5 and 6), t-values are given for a given network's defining contrast using ROIs defined from that network. Such results are not meant as a second non-independent test of the data. Instead, they are given to demonstrate that the tests employed to define each network (SDA, ToM, and Default) based on ROI timecourses were comparable to the GLM results.

Six participants in the SiB experiment also participated in the ToM experiment. For those six participants, we defined individual ROIs from ToM SPMs generated for each person (all thresholds at q(FDR) < 0.05). Although individual SPMs for the SDA contrast were not sufficiently robust for ROI analyses (given the small number of trials per subject), the Default contrast did allow us to define ROIs for consistently activated regions across subjects. For these Default ROIs, a lenient threshold of $p < 0.01$ (uncorrected) was used. For most subjects (17 of 30), q(FDR) < 0.05 produced a p-value in this range, but for the remainder, the p-value was extremely low. This result is likely due to the FDR correction being sensitive to a limited data-set (each subject provided but 140 seconds of imaging data for this contrast). Timecourse extraction and statistical comparisons were extracted and comparisons made in a fashion identical to those in the group ROI analyses.

Results

For complete behavioral and neuroimaging results of the SiB experiment, see Asplund et al. (2010). Briefly, the first two presentations of the surprise stimulus caused a target detection deficit (see Figure 1b). This early deficit was not the result of learning the task because performance was high during the trials preceding the first two surprise trials. Instead, the early deficit reflects stimulus-driven attentional capture (see also Asplund et al., in press). Target detection during search trials (those with a target but without a surprise stimulus) was good but not perfect at 90.4%, confirming that the primary search task was effortful.

For the ToM experiment, there was a significant difference in response time between tasks, with CONTROL times longer than FRIEND times ($t(11) = 2.31$, $p = 0.041$; RT +/- SD: 6.21 +/- 0.99 s versus 5.92 +/- 0.98 s). This response time difference, however, could not account for our neuroimaging results, for the SPMs were virtually identical when trials were removed from both tasks (approximately 6% of total trials per subject) to equilibrate the response times (data not shown).

Overlap quantification

Substantial network overlap was found between ToM and Default, with far less general overlap in other overlap comparisons, specifically those with SDA (Table 1; Figure 2). ToM and Default showed great overlap in the precuneus, posterior cingulate, medial frontal cortex, middle temporal gyri (MTGs), and TPJs (Figure 2; Table 2). Overlaps involving the SDA were far less widespread. The vast majority of the SDA overlap with ToM and Default was concentrated at the TPJ (Tables 2), and with TP at the IFJ (Table 3). At the TPJs, the overlaps between SDA and ToM as well as SDA and Default were similar in degree to the overlap between ToM and Default.

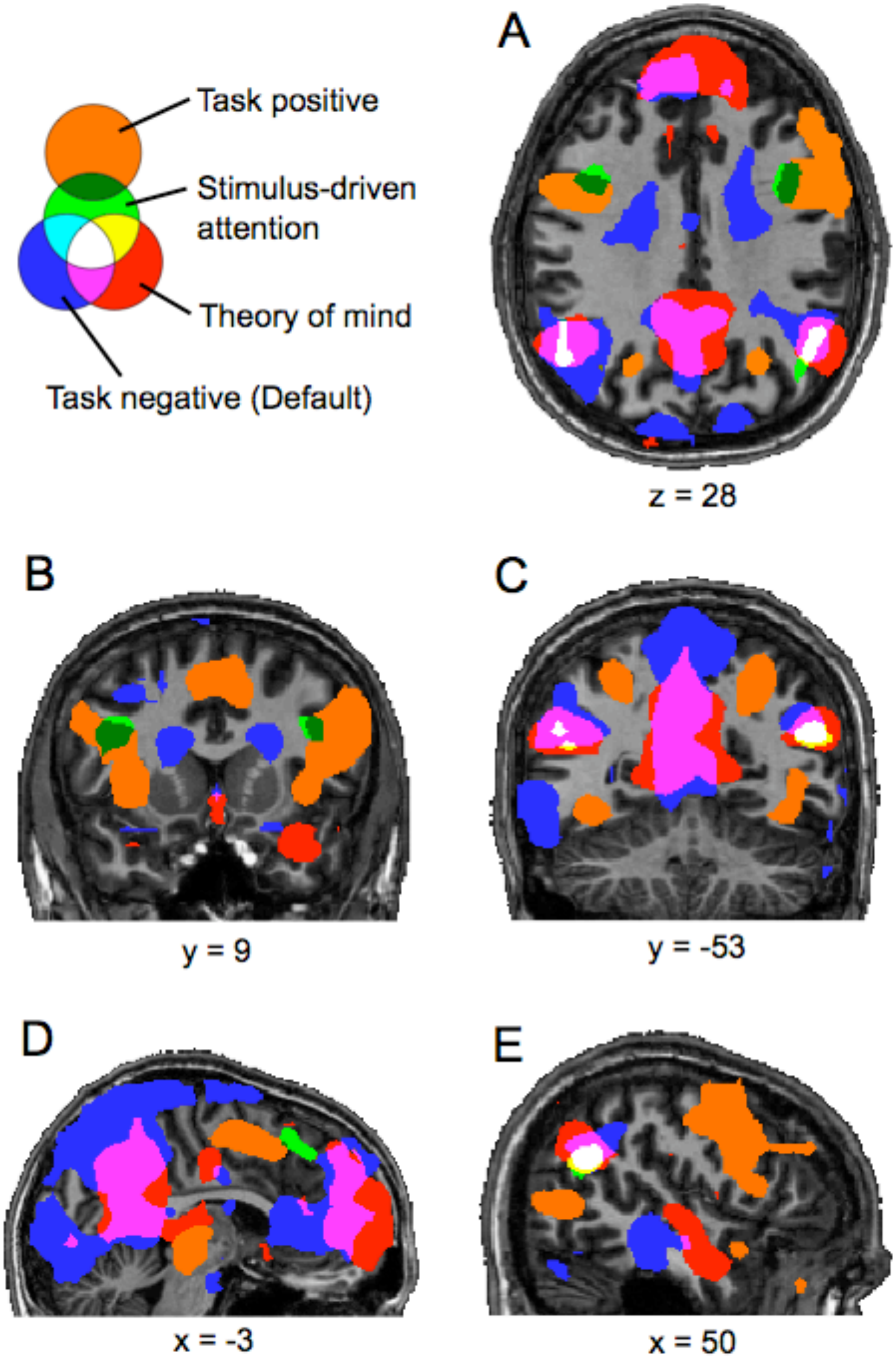

Figure 2. Overlap of network activations. Note especially the triple overlap at the TPJs (white; visible on A, C, and E), the network overlap of ToM and Default (magenta; A, C, D, and E), the overlap at the IFJs (dark green; A and B), and the dissociation in the MFC (D). All SPMs thresholded at q(FDR) < 0.05.

Table 1. Network overlaps.

Network	ROI size (mm^3)	% Overlap (small denominator)	% Overlap (large denominator)	% Overlap (middle denominator)	Average % Overlap
SDA	9,345				
TOM	134,773				
Default	222,733				
TP	126,669				
SDA ∩ TOM	2,008	21	1		11
SDA ∩ Default	1,393	15	1		8
TOM ∩ Default	51,960	39	23		31
SDA ∩ TOM ∩ Default	1,266	14	1	1	5
SDA ∩ TP	2,293	25	2		14

Volume of significantly activated voxels (q(FDR) < 0.05) for each network. A ∩ indicates the intersection between the networks in question. Small, large, and middle refer to the relative volumes of the networks being compared, with each in turn used as the denominator for the percent overlap calculation (see text). SDA = Stimulus-driven Attention, TOM = Theory of Mind, Default = Default Mode of Processing, TP = Task-Positive, ROI = Region of Interest.

Table 2. Overlap of networks at the Temporo-Parietal Junction (TPJ).

Network	Hemisphere	ROI size (mm^3)	% Overlap (small ROI denominator)	% Overlap (large ROI denominator)	% Overlap (middle ROI denominator)	Average % Overlap
SDA	Right	1,994				
TOM	Right	5,376				
Default	Right	6,390				
SDA ∩ TOM	Right	1,251	63	23		43
SDA ∩ Default	Right	836	42	13		28
TOM ∩ Default	Right	2,111	39	33		36
SDA ∩ TOM ∩ Default	Right	836	42	16	13	24
SDA	Left	612				
TOM	Left	9,641				
Default	Left	14,258				
SDA ∩ TOM	Left	540	88	6		47
SDA ∩ Default	Left	486	79	3		41
TOM ∩ Default	Left	5,700	59	40		50
SDA ∩ TOM ∩ Default	Left	430	70	4	3	26

Table 3. Overlap of networks in the Inferior Frontal Junction (IFJ)

Network	Hemisphere	ROI size (mm^3)	% Overlap (small ROI denominator)
SDA	Right	980	
SDA ∩ TP	Right	740	76
SDA	Left	3,895	
SDA ∩ TP	Left	1,307	34

Volume of significantly activated contiguous voxels in the IFJ (which ROI indicated by Hemisphere).

All overlap percentages for the o-ROI analyses were significantly less than 100% (Tables 2, 3), but this result could be caused by many factors other than real functional dissociations between adjoining or partially overlapping regions (see Methods). To estimate what degree of overlap (percentages) obtained in the TPJs could be explained by these other factors, we examined overlaps between different Default TPJ o-ROIs. Different o-ROIs for the Default network were obtained by splitting the data either across or within subjects before o-ROI definition; the different Default data sets are labeled as Default Within 1-2 and Default Between 1-2. For the data split within-subject (Default Within 1 and 2), the overlaps were greater than those obtained when comparing across networks (e.g. SDA versus ToM at the right TPJ), but still well under 100% (Tables 2, 4). This result implies that physiological or random noise cannot explain all of the imperfect overlap results, though it does not rule out a substantial contribution of some tasks simply activating more tissue than others (indeed, this appears to be the case, with SDA o-ROIs far smaller than those for ToM or Default). For the data split between-subject, the Default Between 1 overlaps with Default Between 2 were closer to the values obtained when comparing across networks, demonstrating that there is substantial variability in activated regions across subjects. This substantial variability is still not enough to remove overlaps entirely, at least in our data set (Table 4). More systematic study of what different overlap percentages imply for the degree of actual functional overlap is required.

Table 4. Overlap of different Default ROIs at the TPJ.

Network	Hemi-sphere	ROI size (mm^3)	% Overlap (small ROI denominator)	% Overlap (large ROI denominator)	Average % Overlap
Default Within 1 (N=30, first half of run)	Right	1,228			
Default Within 2 (N=30, second half of run)	Right	6,390			
Default Within 1 ∩ Default Within 2	Right	1,188	97	19	58
Default Between 1 (N=15, first half of subjects)	Right	126			
Default Between 2 (N=15, second half of subjects)	Right	672			
Default Between 1 ∩ Default Between 2	Right	2	2	0	1
Default Within 1 (N=30, first half of run)	Left	13,541			
Default Within 2 (N=30, second half of run)	Left	14,258			
Default Within 1 ∩ Default Within 2	Left	11,658	86	82	84
Default Between 1 (N=15, first half of subjects)	Left	86			
Default Between 2 (N=15, second half of subjects)	Left	4,756			
Default Between 1 ∩ Default Between 2	Left	86	100	2	51

Region-of-interest analyses

The region-of-interest analyses largely confirmed the SPM overlaps. For the group-defined ROIs (Table 5), significant activation was found in the TPJs for SDA, ToM, and Default regardless of the contrast from which they were defined. In contrast, the IFJs showed positive SDA activity but negative Default activity (consistent with the overlap with TP in the SPMs). The individual-defined ROIs for the TPJs and IFJs demonstrated this same pattern. These results confirm that the core members of the ventral attention network do not co-activate during the other examined tasks. In fact, their activity patterns went in opposite directions as measured by their activity during Default processing. Whereas the TPJ showed Default activation, the IFJ showed deactivation; this result indicates that the IFJ was active during the attention-demanding portion of the Surprise-induced Blindness task (searching for and responding to the target). Such activity is characteristic of the task-positive network, which also includes the dorsal attention network. Hence the ROI analysis confirms that the IFJ co-activates with the FEF and IPS.

SDA was dissociated from ToM and Default in the IFJ, and this dissociation held across most other regions as well. In the medial frontal regions, SDA-defined anterior rostral MFC showed activity for neither ToM nor Default, and Default-defined posterior rostral MFC demonstrating ToM but not SDA activity. Medial posterior structures (posterior cingulate and precuneus) also had no significant SDA activity. Conversely, ToM and Default generally showed activity in these regions regardless of the ROI definition, although there were notable exceptions in the cingulate and ToM-defined MFC. ToM and Default also showed a double dissociation in the middle temporal gyrus (MTG). Although the MTG activation overlapped on the SPMs (Figure 2E), the peak activation voxels were distinct. Finally, TP-defined ROIs typically did not show ToM or SDA activation (with the notable exception of IFJ for SDA). The same pattern of convergence and divergence was seen for the individual ROI analysis as well. Taken together, the ROI results support the SPM overlap results. ToM and Default involve most of the same regions, but these networks overlap with SDA only at the TPJ. TP also has only one prominent overlap point, which is at the IFJ.

Curiously, the results were often less clear in the individual-defined ROIs than in the corresponding group-defined ROIs, both in terms of consistency and t-values (though trends were the same). In the case of the ToM-defined ROIs, the reason is obvious: There were few subjects (6) for the comparisons. I return to the values for the Default-defined and TP-defined ROIs in the discussion below.

Table 5. Group-defined ROI analysis results.

Anatomical region of interest	Network from which ROI defined				Talairach coordinates (x, y, z)	T-values for activity in each task versus its baseline		
	SDA	TOM	Default	TP		SDA	TOM	Default
Right TPJ	X				48, -57, 22	4.37***	6.41***	3.22**
		X			51, -58, 27	4.08***	9.90***	4.43***
			X		47, -55, 28	3.78**	7.52***	5.02***
Left TPJ	X				-51, -53, 26	4.08***	7.04***	3.28**
		X			-56, -58, 24	2.53*	8.39***	2.47*
			X		-44, -65, 28	3.11**	4.22**	5.63***
Right IFJ	X				37, 7, 27	5.46***	-0.78	-3.14**
				X	48, 4, 27	2.39*	-0.73	-3.63**
Left IFJ	X				-40, 7, 25	7.52***	-2.07	-3.89**
				X	-49, 3, 27	3.82**	-1.56	-3.81**
Left IFG	X				-44, 19, 14	6.34***	-0.04	-0.83
mSPL			X		3, -58, 56	1.32	3.82**	4.63***
Precuneus		X			-2, -48, 28	1.61	13.5***	2.4*
			X		-2, -51, 35	1.62	8.48***	3.27**
Post Cing		X			-7, -53, 11	1.32	7.62***	4.56***
			X		-3, -50, 6	1.06	5.25***	4.89***
Cingulate		X			0, -19, 36	1.50	5.42***	0.94
mLG			X		2, -86, -2	-0.47	2.88*	7.00***
Right MTG		X			53, -13, -9	3.10**	7.70***	1.94
			X		58, -36, -9	1.10	-1.01	3.68**
Left MTG		X			-54, -13, -11	1.58	6.19***	1.87
			X		-58, -29, -5	3.05**	0.93	4.79***
arMFC		X			2, 60, 7	1.68	5.80***	-0.38
			X		-1, 32, 10	-2.13*	5.18***	4.16***
prMFC	X				-3, 28, 44	5.80***	-0.11	-0.16
cMFC				X	3, 7, 47	2.10*	2.41*	-7.03***
Right aSFS		X			15, 41, 42	2.19*	7.10***	-1.07
Left aSFS		X			-17, 41, 36	1.96	4.32**	0.80
			X		-18, 26, 40	1.90	4.79**	2.19*
Pulvinar	X				8, -31, -1	3.55**	3.59**	-0.90
				X	-2, -26, -6	0.80	4.70**	-5.32***
Right FG	X				33, -47, -11	2.88*	3.47*	-3.54**
				X	38, -49, -9	2.06*	2.44*	-3.76**
Left FG	X				-25, -38, -10	2.32*	2.80*	0.15
				X	-38, -49, -9	2.18*	0.86	-3.54**
Right hippo		X			24, -23, -7	1.00	5.58***	2.17*

Left hippo		X			-18, -25, -14	1.80	4.99***	1.18
Right caudate			X		21, 6, 23	-1.26	0.56	3.68**
Left caudate			X		-17, 5, 22	-0.49	0.58	4.47***
Right IPS				X	28, -54, 43	0.99	-2.04	-5.87***
Left IPS				X	-26, -58, 42	1.91	-3.31*	-4.46***
Right FEF				X	36, -9, 51	0.03	0.74	-4.65***
Left FEF				X	-33, -9, 49	1.17	1.84	-4.68***
Right insula				X	33, 19, 2	3.15	0.72	-6.15***
Left insula				X	-31, 18, 2	3.08	1.80	-7.80***
Right pMTG				X	42, -65, 2	-0.71	2.13	-4.76***
Left pMTG				X	-42, -71, 2	-0.59	2.97*	-5.33***
Left PCG				X	-37, -23, 47	-0.39	1.60	-5.91***

Talairach coordinates and t-test results for each probed region of interest (ROI). For each ROI, the network from which it was defined is indicated with an "X". TPJ = Temporo-parietal Junction, IFJ = Inferior Frontal Junction, IFG = Inferior Frontal Gyrus, mSPL = medial Superior Parietal Lobule, Post Cing = Posterior Cingulate, mLG = medial Lingual Gyrus, MTG = Middle Temporal Gyrus, arMFC = anterior rostral Medial Frontal Cortex (MFC divisions from Amodio & Frith, 2006), prMFC = posterior rostral MFC, cMFC = caudal MFC, aSFS = anterior Superior Frontal Sulcus, FG = Fusiform Gyrus, hippo = hippocampus, IPS = Inferior Parietal Sulcus, FEF = Frontal Eye Fields (junction of Superior Frontal Sulcus and Precentral Sulcus), pMTG = posterior Middle Temporal Gyrus, PCG = Postcentral Gyrus. Significance of comparisons given as *p<0.05, **p<0.005, and ***p<0.0005.

Table 6. Individual-defined ROI analysis results.

Anatomical region of interest	Network from which ROI defined			Talairach coordinates (x, y, z)	T-values for activity in each task versus its baseline		
	TOM	Default	TP		SDA	TOM	Default
Right TPJ	6			49 (5), -56 (8), 23 (8)	2.85*	5.80**	2.51
		5		48 (7), -58 (8), 27 (9)	1.24	3.08*	4.49*
		23		49 (7), -53 (7), 27 (5)	2.13*		9.61***
Left TPJ	6			-48 (6), -56 (4), 25 (4)	1.98	8.15***	0.25
		6		-49 (9), -58 (8), 25 (5)	1.90	6.47**	2.57
		25		-49 (7), -57 (7), 26 (4)	2.38*		7.49***
Right IFJ			5	47 (10), 3 (4), 26 (6)	0.62	-1.39	-5.48*
			23	47 (7), 4 (3), 26 (3)	1.92		-11.2***
Left IFJ			5	-43 (9), 4 (2), 27 (4)	0.74	-1.12	-8.04**
			26	-44 (6), 3 (3), 26 (3)	3.39**		-11.0***
PC	6			-2 (6), -51 (5), 32 (5)	2.18	11.1***	2.15
		5		-1 (4), -56 (4), 25 (13)	1.80	3.73*	3.48*
		25		0 (6), -54 (8), 23 (11)	1.07		7.96***
Right MTG	6			53 (3), -10 (6), -11 (5)	1.44	7.63**	-0.34
		4		54 (8), -23 (13), -3 (2)	1.17	1.44	4.99*
		21		53 (5), -21 (9), -7 (6)	2.17*		8.31***
Left MTG	6			-53 (5), -11 (7), -11 (8)	1.38	4.52*	0.38
		5		-54 (7), -33 (4), -3 (3)	0.33	-1.79	7.40**
		24		-52 (6), -25 (9), -7 (5)	-0.07		7.67***
arMFC	6			2 (4), 55 (5), 10 (9)	2.63*	9.08***	-0.24
		6		-1 (11), 49 (10), 8 (7)	0.64	3.39*	3.48*
		27		0 (7), 48 (7), 11 (9)	0.14		10.4***
cMFC			5	-2 (5), -1 (4), 48 (4)	0.32	1.66	-7.02**
			26	-1 (4), 1 (7), 49 (3)	1.52		-11.1***
Pulvinar			3	-1 (3), -28 (7), 1 (5)	0.79	2.42	-2.44
			20	-2 (6), -25 (4), 2 (4)	1.88		-9.71***
Right FG			5	34 (6), -50 (8), -6 (5)	-0.92	1.47	-4.26*
			21	36 (5), -52 (6), -9 (4)	0.85		-9.48***
Left FG			5	-30 (6), -52 (6), -6 (5)	-0.28	1.29	-1.86
			23	-35 (5), -52 (5), -8 (4)	2.51*		-7.47***
Right IPS			5	26 (3), -55 (6), 44 (8)	0.86	-1.13	-13.1***
			25	27 (4), -57 (7), 44 (6)	1.69		-8.03***
Left IPS			5	-27 (4), -58 (4), 46 (6)	0.15	-4.33*	-9.33**
			24	-26 (4), -59 (4), 45 (5)	1.72		-12.3***
Right FEF			5	30 (4), -9 (4), 48 (6)	-1.43	1.37	-8.59**
			25	33 (5), -8 (3), 49 (6)	0.29		-8.47***
Left FEF			6	-28 (10), -8 (4), 50 (6)	0.26	1.55	-14.5***
			25	-31 (7), -8 (4), 48 (6)	1.76		-9.14***
Right insula			6	31 (3), 18 (5), 4 (6)	-0.21	-0.81	-4.29*
			26	33 (5), 18 (5), 2 (4)	1.59		-10.9***

Left insula			6	-29 (3), 21 (4), 5 (6)	0.23	-1.32	-6.01**
			27	-32 (5), 19 (4), 2 (5)	2.58*		-10.8***
Right pMTG			6	38 (5), -70 (6), 2 (7)	0.15	2.50	-11.8***
			28	41 (6), -67 (6), 4 (6)	0.14		-5.88***
Left pMTG			6	-40 (5), -69 (7), 6 (4)	-0.51	0.67	-4.32*
			27	-41 (4), -68 (5), 3 (5)	0.22		-7.94***

Talairach coordinates (with standard deviations in parentheses) and t-test results for each area for which regions of interest (ROIs) in individuals were defined. For each area, the network from which the ROIs were defined is indicated by the number of these ROIs. For initialism key, see Table 5.

Discussion

The different patterns of network overlap aid us in determining the processing components of the eliciting tasks. Foremost, the ToM and Default networks show great overlap, both within specific regions (Table 2; Figure 2) and across the brain as a whole (Table 1). This result implies a high degree of similarity in the psychological processes associated with ToM and Default activity. It is possible that this Default-related activity may be associated with participants thinking of other people's mental states (ToM reasoning) during the fixation periods of the SiB task, though the brevity of the fixation periods (3.4 seconds each) would not be conducive to such processing. Instead, participants may have been engaging in a style of internal, self-directed processing (Raichle, 2006) similar to ToM, even if only briefly (Grecius & Menon, 2004). This processing includes self-projection operations such as recalling autobiographical memories, thinking of one’s future self (prospection), and imagining routes to be navigated (Buckner & Carroll, 2007). Each of these processes activates a network very similar to the Default and ToM networks observed in the present study (Spreng & Grady, 2009; Buckner & Carroll, 2007). Consequently, our results are consistent with the notion that ToM reasoning is akin to projecting oneself into another person's situation, simulating their physical and mental perspective. This idea is both conceptually sensible and neurally supported.

One piece of evidence in support of the idea that the Default network reflects a coherent psychological process is that it a coherent neural network, not the result of a vascular artifact. Diffusion-tensor imaging (DTI) in humans demonstrates strong connections between the medial components of the Default network (Catani & Thiebaut de Schotten, 2008) and lesser ones from the posterior cingulate and precuneus to the TPJs and middle temporal gyri (Teipel et al., 2010). Anatomical tracer studies in monkeys corroborate these connectivity results. The portion of macaque MFC thought to be homologous to the Default's MFC links to posterior cingulate, retrospenial cortex, and the hippocampus (Barbas et al., 1999; Price, 2007), while posterior cingulate connects with the hippocampus and area 7a (Kobayashi & Amaral, 2003, 2007), the area thought to be the homologue of human TPJ (Corbetta & Shulman, 2002; Buckner et al., 2008). This idea was given additional support by the discovery of a monkey default network using fMRI (Vincent et al., 2007). These anatomical findings are complemented by an [18F]fluorodeoxyglucose (FDG) PET study of the Default (Vogt et al., 2006), which demonstrated that resting state glucose metabolism (a measure independent of vascular coupling (Buckner et al., 2008)) was correlated between the structures of the Default network across participants. Consequently, the overlap we and others have observed between Default processing and ToM is not likely a vascular artifact, but a psychologically meaningful result.

Despite the extensive network-level overlap between Default processing and ToM, there were significant dissociations as well. Foremost, the contrasts from our tasks identified different regions of MTG for each network, with the Default MTG more anterior to the ToM activation in both hemispheres. Such a dissociation does not appear to be consistent across studies of the Default network (Spreng et al., 2009; Buckner & Carroll, 2007). It is therefore possible that the specific demands of our tasks (and their respective baseline conditions), not general differences between Default and ToM networks, led to the difference. The same is likely true for the apparent dissociations at the hippocampus and MFC. Neither the pulvinar nor FG are commonly included in the Default or ToM networks, so their differential activation in our tasks is also probably due to specific task demands.

TPJ overlap (SDA, ToM, Default)

In contrast to the widespread overlap between ToM and Default, the vast majority of the overlap between these networks and SDA is at the TPJ. This convergence has been found before for ToM and SDA (Scholz et al., 2009; Mitchell, 2008; Decety & Lamm, 2007) and suggested for Default and SDA (Shulman et al., 2007), although exclusively in the right hemisphere. Our results indicate that the overlap can be bilateral. This finding is unsurprising for Default, as this network is generally bilateral (Raichle et al., 2001; Buckner et al., 2008;

Spreng et al., 2009). Although SDA and ToM activations are often right-lateralized, there are copious examples of left TPJ participation in the former (Downar et al., 2000; Downar et al., 2002; Marois et al., 2000; Linden et al., 1999; Horovitz et al., 2002; Asplund et al., 2010) and the latter (Apperly et al., 2007; Samson et al., 2004; Spreng & Grady, 2009; Spreng et al., 2009; Young et al., 2010; Buckner & Carroll, 2007). Saxe & Kanwisher (2003), however, argue that only right TPJ is specific to reasoning about the beliefs of others, whereas left TPJ has a more general reasoning function. Nevertheless, left TPJ lesions induce ToM reasoning deficits, sometimes in the absence of concomitant deficits in executive function (Apperly et al., 2007; Samson et al., 2004).

Although our results indicate functional overlap at the TPJs, the degree of overlap remains an open question. Given our fairly large voxel size (4-7 x 3.75 x 3.75 mm^3), partial volume averaging could account for some of our overlap. In studies of ToM and SDA with higher spatial resolutions, functional overlap--from both SPM and ROI-based analyses--was still observed (Mitchell, 2008; Scholz et al., 2009). The overlap percentages were generally lower than those in the present study, which could reflect some degree of genuine neural separation or simply the results of underpowered SPMs (especially true for SDA). Nevertheless, such studies and meta-analyses of ToM and SDA activations do suggest a consistent pattern of peak separation: Peak SDA activations tend to fall approximately 7-10 mm superior to peak ToM activations (Scholz et al., 2009; Mitchell, 2008; Decety & Lamm, 2007). On the other hand, the center of mass of SDA and ToM activations differs by only 2 mm (Decety & Lamm, 2007). Our present results show no evidence of consistent ToM and SDA separation at either the group or individual level. Moreover, previous statistical claims of a separation are unconvincing (Scholz et al., 2009). In particular, the bootstrap analysis purporting to test whether ToM and SDA activation peaks were different was performed incorrectly. The bootstrap distribution was treated as the distribution of the random variable (the separation between ToM and SDA peaks in mm) instead of a sampling distribution of the mean; properly interpreted, their results actually show no significant difference between the peak locations (14 of 150 bootstrap samples against their hypothesis, two-tailed p = 0.19; see Figure 3 of Scholz et al., 2009). In sum, there appears to be some degree of functional overlap between SDA and ToM in the TPJs, but whether that overlap is complete or partial remains unclear.

Unlike with ToM and SDA, systematic comparisons of Default processing and SDA activations at the TPJ had yet to be made (Shulman et al., 2007). In our data, no consistent differences appeared between Default and SDA peaks in the TPJ, and ROI cross-probes were significant (Tables 5 and 6). While still statistically significant, the SDA activity in the individual-defined Default ROIs was statistically weaker (approximately 40%) than that reported in Asplund et al. (2010). This difference is likely due to signal attenuation across the run (Search1 > Search2, data not shown). Importantly, this attenuation does not affect the primary conclusions of Asplund et al. (2010). First, the main comparison used to identify regions responsive to the surprise stimulus was between all of the surprise trials and search trials (see Methods). These trials were distributed randomly throughout the run, so attenuation across the run would affect both trial types equally. Second, some of the regions identified with this contrast, including the orbitofrontal cortex (OFC) and fusiform gyrus (FG) showed responses to the face surprise stimuli that did not attenuate. The SDA activity in the individual-defined ROIs, however, was also less significant than the group-defined ROIs. One possibility is that the individual SPMs from which the ROIs were defined were not robust enough to ensure reliable Default activation. A second possibility is that Default and SDA TPJ regions only partially overlap, but without a consistent direction of separation (unlike what has been claimed for ToM and SDA). Group-defined Default ROIs may then better capture the most consistently activated SDA regions across subjects.

Although the degree of functional overlap within the TPJs is not yet clear, it is likely that neurons from the three networks (SDA, ToM, and Default) commingle there. The TPJs are also the only place where these three networks consistently converge. Such overlap implies that a common process, or a family of processes, is carried out in the region (Poldrack, 2006). If so, what type of processing can we assign to TPJ? We propose that the TPJ compares actual states of affairs with internal simulations or schema, reconciling conflicts or maintaining that segregation, as the tasks demand (for similar ideas, see Decety & Grezes, 2006; Decety & Sommerville, 2003; Buckner & Carroll, 2007; Donchin, 1981). In the case of stimulus-driven attention, one is presented with a mismatch between what is expected (the ongoing task) and what is presented (a surprising stimulus), requiring an update of one's internal model of the task. For theory of mind and self-projection (a Default function), one segregates what is actually known about the world from a simulated state of affairs; the brain creates a mismatch in order to reason about mental states of others or abstractions of one’s own mental states. Consequently, the TPJ often handles misinformation (Aichhorn et al., 2009; Mitchell, 2008), whether generated intentionally or when a prediction is discovered to be incorrect.

This proposed TPJ function is consistent with other known TPJ roles. For example, the TPJ is a primary generator of the P300 (Knight et al., 1989; Verleger et al., 1994; Horovitz et al., 2002; Bledowski et al., 2004), an evoked potential associated with the processing of rare and relevant items (Sutton et al., 1965). Donchin (1981) interpreted the P300 as marking a cognitive updating function. When something unexpected occurs, predictive schema are updated with new information about the probability characteristics of events in the world (see also Donchin & Coles, 1988). Integrating information and forming predictions about one's relationship to the environment appears to be a general function of the TPJ, likely why it has been associated with neglect (Driver & Vuilleumier, 2001; Driver & Mattingley, 1998), bodily position in space (Zacks et al., 2003), embodiment (Lenggenhager et al., 2006; Arzy et al, 2006), agency (Decety & Grezes, 2006; Decety & Sommerville, 2003), and integration of sensory information across multiple modalities (Downar et al., 2000; Macaluso et al., 2002). Although the TPJ has been associated with all of these functions, it is unlikely that the same subregions of it underlie all of these various functions. Indeed, there may be specialized pockets within the TPJ (Saxe & Kanwisher, 2003). Our contention is that such specialized subregions can be understood as performing a certain type of processing, possibly because they share a similar developmental and evolutionary history with the TPJ as a whole.

IFJ overlap (SDA, TP)

In contrast to the overlap between SDA, ToM, and Default at the TPJ, the IFJ demonstrated a functional overlap between SDA and TP. This result is consistent with resting state functional connectivity data showing that the IFJ (or nearby regions) is connected to both the task-positive (Fox et al., 2005; Fox et al., 2006) and ventral attention networks (Fox et al., 2006; Corbetta et al., 2008; He et al., 2007). The IFJ also often coactivates with the dorsal attention network (Toro et al., 2008), which is part of the TP network (Fox et al., 2005). Nevertheless, until recently it was unclear whether the IFJ was a site of neural convergence during a task that contained both stimulus-driven and goal-directed attentional elements (Asplund et al., 2010). In addition to coordinating these two forms of attention, the IFJ has been shown to coordinate internal goals with actions. This coordination includes cognitive control (Brass et al., 2005), response selection (Marois et al., 2006; Dux et al., 2006), and rule retrieval (Bunge, 2004).

The IFJ's involvement in such a diverse array of tasks does suggest a potential common role for it in stimulus-driven attention and task-positive activation (goal-directed attention). In Surprise-induced Blindness, an unexpected stimulus causes the disruption of ongoing goal-directed behavior.

This change to goal-directed behavior occurs in the absence of dorsal attention network activity; given the IFJ's task-positive activation and role in control in other tasks, it is plausible that the IFJ alters the ongoing task, modifying attentional weights with the appearance of the surprise stimulus. This attentional role may extend to goal-directed attention as well, with the IFJ interacting with and perhaps directing activity in the dorsal attention network with which it has been shown to co-activate.

Medial Frontal Cortex dissociations

In addition to the IFJ and TPJ dissociations, different regions of the MFC were found to belong to different networks. TP involved an MFC region posterior to the one activated by SDA; in turn, SDA recruited a more posterior portion of MFC than did ToM and Default. This segregation is largely consistent with the proposal of Amodio & Frith (2006), who divided MFC into three zones: orbital (oMFC), anterior rostral (arMFC), and posterior rostral (prMFC). Punishment and reward activates the first, emotional judgment and mentalizing (ToM) tasks the second, and action monitoring and error processing the third. In our tasks, ToM and Default activated arMFC and SDA recruited prMFC. A similar prMFC region has been associated with stimulus-driven attention in other contexts (Downar et al., 2000; Downar et al., 2002; Linden et al., 1999), suggesting that non-motoric errors are processed in prMFC. The TP MFC region lies caudal to prMFC and may correspond to the supplementary eye fields (SEF; Kastner et al., 1999).

Conclusion

We examined the functional overlaps of networks underlying four seemingly disparate task types: Stimulus-driven Attention (SDA), Theory of Mind (ToM), Default Mode of Processing (Default), and Task-positive (TP). ToM and Default overlapped well at both the network level and within most activated regions. Overlaps between SDA and other networks, by contrast, were limited to the TPJ and IFJ. These two regions were dissociated based on these overlaps, with the TPJ recruited by ToM and Default while the IFJ participated in TP. Whereas earlier studies of overlaps between SDA and these other networks had only examined the overlap at the right TPJ, our results demonstrate that the TPJs--both left and right--are the only site of overlap between these networks that extend through much of the brain. In addition, the results show that the TPJ overlaps between Default and SDA hold in individual subjects as well as at the group level.

The revealed pattern of associations and dissociations can shed light on the psychological processes performed in different brain regions (Poldrack, 2006; Henson, 2006). Specifically, ToM and Default likely involve common self-referential mental processes. The TPJ overlap suggests a common process among SDA, ToM, and Default. I hypothesize that the TPJ is involved in the segregation or reconciliation of the actual state of the world and a simulated alternative. Since the IFJ did not overlap with ToM and Default, its role in SDA is likely different. Instead, the TP and SDA overlap at the IFJ suggests that this region is involved in a goal-directed process, consistent with Asplund et al., 2010.

I hypothesize that this process is the modulation of attentional weights, setting priorities to assist in the proper mappings between stimuli and responses to them, whether they are overt (e.g. manual responses) or covert (e.g. a dispositional or task goal change). The IFJ and TPJ co-activate during stimulus-driven attention, and they probably interact. The nature of that interaction is unknown, but could include the IFJ adjusting representations of the actual state of the world in the TPJ, or the TPJ signaling the IFJ about a detected mismatch between expectations and events.

Although discovering for what purpose and how the IFJ and TPJ interact remains for future research, the functional overlap approach assisted in triangulating what the component processes in each region could be. It is important to note that few would have expected a common psychological process to underlie SDA, ToM, and Default. This common mental process was suggested by the imaging results. Consequently, this study and others like it demonstrate how neuroimaging results can inform psychological theories

References

Aichhorn, M., Perner, J., Weiss, B., Kronbichler, M., Staffer, W., & Ladurner, G. (2009). Temporo-parietal junction activity in Theory-of-Mind tasks: Falseness, beliefs, or attention. Journal of Cognitive Neuroscience, 21(6), 1179-1192.

Amodio, D. M. & Frith, C. D. (2006). Meeting of minds: the medial frontal cortex and social cognition. Nature Reviews Neuroscience, 7, 268-277.

Apperly, I. A., Samson, D., Chiavarino, C., Bickerton, W.-L., & Humphreys, G. W. (2007). Testing the domain-specificity of a theory of mind deficit in brain-injured patients: Evidence for consistent performance on non-verbal, “reality-unknown” false belief and false photograph tasks. Cognition, 103, 300-321.

Arzy, S., Seeck, M. Ortigue, S. Spinelli, L. & Blanke, O. (2006). Induction of an illusory shadow person. Nature, *443, 287*.

Asplund, C. L., Todd, J. J., Snyder, A. P., & Marois, R. (2010). A central role for the lateral prefrontal cortex in goal-directed and stimulus-driven attention. Nature Neuroscience, 13(4), 507-512.

Asplund, C. L., Todd, J. J., Snyder, A. P., Gilbert, C. M., & Marois, R. (in press). Surprise-induced Blindness: a stimulus-driven attentional limit to conscious perception. Journal of Experimental Psychology: Human Perception and Performance.

Barbas, H., Ghashghaei, H., Dombrowski, S. M., & Rempel-Clower, N. L. (1999). Medial prefrontal cortices are unified by common connections with superior temporal cortices and distinguished by input from memory-related areas in the rhesus monkey. Journal of Comparative Neurology, 410, 343-367.

Bledowski, C., Prvulovic, D., Hoechstetter, K., Scherg, M., Wibral, M., Goebel, R., and Linden, D. E. J. (2004). Localizing P300 generators in visual target and distractor processing: a combined event-related potential and functional magnetic resonance imaging study. The Journal of Neuroscience *24, 9353-9360*.

Brainard, D. H. (1997). The psychophysics toolbox. Spatial Vision, 10, 433-436.

Brass, M., Derrfuss, J., Forstmann, B., & von Cramon, D. Y. (2005). The role of the inferior frontal junction area in cognitive control. Trends in Cognitive Sciences, 9(7), 314-316.

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain’s default network: Anatomy, function, and relevance to disease. Annals of the New York Academy of Sciences, 1124, 1-38.

Buckner, R. L. & Carroll, D. C. (2007). Self-projection and the brain. Trends in Cognitive Sciences, 11(2), 49-57.

Bunge, S. A. (2004). How we use rules to select actions: A review of evidence from cognitive neuroscience. Cognitive, Affective, & Behavioral Neuroscience, 4(4), 564-579.

Catani, M. & Thiebaut de Schotten, M. (2008). A diffusion tensor imaging tractography atlas for virtual in vivo dissections. Cortex, 44, 1105-1132.

Cavanna, A. E. & Trimble, M. R. (2006). The precuneus: A review of its functional anatomy and behavioral correlates. Brain, 129(3), 564-583.

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: From environment to theory of mind. Neuron, 58, 306-324.

Corbetta, M. & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews Neuroscience, 3, 201-215.

Decety, J. & Grèzes, J. (2006). The power of simulation: Imagining one's own and other's behavior. Brain Research, 1079, 4-14.

Decety, J. & Lamm, C. (2007). The role of the right temporoparietal junction in social interaction: How low-level computational processes contribute to meta-cognition. The Neuroscientist, 13, 580-593.

Decety, J. & Sommerville, J. A. (2003). Shared representations between self and others: A social cognitive neuroscience view. Trends in Cognitive Sciences, 7, 527-533.

Donchin, E. (1981). Surprise!...Surprise? Psychophysiology, *18, 493-513*.

Donchin, E., and Coles, M. G. H. (1988). Is the P300 component a manifestation of context updating? The Behavioral and Brain Sciences, *11, 355-425*.

Downar, J., Crawley, A. P., Mikulis, D. J., & Davis, K. D. (2002). A cortical network sensitive to stimulus salience in a neutral behavioral context across multiple sensory modalities. Journal of Neurophysiology, 87, 615-620.

Downar, J., Crawley, A. P., Mikulis, D. J., & Davis, K. D. (2000). A multimodal cortical network for the detection of changes in the sensory environment. Nature Neuroscience, 3(3), 277-283.

Driver, J. & Mattingley, J. B. (1998). Parietal neglect and visual awareness. Nature Neuroscience, 1(1), 17-22.

Driver, J. & Vuilleumier, P. (2001). Perceptual awareness and its loss in unilateral neglect and extinction. Cognition, 79, 39-88.

Dux, P. E., Ivanoff, J., Asplund, C. L., & Marois, R. (2006). Isolation of a central bottleneck of information processing with time-resolved fMRI. Neuron, 52, 1109-1120.

Fletcher, P. C., Happé, F., Frith, U., Baker, S. C., Dolan, R. J., Frackowiak, R. S. J., & Frith, C. D. (1995). Other minds in the brain: A functional imaging study of "theory of mind" in story comprehension. Cognition, 57, 109-128.

Fox, M. D., Corbetta, M., Snyder, A. Z., Vincent, J. L., & Raichle, M. E. (2006). Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. Proceedings of the National Academy of Sciences, 103(26), 10046-10051.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. Proceedings of the National Academy of Sciences, 102(27), 9673-9678.

Greicius, M. D. & Menon, V. (2004). Default-mode activity during a passive sensory task: Uncoupled from deactivation but impacting activation. Journal of Cognitive Neuroscience, 16(9), 1484-1492.

He, B. J., Snyder, A. Z., Vincent, J. L., Epstein, A., Shulman, G. L., & Corbetta, M. (2007). Breakdown of functional connectivity in frontoparietal networks underlies behavioral deficits in spatial neglect. Neuron, 53, 905-918.

Henson, R. (2006). Forward inference using functional neuroimaging: Dissociations versus associations. Trends in Cognitive Sciences, 10(2), 64-69.

Horovitz, S. G., Skudlarski, P., and Gore, J. C. (2002). Correlations and dissociations between BOLD signal and P300 amplitude in an auditory oddball task: a parametric approach to combining fMRI and ERP. Magnetic Resonance Imaging, *20, 319-325*.

Kastner, S., Pinsk, M. A., De Weerd, P., Desimone, R., & Ungerleider, L. G. (1999). Increased activity in human visual cortex during directed attention in the absence of visual stimulation. Neuron, 22, 751-761.

Kobayashi, Y. & Amaral, D. G. (2003). Macaque monkey retrosplenial cortex: II. Cortical afferents. Journal of Comparative Neurology, 466, 48-79.

Kobayashi, Y. & Amaral, D. G. (2007). Macaque monkey retrospenial cortex: III. Cortical efferents. Journal of Comparative Neurology, 502, 810-833.

Knight, R. T., Scabini, D., Woods, D. L., and Clayworth, C. C. (1989). Contributions of temporal-parietal junction to the human auditory P3. Brain Research *502, 109-116*.

Kung, C.-C., Peissig, J. J., & Tarr, M. J. (2007). Is region-of-interest overlap comparison a reliable measure of category specificity? Journal of Cognitive Neuroscience, 19(12), 2019-2034.

Laufs, H., Krakow, K., Sterzer, P., Eger, E., Beyerle, A., Salek-Haddadi, A., & Kleinschmidt, A. (2003). Electroencephalographic signatures of attentional and cognitive default modes in spontaneous brain activity fluctuations at rest. Proceedings of the National Academy of Sciences, 100(19), 11053-11058.

Lenggenhager, B., Smith, S. T., & Blanke, O. (2006). Functional and neural mechanisms of embodiment: Importance of the vestibular system and the temporal parietal junction. Reviews in the Neurosciences, *17(6), 643-657*.

Linden, D. E. J., Prvulovic, D., Formisano, E., Völlinger, M., Zanella, F. E., Goebel, R., & Dierks, T. (1999). The functional neuroanatomy of target detection: An fMRI study of visual and auditory oddball tasks. Cerebral Cortex, 9, 815-823.

Macaluso, E., Frith, C. D., & Driver, J. (2002). Supramodal effects of covert spatial orienting triggered by visual or tactile events. Journal of Cognitive Neuroscience, 14(3), 389-401.

Marois, R., Leung, H. C., & Gore, J. C. (2000). A stimulus-driven approach to object identity and location processing in the human brain. Neuron, 25, 717-728.

Marois, R., Larson, J. M., Chun, M. M. & Shima, D. (2006). Response-specific sources of dual-task interference in human pre-motor cortex. Psychological Research, 70(6), 436-447.

Pelli, D. G. (1997). The VideoToolbox software for visual psychophysics: transforming numbers into movies. Spatial Vision, 10, 437-442.

Poldrack, R. A. (2006). Can cognitive processes be inferred from neuroimaging data? Trends in Cognitive Sciences, 10(2), 59-63.

Price, J. L. (2007). Definition of the orbital cortex in relation to specific connections with limbic and visceral structures, and other cortical regions. Annals of the New York Academy of Sciences, 1121, 54-71.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. Proceedings of the National Academy of Sciences, 98(2), 676-682.

Raichle, M. E. (2006). The brain's dark energy. Science, 314(5803), 1249-1250.

Samson, D., Apperly, I. A., Chiavarino, C., & Humphreys, G. W. (2004). Left temporoparietal junction is necessary for representing someone else's belief. Nature Neuroscience, 7(5), 499-500.

Saxe, R. & Kanwisher, N. (2003). People thinking about thinking people: The role of the temporo-parietal junction in "theory of mind". Neuroimage, 19, 1835-1842.

Saxe, R., Moran, J. M., Scholz, J., & Gabrieli, J. (2006). Overlapping and non-overlapping brain regions for theory of mind and self reflection in individual subjects. Social, Cognitive, and Affective Neuroscience, 1, 229-234.

Scholz, J., Triantafyllou, C., Whitfield-Gabrieli, S., Brown, E. N., & Saxe, R. (2009). Distinct regions of right temporo-parietal junction are selective for theory of mind and exogenous attention. PLoS ONE 4(3): e4869. doi:10.1371/journal.pone.0004869

Serences, J. T., Shomstein, S., Leber, A. B., Golay, X., Egeth, H. E., & Yantis, S. (2005). Coordination of voluntary and stimulus-driven attentional control in human cortex. Psychological Science, 16(2), 114-122.

Shulman, G. L., Astafiev, S. V., McAvoy, M. P., d'Avossa, G., & Corbetta, M. (2007). Right TPJ deactivation during visual search: Functional significance and support for a filter hypothesis. Cerebral Cortex, 17, 2625-2633.

Shulman, G. L., Astafiev, S. V., Franke, D., Pope, D. L. W., Snyder, A. Z., McAvoy, M. P., & Corbetta, M. (2009). Interaction of stimulus-driven reorienting and expectation in ventral and dorsal frontoparietal and basal ganglia-cortical networks. Journal of Neuroscience, 29(14), 4392-4407.

Spreng, R. N. & Grady, C. L. (2009). Patterns of brain activity supporting autobiographical memory, prospection, and Theory of Mind, and their relationship to the default mode network. Journal of Cognitive Neuroscience, 22(6), 1112-1123.

Spreng, R. N., Mar, R. A., & Kim, A. S. N. (2009). The common neural basis of autobiographical memory, prospection, navigation, Theory of Mind, and the default mode: A quantitative meta-analysis. Journal of Cognitive Neuroscience, 21(3), 489-510.

Sutton, S., Braren, M., Zubin, J., and John, E. R. (1965). Evoked-potential correlates of stimulus uncertainty. Science, *150, 1187-1188*.

Talairach, J. & Tournoux, P. Co-planar steotaxic atlas of the human brain (Thieme Medical Publishers, New York, 1988).

Teipel, S. J., Bokde, A. L. W., Meindl, T., Edson, A., Soldner, J., Reiser, M. F., Herpertz, S. C., Möller, H.-J., & Hampel, H. (2010). White matter microstructure underlying default mode network connectivity in the human brain. Neuroimage, 49, 2021-2032.

Todd, J. J., Fougnie, D., & Marois, R. (2005). Visual short-term memory load suppresses temporo-pareital junction activity and induces inattentional blindness. Psychological Science, 16, 965-972.

Toro, R., Fox, P. T., & Paus, T. (2008). Functional coactivation map of the human brain. Cerebral Cortex, 18, 2553-2559.

Verleger, R., Heide, W., Butt, C., and Kompf, D. (1994). Reduction of P3b in patients with temporo-parietal lesions. Brain Research Cognitive Brain Research 2*, 103-116*.

Vincent, J. L., Patel, G. H., Fox, M. D., Snyder, A. Z., Baker, J. T., Van Essen, D. C., Zempel, J. M., Snyder, L. H., Corbetta, M., & Raichle, M. E. (2007). Intrinsic functional architecture in the anaesthetized monkey brain. Nature, 447, 83-86.

Vogeley, K., Bussfeld, P., Newen, A., Herrmann, S., Happé, F., Falkai, P., Maier, W., Shah, N. J., Fink, G. R., & Zilles, K. (2001). Mind reading: Neural mechanisms of theory of mind and self-perspective. Neuroimage, 14, 170-181.

Vogt, B. A., Vogt, L., & Laureys, S. (2006). Cytology and functionally correlated circuits of human posterior cingulate areas. Neuroimage, 29, 452-466.

Young, L., Dodell-Feder, D., & Saxe, R. (2010). What gets the attention of the temporo-parietal junction? An fMRI investigation of attention and theory of mind. Neuropsychologia, in press. doi:10.1016/j.neuropsychologia.2010.05.012

Zacks, J., Vettel, J. M., & Michelon, P. (2003). Imagined viewer and object rotations dissociated with event-related fMRI. Journal of Cognitive Neuroscience, *15(7), 1002-1018*.

CHAPTER IV

THE FUNCTIONAL SEGREGATION OF THE INFERIOR FRONTAL JUNCTION FROM THE DORSAL ATTENTION NETWORK

In Chapter II, I demonstrated that the IFJ participates with the dorsal attention network (specifically the FEF and IPS) in goal-directed attention, specifically during the cue interpretation and attentional shift portion of an endogenous Posner cueing task (Posner et al., 1980). Like many tasks in the laboratory and real-world behaviors, the Posner cueing task involves several component processes. These include perception of the cue, interpretation of the cue (what action does it suggest), shifting attention to a new spatial location, maintaining attention at that location, detecting the target, and responding to the target. Although the IFJ and the dorsal attention network are involved in some of these processes, they may not be involved in all of them. So how can each region's contribution to a multi-part task be determined?

In a typical fMRI experiment, the component processes (or stages) of most tasks appear sufficiently close in time to be largely inseparable. Several approaches have been employed to explore their processing components, ranging from selectively manipulating a given stage of processing (Dux et al., 2006; Sigman & Dehaene, 2008) to removing a stage altogether (Corbetta et al., 2000). Another strategy is to separate different stages of a given task by several seconds, thereby allowing the hemodynamic response to return to baseline between each stage (Courtney et al., 1998; Todd & Marois, 2004). In this chapter, I use this latter strategy to ascertain the involvement of the IFJ and the dorsal attention network (FEF and IPS) in the component processes of two simple tasks, a Posner cueing task and a response selection task. By dissecting the role of these regions in different goal-directed processes, I aim to characterize better their roles in attention, especially the differences between the regions supporting goal-directed attention.

The Posner cueing task from Chapter II separated cue interpretation and attention shifts from target detection and manual responses to confirm that the IFJ has a role in goal-directed attention. Although the IFJ and the dorsal attention regions were all activated during the first part of each trial, close examination of the hemodynamic response profiles showed that the FEF and IPS activation was relatively prolonged (Chapter II, Figure 8). This result could indicate that the FEF and IPS are active during the delay period between cue and response. Indeed, both regions have been implicated in holding attention or anticipating an event (Curtis & Connolly, 2008; Kastner et al., 1999; Yantis et al., 2002) in addition to shifting attention between spatial locations (Ozaki & Ogawa, 2009; Yantis et al., 2002; Corbetta & Shulman, 2002). The IFJ, in contrast, has not been implicated in holding attention, and it may have a more transient role in attentional control. A transient role, such as interpreting the cue and then passing that information to other brain regions, would be consistent with the IFJ's known role in cognitive control (Brass et al., 2005; Derrfuss et al., 2005) and its hypothesized position in the prefrontal cortex control hierarchy (Koechlin et al., 2003; Koechlin &

Summerfield, 2007; Badre, 2008; Badre et al., 2009; Badre & D'Esposito, 2009). The results of Chapter II demonstrating that the IFJ was the site of convergence for stimulus-driven and goal-directed attention are also consistent with the idea that its attentional role may be one of coordination between these networks rather than the maintenance of attentional settings within each network (Asplund et al., 2010).

Cue interpretation itself involves multiple processes. Each cue must be perceptually selected, after which a response can be selected. Both types of selection recruit the IFJ (Attention: Marois et al., 2000; Marois et al., 2004; Response selection: Dux et al., 2006; Dux et al., 2009; Marois et al., 2006), though these same studies suggest that the right IFJ may be more involved in perceptual selection and the left in response selection. This laterality effect may not be specific to the IFJ, as many regions of the left hemisphere have been shown to be preferentially involved in response selection and the learning of response mappings (Rushworth et al., 1998), while the right hemisphere houses more visuospatial attention functions (Corbetta & Shulman, 2002; Corbetta et al., 2008). Therefore, I conclude this chapter with an experiment that compares the roles of the IFJ and dorsal attention network regions in perceptual selection, response selection, and response execution. Taken in conjunction with the Posner cueing task experiment, the experiments in this chapter delineate the roles of the IFJ, FEF, and IPS, demonstrating that the IFJ has a unique instructional role that puts it above the FEF and IPS in an attentional control hierarchy.

Experiment 1: Endogenous Posner Cueing Task

In this first experiment, we use a Posner cueing task with a long delay between cues and targets to examine the brain regions that support holding spatial attention at a given location away from fixation. Ten right-handed individuals (3 females) participated in the experiment. Participants in this experiment and all others in this chapter had normal or corrected-to-normal vision and received monetary compensation. In addition, the Vanderbilt University Institutional Review Board approved the experimental protocol and written informed consent was obtained from each participant.

Methods

The task consisted of a slow event-related variant of the endogenous Posner cuing task (Asplund et al., 2010). Each trial began with a central dot (0.25° in diameter) changing from black to white for 1000 ms, a warning which ensured that participants were attending to the fixation point after the inter-trial interval (ITI). Next, the fixation dot changed from white to one of four colors (red, green, blue, or yellow) for 500 ms (Figure 1). This cue indicated the location in which a target was likely to appear (80% validity) after a delay; participants were instructed to shift their attention (but not their eyes, which were monitored with an ASL long-range eye-tracker) to the indicated box. To increase response selection load (known to increase activation in IFJ and possibly FEF and IPS as well; see Dux et al., 2006; Marois et al., 2006), there were four boxes, with each 5.2° from fixation and 1.0° across. Participants were told of the cue's color-location mapping just prior to the scan, and they were reminded of the mapping before each fMRI run. The target, a light gray square that appeared inside one of the boxes for 100 ms, was presented after a variable delay (see below). Regardless of whether the target was validly cued, participants responded to the target with a speeded button press during a 1900 ms window. For some trials at the longest cue-target delay, no target was presented (see below). At the conclusion of the response window, the fixation dot turned black to indicate that the trial had ended. The next trial commenced after an ITI of 11.5-12.5 s.

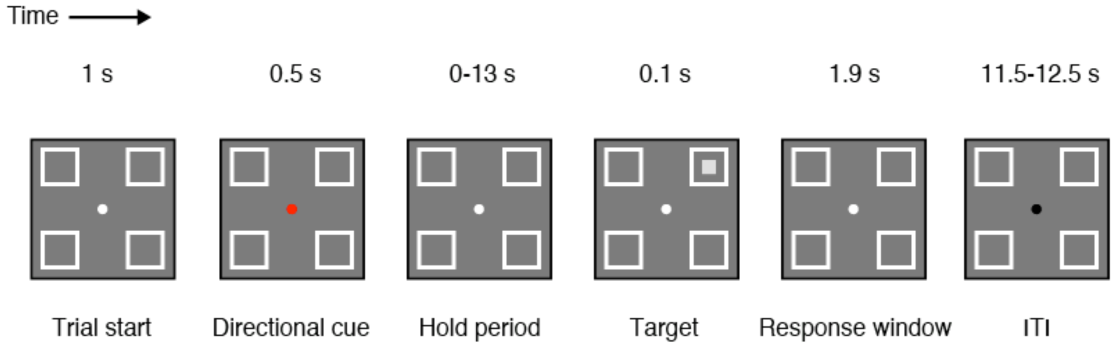

Figure 1. Design for the slow-event Posner cueing task experiment. Each directional color cue indicated that attention should be shifted to one of the four boxes. A target did not appear for some trials with the longest (12-13 s) hold period interval. ITI = Inter-trial interval.

The variable delay between cue and target presentations was the key manipulation of the experiment. In addition to obtaining long cue-target delays that allow us to distinguish between transient and sustained responses during the deployment of attention, we attempted to keep anticipatory neural activity to a minimum. Owing to the Hazard rate function (Trillenberg et al., 2000; Los &

Agter, 2005; Nobre et al., 2007), a target that is bound to appear once at some random point in a given time interval becomes more likely to occur as more of the time interval has already passed. People are sensitive to this relationship, and consequently show behavioral effects in the form of faster RTs (Trillenberg et al., 2000; Los & Agter, 2005) and neurobiological effects such as anticipatory activity (Ivanoff et al., 2008; Nobre et al., 2007). To counteract these effects in the present experiment, we employed an exponential distribution of cue-target delay frequency so that at each time point in the trial, the target was equally likely to occur during the next 4-second time window as it had been in the previous one, given that it had not yet appeared (33% probability of target appearance per time window). Such a manipulation removes anticipatory effects behaviorally (Trillenberg et al., 2000), but to the best of our knowledge, no one has examined its neural consequences. We used five different cue-target delays, with 500 ms of temporal jitter to ensure that participants could not time their responses with the scanner noises. Given our exponential distribution of these delays, we had 32 trials with 0.5-1.5 s SOA (stimulus onset asynchrony), 21 with 4.5-5.5, 14 with 8.5-9.5, 10 with 12.5-13.5, and 19 with no target (14.5-15.5 seconds from colored directional cue to ITI; see Figure 1). Target location was assigned randomly to each of these 96 trials, but validity was assigned so that each delay condition had approximately 80% valid cues. Delays were randomized across the 8 runs, which had 12 trials each.

To localize our regions of interest (ROIs) for subsequent analysis, we employed two different functional localizers. For the first, subjects were presented with a single fMRI run of 8 fixation blocks and 7 saccade task blocks, each lasting 20 s and presented in an alternate order. For the saccade task, a small dot (0.25°) jumped from one random location on the screen to another every 500 ms. Participants were required to track this dot with their eyes, which were monitored using an ASL long-range eye-tracker. Kastner and colleagues (Kastner et al., 2007) employed a similar task to identify FEF and IFJ, and we expected IPS activation as well given that region's role in saccades (Curtis & Connolly, 2008; Connelly et al., 2000). A response selection localizer modeled after those of Dux and colleagues (Dux et al., 2006; Dux et al., 2009) was also used. The block timing was identical to the saccade localizer, but the task was a sensory-motor mapping task, with each of four shapes (two different ovals and two different rectangles) mapped to one of four fingers (index and middle of each hand). Participants were presented with one shape for 100 ms every two seconds (2000 ms stimulus onset asynchrony), to which they had to respond before the next shape was presented. Participants learned the shape mapping by being instructed via intercom just before the localizer run. The saccade localizer gave more specific and consistent activation than the response selection localizer, so it was used to identify the ROIs for IFJ, FEF, and IPS, though the ROIs defined with the response selection localizer showed the same pattern of results (data not shown).

fMRI procedure

Anatomical 3D high-resolution images were acquired using conventional parameters on a 3T Philips Intera Achieva scanner at the Vanderbilt University Institute of Imaging Science. Thirty-three 3.0 mm thick axial slices (0.5 mm skip; 1.875 x 1.875 mm in-plane) were acquired parallel to the AC-PC line. T2*-weighted image parameters were as follows: 35 ms echo time, 79° flip angle, 240 mm FOV, 128 x 128 matrix, 2000 ms repetition time. The functional scan included between 125 and 161 brain volumes, depending on the distribution of delays in each run. The experiment was presented using Psychophysics ToolBox (Brainard, 1997; Pelli, 1997) for Matlab on an Apple MacBook Pro. Stimuli were back-projected from an LCD projector onto a screen viewed through a prism mirror by the supine participant. Manual responses were collected using MR-compatible hand pucks.

Data analysis

Data analysis was performed using BrainVoyager QX 1.10.2 (Brain Innovation, Maastricht, The Netherlands), and custom Matlab software. Data preprocessing for the functional images included image realignment, 3D motion correction, linear trend removal, correction for slice acquisition timing, spatial smoothing with a 6-mm Gaussian kernel (full width at half maximum), and high pass filtering (3 cycles per run cutoff). The data were then transformed to Talairach space (Talairach & Tournoux, 1988) for comparison across participants.

Statistical parametric maps (SPMs) of BOLD activation were created using general linear models (GLMs) with multiple regression. Regressors were created for the localizer runs by convolving a boxcar representing each block type with a canonical double gamma hemodynamic response function (HRF; SPM2, http://www.fil.ion.ucl.ac.uk/spm). To check whether the localizers were identifying regions whose activity was elevated during the delay period, I created regressors for the cue period, target period, and delay period. Cue and target period regressors were single TR boxcars convolved with the HRF; delay period regressors were the result of convoluting boxcars that included all TRs between the cue and the target inclusive with the HRF. After the GLM had been calculated, the open contrast of [+Delay] showed regions with significant activity during the delay (Figure 2, upper right), as this regressor accounted for activity during the trial other than cue- or response-related activity. We created both individual and group GLMs (random effects for the latter) for the localizers and the main task.

Regions of Interest (ROIs) were defined for individual subjects using the saccade localizer [+Saccade -Fixation]. These ROIs were defined for IFJ, TPJ, and FEF in each hemisphere. Each ROI was identified as the peak voxel and significantly surrounding area up to 1 cm^3 (threshold for significance set at $q(FDR) < 0.05$; in the rare cases in which no activity could be found at this level, $p < 0.001$, uncorrected was used; see Dux et al., 2006). Anatomical landmarks (FEF at the junction of the superior frontal sulcus and precentral sulcus; IPS in the intraparietal sulcus; IFJ at the junction of the inferior frontal sulcus and precentral sulcus) were used to identify each region, consistent with earlier work (Kastner et al., 2007; Derrfuss et al., 2009; Corbetta et al., 2000; Serences et al., 2005; Corbetta et al., 2008; Marois & Ivanoff, 2005). We then used these ROIs to probe the activity in each region during the main task. The timecourse for each validly-cued trial for which a response was recorded was extracted from each ROI for each participant. The timecourse was then converted to percent signal change (baseline from the time point of the directional cue onset and the preceding point, averaged across all conditions and trials). The average time courses for each delay length were next computed for each participant. Averages across participants were computed for display purposes (Figure 2).

For statistical tests of the cue period and response period, I calculated the value of each subject's timecourse for each condition at the group-average peak for that condition and region (e.g. the peak is at 8 s for the cue period in the 1 s SOA condition in Left IPS). A one-sample t-test was then used to test whether this list of values from each subject (by ROI and condition) was different than zero (baseline). For tests of delay period activity, the minimum point of the group average across subjects and the 9 s, 13 s, and 15 s delay period conditions was first identified. The minimum point was used because all conditions showed gradual ramping of activity toward the response; similar results were obtained using 10 s and 12 s from cue onset as the selected volumes. The timecourse values were then extracted for each subject at the identified timepoint. These values were then compared to baseline (0) with a one-sample t-test. Because there were no interhemispheric differences across matched ROIs (all $|t(9)|$'s <

2.20, p 's > 0.055) and to increase power for subsequent comparisons, the timecourses were averaged across the hemispheres. Results were qualitatively the same when the data were split by hemisphere (Results not shown).

The data collapsed across hemispheres were used for three additional comparisons. First, the 1 s SOA condition was expected to have greater early activity than other conditions because the neural response to the cue and target would sum over time. To test whether this effect did occur, I first created a timecourse that was a weighted average of the conditions except 1 s SOA (weighted because there was an unequal number of trials in each condition). Using this timecourse and the 1 s SOA condition timecourse, I identified the peak for each in each subject, and compared these peaks using paired t-tests. I then used paired t-tests on the peak differences between conditions to determine whether the IFJ difference between these timecourses was greater than the FEF or IPS difference, Second, the peak time in Experiment 4 of Chapter II appeared to be delayed (Figure 8), so I tested for the same effect in the present experiment. To compare the peak timing of the cue period in IFJ versus FEF and IPS, I created a weighted average of the three delay periods whose cue and response peaks were clearly separated: 9, 13, and 15 s. I next found the peak volume between 2 and 10 seconds after cue onset for each ROI for each subject. These peak volume times were then compared by paired t-test. Finally, to ensure that any effects from comparing the 1 s SOA to the other conditions were not driven by overall response amplitude differences across regions, I compared the response peaks across regions. To do so, I determined the peak values for the same three conditions (9, 13, 15 s) in each ROI in each subject. After weighted averages of these peak values were created by subject, paired t-tests were used to compare these values across ROIs.

Results and Discussion

The behavioral results revealed a classic validity effect in reaction times (RTs) with good overall accuracy. Specifically, there was a main effect of validity on RTs (F(1,9) = 44.62, $p < 0.0001$), with neither a main effect of delay length nor an interaction present (Duration: F(3, 27) = 0.78, p = 0.52; Validity x Duration: F(3, 27) = 0.75, p = 0.53). The size of this validity effect was large (Validity effect: 127 ms, SD = 55 ms; Valid: 436 ms, SD = 50; Invalid: 562 ms, SD = 81), approximately two to three times that reported elsewhere (Corbetta et al., 2000; Asplund et al., 2010; Posner et al., 1980). This large validity effect may be due to our using four locations instead of the common two. Overall accuracy was very high, at 98.7% (SD = 2.0%). With such high accuracy, there were no effects of validity or duration on accuracy (Validity: F(1, 9) = 1.83, p = 0.21; Duration: F(3, 27) = 0.41, p = 0.75; Validy x Duration: F(3, 27) = 0.95, p = 0.43). In sum, the behavioral effects demonstrate that subjects remained vigilant throughout the session, shifting their attention and maintaining it on the cued location.

The saccade localizer was used to identify six regions in each subject (Table 1). The activation from the saccade localizer (group-level) and the delay period from the main experiment (see methods) overlapped well (Figure 2, upper right).

Table 1. Anatomical regions defined from the saccade localizer. Standard deviations of Talairach coordinates across subjects are in parentheses.

Region of Interest	Talairach coordinates (x, y, z)
Right IFJ	45 (5), 5 (4), 27 (4)
Left IFJ	-45 (8), 3 (3), 27 (4)
Right FEF	25 (4), -7 (4), 46 (2)
Left FEF	-25 (3), -7 (3), 47 (3)
Right IPS	21 (2), -54 (4), 45 (3)
Left IPS	-23 (3), -55 (4), 47 (3)

All regions identified (IPS, FEF, IFJ) with the saccade localizer showed significant activation during the cue period and the response period (all $t(9)$'s > 2.37, p's < 0.042). But only the IPS and FEF demonstrated consistently elevated activity during the delay period (IPS: $t(9) = 5.26$, $p < 0.001$; FEF: $t(9) = 5.26$, $p < 0.001$; IFJ: $t(9) = 1.25$, $p = 0.24$). This crucial difference between the IFJ and the dorsal brain regions was corroborated with examination of the delay task SPM, as no delay period activity was observed in the IFJ, even at a very lenient threshold of $p < 0.01$ (uncorrected). These results suggest that the IFJ has a goal-directed attentional role that is distinct from the FEF and IPS. Whereas the latter regions maintain attention on the cued location during the delay, the IFJ's activation is transient.

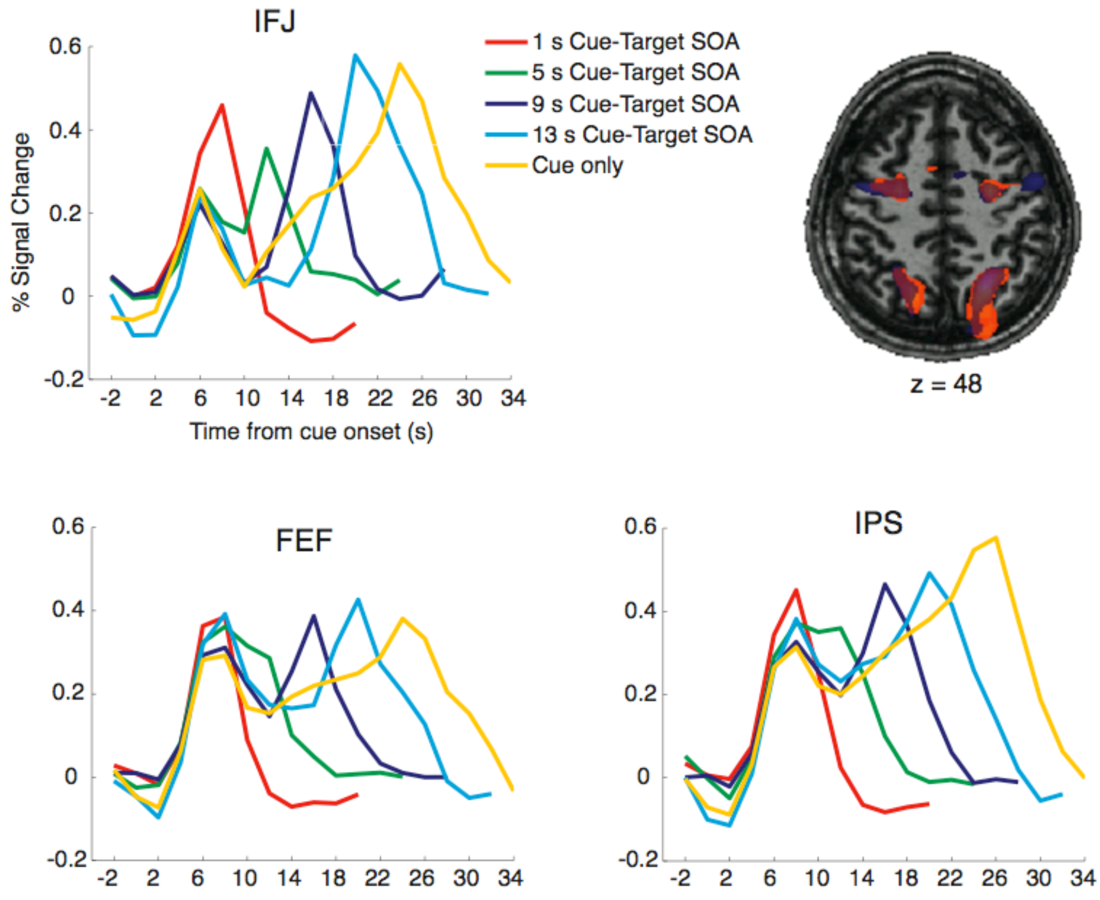

Figure 2. Event-related averages for IFJ, FEF, and IPS in the slow-event Posner cueing task experiment and SPMs of saccade and delay activity. For the timecourses, cue onset occurs at time 0. Note that the FEF and IPS show more sustained activity between the cue and the end of the trial. For the SPMs, saccade task activity is shown in blue and activity during the delay in the main experiment in orange. Both SPMs thresholded at $p < 0.001$ (uncorrected) for visualization purposes. SOA = Stimulus onset asynchrony.

Detailed examination of the activation timecourses further distinguishes the IFJ from the dorsal attention network regions. Foremost, although all three regions show greater activity during the cue period (the first peak in each timecourse) of the 1 s SOA condition compared to the average of the other delay conditions (IPS, $t(9) = 3.10$, $p = 0.013$; FEF, $t(9) = 3.47$, $p = 0.0071$; IFJ, $t(9) =$

3.64, p = 0.0054), that difference is larger in the IFJ than in the FEF or IPS (IFJ vs. IPS: t(9) = 2.42, p = 0.038; IFJ vs. FEF: t(9) = 3.19, p = 0.011). This larger peak is likely caused by the conflation of cue and response period during the 1 s SOA condition. One possible explanation for the greater difference in IFJ activation is that it simply responds more during the response period than do the IPS and FEF. A comparison of the average of the last three response peaks (9, 13, 15 s delay) across regions, however, does not support this hypothesis (IFJ vs. IPS: t(9) = 0.91, p = 0.38; IFJ vs. FEF: t(9) = 1.51, p = 0.17).

Another difference between IFJ and dorsal activity is found in the timing of cue-related activity. The IPS and FEF cue-related peak activity is prolonged relative to the IFJ (IPS vs. IFJ: (t(9) = 4.58, p = 0.0013; FEF vs. IFJ: t(9) = 2.45, p = 0.037), but this is not true for the response peak. The prolonged hemodynamic response in the dorsal regions suggests that an additional neural process is occurring in those regions. This additional process may even continue throughout the delay period. To explore what timecourse would be expected if neural activity was sustained through the delay, I created a simple hemodynamic model (Figure 3). In this model, the initial neural activity related to cue presentation is assumed to be identical in two hypothetical regions, but one region (black curve) then sustains its activity--albeit at a low level--through the delay period while the other does not (gray curve). This simple model captures a number of features observed in the experimental results. First, the delay activity boosts the amplitude of the initial peak despite identical cue-related activity. Second, the delay activity prolongs the initial peak. Third, although delay activity is present, the response falls during the delay period. This lower level of neural activity is consistent with fMRI studies that use delay periods during which an item must be maintained in memory (Todd & Marois, 2005; Courtney et al., 1998).

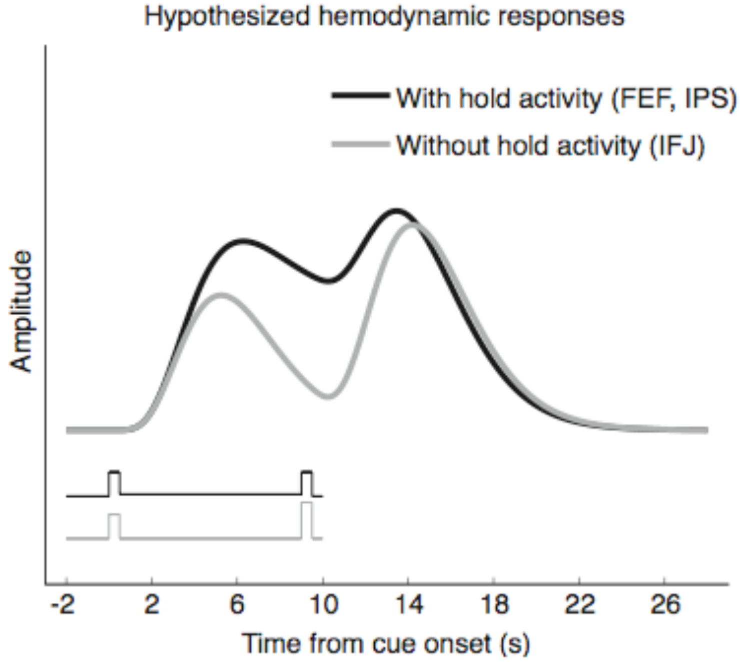

Figure 3. Hemodynamic predictions for the slow-event Posner cueing task experiment. The black curve shows the result of convolving the black boxcar function (representing levels of neural activity related to the cue, response, and holding attention during the delay period) with a standard hemodynamic response function. The gray curve shows the result when no delay activity is assumed. Activity most closely models the dark blue curve in Figure 2.

Despite the hemodynamic model's appeal, it fails to capture a salient aspect of the observed timecourses, namely the slow accumulation of activity in all three regions during the delay period. This accumulation is most dramatically evidenced in the 15 s delay condition, as no target appears and no response is made. Anticipatory activation has been observed in fMRI studies before (Ivanoff et al., 2008; Nobre et al., 2007; Curtis & Connolly, 2008), likely because subjects are sensitive to the fact that the probability of an event's occurrence increases over time, given that the event has not yet occurred (Hazard rate; Trillenberg et al., 2000; Los & Agter, 2005). We designed our experiment to counter these effects by using an exponential distribution of delay periods. Although effective at removing anticipatory RT effects in behavioral experiments (Trillenberg et al., 2000; Los & Agter, 2005), anticipatory signal was still prominent in the present experiment. Three possible explanations present themselves. First, subjects may not have believed the manipulation, potentially because the end of the trial (not the target presentation) did become more likely as the trial continued. Second, response preparation signals may build over time even if the level of anticipation remains constant. These preparation signals may have been for the manual response, as FEF and parietal cortex in humans and macaques supports preparation for forelimb movement (Connolly et al., 2000; 2007; Lawrence & Snyder, 2006; Dickinson et al., 2003). Alternatively, holding spatial attention away from fixation serve as the plan for an unexecuted saccade (Andersen et al., 1992; Bruce & Goldberg, 1985), consistent with the premotor theory of attention (Rizzolatti et al., 1987; Curtis & Connolly, 2008). Third, the sustained maintenance of attention away from fixation is effortful, perhaps becoming increasingly so over time as fatigue sets in (Grier et al., 2003; Szalma et al., 2004; Warm et al., 2008). Although participants verbally reported the strain of the long delays when questioned after the experiment, a systematic neuroimaging study of the exhaustion of attention has yet to be conducted.

This last explanation, that the ramping of activity actually represents increased effort as regions fatigue, is also consistent with the IFJ's role in cognitive control (Derrfuss et al., 2005; Brass et al., 2005). The IFJ may exert more control as fatigue sets in. Regardless of whether the ramping of activity represents the application of cognitive control, the IFJ's activation profile in this experiment--a response to the cue followed by no significant delay activity, and then by a robust target response--better matches a region that is controlling the deployment of attention than maintaining it at a certain spatial location (Asplund et al., 2010; see also Curtis & Connolly, 2008). In other words, the IFJ sets attentional weights but is not involved in their maintenance. In contrast, the robust sustained activity in the FEF and IPS suggests that these regions do maintain goal-directed attentional settings across delay periods. Such a division of labor may indicate an attentional hierarchy similar to the cognitive control hierarchy in prefrontal cortex (Koechlin et al., 2003; Koechlin & Summerfield, 2007; Badre, 2008; Badre et al., 2009; Badre & D'Esposito, 2009).

Experiment 2: Response Selection Load

Although the Posner cueing task experiment above demonstrated clear IFJ activity following cue presentation, perhaps because IFJ interprets the cue and then instructs other regions, a much lower-level possibility also exists: the response could have been visually evoked. To test whether the specific IFJ, FEF, and IPS regions identified participate in response selection, we employed a response selection load experiment (Dux et al., 2006; Marois et al., 2006). Brain regions involved in response selection should be increasingly engaged as the number of response choices increases. Like Dux et al. (2006), here we compared blocks in which subjects selected from 6 alternatives (6 AD) from 2 alternatives (2 AD). This manipulation has been successful with visual-manual and auditory-manual tasks (Dux et al., 2006; Marois et al., 2006), but it is unclear whether an internal response (a shift of visuo-spatial attention) will do the same. For Experiment 2, I use a modified Posner cueing task to test whether response selection of an attentional shift involves the IFJ, IPS, and FEF.

Methods

Six subjects who participated in the Posner cueing task experiment (Experiment 1) also participated in this control. In each trial (see Figure 4), subjects shifted their attention to one of eight locations, with each location mapped to a distinct color cue (same colors as in Dux et al., 2006). This cue was presented at fixation for 1000 ms. Following cue presentation and a 500-1500 ms hold period, a light gray square target was presented in one of the eight locations for 100 ms (each box was 4.1° from fixation and 1.0° across). The cue correctly predicted the target location on 85% of the trials. Regardless of trial validity, subjects responded to the target's presence as quickly as possible during a 1.4 s response window. The next trial commenced after a variable delay of 0-7 s (see below).

Before scanning, each participant was briefly trained on the stimulus-response mapping. Subjects completed 66 trials (equivalent to one fMRI run; see below) with a response diagram sheet; they then completed an additional 66 trials without the sheet. During training, all blocks were 8 AD; participants were not aware of the load manipulation until the scan session. Training was kept brief to ensure maximum response selection activation during that session.

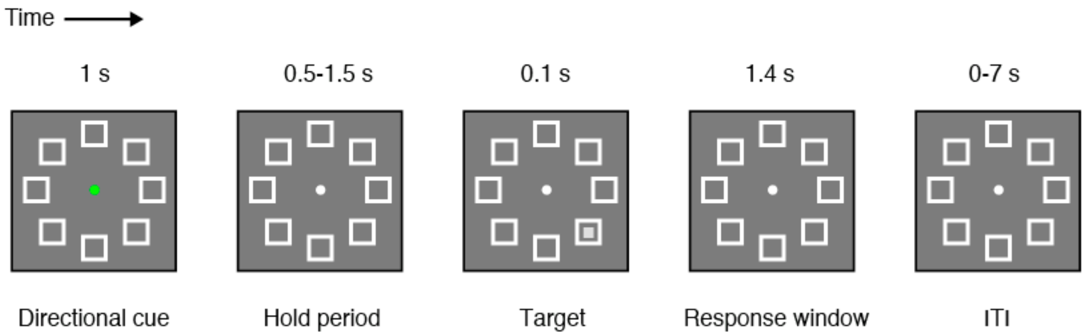

Figure 4. Task design for the response selection load experiment. ITI = inter-trial interval.

In each of seven fMRI runs, subjects were presented with three blocks of 2 AD trials interleaved with three blocks of 6 AD trials. Each block lasted 70 s, including 4 s of instructions ("6 AD condition" versus "2 AD condition"). Each block contained 11 trials with the TOA (trial onset asynchrony) distributed exponentially to aid in deconvolution efficiency: 5 trials at 4 s, 3 at 6 s, 2 at 8 s, and 1 at 10 s. The condition for the first block of each run was counterbalanced across subjects and runs. Just prior to the experiment, subjects were informed as to which stimulus-location pairings would be part of the 6 AD and 2 AD blocks. For the latter, the two locations were directly opposite each other and varied by subject.

fMRI procedure

The fMRI procedure was identical to that used in Experiment 1.

Data analysis

Preprocessing steps were identical to those in Experiment 1, save high pass filtering was not employed because the block structure would introduce low frequency signal (3 cycles per run). Manipulations of response selection load have been shown to affect baseline signal (possibly due to mnemonic demands; Marois et al., 2006), so we derived the response to each trial using deconvolution and then compared the peak amplitude of the resulting time courses. Using the ROIs from Experiment 1, timecourses for each validly-cued trial were constructed using a deconvolution analysis. Z-transformed beta estimates, corrected for serial auto-correlations, were derived for the 10 volumes following cue onset. These timecourses were then averaged across hemispheres for statistical purposes and across individuals for display purposes (Figure 5). The peak of each timecourse by condition and subject was then compared across participants using paired t-tests (one-tailed, owing to the a priori directional hypothesis about response selection load effects; see Dux et al., 2006; Marois et al., 2006).

Results and Discussion

As expected of a Posner cueing task variant, a robust validity effect was found for reaction times (F(1, 5) = 20.3, p = 0.0064). As in Experiment 1, the magnitude of the validity effect was rather large (100 ms, SD = 54; Valid: 389 ms, SD = 30; Invalid: 489 ms, SD = 61), likely for the same reason that there are many different locations that could be cued. No effect of Load (2 AD versus 6 AD) on RT was observed, and there was also no interaction (Load: F(1, 5) = 1.63, p = 0.26; Validity x Load: F(1, 5) = 1.80, p = 0.24). This null effect of Load (2 AD versus 6 AD) is important, for it implies that participants were able to shift their attention successfully before the target arrived. This result makes sense because that the cue-target SOA was at least 1500 ms, and mean RTs with an auditory-manual response selection task found mean RTs that were shorter than this minimum gap (6 AD: 968 ms; 2 AD: 656 ms; Dux et al., 2006). Consequently, the imaging results cannot be explained by subjects failing to complete their attentional shift quickly and then being surprised by the target onset. Subject performance is further commendable because each participant responded to the cue within the allotted time window on every trial.

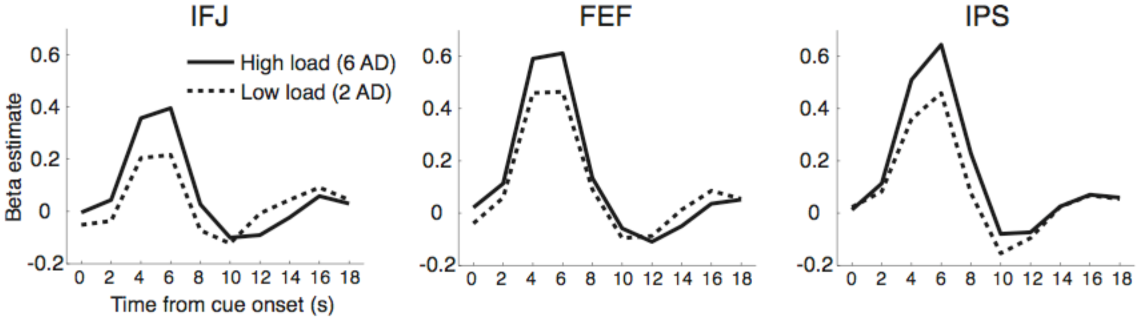

Figure 5. Hemodynamic responses (recovered through deconvolution) from the response selection load experiment (Experiment 2) for IFJ, FEF, and IPS. Timecourses have been averaged across participants and hemispheres.

Despite the lack of load effects on behavior, response selection load had a significant effect on participant's brain activity. Increased load caused greater activity in all three key regions: IPS (t(5) = 3.75, p = 0.007), FEF (t(5) = 2.27, p = 0.036), and IFJ (t(5) = 2.09, p = 0.046). These results are consistent with those found in studies with overt actions following response selection (Dux et al., 2006; Marois et al., 2006). The present results do have two caveats. First, the general increase of activity across all three brain regions could indicate a general increase across the brain for more difficult trials (though not an overall arousal level change by block; see Marois et al., 2006). Dux et al. (2006) found that only the Left IFJ was sensitive to their response load manipulation, but such specificity may not be expected for visuospatial selection. Indeed, using a visual-manual experiment (instead of the auditory-manual one in Dux et al., 2006), Marois et al. (2006) found activity in IFJ, FEF, and IPS. The second caveat is that the observed load effect may be caused, at least in part, by perceptual demands instead of response demands. All three of these regions are sensitive to perceptual difficulty (Marois et al., 2000; Marois et al., 2004a; Serences et al., 2005; Nee & Jonides, 2009; Sylvester et al., 2008; Corbetta & Shulman, 2002) and so play a role in perceptual selection, a point to which I return in Experiment 3. While perceptual effects may contribute to the observed activity, response selection is still likely the primary cause of the effects. Dux et al. (2006)'s 6 AD versus 2 AD manipulation led to a 312 ms reaction time effect, and it is reasonable to assume that a similar delay occurred in the present experiment. In addition, the perceptual effects were likely small because the color cue was easy to see (on screen for a full second) and easy to distinguish from the other cue colors.

One final aspect of the results is worth noting: All three regions appear to peak at the same time. This result is different from those in Experiment 1 above and in Chapter II's Experiment 4. I surmise that the delay period in the present experiment was sufficiently short that no peak timing difference developed across regions. Indeed, in Experiment 1, the three regions peaked at the same time in the 1 s SOA condition. In contrast, whenever a longer delay occurs, the FEF and IPS peak later than the IFJ. The results from the present experiment are thus consistent with Experiment 1's conclusion that the FEF and IPS are active during the delay period of a Posner cueing task to support the maintenance of attentional settings.

Experiment 3: Perceptual Selection versus Response Selection

The Posner cueing experiment (Experiment 1) separated the establishment of attentional settings (i.e. cue interpretation) from the maintenance of these attentional settings, while the response selection load experiment (Experiment 2) demonstrated that the IFJ, FEF, and IPS regions from Experiment 1 were performing cue-location response selection in a Posner endoneous cuing task. As was discussed above, these regions may also play a role in perceptual selection (Marois et al., 2000; Marois et al., 2004a; Serences et al., 2005; Nee & Jonides, 2009; Sylvester et al., 2008; Corbetta & Shulman, 2002). Although the IFJ participates in both forms of selection, the right IFJ appears to activate more consistently in studies of perceptual selection and visuospatial attention (Marois et al., 2000; Marois et al., 2004a; Serences et al., 2005; Corbetta & Shulman, 2002; Corbetta et al., 2008; Corbetta et al., 1998), whereas the left IFJ activates more for response selection (Dux et al., 2006; Dux et al., 2009) and rule selection (Bunge, 2004; Crone et al., 2006; Derrfuss et al., 2004)--a possible component of response selection.

The IFJs are not the only regions that appear to show functional differences across hemispheres on account of the type of selection they perform. For example, the selection of learned actions has been proposed to be left-lateralized, with many different parts of the left hemisphere implicated (Rushworth et al., 1998; Schluter et al., 2001). Visuospatial attention, on the other hand, shows a right-hemisphere bias (Driver & Mattingley, 1998; Corbetta & Shulman, 2002), though it has recently been claimed that this bias does not include the dorsal attention network (Shulman et al., 2010). In this final experiment, I employ a task that separates the perceptual selection and response selection components (also separating out response execution) to determine whether the IFJ does show preferential processing for response selection or perceptual selection by hemisphere. I then compare these results to the results in the dorsal attention network, as these laterality effects present another possible opportunity to dissociate the IFJ from the FEF and IPS.

Methods

Eleven right-handed subjects participated in the experiment; one subject was removed due to failure to follow task instructions. The task consisted of three phases--perceptual selection, response selection, and response execution--each separated by 14 s to allow the hemodynamic response to return to baseline (see Figure 6). Each trial began with the fixation dot changing from black to white, which served as a warning cue (500 ms). A 15-item rapid serial visual presentation (RSVP) stream was next presented at fixation (100 ms per item, no gap). The stream consisted of distractor digits 2-9 (White Helvetica font, 0.8° across), with the restriction that no distractor could be shown within three frames of another presentation of itself. The subjects' task was to search for the target letter, which replaced one of the digits in position 5-13.

After a 14 s fixation period, a colored letter was shown at fixation. This letter matched the target letter from the RSVP stream on 80% of trials. If the presented letter matched the remembered one, subjects were to perform response selection, mapping the color to one of six fingers; if the presented letter was not a match, subjects simply fixated for the remainder of the trial. These ‘catch’ trials allowed us to determine whether subjects did encode the target during the perceptual selection phase. After response selection was complete, the selected finger was remembered for an additional 14 seconds, at which time the fixation dot changed to a slightly larger square. Upon seeing the square, subjects made their response. This response execution period was followed by another 14 s of fixation, at which time the next trial began.

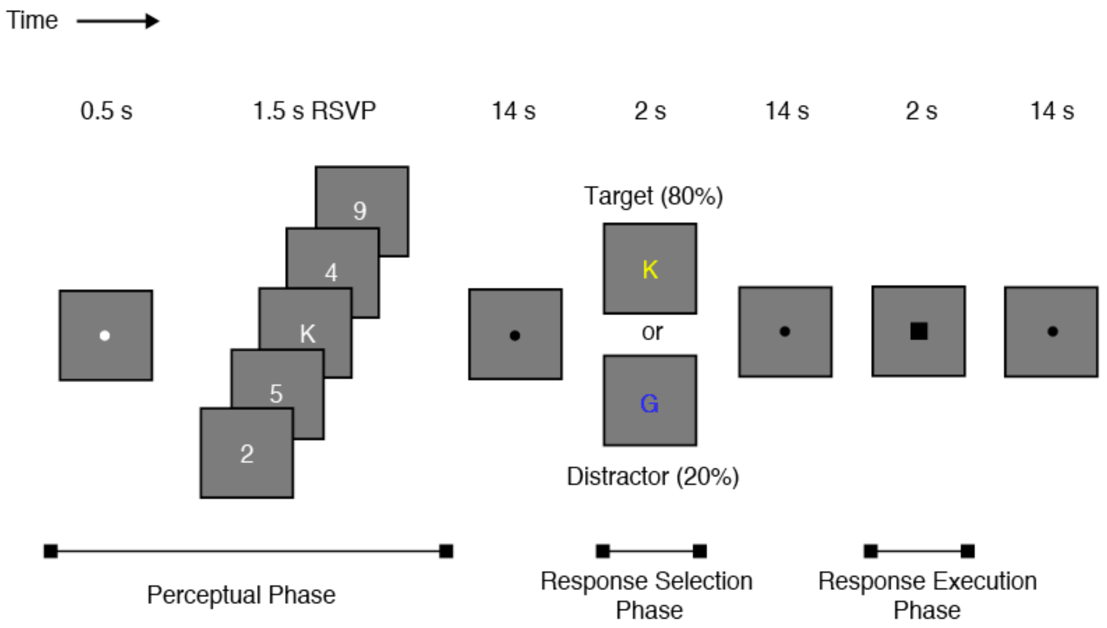

Figure 6. Task design for the Experiment 3. The RSVP was comprised of 15 frames and each color during the response selection phase mapped onto one of six fingers.

Subjects completed a total of six trials per fMRI run, and a total of eight main runs (48 trials total). Before the scan session, subjects practiced the task at a higher speed, with only one second between each phase instead of 14. Subjects practiced with two runs of 44 trials each. During the first, a task diagram was provided that gave the color-finger mappings; for the second, the mappings were performed from memory.

Two runs during the fMRI session used this faster timing and served as localizers. For these runs, there were 11 blocks, 5 of which were 36-second task periods (4 trials) and 6 of which were 24-second fixation periods. One was the first run of the session, the other the last. Thus the first localizer run allowed subjects to become accustomed to the stimuli in the scanner environment without affording them too much additional practice (Dux et al., 2006).

fMRI procedure

The fMRI procedure was identical to that used in Experiment 1.

Data analysis

Preprocessing steps were identical to those in Experiment 1. Statistical parametric maps (SPMs) of BOLD activation were created using general linear models (GLMs) with multiple regression. Regressors were created for the localizer runs by convolving a boxcar representing each block type with a canonical double gamma hemodynamic response function (HRF; SPM2, http://www.fil.ion.ucl.ac.uk/spm). One localizer GLM was created for each subject for use during ROI definition.

ROIs were defined as in Experiment 1 with the exception of the primary motor cortex ROIs, which were defined based on anatomical coordinates from Indovina & Sanes (2001). We then used these ROIs to probe the activity in each region during the main task. The timecourse for each phase of every trial for which the response selection letter matched the target and to which the subject responded (a hit) was extracted from each ROI for each participant. The timecourse was then converted to percent signal change (baseline from the time point of the directional cue onset and the preceding point, averaged across all trials). The average timecourses for each phase were next computed for each participant. Averages across participants were computed for display purposes (Figure 7).

For statistical tests of activation during each phase, I calculated the value of each subject's timecourse for each phase at the group-average peak for that phase and region (e.g. the peak is at 6 s for the perceptual selection phase in Left IFJ). A one-sample t-test was then used to test whether this list of values from each subject (by ROI and phase) was different than zero (baseline; Table 2a). For tests of the interaction between the right and left hemisphere representatives of a given region, these lists of values were compared using paired t-tests (Table 2a). For tests comparing phases, I first determined the peak of each phase response for each subject. Next, these values were compared using paired t-tests (Table 2b). To test for the interaction of phase by region, I took the difference between the left and right hemisphere representatives of a given region and then compared the difference scores across phases using paired t-tests (Table 2b).

Results and Discussion

To assess whether subjects were successfully detecting the target in the RSVP stream, I examined whether subjects performed response selection. They did so on 96.4% (SD = 7.8%) of trials in which the presented letter matched the RSVP target letter (hits), and also on 21.8% (SD = 19.2%) of trials in which it did not (false alarms). This false alarm rate is rather high, and likely reflects a subject bias to respond (80% of trials did contain the target). Two subjects account for most of these errors, with both at over 50%. Their imaging data, however, do not appear different from the rest of the group, so we assume that they were performing the task, albeit poorly. Performance on the response selection component of the task was very good; given that a response was ultimately made, 96.1% (SD = 8.6%) of trials had a correct one.

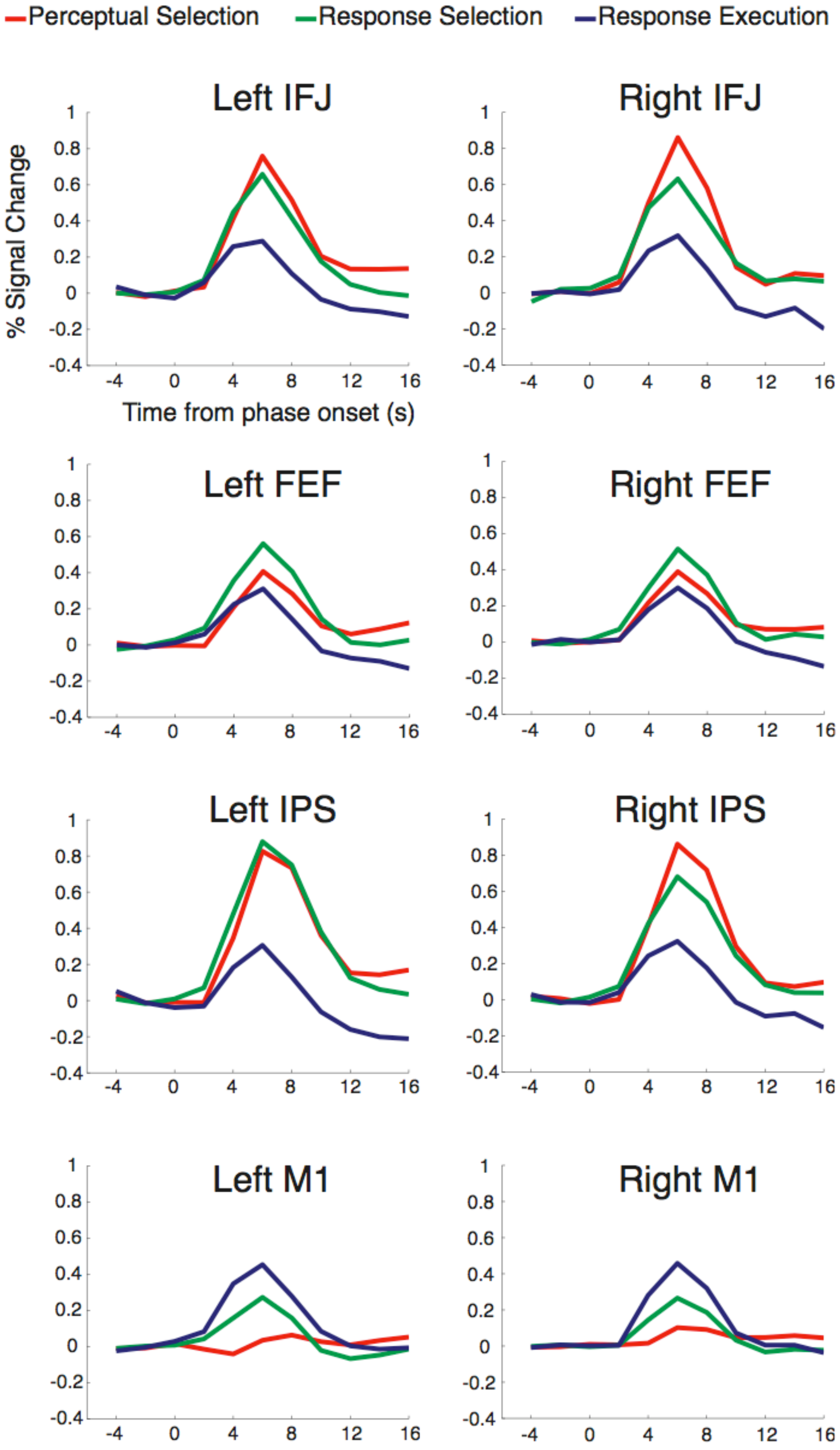

Figure 7. Timecourses from each phase for the regions of interest (ROIs) probed in Experiment 3.

The imaging results show that each ROI was activated by all phases of the experiment, with the exception of Left M1 during the perceptual phase (Table 2a; Figure 7). Motor cortex did show robust motor related activity, and also preparatory activity during response selection. Although subjects were instructed not to move their fingers as a mnemonic device during response selection, some may have done so. Alternatively, manual motor cortex may have a role in response selection when the effector is a finger.

Both the IFJ and IPS were more active during the perceptual and response selection phases than during response execution (Table 2b), with the FEF showing less of a distinction between the phases (Table 2b). Consequently, in this experiment, the IFJ and IPS behave similarly, much as they do during attentional blink tasks or tasks with high perceptual difficulty (Marois et al., 2000; Marois et al., 2004a; Marois et al., 2004b). The FEF, by contrast, shows relatively more response execution and response selection activity (Table 2b). Nevertheless, the FEF does not behave like M1, as the former has more response selection than response execution activity, whereas the latter shows the opposite pattern (Figure 7; Table 2b). This result could be the consequence of FEF's responses to forelimb movement and the preparation for such movement (Connolly et al., 2000; 2007; Lawrence & Snyder, 2006; Dickinson et al., 2003). It is also consistent with dorsal premotor cortex's being in close proximity to FEF (Amiez et al., 2006).

Table 2a. Anatomical regions probed in Experiment 3; Main statistical results.

ROI	Talairach coordinates	PS	PS interaction (R vs. L)	RS	RS interaction (R vs. L)	RE	RE interaction (R vs. L)
Right IFJ	43 (6), 8 (5), 27 (4)	6.86*	1.17	9.71*	-0.30	4.25*	0.40
Left IFJ	-46 (7), 7 (5), 30 (5)	8.86*		6.19*		3.77*	
Right FEF	30 (3), -5 (2), 50 (3)	5.73*	-0.25	9.51*	-0.66	8.01*	-0.26
Left FEF	-29 (4), -7 (3), 50 (2)	7.07*		14.4*		5.73*	
Right IPS	29 (5), -57 (3), 46 (3)	12.9*	0.27	10.4*	-2.38*	7.72*	0.32
Left IPS	-29 (2), -60 (4), 47 (3)	6.74*		13.8*		6.16*	
Right M1	35 (2), -24 (3), 56 (2)	2.42*	1.97	3.38*	-0.10	7.10*	0.06
Left M1	-36 (2), -25 (4), 55 (2)	0.95		4.01*		5.71*	

The six rightmost columns provide t-values for comparisons between phase activity and zero (PS, RS, RE) or between the activity in each phase compared across hemispheres (Interaction (R vs. L)). PS = Perceptual Selection; RS = Response Selection; RE = Response Execution. *$p<0.05$.

Table 2b. Anatomical regions probed in Experiment 3; Interaction statistical results.

ROI	PS vs. RS	PS vs. RS Interaction (R vs. L)	PS vs. RE	PS vs. RE Interaction (R vs. L)	RS vs. RE	RS vs. RE Interaction (R vs. L)
Right IFJ	2.97*	1.81	4.73*	0.70	4.55*	-0.58
Left IFJ	1.19		5.97*		3.51*	
Right FEF	-1.85	0.52	1.26	-0.11	3.47*	-0.81
Left FEF	-2.29*		1.32		4.64*	
Right IPS	6.64*	3.57*	8.99*	0.20	6.12*	-4.20*
Left IPS	-0.64		5.29*		9.96*	
Right M1	-2.04	1.32	-8.09*	0.84	-2.29*	-0.29
Left M1	-2.69*		-6.13*		-2.11	

The right six columns provide t-values for comparisons between the activity in different phases (e.g. PS vs. RS) or between the difference in activity between any two phases compared across hemispheres (Interaction (R vs. L)). PS = Perceptual Selection; RS = Response Selection; RE = Response Execution. *p<0.05.

Few interhemispheric differences were found. Foremost, the IPS showed a significant interaction between phases (perceptual versus response selection) across hemispheres (Table 2b). This effect was driven by greater left IPS activity during response selection (Table 2a), consistent with the idea that the left hemisphere is specialized for response-related processing (Rushworth et al., 1998; Schluter et al., 2001). In addition, there was no difference in perceptual selection across the left and right IPS, consistent with Shulman et al.'s (2010) contention that the right hemisphere bias for visuospatial attention does not involve the dorsal attention network (but see Marois et al., 2000; Marois et al., 2004b). Although the statistical tests are not significant with the current n (Table 2b), the IFJ shows a similar pattern to the IPS, with a perceptual selection tending to be greater than response selection in the right hemisphere (Figure 7). Unlike the IPS, however, this potential effect looks to be driven primarily by an increase in perceptual selection activity in the right hemisphere instead of left hemisphere dominance in response selection. These results are consistent with previous studies showing greater right IFJ sensitivity to perceptual selection (Marois et al., 2000; Marois et al., 2004b). Although we predicted greater response selection load activity on the left, many response selection tasks do still find right IFJ activation, just not with the temporal profile that would suggest that it was actually performing response selection (Dux et al., 2006; Tombu et al., unpublished data). Instead, the right IFJ activation may reflect the fact that response selection tasks always have a perceptual component to them. The present task also had such a component, and it may have driven the right IFJ to have greater activity than the left during the response selection phase. Nevertheless, the right IFJ is even more active during the perceptual phase (Table 2b).

Overall, there were few differences between perceptual selection and response selection activity in the ROIs examined (with the exception of the motor cortex, which appeared to have little or no perceptual selection activity). Such common activation is consistent with previous work suggesting that perceptual and response processes draw on common resources (Marois et al., 2006; Jolicoeur, 1998; Jolicoeur et al., 2001; Arnell & Duncan, 2002; Ruthruff & Pashler, 2001). Such convergence has also been demonstrated in single unit recordings (Gold & Shadlen, 2001; Hernandez et al., 2002; Schall, 2001), implying that the mechanisms of perceptual and response selection may be intertwined. Naturally, one should not ignore the confound that the response selection stage of the present experiment included a perceptual component (identify the letter and its color). Nevertheless, despite seemingly disparate response and perceptual processes as the major component of each phase, the activation patterns across these phases are remarkably similar.

General Discussion

The experiments in this chapter clarify the function of the IFJ in goal-directed attention, dissociating it from members of the dorsal attention network. A Posner cueing task with an extended delay time between the cue and target (Experiment 1) revealed that the IFJ is not involved in holding spatial attention at a location away from fixation. Put another way, it does not maintain attentional weights. Instead, this maintenance function is the role of the IPS and FEF. The IFJ does still activate during the task, albeit transiently. This transient nature of the IFJ response may explain why it is not regularly observed co-activating with the dorsal attention network (Kastner et al., 1999; Yantis et al., 2002; Corbetta et al., 2002).

The transient nature of this response implies that the IFJ was involved in cue interpretation and response to the target, but it did not in actively hold attention in the cued location. Put another way, the IFJ set attentional weights, but it was not responsible for maintaining those attentional settings. This function is similar to that proposed for the superior parietal lobule (SPL) in spatial shifts of attention (Yantis et al., 2002). In contrast, the FEF and IPS were involved in all three phases. This suggests that these dorsal attention network regions maintain attentional weights while spatial attention is being held away from fixation. Given this dissociation of roles, it seems likely that the IFJ instructs or interacts with the FEF and IPS to determine the attentional weights. Such a relationship would be consistent with the IFJ's known involvement in coordinating attention (Asplund et al., 2010), response selection (Dux et al., 2006; Marois et al., 2006; Dux et al., 2009), and cognitive control (Derrfuss et al., 2004; 2005; Brass et al., 2005).

A follow-up experiment (Experiment 2) confirmed that all three regions were sensitive to response selection load. This result indicated that the IFJ (and FEF and IPS, for that matter) activation in Experient 1 was not simply visually evoked. The experiment also demonstrated that the IFJ is involved in response selection even when the response being selected is covert. Previous studies of response selection have used manual or vocal responses (Dux et al., 2006; Dux et al., 2009; Marois et al., 2006), but the response being selected in Experiment 2 was a shift of attention.

In a final experiment, we examined the roles of the IFJ, FEF, and IPS in two different forms of attentional selection: perceptual selection and response selection. All three regions were active for both types of selection, consistent with many studies demonstrating a tight link between perception and action (Marois et al., 2006; Jolicoeur, 1998; Jolicoeur et al., 2001; Arnell & Duncan, 2002; Ruthruff & Pashler, 2001). Nevertheless, the IFJ and IPS showed a small preference for perceptual selection in the right hemisphere and response selection in the left, a finding also consistent with the literature (Rushworth et al., 1998; Schluter et al., 2001; Dux et al., 2006; Dux et al., 2009; Marois et al., 2006; Marois et al., 2000; Marois et al., 2004b; Marois et al., 2004a; Corbetta & Shulman, 2002; Driver & Mattingley, 1998). Why such specialization--albeit partial--across hemispheres would develop is not clear. Perhaps linguistic processing requires rule-selection abilities, so these clustered in the left hemisphere (Bunge, 2004; Crone et al., 2006; Brass et al., 2005). That is to say, left hemisphere activation may be dominant because rule retrieval in language and in the selection of stimulus-response mappings share fundamental computations.

Taken together, the results from the experiments in Chapter IV suggest that the IFJ, FEF, and IPS have many roles in attention and selection, but the IFJ's transient activation during the first experiment suggests that it exerts control only when changes to current attentional settings are required, perhaps by instructing the FEF and IPS.

References

Amiez, C., Kostopoulos, P., Chapod, A.-S., & Petrides, M. (2006). Local morphology predicts functional organization of the dorsal premotor region in the human brain. The Journal of Neuroscience, 26(10), 2724-2731.

Arnell, K. M., & Duncan, J. (2002). Separate and shared sources of dual-task cost in stimulus identification and response selection. Cognitive Psychology, 44, 105-147.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. Trends in Cognitive Sciences, 8(4), 170-177.

Asplund, C. L., Todd, J. J., Snyder, A. P., & Marois, R. (2010). A central role for the lateral prefrontal cortex in goal-directed and stimulus-driven attention. Nature Neuroscience, 13(4), 507-512.

Badre, D. (2008). Cognitive control, hierarchy, and the rostro-caudal axis of the prefrontal cortex. Trends in Cognitive Science, 12(5), 193-200.

Badre, D., Hoffman, J., Cooney, J. W., & D'Esposito, M. (2009). Hierarchical cognitive control deficits following damage to the human frontal lobe. Nature Neuroscience, 12(4), 515-522.

Badre, D. & D'Esposito, M. (2009). Is the rostro-caudal axis of the frontal lobe hierarchical? Nature Reviews Neuroscience, 10, 659-669.

Brainard, D. H. (1997). The Psychophysics Toolbox. Spatial Vision 10, 433–436.

Brass, M., Derrfuss, J., Forstmann, B., & von Cramon, D. Y. (2005). The role of the inferior frontal junction area in cognitive control. Trends in Cognitive Sciences, 9(7), 314-316.

Bruce, C. J. & Goldberg, M. E. (1985). Primate frontal eye fields. I. Single neurons discharging before saccades. Journal of Neurophysiology, 53, 603-635.

Bunge, S. A. (2004). How we use rules to select actions: A review of evidence from cognitive neuroscience. Cognitive, Affective, & Behavioral Neuroscience, 4(4), 564-579.

Connolly, J. D., Goodale, M. A., Desouza, J. F., Menon, R. S., & Vilis, T. (2000). A comparison of frontoparietal fMRI activation during anti-saccades and anti-pointing. Journal of neurophysiology, 84, 1645-1655.

Connolly, J. D., Goodale, M. A., Cant, J. S., & Munoz, D. P. (2007). Effector-specific fields for motor preparation in the human frontal cortex. Neuroimage, 34, 1209-1219.

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: From environment to theory of mind. Neuron, 58, 306-324.

Corbetta, M. & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews Neuroscience, 3, 201-215.

Corbetta, M., Kincade, J. M., Ollinger, J. M., McAvoy, M. P., & Shulman, G. L. (2000). Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nature Neuroscience, 3(3), 292-297.

Corbetta, M., Akbudak, E., Conturo, T. E., Snyder, A. Z., Ollinger, J. M., Drury, H. A., Linenweber, M. R., Petersen, S. E., Raichle, M. E., Van Essen, D. C., & Shulman, G. L. (1998). A common network of functional areas for attention and eye movements. Neuron, 21, 761-773.

Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. Science, 279, 1347-1351.

Courtney, S. M, Ungerleider, L. G., Keil, K., & Haxby, J. V. (1997). Transient and sustained activity in a distributed neural system for human working memory. Nature, 386, 608-611.

Crone, E. A., Wendelken, C., Donohue, S. E., & Bunge, S. A. (2006). Neural evidence for dissociable components of task-switching. Cerebral Cortex, 16, 475-486.

Curtis, C. E. & Connolly, J. D. (2008). Saccade preparation signals in the human frontal and parietal cortices. Journal of Neurophysiology, 99, 133-145.

Derrfuss, J., Brass, M., Neumann, J., & von Cramon, D. Y. (2005). Involvement of the inferior frontal junction in cognitive control: Meta-analyses of switching and Stroop studies. Human Brain Mapping, 25(1), 22-34.

Derrfuss, J., Brass, M., von Cramon, D. Y., Lohmann, G., & Amunts, K. (2009). Neural activations at the junction of the inferior frontal sulcus and the inferior precentral sulcus: Interindividual variability, reliability, and association with sulcal morphology. Human Brain Mapping, 30(1), 299-311.

Derrfuss, J., Brass, M., & von Cramon, D. Y. (2004). Cognitive control in the posterior frontolateral cortex: evidence from common activations in task coordination, interference control, and working memory. Neuroimage, 23(2), 604-612.

Dickinson, A. R., Calton, J. L., & Snyder, L. H. (2003). Nonspatial saccade-specific activation in area LIP of monkey parietal cortex. Journal of Neurophysiology, 90, 2460-2464.

Doricchi, F., Macca, E., Silvetti, M., & Macaluso, E. (2009). Neural correlates of the spatial and expectancy components of endogenous and stimulus-driven orienting of attention in the Posner task. Cerebral Cortex, 20, 1574-1585.

Driver, J. & Mattingley, J. B. (1998). Parietal neglect and visual awareness. Nature Neuroscience, 1(1), 17-22.

Dux, P. E., Ivanoff, J., Asplund, C. L., & Marois, R. (2006). Isolation of a central bottleneck of information processing with time-resolved fMRI. Neuron, 52, 1109-1120.

Dux, P. E., Tombu, M. N., Harrison, S., Rogers, B. P., Tong, F., & Marois, R. (2009). Training improves multitasking performance by increasing the speed of information processing in human prefrontal cortex. Neuron, 63, 127-138.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., et al. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. Proceedings of the National Academy of Sciences of the United States of America 102, 9673–9678.

Gold, J. I. & Shadlen, M. N. (2001). Neural computations that underlie decisions about sensory stimuli. Trends in Cognitive Science, 5, 10-16.

Grier, R. A., Warm, J. S., Dember, W. N., Matthews, G. Galinsky, T. L., Szalma, J. L., & Parasuraman, R. (2003). The vigilance decrement reflects limitations in effortful attention, not mindlessness. Human Factors, 45, 349-359.

Hernandez, A., Zainos, A., & Romo, R. (2002). Temporal evolution of a decision-making process in medial pre-motor cortex. Neuron, 33, 959-972.

Indovina, I. & Sanes, J. N. (2001). On somatotopic representation centers for finger movements in human primary motor cortex and supplementary motor area. Neuroimage, 13, 1027-1034.

Ivanoff, J., Branning, P., & Marois, R. (2008). fMRI evidence for a dual process account of the speed-accuracy tradeoff in decision-making. PLoS ONE, 3, e2635.

Jolicoeur, P. (1998). Modulation of the attentional blink by on-line response selection: Evidence from speeded and unspeeded Task-1 decisions. Memory & Cognition, 26, 1014-1032.

Jolicoeur, P., Dell'Acqua, R. & Crebolder, J. M. (2001). The attentional blink bottleneck. In K. Shapiro (Ed.), The limits of attention: Temporal constraints in human information processing. OU Press, New York, 82-99.

Kastner, S., DeSimone, K., Konen, C. S., Szczepanski, S. M., Weiner, K. S., & Schneider, K. A. (2007). Topographic maps in human frontal cortex revealed in memory-guided saccade and spatial working-memory tasks. Journal of Neuophysiology, 97, 3494-3507.

Kastner, S., Pinsk, M. A., De Weerd, P., Desimone, R. & Ungerleider, L. G. (1999). Increased activity in human visual cortex during directed attention in the absence of visual stimulation. Neuron 22, 751–761.

Koechlin, E., Ody, C., & Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. Science, 302, 1181-1185.

Koechlin, E. & Summerfield, C. (2007). An information theoretical approach to prefrontal executive function. Trends in Cognitive Science, 11(6), 229-235.

Lawrence, B. M. & Snyder, L. H. Comparison of effector-specific signals in frontal and parietal cortices. Journal of Neurophysiology, 96, 1393-1400.

Los, S. A. & Agter, F. (2005). Reweighting sequential effects across different distributions of foreperiods: Segregating elementary contributions to nonspecific preparation. Perception & Psychophysics, 67(7), 1161-1170.

Marois, R., Chun, M. M., & Gore, J. C. (2000). Neural correlates of the attentional blink. Neuron, 28, 299-308.

Marois, R., Chun, M. M., & Gore, J. C. (2004a). A common parieto-frontal network is recruited under both low visibility and high perceptual interference conditions. Journal of Neurophysiology, 92, 2985-2992.

Marois, R., Yi, D.-J., & Chun, M. M. (2004b). The neural fate of consciously perceived and missed events in the attentional blink. Neuron, 41, 465-472.

Marois, R. & Ivanoff, J. (2005). Capacity limits of information processing in the brain. Trends in Cognitive Sciences, 9(6), 296-305.

Marois, R., Larson, J. M., Chun, M. M. & Shima, D. (2006). Response-specific sources of dual-task interference in human pre-motor cortex. Psychological Research, 70(6), 436-447.

Nee, D. E. & Jonides, J. (2009). Common and distinct neural correlates of perceptual and memorial selection. Neuroimage, 45(3), 963-975.

Nobre, A. C., Correa, A. & Coull, J. T. (2007). The hazards of time. Current Opinion in Neurobiology, 17(4), 465-470.

Ozaki, T. J. & Ogawa, S. (2009). Causality analysis defines neural streams of orienting and holding of attention. Neuroreport, 20, 1371-1375.

Pelli, D. G. (1997). The VideoToolbox software for visual psychophysics: Transforming numbers into movies. Spatial Vision 10, 437–442.

Posner, M. I., Snyder, C. R. R. & Davidson, B. J. (1980). Attention and the detection of signals. Journal of Experimental Psychology: General 109, 160–174.

Rizzolatti, G., Riggio, L., Dascola, I. & Umiltá, C. (1987). Reorienting attention across the horizontal and vertical meridians: Evidence in favor of a premotor theory of attention. Neuropsychologia, 25, 31-40.

Rushworth, M. F. S., Nixon, P. D., Wade, D. T., Renowden, S., & Passingham, R. E. (1998). The left hemisphere and the selection of learned actions. Neuropsychologia, 36(1), 11-24.

Ruthruff, E. & Pashler, H. (2001). Perceptual and central interference in dual-task performance. In K. Shapiro (Ed.), The limits of attention: Temporal constraints in human information processing. (Oxford University Press, New York), 100-123.

Schall, J. D. (2001). Neural basis of deciding, choosing, and acting. Nature Reviews Neuroscience, 2, 33-42.

Serences, J. T., Shomstein, S., Leber, A. B., Golay, X., Egeth, H. E., & Yantis, S. (2005). Coordination of voluntary and stimulus-driven attentional control in human cortex. Psychological Science, 16(2), 114-122.

Shulman, G. L., Pope, D. L. W., Astafiev, S. V. McAvoy, M. P., Snyder, A. Z., & Corbetta, M. (2010). Right hemisphere dominance during spatial selective attention and target detection occurs outside the dorsal frontoparietal network. The Journal of Neuroscience, 30(10), 3640-3651.

Sigman, M. & Dehaene, S. (2008). Brain mechanisms of serial and parallel processing during dual-task performance. The Journal of Neuroscience, 28(30), 7585-7598.

Sylvester, C. M., Jack, A. I., Corbetta, M., & Shulman, G. L. (2008). Anticipatory suppression of non-attended locations in visual cortex marks target location and predicts perception. Journal of Neuroscience, 28(26), 6549-6556.

Szalma, J. L., Warm, J. S., Matthews, G., Dember, W. N., Weiler, E. M., Meier, A., & Eggemeier, F. T. (2004). Effects of sensory modality and task duration on performance, workload, and stress in sustained attention. Human Factors, 46, 219-233.

Talairach, J. & Tournoux, P. (1988). Co-planar stereotaxic atlas of the human brain (Thieme Medical Publishers New York).

Todd, J. J. & Marois, R. (2004). Capacity limit of visual short-term memory in human posterior parietal cortex. Nature, 428, 751-754.

Trillenberg, P., Verleger, R., Wascher, E., Wauschkuhn, B., & Wessel, K. (2000). CNV and temporal uncertainty with 'ageing' and 'non-ageing' S1-S2 intervals. Clinical Neurophysiology, 111, 1216-1226.

Warm, J. S., Parasuraman, R., & Matthews, G. (2008). Vigilance requires hard mental work and is stressful. Human Factors, 50, 433-441.

Yantis, S., Schwarzbach, J., Serences, J. T., Carlson, R. L., Steinmetz, M. A., Pekar, J. J., & Courtney, S. M. (2002). Transient neural activity in human parietal cortex during spatial attention shifts. Nature Neuroscience, 5, 995-1002.

CHAPTER V

SUMMARY AND CONCLUSION

The purpose of this final chapter is threefold. First, the aims and primary findings of each chapter (II-IV) are summarized. Second, the novel findings of the experiments therein are discussed in the context of the control and coordination of attention and selection, focusing specifically on the contribution of the inferior frontal junction (IFJ). Third, I discuss remaining challenges and directions for future research.

Chapter II: The central role of the inferior frontal junction in stimulus-driven and goal-directed attention

Selective attention, the process by which sensory information is preferentially processed, is not a unitary phenomenon. One fundamental division is between stimulus-driven (when attention is captured by unexpected or salient events) and goal-directed (when attention is deployed under voluntary control) attention (Egeth & Yantis, 1997; Corbetta & Shulman, 2002). These two forms of attention draw on two largely distinct fronto-parietal networks, ventral and dorsal, but must be coordinated for coherent behavior to emerge. Using a novel behavioral paradigm (Surprise-induced Blindness), we showed that the inferior frontal junction (IFJ) is activated by both forms of attention and may therefore coordinate them. A follow-up endogenous Posner cueing task confirmed the IFJ's goal-directed attention role. Finally, in conjunction with fellow ventral attention network member the temporo-parietal junction (TPJ), the IFJ also accounted for the stimulus-driven attentional limits to conscious perception revealed by Surprise-induced Blindness.

Chapter III: The functional segregation of the ventral attention network: Separating the inferior frontal junction from the temporo-parietal junction

Although the IFJ and TPJ both activate during stimulus-driven attention, only the former also participated in goal-directed attention (Chapter II). To further investigate the dissociation between these core members of the ventral attention network, we employed a functional overlap approach. The activation patterns from two tasks known to involve the TPJ--reasoning about another person's mental states (theory of mind) and self-directed processing during periods of rest in an otherwise demanding task (default mode of processing)--were compared to stimulus-driven attention activations. Both theory of mind and default processing involved the same TPJ region as stimulus-driven attention. In stark contrast, neither of these tasks recruited the IFJ. This dissociation between the IFJ and the TPJ implies that they have different cognitive functions, even in stimulus-driven attention. More broadly, stimulus-driven attention overlapped with the other two tasks only at the TPJ, while overlap between theory of mind and default networks occurred in many regions throughout the cortex. These results imply that the cognitive processes involved in stimulus-driven attention are largely distinct from those in theory of mind and default processing.

Chapter IV: The functional segregation of the inferior frontal junction from the dorsal attention network

Whereas Chapter III functionally segregated the IFJ from the TPJ, another core member of the ventral attention network, Chapter IV aimed to segregate the IFJ from the dorsal attention network. To do so, we examined the activity of the IFJ, FEF, and IPS during an endogenous Posner cueing task with a long delay between the cue and target. This experiment revealed that the IFJ was involved in cue interpretation and response to the target, but not in actively holding attention in the cued location. Put another way, the IFJ set attentional weights, but it was not responsible for maintaining those attentional settings. In contrast, the FEF and IPS were involved in all three phases. A follow-up experiment confirmed that all three regions were sensitive to response selection load. In a final experiment, we examined the roles of these three regions in two different forms of attentional selection: perceptual selection and response selection. Although all three regions were active for both types of selection, only the IFJ and IPS showed a preference for perceptual selection in the right hemisphere and response selection in the left. Taken together, the results from the experiments in Chapter IV suggest that the IFJ, FEF, and IPS have many roles in attention and selection, but the IFJ's transient activation during the first experiment suggests that it exerts control only when changes to current attentional settings are required, perhaps by instructing the FEF and IPS.

General discussion

This dissertation has demonstrated that the IFJ has a unique and important role in the control and coordination of attention and selection. As shown in Figure 1, the IFJ was the only region involved in both stimulus-driven attention and goal-directed attention. Its role in goal-directed attention, however, was shown to be different than the roles of the IPS and FEF. This role was a transient one, suggesting that the IFJ adjusts attentional settings but does not maintain them, as the FEF and IPS do. Such a result suggests that the IFJ sits above the IPS and FEF in an attentional control hierarchy.

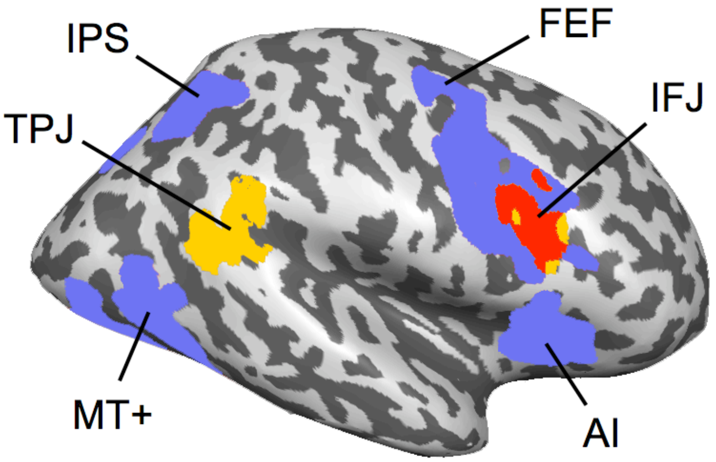

Figure 1. Inflated brain showing activated regions from the Surprise-induced Blindness Experiment (Chapter II). Stimulus-driven attention regions are shown in orange and goal-directed ones in violet. Regions supporting both forms of attention (the IFJ) are red. IPS = Intra-parietal Sulcus, FEF = Frontal Eye Field, TPJ = Temporo-Parietal Junction, IFJ = Inferior Frontal Junction, MT+ = Middle Temporal Complex, AI = Anterior Insula.

Although these findings generally resonate with the attention and control literature, they do invite some important revisions to current models. In an update to their influential model of attentional control, Corbetta and colleagues (Corbetta et al., 2008) conclude that the right IFJ (labeled as middle frontal gyrus--MFG--in their work; the inferior MFG is the superior bank of the IFJ) acts as a relay station between the dorsal attention network and the ventral attention network (see Figure 2). According to this model, the IFJ interrupts ongoing goal-directed attentional processing by modulating activity in the dorsal attention network. This disruption is only considered for stimulus-driven attention. Our results conflict with such a limited role for the IFJ in two ways. First, the IFJ co-activates and presumably interacts with the dorsal attention network during goal-directed behavior. Second, in the Surprise-induced Blindness experiment, the unexpected event disrupted ongoing goal-directed attention without modulating activity in the dorsal attention network. We conclude that the IFJ is more than a relay station; it is a control station, capable of adjusting goal-directed attentional settings itself and of participating with the dorsal attention network in goal-directed attentional processes.

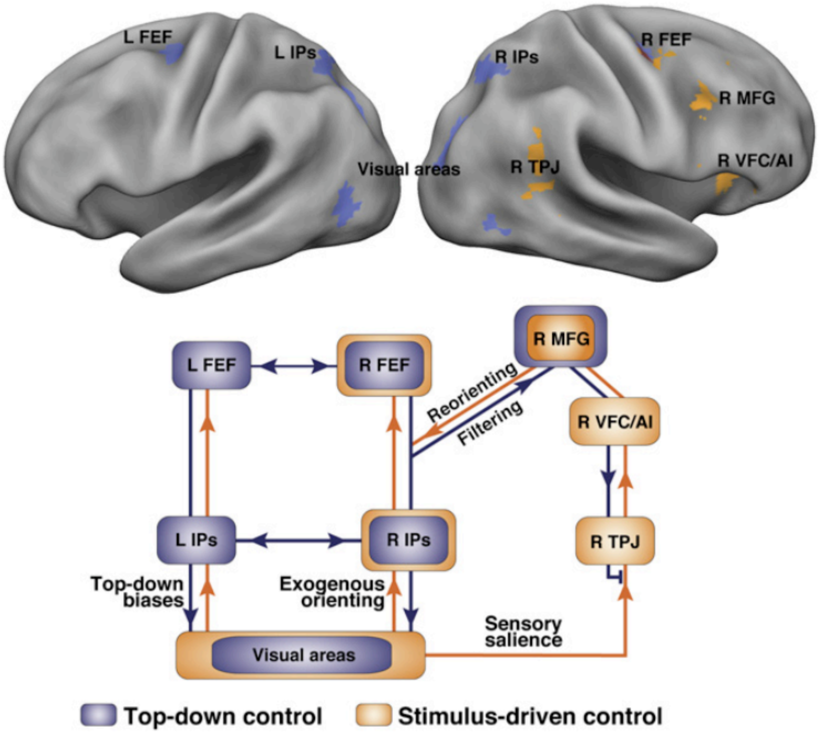

Figure 2. Model of attentional control from Corbetta et al., 2008. IPS = Intra-parietal Sulcus, FEF = Frontal Eye Field, TPJ = Temporo-Parietal Junction, MFG = Middle Frontal Gyrus (the superior bank of the IFJ), VFC/AI = Ventral Frontal Cortex/Anterior Insula.

Other aspects of our results suggest that the dorsal attention network has a more circumscribed role in stimulus-driven attention than that posited in Corbetta et al. (2008). Foremost, we show that the dorsal attention network need not be involved in exogenous orienting when the triggering stimulus does not require a shift of attention. When our unexpected stimuli were presented away from fixation, the dorsal network was robustly activated (Asplund et al., 2010). Studies using singletons presented away from fixation have also observed dorsal attention network activation (de Fockert et al., 2004; Kincade et al., 2005; Peelen et al., 2004), but with the exception of Peelen et al. (2004), they did not find ventral attention network activity. The likely explanation is that the singleton's attention-grabbing effects were weak, especially after multiple presentations. Indeed, ventral attention network activity in our Surprise-induced Blindness experiment showed strong attenuation after only three presentations of the surprise stimulus.

A final difference between our results and the Corbetta et al. (2008) model concerns the degree to which the ventral attention network is right-lateralized. Although we found some evidence of hemispheric specialization in the IFJ, there was no evidence of right-dominant responses in the IFJ or TPJ during stimulus-driven attention. One possibility is that non-spatial reorienting does not reveal a lateralized pattern of activity. The spatial version of the Surprise-induced Blindness task and other studies (Serences et al., 2005; Marois et al., 2000a) have revealed left TPJ activity, so this explanation is not entirely satisfactory. Other task variations yet to be identified likely account for the difference.

Laterality effects were observed when comparing perceptual selection to response selection. For example, the right IFJ was found to be more active for perceptual selection than for response selection, consistent with earlier work with perceptual selection and visuospatial attention (Marois et al., 2000b; Marois et al., 2004a; Serences et al., 2005; Corbetta & Shulman, 2002; Corbetta et al., 2008; Corbetta et al., 1998). More striking than the small laterality effects was the general convergence of perceptual and response selection processes, consistent with previous behavioral, imaging, and neurophysiological work (Marois et al., 2006; Jolicoeur, 1998; Jolicoeur et al., 2001; Arnell & Duncan, 2002; Ruthruff & Pashler, 2001; Gold & Shadlen, 2001; Hernandez et al., 2002; Schall, 2001). Our results confirm that perceptual and response selection processes are closely intertwined, but subtle differences in specialization across the hemispheres do exist.

Despite the IFJ's co-activation with the dorsal attention network in several of this dissertation's experiments, it has not generally been identified with this network (Kastner et al., 1999; Corbetta & Shulman, 2002; Yantis et al., 2002). Our results from the Posner cueing task suggest that the IFJ's activation in the task is transient, indicating that the IFJ supports changes to attentional weights but is not active in maintaining them. Since the dorsal attention network is often identified as the regions that maintain activity in preparation for a stimulus to be presented or an action performed, the IFJ would not have been found with such a contrast (Kastner et al., 1999; Corbetta & Shulman, 2002). Instead, the IFJ may instruct the dorsal attention network as to what attentional settings should be maintained (see Yantis et al., 2002, for a similar idea about the superior parietal lobule's role). Such an instructional role fits well with the suggestion that the IFJ supports low-level forms of cognitive control, which refers to the ability to coordinate behavior in accordance with internal goals (Derrfuss et al., 2005; Brass et al., 2005). It is hypothesized that cognitive control is hierarchically organized (Koechlin et al., 2003; Koechlin & Summerfield, 2007; Badre, 2008; Badre et al., 2009; Badre & D'Esposito, 2009). Our results suggest that attentional control also has a hierarchical organization, with the IFJ above the dorsal attention network. According to this account, the IFJ controls and coordinates this network's activity with the ventral attention network. This conclusion builds upon and extends the existing literature on attentional control by demonstrating how different forms of attention are coordinated and by suggesting that attentional control is hierarchical (Miller & Cohen, 2001; Desimone & Duncan, 1995; Corbetta et al., 2008; Corbetta & Shulman, 2002; Serences et al., 2005; Yantis et al., 2002).

The IFJ's role in coordination extends beyond the control of the two attention networks, as evidenced by its roles in cognitive control (Derrfuss et al., 2005; Brass et al., 2005) and response selection (Dux et al., 2006; Dux et al., 2009; Marois et al., 2006). Rather, a form of coordination appears to be a general feature of the region. I conclude that the IFJ's function is to connect incoming sensory information or internal dispositions to responses, whether they are overt behaviors such as finger movements or covert adjustments such as a change in attentional priorities. In this way, the IFJ acts like a telephone operator routing calls through a switchboard. The power of the IFJ is that this routing need not be obvious. It can forge conceptual connections between physically separate items, using those established connections to reason and select (Diamond, 2006).

Because the IFJ has such a central role in information processing, it is also associated with commonly-observed limitations in processing. These limitations arise because the brain has a restricted capacity of neural processing, meaning that we can only attend or respond to a surprisingly small number of items at any given time (Chun & Marois, 2002). Previous research has linked the IFJ to limitations in response selection, as revealed by the Psychological Refractory Period paradigm (Dux et al., 2006; Dux et al., 2009; Marois et al., 2006; Sigman & Dehaene, 2008), and to failures of visual attention, as demonstrated in both attentional blink (Marois et al., 2000b; Marois et al., 2004b) and contingent capture (Serences et al., 2005) paradigms. Our results from the Surprise-induced Blindness experiment add a stimulus-driven attentional limitation to this list. This limitation was observed in both spatial and non-spatial domains. Taken together, our results resonate well with the proposal that the IFJ is a critical neural substrate of our severely limited attentional capacities (Marois & Ivanoff, 2005).

Future directions

Although this dissertation has elucidated much about the IFJ, much still remains to be learned about its functional and anatomical properties. Foremost, I have suggested throughout this dissertation that the IFJ coordinates activity in other regions. The nature of this interaction, however, is not yet known. One possibility is that the IFJ processes incoming sensory information (from outside the visual domain) and then passes the result of its processing to the dorsal attention network. Such a sequence of events would suggest that the IFJ would activate first, followed by the dorsal attention network. We plan to use functional connectivity measures such as Granger Causality (Rogers et al., 2010) and Dynamic Causal Modeling (Friston et al., 2006) in conjunction with curve-fitting (Henson, 2005) to test whether such a timing relationship exists. Although preliminary results have not yet revealed any timing differences in activity across the regions, further development of these methods is an ongoing priority.

In addition to studying the relationship of the IFJ to the dorsal attention network, another avenue of study would examine its relationship with the TPJ. In Chapter III, I found that these regions were likely performing different functions within stimulus-driven attention because they are dissociable in other tasks such as theory of mind reasoning and the default mode of processing. Both of these tasks recruit the TPJ, suggesting a common function. This common function may involve detecting or maintaining mismatches between internal representations of the current state of the world and imagined alternatives. In contrast, the IFJ's role is likely one of modifying attentional weights. Given these different roles, there are a number of different possible interactions between the IFJ and TPJ during stimulus-driven attention. First, the IFJ may interact with the TPJ to adjust the latter's representations after incoming sensory information requires them to be altered. Second, the IFJ may switch attention to the surprising event so that the TPJ can evaluate it, comparing it against internal predictions and schema. Third, the TPJ may determine that the perceived stimulus does not match expectations and then signal the IFJ to switch attention to it.

Electrophysiological and neuroimaging results do not support this third possibility, though they do not clearly support one of the other hypotheses either. Two evoked response potentials (ERPs) related to stimulus novelty or rarity (P3a and P3b) show different timings in the frontal and temporo-parietal cortex (Bledowski et al., 2004). The IFJ and TPJ are known to support these signals (Bledowski et al., 2004; Horovitz et al., 2002), and those associated with the IFJ generally occur slightly (on the order of tens of milliseconds) earlier than those in the TPJ. Although these results do not distinguish between the first two possibilities for IFJ-TPJ interaction, a clever fMRI experiment could do so. As suggested by the IFJ's transient activation during goal-directed attention, the IFJ may only transiently interact with the TPJ during stimulus-driven attention. Consequently, a study with an "extended surprise" (a continuous episode that disrupts goal-directed attentional processing) may segregate the functions of these two regions. If the IFJ interaction is transient, its activity would quickly fall off during the extended surprise episode, while the TPJ's activity would continue throughout.

In addition to further exploration of IFJ connectivity (both functional and anatomical), the organization and functional localization of the IFJ deserve more study. Foremost, it is currently unknown whether the same tissue is being identified across the many tasks that activate the IFJ. Examination of the Talairach coordinates for peak responses in this region (see Table 1) suggests no consistent differences across task types. This finding is consistent with the underlying anatomy in two ways. First, there is preliminary evidence that the IFJ is cytoarchictetonically distinct from neighboring tissue (Amunts et al., 2004; Amunts et al., 2006), suggesting that there is anatomical specialization that would support functional specialization. Second, the IFJ's location (the junction of the inferior frontal and precentral sucli) has a fairly high degree of anatomical variation across subjects (Derrfuss et al., 2009). Task-switching activity tracked this anatomical variability across subjects. This variability could explain why there is moderate variability in the group averages in Table 1.

Table 1. IFJ peak Talairach coordinates for a sampling of experiments.

Experiment	Left IFJ	Right IFJ
Surprise-induced Blindness (Chapter II, Expt. 1)	-42, 8, 25	40, 6, 27
Spatial Surprise-induced Blindness (Chapter II, Expt. 2)	-38, 7, 27	38, 5, 27
Posner cueing task (Chapter IV, Expt. 1)	-45, 3, 27	45, 5, 27
Perceptual, Response selection (Chapter IV, Expt. 3)	-46, 7, 30	43, 8, 27
Task-switching (Derrfuss et al., 2009)	-39, 2, 32	
Task-switching (Derrfuss et al., 2005)	-40, 4, 30	44, 10, 34
Stroop (Derrfuss et al., 2005)	-40, 4, 32	
Response selection (Dux et al., 2006)	-37, 14, 25	42, 18, 28
Response selection (Dux et al., 2009)	-43, 8, 29	
Perceptual selection (Marois et al., 2000)		48, 8, 35

Naturally, another possibility is that the IFJ contains functional topography, as part of the topography that the prefrontal cortex as a whole is thought to contain (Koechlin et al., 2003; Koechlin & Summerfield, 2007; Badre, 2008; Badre et al., 2009; Badre & D'Esposito, 2009). Further experimentation, perhaps using a within-subjects overlap approach as we did in Chapter III, is needed to reveal the answer.

One possible result of such a study would be a partial functional overlap. What would this result indicate? Partial overlap may reflect spatial gradients in the cell types and properties in a given region (Petrides & Pandya, 2001). Although we tend to think of anatomical regions as distinct, transition zones often mark their boundaries, and the cytoarchitecture is slightly varied across a region's extent. These variations may have functional consequences. I propose that in addition to thinking of regions as defined areas, much like countries on a map, another cognitive model should be employed. A given cognitive function may have a range like that of a species of bird; as the bird dwells in its range because it provides certain resources, the cognitive function is localized to a given region because of the neural resources present.

In addition, partial overlaps may represent the gradual splitting of one region into two or the development of a new region de novo over evolutionary time. For example, marsupials possess no motor cortex, but they do have a motor component embedded in somatosensory cortex (Kaas, 2004; Wong & Kaas, 2009). Placental mammals, however, have a primary motor cortex that contains ever more specific subdivisions as one moves to more complex animals (Kaas, 2004). The functional overlap in the human TPJ among stimulus-driven attention, default mode of processing, and theory of mind reasoning may be developing along similar lines. Perhaps the simple function of comparing sensory information with internal representations is the oldest function, with that function being co-opted for more advanced processing such as theory of mind (Decety & Lamm, 2007). The TPJ may even be evolving toward separate processing units for its different processes, yielding partial functional overlaps for now. Clearly, much anatomical and functional work is required before any of these ideas are proven to be true or false. Nevertheless, the properties of cortex still developing in evolutionary time (Hill et al., 2010), such as the IFJ, can potentially be leveraged to take the next step in associating cognitive function to brain structure.

I began this thesis by asking you to imagine a cockroach, and I find it fitting to close with the same request. After all, while a cockroach lacks the neural processing power to flexibly adapt its behavior, we humans flexibly adapt ours at the sight of one. A scurrying cockroach may disrupt our ongoing goal-directed behavior of fetching something from the refrigerator. We may also have to select an appropriate response to deal with the insect. As I have demonstrated in this dissertation, these abilities are made possible by our highly developed frontal lobes. In particular, they are the province of the inferior frontal junction.

References

Amunts, K. & von Cramon, D. Y. (2006). The anatomical segregation of the frontal cortex: What does it mean for function? Cortex, 42, 525-528.

Amunts, K., Palomero-Gallagher, N., Brass, M., Derrfuss, J., Zilles, K., & von Cramon, D. Y. (2004). A receptor- and cytoarchitectonic correlate of the functionally defined inferior-frontal junction area. Neuroimage, 22 (Supplemental), 50.

Arnell, K. M., & Duncan, J. (2002). Separate and shared sources of dual-task cost in stimulus identification and response selection. Cognitive Psychology, 44, 105-147.

Asplund, C. L., Todd, J. J., Snyder, A. P., & Marois, R. (2010). A central role for the lateral prefrontal cortex in goal-directed and stimulus-driven attention. Nature Neuroscience, 13(4), 507-512.

Badre, D. (2008). Cognitive control, hierarchy, and the rostro-caudal axis of the prefrontal cortex. Trends in Cognitive Science, 12(5), 193-200.

Badre, D., Hoffman, J., Cooney, J. W., & D'Esposito, M. (2009). Hierarchical cognitive control deficits following damage to the human frontal lobe. Nature Neuroscience, 12(4), 515-522.

Badre, D. & D'Esposito, M. (2009). Is the rostro-caudal axis of the frontal lobe hierarchical? Nature Reviews Neuroscience, 10, 659-669.

Bledowski, C., Prvulovic, D., Hoechstetter, K., Scherg, M., Wibral, M., Goebel, R., & Linden, D. E. (2004). Localizing P300 generators in visual target and distractor processing: A combined event-related potential and functional magnetic resonance imaging study. The Journal of Neuroscience, 24(42), 9353-9360.

Brass, M., Derrfuss, J., Forstmann, B., & von Cramon, D. Y. (2005). The role of the inferior frontal junction area in cognitive control. Trends in Cognitive Sciences, 9(7), 314-316.

Brodmann, K. (1909). Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipin Dargestellt auf Grund des Zellenbaues. Barth, Leipzig.

Bunge, S. A. (2004). How we use rules to select actions: A review of evidence from cognitive neuroscience. Cognitive, Affective, & Behavioral Neuroscience, 4(4), 564-579.

Chun, M. M. & Marois, R. (2002). The dark side of visual attention. Current Opinion in Neurobiology, 12, 184-189.

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: From environment to theory of mind. Neuron, 58, 306-324.

Corbetta, M. & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews Neuroscience, 3, 201-215.

Corbetta, M., Akbudak, E., Conturo, T. E., Snyder, A. Z., Ollinger, J. M., Drury, H. A., Linenweber, M. R., Petersen, S. E., Raichle, M. E., Van Essen, D. C., & Shulman, G. L. (1998). A common network of functional areas for attention and eye movements. Neuron, 21, 761-773.

de Fockert, J., Rees, G., Frith, C., & Lavie, N. (2004). Neural correlates of attentional capture in visual search. Journal of cognitive neuroscience, 16(5), 751-759.

Decety, J. & Lamm, C. (2007). The role of the right temporoparietal junction in social interaction: How low-level computational processes contribute to meta-cognition. The Neuroscientist, 13, 580-593.

Derrfuss, J., Brass, M., von Cramon, D. Y., Lohmann, G., & Amunts, K. (2009). Neural activations at the junction of the inferior frontal sulcus and the inferior precentral sulcus: Interindividual variability, reliability, and association with sulcal morphology. Human Brain Mapping, 30(1), 299-311.

Derrfuss, J., Brass, M., Neumann, J., & von Cramon, D. Y. (2005). Involvement of the inferior frontal junction in cognitive control: Meta-analyses of switching and Stroop studies. Human Brain Mapping, 25(1), 22-34.

Desimone, R. & Duncan, J. (1995). Neural mechanisms of selective visual attention. Annual Review of Neuroscience, 18, 193-222.

Diamond, A. (2006). Bootstrapping conceptual deduction using physical connection: Rethinking frontal cortex. Trends in Cognitive Sciences, 10(5), 212-218.

Dux, P. E., Ivanoff, J., Asplund, C. L., & Marois, R. (2006). Isolation of a central bottleneck of information processing with time-resolved fMRI. Neuron, 52, 1109-1120.

Dux, P. E., Tombu, M. N., Harrison, S., Rogers, B. P., Tong, F., & Marois, R. (2009). Training improves multitasking performance by increasing the speed of information processing in human prefrontal cortex. Neuron, 63, 127-138.

Egeth, H. E. & Yantis, S. (1997). Visual attention: Control, representation, and time course. Annual Review of Psychology, 48, 269-297.

Gold, J. I. & Shadlen, M. N. (2001). Neural computations that underlie decisions about sensory stimuli. Trends in Cognitive Science, 5, 10-16.

Hernandez, A., Zainos, A., & Romo, R. (2002). Temporal evolution of a decision-making process in medial pre-motor cortex. Neuron, 33, 959-972.

Hill, J., Inder, T., Neil, J., Dierker, D., Harwell, J., & Van Essen, D. (2010). Similar patterns of cortical expansion during human development and evolution. Proceedings of the National Academy of Sciences, 107(29), 13135-13140.

Horovitz, S. G., Skudlarski, P. & Gore, J. C. (2002). Correlations and dissociations between BOLD signal and P300 amplitude in an auditory oddball task: a parametric approach to combining fMRI and ERP. Magnetic Resonance Imaging 20, 319-325.

Jolicoeur, P. (1998). Modulation of the attentional blink by on-line response selection: Evidence from speeded and unspeeded Task-1 decisions. Memory & Cognition, 26, 1014-1032.

Jolicoeur, P., Dell'Acqua, R. & Crebolder, J. M. (2001). The attentional blink bottleneck. In K. Shapiro (Ed.), The limits of attention: Temporal constraints in human information processing. OU Press, New York, 82-99.

Kaas, J. H. (2004). Evolution of somatosensory and motor cortex in primates. The Anatomical Record Part A: Discoveries in Molecular, Cellular, and Evolutionary Biology, 281A(1), 1148-1156.

Kincade, J. M., Abrams, R. A., Astafiev, S. V., Shulman, G. L., & Corbetta, M. (2005). An event-related functional magnetic resonance imaging study of voluntary and stimulus-driven orienting of attention. The Journal of Neuroscience, 25(18), 4593-4604.

Koechlin, E., Ody, C., & Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. Science, 302, 1181-1185.

Koechlin, E. & Summerfield, C. (2007). An information theoretical approach to prefrontal executive function. Trends in Cognitive Science, 11(6), 229-235.

Marois, R., Leung, H.-C., & Gore, J. C. (2000a). A stimulus-driven approach to object identity and location processing in the human brain. Neuron, 25, 717-728.

Marois, R., Chun, M. M., & Gore, J. C. (2000b). Neural correlates of the attentional blink. Neuron, 28, 299-308.

Marois, R., Chun, M. M., & Gore, J. C. (2004a). A common parieto-frontal network is recruited under both low visibility and high perceptual interference conditions. Journal of Neurophysiology, 92, 2985-2992.

Marois, R., Yi, D.-J., & Chun, M. M. (2004b). The neural fate of consciously perceived and missed events in the attentional blink. Neuron, 41, 465-472.

Marois, R., Larson, J. M., Chun, M. M. & Shima, D. (2006). Response-specific sources of dual-task interference in human pre-motor cortex. Psychological Research, 70(6), 436-447.

Peelen, M. V., Heslenfeld, D. J., & Theeuwes, J. (2004). Endogenous and exogenous attention shifts are mediated by the same large-scale neural network. Neuroimage, 22, 822-830.

Petrides, M. & Pandya, D. N. (2001). Comparative cytoarchitectonic analysis of the human and macaque ventrolateral prefrontal cortex and coritocortical connection patterns in the monkey. European Journal of Neuroscience, 16, 291-310.

Ruthruff, E. & Pashler, H. (2001). Perceptual and central interference in dual-task performance. In K. Shapiro (Ed.), The limits of attention: Temporal constraints in human information processing. (Oxford University Press, New York), 100-123.

Schall, J. D. (2001). Neural basis of deciding, choosing, and acting. Nature Reviews Neuroscience, 2, 33-42.

Serences, J. T., Shomstein, S., Leber, A. B., Golay, X., Egeth, H. E., & Yantis, S. (2005). Coordination of voluntary and stimulus-driven attentional control in human cortex. Psychological Science, 16(2), 114-122.

Sigman, M. & Dehaene, S. (2008). Brain mechanisms of serial and parallel processing during dual-task performance. The Journal of Neuroscience, 28(30), 7585-7598.

Wong, P. & Kaas, J. H. (2009). Architectonic subdivisions of neocortex in the short-tailed opossums (Monodelphis domestica). Brain, Behavior and Evolution, 73(3): 206-228.

Yantis, S., Schwarzbach, J., Serences, J. T., Carlson, R. L., Steinmetz, M. A., Pekar, J. J., & Courtney, S. M. (2002). Transient neural activity in human parietal cortex during spatial attention shifts. Nature Neuroscience, 5, 995-1002.