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The Impact of Motivation on Object-Based Visual Attention Indexed by Continuous Flash Suppression.

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Abstract

Motivationally-relevant stimuli summon our attention and benefit from enhanced processing, but the neural mechanisms underlying this prioritization are not well understood. Using an interocular suppression technique and functional neuroimaging, this work has the ultimate aim of understanding how motivation impacts visual perception. In Chapter 2a, we demonstrate that novel objects with a more rich reward history are prioritized in awareness more quickly than objects with a lean reward history. In Chapter 2b, we show that faces are prioritized in awareness following social rejection, and that the amount faces are prioritized correlates with individual differences in social motivation. Chapters 3 & 4 use a combination of functional neuroimaging and flash suppression to suppress fearful faces and houses from awareness. Using binocular rivalry and motion flash suppression in Chapter 3, we find that suppressed fearful faces activate the amygdala relative to suppressed houses, and the amygdala increases coherence with a network of regions involved in attention, including bilateral pulvinar, bilateral insula, left frontal eye fields, left inferior parietal cortex, and early visual cortex. Using the more robust technique, continuous flash suppression, in Chapter 4, we find no differentiation between stimuli based on mean amygdala responses. However, we show increased connectivity between the amygdala, the pulvinar, and inferior parietal cortex specific to fearful faces. Overall, these results indicate that motivationally-relevant stimuli activate the amygdala prior to awareness. Enhanced connectivity between the amygdala and regions involved in attention may underlie the enhanced processing seen for salient stimuli.

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THE IMPACT OF MOTIVATION ON OBJECT-BASED VISUAL ATTENTION INDEXED

BY CONTINUOUS FLASH SUPPRESSION.

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Motivationally-relevant stimuli summon our attention and benefit from enhanced processing, but the neural mechanisms underlying this prioritization are not well understood. Using an interocular suppression technique and functional neuroimaging, this work has the ultimate aim of understanding how motivation impacts visual perception. In Chapter 2a, we demonstrate that novel objects with a more rich reward history are prioritized in awareness more quickly than objects with a lean reward history. In Chapter 2b, we show that faces are prioritized in awareness following social rejection, and that the amount faces are prioritized correlates with individual differences in social motivation. Chapters 3 & 4 use a combination of functional neuroimaging and flash suppression to suppress fearful faces and houses from awareness. Using binocular rivalry and motion flash suppression in Chapter 3, we find that suppressed fearful faces activate the amygdala relative to suppressed houses, and the amygdala increases coherence with a network of regions involved in attention, including bilateral pulvinar, bilateral insula, left frontal eye fields, left inferior parietal cortex, and early visual cortex. Using the more robust technique, continuous flash suppression, in Chapter 4, we find no differentiation between stimuli based on mean amygdala responses. However, we show increased connectivity between the amygdala, the pulvinar, and inferior parietal cortex specific to fearful faces. Overall, these results indicate that motivationally-relevant stimuli activate the amygdala prior to awareness. Enhanced connectivity between the amygdala and regions involved in attention may underlie the enhanced processing seen for salient stimuli.

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CHAPTER 1: Introduction

Everything beckons to us to perceive it,

murmurs at every turn 'Remember me!' –Rainer Marie Rilke

We live in a world that is rich with visual information. Because our visual system is so efficient, it is easy to forget that what we are not simply walking video cameras, obtaining high-resolution and continuous snapshots of our environment. Rather, we "see" a reconstructed version of the world- a representation that is much more impoverished than one might assume.   Attention is the mechanism by which the brain deals with the bombardment of information in our environment. Frequently described as a filter, attention characterizes the way we select meaningful information from the noisy sensory world in which we live. Theories of attention have proposed that at a given moment, we have a limited capacity of mental resources to allocate to any given task. Thus, to make sense of our environment, we must filter out irrelevant information in order to process pertinent information.

Theories of attention additionally propose that computations are done across a visual scene and regions of highest salience are determined based on inputs from primary visual feature-based maps (Itti & Koch, 2000). The conceptual outcome of this process is a salience map, which is thought to automatically elicit orienting responses

and ultimately drive target selection. Yet, an efficient perceptual system must flexibly respond to a multitude of stimuli in a variety of environments. Thus, determining the most relevant stimuli in complex settings likely relies on the coordination of a distributed network of cortical and limbic regions involved in various aspects of perception. Recently, it has been proposed that stimulus-driven salience maps are integrated with non-visual features, such as observer goals and object relevance in order to determine attention allocation (Fecteau & Munoz, 2006). Thus, a combination of stimulus salience (determined by physical properties) and relevance (determined by goal-oriented strategy, learned associations, or motivation) likely contributes to a comprehensive priority map for target selection. Consistent with this idea, recent work has focused on a more systems-based perspective, reflecting an interaction of limbic and emotional modulation of non-conscious attention (Pessoa & Adolphs, 2010). Beyond early visual features, it is unknown what cognitive and motivational features are capable of influencing such a priority map and mechanisms by which this influence may be accomplished have not yet been elucidated.

Anecdotally, we know that personal experience and motivations influence the objects we pay attention to. Also, studies in psychology have indicated that individual experiences and motivations impact what we see. For example, people overestimate the size of a bottle of water when they are thirsty (Balcetis & Dunning, 2010). In a mood induction paradigm, children primed with sad music were faster to locate a simple shape in a complex figure, indicating an effect of mood on global/local perception

(Schnall, Jaswal, & Rowe, 2008). These studies indicate that motivational state impacts

attention. However, more precisely controlled, psychophysical studies are necessary for

identifying the precise mechanisms by which altered motivation produces this influence.

1.1 A motivational framework: Factors that influence object prioritization

To determine the most relevant stimuli in our environment, the brain must

weigh a combination of reflexive and suppressive mechanisms that interact to guide the

eye towards a central focus of attention. Stimulus driven or exogenous attention is

known as "bottom-up" attention, indicating that the attentional processing is driven by

low-level sensory properties of the objects themselves. Goal-directed or exogenous

attention (sometimes referred to as "top-down") refers to a process informed by

intrinsic factors from the observer, including memory, expectations, and goal-directed

behavior. Bottom-up mechanisms are thought to be more closely linked with automatic

salience, while controlled suppression of these automatic processes are linked to top-

down control. Both of these highly interactive mechanisms help to determine the

salience of an object.

A useful framework for factors determining visual attention (and thus, influenced

by stimulus salience) is one of motivational state. We know that low-level visual

features drive automatic visual attention, but beyond these features, there are multiple

factors that may influence whether a stimulus is prioritized, including primary

reinforcers (food, sex), secondary reinforcers (learned associations), and state-dependent motivations (strategy). Several studies have demonstrated the influence of these factors on visual attention. Adults responded with increased spatial attention to pictures depicting food stimuli relative to tools only after food and water deprivation (Mohanty, Gitelman, Small, & Mesulam, 2008). Arousing, erotic images rendered invisible with CFS can attract or repel observers' attention, influenced by gender and sexual orientation (Jiang, Costello, Fang, Huang, & He, 2006). Learned associations also influence visual attention: Advantages in overcoming suppression induced by CFS have been demonstrated for Chinese vs. Hebrew characters for Chinese observers, and vice-versa for Hebrew observers (Jiang, Costello, & He, 2007). In a study pairing biological reward with line gratings suppressed from awareness using CFS, individuals were more accurate in discriminating gratings previously paired with water rewards (even when "unseen") (Seitz, Kim, & Watanabe, 2009). Thus, results from several veins of research implicate contributions of food, sex, learned associations, and strategy to stimulus prioritization.   Finally, top-down strategies must be considered, as goal-directed selection induces substantial biases. A strong example of this is the observation that participants will "see" a face pattern in complete noise (Smith, Lestou, Gosselin, & Schyns, 2009). This perception may be induced by internal representations, driven by a search template mechanism in object-selective cortex. Evidence for this search template mechanism comes from studies demonstrating that activation patterns in object-selective cortex contain information regarding target category in a search

detection task, regardless of whether stimuli were task-relevant or within the focus of spatial attention (Peelen, Fei-Fei, & Kastner, 2009).

1.2 Social Motivation

When thinking about motivation in research, it is perhaps most common to think of motivation towards food or sex, or even the impact of learning reward associations. One type of motivation that is important for the following studies but that has not been well-defined until recently is that of social motivation (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012). This is the natural propensity to attend preferentially to the social world. This proclivity is present from early in life and can impact development and numerous behaviors. For example, infants have a preference for human speech over noise and prefer direct eye contact over averted eyes (Gliga & Csibra, 2007). Circuits involved in social motivation appear to overlap with other motivational circuits, as viewing smiling faces activates brain structures that also respond to rewards such as food and money (Aharon, Etcoff, Ariely, Chabris, O'Connor, & Breiter, 2001). Social interest can be so rewarding that humans experience a state similar to physical pain when socially excluded (Eisenberger, Lieberman, & Williams, 2003). Being deprived of social experiences can have detrimental health effects. Chronically lonely people as well as people induced to be lonely have been found to pay more attention to social cues (Bernstein, Young, Brown, Sacco, & Claypool, 2008; Pickett, Gardner, & Knowles, 2004), even to the extent of inventing humanlike agents in their environment (e.g., seeing

faces in the clouds, anthropomorphizing pets, feeling the presence of supernatural agents) (Epley, Akalis, Waytz, & Cacioppo, 2008). Although the exact origin of these phenomena remains to be delineated, it has been argued that they arise through the increased attention to social cues activated by social disconnection (Jonason, Webster, & Lindsey, 2008). A simplified view of brain structures involved in social motivation are the amygdala (important for orienting automatically to social stimuli) and the orbitofrontal cortex and other reward structures for computing the value of social stimuli and generating 'wanting' and 'liking' signals important for social learning. With regard to the following experiments, the amygdala's involvement in bottom-up prioritization of biologically-relevant stimuli is particularly significant.

1.3 Neural information flow, the amygdala, and parietal cortex

As we shift to a discussion of the neural regions involved in attentional selection, it is necessary to emphasize an alternate meaning of the terms "bottom-up" and "top-down". In terms of anatomy, this refers to the direction of information flow, with bottom-up indicating feedforward information flow through a hierarchy and top-down influences equated with feedback connections. For example, within an overly simplified view of the visual system, information in the feedforward direction would travel from the retina→ thalamus → V1 → V2, with feedback occurring in the opposite direction. This differentiation becomes important (and potentially quite confusing) when discussing information processed outside of awareness. For example, if a stimulus, such

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as a fearful face, is processed with increased efficiency due to some meaning the observer attributes to the stimulus, this would be considered a top-down (user-driven) influence. However, anatomically, this could be attributed to either a bottom-up (feed-forward) or top-down (feed-back) mechanism. This differentiation becomes important when considering the potentially automatic activation of subcortical regions involved in relevance processing. In particular, a continuing question in processing stimuli without awareness is whether a signal can reach the amygdala in a feed-forward mechanism that bypasses cortex.

This idea was originally proposed as a parallel subcortical visual pathway that proceeds from the retina to the superior colliculus, the pulvinar (a posterior nuclei of the thalamus), and onto the amygdala. This pathway is thought to process low spatial frequency information quickly in order to provide fast yet coarse visual information to aid in threat detection (Johnson, 1990, 2005). Evidence for the existence of this pathway comes from patients with "blindsight", who exhibit residual localization and detection abilities, despite primary visual cortex lesions (Kentridge, Heywood, & Weiskrantz, 1999, 2004; Kentridge, Nijboer, & Heywood, 2008). Such patients can also experience "affective blindsight", in which the emotion of faces presented in their blind hemi-field is reported with above chance accuracy (De Gelder & Hadjikhani, 2006; De Gelder, Vroomen, Pourtois, & Weiskrantz, 1999). These abilities are thought to emerge from intact subcortical processing, capable of performing rudimentary visual processing, as well as emotional information extraction.

However, because of the profuse bidirectional connections in the brain, it is nearly impossible to limit information processing to a specific region. For example, if information reaches the pulvinar via the superior colliculus, the pulvinar may still use its abundant cortical connections to perform computations necessary to fully evaluate the signal. For this reason, there has been a shift towards examining networks of information, as opposed to responses of individual regions. This shift is especially apparent in research of motivation, since these processes quite clearly involve numerous interactive regions. In fact, it has been suggested that it is not the function of singular regions that contribute to altered attention due to motivational changes, but the increased coherence and communication between regions in distinct networks (Kinnison, Padmala, Choi, & Pessoa, 2012).

The amygdala, an almond-shaped nucleus within the medial temporal lobes, has been consistently associated with emotional responses, and has a role in fear conditioning (LeDoux, 1998). Essential for arousal, the amygdala mediates the formation of visual-reward associations by assigning significance to environmental stimuli (i.e. "emotional learning") (Anderson & Phelps, 2001). It can be activated by conscious facial expressions, as well as those presented outside of conscious awareness (Pasley, Mayes, & Schultz, 2004; Whalen et al., 2004; Whalen et al., 1998). With dense reciprocal ventral visual connections, the amygdala may represent a key node in motivational networks, particularly those involved in social motivation. While originally implicated in emotion and fear, it has been recently proposed that the amygdala plays a more general role in

assessing the biological relevance of a stimulus and guiding attention towards salient

regions of these biologically relevant stimuli (Pessoa & Adolphs, 2010). Evidence for this

hypothesis comes from a patient with bilateral amygdala lesions who does not show the

automatic orientation towards the eye region of faces that is seen in healthy adults

(Tsuchiya, Moradi, Felsen, Yamazaki, & Adolphs, 2009). Other evidence comes from the

previously described patients with "blindsight", who show amygdala activation to

relevant stimuli presented in their blind hemifield (Morris, DeGelder, Weiskrantz, &

Dolan, 2001).

A final region that deserves mention prior to the discussion of the experiments

to follow is parietal cortex. Parietal cortex is generally associated with visual attention

and spatial processing. Specific sub-regions have been associated with visual attention,

linking vision to action, numerical calculation, mental rotation, and even a general

involvement in human memory. Parietal cortex activation has also been associated with

stimulus salience in a wide variety of cognitive and sensory tasks in primate and human

literature and is a likely candidate region for housing a salience map. For example,

parietal cortex is activated in response to detection of salient items embedded in a

sequence of events (i.e. "oddball paradigms") (Balan & Gottlieb, 2006). Increased

parietal activity is associated with the probability that a particular response will result in

the gain (or reward) in monkeys (Platt & Glimcher, 1999). In humans with partial cortical

blindness, parietal activation is enhanced when non-conscious aversive stimuli are

presented to the patients' blind field (Anders, Birbaumer, Sadowski, Erb, Mader, Grodd,

& Loztze, 2004). Typically referred to as "association cortex" due to its complex, multimodal responses, parietal cortex may represent a region suitable for integrating primary visual object features along with motivation and learned associations.

1.4 Investigating Implicit Perception

To measure the influence of motivation on attention, research in this field has relied on the phenomenon of binocular rivalry, in which conflicting monocular images presented to each eye result in perceptual awareness of a dominant image. This perceptual dominance fluctuates, such that each image is perceived for a few seconds, oscillating spontaneously. The duration at which a stimulus remains dominant has been taken as a correlate of the stimulus' meaning or salience. Although the underlying neural mechanisms regarding rivalry are still under debate (Tong, Meng, & Blake, 2006), this phenomenon has been utilized to investigate the brain structures important for visual awareness. When a stimulus is completely suppressed from awareness, any processing is thought to reflect more automatic cognitive processes.

Neuroimaging visual processing in the absence of awareness presents a number of methodological challenges. Chief among these is the difficulty in suppressing stimuli from awareness for long durations. The popular suppression technique of backward masking is insufficient for complete disruption of the ventral visual pathway, and binocular rivalry is only capable of disrupting cortical processing for short periods of

time, making functional neuroimaging data difficult to interpret.

More recently, continuous flash suppression (CFS) has been utilized to manipulate or enhance dominance of one percept for longer durations (Tsuchiya & Koch, 2005). CFS consists of a changing pattern (mondrian) flashed to one eye at a rate of 10 Hz. This prevents the perception of a stimulus presented to the opposite eye for up to several minutes, and revealing aspects of stimuli that can be processed even before awareness. This method can be used in several ways: (1) A prime stimulus can be suppressed from awareness using CFS and the impact of this non-conscious prime on a conscious percept assessed, (2) A stimulus of interest can be presented to the opposite eye of the mondrian pattern and the time for the stimulus to overcome suppression and "break through" to awareness used as an index of stimulus value or meaning, (3) A CFS task presented while participants undergo fMRI can be used to measure the neural correlates of object processing in the absence of awareness.

1.5 Previous Work using CFS

Previous work in non-conscious object processing has focused on one of two domains: (1) examining the prioritization of objects based on the dorsal/ventral stream dichotomy and (2) examining the influence of brain regions involved in the automatic processing of emotion-laden stimuli. The first of these domains has exclusively used the priming CFS method described above to explore the hypothesis that information about

tools are processed in the brain faster based on their associations with the dorsal stream and "vision for action". Thus, under this framework, activation to non-conscious stimuli in parietal cortex is typically thought to underlie semantic category distinctions and a role for manipulation in service of comprehension of certain stimuli (tools compared to animals, for example). In a seminal study, Fang & He found that information can break through interocular suppression and reach the dorsal processing stream, even without stimulus awareness. (Fang & He, 2005) Almeida et al. substantiated this finding with a study in which priming effects were observed for objects associated with dorsal stream processing (i.e. tools), even when primes were rendered non-conscious with flash suppression(Almeida, Mahon, Nakayama, & Caramazza, 2008). In a follow-up study, Almeida et al suggest that these dorsal stream computations reflect motor-relevant information that influences identification of manipulable objects (Almeida, Mahon, & Caramazza, 2010).

Another set of experiments explores implicit processing of motivational stimuli without awareness and several studies have demonstrated the influence of motivational factors on visual attention. Using the CFS priming paradigm in conjunction with fMRI, arousing, erotic images rendered invisible with CFS were found to attract or repel observers' attention, influenced by gender and sexual orientation (Jiang, Costello, Fang, Huang, & He, 2006). Even without awareness, food and water deprived observers can learn to discriminate a particular line grating that has been paired with an imperceptible drop of water (Seitz, Kim, & Watanabe). Advantages in overcoming suppression induced

by CFS have been demonstrated for upright vs. inverted faces (Jiang, Costello, & He, 2007), fearful vs. neutral faces, and direct vs. averted gaze. The influence of motivation has even been shown to be state-dependent. For example, a recent study found that individuals who had fasted perceived words that were associated with food items faster than non-food words (Radel & Clément-Guillotin, 2012). Thus, results from several veins of research implicate contributions of motivational relevance to stimulus prioritization in breakthrough from interocular suppression.

Overall, CFS is a powerful suppression method, allowing for more behaviorally precise responses to the fluctuations of rivalrous stimuli. We incorporate the b-CFS technique and CFS in combination with fMRI in the following chapters.

1.6 Experimental Approach

The goal of this dissertation was to examine the impact of various motivational factors on object-level prioritization using continuous flash suppression, with the hope that this work will serve as a first step towards better understanding motivated attention and ultimately, pathologically (un)motivated attention. We begin, in Chapter 2a, by first establishing that objects that only differ in motivation (learned monetary reward value) result in altered prioritization as measured with a break from CFS paradigm. Through a training study, participants were visually exposed to two families of stimuli, while one family was more highly associated with reward, creating one family

with a rich reward history and one with a lean reward history. We then investigated

whether subjects became aware of stimuli faster when associated with a rich (compared

to lean) reward history. This is the first novel-object/reward training study of its kind

and we sought to examine whether stimuli with only a difference in value could impact

the rate at which objects are prioritized in awareness. An effect of reward history would

provide evidence that reward value of stimuli contributes to stimulus prioritization and

that this process occurs prior to awareness. This also indicates that CFS is a useful

method for examining differences in motivation on object prioritization.

In order to influence the motivational value of a stimulus, one can 1) reward a

stimulus to change its reinforcing value or 2) alter baseline homeostasis to increase

motivation towards the deprived stimulus. Having established that break from CFS is

valid to measure differences in motivation by changing an objects reinforcing value in

Chapter 2a, we then examine whether altering baseline homeostasis can also result in

changes in object prioritization as measured with CFS. In Chapter 2b, social homeostasis

was altered using a priming technique in which participants wrote about a time in their

life where they experienced social exclusion or social acceptance. The dependent

variable was the difference in breakthrough speed between houses (a non-social

stimulus) and faces (a social stimulus). Participants were randomly assigned to a social

rejection or a social acceptance condition, which allowed us to measure the effect of the

subject's current social state on preconscious processing of social cues. More generally,

this experiment allowed us to assess whether differences in object-based prioritization occur before awareness, following state-based changes in motivation.

In Chapter 3, we turn to the neural correlates of processing motivational stimuli without explicit awareness. That is, we know from the studies outlined in Chapter 2 that certain stimuli benefit from enhanced processing earlier in awareness. What brain regions participate in this process? To answer this question, we used a combination of binocular rivalry and motion flash suppression to suppress fearful faces and houses from awareness for the duration of an fMRI scan. Participants performed an orthogonal task in the scanner (detecting whether the first letter of a centrally presented word was a vowel or consonant), while fearful faces and houses were presented to their opposite eye, unbeknownst to the participant. Because participants are performing the vowel-detection task in all blocks, the only difference between the blocks is the stimulus type presented (fearful faces or houses). By presenting two categorically distinct stimuli while participants undergo fMRI, category-specific activity can be isolated via cognitive subtraction. We reasoned that any category-specific differences would reflect altered stimulus-driven attention allocated to a stimulus category before awareness. Thus, this experiment allowed us to assess whether there are neural differences between motivational and non-motivational stimuli processed before awareness.

In Chapter 4, we consider whether inducing a more robust state of suppression will help to elucidate the brain regions impacted earliest in the process of visual selection. More specifically, Chapter 4 uses continuous flash suppression presented

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through specialized dual display fMRI safe goggles, which allowed us to ensure that no information is 'leaking through' certain wavelengths of the anaglyph glasses. We additionally optimize by adding a no-stimulus control condition and presenting the stimuli at a smaller size- since larger rivalrous stimuli can suffer from piecemeal breakthrough. Using these optimizations, we can examine whether stimulus information can reach the amygdala even under conditions of robust suppression and potentially isolate the earliest regions that contain differential object-based information.

Our motivations impact our visual reconstructions of the world- thus, what we "see" is influenced by our bodily state and goals even before we are aware of the visual stimulus. Thus, taken together, the work presented in Chapters 2-4 sought to shed light on some of the types of motivational associations that are capable of influencing object prioritization and then neural concomitants of this prioritization process.

CHAPTER 2: Behavioral Studies with CFS

A. Reward Associations Modulate Awareness of Novel Objects

Abstract

Although we clearly attend to stimuli that are high in value (i.e. faces, objects of interest), reward value in the natural environment is highly conflated with visual experience. Over time, the objects we find the most rewarding are attended more frequently, consequently altering our visual experience with certain percepts more than others. Because reward value impacts visual experience, it remains difficult to disentangle the effect of each individually on object prioritization. In the current study, novel visual objects were paired with monetary reward during a training task in which one category was associated with monetary reward more than another category. We then used a break from continuous flash suppression paradigm to examine whether perceptual mechanisms that control access to visual awareness incorporate the previous reward history of an object. Results show that subjects become aware of stimuli faster when they have been associated with a more rich reward history and suggest that reward value is a dimension that is processed prior to awareness.

Introduction

To deal with a cluttered visual world, visual attention has a capacity limit, through which only the most salient information is extracted. That is, the spatial locations and objects with the most relevant information are prioritized above other less-relevant parts of a visual scene- in order to select and attend to the most informative visual input. Conceptually, this has been described as a global attention priority map that receives inputs from various low-level feature layers, including orientation, color, and luminance (Treisman & Gelade, 1980). Computational algorithms based on such an approach can accurately predict regions of an image that will capture attention, based on a combination of low-level feature inputs in a winner-take-all mechanism (Itti & Koch, 2000). Although these visual salience algorithms are not new, it is increasingly being realized that factors beyond visual salience influence attentional prioritization. For example, in an overt search task of line orientation gratings, participants associated two different line orientations with a specific monetary value. Stimulus contrast was varied by trial to further modulate the visual salience of the valuable stimuli. The best model of the data was one in which observers combined both the reward value and the salience of lines to achieve optimal search (Navalpakkam, Koch, Rangel, & Perona). Even when features with associated value are no longer useful, they continue to attract attention. For instance, when people were trained to associate

a reward value with a particular colored shape, this color continued to distract observers even after the color feature was no longer relevant to the task (Anderson, Laurent, & Yantis, 2011).

The brain can also attend to certain aspects of visual stimuli prior to awareness, a process that is influenced by reward. Awareness can be modulated using interocular suppression techniques that prevent awareness of stimuli, although the stimulus of interest is still processed by the retina and some regions of the brain. Suppression methods make use of the phenomenon of binocular rivalry, which refers to the fact that when conflicting monocular images are presented to each eye, an observer is only perceptually aware of one image. Perception can be biased towards one stimulus (deemed the dominant stimulus) by increasing the visual attributes (e.g. contrast, luminance, or motion) of one stimulus relative to another (Tsuchiya & Koch, 2005). In a previous study using continuous flash suppression (CFS), participants learned to discriminate a line orientation that was associated with a biological reward (Seitz, Kim, & Watanabe, 2009). Participants were never aware of the reward (imperceptible drops of water) or the stimulus (line orientation suppressed with CFS), indicating that reward can influence discrimination in a feature-based manner, in the complete absence of awareness. However, it remains unknown whether the reward value of complex visual objects influences prioritized selection.

In Seitz, Kim, & Watanabe (2009), participants remained unaware of the stimuli for the duration of the experiment. Another useful method employing the CFS technique is the break from continuous flash suppression (b-CFS) paradigm (Jiang, Costello, & He, 2007). In this paradigm, the contrast of the dominant, suppressive image is ramped down while the contrast of the stimulus of interest is ramped up. The salience of the non-dominant stimulus can then be quantified by the time it takes the participant to perceive the non-dominant stimulus. If the effectiveness of suppression differs between two stimuli, differences are thought to reflect dimensions that are processed prior to awareness, thus causing one stimulus to break through faster than the other. Multiple dimensions appear to influence the speed at which objects break through suppression, including motivational meaning. Fearful faces (highly motivational) break through faster than neutral expressions (Yang, Zald, & Blake, 2007). Similarly, direct gaze breaks through faster than averted gaze, potentially due to the value of direct gaze as a motivational approach signal (Stein, Senju, Peelen, & Sterzer, 2011). However, visual experience can also influence differential prioritization. For example, familiar orthographic characters break through faster than unfamiliar ones (Jiang, Costello, & He, 2007). Thus, it remains unclear whether a purely motivational dimension can influence object prioritization prior to awareness in stimuli equated for visual experience and low-level visual features.

The current study examines the influence of motivation (monetary reward history) on how quickly novel visual objects gain access to awareness. Participants were introduced to two novel "categories" of stimuli. Stimulus category consisted of 4 objects that share a common template of physical characteristics, but are distinguishable from each other (see Fig 1A). Participants first learned about the stimuli in a training procedure that consisted of a reward-induced performance bias experiment, during which they performed a forced-choice categorization task. Correct responses were rewarded on half of the trials, while a bias towards one family of stimuli was introduced, unbeknownst to the participant. This bias was counterbalanced, such that half of the participants received more rewards for stimuli in Category A and half received more rewards for stimuli in Category B. Following the reward bias experiment, a post-training procedure consisted of a b-CFS task that assessed whether stimuli with a more rich reward history were prioritized faster than those with a meager reward history.

Materials & Methods

Novel Object Stimuli

Eight stimuli were selected from the novel objects (called "Ziggerins") used in Wong, Palmeri, & Gauthier (2009). Gray scale versions of these stimuli were used in both the training procedure and the break from continuous flash suppression task. The

stimuli were divided into two groups, Ziggerin Category A and Ziggerin Category B (see

Figure 1A).

Subjects

Informed written consent was obtained from 42 undergraduate students (16

men, 24 women; age 24.2 ($\pm$3.1) years) recruited from the surrounding community of

Philadelphia, including students at nearby universities (Drexel, University of

Pennsylvania). All participants received $10 per hour for participation in this study ($+$

additional monetary incentive for rewards during the study). The study was approved by

the IRB at the Children's Hospital of Philadelphia. Two participants were excluded from

the study due to inability to focus the 2 screens into one image. Twenty-two

participants were randomly assigned to Training Group A or Training Group B. The

training group letter corresponded to the family of stimuli that received the more rich

reward contingencies. Another 18 participants did not undergo the training paradigm to

learn reward associations with the novel objects, but completed the identical test

procedure as that given to the training groups. Therefore, at test, the control groups

had never seen the novel stimuli. These Control participants were included to ensure

that low-level visual differences between the novel stimuli did not influence

breakthrough from suppression.

Training Procedure: Object-Reward pairing

The goal of the training procedure was to expose participants to all of the novel

stimuli equally, such that visual experience was equated across groups, while controlling

reward associations with the objects. Participants were given verbal instructions about

the task and told that the aim of the task was to earn money by pressing the correct

button corresponding to each object category. Participants were not exposed to the

novel stimuli prior to the training task. Instead, they had to use the feedback from the

task to learn to discriminate the stimuli.

The task consisted of 3 blocks of 100 trials and was adapted from Pizzagalli, Jahn,

& O'Shea (2005). Each trial started with the presentation of a fixation cue (Figure 1).

After 500 msec, an object appeared in the center of the screen for 100 msec.

Participants were asked to identify which type of object had appeared by pressing a

particular key on the keyboard (labeled with colored stickers). For each block, both

categories of objects were presented equally often in a randomized sequence. An

asymmetrical reinforcer ratio (the relative number of reinforcers received after a given

correct response vs. another correct response) was used to produce a response bias. In

this task, the only type of feedback provided was reward feedback for correct

responses. Subjects were specifically instructed that not all correct responses would

receive reward feedback. For each block, 40 correct trials were followed by reward

feedback (picture of a coin indicating 5 cents had been won), presented for 1750 msec

immediately after the correct response. For half of the participants, correct

identification of Ziggerin Category A was associated with three times more positive

feedback (30 of 40) than correct identification of Ziggerin Category B (10 of 40). For the

other half of participants, the contingencies were reversed. A controlled reinforcer

procedure was used so that reward feedback was given according to a pseudorandom

schedule that determined which specific trials were to be rewarded for correct

identifications. If a subject failed to make a correct identification in a trial for which

reward feedback was due according to the schedule, the feedback was delayed until the

next correct identification of the same stimulus type. For the entire task, participants

could earn an additional $6, based on task performance.

Post-training Procedure: Continuous Flash Suppression

Noise images were generated with Matlab and presented using Psychopy.

Participants viewed the stimuli through two OLED SVGA microdisplays mounted to a

Z800 3DVisor (800 x 600 per display, at 85Hz), spanning a visual angle of 32 degrees

horizontally and 24 degrees vertically. Visual stimuli were 24 images of novel objects,

including the 8 stimuli from training and 16 other foil stimuli, which were drawn from

other Ziggerin families (Wong et al., 2009). Each stimulus was repeated 3 times, for a

total of 96 trials. At the start of each trial, a centrally presented cross served as a fixation point. A full contrast dynamic noise pattern was presented to each eye at the beginning of a trial. Then, the test image was presented to the opposite eye at a random location within a region corresponding to the location of the noise image. The contrast of the test image was systematically ramped up from 0 to 100% over a period of 10 seconds, while the noise image was ramped down at the opposite rate. Test images subtended 5.2 degrees by 7.8 degrees visual angle and were presented in a random position either to the left or to the right of fixation. Observers pressed a key affixed with a left or right arrow image, corresponding to the side of fixation on which the test image appeared. They were instructed to respond to the appearance of any part of a test image as soon as possible, even if they were unable to identify the precise content of the image.

Results

Training Procedure: Object-Reward pairing

Both training groups showed a significant increase in overall accuracy from Block1 to Block 3 (Group A, $t(9)=6.04$, $p=0.0002$, $d=1.17$; Group B, $t(10)=4.37$, $p=0.001$, $d=1.35$), demonstrating that participants learned the appropriate response for each family of stimuli. Both groups also became significantly faster at the task over the course of the experiment (Group A, $t(9)=3.38$, $p=0.008$, $d=1.33$; Group B, $t(10)=3.39$,

p=0.007, d=0.88). There were no significant differences between the two groups on accuracy or reaction time to either stimulus type.

Post-Training Procedure: Continuous Flash Suppression

We use difference scores to remove the large variance in overall sensitivity to interocular suppression between subjects. Difference scores were computed by calculating the average reaction time for each subject to objects from Family A and subtracting the average reaction time to objects from Family B. Thus, if participants are faster to respond to objects in Family A, this will result in a negative difference score. If participants are faster to respond to objects in Family B, this will result in a positive difference score. This method was used to calculate difference scores for the two control groups, and no difference was found between the groups. That is, the reaction time biases were significantly different between the training groups (t(20)=-2.2, p=0.040, d=0.94; Figure 2C. In contrast, the control groups did not show a bias towards one Family of Ziggerins (t(17)=0.26, p=0.80, n.s.; Figure 2B).

Discussion

Utilizing a training study in conjunction with a post-training CFS breakthrough task, we demonstrate an awareness bias towards objects that only differ only in their reward history. We observed this directional effect in two groups, rewarded for

different objects, indicating object-reward associations (and not merely visual properties) drive this advantage. More specifically, we find that motivational value can influence object-based attention, extending findings from Chou & Yeh (2012) that demonstrated object-based attention without object awareness. To our knowledge, this is the first evidence of a category advantage based solely on differences in reward value. In a recent study, Radel & Clement-Guillotin (2012) demonstrated that food deprived participants were more likely to perceive masked food-related words compared to sated participants. Thus, this work adds to a growing body of evidence that the motivational value of a stimulus can influence its prioritization and that some of the mechanisms in support of this prioritization bias take place prior to stimulus awareness.

Now, we turn to potential mechanisms that lead to this prioritization, of which there are several possibilities. Reward may amplify the signal of features that have been associated with a more rich reward history, sharpening the tuning of regions that process particular features along a certain dimension. Previous evidence suggests that subjects become perceptually attuned to diagnostic physical features that facilitate discrimination between presented stimuli (e.g. B. T. Gardner & Wallach, 1965; Gibson & Gibson, 1955). In the case of the Ziggerin stimuli used here, this dimension would be the rounded or squared edges. Another possibility is that reward may function to drive stimulus expertise by heightening attention to a particular dimension of the stimuli. The result would be a selective weighting of appropriate dimensions associated with a more

rich reward history, with heightened attention paid to particular dimensions. This effect

could also result from a conditioned visual response to preferentially see the trained

stimulus (Seitz et al., 2009). However, at debriefing, subjects were not necessarily

aware that they were being presented with the previously learned novel stimuli during

the post-training CFS task. Thus, this effect doesn't seem to arise from an explicit top-

down cognitive strategy. Regardless of the precise mechanism, our results show that

reward influences the earliest stages of a process that may drive a great deal of

perceptual and conceptual learning.

Learning to prioritize the objects most relevant to us is critical to learning to

optimize our goals and behaviors. We show that participants become more sensitive to

stimuli associated with a more rich reward history, indicating that value-based

information can influence the prioritization of object-level information in the absence of

awareness. Because multiple dimensions have been shown to influence information

break through from CFS, including emotional value, social value, biological relevance,

stimulus familiarity, associations of the stimulus with grasping or complex motor

behavior, and contextual concordance of a foreground object with its background.

Future work should focus on the integration of these features and potential limits and

biases for weighting particular dimensions.

Figure 2.1

(A) Stimuli used in the current experiment, originally published in Wong et al., 2009. (B) Schematic diagram of the training task. After presentation of the object, subjects selected whether the stimulus belonged to Category A or Category B.
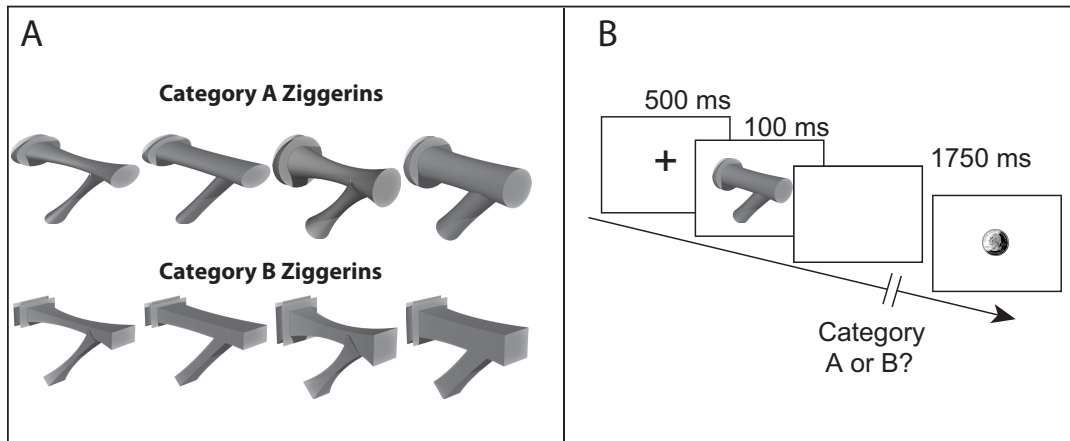
Figure 2.2

(A) Schematic representation of experimental paradigm. A test figure was gradually introduced to one eye to compete with a dynamic noise pattern presented to the other eye. The contrast of the test figure was linearly ramped up from 0 to 100% within a period of 10 seconds from the beginning of the trial, while the noise pattern was gradually ramped down in a corresponding manner. Observers made a response to indicate the side on which the test figure appeared. (B) Reaction Time difference scores for two control groups indicating no bias towards either stimulus group. (C) Reaction Time different scores for two training groups, indicating a bias towards the stimuli with a more rich reward history.
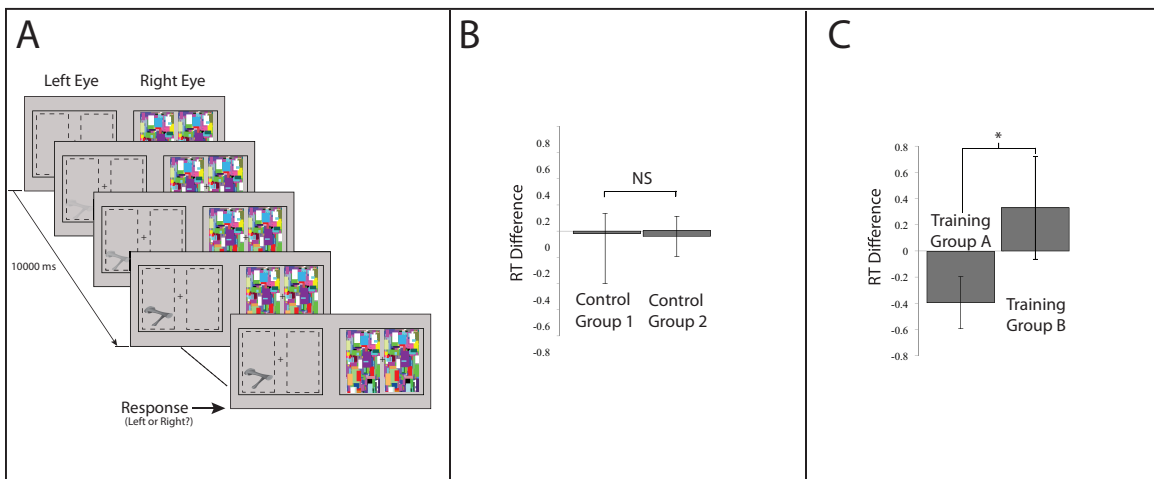
B. Social rejection enhances preconscious processing of faces

Introduction

Social motivation can be construed as one of the many homeostatic systems, like thirst or hunger, which contribute to maintaining an individual's internal balance. Altered social homeostasis impacts perception, decision-making, and behavior, in order to enable the individual to flexibly respond to her environment and restore balance (Cacioppo & Patrick, 2008; Chevallier et al., 2012). When social rejection is experienced, for instance, negative feelings akin to physical pain (DeWall et al., 2010) arise and signal the individual that their social needs are thwarted.

While several studies indicate that altered social homeostasis (in the form of social rejection) enhances processing of social information (Maner, DeWall, Baumeister, & Schaller, 2007; Pickett, Gardner, & Knowles, 2004), none have examined the earliest, and non-volitional, stages of attention.

In this study, we used continuous flash suppression (Tsuchiya & Koch, 2005) to suppress faces and houses from participants' conscious perception following a social acceptance or exclusion prime (Gardner, Pickett, & Brewer, 2000). In CFS, the speed with which stimuli overcome suppression is regarded as an index of preconscious processing (Costello, Jiang, Baartman, McGlennen, & He, 2009; Jiang et al., 2007;

Tsuchiya et al., 2009; Yang & Yeh, 2011). We hypothesized that social exclusion would lead to enhanced processing of social images even in the absence of conscious awareness, and that participants would therefore become aware of faces more quickly following the exclusion prime.

Methods

Participants.

34 adults were recruited from the Philadelphia community and randomly assigned to the acceptance (N=16) or rejection (N=15) condition. Three participants were excluded because they were unable to focus both visual inputs into one image. The final sample included 31 participants (14 males, Mean age=24) with normal or corrected to normal vision and no history of an Axis 1 disorder. All participants gave written informed consent in a procedure approved by the local ethics committee.

Stimuli.

Gray-scale house and face pictures were cropped to fit a standard oval frame and matched on average luminosity (M(SD) faces=153(13), M(SD) houses=158(12), p=.19) and contrast (M(SD) faces=48(3), M(SD) houses=48(4), p=.16). The 30 faces (15 female) were selected from an in-house database among stimuli previously rated as likeable and

matched the ethnic distribution of the Philadelphia area (24 Caucasian, 5 African

American, and 1 Asian).

Procedure.

In both the acceptance and rejection condition, participants were asked to recall

and re-live in their mind a time in their life when they felt socially accepted or socially

rejected and to then write a short essay about this event and the feelings that they

experienced at the time.

The CFS experiment started immediately after the social prime. The stimuli were

presented using Psychopy through a Z800 3DVisor (800 x 600 per display, at 85Hz). At

the beginning of each trial, participants fixated on a centrally presented cross while a

full contrast dynamic noise pattern was presented to one eye. The test image was then

presented to the opposite eye within a region corresponding to the location of the noise

image. The contrast of the test image was ramped up from 0 to 100% over 10 seconds,

while the noise image was ramped down at the opposite rate. Test images subtended

5.2 by 7.8 degrees visual angle and were presented either to the left or to the right of

the fixation cross. Participants were instructed to answer as soon as they detected a

stimulus (without identifying its precise content) by pressing the key corresponding to

the side on which the stimulus had appeared (see Figure 1A).

Following a break of at least 30 minutes, participants also completed physical and social pleasure scales, administered using E-Prime. These true-false scales measure the lowered ability to experience pleasure in various situations. Two subscales were included: the Social Anhedonia scale (typically 40 items; 32 item version used here due to computer error) and the Physical Anhedonia scale (61 items) (Chapman, Chapman, & Raulin, 1976). The physical anhedonia scale measures physical pleasures linked to eating, touching, feeling, sex, temperature, movement, smell and sound. The social anhedonia scale measures the interpersonal pleasure of being with people, talking, exchanging expressions of feelings, doing things with them, competing, loving, and interacting in multiple other ways.

Results & Discussion

All correct trials with reaction times below 10 seconds were included in the analysis (SPSS 19). Average accuracy was above 98% in all conditions with no difference between rejection (M=98.1, SD=2.4) and acceptance (M=98.1, SD=1.9) conditions, t(29)=-.27, p=.79. Because of individual variations in sensitivity to interocular suppression, we computed within subject z-scores on RT to faces and houses. In line with our hypothesis, a repeated measures ANOVA with Condition (Rejection, Approval) as a between-subjects factor and Stimulus Type as a within-subjects factor revealed a significant Condition X Stimulus Type interaction, F(1,29)=4.29, p=.047 (see Figure 1B). In order to further investigate this effect, we computed the RT difference between houses and faces and

found it to be larger in the Rejection (*M*=.69, *SD*=.33) than in the Approval condition

(*M*=.33, *SD*=.55), two-tailed independent t-test: *t*(29)=-2.15, *p*=.04, Cohen's *d*=0.79.

Because humans are generally socially motivated, faces tend to break through

faster than houses across all participants. We wondered if social exclusion actually

impacts the distribution of face and house prioritization, such that highly prioritized

objects are shifted to the lower end of this distribution. To better understand the

mechanism by which social exclusion impacts object prioritization, we divided the

responses for each subject into eight bins, with each bin corresponding to an octile of

subject responses based on reaction time. We then computed the number of stimuli of

each type (faces and houses) that fell into each octile (Figure 2A). While these profiles are

generally similar across both rejection and acceptance groups, the biggest difference is in

the first bin. Subject's that have experienced rejection significantly prioritize more faces

(t(29)=2.14, p=0.04) and less houses (t(29)=2.04, p=0.05) in the first bin compared to the

acceptance group (Figure 2B). This shift in distribution appears to be behaviourally

relevant. Within the rejection group, when we compute a score that reflects how much

an individual prioritizes faces (difference in number of faces in the first quartile compared

to the last quartile), this metric correlates significantly with social anhedonia (r=-.549,

p=0.034; Figure 2C). More specifically, experiencing more social pleasure is associated

with an increased difference between the numbers of faces prioritized in the lowest part

of the object distribution compared to the highest part of the distribution. This

correlation was specific to social anhedonia, as there was not a significant correlation between the prioritization metric and physical pleasure (r=-0.033, p=0.453, N.S.).

Social orienting is a paramount first step towards social inclusion. Our results indicate that a threat to social inclusion enhances social perception even at preconscious stages of processing. This finding adds to a rich literature in social psychology demonstrating that social exclusion has a drastic impact on social attention (DeWall & Bushman, 2011). Although the exact origin of these phenomena is unknown, it has been argued that they arise through increased attention to social cues activated by social disconnection (DeWall & Richman, 2011). While the neural bases of this phenomenon have yet to be elucidated, one possibility is that this mechanism functions similarly to explicit searches for social stimuli. Seidl, Peelen, and Kastner (2012) recently demonstrated that efficient visual search functions through activation of object-selective cortex associated with the percept of interest (e.g. fusiform gyrus for faces) and simultaneously suppress activation in object-selective cortex not associated with the percept (e.g. parahippocampal cortex for houses). This mechanism may also support automatic attentional changes in response to altered homeostasis. This interpretation is supported by our results showing an increase in awareness of faces after reliving a personal rejection episode, along with a decrease in sensitivity to house detection.

Figure 2.3

(A) Schematic representation of experimental paradigm. A test figure was gradually introduced to one eye to compete with a dynamic noise pattern presented to the other eye. The contrast of the test figure was linearly ramped up from 0 to 100% within a period of 10 seconds from the beginning of the trial, while the noise pattern was gradually ramped down in a corresponding manner. Observers made a response to indicate the side on which the test figure appeared. (B) Z-Scored reaction times for Acceptance and Rejection groups. Asterisk above the "x" indicates a significant condition (Acceptance or Rejection group) by stimulus type (face or house) interaction.
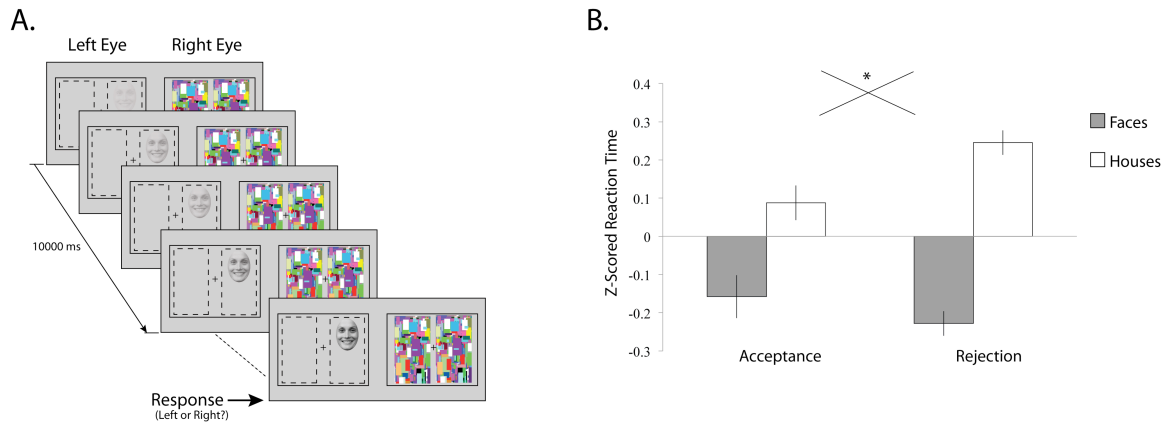
Figure 2.4

(A) Bar graphs depicting the number of stimuli in each octile for faces (red) and houses (blue). (B) Number of faces and houses in the first octile for approval and rejection groups, separated by stimulus type. Z-Scored reaction times for Acceptance and Rejection groups. Asterisk indicates a significant difference between groups. (C) Scatterplot depicting relationship between social anhedonia (orange), physical anhedonia (gray) and face prioritization score. Face prioritization score was calculated as the difference between faces appearing in the first quartile and faces appearing in the last quartile.
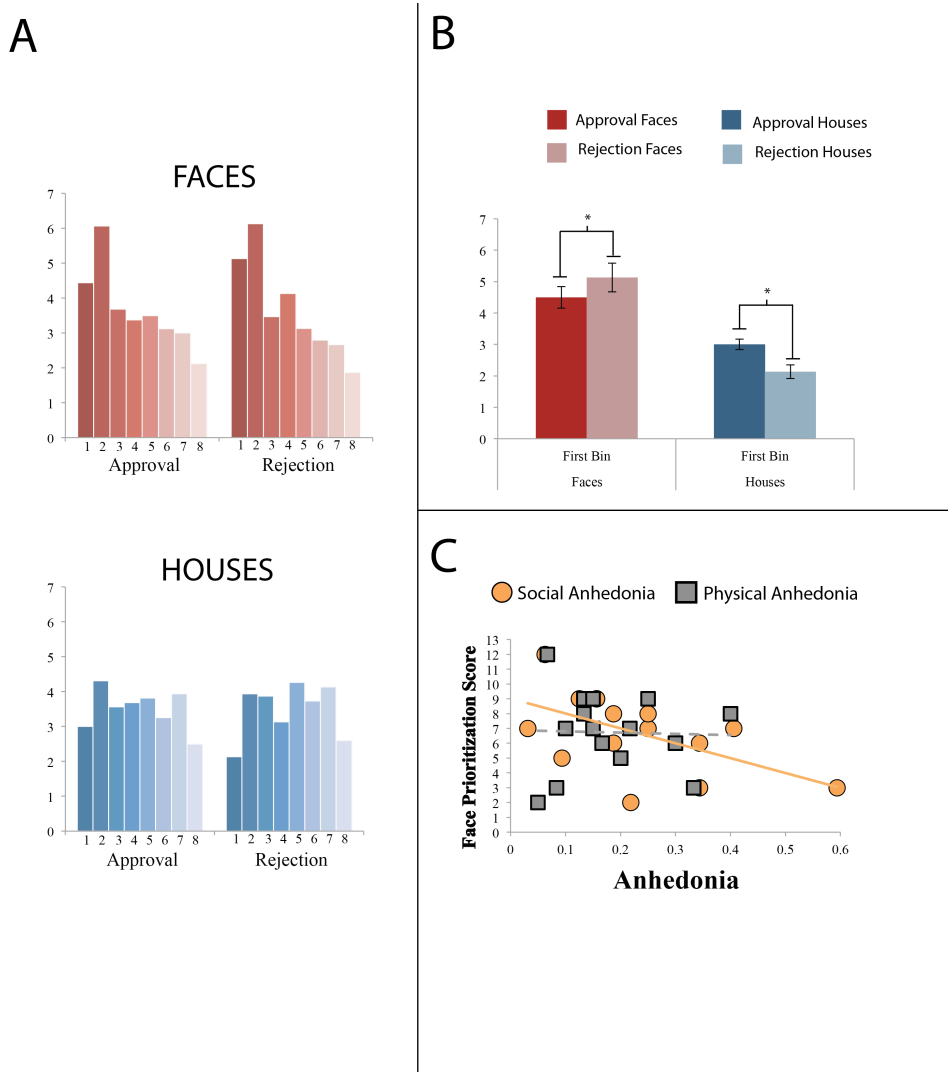
CHAPTER 3: Unseen Fearful Faces Promote Amygdala Guidance of Attention

Vanessa Troiani, Elinora Price, & Robert T. Schultz. *Social, Cognitive, and Affective Neuroscience*, in press.

Abstract

Little is known about the network of brain regions activated prior to explicit awareness of emotionally salient social stimuli. We investigated this in an fMRI study using a technique that combined elements of binocular rivalry and motion flash suppression in order to prevent awareness of fearful faces and houses. We found increased left amygdala and fusiform gyrus activation for fearful faces compared to houses, despite suppression from awareness. Psychophysiological interaction analyses showed that amygdala activation was associated with task-specific (fearful faces greater than houses) modulation of an attention network, including bilateral pulvinar, bilateral insula, left frontal eye fields, left intraparietal sulcus, and early visual cortex. Furthermore, we report an unexpected main effect of increased left parietal cortex activation associated with suppressed fearful faces compared to suppressed houses. This parietal finding is the first report of increased dorsal stream activation for a social object despite suppression, which suggests that information can reach parietal cortex for a class of emotionally salient social objects, even in the absence of awareness.

Introduction

Emotional stimuli summon our attention more than neutral stimuli. Fearful faces, an emotive social stimulus, are particularly compelling, and effectively capture our attention. This is potentially due to the role of fearful faces as a warning to other conspecifics of nearby threat and represents an evolved mechanism to automatically detect stimuli important for survival (Anderson & Phelps, 2001; Ekman, Friesen, & Press, 1975; LeDoux, 1998; Öhman, Flykt, & Lundqvist, 2000). Emotional stimuli have a privileged processing status, attributed to the automatic engagement of selective attention by emotionally salient objects (Vuilleumier, 2005; Vuilleumier & Schwartz, 2001).

Even when emotional stimuli are presented very briefly or outside of the focus of attention or awareness, they are processed with increased efficacy compared to non-emotional stimuli. One paradigm that has been used to investigate processing of emotional or arousing stimuli is the interocular technique of continuous flash suppression (Tsuchiya & Koch, 2005). Behaviorally, this technique can be used to measure differences in the detectability of different stimuli. Briefly, a target is presented to the participant's non-dominant eye and a continuous flow of "noise" images (e.g., Mondrian like patterns) is presented to the participant's dominant eye. CFS causes awareness of target stimuli to be temporarily suppressed from conscious

perception. The target stimulus eventually "breaks through" to conscious perception and time to break through of various stimuli can be compared. Using CFS, it has been demonstrated that highly salient social stimuli such as fearful faces (vs. neutral faces), upright faces (vs inverted faces), and faces with direct gaze (vs. averted gaze) break through to awareness faster (Jiang et al., 2007; Stein et al., 2011; Yang et al., 2007). Thus, arousing or motivationally relevant stimuli are prioritized during visual processing, but how this occurs is not well understood.

At the neural level, fearful faces and other emotional stimuli engage the amygdala, which is particularly reactive to signals of impending threat or biological relevance, such as fearful faces (Adolphs, 2002; Davis & Whalen, 2001; LeDoux, 1998; Phelps & LeDoux, 2005). Regardless of whether fearful stimuli are presented subliminally or supraliminally, the amygdala is robustly activated in many neuroimaging studies (Anderson, Christoff, Panitz, De Rosa, & Gabrieli, 2003; Gläscher & Adolphs, 2003; Wager, Phan, Liberzon, & Taylor, 2003; Whalen et al., 1998). The amygdala plays a role in guiding endogenous attention towards emotionally salient stimuli (Adolphs, 2008; Pessoa & Adolphs, 2010). For social perception, it is important for spontaneously attending to salient parts of the face, such as the eyes (Adolphs, 2008, 2010; Adolphs, et al., 2005; Adolphs & Spezio, 2006; Whalen, et al., 2004; Whalen, et al., 1998). Patients with bilateral amygdala damage do not show this automatic fixation towards the eye region of faces, nor do they show the enhanced perception for aversive stimuli present in healthy observers (Anderson & Phelps, 2001; Tsuchiya et al., 2009). This is thought to

be due to impaired bottom-up (e.g. stimulus-driven or feature-based) attention in patients with amygdala lesions (Kennedy & Adolphs, 2010).

One proposed route through which the amygdala may receive low-level visual information is via a subcortical visual pathway, although its existence is controversial (Pessoa & Adolphs, 2010). We have previously demonstrated differential responses in regions associated with the subcortical visual pathway (including the amygdala, pulvinar, and superior colliculus) for unperceived faces compared to chairs using binocularly rivalry and motion suppression (Pasley et al., 2004). Additional evidence for the processing of emotional stimuli in the absence of awareness comes from patients with "blindsight" who have sustained a primary visual cortex (V1) lesion that prevents conscious vision in the corresponding portion of the visual field. Despite these lesions, patients with blindsight exhibit residual abilities to detect visual stimuli, suggesting this information can be still be processed. Morris and colleagues (2001) used fMRI to demonstrate increased amygdala activation in response to emotionally expressive faces in a blindsight patient, and these patients can also learn aversive associations with neutral stimuli presented in their blind hemifield (Anders et al., 2004). This suggests information can reach the amygdala and influence behavior without conscious awareness.

Conscious awareness is likely a continuum, rather than a dichotomous event. Between unawareness and awareness exist other states. For example, *implicit*

awareness refers to a state during which stimuli cannot be explicitly reported, but have

a measureable impact on subject performance. *Explicit awareness* occurs when visual

events can be explicitly reported by the subject (Kihlstrom, Barnhardt, & Tataryn, 1992;

Mack & Rock, 1998). Selective attention can operate at any stage of this continuum,

with largely unconscious attentional mechanisms thought to operate on stimuli with

visual awareness typically resulting from this attentional step (Crick & Koch, 1990).

Thus, attention can select invisible objects. Although we do not manipulate attention in

the current design, any processing differences between stimulus categories may reflect

attentional mechanisms operating prior to awareness.

CFS in conjunction with fMRI provides a useful framework for examining neural

responses to objects that are not explicitly perceived but nevertheless processed. Prior

studies utilized binocular rivalry and CFS techniques to understand neural responses to

different object categories. Most early binocular rivalry neuroimaging studies examined

neural responses to alternations in stimulus dominance (Polonsky, Blake, Braun, &

Heeger, 2000; Tong, Nakayama, Vaughan, & Kanwisher, 1998). More recent

neuroimaging studies utilized CFS and required participants to search for object stimuli

and report when they detect such stimuli (Jiang, et al., 2006; Pessoa, Japee, &

Ungerleider, 2005). These experiments answer specific questions regarding the

threshold of awareness.

The current study used a CFS-like paradigm to examine neural responses to fearful faces compared to a class of neutral stimuli – houses. Unlike most other CFS studies, the current design does not involve an explicit search task, and was not designed to compare brain activity when targets are seen vs. unseen. Rather, the goal here was to examine purely non-conscious processing of emotional stimuli. Participants performed a task that was orthogonal to the underlying fearful face vs. house manipulation, and trained to respond if they saw anything other than the blue disk or the dynamically moving checkered grid. Using this approach, we were able to capture neural responses to suppressed stimuli in the absence of search strategies. This study follows up our previous work, which found significant subcortical activation in the amygdala, pulvinar, and superior colliculus in response to suppressed fearful faces but not suppressed chairs (Pasley et al., 2004). The current study improves upon our previous work in several ways: Use of a more visually complex suppressed control (houses instead of chairs) allowed us to examine responses in the fusiform and another higher-level control region (PPA). We also employed a language-based instead of object-based orthogonal task, which allows for detection of differences in the ventral visual pathway that could have been obscured by the complex visual object task used previously. Finally, while our previous work imaged only the ventral visual pathway and subcortical structures, the full brain coverage collected in the current design is crucial to understanding the whole-brain network involved in non-conscious processing of emotional stimuli. Because amygdala responses in the absence of explicit awareness are

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thought to play a role in prioritizing selection mechanisms and ultimately influencing behavior, we additionally employed a psychophysiological interaction analysis to characterize the network of activity associated with a fearful-face specific amygdala response.

Materials & Methods

Subjects

Sixteen adults from Yale University with normal or corrected-to-normal vision were recruited to participate in the study. Four subjects were excluded from analysis: Three subjects experienced failure of binocular suppression during fMRI scanning: one reported clear, conscious perception of faces and houses during the task, and two participants reported seeing intermittent eyes or "parts of faces". The fourth subject excluded from the study reported that he "guessed" the content of the suppressed stimuli based on his knowledge of the laboratory's research interests. All 12 remaining subjects (6 female, mean age = 22.9 years) reported complete unawareness of the face and house stimuli. All participants gave written informed consent in accordance with procedures approved by the Yale Institutional Review Board and were paid for their participation.

Experimental Procedure

Participants wore custom red/blue anaglyph glasses, made to accommodate both left and right-eye dominance. Eye dominance was determined using a variant of the Miles test (Miles, 1929, 1930). Because of the importance of full suppression of the non-dominant stimulus to the current investigation, participant eligibility for study inclusion was determined through individual behavioral pretesting of the rivalry effect. Only individuals reporting complete suppression and dominance in response to rivalrous stimuli were considered for fMRI scanning. Pretesting was completed in the context of unrelated behavioral testing for other laboratory experiments, and participants were unaware that their responses to presented stimuli impacted eligibility for the current investigation. The experimenter briefed participants on the binocular rivalry effect and explained that they would be asked to view and comment on a set of rivalrous stimuli. Participants were told that the stimuli would be utilized in future fMRI studies and the importance of honest, thorough reporting was emphasized. Using anaglyph glasses, participants viewed rivalrous stimuli with a dynamic red checkerboard and centrally presented word presented to the dominant eye and blue abstract shapes to the non-dominant eye. Participants were introduced to the phenomenon of breakthrough to prepare them for reporting any experiences of breakthrough during the test procedure.

Participants viewed 14 alternating blocks of suppressed faces and suppressed houses. Seven 10s blocks of each rivalrous condition appeared across the duration of

the experiment, separated in each instance by an equal-duration block of rest. Four

2.5s trials were presented consecutively within each block. Participants wore custom

red/blue anaglyph glasses, made to accommodate both left and right-eye dominance.

During the test procedure, stimuli were back-projected onto a translucent screen

mounted at the rear of the MRI gantry and were viewed through a periscope prism

system on the head coil. Each trial began with a 500ms monocular presentation of a

blue disk to the non-dominant eye. In order to induce independent perception of the

intended dominant and suppressed stimuli through the anaglyph glasses, checkerboard

images were defined by red luminance and suppressed stimuli were defined by blue

luminance. Following presentation of the blue disk, a red checkerboard with a centrally

presented word appeared to the dominant eye and began moving sharply back and

forth (Figure 1). Accompanying the checkerboard display, the blue disk displayed to the

non-dominant eye gradually faded into the target presentation of a blue fearful face or

blue house. The target stimulus faded again to a blue disk after approximately 1.5s. The

participant's task was to identify the first letter of each word as a consonant or vowel as

soon as they were able to identify the letter. If participants saw anything other than the

blue disk or checkerboard (such as objects or parts of objects) in any trial, they were

trained to press a third key. A single catch trial at the end of the experiment (in which

breakthrough from interocular suppression is mimicked by presenting stimuli to both

eyes) was used as an additional probe to determine if participants perceived the

subliminal stimuli presented prior to the catch trial. All subjects responded

appropriately to the catch trial that simulated breakthrough. If it was determined via button press, catch trial, or post-scan debriefing that subjects perceived objects or parts of objects, this data was not used in the analysis (see Subjects section for individual subject details). This method allowed us to obtain a report of participant awareness of the stimuli, without biasing participants to look for stimuli, allowing us to achieve the ultimate goal of a long duration scanning session in the absence of awareness.

A functional localizer scan followed the main scan, in which participants made same or different identity judgments (i.e. subordinate-level discrimination) on unfamiliar faces or houses, presented in a blocked design. Two images of unfamiliar faces or houses were presented side-by-side on a black background for 3500 ms (followed by a 1000 ms interstimulus interval), with four 22.5 s blocks of each stimulus type separated by a 10 s rest period during which two asterisks were presented side-by-side on the screen. This localizer scan served to identify face- and house-selective regions (fusiform face area; FFA and parahippocampal place area; PPA) for functional region of interest analyses.

Magnetic Resonance Imaging Acquisition

Scans were performed at Yale University on a 3T Siemens Trio scanner equipped with a standard quadrature head coil (40 axial slices parallel to the AC-PC plane, whole-

brain coverage, in-plane voxel size = 3.516 x 3.516 mm, slice thickness/gap = 3.5/0 mm,

TR = 2320 ms, TE = 25 ms, flip angle = 60°, 127 volumes collected in 1 functional run).

High resolution T1-weighted 3D anatomical data was also acquired (MPRAGE, TR = 2530,

TE = 3.66, TI = 1100, flip angle = 7°, resulting in 1 mm^3 voxels).

Stimuli

Visual stimuli were black and white images of 32 fearful faces and 32 houses.

Faces were from the Ekman stimuli (Ekman, et al., 1975) and face photos taken from a

Yale theater group. Houses were from a locally collected set of photos of homes from

New Haven County, CT. All stimuli were 450 x 450 pixels. Each face and house image

was presented once, with no repetition. Each block contained either 4 faces or 4

houses.

Face and house stimuli were matched for mean and standard deviations of

luminance values (mean: t(64)=1.34; SD: t(64)=0.580, both p>.05, *n.s.).* Spatial

frequency for each stimulus was determined using a 2-dimensional discrete Fourier

transform, shifting the zero-frequency component to center, and averaging frequencies

within a stimulus. We then compared these values, but found no differences between

face and house stimuli (face mean=10774 (S.D. 1003); house mean = 10792 (S.D. 1346);

t=0.06, p>.05, *n.s.*).

Words of low imagability and relatively low age of acquisition were chosen for the experiment from the UWA MRC Psycholinguistic Word database. The thirty-two words were: Might, Excuse, Lie, Age, Luck, Aim, Sense, Edge, Amount, Escape, Gain, Whole, Ideal, Moment, Act, Reason, Bother, Try, Extra, Object, Find, Answer, Clever, Usual, Wonder, Order, Issue, Bet, Area, Item, Normal and Repeat. Words were repeated one additional time across the length of the experiment, such that suppressed face and suppressed house conditions contained the same number of repeated words. Centered within the checkerboard, each word was displayed in Arial font of mixed case, with the first letter of each word capitalized and the other letters lowercase. Participants performed near ceiling on this task (96.8 ($\pm$0.05) % accuracy overall) and there were no differences in accuracy between the face and house blocks.

Data Analysis

Anatomical Region of Interest

Functional data were processed using tools from the FMRIB ((Oxford University Centre for Functional MRI of the Brain) Software Library (FSL 4.1); online at http://www.fmrib.ox.ac.uk/fsl/). Data were motion corrected, with resulting movement parameters subsequently entered as covariates in statistical analysis. We used FEAT (FMRI Expert Analysis Tool) version 5.2 to submit functional data to a mixed model random effects analysis. Data were spatially smoothed using a Gaussian filter with a

full-width half-maximum (FWHM) of 5 mm, a 40s high pass filter was applied to remove

low frequency artifacts, pre-whitened using FILM to minimize temporal autocorrelations

in the data, and non-linearly registered to the MNI template using FNIRT

(http://www.fmrib.ox.ac.uk/fsl/fnirt). We included two regressors of interest (faces and

houses), which were convolved with a double gamma HRF waveform, and a voxel-wise

general linear model was implemented to identify regions showing significant task-

related activation for each condition. Region of interest (ROI) analyses were

implemented to identify task-related differences in the amygdala, based on our a priori

hypothesis. Normalized estimates from the main effects of suppressed faces and

suppressed houses were extracted from left amygdala using the Harvard-Oxford

subcortical atlas, distributed with FSL. Average values for each individual were entered

into a t-test for significance testing.

Functional Regions of Interest

Data from the functional localizer were preprocessed and analyzed identically to

experimental data, with face and house blocks included as regressors of interest. Two

ROIs were defined in each subject using data from functional localizer scans. Both were

4mm spherical ROIs drawn around the peak voxel from the appropriate contrast of

interest. The fusiform ROI was selected based on the region surrounding the most

selective voxel (voxel with highest t-statistic) within the fusiform gyrus responding more

to faces than houses. The parahippocampal region of interest was selected as the

region surrounding the most selective voxel within the posterior

parahippocampal/collateral sulcus region.

Connectivity

In order to perform a psychophysiological interaction analysis incorporating the

hemodynamic deconvolution procedure implemented in SPM, individual participants'

data were remodeled in SPM8 (Wellcome Trust Centre for Neuroimaging). Individual

subject-level analyses were remodeled by realigning to the first image, coregistering to

the structural image, and normalizing to the Montreal Neurological Institute (MNI)

space. Images were then spatially smoothed with a 5mm FWHM Gaussian Kernel. Each

block was convolved with a hemodynamic response function to produce a predicted

neural response, with additional regressors included for motion. Subject-specific

amygdala peaks were identified as a 4mm sphere surrounding the maxima within the

amygdala ROI, for the suppressed face > suppressed house contrast. For each ROI, the

first eigenvariate of the timeseries was extracted to summarize the timecourse of

activation. Neural activity was then estimated using a simple deconvolution model; the

estimated neural activity was then multiplied by the psychological variable (faces vs.

houses) and reconvolved with a canonical HRF to obtain an interaction term. Individual

subjects' data were then modeled using the ROI timecourse, psychological variable (i.e.,

stimulus type: suppressed faces vs. suppressed houses), and interaction term as regressors. Contrast images were created for the interaction term, which reflected correlations between the seed region that differed depending on stimulus category. These single-subject contrast images were then entered into a second level analysis to test for group effects. To control for multiple comparisons, we used threshold-free cluster enhancement (TFCE) (Smith & Nichols, 2009), which determines statistical significance using permutation labeling, with the α level set at $P < 0.05$.

Whole Brain General Linear Model

In addition to the ROI & PPI analyses, we also performed a whole brain general linear model in order to assess whether unexpected regions were activated for one condition compared to another. As with the PPI analyses, multiple comparisons were controlled using a permutation method with the α level set at $P < 0.05$ (corrected using TFCE for whole-brain significance).

Results

Region of Interest Analysis

We defined an a priori left amygdala region of interest, based on our previous finding of increased left amygdala response to unperceived faces (Pasley et al., 2004).

Increased amygdala activation is associated with fearful face processing (Morris et al., 1996), and is thought to influence a rapid fear- or threat-related response. We examined differences in bilateral amygdala activation for the two suppressed conditions and found greater left amygdala activation for suppressed faces than suppressed houses (t=2.5, p<.05; Figure 2a), consistent with our a priori hypothesis and previous work. There were no significant differences between the two suppressed conditions in the right amygdala.

Next, we examined activation in our functional regions of interest, including the fusiform face area (FFA) and parahippocampal place area (PPA), separately for each hemisphere (Figure 2b). We find significantly greater activation in left FFA for suppressed fearful faces compared to suppressed houses (t=2.2, p<0.05), while this same comparison in right FFA was not significant (t=1.1, p=.299,ns). There was no significant difference in activation in left or right PPA for suppressed fearful faces compared to suppressed houses (left: t=1.4, p=.204,ns; right: t=1.2, p=.267,ns). In our previous study, we found that amygdala activation associated with suppressed fearful faces was not accompanied by increases in fusiform cortex, which is contrary to the current findings.

Functional Connectivity Analysis

The amygdala is thought to guide attention towards objects of biological relevance. Based on our previous finding of amygdala-pulvinar connectivity (Pasley et al., 2004), we anticipated that amygdala activation would be associated with increased connectivity to the pulvinar and potentially other regions not covered by our previous slice selection. In order to examine this hypothesis, we employed a psychophysiological interaction (PPI) analysis (Friston et al., 1997). A PPI analysis identifies regions that covary with a given reference region in a condition-specific manner. The PPI analysis revealed increased connectivity between amygdala and multiple regions implicated in visual attention, including bilateral pulvinar, bilateral insula, left frontal eye fields, left inferior parietal, and early visual cortex for non-conscious faces compared to houses (Table 1, Figure 3a & b).

Whole-Brain General Linear Model

In addition to our a priori ROIs and functional connectivity analyses, we performed a whole-brain analysis to determine if any unexpected regions were activated for one condition compared to another. Perceptually suppressed fearful faces produced significantly greater activation compared to suppressed houses in left parietal cortex (Figure 4). Regions included the left angular gyrus (42,-56,32; t-value: 4.8) and left posterior parietal cortex (30,-70,50; t-value: 5.7). These two parietal regions were

the only regions of significant activation. There were no regions of increased activation for suppressed houses greater than suppressed fearful faces.

Discussion

We hypothesized that the tendency for people to prioritize fearful faces compared to neutral, non-social stimuli corresponds to differences in amygdala responsivity. To test this, we suppressed fearful faces and houses while participants performed an orthogonal letter-detection task. This method allowed us to examine neural responses to two object categories without invoking a search strategy in participants (e.g. "Search for a face and report when this search is successful"). Because search is known to heighten perceptual awareness and activate object-selective cortices (Peelen et al., 2009), any corresponding activation would conflate stimulus-driven attention (e.g. bottom-up) and goal-directed search (top-down) influences. By explicitly not using a search paradigm, our results should better reflect stimulus-driven networks. We found increased left amygdala activation for suppressed fearful faces as compared to suppressed houses, replicating our previous work (Pasley, et al., 2004). The increased amygdala response was accompanied by significant fearful face-specific activation in object-selective cortices, with fearful faces increasing activation in left fusiform cortex. Examination of whole-brain and PPI analyses revealed significant differential findings in regions involved in attention, including bilateral insula, pulvinar, and early visual cortex,

as well as a region of left inferior parietal cortex and left frontal eye fields. Together,

these results suggest that the amygdala guides attention to emotionally salient objects,

like fearful faces, even in the absence of visual awareness.

These findings represent an advance on previous work, which typically focused

on differentiating neural activation to faces below and above the threshold of implicit

awareness. Implicit awareness refers to seeing that occurs when visual stimuli cannot

be explicitly reported, but have measurable impact on subject performance. In contrast,

explicit awareness occurs when subjects can explicitly report a visual event (Kihlstrom et

al., 1992; Mack & Rock, 1998). This differentiation is not necessarily dichotomous,

however, and may represent a continuum of awareness. Participants included in the

current analysis had no explicit awareness of the stimuli, and thus we interpret

associated activation to reflect processes prior to explicit awareness. Because we found

that fearful faces engage both emotional (amygdala) and attentional (pulvinar, parietal)

resources prior to explicit awareness, this activation may represent the mechanism by

which motivationally salient stimuli are prioritized in attention and enhanced by

amygdala activation. Thus, we expect that with a longer presentation, fearful faces

would reach awareness more quickly as a result of pre-conscious attention. Consistent

with this expectation, results of a behavioral breakthrough from continuous flash

suppression study using the same face and house stimuli found that participants detect

suppressed fearful faces much more quickly than suppressed houses (p<0.001; See

Supplement for details).

We found unexpected activation in aspects of the inferior parietal cortices to suppressed faces vs. houses. An important unresolved question is how this information reaches parietal cortex. We see three possibilities. One possibility is that information can "leak through" suppression from a magnocellular pathway, projecting more heavily to dorsal visual regions involved in spatial processing, rather than to ventrotemporal object recognition regions (Livingstone & Hubel, 1987). Under this hypothesis, information reaching parietal cortex may influence behavior by shifting attention to the regions of space where this information is "leaking through". Another hypothesized route by which information from the suppressed eye can reach parietal regions is the subcortical pathway. This phylogenetically older pathway consists of the superior colliculus, pulvinar nucleus of the thalamus, and the amygdala, and is thought to process crude visual information quickly, in order to activate a rapid response to threatening stimuli (Johnson, 2005). A final path by which visual information from a suppressed stimulus may influence allocation of neural resources and consequently, behavior, is via integrative functions in the pulvinar nucleus of the thalamus. The pulvinar is a retinotopically organized nucleus of the thalamus, with robust bidirectional connections to multiple cortical and subcortical regions (Sherman & Guillery, 2002; Shipp, 2003) and rudimentary visual abilities (Fischer & Whitney, 2009). Pulvinar-amygdala connections are thought to underlie increased amygdala activation to fearful stimuli in the absence of awareness. This is supported by our previous functional imaging work (Pasley et al., 2004), as well as observations from patients with lesions to either amygdala

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(Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004) or pulvinar (Ward, Calder, Parker, & Arend, 2006), who show impaired processing of social stimuli. Transient inactivation of the pulvinar leads to a spatial neglect syndrome in macaque monkeys, while lesions of the pulvinar in humans can lead to inabilities to filter out salient distractors (Snow, Allen, Rafal, & Humphreys, 2008; Wilke, Turchi, Smith, Mishkin, & Leopold, 2010). On the basis of the connectivity of the human pulvinar, it may serve as one nexus to integrate signals from multiple regions (including the amygdala and insula in the current study), in order to generate signals regarding the biological relevance of the stimulus.

Other evidence that emotional stimuli can be processed without awareness comes from patients with partial cortical blindness or "blindsight". Despite absence of awareness, blindsight patients nevertheless are influenced by and act on stimuli within their blind hemifield. In a particularly informative study, blindsight patients were trained to associate neutral face expressions with a threatening sound prior to an fMRI experiment. When the conditioned visual stimulus was presented to the blind hemifield of these patients during an fMRI scan, activation in left parietal cortex was enhanced compared to unconditioned faces (Anders et al., 2004). The locus of the left parietal activation in the study by Anders et al. is very similar to the left parietal activation demonstrated in the current design for suppressed fearful faces compared to houses. In another study, emotionally expressive faces presented in the blind hemifield

of a blindsight patient increased amygdala activation (Morris et al., 2001). Thus, this enhanced processing is thought to be due to engagement of the amygdala.

In another study using an active search paradigm, healthy participants were cued to spatial locations prior to performing a search task, in which they had to locate a tilted face amongst an array in a cued visual search task (Mohanty, Egner, Monti, & Mesulam, 2009). The cues could either be spatially and/or emotionally informative or uninformative. Spatially informative cues enhanced regions of the IPS, FEF, and fusiform gyrus, as well as superior parietal cortex and supplementary motor areas. Negative emotional cues activated the amygdala, insula, and fusiform, as well as the orbitofrontal cortex, subcollosal gyrus, and posterior cingulate. Authors concluded that active search for threatening stimuli may benefit from amygdala input to the spatial attention network and contribute to the compilation of a salience map that combines the spatial coordinates of an event with its motivational relevance. We show a very similar network of activation, but participants are performing a completely orthogonal task that does not engage an active search for stimuli. Thus, this is the first report of amygdala guidance of attention using an interocular suppression technique while participants are not engaged in active search for the stimulus. These results suggest emotionally relevant stimuli may also inform such a salience map even when they are not explicitly perceived, and even when participants are not actively searching for a motivationally relevant target.

A notable difference between the current findings and our prior study (Pasley et al., 2004) is activation in higher-level visual regions for suppressed fearful faces instead of houses. One potential role of amygdala activation is to prime the computational activities of the FFA, in order to increase the likelihood that visual representations with affective value reach awareness (Duncan & Barrett, 2007). The current results are consistent with this role for the amygdala. In addition, our prior design used a complex visual object task that might lead to a ceiling effect in the detectable activation differences between subliminal object images. Thus, perhaps using a language-based orthogonal task in the current design allowed us to better detect signal in higher-level visual cortex caused by the undetected images. Increased fusiform in the absence of awareness is consistent with work by Jiang & He (Jiang & He, 2006). Authors examined activation in regions of the face network (FFA & superior temporal sulcus; STS) while face stimuli were rendered invisible using CFS. Bilateral FFA activation was measurable, albeit much reduced, compared to a fusiform activation in response to visible faces. However, it should be noted that Jiang & He used an explicit face search task. Thus, any corresponding activations could be due to the activation of a search template, as merely searching for faces can activate ventral visual cortex (Peelen et al., 2009). Because participants in the current study were not searching for faces, our results are more consistent with an amygdala priming fusiform account.

Although parietal activation has been previously found in the absence of awareness, this is the first report of parietal activation in response to emotional, social

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stimuli (fearful faces) compared to non-emotive, non-social stimuli (houses). We

interpret these findings from 2 potential perspectives: (1) An increased parietal

response due the link between fear and action (e.g., to mitigate potential personal

harm), similar to how tools are related to action and (2) An increased parietal response

reflects increased demands on attentional resources or altered spatial attention. The

first possibility stems from previous studies using CFS to test the hypothesis that

information processing in parietal cortex/dorsal stream regions is biased towards

manipulable objects. One fMRI study examined categorical activation differences for

CFS-suppressed tools compared to suppressed neutral faces, and found greater

activation in dorsal stream regions for tools (Fang & He, 2005). Dorsal steam activation

was ascribed to its association with tools, due to its importance in reaching and

grasping. In a behavioral priming study using CFS, unperceived category congruent

primes facilitated object categorization for man-made tools, but not for animals

(Almeida et al., 2008). Again, these findings were interpreted as a category-specific

processing advantage for objects associated with grasping or manipulation (and thus,

increased reliance on the dorsal stream), although recent work suggests this effect is for

any elongated or manipulable shape (Sakuraba, Sakai, Yamanaka, Yokosawa, &

Hirayama, 2012). Thus, prior work has interpreted parietal activation as due to the

manipulable/action-related nature of the objects under study. However, we report

similar activations using classic ventral stream-associated objects – ie. faces. From an

evolutionary perspective, fear is very closely linked to action, and thus fearful faces may

activate a similar pathway to non-conscious tools, with parietal cortex activation reflecting the launch of a motor preparation plan. Thus, emotionally-laden information might also reach parietal cortex in order to serve action preparation. Because we only used fearful faces in the current design, we cannot parse whether this effect is due to the emotional or social nature of these stimuli. Other studies have found faster breakthrough from suppression for fearful faces compared to happy or neutral faces (Yang et al., 2007), suggesting a fearful face advantage. However, we cannot be sure the current fMRI findings will not generalize to other emotional or salient facial expressions.

An alternate interpretation within an attentional framework is that the increased parietal activation is associated with altered attention due to the increased effort devoted to the vowel/consonant detection task. Emotional stimuli could produce increased processing and serve as a distractor, creating competition for resources and thus requiring increased effort and attention in order to complete the language-based task presented to the dominant eye.

A second possibility is that parietal cortex activation reflects altered spatial attention. More specifically, this region may reflect a comprehensive priority map for target selection that integrates bottom-up demands on attention and top-down goals. Determining the most relevant stimuli in complex settings likely relies on the coordination of a distributed network of cortical and limbic regions involved in various aspects of perception. Consistent with this idea, recent work has focused on systems-

based perspectives, reflecting limbic modulation of non-conscious vision when the content is emotional (Pessoa & Engelmann, 2010; Tamietto & De Gelder, 2010). Several studies have demonstrated the influence of arousal on visual attention. Adults responded with increased spatial attention to pictures depicting food stimuli relative to tools only after food and water deprivation (Mohanty et al., 2008).   Arousing, erotic images rendered invisible with CFS can attract or repel observers' attention, influenced by gender and sexual orientation (Jiang et al., 2006). Learned associations also influence visual attention: Advantages in overcoming suppression induced by CFS have been demonstrated for fearful vs. neutral faces, and Chinese vs. Hebrew characters for Chinese observers (Jiang et al., 2007). In a study pairing biological reward with line gratings suppressed from awareness using CFS, individuals were more accurate in discriminating gratings previously paired with water rewards (even when "unseen") (Seitz et al., 2009). Thus, results from several veins of research implicate contributions of emotion, arousal, or biological relevance to stimulus prioritization in breakthrough from interocular suppression.

To summarize, we found that suppressed fearful faces were associated with increased activation in the left parietal cortex, left amygdala and left fusiform gyrus, and increased task-dependent correlations between the left amygdala and the pulvinar, insula, frontal eye fields, intraparietal sulcus, and early visual cortex. This suggests that these regions evaluate visual stimuli despite a lack of explicit awareness. We interpret these correlations as amygdala-dependent modulation of a network of regions that

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serve to evaluate pre-attentive stimulus value in order to prioritize locations of future

target selection. Contributions of several regions can then be integrated via thalamo-

cortical connections and an overall salience value computed in parietal cortex. When

this information is integrated, the pulvinar has the anatomical connections necessary to

generate a signal to re-orient attention via eye-gaze shifts, generated by intraparietal

cortex and frontal eye fields.

Table 3.1

Peaks of significant clusters identified in the PPI analysis. Seed region was a 4mm sphere around each individual's left amygdala peak. Results are corrected for multiple comparisons using TFCE (see methods for details). Regions correspond with Figure 3a.

Region	Hemisphere	X	Y	Z	T-value
pulvinar	R	26	-30	-6	4.89
pulvinar	L	-14	-30	-4	5.17
Insula	R	44	6	-2	4.07
Insula	L	-38	12	-8	4.06
Inferior parietal	L	-32	-54	48	4.16
Early visual cortex	Bilateral	-12	-92	-16	7.93
Frontal Eye Fields	L	-44	-4	32	4.09

Figure 3.1

Schematic of Binocular Rivalry Stimulus Presentation. Without Glasses. Example view of stimulus as seen without anaglyph glasses. Through Anaglyph Glasses. Words were presented into the dominant eye through the red lens of anaglyph glasses while thirty-three faces and houses were presented into the suppressed eye through the blue lens.
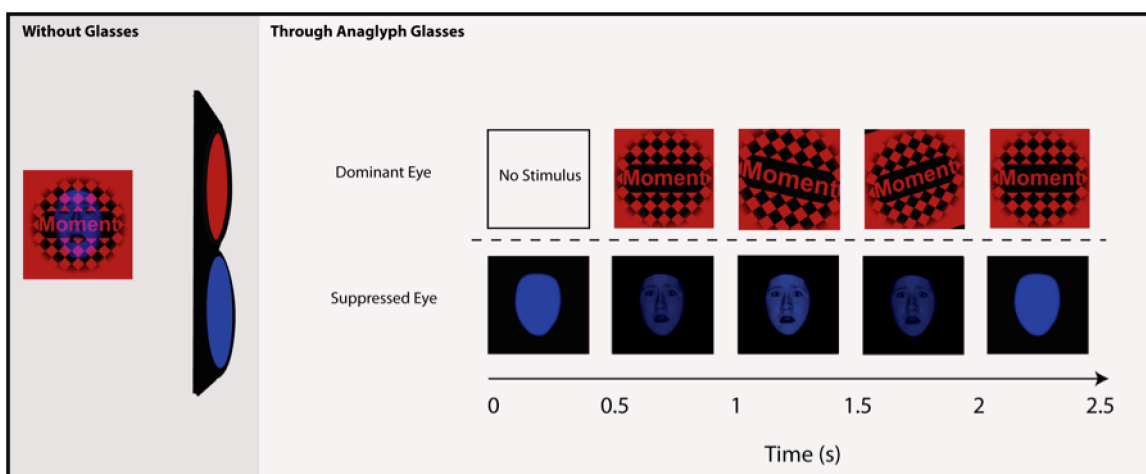
Figure 3.2.

Effects of Unconscious faces and houses in (A) Amygdala and (B) FFA & PPA.   (A) Amygdala regions determined by the Harvard-Oxford atlas. Significantly greater activation for left amygdala for suppressed faces than suppressed houses (p<.05). (B) Fusiform face area (FFA) and Parahippocampal Place Area (PPA) regions of interest. Regions of interest were defined as a 4mm sphere around the peak voxel for face- and house- selective regions with peaks defined based on an independent localizer scan. Significant activation for suppressed fearful faces (compared to suppressed houses) were only observed in the left FFA.
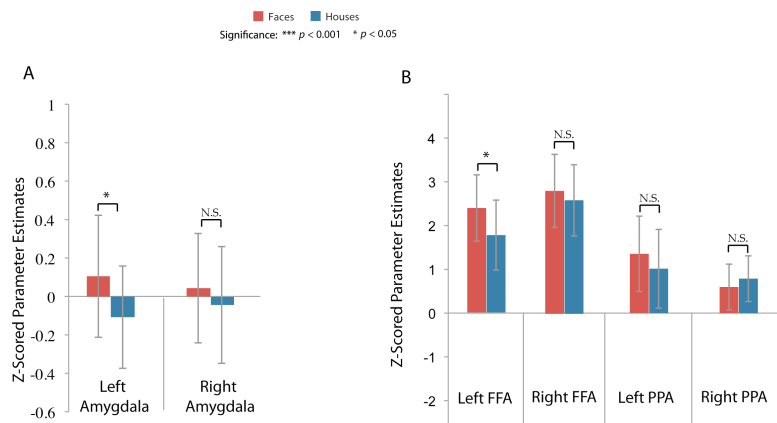
Figure 3.3

(A) Regions that interact with the amygdala in a task-dependent manner (suppressed face blocks greater than suppressed house blocks). (B) Correlations between amygdala (x-axis) and pulvinar (y-axis) for two representative subjects, with suppressed face blocks represented in blue and suppressed house blocks in red.
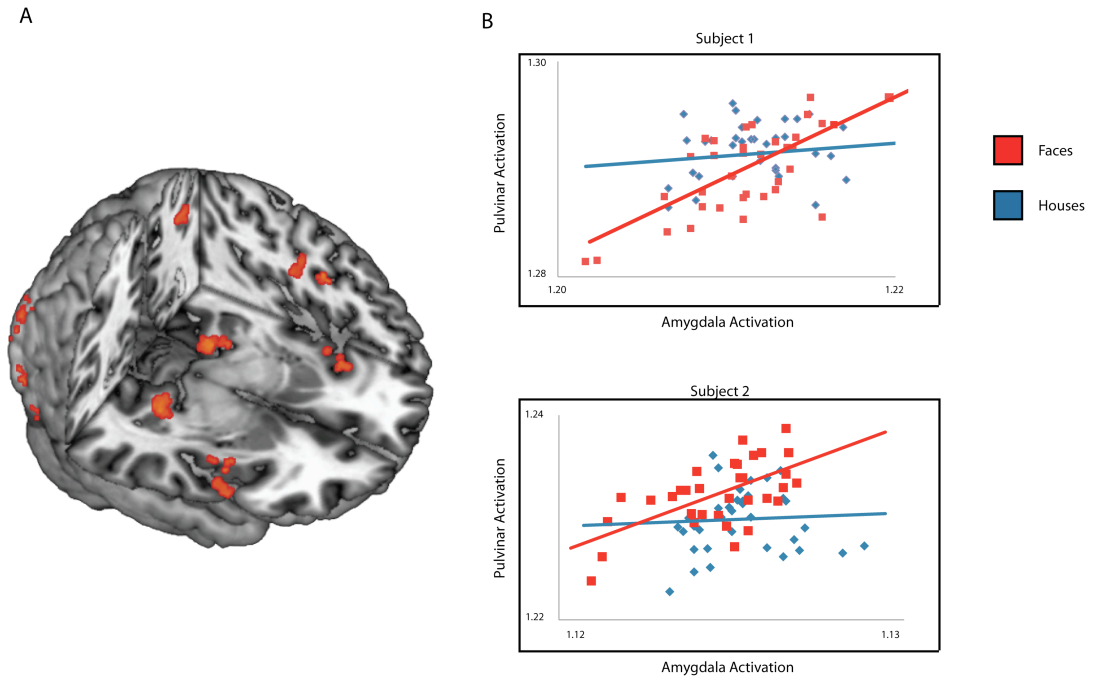
Figure 3.4

Whole-brain analysis for Perceptually Suppressed Faces. Voxels showing significant activation are plotted on coronal slices and a left lateral view of the MNI template brain. Perceptually suppressed faces led to increased fMRI response in the left posterior superior parietal sulcus and left angular gyrus, when compared to perceptually suppressed houses. This was the only region of significant activation at the whole-brain level after correcting for multiple comparisons.
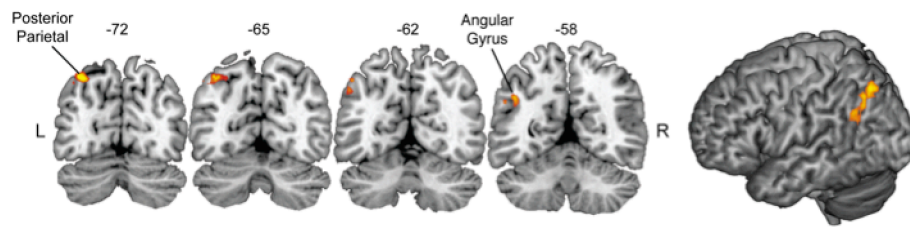
Supplementary Data

Method

Participants

Ten observers (5 female) with normal or corrected-to-normal vision from the University of Pennsylvania community participated. Participants had a mean age of 25.8 years (S.D. 4.2 years).

Experimental Procedure

Noise images were generated with MATLAB and presented using Psychopy. Participants viewed the stimuli through two OLED SVGA microdisplays mounted to a Z800 3DVisor (800 x 600 per display, at 85Hz), spanning a visual angle of 32 degrees horizontally and 24 degrees vertically.

Face and houses stimuli were identical to those used in the main fMRI experiment. At the start of each trial, a centrally presented fixation cross appeared as a fixation point. A full contrast dynamic noise pattern was presented to each eye at the beginning of a trial. Then, the test image was presented to the opposite eye at a random location within a region corresponding to the location of the noise image. The contrast of the test image was systematically ramped up from 0 to 100% over a period of 10 seconds, while the noise image was ramped down at the opposite rate (See

supplementary Figure 1). Test images subtended 5.2 degrees by 7.8 degrees visual

angle and were presented in a random position either to the left or to the right of

fixation. Observers pressed a key affixed with a left or right arrow image, corresponding

to the side of fixation on which the test image appeared. They were instructed to

respond to the appearance of any part of a test image as soon as possible, even if they

were unable to identify the precise content of the image.

Results

      We observed significantly faster breakthrough for fearful faces compared to

houses ($p<.001$, Supplementary Figure 2). Fearful faces may breakthrough suppression

faster than houses due to their increased relevance and inherent social value as faces

and/or due to association with threat and concerns over safety.

Figure 3.5

Schematic representation of experimental paradigm. A test figure (upright face, as shown) was gradually introduced to one eye to compete with a dynamic noise pattern presented to the other eye. The contrast of the test figure was linearly ramped up from 0 to 100% within a period of 10 seconds from the beginning of the trial, while the noise pattern was gradually ramped down in a corresponding manner. Observers made a response to indicate the side on which the test figure appeared.
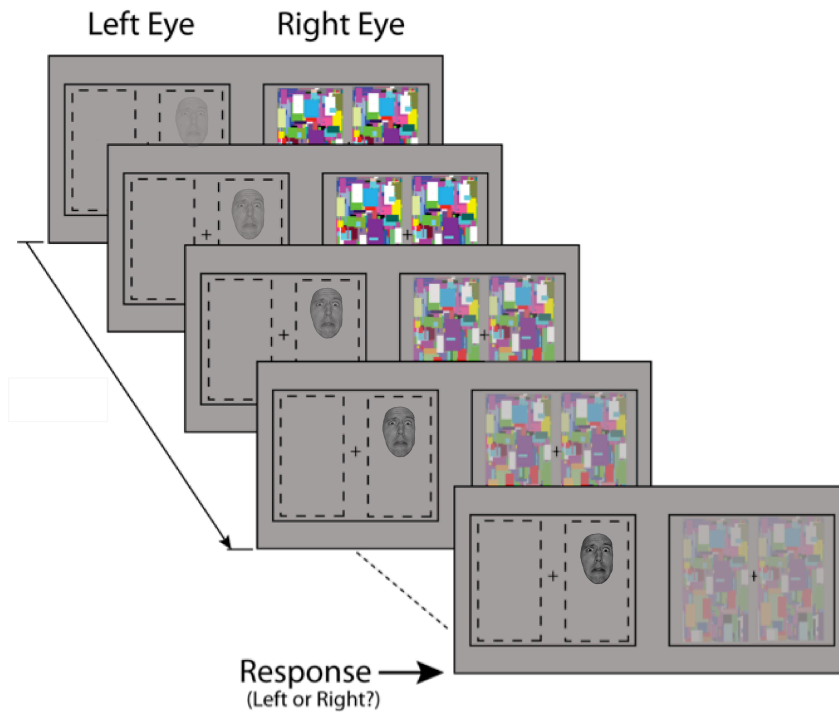
Figure 3.6

Suppression times for faces and house. Left side of figure shows the suppression times for 10 individual observers, with average suppression times presented on the right. Asterisks indicate a significant difference between faces and houses, ***p<.001.
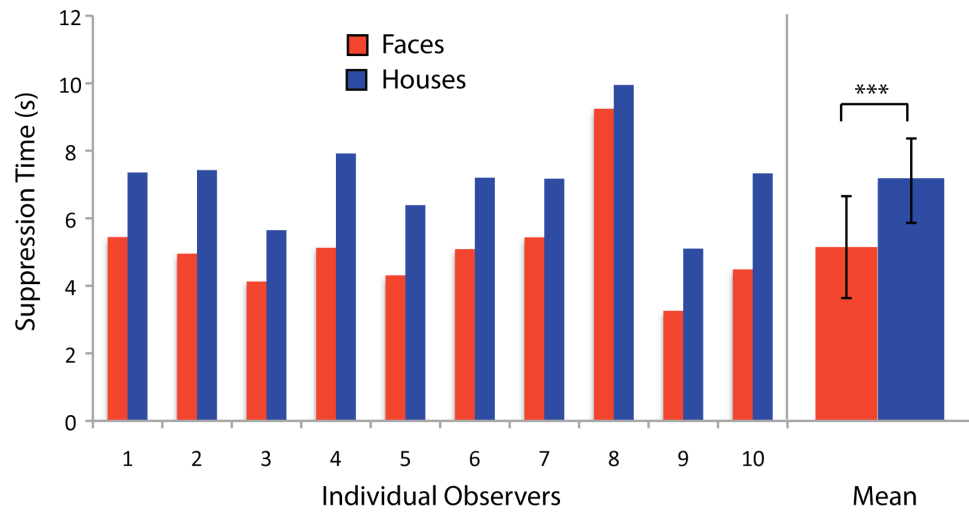
CHAPTER 4 :Amygdala, Pulvinar & Inferior Parietal Cortex Contribute to Early Processing of Faces without Awareness

Abstract

The goals of the present study were twofold. First, we wished to investigate the neural correlates of stimulus-driven processing of stimuli strongly suppressed from awareness and in the absence of top-down influences. We accomplished this using a novel approach in which participants performed an orthogonal task atop a flash suppression noise image to prevent top-down search. Second, we wished to investigate the extent to which amygdala responses differentiate between suppressed stimuli (fearful faces and houses) based on their motivational relevance. Using continuous flash suppression in conjunction with fMRI, we presented fearful faces, houses, and a no stimulus control to one eye while participants performed an orthogonal task that appeared atop the flashing Mondrian image presented to the opposite eye. In 29 adolescents, we show activation in subcortical regions, including the superior colliculus, amygdala, thalamus, and hippocampus for suppressed objects (fearful faces and houses) compared to a no stimulus control. Suppressed stimuli showed less activation compared to a no stimulus control in early visual cortex, indicating that object information was being suppressed from this region. Additionally, we find no activation in regions associated with conscious processing of these percepts (fusiform gyrus and/or parahippocampal cortex) as assessed by mean activations and multi-voxel patterns. A psychophysiological

interaction analysis that seeded the amygdala showed task-specific (fearful faces greater than houses) modulation of right pulvinar and left inferior parietal cortex. Taken together, our results support a role for the amygdala in stimulus-driven attentional guidance towards objects of relevance and a potential mechanism for successful suppression of rivalrous stimuli.

Introduction

We are automatically drawn to objects that are relevant to our needs and desires. For example, as human beings, we tend to pay more attention to faces and bodies compared to other objects. Emotional stimuli are also processed earlier in this object-relevance hierarchy, potentially due to selective attention mechanisms that are automatically engaged by emotionally salient objects (Vuilleumier and Schwartz, 2001; Vuilleumier, 2005). These category-based preferences are thought to relate to the stimulus meaning or value: Conspecifics are valuable to us due to the important information faces can convey. Emotional stimuli indicate a potential threat, which is meaningful in terms of survival (Ekman and Friesen, 1971; LeDoux, 1998; Öhman et al., 2000; Anderson and Phelps, 2001). Object relevance is also state-dependent: Food stimuli are captured by attention more quickly when we're hungry than when we're sated. While it is clear stimulus meaning and motivational value modulate object-based prioritization, it is not fully understood how highly relevant objects are prioritized in attention and how this process is reflected in the human brain.

Though it has been known for quite some time that meaningful stimuli benefit from enhanced attentional capture, the recent development of the continuous flash suppression (CFS) technique has facilitated the study of visual processing that occurs prior to awareness and its influence on object prioritization (Tsuchiya and Koch, 2005). CFS uses rapidly flashing colored images (mondrians) presented to one eye to prevent awareness of a stimulus presented to the opposite eye. One behavioral use of this technique is the break from CFS paradigm (b-CFS), in which the relevance of a target is determined based on the time it takes to break through the flashing stimulus and reach awareness (Jiang et al., 2007). Using this technique, it has been shown that social signals are prioritized more quickly. For example, observers become aware of a face with a direct gaze faster than one with indirect gaze and upright conspecifics faster than an inverted visual control (Stein et al., 2011; Stein et al., 2012). Stimuli that contain both social/emotional signals, like fearful faces, are a particularly potent stimulus. Observers become aware of fearful faces much more quickly than a non-social visual control (houses) and emotional faces break through faster than non-emotional faces (Yang et al., 2007; Troiani et al., in press). These differences in stimulus break through are thought to reflect enhanced processing that occurs prior to stimulus awareness. The amygdala plays a particularly important role in spontaneous orienting towards salient parts of a stimulus (such as the eye region of a face) and is thought to facilitate enhanced processing of biologically-relevant stimuli prior to awareness (Whalen et al., 1998; Whalen et al., 2004; Adolphs et al., 2005; Adolphs, 2008, 2010; Pessoa, 2010).

Patients lacking bilateral amygdalae suffer from impaired automatic orientation towards

the salient portions of a face, potentially due to impaired stimulus-driven attention

(Tsuchiya et al., 2009; Kennedy and Adolphs, 2010). Within the realm of non-conscious

vision research, connections between the amygdala and the pulvinar nucleus of the

thalamus are associated with a hypothesized fast-track route for processing emotional

stimuli. This alternate visual pathway is thought to project from the superior colliculi to

the pulvinar and onto the amygdala. Critically, this pathway is described as bypassing

cortex to provide fast yet coarse visual information with the potential to aid in threat

detection (Johnson, 1990, 2005). However, due to the profuse interconnections present

between the regions of the hypothesized colliculus-pulvinar-amygdala pathway and

cortex, it is difficult to limit processing exclusively to these regions. An alternative

hypothesis is that the pulvinar and amygdala serve to coordinate the function of cortical

networks in the process of evaluating the biological significance of a stimulus (Pessoa

and Adolphs, 2010). Under this framework, the cortex remains significantly involved in

this process, and processing is not limited to the three regions of the subcortical

pathway.

Consistent with the idea of amygdala and cortical involvement in the evaluation

of important stimuli, recent work has shown enhanced processing of motivationally

relevant stimuli to be reliant on a combination of highly interactive cortical and

subcortical structures. It may be the case that it is not merely the involvement of

specific brain regions in emotional and motivational processes, but the enhanced

communication between cortical and subcortical regions induced by motivational states

(Kinnison et al., 2012). Mohanty and colleagues showed that following a period of food

and water fasting, participants activated a network of regions involved in spatial

attention in response to donuts (a food) compared to hexnuts (a visually similar tool).

This network included posterior parietal cortex, intraparietal sulcus, frontal eye fields,

posterior cingulate, and the amygdala (Mohanty et al., 2008). We recently found a

similar network of activation for suppressed motivationally relevant faces compared to a

suppressed non-social stimulus (houses) (Troiani et al., in press). In our previous study,

we successfully implemented a novel paradigm designed to limit top-down influences in

order to measure stimulus-driven components of object prioritization. In this paradigm,

participants perform a demanding task that is unrelated to the suppressed stimuli,

which serves to increase the duration of suppression, allowing stimuli to remain

suppressed for minutes (compared to the seconds at which binocular stimuli typically

rival). This allows for the examination of stimulus-driven neural responses to

suppressed stimuli in the absence of top-down search strategies. Here, we combine CFS

with a demanding task that appeared atop the flashing Mondrian images in order to

suppress images from awareness for the duration of the fMRI study. We further

optimized this method in order to increase the depth of stimulus suppression by 1)

using a more robust form of suppression, 2) making stimuli smaller to prevent

piecemeal breakthrough, 3) using MR compatible goggles with a dual LCD display to

prevent escape of certain wavelengths from the suppressed stimulus into the dominant

eye, and 4) adding a no-stimulus control condition. With these optimizations, we hoped to strengthen stimulus suppression in order to isolate the earliest regions of the network that contributes to the differential prioritization of stimuli prior to awareness.

Materials & Methods

Subjects

Twenty-nine adolescents (2 females; ages 11 to 17 years (mean =14.3); 2 left-handed) with normal or corrected-to-normal vision were recruited from the Philadelphia community to participate in the main fMRI experiment. All participants gave written informed consent in accordance with procedures approved by the Children's Hospital of Philadelphia Institutional Review Board and were paid for their participation. Prior to the fMRI session, subjects completed a mock scan procedure, allowing the participants to acclimate to the scanner environment and train to minimize movement while scanning. Only participants who were under a minimum movement criterion proceeded to the scanning session. None of the participants moved more than 3 mm during any scanning run. Three subjects were eliminated from the connectivity analysis because they did not show activation within the region of interest used to define the seed region.

Piloting: In order to establish the effectiveness of the method, six pilot subjects also completed the task while undergoing fMRI. Pilot subjects were six adults (all female) with knowledge of the suppressed stimuli and the goal of the study. The objective of piloting was to determine whether participants with knowledge of the

stimuli experienced break from interocular suppression while performing the task.

None of the pilot subjects experienced break through of the suppressed stimuli while

performing the task. Even when these participants had knowledge of the presence of

the suppressed stimuli, they experienced no break through, indicating the effectiveness

of this suppression method.

Magnetic Resonance Image Acquisition

Imaging data were collected using a 3T Siemens Verio scanner and a 12 channel

head coil. Two structural MR images were acquired for the registration of fMRI data to

standard space: A high-resolution T1-weighted MPRAGE sequence of the entire brain

(176 sagittal slices, isotropic voxel size = 1 mm, TR = 1900 ms, TE = 2.54 ms, flip angle = 9

degrees), and a high-resolution FLASH sequence collected in the same axial plane as the

fMRI data (number of slices = 40, slice thickness = 3.5 mm, TR = 300 ms, TE = 2.46 ms,

flip angle = 60 degrees). Functional data consisted of two 4-minute runs of whole-brain

T2* weighted BOLD echoplanar images with 107 volumes acquired per run (40 oblique

axial slices, isotropic voxel size = 3.5 mm, TR = 2340 ms, TE = 25 ms, flip angle = 90

degrees).

Stimuli

Stimuli of interest were 32 gray scale fearful faces and 32 houses presented

within 2 degrees of visual angle into the left lens of MR compatible dual display LCD

goggles (Resonance Technology Inc., Northridge, CA). Responses were recorded with a

four-key fiber optic response box. Task stimuli consisted of movies of colorful Mondrian

images changing at a rate of 10 Hz. Mondrian images were created using Matlab, with

each 28-second block movie consisting of 280 unique dynamic noise images, each

presented for 100ms. Images were made into movies using Corel Video, with letters

and fixation cross images added to these movies before exporting the movies to

Quicktime. Experimental presentation was done with Psychopy.

A fixation cross appeared in the center of the Mondrian movies, and uppercase

letters from the English alphabet appeared in one of four quadrants immediately

adjacent to the fixation cross. Letters consisted of 5 vowels (A, E, I, O, U) and 5

consonants (C, H, N, T, S). The task consisted of 12 28-second blocks (12 TRs, 2340ms

each TR). Within a block, letter trials appeared in the right eye and stimulus trails to the

left, which was experienced by the subject as one image (See Figure 1A). Following is a

description of these trials as incorporated into a block (For visual schematic, see Figure

1B). Each trial was a total of 2340ms, the length of one TR. Projected through the right

lens, a block began with a continuous stream of Mondrian images changing at a rate of

10 Hz. After 2340ms, the first of 10 letter trials was presented. A letter trial consisted

of a 300ms fixation cross, followed by the appearance of a letter in one of the four

quadrants for a duration of 1500ms. Onset of the letter trials was varied by 300-600ms

from the start, with the difference in onset accounted for at the end of a trial, such that

each letter trial was 2340ms. At the end of 10 trials, only the Mondrians appeared for

2340ms (no letters or fixation) and then the block was complete. In each block, all 10

letters were presented, with letter order and onset variance randomized between

blocks.

Stimuli of interest were projected through the left lens, blocked by stimulus

category, with category order counterbalanced across participants. Eight fearful faces,

eight houses, or a no-stimulus control were presented in each block. A block began with

a black screen for the first 4680ms. After this period, 8 stimulus trials were presented.

A stimulus trial began with a stimulus that appeared after 600ms. The stimulus was

slowly ramped from a contrast level of 0 to 100 over 750ms and ramped back down

over the following 750ms (total duration: 1500ms). The left screen was then blank for

another 340ms until another trial began. Following the presentation of 8 trials, no

stimulus appeared for another 4680ms until block completion. Task blocks were

separated by 11,700ms of rest, with a black screen presented to both eyes. It should be

noted that for the no stimulus control condition, a black screen was presented to the

left eye for the entire 28-second block, while the task still appeared in the right eye.

Procedure

The main fMRI experiment consisted of two 4 min 20 second scan runs, each of which was divided into 6 task blocks and 7 periods of rest. During each block, participants viewed letters that appeared surrounding a central fixation. They were instructed to press the right button if the letter was a vowel and the left button if the letter was a consonant. Following the presentation of the 2 runs, a catch trial was presented. A catch trial consists of a fearful face or house image presented atop of the mondrian image to both eyes, in order to mimic break from interocular suppression. This trial is used as a probe to assess whether participants experienced break from interocular suppression earlier in the experiment. Following the catch trial, participants were asked, "Did you notice anything different about the last 2 trials?" All participants reported the presence of a face and a house. They were then asked if they saw any objects or parts of objects earlier in the experiment. All participants reported that they did not see objects prior to the catch trial, indicating successful suppression of the objects for the duration of the experiment.

Following the main experimental scans, a 5-minute functional localizer scan was administered, in which subjects detected when a centrally presented white crosshair appeared on full color faces, scenes, objects and scrambled objects, presented in a blocked design. Four, 14-second blocks of each image category were presented as "superblocks", in which the stimulus category blocks were presented in succession and separated by 14 seconds of rest. Each "superblock" sequence was presented four times, with object categories in a different order for each "superblock".

Data Analysis

Image preprocessing and statistical analyses were performed using SPM8

(Wellcome Trust Centre for Functional Neuroimaging, London, UK). Functional images

from both experimental and localizer scan runs were initially analyzed separately for

each participant. Low-frequency drifts were removed with high-pass filtering with a

cutoff period of 128 seconds and autocorrelations modeled using a first-order

autoregressive model. Images for each participant were realigned to the first image in

the series (Friston et al., 1995) and coregistered with the structural image (Ashburner &

Friston, 1997). The transformation required to bring a participant's images into

standard MNI152 space were calculated using tissue probability maps (Ashburner &

Friston, 2005), and these warping parameters were then applied to all functional images

for that participant. The data were spatially smoothed with a 4 mm FWHM isotropic

Gaussian kernel.

Whole Brain Analysis

Whole-brain analyses were implemented using a standard linear modeling

approach. These models included three categorical regressors indicating whether the

suppressed stimulus for each block was a fearful face, house, or no stimulus control.

Categorical regressors were boxcar functions at stimulus onset convolved with a

canonical hemodynamic response function. Whole brain analyses were corrected for

multiple comparisons using a cluster corrected family wise error (FWE) threshold of

p<0.05.

Region of Interest Analysis

Our main region of interest was the amygdala, based on its involvement in

implicit processing of social and emotional stimuli. The amygdala is composed of

multiple subnuclei, with each nucleus displaying different response profiles and

structural connectivity. We used the three amygdala sub-regions of the

cytoarchitectonic probability maps to explore response profiles to the suppressed image

conditions and the no stimulus control (Amunts et al., 2005). For these analyses,

average parameter estimates were extracted for each sub-region in both hemispheres

using Marsbar (Brett, Anton, Valabregue, & Poline, 2002).

We were also interested in responses in ventral visual cortex to the suppressed

images. Because of the variance between subjects in object-selective cortex, we

defined two functional regions of interest in each subject using data from the functional

localizer scans. The fusiform face area (FFA) was defined as the region of the fusiform

gyrus responding more to faces than to scenes. The Parahippocampal Place Area (PPA)

was defined as the set of contiguous voxels responding more strongly to scenes than

objects in the posterior parahippocampal/collateral sulcus region. Significance

thresholds (ranging from t > 3.0 to t > 4.0) were set for each ROI on a subject-by-subject

basis.

For individual parameter estimate ROI analyses, the time course of response during the main experiment was extracted from each ROI and response estimates (i.e. Beta values) were obtained for each regressor and covariate, which were then compared between conditions using a repeated measures ANOVA with follow-up t-tests, when appropriate.

Multivoxel Pattern Analysis

In the FFA & PPA, we performed multivoxel pattern classification in addition to the univariate analyses. Preprocessing for the MVPA analysis was identical, except data were not spatially smoothed. Three regressors were created to model each of the conditions of interest (fearful faces, houses, control) separately within the two experimental runs. After using these regressors to extract beta values for each condition at every voxel, we performed multivoxel pattern classification on these values using custom MATLAB code based on the method described by Haxby et al. (Haxby et al., 2001). In this analysis, we calculated a cocktail mean pattern for each of the two runs and subtracted this mean from each of the individual patterns prior to classification. Pattern classification was performed by pairwise comparisons across all 3 conditions (fearful faces, houses, and control). If the average pattern correlation between fearful faces in opposite halves of the data was higher than between fearful faces and houses in opposite halves of the data, this was considered a correct

classification. Classification accuracy was then averaged across all possible pairwise comparisons for a given ROI and tested against random chance (i.e., 0.5) using a one-tailed t-test.

Connectivity Analysis

In order to examine whether the amygdala increases in coherence with regions of an attention network that we identified previously (Troiani et al., in press), we employed a psychophysiological interaction analysis (PPI) (Friston et al., 1997). In this analysis, a seed region is identified and the interaction of this seed region and a covariate of interest (in this instance, suppressed Faces > suppressed Houses) is computed. The resultant interaction term is then entered as a covariate in a general linear model, along with additional covariates for the response of the seed region and the covariate of interest. Any significant effects corresponding to the interaction term are thought to reflect increased coherence or functional connectivity with the seed region. We have used this method previously with an amygdala seed and identified a network of activation, including the pulvinar nucleus of the thalamus, insula, frontal eye fields, early visual cortex, intraparietal sulcus, and frontal eye fields. Subject-specific amygdala peaks were identified as a 4mm sphere surrounding the maxima within a superficial amygdala ROI, for the suppressed face > suppressed house contrast. For each ROI, the first eigenvariate of the timeseries was extracted to summarize the timecourse of activation. Neural activity was then estimated using a simple

deconvolution model; the estimated neural activity was then multiplied by the psychological variable (faces vs. houses) and reconvolved with a canonical HRF to obtain an interaction term. Individual subjects' data were then modeled using the ROI timecourse, psychological variable (i.e., stimulus type: suppressed faces vs. suppressed houses), and interaction term as regressors. Contrast images were created for the interaction term, which reflected correlations between the seed region that differed depending on stimulus category. We then extracted average beta values from each subject for each of 7 regions of interest, based on connectivity results from our previous work (Troiani et al., in press).

Results

Whole Brain Analysis

We first assessed the activation pattern evoked by the conscious task (flashing mondrian images presented to the right eye). To examine this, we averaged activation across the three covariates (fearful faces, houses, and control) compared to a resting baseline (12 second blocks of rest). Because the mondrian images are consistent across these three conditions, we expected activation in regions of the central visual system. Indeed, participants activated bilateral lateral geniculate nucleus (LGN) and early visual cortex (EVC) (Figure 2A). We then explored whether there were differences in EVC between three conditions by extracting subject's parameter estimates from each

condition, separately, using a mask defined by the regions reaching whole brain significance. (We chose not to explore the LGN signal further, as there is a great deal of anatomical variability in subject anatomy and we would be unable to differentiate the LGN from surrounding structures). We observed a significant effect of condition in EVC, bilaterally (left F_2=6.83, p=0.002; right F_2=12.01, p<0.001). However, this was driven by stronger activation when there was no stimulus presented to the left eye compared to a fearful face or house stimulus (RIGHT: faces t_{28}=3.92, p=0.001; houses t_{28}=5.17, p<0.001; LEFT: faces t_{28}=2.98, p=0.006; houses t_{28}=3.54 p=0.001). We find no significant differences between fearful face and house conditions in EVC.

When contrasting the conditions with a stimulus (fearful faces or houses) with the no stimulus control condition, we find a single cluster of activation that encompasses right lateralized superior colliculus, thalamus, amygdala, and hippocampus. These results are consistent with an abundance of previous work implicating these regions in implicit perception and vision without awareness (De Gelder et al., 1999; De Gelder and Hadjikhani, 2006; Tamietto et al., 2009; Stienen and de Gelder, 2011; Van den Stock et al., 2011; De Gelder et al., 2012). However, there are no differences between fearful faces and houses based on mean activation in these subcortical regions. Even when we lower this contrast to an excessively liberal threshold (p<0.05, uncorrected), the regions showing mean differences to stimulus vs. no stimulus are only in subcortical areas. Based on our a priori hypothesis regarding the amygdala,

we examine responses in this region statistically using a region of interest approach, described below.

Amygdala ROI Analysis

The amygdala is frequently activated by social information and is thought to play a particular role in guiding orientation responses to visual social stimuli (Adolphs, 2010; Adolphs & Spezio, 2006). We have previously found amygdala activation to fearful faces (an emotional, social stimulus) in the absence of awareness (Troiani et al., in press). Thus, we expected a differentially stronger response in the amygdala for fearful faces compared to houses. We explored this hypothesis by examining responses in bilateral amygdala, for each of three regions defined by cytoarchitectonic probabilistic maps (Amunts et al., 2005). Contrary to our hypothesis, we did not find amygdala activation that was specific to fearful faces. Instead, in all amygdala ROIs, we observed an effect of condition (stimulus vs. no stimulus) in bilateral superficial amygdala and the right centromedial amygdala (Left SF: F_2=3.18, p=0.049; Right SF: F_2=7.15, p=0.002; Right CM: F_2=6.74, p=0.002), but there were no differences in activation between fearful faces and houses (Figure 3B). Please note that these are relative differences in activation, such that in the control condition, the amygdala is quite suppressed compared to baseline. The amygdala is known to undergo suppression compared to a resting baseline during an attention-demanding task (such as detecting letters in a noise pattern). Thus, we interpret the less negative amygdala response to fearful face and house stimuli as a

small break from the suppression of the amygdala. While we did not observe a

category-specific response in the amygdala to fearful faces, we go on to explore the

connectivity profile of the right superficial amygdala, based on its involvement in social

processing (Bos, van Honk, Ramsey, Stein, & Hermans, 2012; Bzdok, Laird, Zilles, Fox, &

Eickhoff, 2012; Goossens, et al., 2009).

Amygdala Connectivity Analysis

We previously identified a network of increased coherence with the left

amygdala BOLD signal for suppressed fearful face presentations compared to

suppressed houses (Troiani et al., in press). One goal of the current study was to

examine whether this network existed with a more robust form of interocular

suppression. Based on our finding of right superficial amygdala activation to both faces

and houses, we used this region to guide a connectivity analysis. We reasoned that

despite the lack of differential mean activation in this region based on the category of

the stimulus, perhaps this activation leads to increased connectivity for one stimulus

(fearful faces) more than another (houses), based on its motivational value. We used

regions of interest from the results of our previous connectivity analysis to guide our

search. These seven ROIs included bilateral pulvinar, bilateral insula, left inferior

parietal cortex, left frontal eye fields, and early visual cortex (Figure 4A). We find

increased coherence between the right superficial amygdala seed and two regions,

including the right pulvinar and left inferior parietal cortex (Figure 4B). These results

suggest that the pulvinar and parietal cortex may be amongst the earliest regions to differentiate between motivational stimuli, a point we will take up further in the discussion.

Univariate Ventral Visual Responses

The fusiform face area (FFA) and Parahippocampal place area (PPA) are regions typically defined based on their category-selectivity. In conscious vision, the FFA responds most strongly to faces compared to other objects, while the PPA responds most robustly to scenes or houses and not at all to faces. In studies of non-conscious vision, activation in category specific regions is thought to reflect stimulus awareness, as activation in these regions may indicate that the signal from the visual stimulus has escaped suppression enough to proceed beyond early regions in the visual processing hierarchy and reach higher level processing regions. Although, some studies have found activation in category-specific visual cortex without awareness albeit at much lower levels compared to responses to conscious stimuli (Jiang & He, 2006; Troiani et al., in press). Given the link between conscious awareness and activation in category-selective cortex, we examine mean responses in the FFA & PPA to all three conditions (fearful faces, houses, no stimulus control). We find no differences between the three conditions in either FFA or PPA, indicating that the stimuli are not escaping suppression enough to reach ventral visual cortex.

Multivariate Ventral Visual Responses

A previous study found that faces and houses presented in the absence of awareness were associated with distinct multi-voxel patterns in object-selective cortices (Sterzer, Haynes, & Rees, 2008). These results suggested that some amount of information escapes suppression and reaches object-selective cortex differentially by object type (i.e. FFA for faces and PPA for houses). To examine whether object-related information was present in our own data, we employed a multi-voxel pattern analysis. We find no evidence that signals in subject-specific FFA or PPA are able to discriminate between fearful faces and houses, or stimulus vs. control. In conjunction with the null univariate results described above, these results suggest that stimulus information does not escape suppression enough to reach higher-level cortex in the current experiment.

Discussion

The goal of this study was to capture stimulus-driven activation that is uncontaminated by top-down mechanisms. We achieve this goal by using an interocular suppression technique accompanied by an orthogonal task that appears atop the dominant image—this task serves to further prevent perception of the stimuli presented to the opposite eye. We successfully implemented this novel paradigm in previous work (Troiani et al., in press), but optimized the current design by 1) using a more robust

version of interocular suppression, 2) making stimuli smaller to prevent piecemeal

breakthrough, 3) using MR compatible dual-display goggles to ensure stimuli were

uniquely presented to one eye, and 4) including a no stimulus control condition.

Despite the strong suppression that resulted from these optimizations, we find that

stimuli (compared to a no stimulus control) can escape interocular suppression and

activate regions involved in subcortical vision, including the superior colliculus,

thalamus, hippocampus, and a region of particular interest—the amygdala. In our

previous work, we identified greater mean amygdala activation for fearful faces

(compared to houses) as well as a network of regions that increased in coherence with

the amygdala that was specific to fearful faces. Thus, we expected to replicate our

previous finding of category-specific activation in the current study, despite employing

several methods to further prevent escape from suppression. In contrast to our

hypothesis, we show equally robust amygdala activation to both fearful faces and

houses presented outside of awareness. At the whole brain level, both suppressed

stimulus categories activated the right superficial amygdala, a result that was confirmed

with a more thorough analysis of amygdala subregions. Although the mean activation in

the superficial amygdala was equivalent for fearful faces and houses, the connectivity

profile showed differential increases in connectivity for suppressed fearful faces

compared to suppressed houses. Specifically, we find increased task-specific coherence

between the amygdala and two regions that are part of the attention network identified

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in our previous work: the right pulvinar nucleus of the thalamus and left inferior

parietal cortex.

We also examined mean activation and multivoxel pattern differences in cortical

regions associated with category-specific processing of faces (FFA) and houses (PPA). In

our previous study, we found that fearful face-specific amygdala activation was

accompanied by activation in the left FFA, but no activation in PPA for either suppressed

faces or houses. In the current study, we find no category-specific activations to the

suppressed stimuli. Furthermore, there seems to be no information at all about the

presence of a stimulus in high-level visual cortex, as there were no activation differences

in either FFA or PPA for the presence of a suppressed stimulus vs. no stimulus.

Additionally, neither the FFA nor PPA could discriminate between the presence of a

stimulus vs. no stimulus based on multi-voxel patterns, providing further evidence that

stimulus information was not reaching high-level visual cortex and indicating that these

stimuli were robustly suppressed from awareness.

Unsurprisingly, we show that the main task activates bilateral LGN and early

visual cortex, consistent with information processing by a retino-geniculate-cortical

pathway. When further exploring activation in EVC to each condition separately, we

find significant differences between stimulus presentation and control. More

specifically, the control condition correlated with more activation in EVC than the two

suppressed stimulus conditions. V1 is the first stage in the visual processing hierarchy at

which the information from both eyes is combined. In previous studies examining the

neural bases of binocular rivalry, activation in V1 has been concomitant with awareness. That is, when subjects were asked to report whether they perceived one rivalrous stimulus compared to another, activation in V1 strongly correlated with the reported percept (Polonsky et al., 2000; Tong and Engel, 2001; Lee et al., 2007). When stimuli are reliably suppressed, this is associated with suppression in V1 (Lee and Blake, 2002). Because observers remained unaware of the stimuli presented to their left eye for the duration of the study, this pattern of activation in EVC likely reflects successful suppression of the fearful face and houses stimuli.

These results are also informative with regard to the idea of parallel visual pathways. Visual signals originate from the retina and project to the lateral geniculate nucleus (LGN) to primary visual cortex (V1), located in the posterior occipital lobe, surrounding the calcarine fissure. It is thought that a parallel pathway exists which projects from the superior colliculli to the thalamus, and onto the amygdala. In our data, we show that the presence of a stimulus appears to reduce activation in EVC. In contrast, we show that stimulus information activates regions of the superior colliculus, thalamus, hippocampus, and amygdala, indicating that that information has reached structures of the superior colliculus-pulvinar-amygdala pathway. This suggests that information can reach subcortical regions and influence the amygdala without corresponding information representation in higher-level visual regions (FFA/PPA) or even lower level cortical visual regions (EVC).

We also find hippocampal activation when stimuli are present (but suppressed). This finding is consistent with models of fear conditioning that implicate hippocampal-amygdala connections in contextual fear conditioning. For example, Alvarez & colleagues found right anterior hippocampus and bilateral amygdala activation for the conditioned stimulus in a foot shock fear conditioning paradigm, but only when preceded by the associated context (Alvarez et al., 2008). Amygdala-hippocampal connectivity increases bidirectionally when retrieval of emotional information is relevant to the current behavior (Smith et al., 2006). Furthermore, unseen primes have been shown to generate predictive signals related to stimulus history and influence the precept selected in a binocular rivalry paradigm (Denison et al., 2011). Thus, it may be that predictive signals are generated by the hippocampus even with the minimal amount of information that leaks though interocular suppression. Such a predictive signal would aid in the prioritization of particularly relevant stimuli.

There are several differences between the current study and our previous study, both in design and results. Although the combination of flash suppression and rivalry used in our previous study is referenced as a form of continuous flash suppression, there are a few, important differences. In our previous design, we used a single red/blue rivalrous image that was viewed through anaglyph glasses. Because it is difficult to exactly match the colored lenses of the anaglyph glasses and the color of the rivalrous stimuli, it is possible that certain wavelengths can "leak through" from the suppressed image into the dominant eye. Here, we used MR compatible goggles with a

dual LCD display, which allowed for stimulus presentation directly into one eye without the possibility of wavelength-based "leak through" of information. Previously, we induced motion suppression through the use of a centrally presented word/checkerboard stimulus that moved around the screen. In practice, this was quite suppressive—and participants were still not explicitly aware of the stimuli. However, completely changing a colorful, dominant stimulus at a rapid rate (as in the type of continuous flash suppression described by (Tsuchiya and Koch, 2005) is a much stronger form of suppression. In our previous study, stimuli could be differentiated based on mean amygdala activation. Accompanying this greater amygdala activation was left parietal activation for suppressed fearful faces compared to suppressed houses and increased connectivity with multiple regions involved in attention. Taking the results of both studies together, we speculate that under the less robust suppression induced previously, more information was able to escape suppression and activate a broader network involved in preattentive stimulus processing. With this greater information breaking through, feedforward and feedback signals between regions in this network may strengthen their communication and lead to the mean activation differences observed in our previous study.

Here, we find amygdala activation for stimuli (vs. no stimulus) presented in the absence of awareness despite apparent suppression of early visual cortex and a lack of information in category-specific cortices. These results indicate that information can proceed in a feed-forward manner to the amygdala. We additionally show increased

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connectivity from the right amygdala to the right pulvinar and left inferior parietal

cortex. These results suggest that in addition to the amygdala, the pulvinar and parietal

cortex may be amongst the earliest regions to differentiate between motivational

stimuli. Recently, these regions have been implicated in information integration and

motivational relevance. Parietal cortex has long been implicated in spatial attention and

has been more recently implicated in housing a salience map that integrates top-down

and bottom-up attention (Balan and Gottlieb, 2006; Bendiksby and Platt, 2006; Fecteau

and Munoz, 2006; Geng and Mangun, 2009; Zenon et al., 2010). In particular, the lateral

intraparietal cortex (LIP) integrates sensory and reward information (Rorie et al., 2010),

is modulated by sensory, motivational, and motor factors (Gottlieb et al., 2009), and has

sharpened tuning responses in response to motivational relevance (Falkner et al., 2010).

Recently, baseline fluctuations in LIP response were found to reflect motivational

fluctuations, independent of spatial attention (Wang et al., 2012). The pulvinar nucleus

of the thalamus is a second region implicated in modulating information flow in

response to altered motivation. Although this region was previously thought to be

merely a relay nucleus, recent evidence highlights the pulvinar's role in selecting salient

information, as pulvinar lesions lead to inabilities to filter out distracting information

(Snow et al., 2009; Wilke et al., 2010). The pulvinar has also been specifically implicated

in processing salient face information, as emotional expressions of human faces activate

neurons in the monkey pulvinar (Maior et al., 2010). Most recently, the pulvinar was

shown to synchronize activity between multiple cortical areas (Saalmann et al., 2012),

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highlighting a complex role in information integration that would be necessary for combining the wide array of information important for assessing motivational relevance. Thus, our finding adds to previous work implicating the amygdala, pulvinar and parietal cortices in early processing of motivational stimuli.

Table 4.1.

Peaks of significant clusters for all conditions and for the contrast of stimulus (faces & houses) compared to no stimulus. Results are cluster FWE corrected for multiple at p<0.05. Regions correspond with Figure 2a & 3a.

Contrast	Region	Hemi-sphere	X	Y	Z	T-value
All Conditions	LGN	R	24	-28	0	6.63
	LGN	L	-26	-32	0	7.53
	EVC	R	24	-96	8	15.31
	EVC	L	14	-102	8	16.1
Stimulus > No Stimulus	amygdala	R	26	-2	-16	3.91
	thalamus	R	12	-2	0	4.09
	Superior colliculus	R	4	-22	-6	3.60
	hippocampus	R	28	-12	-10	5.03

Figure 4.1

Stimulus Schematic & Experimental Design. (A) Participants performed a vowel/consonant detection task, projected into the right eye atop flashing noise images presented at a rate of 10 Hz. In the left eye, 32 fearful faces, 32 houses, and a no stimulus control were projected to the left eye. (B) Overall block design, with 28-second blocks of noise images separated by 12 seconds of rest. Ten letters were presented for a duration of 1500ms each, with letter onset jittered by 300-600ms. Eight houses or fearful faces appeared within each block, with block order counterbalanced and randomized across participants.
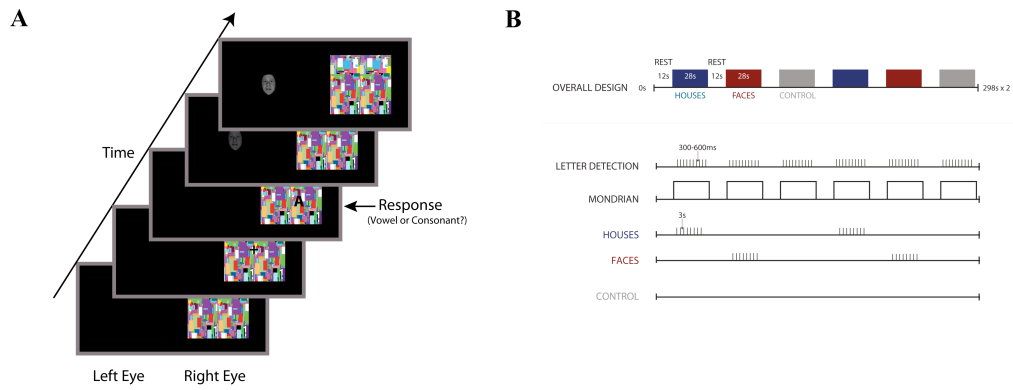
Figure 4.2.

Effects across all conditions. (A) Whole brain fMRI response to fearful faces, houses, and control compared to resting baseline. Data show effects in bilateral lateral geniculate nucleus and early visual cortex, FWE cluster corrected for multiple comparisons, p<0.05. (B) fMRI response in early visual cortex for each condition, plotted individually by hemisphere. Differences between stimulus presentation (fearful face or house) and no stimulus (control) were significant in both hemispheres, with stronger activation for the control condition than the two stimulus conditions. There were no differences between the two stimulus categories (fearful faces compared to houses).
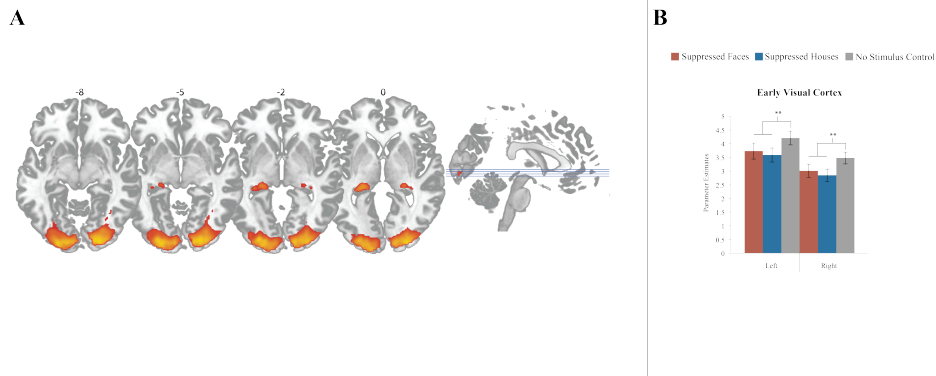
Figure 4.3

(A) Regions showing greater fMRI response to suppressed fearful faces or suppressed houses compared to control. Activation to stimulus (fearful faces & houses) compared no stimulus was computed. The region of activation identified with the conjunction (p<0.05, uncorrected) is depicted with a yellow outline. Suppressed stimuli activated the right amygdala, superior colliculus, thalamus, and hippocampus compared to the no stimulus control condition. (B) Region of interest analysis using amygdala cytoarchitectonic probabilistic maps. An average parameter estimate for the centromedial (yellow), laterobasal, and superficial subregions was computed for each individual across all three conditions. While every subregion show the same pattern of response (stronger response for fearful faces and houses compared to control), this reached significance in bilateral superficial amygdala and the right centromedial amygdala.
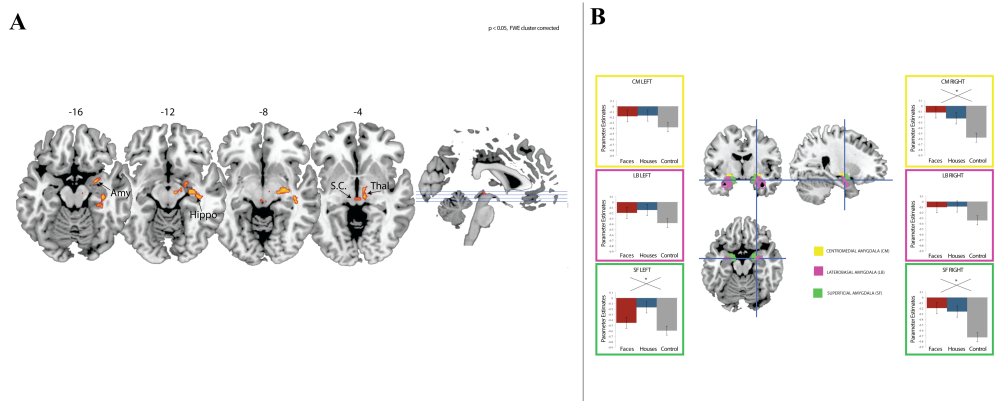
Figure 4.4.

Connectivity regions of interest and results. (A) Regions of interest were defined based on a result from our previous work: Regions that showed increased coherence with the amygdala for fearful faces compared to houses included early visual cortex (EVC), left inferior parietal cortex, bilateral pulvinar (Pul), left frontal eye fields (FEF), and bilateral insula (Ins) (Troiani et al., in press). (B) Region of interest results from a psychophysiological interaction (PPI) analysis with a right superficial amygdala seed. Significant effects were observed in left inferior parietal cortex (red) and the right pulvinar (green).
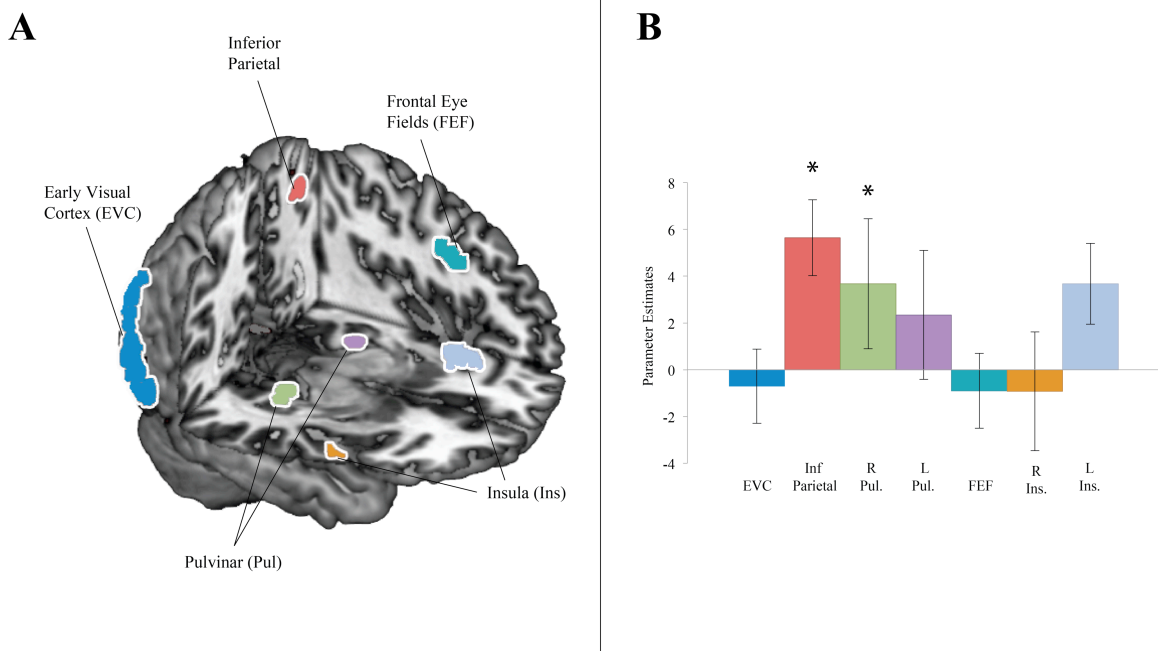
CHAPTER 5: General Discussion and Future Directions

Altered motivations impact our perception, decision-making, and behaviors to enable us to flexibly respond to our internal and external environment. Although it is generally accepted that we pay more attention to stimuli that are motivating and even process motivating stimuli more quickly, little is known about the psychological and neurobiological mechanisms that support this process. The major goal of the studies described above was to investigate the impact of various types of motivation on visual selection, in order to understand the influence of altered motivation on the earliest stages of visual selection.

In Chapter 2a, we used a break from continuous flash suppression paradigm to show that the reward history of an object can influence how quickly the object is prioritized. In Chapter 2b, we demonstrated that altered social motivation impacts the rate at which social stimuli are prioritized in awareness. Furthermore, we found the amount of face prioritization was behaviorally relevant: those individuals that prioritized faces the most in response to rejection were also the most socially motivated, as measured by a social anhedonia questionnaire. In Chapter 3, we established that a motivational stimulus (fearful faces) evoked an amygdala response and activated a network of regions involved in attention. In Chapter 4, we used a more robust form of suppression and a number of design improvements to assess whether this amygdala

response was activated in a feed-forward stimulus-driven mechanism. This study showed robust amygdala activation with no mean or multi-voxel pattern differences in higher-level visual cortices, indicating the signal originated in subcortical visual processing regions. Furthermore, we show that the amygdala increases its connectivity with the pulvinar and inferior parietal cortex, suggesting that these may be the regions that differentiate stimuli earliest in this motivational attention network. Combining the results from these studies allow us to suggest future directions for this work, with a particular interest in implications for autism spectrum disorders.

5.1 The salience filter: Bottom-up mechanisms

Attention is frequently described as a filter that serves as a selection mechanism to obtain the most meaningful information from our environment. Its thought that attention determines the most salient parts of our environment in order to maximize the information we obtain from our environment. While it is clear that altered motivation influences this salience filter, the important underlying neural structures are unclear, and the pursuit of this knowledge lays the foundation for many future research questions: What regions of the brain register a dip in social homeostasis? What changes occur in the brain to increase the potential of restoring balance to the organism? Do efficiencies in processing certain types of visual signals influence these abilities?

To begin the discussion of a salience filter, it is useful to consider how selective attention was originally described and tested. One informative framework is Feature-integration Theory (FIT). FIT was originally put forward by Treisman and Galade (1980) and sought to differentiate between the role of primary visual features, how these are integrated in the visual system, and whether the process of detecting conjunctions of these features requires focused attention. In this framework, different sensory features are coded automatically in specialized modules, in parallel with other modules. Each module forms a feature map of the dimension it encodes (i.e. colors or orientations). In order to bind different features into a conjoined object, both a spatial map and attention are required (see Figure 5.1). From this perspective, a spatial map contains feature boundaries for all encoded features, with each partition of space identified as "filled" or "empty". Focal attention is necessary to access the various feature maps via the master spatial map and integrate them (Treisman, 1988). While this idea was originally proposed in an attempt to understand whether the human brain is capable of accessing and combining multiple feature levels, it is quite interesting to consider with respect to motivated selection.   Studies examining FIT have focused on whether multiple features can be combined at an individual location. However, part of this theory states that sensory features are coded *automatically* and in *parallel*. This would indicate that information is present in each feature layer for all sensory features, even if it cannot be accessed. Thus, an alternative question is what is the quality of information present in each feature layer, even if it cannot be accessed by attention? And does the

quality of the information in each feature layer influence a bias in what spatial locations are selected for further processing? Furthermore, this biasing mechanism would be consistent with the Reverse Hierarchy Theory, proposed by Hochstein and Ahissar (2002). Part of this theory suggests that the computational results (or mean estimates) of implicit processing of basic information are only available to conscious perception. Determining the quality of information encoded automatically in sensory feature layers and how information quality impacts visual selection would be an interesting question for follow-up work.   The behavioral CFS method used in Chapter 2 is potentially useful for assessing this particular research question. For instance, if features (such as line orientation or color) are presented but suppressed from awareness using CFS, are some more likely to influence a decision following this prime? Can this influence be altered by the current state of the participant?

One possibility is that the information in each feature layer is only available as a summary measure. That is, information that is processed very quickly or unattended is pooled across a particular feature. These summary or ensemble statistics in vision are thought to provide a useful mechanism for dealing with the visual information bottleneck in order to increase visual processing efficiency. Daniel Ariely (2001) published the first behavioral data establishing that humans represent the mean size of a stimulus set, but none of the individual values of the set. In three experiments using static stimuli composed of different size dots, participants were asked to report whether or not a preceeding dot was part of the original stimulus.   Observers represented the

original stimulus set's mean and range, but little to no information about the individual

components. Chong and Treisman (2003) replicated Ariely's results, confirming that

observers can easily judge a mean value of a parameter but cannot judge whether a

particular value was present in the scene. Additionally, Chong and Treisman (2003)

added an attentional component to the experiment, providing evidence that mean size

judgments can be done without interference from simultaneous tasks that affected

distributed or global attention. Mean size judgments can be performed equally well for

normal, rectangular, and homogenous distributions, in addition to distributions with just

2 equal peaks and performance was not affected by a secondary task. Another

interesting question is whether there is relative influence of summary information in

different feature layers and whether this influence is altered by motivational state.

5.2 The salience filter: Top-down mechanisms

The mechanisms described above would be considered "bottom-up" in terms of

the visual processing hierarchy. Other more "top-down" mechanisms have been

studied in the attentional literature and may also be points of influence for motivated

attention. These two mechanisms include altering spatial attention and altering object-

based attention.

Visual attention can be directed towards different levels of a scene- typically differentiated as "global" and "local" levels. This type of attention is classically assessed via Navon figures (Navon, 1977). These figures consist of a large letter that is made up of smaller letters (Figure 5.2). Typically, there is global precedence, in that the global level is processed first. However, this can be influenced by individual experience and mood and can be altered in certain neuropsychological pathologies. For example, individuals from a remote culture have a local (instead of global) bias (Davidoff, Fonteneau, & Fagot, 2008) and this bias is altered after experience with an urban environment (Caparos et al., 2012). Personality traits of positive mood and optimism are associated with a global bias and negative mood with local bias (Basso, Schefft, Ris, & Dember, 1996). Positive mood that has been induced via music shifts perceptual bias towards global features and negative induced mood towards local features (Poirel, Cassotti, Beaucousin, Pineau, & Houdé, 2012; Schnall, Jaswal, & Rowe, 2008). Individuals with autism frequently show locally-oriented perception without a deficit in global perception (Bölte, Holtmann, Poustka, Scheurich, & Schmidt, 2006; Mottron, Belleville, & Menard, 1999; Mottron, Burack, Iarocci, Belleville, & Enns, 2003; Wang, Mottron, Peng, Berthiaume, & Dawson, 2007). It has been suggested that global perception is associated with low spatial frequency channels and local perception with high spatial frequency channels (Shulman, Sullivan, Gish, & Sakoda, 1986).

As to the neural bases underlying local and global perception, this has been studied in a separate literature regarding a theory of "neural object-files". Distinct

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regions of parietal cortex are thought to be involved in object individuation vs. object

identification (Xu & Chun, 2007; Xu & Chun, 2009; Xu, 2009). Object individuation

involves a selection and course representation of about 4 object-files selected via their

spatial location and relies on the inferior intraparietal sulcus (IPS). This is distinguished

from object identification, which represents detailed featural information, reliant on

superior IPS. These two processes are thought to be differentially reliant on spatial

frequency information, with object individuation utilizing low spatial frequencies and

object identification requiring high spatial frequencies. This theory is substantiated with

an fMRI task in which observers viewed a variable number of shapes, briefly displayed in

one of 8 possible locations (Xu, 2009). These shapes could be simple or complex (two

simple shapes combined) and observers performed a change detection task. Inferior IPS

activation increased for set size, but plateaued at four objects, and was not differentially

responsive for complexity of the stimulus. Superior IPS activity was modulated by

object complexity. In a second change-detection fMRI study, observers viewed four

identical or different shapes. While superior IPS activity was much greater when the

shapes were different, activity in inferior IPS was no different for identical and different

shapes. The authors attribute these distinct activation profiles as separate neural

mechanisms, with inferior IPS selecting object-files in an individuation process

consistent with visual short-term memory capacity limitations.

Taken together, research in global/local perception suggests that mood can shift

perception and this is potentially accomplished via different spatial frequency channels.

The neural object file theory suggests this is driven by different parts of parietal cortex.

Future work should assess whether altered motivation influences spatial frequency

channel selection. This could be assessed through a covert attention task (Posner cuing

paradigm), in which spatial frequency filtered versions of objects are presented

following a directional cue. One would expect that in an altered motivational state,

attention towards a specific spatial frequency channel might be particularly enhanced,

as indicated by faster response to these cues in valid trials.

Motivation might influence perception via an object-based mechanism that is

independent from spatial attention. It is thought that a top-down biasing mechanism is

present during real-world search, which essentially results in a pattern-matching

mechanism driven by a category-specific search template in object-selective cortex

(OSC) (Peelen, Fei-Fei, & Kastner, 2009; Peelen & Kastner, 2011). This was tested in an

fMRI study, during which subjects identified the presence of a body or car (in separate

tasks) in either attended or unattended scenes (Peelen et al., 2009). Prior to the task,

category localizer scans identified activation patterns in OSC associated with viewing

bodies or cars. Using multi-voxel pattern (MVP) analysis of OSC, activity patterns in the

category localizers were correlated with activity patterns in the body and car conditions

of the main experiment. Response patterns correlated more highly within an object

category than between object categories, regardless of whether the stimulus was

attended. That is, the activity pattern in object-selective cortex when viewing isolated

images of cars (as in the category localizer) is more highly correlated with the pattern of

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activity in OSC during the car search task than the body search task, and vice-versa. This is thought to reflect a category-specific biasing mechanism, in which detection is aided by activation of a "search template" in OSC. Because this bias can apply to unattended stimuli, it appears to be independent of spatial attention. In follow-up work, efficient object-selective search was found to both increase object-selective patterns as well as decrease object patterns that were not associated with the relevant search goal (Seidl, Peelen, & Kastner, 2012). It would be interesting to follow-up this work to test whether altered motivation (via social exclusion, for example) impacts object-selective cortices in a similar manner.

5.3 Social Motivation

While the majority of motivation-based research has focused on biological or monetary motivation, it has become increasingly clear that social motivation is an equally powerful drive. In the collaborative context in which humans live, pursuit of collaborative activities makes a range of benefits accessible (Kaplan, Hooper, & Gurven, 2009). Therefore, a drive to be included in social interactions is vital and social motivation can be seen as an adaptation to this highly collaborative environment. Given the importance of social inclusion for survival, social exclusion is perceived as highly detrimental. Social motivation functions just like any other basic need: when human's need to belong is not met, negative feelings arise in order to signal to the individual that

social homeostasis is disrupted. Formally, social motivation refers to the preferential orientation towards social objects, the pursuit of rewarding social interactions, and the maintenance of social relationships (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012).

In the Social Motivation Hypothesis of Autism, diminished social motivation, mediated by dysfunction of the mesocorticolimbic reward circuitry, contributes to deficits in social attention, social perception, and social cognition in autism spectrum disorders (ASD) (Chevallier et al., 2012; Schultz, 2005).   ASDs are a heterogeneous group of neurodevelopmental disorders defined by a triad of deficits: repetitive and stereotyped behaviors, delays in early language and communication skills, and impairments in social interaction (DSM-IVR). Social deficits are a cardinal feature of ASD and diminished social interest is one of the earliest and most persistent symptoms of the condition. Thus, autism can be described as a disorder of social motivation, or the failure to prioritize social entities as valuable and important. Face processing deficits in ASD could arise from a malfunctioning reward system, sensory systems, or a composite of both. The possibility that reward systems in ASD are altered lends further credence to the possibility that autism symptomology results from cascading effects of an early malfunctioning motivational system.

Follow-up experiments in autism for each of the studies described in the previous chapters would offer important information as to the origin of their face processing deficits. In autism, face processing deficits (and corresponding hypoactivation of the fusiform gyrus when doing face processing tasks) could be due to

a lack of experience with faces due to inattention to faces from early in life. Thus, a next step with regard to autism is to identify whether they display similar abilities to learn novel object-reward associations. Furthermore, do they demonstrate similar abilities to prioritize objects with more motivational value? Recent work has begun to characterize the integrity of reward responses to different types of reward in ASD, including response to biological, monetary, and social reward (Kohls et al., 2011; Scott-Van Zeeland, Dapretto, Ghahremani, Poldrack, & Bookheimer, 2010). Results from these studies suggest hypoactive ventrostriatal responses to reward in ASD, most notably in response to social forms of reward.

The amygdala is thought to guide attention towards biologically relevant stimuli, and in conjunction with the fusiform face area, forms a network for effective face processing (Adolphs, 2008). Face processing difficulties in ASD have been linked to hypoactivation of both the amygdala and fusiform gyrus in face perception tasks (Critchley, H.D. et al., 2000; Schultz et al., 2000), yet the network underlying these abnormalities is not fully understood. The consistent hypoactivity of the fusiform in people with ASD suggests it may serve as a cortical locus of their face-processing deficits. Given the complexity of the perceptual and social demands tested in face perception tasks, the origin of face processing deficits in ASD could be a consequence of differences in any number of highly interactive brain regions belonging to multiple neural systems. A pathophysiological model of autism suggests an early failure of the amygdala results in abnormal development of cortical regions important for visual social

perception, specifically the fusiform gyrus in the ventrotemporal cortex (Schultz, 2005). This amygdala-fusiform system may also serve an important role in scaffolding other social cognitive skills deficient in autism.

One goal of the current research was to develop a paradigm that could examine the integrity of stimulus-driven amygdala responses in individuals with autism. In Chapter 4, we show robust activation in the amygdala to suppressed stimuli in typically developing adolescents. Future work should examine the integrity of this response in ASD. Hypoactivation of the amygdala in autism compared to controls would indicate impaired stimulus-driven processing in autism.

The research described in this dissertation focused on the influence of motivation on prioritization of objects. The results of these studies are a first step in understanding the neural mechanisms underlying how we select the most meaningful information in our noisy sensory world. The studies described here have demonstrated that we prioritize objects of value, that visual information can reach the amygdala without explicit awareness, and that this amygdala response guides nodes of an attention network towards objects of relevance. In particular, the results presented here suggest that there is a network of subcortical visual regions involved in processing motivationally relevant stimuli. The results of these studies may form the basis for understanding how we select relevant information in our environment to satisfy our motivational needs.

Figure 5.1

Depiction of Feature Integration Theory, in which individual sensory feature maps (Color, Orientation, etc.) are combined onto a master map of locations. An attentional filter than serves as a "spotlight" which can access information about various features at a particular location.
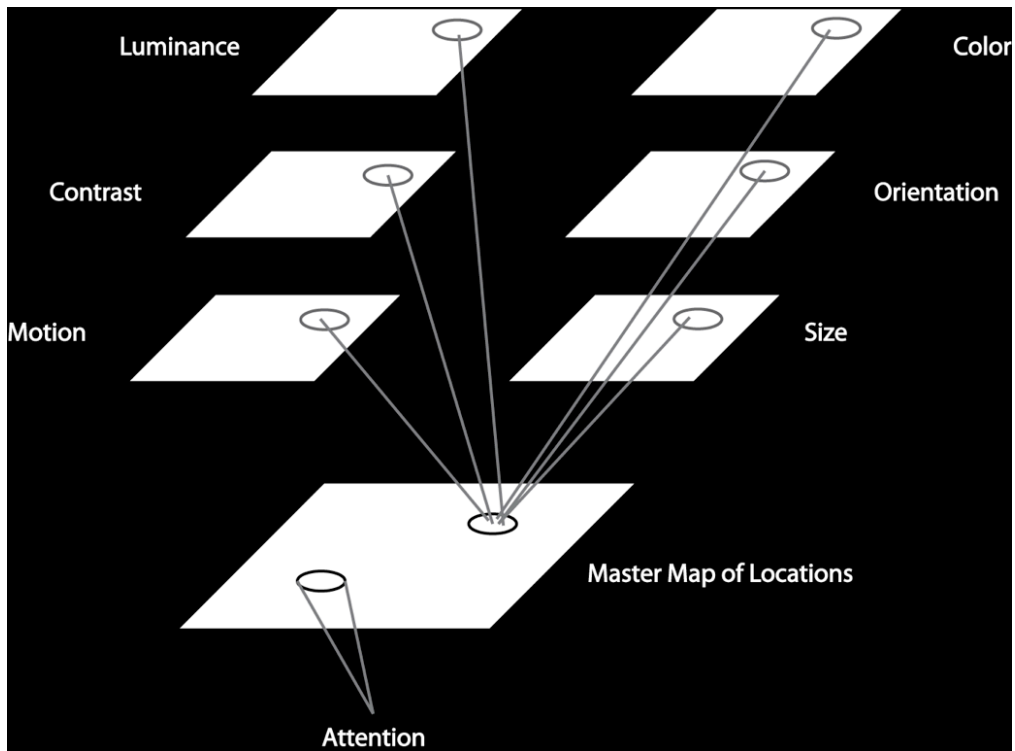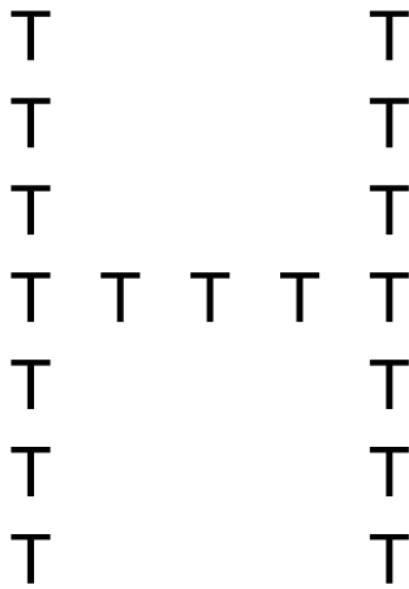
Figure 5.2

Navon Figure. A global letter (H) is made from many local letters (T).

```
T           T
T           T
T           T
T  T  T  T  T
T           T
T           T
T           T
```

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