AFFECTIVE MODULATION OF SCENE PERCEPTION: HEMODYNAMIC AND ELECTROCORTICAL RELATIONSHIPS

by

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(Under the Direction of Dean Sabatinelli)

ABSTRACT

Research suggests that human emotional discrimination is initiated through an interaction of inferotemporal cortex (IT) and amygdala that then modulates activity across the visual system. However, the temporal dynamics of activity in these downstream regions is unclear. Fast sampled functional magnetic resonance imaging (fMRI) was used to investigate the timing of emotional discrimination in amygdala and IT relative to frontoparietal structures, including frontal eye fields (FEF) and intraparietal sulcus (IPS). A subset of subjects also participated in an electrocortical recording session to enable a comparison of middle and late emotional-modulated event related potentials (ERP) with the fMRI data. Amygdala and IT differentiated emotional from neutral scenes prior to IPS and FEF. Correlations were found between hemodynamic and late ERP modulation across stimulus pleasantness and semantic categories. These data suggest that visual emotional information may be registered in a ventral network, and distributed to dorsal attention structures thereafter.

INDEX WORDS: Emotion, frontal eye fields, intraparietal sulcus, amygdala, inferotemporal cortex, LPP, EPN, fMRI, EEG.

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CHAPTER 1

LITERATURE REVIEW

Introduction

Emotional events play a significant role in our daily decision-making and attention processes. While it is common to view emotion as a manifestation of conscious thought, it is more practical and quantifiable to express it as a disposition to action (Frijda, 1986). An organism must be able to attain certain resources to sustain life while avoiding dangerous encounters that may end it. It is thus imperative to quickly identify if an object or event possesses emotional qualities in order to respond accordingly. Such survival related environmental stimuli are therefore considered emotionally relevant. One can further separate affective stimuli into appetitive and defensive categories that lead to approach and avoidance behaviors, respectively (Dickinson & Dearing, 1979). In this case we are motivated to attain, and therefore approach pleasant stimuli, while trying to avoid unpleasant stimuli. Both pleasant and unpleasant environmental events are affectively arousing, thus the arousal characteristics of the environment around us begin the cascade of preparatory activity that precedes action, while hedonic valence determines the direction of that action (Lang et al., 1997). In this literature review, the emotional process will be viewed as activation of a survival circuit shared across species that, at least in humans, results in conscious feelings (Ledoux, 2012). The purpose of this review is to explore the physiological and neural mechanisms involved in recognizing, categorizing, and responding to emotional stimuli.

A survival mechanism

The study of the neurobiological circuits of emotion, specifically fear, initially received great attention in the animal model. The state of fear seems to be tied closely with the primal mammalian defense system, expressed by the organism's sensory intake and preparation for the flight or fight response (depending on the availability of an escape option). Fear in rodents is readily conditioned, often by pairing an auditory tone with an electrical foot shock, after which the tone by itself will cause an expressed freezing response in the animal. This fear state can be quantifiably measured by imposing a sudden stimulus that will generate a measurable startle response. Many of these studies have implicated the amygdala, a small bilateral subcortical limbic structure located within the medial temporal lobe, as a common pathway of this fear network, and have demonstrated that electrical stimulation of the amygdala will elicit many of the same responses seen under normal fear conditioning paradigms (Sarter & Markowitsch, 1985). The amygdala also possesses the anatomical connections to process the emotionality of environmental stimuli, as it both receives connections from sensory areas and diffusely projects to a variety of cortical and subcortical structures to mediate the fear response (Lang et al., 2000).

Emotional reactivity may also be elicited in humans, using stimuli such as emotional faces or scenes. Studies involving faces typically compose of males and females making a variety of emotional facial expressions facing the viewer, often based off of the work of Ekman and Friesen (1976). Those involving scenes generally use the International Affective Picture System (IAPS; (Lang et al., 2008), which is composed of pictures that are normatively rated for arousal level and valence (pleasantness). Examples include scenes depicting household objects, landscapes, and people engaged in routine activities as neutral images, animal attack, human threat, and bodily mutilations for unpleasant images, and happy babies, sport scenes, and erotica for pleasant

images. Picture sets chosen for experiments may thus be created to occupy distinct, yet balanced, areas of a two dimensional "affective space" of valence and arousal.

Using these methods, a similar startle response to that found in animals can also be seen in both infant and adult humans (Balaban, 1995; Vrana et al., 1988), consistent with a common evolutionary adaptive defense mechanism common across mammalian species. Emotional reactivity was prompted using either human faces or emotional scenes, with both stimulus types eliciting a linear increase in the startle response for pleasant, neutral, and unpleasant images, respectively. Startle magnitude may therefore be used as an index of motivational circuitry that engages both appetitive and defensive mechanisms. In addition to the startle reflex, peripheral physiology may also reflect these underlying dimensions of emotion.

Orienting and peripheral physiology

An emotionally arousing event, whether pleasant or unpleasant, will initiate distinct physiological changes. For example, humans and animals show a marked cardiac deceleration when exposed to arousing stimuli, which is hypothesized to reflect a period of sensory intake (Graham & Clifton, 1966) and is, at least in part, mediated by the amygdala (Veening et al., 1984). It is at this time that an organism detects an arousing stimulus and pauses to process all relevant environmental information. This is consistent with studies of fear in animals, which exhibit a freezing response to aversive stimuli (LeDoux, 2003). In keeping with this idea, this sensory cardiac deceleration disappears when humans imagine emotional events (Schwartz, 1971), as there is no perceptual information from the external environment to process. Furthermore, unpleasant events accompany a larger decrease in initial cardiac deceleration than pleasant (Bradley, 2000). After an early deceleration, there is a marked period of cardiac acceleration, which reflects the switch from sensory intake to action (fight or flight).

Interestingly, phobic individuals show a prominent cardiac acceleration for phobic items with little to no deceleration (Hamm et al., 1997). This period of minimal sensory intake may reflect a learned fear that has developed a more efficient sensory processing pathway in order to recognize the feared object more readily.

Skin conductance is another physiological measure reliably modulated by emotional arousal, and reflects sympathetic nervous system activity, which stimulates sweat glands on the palms and soles (Critchley, 2002). Since emotion seems to drive action, any item in the environment that is significantly arousing would increase this reaction. Accordingly, the recorded skin conductance response (SCR) shows a linear increase with stimulus arousal, regardless of valence (Bradley et al., 2001b). Studies have also demonstrated that this increase in SCR occurs during emotional imagery (Fiorito & Simons, 1994), emotionally arousing auditory scripts (Bradley & Lang, 2000), and during the anticipation of an emotionally arousing image (Hamm & Vaitl, 1996). An emotionally modulated SCR can also be recorded when arousing images are presented for as briefly as 80ms (Codispoti et al., 2009), and even when individuals can not consciously identify an unpleasant object they have seen, they will still exhibit an increased electrodermal response to that object (Ohman & Soares, 1994). Therefore, the SCR is a dependable measure of sympathetic arousal across modalities, even after only brief exposure to arousing stimuli, and appears to be independent of conscious identification of unpleasant objects. Interestingly, patients with bilateral or unilateral amygdala lesions show an absent or diminished (respectively) conditioned SCR response to noxious stimuli, while still able to declare the conditional rules, suggesting that the amygdala also plays a role in SCR modulation (Bechara et al., 1995; LaBar et al., 1995).

Electrocortical correlates and stimulus characteristics

Peripheral physiological responses co-occur with brain regions that are preferentially active for perceived emotionally arousing stimuli, and can be measured non-invasively using techniques such as electroencephalography EEG. Evidence for differential brain processing for arousing scenes is provided via the Late Positive Potential (LPP), a delayed event related potential (ERP) present over the centro-parietal region of the scalp (Cuthbert et al., 2000a; Keil et al., 2002) typically beginning around 400ms with a duration dependent upon recording methods. This ERP is thought to extend from the P300 component (Cuthbert et al., 2000b; Schupp et al., 1997). Cuthbert and colleagues (2000a) observed sustained LPP modulation for almost the entire 6s duration of the picture, reflecting continuous processing of each image. The LPP amplitude increases in positivity with stimulus arousal, regardless of hedonic content (Schupp et al., 2004a; Schupp et al., 2000), and will therefore undergo a roughly equivalent increase in positivity for scenes depicting aversive threat and erotic couples compared to neutral faces and household objects.

To verify that the LPP is an index of emotional arousal and not a simple sensory characteristic of picture stimuli, Bradley and colleagues (2007) presented subjects with a series of affectively arousing and non-arousing images that were composed of either simple figure ground objects or visually complex scenes. While occipital regions exhibited increasing activation for complex scenes shortly after picture onset (~150ms), the physical characteristics of the images did not affect the increased LPP response to arousing scenes (~400-700ms in this study). Nor did differences between colored and grayscale images change the affective modulation measured by the LPP, even for short stimulus presentations (Codispoti et al., 2012; Weymar et al., 2009). This emotional modulation of the LPP is also slow to habituate to repeated

stimuli; after many repetitions of the same affective and neutral objects, LPP amplitude, while decreasing slightly overall, is consistently larger for arousing compared to neutral images (Codispoti & De Cesarei, 2007; Codispoti et al., 2006). Affective modulation of the LPP also reliably occurs for stimuli presented very briefly (without a mask), even as short as 25ms in duration (Codispoti et al., 2009). Thus, it appears that the LPP is reflective of the emotional meaning of objects, and does not depend on an ongoing stimulus.

Earlier neural modulation of emotionally arousing scenes can be recorded during visual processing, as indexed by the early posterior negativity (EPN) ERP over lateral occipital sensors from approximately 200-300ms after stimulus onset. Scalp potentials during emotionally arousing images are associated with more negativity (or less positivity) when compared to neutral images (Schupp et al., 2003b), even when pictures were presented briefly (Junghöfer et al., 2001; Schupp et al., 2004b). Interestingly, threatening faces also elicit a greater negativity compared to neutral, while happy faces do not (Schupp et al., 2004c). Since the LPP occurs later and over a large region of sensory regions, it may reflect post-sensory, higher order processing. The EPN may be reflective of the initial visual processing areas marking environmental stimuli as motivationally relevant and necessary for the additional downstream visual processing reflected by the LPP (Junghöfer et al., 2001; Schupp et al., 2004b).

Emotional imminence

Mammals undergo physiological changes as a function of their proximity to an emotionally arousing stimulus. Lang and colleagues (1997) proposed a defense cascade model in which prey animals experience changing physiological states as threat distance decreases. Additionally, animals will approach a goal that is associated with both reward and punishment up to a certain point, at which time the avoidance of punishment supersedes the drive for reward (Miller, 1959). Taken together, when a distant threat is detected an animal will freeze and engage attentional resources to evaluate the threat. As the threat grows more proximal the animal will undergo physiological changes in preparing for a flight or fight reaction, which is triggered when the threatening object closes to a certain distance. A similar chain of events occurs in predatory animals in which the predator will decrease movement on detection of prey as a hunting tactic, and at a specific distance the initiation of prey capture is triggered.

The defense cascade model has been supported in humans using computer simulations and recorded ERPs (Löw et al., 2008). In this study, subjects viewed a series of three pictures that were presented in six different sizes to simulate gradual approach. The three pictures consisted of a clock, which served as a neutral stimulus, an appetitive bundle of money, and an aversive gun pointed toward the subject. After the sixth ("imminent") image, the subject was required to press a button to either prevent an image of the gun firing or the money from burning. The standard affective LPP modulation was elicited at all six "distances". Distance differentially affected ERP magnitude in which the average amplitude differences (e.g. emotional stimulus > neutral stimulus) of the LPP exhibited a u-shaped curve with the "furthest" and "closest" images eliciting the largest overall activation. While there was no difference between appetitive and aversive images for the first 5 picture positions, the threatening pointed gun elicited greater

activation for the closest image (consistent with Miller, 1959). Skin conductance level was also higher for the appetitive and aversive conditions than the neutral conditions (which steadily declined across all image presentations), and both showed a marked increase in amplitude during the imminent image. Heart rate also decreased across the fourth and fifth presentations, with a sudden acceleration during the last picture. The peripheral physiological measures during this simulated approach of appetitive, neutral, and aversive objects are consistent with the defense cascade model where SC increases steadily as the time for action draws near, and heart rate decelerates up until the point of action, at which time it rapidly accelerates. The reason for the diminished LPP amplitude differences between the first and last versus middle picture presentations was thought to reflect the arrival of the imperative stimulus. This study thus demonstrates that emotional processing is dynamic, and relies on object proximity in addition to identity.

Affective visual processing using fMRI

Visual processing throughout the brain is thought to contain an iterative component that cortically originates in the striate area and spreads forward across dorsal and ventral streams (Grill-Spector & Malach, 2004), and non-hierarchical components that contain various recurrent pathways (de Graaf et al., 2011; Hegde & Felleman, 2007; Lamme & Roelfsema, 2000). Results from the aforementioned electrocortical studies suggest that the brain initially identifies emotionally relevant information around early visual cortex (as indexed by the EPN), followed by higher order sensory temporal and parietal areas (as indexed by the P300 and LPP). These findings suggest that emotional stimuli influence vision at an early stage in processing, and may subsequently influence higher-order visual areas in a feed-forward manner. However, the spatial insensitivity of ERP measures limits our ability to locate affectively modulated cortical or

subcortical loci of activity with specificity. For improved spatial localization, fMRI methodologies have been used to investigate specific structures that show differential activity to emotionally arousing items. Several of these key structures will be reviewed.

In occipital cortex, pleasant and unpleasant arousing images elicit enhanced blood oxygenation level dependent (BOLD) activation relative to neutral or weakly arousing images (Bradley et al., 2003; Lang et al., 1998b). Like in the ERP studies mentioned above, Bradley and colleagues (2003) found no affective modulatory differences between colored and grayscale images. Furthermore, these arousal differences can be seen in the middle occipital gyrus when stimuli are presented for a very short duration (116ms; (Junghöfer et al., 2006). Extra-striate occipital cortex activity also appears to reflect gender differences, with males exhibiting a larger average blood oxygen level dependent (BOLD) response to erotica than women, and women exhibiting a larger average BOLD response to aversive images than men (Sabatinelli et al., 2004). Other areas, such as the Inferior Temporal cortex (IT), also appear crucial in processing emotion. The IT seems particularly involved in processing emotional faces (Breiter et al., 1996; Sprengelmeyer et al., 1998) and scenes (Bradley et al., 2003; Lang et al., 1998b; Norris et al., 2004), and is sensitive to motivationally relevant hunger states (LaBar et al., 2001).

As mentioned previously, it is well established that the amygdala plays a key role in processing emotionally evocative stimuli and projects to multiple brain regions to modulate responses to environmental stimuli (Everitt et al., 2003; Zald, 2003). This structure also appears to be crucially involved in fear learning by forming pathways with thalamus and hippocampus for sensory and contextual conditioning, respectively (Davis, 1992; LeDoux, 1993). Using intracranial recordings, researchers have demonstrated amygdala activation for both auditory and visual emotional stimuli in monkeys (Kuraoka & Nakamura, 2007; Nakamura et al., 1992).

Research in human clinical patients has also found amygdala activation in response to fearful faces and scenes using intracranial recording (Krolak-Salmon et al., 2004; Oya et al., 2002; Pourtois et al., 2010).

The re-entrant pathway: A model for affective visual processing

A framework explaining the emotionally modulated brain activity that we have seen in the LPP, EPN, and early occipital structures could involve a re-entrant pathway from amygdala to visual regions. Researchers have found dense recurrent amygdala-IT connections (Amaral & Price, 1984; Spiegler & Mishkin, 1981), and projections from the amygdala to the visual cortex in monkeys (Amaral et al., 2003). These studies suggest that visual information travels along the ventral visual pathway to IT, where it projects to the amygdala. The amygdala then feeds back to IT and to extra-striate visual structures such as V2. Theoretically, when viewing an emotionally arousing object, the amygdala-IT feedback loop promotes increased and sustained visual processing of that object in the extra-striate cortex and other ventral visual areas, which then spreads to the dorsal regions.

Support for this re-entrant model in humans was provided by Sabatinelli and colleagues (2005), in which six categories of visual scenes that differed in arousal were presented to both snake-phobic and non-phobic participants. The BOLD activation in both amygdala and IT showed a positive linear increase with picture arousal level in non-phobics, with similar increases in activation for both appetitive and aversive, relative to neutral, pictures. Interestingly, a similar pattern was found in snake phobics, but with a particularly large increase in BOLD activation for snake pictures. IT and amygdala activity did not significantly differ across categories between groups. When considering inter-subject variability during emotional processing tasks, this bilateral co-activation of amygdala and IT cortex provides support for the

feedback loop between these structures. Weaker or non-significant correlations were observed between amygdala and V2, and between IT and other active subcortical structures, such as the caudate. Further evidence supporting the physiological viability of the re-entrant model in humans has been found using Diffusion Tensor Imaging (DTI), which has identified dense white matter tracts projecting from ventral visual areas to the anterior temporal lobe, and back projections from the amygdala to ventral visual areas (Catani et al., 2003; Pugliese et al., 2009). Additionally, functional connections between IT and early visual areas were illustrated using Granger causality analysis of steady state visually evoked potentials (ssVEP) in a similar affective picture perception paradigm (Keil et al., 2009).

We know from ERP studies that emotional discrimination of visual scenes occurs rapidly. Animal and human imaging has also demonstrated that the amygdala and IT cortex play a role in emotional discrimination. However, the temporal order of the hypothesized amygdala-IT reentrant pathway and other regions implicated in higher order visual perception had not been demonstrated in humans. To address this issue, Sabatinelli and colleagues (2009) capitalized on the consistency of the hemodynamic response function (HRF) timing and shape when recorded within subject, within a brain region. Using a rapid data acquisition fMRI protocol, the authors were able to quantify the time at which relevant structures showed differential activation between arousing and non-arousing images. As would be expected, primary visual cortex did not differentiate emotional scenes while amygdala, IT, and extra-striate cortex did. The key finding, however, was that amygdala and IT discriminated both pleasant and unpleasant images approximately one second before extra-striate V2. These results support the concept that the amygdala and IT identify emotional stimuli and feed back to extra-striate visual areas before higher order visual processing occurs in the dorsal pathway; consistent with the re-entrant model.

Uncovering affective neural networks: A multimodal approach

Two of the most popular methodologies for the noninvasive recording of neural activity are EEG and fMRI. Given that fMRI and EEG are complementary in nature, with fMRI's excellent spatial resolution and EEG's temporal resolution, combining the two to locate common areas of neural activation is advantageous. Few studies have used this combination to study emotion, which may be partially due to the inherent technical and inferential challenges involved. Simultaneous fMRI-EEG acquisition allows data to be collected from the same participant for the same temporal events, though it is necessary to overcome a variety of technical issues induced by the MR environment such as rapid gradient switching, amplified physiological changes, and hardware vibration. These problems are not insurmountable, but require specialized equipment and careful data preprocessing. In fact, several event-related components have been shown to correlate well with BOLD signals using this method (Bak et al., 2011; Hesselmann et al., 2011; Novitskiy et al., 2011). Another option is to record EEG and fMRI in separate, but equivalent sessions, and compare the results. While the technical difficulties are greatly reduced, claims made from these paradigms are more restricted, as session variability and habituation are difficult to control. Additionally, the physical recording environments are considerably different (unless EEG is recorded in a mock MR scanner). Nevertheless, an association between the two signals has been verified using several cognitive tasks in separate recording sessions (Horovitz et al., 2002; Vitacco et al., 2002).

Emotional reactivity has been explored with combined EEG-fMRI collected separately using identical emotional paradigms (Sabatinelli et al., 2007b). In this study, subjects viewed pleasant, unpleasant, and neutral images, with the typical arousal effects seen in LPP, and BOLD change in lateral occipital, IT, and medial parietal cortex (anterior subcortical structures were not

sampled). During picture viewing, the LPP was significantly correlated with the lateral occipital, parietal, and IT cortex. Importantly, the LPP did not correlate with primary visual cortex, as this region does not typically differentiate emotional images. This suggests that the re-entrant pathway may, at least in part, modulate activity observed over the parietal cortex. Sabatinelli and colleagues (2012) replicated and extended this study by investigating the correlations between EPN, LPP, and BOLD activity in various limbic, ventral visual and dorsal visual pathways during emotional picture viewing. The LPP showed covariation with limbic structures including amygdala, anterior cingulate (ACC), nucleus accumbens (NAc), insula, and visual regions such as IT, IPS, and extra-striate cortex. However, EPN was only moderately correlated with amygdala and ACC. This weaker EPN-BOLD relationship calls into question the extent to which the EPN reflects emotion in relation to other perceptual qualities of the stimuli. For example, the authors suggest that the EPN may also be sensitive to image perceptual complexity (Codispoti et al., 2007b). It was also surprising that the EPN was uncorrelated with emotional modulation in extra-striate visual regions, over which the EPN is seen. However, the correlations between BOLD and ERP amplitudes were performed on separate groups of participants, and thus a within-group comparison (as done here) may provide clarification of these findings. The EPN signal may also rely more on phase locking, which is not detected by fMRI, than EEG power (Fell et al., 2004; Makeig et al., 2002). It may also be valuable to look for LPP and EPN correlations with additional affectively modulated brain regions to further investigate the circuitry that drives this activity in the dorsal visual pathway. Since the dorsal visual pathway is implicated in the voluntary and involuntary redirection of attention (Corbetta et al., 2008), these studies may clarify the role of emotional stimuli on attention processes.

In summary, emotional stimuli are considered to motivate an organism to act such that appetitive items are approached and aversive items are avoided. Animals and humans both experience changes in peripheral physiology modulated by the distance from the emotional object, and the object's subjective valence. Electrocortical studies have implicated early and late regions of the visual cortex in emotional processing, while intracranial and fMRI studies have suggested the amygdala as a central structure involved in the processing of emotion (regardless of stimulus modality or category). A re-entrant hypothesis suggests that the amygdala modulates processing of emotional stimuli in the ventral visual pathway, which may then increase subsequent dorsal visual processing. Other brain regions, such as the mPFC, IFG, ACC, IPS, and NAc, are also involved in affective processing. It is probable that these regions form multiple networks that allow objects in the environment to dynamically change perceptual acuity and overt behavior based on emotionally relevant characteristics, thus increasing an animal's chances of survival.

CHAPTER 2

INTRODUCTION

The mammalian brain has developed a specialized network of neural pathways to process the emotional quality of stimuli. The amygdala is a key structure in this network, responding to arousing (appetitive and aversive) cues across species and stimulus modality (Lang et al., 2000; Sarter & Markowitsch, 1985; Zald, 2003). As humans view emotionally arousing images, blood oxygen level dependent (BOLD) increases can be seen in other structures as well, including extra-striate and inferotemporal (IT) visual cortex (Bradley et al., 2003; Lang et al., 1998c; Norris et al., 2004; Sabatinelli et al., 2005), reflecting enhanced perceptual processing of motivationally relevant stimuli.

Cortical processing of visual information in the primate visual system originates in striate regions (v1), proceeds to extra-striate cortex (v2), and is then generally divided into the canonical ventral object recognition ("what") and the dorsal object location ("where") pathway, with higher order visual percepts resolved later in time, and feeding back to earlier visual areas (de Graaf et al., 2011; Grill-Spector & Malach, 2004; Hegde & Felleman, 2007; Lamme & Roelfsema, 2000). Visual emotional discrimination is thought to involve re-entrant feedback from amygdala to extra-striate and ventral visual regions. Amaral and colleagues have identified recurrent amygdala-IT connections in the primate that may enable this process (Amaral et al., 2003; Amaral & Price, 1984; Freese & Amaral, 2005; Spiegler & Mishkin, 1981). Support for this re-entrant model in humans can be found from parallel amygdala and IT BOLD modulation by arousing images (Morris et al., 1998; Sabatinelli et al., 2005; Vuilleumier et al., 2004).

According to this perspective, image processing undergoes an initial feed forward sweep through the ventral pathway where information eventually reaches the amygdala. The amygdala then processes the emotionality of the image and feeds back to visual (and presumably extra-visual) structures along the length of the ventral visual pathway, with decreasing modulatory influence with caudal extent. It is possible that this particular feedback is captured by the early posterior negativity (EPN) event related potential (ERP) that is maximally recorded over lateral occipital areas around 200-300ms after stimulus presentation (Junghöfer et al., 2001; Schupp et al., 2003a). This emotionally modulated visual processing is also seen in higher order ventral and dorsal visual areas (Sabatinelli et al., 2005; Sabatinelli et al., 2007b), as reflected by the late positive potential (LPP) that is maximally recorded over the centro-parietal area from 400-900ms after stimulus presentation (Cuthbert et al., 2000a; Keil et al., 2002).

While the structural mechanisms supporting the emotional re-entrant model are established in the animal model, the consistency and timing of these processes in humans is less clear. Sabatinelli and colleagues (2009) investigated the timing of emotionally modulated BOLD response in the amygdala and the IT, striate, and extra-striate cortices using fast sampling fMRI. Results indicated that the amygdala and IT cortex differentiated emotional from non-emotional stimuli earlier than extra-striate cortex, while primary visual areas exhibited no emotional differentiation. Thus despite the delayed and indirect nature of BOLD signal, the relative timing of emotional discrimination across sampled structures was consistent with re-entrant connectivity between amygdala and the ventral visual system.

Previous research has also demonstrated that the affectively modulated LPP is associated with BOLD activation in various ventral visual, dorsal visual, and limbic regions, while the EPN is moderately associated with BOLD activity in the amygdala and anterior cingulate cortex

(Sabatinelli et al., 2012; Sabatinelli et al., 2007b). However, the weaker affectively modulated EPN-BOLD correlations call into question the extent to which the EPN reflects emotion in relation to other perceptual qualities of the stimuli. However, since the correlations between BOLD and ERP amplitudes were performed on separate groups of participants, a within group comparison may provide clarification of this previous study.

One aim of the present study was to extend the investigation of the timing of emotional discrimination to dorsal visual and frontal structures involved in the orienting of visual attention, including the intraparietal sulcus (IPS) and frontal eye fields (FEF), respectively (Curtis & D'Esposito, 2006; Dyckman et al., 2007). The IPS has been implicated in representing visual space while the FEF is involved in planning eye movements, both working together to coordinate the exogenous orienting of attention (Corbetta et al., 2002; Corbetta et al., 2008; Curtis et al., 2004). Since attending to emotional content is environmentally adaptive, these regions were chosen as late stage processing areas. A subgroup of the participants also participated in a separate EEG session in order to investigate potential individual correlations between EPN and LPP measures with BOLD signal to further clarify which brain structures may underlie these electrocortical measures, thus extending our knowledge regarding the timing of emotional discrimination. In line with the re-entrant model, it was hypothesized that amygdala and IT cortex would differentiate arousing from non-arousing images close in time, and prior to emotional modulation in IPS and FEF. Additionally, these ERPs were expected to reflect the relative timing of the emotional re-entrant feedback model. Therefore the EPN would correlate with all emotionally modulated structures, but most strongly with amygdala and extra-striate and IT cortices. A similar finding should be observed with the LPP, but with the strongest correlation with the IPS, FEF, and extra-striate cortex (Sabatinelli et al., 2007b).

CHAPTER 3

METHODS

Participants

A total of 42 undergraduate students (20 females) from the University of Georgia participated in an fMRI session, receiving \$20 in compensation for two hours of participation. All subjects were invited to participate in a second EEG session, and 19 of these participants (9 females) agreed, receiving an additional \$20 in compensation for two hours of participation. For each session participants reviewed and signed an informed consent form, approved by the University of Georgia human subjects review board, detailing the study and scanning procedures that would occur during that particular session.

<u>Stimuli</u>

During both sessions, participants viewed a series of pleasant, unpleasant, and neutral pictures in grayscale. The picture stimuli were composed of 8 categories, which included scenes depicting erotica, romantic partners, families and babies, people performing daily activities, landscapes, animal threat, human threat, and bodily mutilations. Participants rated the pleasantness and arousal of the images on the self-assessment manikin scale (Lang et al., 2008) after the first session. This scale was introduced approximately halfway into the study, therefore only 26 participant ratings were collected. All pictures were balanced by category for luminosity. Due to a computational error only 75% of the categories were matched on visual complexity. The pictures that were unbalanced consisted of one picture block (20pics). Before both sessions, participants were asked to attend to a central fixation dot at the center of each image and keep

eye movements to an absolute minimum. Eye movements were not tracked, however a previous study using the same fixation paradigm tested this directly, reporting no differential effect of emotional arousal on eye movement (Lang et al., 1998c).

fMRI procedure

Participants were scanned in a General Electric 16-channel Signa HDx 3T MRI magnet, and were provided with cushions and explicit instructions to restrict head motion. Images were delivered via MRI compatible goggles (Resonance Technology Inc.) at a resolution of 800 x 600 pixels (30° horizontal FOV). Each picture block was comprised of an initial 2s checkerboard acclimation image followed by a series of 20 pictures with a duration of 2s and a variable inter stimulus interval (ITI) of 9-11s. The images were pseudo-randomized so that no more than two pictures of the same category were presented in succession. Four picture blocks were presented, however only two blocks were used in any given participant (see fMRI parameters below). The order of picture block presentation was counterbalanced across participants.

fMRI parameters

Once participants were situated inside the magnet, a T1-weighted structural volume was collected consisting of 156 sagittal slices with a 256x256 matrix and 1mm isotropic voxels. The four functional blocks each comprised of four oblique axial slices (64x64 EPI, 18cm FOV, 5mm thickness, 1.5mm gap, 25° flip angle, 30ms TE, 250ms TR) situated over four different regions of the brain in order to obtain maximal coverage of amygdala, IT, IPS, and FEF regions of interest (ROI). Four slices were used to enable fast sampling at 250ms TR. Each set of four axial slices (constituting one 20-picture block) was manually positioned using the T1 image for visual identification of landmarks based on each participant's anatomy, with one set of slices covering amygdala and IT, and a second set covering IPS and FEF. The set covering amygdala and IT was

centered on amygdala and tilted to cover the occipital lobe. The set covering IPS and FEF was centered on the intraparietal sulcus and tilted to cover the superior frontal lobe. In this way, activation in any ROI represents a response to 20 pictures per participant.

fMRI data processing

Each time series was motion corrected using trilinear interpolation, spatially smoothed across two voxels (5.625mm full width at half maximum), linearly de-trended with a 0.02 Hz high pass filter, and temporally smoothed with a 1s Gaussian filter using BrainVoyager QX 1.10 (Brain Innovation; brainvoyager.com). Single-subject ANOVAs were then performed on the time-series data to differentiate BOLD signal arising from the picture stimuli. A false discovery rate of p<0.05 (Genovese et al., 2002) was used to control for multiple comparisons. Four pre-defined regions of interest were identified from the resulting functional maps; the amygdala, IT, IPS, and FEF (Table 1 & Figure 1). The peak cluster of activity (10x10 voxels) was sampled for each ROI. The coordinates for these functionally active clusters were guided a priori by those observed in previous work involving emotional discrimination (Liu et al., 2012; Sabatinelli et al., 2012) and goal directed attention in IPS and FEF (Dyckman et al., 2007). Signal change scores (deviating from pre-trial baseline) were calculated using the average BOLD signal from 5-8s post stimulus onset. Due to the large extent of BOLD activation in IT cortex, the ROI from this area was functionally derived based on an arousal contrast (pleasant + unpleasant > neutral).

Table 1				
Region	Hemisphere	х	У	z
Amygdala	L	-20	-6	-13
Amygdala	R	20	-5	-13
IT	L	-38	-63	-14
IT	R	37	-62	-14
IPS	L	-28	-59	50
IPS	R	26	-60	52
FEF	L	-38	-7	51
FEF	R	37	-5	51

Table 1: ROI coordinates. Talairach coordinates listed for the peak cluster of active voxels within each ROI in the current study.

Figure 1



Figure 1: fMRI regions of interest. Statistical overlay of functional BOLD activity in amygdala and IT cortex (A), and IPS and FEF (B) for a representative participant.

EEG procedure

Electrocortical data were recorded using a 64 channel Biosemi ActiveTwo system (biosemi.com). Stimuli were viewed on a Westinghouse 32-inch LCD television at a resolution of 800x600 pixels (31° horizontal FOV). Participants were seated in a chair in a dark shielded chamber and provided instructions to keep their eyes focused on the center of each picture and to keep blinking to a minimum. Each picture block was comprised of an initial 2s checkerboard acclimation image followed by a series of 20 pictures with a duration of 2s and a variable ITI of 4-6s. The images were presented in the same pseudo-randomized order as in the fMRI portion. Each of the four picture blocks from the fMRI portion was presented twice, consisting of a total of 160 pictures (80 unique), and the order of picture block presentation was counterbalanced across participants. Pictures were repeated in order to improve data quality after averaging across trials. Consistent with previous findings indicating that the ERP signals of interest are resistant to picture habituation (Codispoti et al., 2007a), we found neither a difference in activation between the first and second viewing of arousing pictures for LPP and EPN ($F_{(1,1984)}=2.05, p>.05$; $F_{(1.1984)}=3.21, p>.05$, respectively), nor neutral images ($F_{(1.495)}=2.05, p>.05$; $F_{(1.495)}=0.70, p>.05$, respectively).

EEG parameters and data processing

Electrocortical data were recorded using ActiView640 software (biosemi.com) and analyzed using EMEGS (emegs.org) in Matlab (Mathworks, Inc.). All 64 scalp electrodes were sampled at 512Hz and their offsets were brought below $40\mu v$ prior to data acquisition. A Butterworth low-pass filter from 30-40Hz and high-pass filter from 0.05-0.1Hz was used to preprocess the data. Epochs extending from 200ms prior to stimulus onset to 2s after onset were extracted, and the SCADS procedure was used for artifact removal (Junghöfer et al., 2000) while

retaining no less than 80% of each participant's original data. Centro-parietal sensors Cz, CPz, Pz, CP1, and CP2 were averaged to attain the LPP time-course, and occipito-temporal sensors P7, P8, PO7, and PO8 were averaged to attain the EPN time-course. The LPP average amplitude from 400-900ms and EPN average amplitude from 200-300ms post stimulus onset was calculated for each participant, and then correlated with average BOLD measures (5-8s after picture onset) from each region of interest.

CHAPTER 4

RESULTS

Picture ratings

Participants rated pleasant and unpleasant images high on arousal, and subjective pleasantness ratings increased linearly with hedonic valence (Table 2). Twelve of those who participated in both fMRI and EEG sessions completed picture ratings, however these participants were consistent with the larger group on both arousal and valence (Table 3; Figures 2a,b).

Table 2		
Category	Pleasantness	Arousal
Pleasant	6.99 (0.87)	5.72 (0.69)
Neutral	5.89 (0.79)	3.65 (1.13)
Unpleasant	3.06 (1.03)	6.62 (0.79)

Table 2: Picture Ratings (fMRI, n=26). Mean (and SD) subjective pleasantness and arousal rated on a scale from 1-9, with nine being most pleasant or arousing.

Table 3

Category	Pleasantness	Arousal
Pleasant	7.09 (0.74)	6.13 (0.73)
Neutral	5.77 (0.46)	3.74 (0.88)
Unpleasant	2.84 (0.73)	6.67 (0.87)

Table 3: Picture Ratings (EEG subgroup, n=12). Subjective pleasantness and arousal rated on a scale of 1-9 (and SD), with nine being most pleasant or arousing, by participants in both fMRI and EEG sessions.



Figure 2: Picture ratings. Average arousal (A) and pleasantness (B) ratings (n=12) from 1-9, with nine being the most arousing or pleasant, for each image. Pictures grouped by category.

Regional BOLD activation

Arousing pictures (both pleasant and unpleasant) elicited a larger BOLD signal change than neutral images in amygdala ($F_{(2,123)}=9.60, p<0.01$), IT ($F_{(2,123)}=11.25, p<0.01$), FEF ($F_{(2,123)}=3.18, p<0.05$), and IPS ($F_{(2,123)}=5.51, p<0.01$; Figure 3b). Time points at which emotional discrimination occurred were then reliably determined using non-parametric permutation tests (to control for family-wise error rate) for each region and time point during the first 6 seconds (24 time points) of picture presentation (Sabatinelli et al., 2009). For each region, trials were randomly assigned to one of three picture conditions (pleasant, neutral, unpleasant) and an Fvalue was computed. This random partitioning was performed 10,000 times, creating a distribution of F-values. The 99th percentile was used as the critical value for the observed F at each time point (Maris, 2004; Maris & Oostenveld, 2007). This analysis revealed that BOLD signal discriminated emotional from neutral picture content at 2750ms in amygdala, 3000ms in IT, 5750ms in IPS, and at no single point in FEF (Figure 3a).



Figure 3: BOLD time course and peak amplitude. Average time courses (n=42) of emotionally driven BOLD response with affective discrimination point (A) and average BOLD amplitudes (5-8s) in amygdala, IT cortex, IPS, and FEF.

Electrocortical activation

The group of 19 participants that returned for the EEG session exhibited an amplified LPP 400-900ms after viewing pleasant and unpleasant images, compared to neutral ($F_{(2,57)}=13.22$, p<0.01; Figure4a), that increased linearly with arousal across pictures (Figure5a). The EPN was also magnified (elicited more negativity) by arousal ($F_{(2,57)}=7.31$, p<0.01; Figure4b), though this effect appeared to be driven more so by pleasant images (Figure 5b). Among arousing stimuli, the EPN displayed a positive linear trend from pleasant to unpleasant pictures. Women consistently exhibited an attenuated EPN magnitude for each picture type.



Figure 4: ERP time course and peak amplitude. Average time courses (n=19) of emotionally driven ERP response (A) and average ERP amplitudes for LPP (400-900ms; Cz, Pz, CPz, CP1, & CP2) and EPN (200-300ms; P7, PO8, PO7, & P8).



Figure 5: ERP amplitude by picture. Average LPP (A) and EPN (B) amplitudes (n=19) are displayed for each image. Pictures grouped by category.

Hemodynamic and electrocortical correlation

Peak BOLD activation increased for each ROI across pictures (Figure 6) among the subset of EEG participants and, as expected, the magnitude of the LPP and EPN increased with arousal (R=0.54 & 0.38, respectively). The LPP exhibited a positive correlation with both IT and FEF (R=0.24 & 0.32, respectively; Figure 7a), but not amygdala or IPS, while the EPN was negatively correlated with IT, IPS, and FEF (R=0.28, 0.25, & 0.22, respectively; Figure 7b), with no relationship with BOLD signal in any other region.





Figure 6: BOLD activation by pictures. Average peak BOLD activation (n=19) from 5-8s after picture onset for amygdala (A), IT cortex (B), IPS (C), and FEF (D) for each image.



Figure 7: ERP – BOLD correlations (by picture; n=80). The LPP (A) and EPN (B) correlates across the picture set with IT and FEF. EPN also correlates with IPS. R-values are located in the top left of each graph if statistically significant.





<u>ERPs</u> 4 3 2 1 0 -1 10 8 6 4 2 0 Ero. Fam. p. H.Thr. A.Thr. Mut. L.scp. Rom. Ppl.

LPP amplitude Δ (μ V)

EPN amplitude Δ (μV)

Figure 8: Peak activation (8 category). Average peak activation (n=19) for ROIs and ERPs across all eight categories.







LPP amplitude Δ (μ V)

EPN amplitude Δ (μ V)



Figure 9: Peak activation (8 category by gender). Average peak activation (n=19) for ROIs and ERPs across all eight categories. Gender is alternating, starting with females.

CHAPTER 5

DISCUSSION

Emotional discrimination among brain regions

In the present study, emotional discrimination was found between the amygdala and IT cortex, consistent with previous work (Bradley et al., 2003; Sabatinelli et al., 2007a). The amygdala is positioned adjacent to the medial-temporal lobe, with a wide array of interconnections with sub-cortical areas, including the thalamus and hypothalamus, and cortical regions, including the orbito-frontal cortex and IT (Catani et al., 2003; Freese & Amaral, 2005; Lang & Bradley, 2010). It is therefore well situated to modulate higher order brain regions and modulate sensory and motor processing. The IT has typically been implicated in complex visual processing, including the processing of emotional faces (Breiter et al., 1996), scenes (Bradley et al., 2003; Lang et al., 1998a; Norris et al., 2004), and has been shown sensitive to motivationally relevant hunger states (LaBar et al., 2001). Due to the dense inter-connections and close proximity with the amygdala, this may be one of the earlier visual regions involved in representing visual information and emotionally charged.

In the current study, both amygdala and IT displayed equivalent signal change across pleasant and unpleasant pictures. However, category effects were also of interest. Using a posthoc paired samples t-test, neutral landscapes elicited lower activation than all other picture categories (Figure 8). Interestingly, there were no reliable differences in signal change across any of the other categories, including neutral people. The increased activation for neutral people was most likely due to this regions' overlap with the fusiform gyrus, the anterior region of which is

particularly involved in facial processing (Kanwisher et al., 1997). A similar comparison of categories in amygdala revealed increased BOLD signal for erotica, animal threat, and human threat over all other neutral and pleasant categories. It appears, then, that amygdala was primarily sensitive to highly arousing pleasant images and threatening images. This could be explained by the survival value of these pictures, as these contents arguably represent the most direct cues for survival. The heightened activation of threatening and arousing over mutilation pictures, in particular, may be due to the lack of threat imminence associated with viewing a mutilated body (i.e., the dangerous event which caused the mutilation may be viewed as no longer present). Future studies with a larger sample size would be necessary to further investigate this finding.

The IPS and FEF were also modulated by picture content in the current study, showing elevated peak BOLD signal during emotionally arousing pictures. These structures are part of a dorsal sensory system involved in goal directed (top-down) attention processing (Corbetta et al., 2000; Hopfinger et al., 2000; Kastner et al., 1999). Specifically, these two regions appear to work in concert when representing a visual scene and planning eye movements (i.e., saccades; (Curtis & D'Esposito, 2006; Dyckman et al., 2007), and are also preferentially active when participants view emotionally laden images (Armony & Dolan, 2002; Pourtois et al., 2006). The emotional discrimination found in the present study may therefore reflect a biasing effect of emotion on goal directed attention (Frank & Sabatinelli, 2012) by allocating more sensory resources to processing an emotional image. This, in turn, may manifest as larger and more widespread activation in the visual attention system (Pourtois et al., 2012). Since a failure to attend to a potentially life threatening situation may pose serious consequences, it is unsurprising that affective discrimination is reflected in these dorsal attention structures.

Unlike BOLD signal change in amygdala and IT, post-hoc tests revealed that pleasant pictures led to greater signal change in both IPS and FEF relative to neutral and unpleasant pictures, and equivalent reactivity during unpleasant and neutral scenes. To further investigate the content specificity of this result, all picture categories were compared (Figure 8). Activity in the IPS was greatest during pictures of erotica and human threat. A similar result was found in FEF, with romance and family categories eliciting more activation than in IPS. These dorsal regions may therefore be particularly sensitive to erotica and human threat, similar to the pattern of amygdala activity across picture categories. Overall, it appears that while, on average, pictures depicting bodily mutilations were rated highest on arousal and lowest on pleasantness, they elicited similar or less activation than threat scenes across our BOLD regions of interest. The human threat condition, however, elicited a similar BOLD signal change as the erotica condition for both dorsal and ventral regions. We hypothesize that these images reflect the most imminent motives of our participants (as mentioned above). Erotic images may cue a direct urge to procreate, whereas viewer-directed threat reflects a motive for self-defense, both of which have clear evolutionary significance. It may therefore be more imperative to attend to erotica and threat, because they are both direct and imminent signals reflecting preservation of life. Bodily mutilations may be less important, because they may reflect a past event and thus lack the same level of imminence.

The current fMRI findings also demonstrate that the amygdala and IT discriminate emotional stimuli in close temporal proximity, replicating previous work (Sabatinelli et al., 2009). Visual processing throughout the brain is thought to contain an iterative aspect, cortically originating in the striate area and spreading forward across dorsal and ventral streams (Grill-Spector & Malach, 2004), and is also conceived as containing non-hierarchical components, with

various recurrent pathways (de Graaf et al., 2011; Hegde & Felleman, 2007; Lamme & Roelfsema, 2000). Our results support the perspective that the amygdala and IT are modulated by emotional arousal prior to IPS and FEF discrimination, which again supports the re-entrant model of emotional discrimination (Freese & Amaral, 2005; Spiegler & Mishkin, 1981). Following the well-characterized identification of the structural relationships between amygdala and ventral visual cortex, this model suggests that emotions are resolved early in the amygdala-IT recurrent loop, which would then presumably be followed by emotional discrimination in dorsal visual structures. Conceivably, this amygdala-IT feedback loop initiates sustained visual processing of an arousing scene in extra-striate and ventral visual cortices, which then spreads along the dorsal visual pathway. The later arousal discrimination in IPS, compared to amygdala and IT, provides support for this affective biasing perspective.

While peak BOLD activation of the FEF was modulated by emotion, a discrimination point was unidentifiable. This may be due to increased variability in the FEF BOLD signal and, the source of which may have included behaviors such as eye movements that could have masked neural processes involved in perceptual attention (Schall, 2004). Since eye movements were not recorded, it was not possible to identify this variability and use it as a regressor. This may be considered in future work.

A critical function of visual scene perception is to identify potentially life threatening or life sustaining events efficiently and quickly, and inform downstream brain regions of this emotional content. These downstream regions may then alter top down goals and instantiate a motor response in response to the environmental stimulus. The current emotional modulation of BOLD peak activation and onset timing of the amygdala, IT, IPS, and FEF is consistent with this view of the mechanisms of visual attention.

ERP indexes of emotional discrimination

The LPP is a highly reliable index of emotional arousal (Cuthbert et al., 2000a; Keil et al., 2002), reflecting higher-order perceptual features (Codispoti et al., 2012). Due to its late onset and sustained arousal differentiation, this waveform appears to represent higher order sensory recognition. Consistent with this idea, in the current work, LPP magnitude was greater during emotionally arousing, relative to neutral pictures, an effect that remained for the entire picture period. No significant difference in LPP magnitude was found across pleasant and unpleasant images. When all eight picture categories were plotted from most to least pleasant (i.e., erotica... \rightarrow ...landscapes... \rightarrow ...mutilations), a U-shaped activation pattern was evident with no significant differences between each adjacent category (Figure 8). These findings support that the LPP is an index of emotional arousal (pleasant and unpleasant) and not a specific semantic category.

The EPN reliably discriminated arousing from non-arousing images, and displayed an enhanced negativity particularly for pleasant images, as seen in previous work (Schupp et al., 2003b; Schupp et al., 2004b). This ERP appears to reflect early affective visual processing, due to its discrimination starting roughly 200ms after picture onset. Since previous studies have reported a preferential effect of pleasant images (Schupp et al., 2007), we computed a post-hoc test that revealed a higher EPN magnitude for pleasant over unpleasant images (t=1.92, p<0.05, one-tailed). A follow-up analysis comparing the difference in EPN magnitude across category (Figure 8) revealed that pictures depicting romantic couples elicited a higher EPN magnitude than every other category, except erotica. Therefore, while the EPN discriminates both pleasant and unpleasant images from neutral, it may show preferential sensitivity towards pleasant images. In particular, it appears that this effect is driven by images of romantic couples.

Interestingly, previous work has demonstrated an EPN sensitivity to erotic images (Schupp et al., 2007), but not romance alone. Previous studies have used romantic couple stimuli, but to our knowledge this category has not been tested in isolation (Schupp et al., 2004a), and warrants future investigation. It should be noted that, unlike the trends seen in BOLD activation across category (Figure 8), no LPP or EPN amplitude differences were found among pictures depicting human threat, animal threat, and bodily mutilations.

Hemodynamic and electrocortical relationships

A correlation between the LPP and both the IT and FEF cortex was found in the group as a whole, providing support for both early and late emotional discriminating structures, modulating later sustained visual cortical activity (Pessoa & Adolphs, 2010; Sabatinelli et al., 2012). The LPP is thought to represent the activity of multiple cortical structures, which is supported by the present results. However, no correlation was found between modulation of the LPP and BOLD signal from the IPS and amygdala. The reason for the lack of replication of the LPP-IPS and LPP-amygdala correlation is unclear, but may have to do with the female subset of the current sample, discussed below. A negative relationship between EPN and all cortical regions of interest was also identified, supporting the idea that the EPN represents emotionally modulated early visual regions, which may then affect downstream processing.

Emotional modulation of the LPP or EPN was not correlated with amygdala BOLD activity. Male subjects (n=10) showed significant correlations between LPP and both amygdala and IT modulation (R=0.39 & 0.28, respectively), whereas females exhibited reliable correlations between LPP and both IPS and FEF (R=0.27 & 0.28). Furthermore, while men maintained the EPN – BOLD correlations, women exhibited no EPN – BOLD relationships. It is unclear what may have led to this gender-specific pattern of results; to further investigate this

gender difference, peak scores were averaged across each category by gender (Figure 9). Only a significant increase in FEF activation for women, compared to men, in response to human threat was revealed (t=2.15, p<0.05), with an overall decrease in EPN magnitude in women. There is some research to suggest that females respond to threat related cues differently than males (Bradley et al., 2001a; Sabatinelli et al., 2004), perhaps relying more heavily on the amygdala and orbito-frontal cortical network (McClure et al., 2004). It will be worthwhile to test these gender effects more rigorously in the future, while also sampling OFC in order to attain a more complete picture of affective neural network processes.

Conclusion

As we have observed in the present study, the human brain differentiates emotional from non-emotional stimuli early in the perceptual process, and the amygdala and IT may be among the first of the modulated regions. The LPP, a reliable index of sustained affective processing, exhibits a positive relationship with IT and FEF, providing support for the idea that these regions contribute to extended late stage affective processing. Future investigations of electrocortical and hemodynamic measures of scene perception will continue to clarify the complex temporospatial relationships among the neural mechanisms of emotional perception.

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