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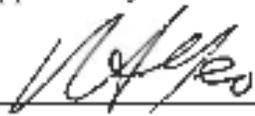
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RESPONSIVITY OF THE HUMAN CALCARINE FISSURE
AND FUSIFORM GYRUS TO THE EMOTION OF VIEWED
FACES**

BY

PER A. LYSNE

**B.S. COMPUTER ENGINEERING
M.S. ELECTRICAL ENGINEERING**

THESIS

Submitted in Partial Fulfillment of the
Requirements for the Degree of

**Master of Science
Psychology**

The University of New Mexico
Albuquerque, New Mexico

December, 2009

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Abstract

Darwin proposed that communication of information concerning psychological state was an evolved mechanism. Much emotional signaling in humans occurs via facial expression. Neuroimaging techniques have identified regions involved in facial emotion perception and, although successively more sophisticated models have sought to explain this processing, results suggest that further development is needed. Neuroimaging research in facial emotion perception is currently focused on characterizing major sources of activation in development of these models. Although facial processing is a visual task, decoding of expression has been theorized to take place not in the primary visual regions of the occipital cortex but later within specialized portions of temporal cortex. Portions of the fusiform gyrus respond preferentially to facial stimuli and, although current models hypothesize that processing of facial expression takes place elsewhere, some evidence suggests that facial expression modulates the fusiform response. Lewis et al. (2003) found differential activation of an equivalent current magnetic dipole in the right fusiform when viewing happy versus disgusted versus neutral faces. The current work sought to replicate and extend these findings by, 1) expanding the stimulus set to all six basic emotions and a non-face control condition, 2) investigating the primary visual response of the calcarine fissure for an emotion-dependent component, and 3) investigating effects

of gender and age. Contrary to expectations, findings here included emotion-related differences in peak amplitude and latency in responses of both the calcarine and fusiform. In the calcarine happy faces were seen to elicit greater amplitude than neutral, swirled, and sad faces, while in the fusiform fearful and surprised faces resulted in greater amplitude than disgusted faces and non-face objects. In the fusiform swirled faces elicited longer response latencies than recognizable faces regardless of emotion with fewer significant comparisons making a similar suggestion in the calcarine. Surprised faces required greater latencies in the right fusiform than happy and neutral faces. Partial support for the findings of Lewis and colleagues is suggested. A main effect was found for gender, with women displaying greater amplitude, shorter-latency responses. The amplitude response of the fusiform was greater than the calcarine and this differential increased with age.

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Chapter 1: Introduction

Background

Within social species, it has been theorized that the ability to rapidly and accurately transmit information between individuals confers a survival benefit, particularly for transmission of information regarding emotional states and behavioral intentions. The ability to appropriately transmit, receive, and interpret these signals has been selected for in members of social species. Further, it has been theorized that the function of emotions in organisms is as motivational mechanisms (Bradley and Lang, 2007). Thus when attempting to predict the behavior of an advanced, social organism, information regarding emotional state may serve to provide advanced warning of possible conflict or to signal opportunities for cooperation. It is not surprising then that mechanisms of emotional signaling are well developed in many social animals including humans. This theory, originally proposed by Darwin in *The Expression of the Emotions in Man and Animals* (1965), is now central to the study of modern psychology, behavior, and other related disciplines. Emotion may be expressed via multiple modalities including speech, tone of voice, and body posture, and the investigation of social signaling via facial expression has become a particularly fruitful avenue for research in recent decades.

The influence of emotion on both the behavior and the self-reported internal states of humans is obvious. Nonetheless, answers to fundamental questions such as how many distinct emotional states exist in humans have not been determined. Researchers are just beginning to investigate the neural bases of emotions, which remain elusive despite an interest dating to the time of Darwin. In the past twenty years, a tentative consensus has been reached that there exist six basic emotions: happiness, sadness, anger, fear, surprise, and disgust (Ekman, 1972). (Ekman and Friesen (1986) now consider contempt to be a basic emotion as well, but their original facial images did not include contemptuous faces and thus this condition is excluded from the current work). Furthermore, considerable evidence has been found indicating that the six basic emotions are universal among human cultures (Ekman, 1987).

Neural Models of Facial Processing
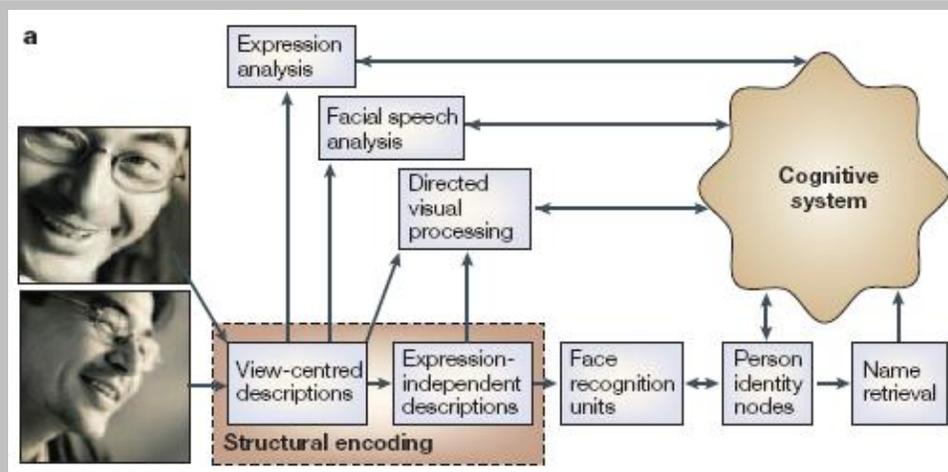
Figure 1: The Bruce and Young Model (1986). Early in processing, encoding of both identity and expression-related features of the face are view-dependent, after which identity and expression analysis bifurcate along two distinct pathways. This model was responsible for the strong delineation between identity and expression processing pathways which is still evident in facial emotion recognition research, although in subsequent work (Calder and Young, 2005), one of the original authors of this model has backed away from this position. Note that this is a functional model, and no direct neural correlates are proposed. (Figure from Calder and Young.)

Much of the progress in neuropsychology research has been made by analyzing the boundaries along which dysfunctions occur. In the realm of facial emotion recognition, one such dysfunction of interest is that of *prosopagnosia*, or a deficit in the ability to recognize the identity of familiar faces. In 1986 Bruce and Young consolidated existing results in the field and proposed a model that has driven the direction of research since then. In developing this model, Bruce and Young reviewed documented cases of prosopagnosia and noticed a double dissociation between the recognition of facial identity and expression; in some cases patients were unable to recognize facial identities but were able to identify facial expression, while in other cases patients had unimpaired identity recognition abilities but were unable to identify facial expressions. This finding led Bruce and Young to propose that the neural processing of facial identity and facial expression took place along two separate and distinct pathways. The boxes in their model (Figure 1) are drawn such that each represents what the authors consider to be an empirically separable function, and it is seen that the first step in facial processing of any kind is the production of view-dependent facial descriptors. Although this model is primarily concerned with identity recognition based on the static features of the face, as opposed to what the authors refer to as the changeable aspects of the face, that is,

expression, direction of gaze, and lip/speech movement, they do note that these analysis pathways branch off into dedicated systems in the early stages of processing and do not reconverge. A significant aspect of the Bruce and Young model is the inclusion of a cognitive component in which specialized face processing structures interact with more generalized cognitive systems. For example, the amygdala is proposed to provide a generalized emotion processing function which is enlisted by many subsystems, including those involved in facial emotion recognition.

The theorized existence of completely separate, non-interacting neural pathways for identity versus expression recognition remains evident in much face processing research today and is widely attributed to the original Bruce and Young model. However, in a recent review of the field, one of the original authors of the Bruce and Young model (Calder and Young, 2005) suggested that the clinically observed evidence for completely separate pathways no longer supports a strong neural separation of these functions. This reversal is based on several new developments, including a questioning of the rigor with which clinical prosopagnosics have been evaluated, neuroimaging results which show structures thought to be unique to one pathway or the other being activated by both identity- and expression-related tasks, and a re-analysis of the neuro-functional boundaries which appear to exist in face processing.

Figure 2: The Haxby, Hoffman, and Gobbini Model (2000) is similar to the Bruce and Young model, with three significant differences; 1) although there exist separate pathways for identity versus expression processing, these pathways are not expected to be completely independent, 2) the earliest stages of visual processing of the face are no longer view-dependent and 3) a distinction is made between dedicated face-processing structures in the core system and more generalized processing regions of the extended system. (Figure from Calder and Young, 2005.)

Haxby, Hoffman, and Gobbini (2000) proposed a model similar to the earlier work of Bruce and Young, but with three significant differences (Figure 2). First, although the Haxby model does contain separate identity and expression pathways, it does not maintain that these pathways are completely independent, as facial emotion is expected to modulate responses along the identity pathway and vice versa. Second, the Haxby model does not require the earliest levels of face processing to be view-dependent. Third, the model distinguished between core and extended systems. The core system consists of structures dedicated to the visual processing of faces that project into an extended system comprised of more general purpose regions. For example, it is proposed that regions of the superior temporal sulcus (STS) dedicated to facial expression processing project to the limbic system, which performs generalized emotion-related analysis.

Unlike the Bruce and Young model, the Haxby model contains hypothesized neural correlates associated with its functional components. Three bilateral structures in the occipito-temporal region, the inferior occipital gyri, the lateral fusiform gyri (FFG), and the STS, make up the core system of dedicated structures. Widespread support has accumulated for face-specific processing beginning in the temporal portions of the

occipital regions and then quickly projecting forward to both the FFG and STS. Although responses in FFG and STS have been shown to be modulated by both identity and expression related features, processing in the FFG is proposed to be dominated by identity, whereas STS is predominantly expression-related. After exiting the structures of the core system, activation is projected into a number of systems which depend upon the aspect of facial perception under consideration. FFG projects into the memory system of the anterior temporal region in order to recall person-specific details. STS projects to, 1) the intraparietal sulcus in order to modulate attention, 2) to the auditory cortices to decipher the facial aspects of speech and, 3) to the amygdala, insula, and other limbic structures in order to process facial emotion. The Haxby model is somewhat conservative in that it does not attempt to identify those regions in the larger cognitive system in which further processing takes place. Additionally, the degree to which systems such as the limbic system function as general purpose processing resources for a number of clients remains an open issue.

Figure 3: The Adolphs Model (2002a, 2002b) extends the Haxby model with the addition of early amygdala activation, orbitofrontal activation in later processing, and somatosensory activation as the peripheral nervous system is enlisted to decipher emotion. Additionally, the sophisticated nature of the model allows for several neural regions to be repeatedly employed as processing progresses. (Figure from Adolphs, 2002b).

The Adolphs model (2002a, 2002b) extends the Haxby model (Figure 3). As proposed by the latter, activation occurs first in the striate cortex and then projects to FFG and STS. However, Adolphs also includes an early activation of amygdala in the initial phases of facial processing. These structures/activations are considered to represent the structural encoding phase of the Bruce and Young model, and the core system of Haxby and colleagues. One of the most notable features of the Adolphs model is that various structures are activated multiple times and from differing sources at various points during processing. This is seen in the second phase of processing where FFG and STS reactivate

amygdala as well as projecting to the orbitofrontal region. This process is analogous to Bruce and Young's recognition modules and Haxby's extended system. Finally, amygdala and the orbitofrontal region project activation into the body, reminiscent of the James-Lange theory of emotion, in which bodily sensation is interpreted to determine the emotion being experienced (Bradley and Lang, 2007). The return projection from the peripheral nervous system, in combination with STS, orbitofrontal regions, and amygdala, activates the somatosensory cortex in what the previous models termed the cognitive processing step.

Summary of Meta-Analytic Results

As work has progressed in the functional neuroimaging of emotion, it has become clear that emotion is a distributed brain process and thus the relevant circuits and pathways will not be easily disentangled. Additionally, a "pure" emotional task has yet to be discovered, and hence experimental results are confounded by other experimental demands on the subject (e.g. differing induction methods and cognitive loads, Phan, Wager, Taylor, and Liberzon, 2003). The body of functional imaging literature covering emotional processes is so vast as to be quite challenging to summarize. Fortunately, review articles and meta-analyses have begun to appear.

Phan et al. (2003) performed a meta-analysis of 55 PET and fMRI studies of emotional activation and drew the following six conclusions:

1. The medial prefrontal cortex has a general role in emotional processing;
2. Fear specifically engages the amygdala;
3. Sadness is associated with activity in the subcallosal cingulate;
4. Emotional induction by visual stimuli activates the occipital cortex and the amygdala;
5. Induction by emotional recall/imagery recruits the anterior cingulate and insula;
6. Emotional tasks with cognitive demands also involved the anterior cingulate and insula.

The same group (Wager, Phan, Liberzon, and Taylor, 2003) performed another meta-analysis of 65 studies in order to assess differences in gender and lateralization as well as to investigate two of the biaxial theories of emotion (positive affect plus negative affect and approach plus withdrawal). Their results show no support for hemispheric

lateralization of emotional function and limited support for a biaxial structure of emotion. However, they did report greater lateralization of emotional function in males and greater subcortical activity in females.

Murphy, Nimmo-Smith, and Lawrence (2003), in a separate meta-analysis of 106 PET and fMRI studies of emotion, identified regions activated exclusively by specific emotions and regions globally activated across all emotions. Fear was found to selectively activate the amygdala, disgust the insula and globus pallidus, and anger the lateral oribito-frontal cortex. The anterior cingulate and medial prefrontal cortices were activated across emotional conditions, including happiness, sadness, fear, disgust, and anger.

Summarizing across Phan et al. (2003) and Murphy et al. (2003), Barrett and Wager (2006) found a similar pattern of activation. Particularly, these studies agree that fear recruits the amygdala, disgust the basal ganglia (or the associated insula/operculum and globus pallidus), and sadness the anterior cingulate and surrounding regions. Happiness, which Murphy et al. assign to the same structures as sadness, is placed by Phan, et al. in the basal ganglia. Anger, located in the lateral orbito-frontal cortex by Murphy et al., is not localized by Phan and colleagues.

Review of Facial Emotion Processing in the Calcarine Fissure

In a 2003 MEG study, Lewis et al. localized an equivalent current magnetic dipole to the right hemisphere fusiform gyrus of six normal control subjects that responded selectively to the emotion displayed on viewed facial images. The peak amplitude of this dipole's timecourse, occurring approximately 150ms after the onset of stimulus, was shown to distinguish between the emotional condition being viewed in the order; happiness > disgust > neutral. This dipole was not found when viewing non-face conditions. Additionally, the early visual activation of each subject's occipital cortex was found to be modeled by bilateral dipoles localizing to the calcarine fissure. No emotion-modulated features were found in the early timecourses of the calcarine dipoles. Since the current work attempts to replicate and extend the findings of Lewis and colleagues, the literature pertaining to neural activation in the calcarine fissure and fusiform gyrus during facial emotion recognition tasks is summarized below. Particular attention is paid to evidence of facial-emotion modulation of the 100ms primary visual response in the

calcarine fissure and to the ability of the 160ms response of the fusiform gyrus to distinguish between emotional conditions.

In a 1999 ERP study Pizzagalli, Regard, and Lehmann found that the personal affective judgment of viewed facial images modulated the response in the posterior cortex. The difference between liked and disliked faces could be distinguished by the topography of the response potential in the window 80-116ms in the right hemisphere and 104-160ms in the left. The stimuli in this work were black and white Szondi portraits of psychiatric patients which were intended to elicit an affective response, although this was done in the absence of an emotional expression on the face. This result was replicated and extended to personally liked, disliked, and neutrally-regarded faces in a 2002 ERP study by the same group (Pizzagalli, Lehmann, Hendrick, Regard, Pascual-Marqui, and Davidson). An often-cited MEG study by Halgren, Raij, Marinkovic, Jousmaki, and Hari (2002) localized a midline occipital dipole, suggestive of the bilateral calcarine fissure, the timecourse of which differentiated between happy, sad, and neutral faces at 110ms, but the relative ordering of amplitudes was not specified. Interestingly the control condition of faces with randomized visual features that was employed in this work was seen to generate greater calcarine amplitude than recognizable facial conditions. This was attributed to the greater visual complexity of randomized versus coherent faces. The randomized faces used here were not recognizable, and no effect was found for another control condition in which the features of faces were scrambled by remained identifiable. Both black and white and color facial photographs were employed in this work as well as numerous control conditions including animal faces and sketches. A 2002 ERP study by Eger, Jedynak, and Skrandies employing schematic facial stimuli (positive, neutral, and negative expressions as well as scrambled faces and checkerboards) revealed a topographical difference over the occipital region which differentiated negative from neutral from positive facial expressions at a mean latency of 85ms. Interestingly, the authors do not describe this as being a face-responsive effect, and it appears that checkerboard stimuli evoked a greater global field power than did faces in an early window of 50-100ms. Batty and Taylor (2003) found a main effect of emotion on the amplitude peak of the ERP field over the occipital region beginning around 90ms with neutral and surprised faces appearing to elicit the smallest responses, but no pairwise

comparisons between particular emotional conditions were significant. Greater overall right-hemisphere activation was seen in this component as well. An MEG study by Bayle, Bostan, and Taylor (2007) localized activation at 90ms to several regions including occipital cortex, which showed greater intensity for happy versus fearful and neutral faces, but only when an identity recognition task was being performed. This effect was not found in an explicit emotion recognition task. Black and white facial photographs of these three conditions were used, and no control condition was present. An MEG study by Peyk, Schupp, Elbert, and Junghofer (2008) revealed increased activation of the occipito-parietal region for pleasant and unpleasant versus neutral scenes in the window 120-170ms. The stimuli used in this work were drawn from the International Affective Picture System. No difference was found between the responses to simple and more complex images. Finally, an MEG study by Okazaki, Abrahamyan, Stevens, and Ioannides (2008) found that category specific regions for faces, hands, and shoes, were differentially activated by these stimuli as early as 100ms in a passive viewing task. Particularly, they found that the fusiform gyrus was preferentially activated by facial stimuli as compared to other objects at this latency. Similarly, an MEG study by Meeren, Hadjikhani, Ahlfors, Hammalainen, and de Gelder (2008) found inversion effects of upright versus inverted stimulus images for faces, houses, and bodies in regions including inferior occipital cortex at latencies of 70-100ms.

Taken together the early visual results suggest that the occipital cortex is performing some function that depends upon the visual properties of the stimulus, but the nature of that function remains unclear. The pair of results from Pizzagalli and colleagues showing that the affective judgment of the viewer modulates the visual response to faces even when no emotion is displayed suggests that an interaction between the viewer and the facial stimuli is present. It seems reasonable to suppose that, when a facial emotion is present, the reaction of the viewer is at least partially related to the valence being displayed. It is also implied that not only does the viewer register a facial stimulus, but in some sense responds to it as well at a notably short latency. The results of Peyk et al. suggest that the presence or absence of emotional content in (non-facial) stimulus amplifies the occipital response although, in this case, the stimuli were known to draw specific emotional responses from the subjects and did not depend solely upon individual

reactions. The inversion effect on several categories of stimuli demonstrated by Meeren et al. seems to imply that some form of object recognition, which is presumably a precursor to judgments of spatial orientation, takes place in the early visual regions prior to 100ms. That Okazaki et al. found category specific activations at a similar latency supports a more rapid timeline of visual processing and categorization than has been historically endorsed. Since this activation was found to include the fusiform at 100ms, it is suggested that the occipital region has not only been activated but has propagated this activity as well.

The combined results of Halgren et al., Eger et al., Batty and Taylor., and Bayle et al. indicate that the occipital region begins to discriminate in some way between facial expressions. That both Halgren et al. and Eger et al. found a checkerboard control stimulus to elicit a greater response than faces, however, indicates that this may not be a true face-specific response as is seen in the fusiform. As Halgren et al. likely surmised when assembling their scrambled face images, there may exist some set of visual cues which are present in emotional faces but which need not be assembled into the likeness of a face in order to generate a calcarine response. Holistic face processing would be assumed to occur at a later stage. An emotion/intensity hypothesis is suggested by the findings of Pizzagalli et al. and Peyk et al. whereby the combination of the emotional content of the stimulus and the affective reaction of the viewer contribute to an amplified occipital response. This hypothesis would indicate that the presence and perhaps intensity of the emotional expression of a face would increase the occipital response.

The detailed results of Batty and Taylor and Bayle et al. allow some further speculation about the emotional responsivity of the early visual processing regions. A "positivity" hypothesis is suggested by Bayle et al.'s finding that happy faces elicited greater calcarine amplitude than fearful and neutral faces. Under this regime the calcarine would respond preferentially to positive valence on faces. This suggestion is further supported by Batty and Taylor's non-significant observation that surprised and neutral faces appear to generate relatively small amplitudes.

Finally, it is well known that several stages of visual processing take place in the occipital and temporo-occipital cortices, and only Halgren et al. directly implicates the primary processes of the calcarine fissure. Overall the evidence for the primary visual

processing function of the calcarine fissure being involved in true facial emotion differentiation is weak, although selective responding to some set of visual cues is supported.

Review of Facial Emotion Processing in the Fusiform Gyrus

In addition to the midline-occipital dipole Halgren et al. (2000) found to select happy and sad faces from neutral expressions, they also localized dipoles to the bilateral fusiform face areas which were found to respond selectively to facial images versus non-face stimuli. The peak activation of this region, occurring at 165ms, was seen to be diminished by scrambled facial images (25%), schematic faces (30%), animal faces (50%) and animal bodies and common objects (80%). The fusiform face area was not seen to distinguish between the emotional conditions employed in this work (happy, sad, and neutral faces). In 2002 Pizzagalli et al. focused on the response of the fusiform gyri and found that liked faces elicited a stronger activation than disliked and neutrally-regarded faces as well as checkerboard stimuli at 160ms. It was also found that both happy and sad faces generated a stronger response than neutral faces and checkerboards. A right hemisphere amplitude bias was also found. The earliest indications of face-responsivity found by Eger et al. (2002) occurred at 150-200ms in the temporal electrodes, where schematic facial stimuli and even eyes in isolation were found to evoke greater amplitude and shorter latency responses than several control conditions (fragmented figures, schematic objects, and animals). Despite a distinct topology, checkerboard stimuli were found to elicit no significant differences in either latency or global field power. The fusiform response was also seen to display greater field power for negative versus neutral and positive faces. A right-hemisphere bias was also observed.

Batty and Taylor (2003) found the amplitude and latency of the 140ms superior- and middle-temporal response to be modulated by facial emotion. The amplitude of the response to fearful faces was greater than that to neutral, happy, disgusted, surprised, sad and angry faces. The latencies of fearful, disgusted, and sad faces were longer than those of happy and surprised faces. A valence-related trend was suggested such that the mean latency response of several positive emotions (happiness and positive expressions of surprise) was shorter than that to a group of negative emotions (fear, disgust and sadness but not anger and negative surprise).

In a 2006 MEG study, Sprengelmeyer and Jentzsch identified bilateral dipoles in the inferior occipto-temporal regions which were responsive to viewed facial images around 170ms. No effect of emotion (happiness, disgust, and fear) was found but amplitude was seen to increase with the intensity of facial emotion, beginning in the 170ms component and becoming most pronounced in the window 200-600ms. The amplitude of the 170ms component was also found to be increased when subjects' engaged in an explicit emotion-recognition task versus an identity-recognition task. In addition to face-preferential activation within 100ms, Okazaki et al. (2008) found that the fusiform gyrus was selectively activated at 170ms and again at 200ms by facial stimuli. Although positive, neutral, and negative facial expressions were utilized no effect of emotional condition is reported. In an additional task including images of faces and hands it was found that the 200ms component was enhanced under task demands which required attention to faces versus to hands. The 100 and 170ms components did not differ based on whether attention was paid to faces or hands.

Together these results well support the assertion that the fusiform gyrus is preferentially activated by facial stimuli (Halgren et al., Eger et al., Batty and Taylor, Sprengelmeyer and Jentzsch, Okazaki et al.), particularly with respect to the well-known 170ms response. In keeping with the Adolphs (2002a, 2002b) model of facial processing the fusiform gyrus is shown by Okazaki et al. to be activated multiple times, first around 100ms, secondly the well documented activation at 170ms, and again beyond 200ms. The 100ms activation was not predicted by Adolphs but the 170 and 200ms activations were, and Okazaki et al showed all three activations to be face-selective. Generally speaking this result suggests that models of facial processing are not yet complete, particularly with regard to the role of the fusiform gyrus. The findings of Sprengelmeyer et al. and Okazaki et al. suggest that the fusiform response is further enhanced when attention is specifically paid to faces. While both groups found this in the response at 200ms and beyond, only Sprengelmeyer et al. found the 170ms response to be amplified by attention.

As with the calcarine fissure, the personal affective reaction of the viewer may also play a role in the fusiform response, as seen in the results from Pizzagalli et al., where liked faces elicited a greater activation than did disliked an neutrally-regarded faces. Intensity of facial expression appears to increase the power of the fusiform

response as well (Sprengelmeyer et al.). Finally, evidence is beginning to accumulate that the emotion of the face being viewed modulates the fusiform response. Pizzagalli et al. found that happy and sad faces caused a greater amplitude response than did neutral faces and a checkerboard pattern. Eger et al. found greater global field power in the response to negative versus positive and neutral facial expressions. Despite using an implicit emotion task, Batty and Taylor found effects on both response amplitude and latency, with fearful faces resulting in greater amplitude than the remaining five basic emotions as well as neutral faces and disgust and sadness having longer latency responses than happiness and surprise. Although it seems generally appropriate to expect that an effect of emotion exists in the response of fusiform gyrus to facial stimuli, it may be premature to speculate any further. That an effect of emotional expression is not seen in many studies which do find a face-specific reaction in the fusiform gyrus (Halgren et al., Sprengelmeyer et al., Okazaki et al.) suggests that the effect size of the former is smaller than of the latter.

Review of Gender Effects on Facial Emotion Processing

Although the popular culture endorses many gender differences in emotion and social perception, empirical support for these difference has often been lacking. Recent work using a large sample size (n=240; Rahman, Wilson, and Abrahams, 2004) and controlling for age and IQ, found no overall difference in accuracy of facial expression recognition between men and women, although women were found to be faster for a given level of accuracy. This work utilized the same Ekman and Freisen Pictures of Facial Affect (1976) as were used as stimuli in the current study. Additional evidence is beginning to accumulate in support of some gender differences, and several investigators have reported a female advantage in either speed or accuracy of facial emotion recognition. Montagne, Kessels, Frigerio, Haan, and Perrett (2005), using video clips of neutral faces morphing into emotional faces, found men to be both less accurate and less sensitive in perceiving facial emotion. Hampson, van Anders, and Mullin (2006) similarly conclude that women are faster than men at recognizing both positive and negative emotion from facial cues. Finally, Proverbio, Matarazzo, Brignone, Zotto, and Zani (2007) conclude that not only do women show greater ability to decode the facial expressions of infants, but also that childcare experience enhances this ability in women but not in men.

In their meta-analysis of the functional imaging of emotion (PET and fMRI, not limited to facial emotion recognition), Wager et al. (2003) investigated gender differences in activation patterns and reported that neither gender displays more frequent overall activation. Gender differences in activation patterns were found however, in that the posterior sensory and association cortices, left inferior frontal cortex, and dorsal striatum were activated more frequently in men, whereas the medial frontal cortex, thalamus, and cerebellum were activated more frequently in women. In general, men displayed greater lateralization of activation while women showed greater activation of subcortical structures. In a facial emotion discrimination task Orozco and Ehlers (1998) found that women displayed a higher amplitude, longer latency P450 ERP component than did men when viewing happy and sad but not neutral faces. In an ERP study of gender differences in emotional perception of infant faces, Proverbio, Brignone, Matarazzo, Zotto, and Zani (2006) showed a greater amplitude of the lateral occipital P110 component in women versus men regardless of facial condition. In the left hemisphere this component was also found to be significantly greater in mothers versus childless women, but there was no effect of parental status in men. A similar gender difference was found in the occipitotemporal N160 component between mothers and fathers, but there was no gender difference between non-parents. Finally, an ERP study by Proverbio, Zani, and Adorni (2008) found significantly greater amplitude of the parietal N2 component between 210 and 270ms when viewing social scenes versus landscapes in women but not in men. Localization showed that both genders activated the middle occipital gyrus, superior temporal gyrus, and fusiform gyrus in this time window. Although the difference between conditions as measured at the scalp was only significant for women, both genders showed significantly greater activation of the fusiform gyrus for social scenes versus landscapes after localization.

Review of Age Effects on Facial Emotion Processing

In a brief review of the cognitive effects of aging from a neuroscience perspective, Hedden and Gabrieli (2004) list emotional processing as a cognitive faculty demonstrating lifelong stability and which is relatively exempt from the declines seen in many other realms. Many other works, however, including a meta-analysis of the age-related effects on multiple modalities of emotion recognition (Ruffman, Henry,

Livingstone, and Phillips, 2008) cite a generalized decline in recognition abilities that crosses modalities and emotions. The inclusion criteria of this meta-analysis accepted only studies in which the older group of participants exceeded 55 years of age, and the younger did not exceed 45. In this field it is often difficult to distinguish the effects of normal aging from the early effects of dementia inducing disease processes. Nonetheless, Chaby and Narme (2008) argue that, even in healthy adults, subtle effects which diminish facial identity and emotion recognition abilities begin to appear by the age of 50 and accelerate after 70. Although this effect is commonly conceptualized as being driven by age-related neural degeneration, Williams et al. (2006) cast the effect in the more positive light of "life experience and wisdom". Across numerous cognitive domains, including facial and emotion recognition, the elderly are seen to enlist frontal and prefrontal regions to a greater extent than young adults. This effect is often explained as an attempt to compensate for the decreasing efficiency of low-level processing with greater cognitive involvement (Hedden and Gabrieli), and is supported by the findings of Tessitore et al. (2005) in which adults over 60 years of age were found to require greater reaction time than younger adults in order to achieve a similar level of accuracy. Noting that emotional stability improves with age however, Williams and colleagues reverse the direction of causality and argue that older adults have developed greater abilities to exercise cognitive control over their emotional reactions. They particularly argue that older adults exert lesser prefrontal control over positive emotional material and greater prefrontal inhibition of negative material. Williams and colleagues included subjects of all ages, and propose that these changes take place in a linear fashion throughout the lifespan. This effect is consistent with the increasingly positive valence and diminished intensity with which older adults view their prior life experiences.

Nonetheless, several studies have uncovered specific age-related deficits in the recognition of facial emotion. The meta-analysis of Ruffman and colleagues (2008) notes that older adults show decreased ability to recognize all facial emotions except disgust. Calder et al. (2003) note a decreased recognition of fear and anger with age but suggest that recognition of disgust may even improve. Keightley, Chiew, Winocur, and Grady (2007) found that older adults had greater difficulty identifying expressions of sadness, anger, and disgust. Varying emotional intensity as well as expression, Orgeta and Phillips

(2008) found that older adults showed diminished ability to recognize anger, sadness, and fear at all intensities but that happiness and surprise remained unaffected by age, and that recognition of disgust may improve. Since visual acuity diminishes with age it remains unclear whether deficits of emotion recognition are driven by visual or other factors. Sullivan and Ruffman (2004) found that aging diminishes the ability to detect anger and sadness but not happiness and that this effect was independent of visual perception. On the other hand, Norton, McBain, and Chen (2009) found that decreased ability to detect faces as well as facial expression was related to decreased visual sensitivity and particularly to diminished contrast detection.

Considerable fMRI-based work has been done to investigate the neural structures associated with emotion recognition and changes with age. Iidaka et al. (2002) found that, although patterns of activation changed over age, in no region did older adults display greater activation than younger. Tessitore et al. (2005) found that, when processing fearful and threatening stimuli, older adults showed greater activity in the prefrontal cortex and reduced activity in the amygdala and posterior fusiform gyrus. Suggesting an age-related movement from subcortical to cortical regions, Fischer et al. (2005) found that, while viewing angry and fearful faces, younger subjects showed greater activation of the right amygdala and hippocampus while older subjects activated the right anterior-ventral insula.

Although ERP studies of emotion perception and aging are rare, Wieser, Muhlberger, Kenntner-Mabiala, and Pauli (2006) showed an early posterior negativity to be associated with highly arousing emotional pictures. This negativity, occurring around 180ms in young subjects, was seen to be delayed until around 220ms in an older group. Amplitude was found to be decreased in the older group as well.

Aims and Hypotheses of Current Work

The current work involved an MEG-based study of the neural response to the viewing of emotional faces in order to explicate the time course of activation of the bilateral calcarine fissure and fusiform gyrus. This work was conducted at the MIND Research Network using a 275-channel CTF MEG scanner, and the experimental protocol was designed as a replication and extension of the prior face-emotion research conducted at the Albuquerque VA Medical Center (Lewis et al., 2003). That this research

was conducted by a separate team using a different make and model of MEG system increased the utility of this replication attempt.

Specific aims of this work were:

Specific Aim 1: To replicate the results of the previous work of Lewis et al (2003) using cortical projection techniques.

Hypothesis 1: The timecourses of the bilateral calcarine fissure of each subject will display an amplitude peak occurring around latencies 80-110ms for the stimulus conditions happiness, disgust, and neutral as well as for the swirled face condition. Within-subjects analysis across these four conditions will reveal no significant differences in either peak amplitude or latency.

Hypothesis 2: The timecourses of the bilateral fusiform gyrus of each subject will display an amplitude peak occurring around latencies 120-170ms for the facial stimulus conditions happiness, disgust, and neutral, and a lesser peak for the swirled face condition. Within-subjects analysis will reveal no significant differences in peak latency between the four conditions, but a significant difference will be found in right hemisphere peak amplitude such that happiness>disgust>neutral.

Specific Aim 2: To extend the previous findings of Lewis et al to all six basic emotions as well as to non-facial, visually complex stimulus images using cortical projection techniques.

Hypothesis 3: The timecourse peaks in the bilateral calcarine fissure corresponding to *Hypothesis 1* will be found for all nine stimulus conditions. Within-subjects analysis will reveal no significant differences among the conditions in either peak amplitude or latency.

Hypothesis 4: The timecourse peaks in the right fusiform gyrus corresponding to *Hypothesis 2* will be found for all facial stimulus conditions, but not for the swirled face and complex, non-face conditions. Similar peaks will be found in the left fusiform gyrus as well. Within-subjects analysis across the nine stimulus conditions will reveal significant differences in peak amplitude and latency including the right hemisphere amplitude difference wherein happiness > disgust > neutral.

Specific Aim 3: To investigate relationships between timecourse peak amplitudes and latencies and gender, age, and cortical hemisphere in the bilateral calcarine fissure and fusiform gyrus. Differences in activation between the calcarine fissure and fusiform gyrus will be noted as well.

Chapter 2: Materials and Methods

Subjects

Twenty-one subjects were recruited on a convenience basis from among the staff at the MIND Research Network, faculty and graduate students of the UNM Psychology and Psychiatry departments, and friends of students, faculty, and staff. Subjects were required to be between 18 and 65 years of age and to be able to give informed consent (UNM North Campus HRRC #07-179). Additionally, since subjects were required to undergo MRI and MEG scans, those with claustrophobia or non-removable metallic objects in the head or upper body were implicitly excluded. Subjects were not excluded on the basis of psychopathology, even if of potential clinical significance. Current medication or substance use was allowed as well.

Of these twenty-one subjects, one became ill during their MRI scan and thus, due to the lack of structural neuroanatomical data, this subject was excluded from data analysis. Prior to formally beginning data collection for this experiment four subjects volunteered to undergo the MEG data collection procedure in a technical development capacity. Of these four subjects, the data from three was collected using the final version of the MEG protocol. These three subjects were re-consented and their data was included in the analysis.

In total, data from twenty-three subjects was used in the final analysis (mean age 29.7, minimum age 22, maximum age 48, standard deviation 7.6). Ten of these subjects were male (mean age 29.4, minimum age 22, maximum age 48, standard deviation 8.9) and thirteen were female (mean age 29.9, minimum age 23, maximum age 43, standard deviation 6.9). A simple t-test reveals that there is no significant difference between the mean age of the male and female groups ($t(21)=-0.159$, $p=0.875$, two-tailed, equal variances assumed according to Levene's test).

It should be noted that many of the subjects participating in this experiment, including the three technical development subjects, already had structural MRI data on file at MRN. In these cases the pre-existing data was used for data analysis purposes. Although this data was collected in a variety of different protocols, using both the 1.5 Tesla and 3.0 Tesla MRI systems, these differences are not anticipated to have any

influence on the results presented here because it was reconfigured into similar format prior to use for MEG localization.
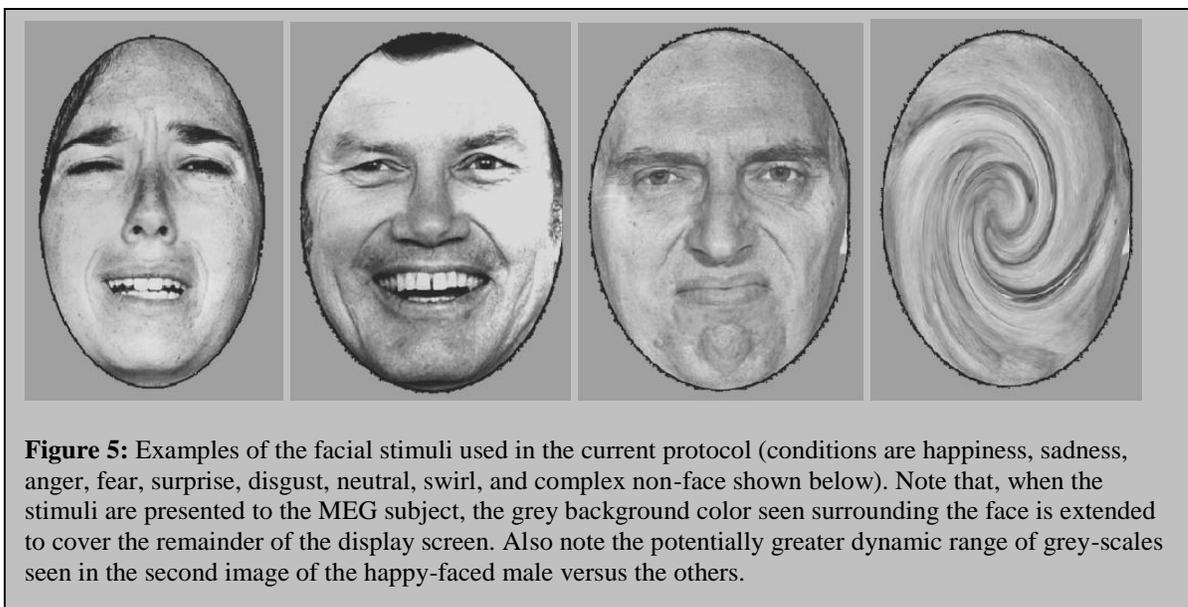
Finally, subjects were paid $50 for each of the MEG and MRI scan procedures, totaling $100 for subjects completing both scans. The cost of scans as well as subject compensation was paid by an MRN internal grant (#07-179).

Materials

The stimulus set for this experiment consisted of images of nine facial conditions: faces displaying the six basic emotions (happiness, sadness, anger, fear, surprise, and disgust), emotion-neutral faces, swirl-filtered facial images, and non-face, visually complex images. Eight separate images were used in each category which, when applicable, were divided into four males and four females. The neutral and emotional faces were derived from the standard Ekman and Friesen set (1976), which consists of black and white photographs of actors depicting expressions of the six basic emotions as well as the neutral condition. A subset of these images was selected and digitized for use in the Lewis, et al (2003) protocol. Since the current experiment was, in part, an attempt to replicate the 2003 results, this stimulus set, with minor modifications, was reused (Figure 4). Faces were selected based on the investigators' judgment of the accuracy of the portrayed expression and thus the same set of actors is not maintained across conditions. Following digitization, each face was processed in Adobe Photoshop such that the face itself was surrounded by an oval bounded approximately by the chin,

Figure 4: Examples of stimuli used in the 2003 Lewis et al. protocol. (Conditions were happiness, disgust, neutral, and swirled faces.) When the stimuli were presented to the MEG subject, the black background color seen surrounding each face was extended to cover the remainder of the display screen.

Figure 5: Examples of the facial stimuli used in the current protocol (conditions are happiness, sadness, anger, fear, surprise, disgust, neutral, swirl, and complex non-face shown below). Note that, when the stimuli are presented to the MEG subject, the grey background color seen surrounding the face is extended to cover the remainder of the display screen. Also note the potentially greater dynamic range of grey-scales seen in the second image of the happy-faced male versus the others.

hairline, and ears. In the Lewis et al. study the background surrounding the face was set to black. This processing step was performed in order to remove distractions such has hair and clothing from the images. The images were then processed for equiluminescence. Although the original Lewis et al. (2003) protocol included only the happiness, disgust, and neutral conditions, the investigators created facial images for all conditions except surprise. In order to maintain continuity with the previous and ongoing work, the same stimulus package, with minor modifications, has been used here.

Of the original stimulus images, three were replaced for this work: 1) a sad-faced female whose eyes were downcast was replaced by an image of the same sad actor but with eyes gazing more directly towards the viewer, 2) a neural-faced male whose expression, on the basis of his low brow-line, could be interpreted as angry was replaced by a different, neutral male face, and 3) a happy female with a closed-lipped smile was replaced by an image of the same happy actor displaying a teeth-bared smile in order to be consistent with the other images in the happiness category. Additionally, only three disgusted-faced male actors were created in the original set so an additional Ekman and Friesen male was selected. Finally, an entire set of surprise-condition facial images was created following the steps used to create the original stimulus images.

Swirled facial images were also created by the original Lewis et al. investigators and these images were reused. These images were created by applying the Photoshop

swirl filter to randomly selected faces from the seven emotional categories (including neutral). The filter was applied prior to the establishment of the oval and black background, so that these features were not modified by the filter.

The current study added the stimulus category of visually complex non-face images as a control condition. For this category, color digital photographs of eight non-human outdoor sculptures were taken around the UNM campus. The sculptures were chosen such that a strong central feature was present and the photographs were framed against an indistinct background. These photographs were converted to grey-scale and processed in the same manner as the facial images.

For use in the MEG protocol described here, the 72 stimulus images were modified in additional ways. First, the average grey scale value of the faces themselves was adjusted to an approximate value of 160. This was done by adding or subtracting the same integer value to/from each pixel identified as being part of the face itself (versus the background). Second, the black background outside of the oval containing each face was converted to a grey scale value of 160. These two steps were performed so that, when the faces were displayed against an inter-stimulus grey background (grey scale value=160), there would be no net change in luminance seen by the subject as faces were displayed and removed. Lastly, the area of the faces within the surrounding ovals was approximately standardized using an image-stretch procedure. This was done so that the visual area occupied by each face would not differ from face to face. These three steps were automated using a script written for Matlab. It should be noted that the dynamic

Figure 6: Examples of the visually complex but non-facial stimuli used in the current protocol.
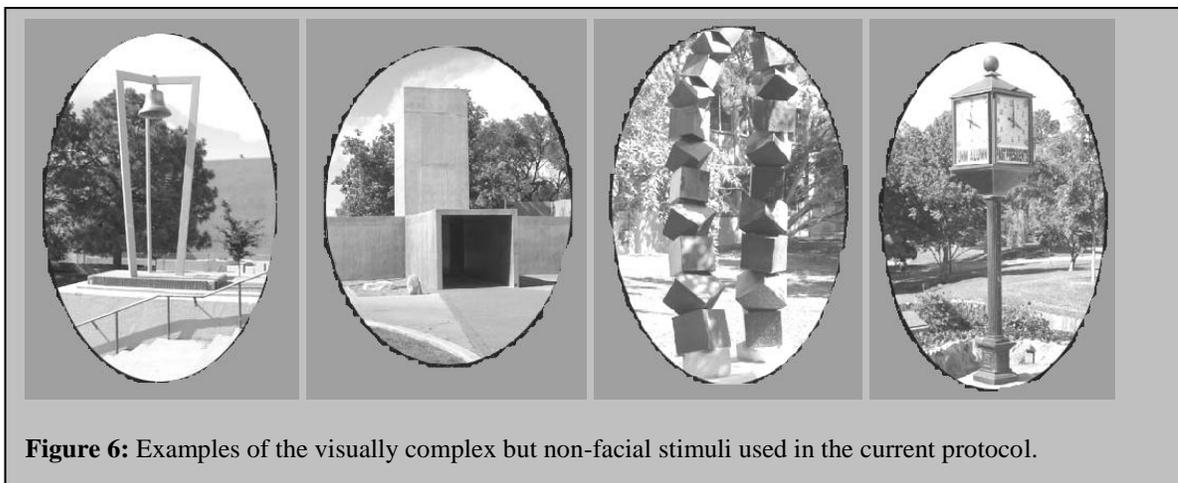
range, or the range of the grey-scale values comprising each face, was not standardized and appeared to be different. Particularly, the images carried over from the original Lewis et al. study, based on an informal visual inspection, appeared to have a more limited range of grey values than did the images developed specifically for this study (replacement faces, surprised faces, and non-face sculptures). It was judged that this disparity was not sufficient to impact the recognizability of the emotions displayed on the faces and it was not corrected (Figures 5 and 6).

Procedures

Data for this experiment was collected in two sessions per subject: 1) an MRI scanning session lasting approximately 60 minutes which included a high resolution structural T1 MRI scan, in addition to MR spectroscopy and diffusion tensor imaging scans to be used in other experiments and, 2) an MEG data collection session lasting approximately two hours including preparation time. During one of these sessions the subjects also completed a battery of psychological self-report instruments related to levels of depression and anxiety. The ordering of these sessions for each subject was determined by convenience, although it is undesirable to perform an MRI scan immediately prior to MEG data collection. As mentioned previously, several subjects recruited from the staff at MRN already had structural MRI scans on file. In these cases the pre-existing scans were used. One informed consent form was used to cover both sessions, and was completed by the subject at the beginning of the first session. The MRI and MEG scans as well as the psychological testing were performed according to established medical, psychological, and research practices.

MEG data were collected on the 275-channel CTF system at MRN. Neuroscan Presentation software was used to present each stimulus image to the subject for 1.5 seconds with an interstimulus interval varying randomly between 1.0 and 3.0 seconds. As the subject sat in the MEG system the images were projected into the chamber and onto a screen approximately 24 inches directly in front of the subject's face. As presented the stimulus faces were approximately 5 inches tall (approximately 12 degrees visual angle), a size which was chosen to allow comfortable viewing of the faces without requiring excessive ocular scanning. Between stimuli a grey background (value=160) with a white fixation cross in the center was displayed. The total stimulus set of 72 images was

presented 15 times, in a separately randomized order each time, for a total of 1080 images over a period of approximately 64 minutes. This resulted in 120 trials of each facial-emotion condition being collected which, in our experience, is a standard but near-minimum number of trials for an MEG experiment. MEG data was collected at 600 samples/second during this time. A 3D spatial digitizer was used to record the subjects' head shapes for later co-registration with the structural MRI data.

Data Analysis

The output from the MEG system was a continuous time-course of data spanning the entire 64 minutes of the experimental protocol for each subject. Before any source localization may be attempted with MEG data several rather complex preprocessing steps must be taken. MEG is sensitive to electromagnetic interference and, in general terms, these steps fall into the two, broad categories of data filtering and artifact rejection. The filtering stage typically takes place in the frequency domain and is used in order to remove information which is not deemed relevant to the research question at hand. Several common forms of data contamination, including DC drift and power-line interference, are also removed by this frequency-specific filtering. The artifact rejection procedure is enacted after the filtering step, and is undertaken in order to remove segments of data that are judged to have been corrupted by processes unrelated to the neural functions of interest. These processes can be related to the subject's own behavior, such as blinking, swallowing, or muscular activity, or can be generated externally from the subject by sources such as vehicles, elevators, and swinging doors.

The data filtering step of this experiment was performed on the continuous data, where a fourth-order band-pass filter (BPF) with cutoff frequencies of 2 and 55 Hz was applied. This filtering was accomplished using the CTF software suite (which employs a Chebeshev-II filter design). The 2 Hz lower cutoff was selected, taking filter roll-off into account, in order to comfortably remove DC and near-DC components from the data while avoiding interference with the 150-200 millisecond face-specific response of the fusiform gyrus (translated into frequency, and making a conservative assumption about the latency at which the fusiform responds, 200 milliseconds is 5 Hz). Note that the selection of a 2 Hz lower cutoff frequency may be inappropriate when investigating longer latency neural activity, such as that approaching 500 ms post-stimulus. The 55 Hz
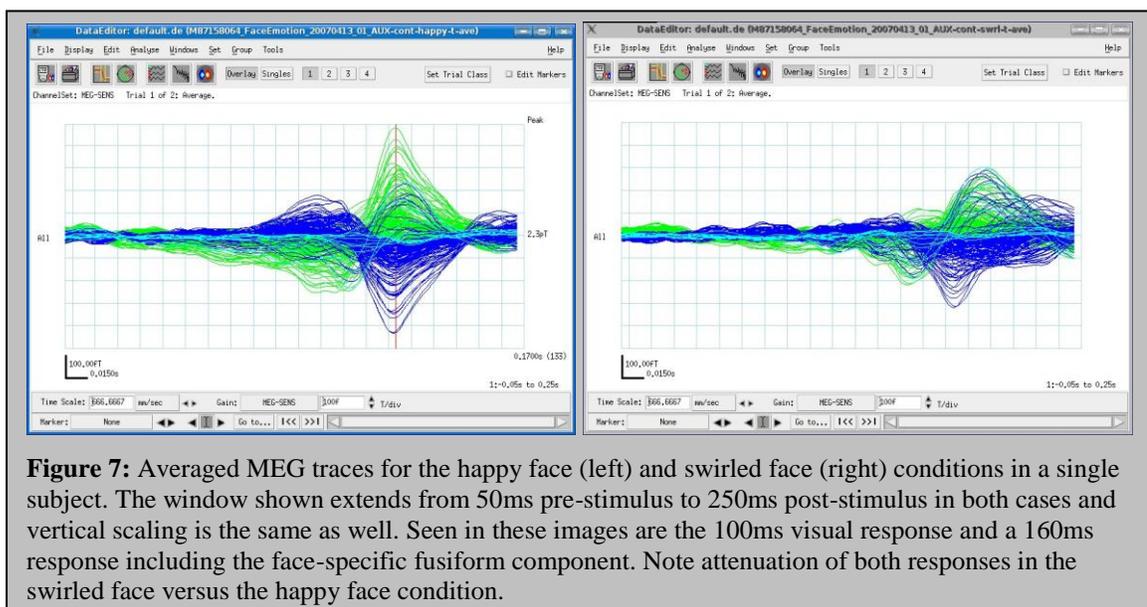
upper cutoff was selected to prevent 60-Hz powerline interference from compromising the experimental data. This artifact, as well as its harmonics at 120 Hz and above, is usually quite prominent in MEG data. Fortunately the power spectrum seen in MEG data suggests that neural activity drops off comfortably below this frequency, so the elimination of data beyond 55 Hz is not anticipated to have influenced our results. Finally data filtering in MEG experiments is often not addressed until the data has been epoched, but experience suggests that epoch-level filtering creates artifacts within the resulting data. These artifacts are characteristically identified by the overlaid MEG traces splaying apart at either or both ends of the epochs, and thus filtering on the continuous data may be considered superior.
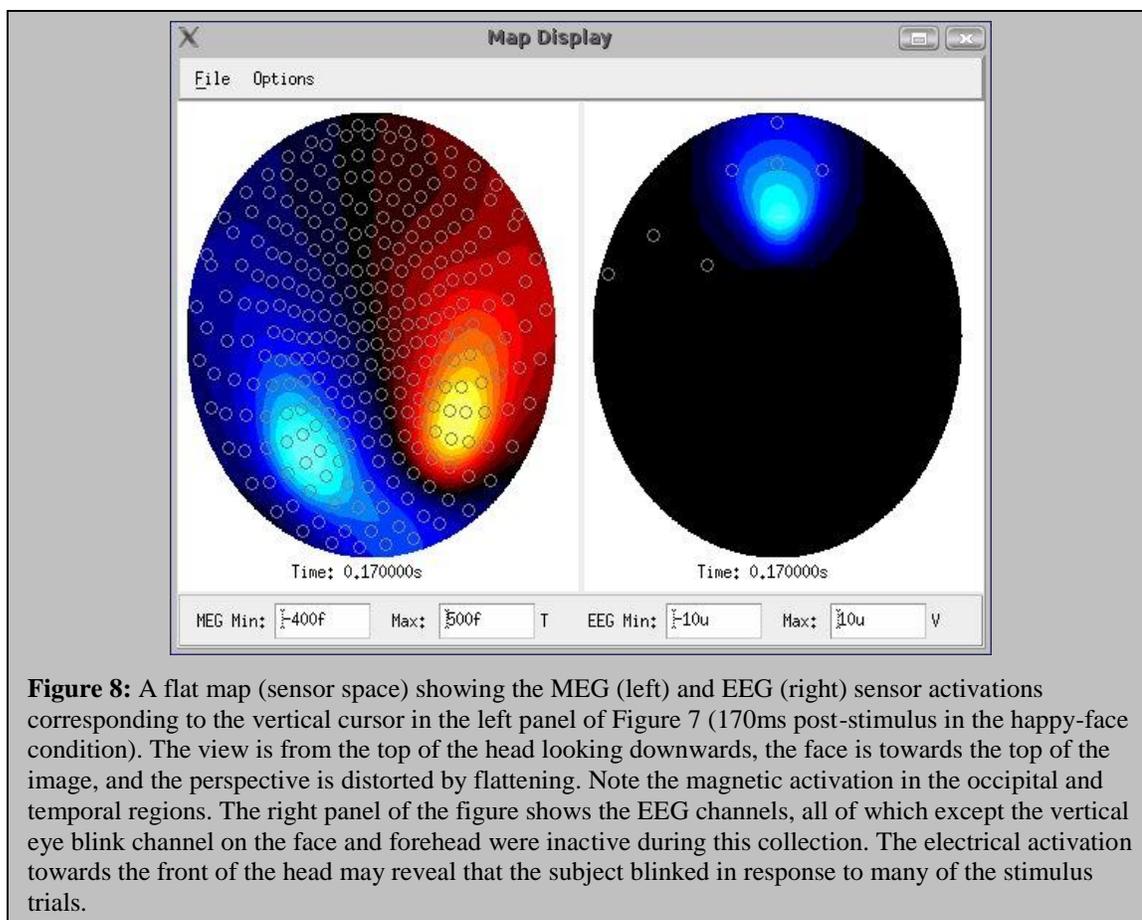
Following filtering on the continuous data, the MEG data was epoched into intervals starting 50ms before and ending 250ms after the presentation of each stimulus image. Thresholds were then applied to the vertical eye movement EEG channel and to all of the MEG channels within these epochs in order to identify trials contaminated by eye blink activity, motion artifacts, or external electromagnetic noise. The threshold levels were set individually for each subject dataset such that as nearly as possible to 25% of the total trials were rejected. This was done in order to control the number of trials which passed onwards to the averaging stage, as this number directly influences the resulting signal-to-noise ratio (SNR). Of the 1080 total stimulus trials viewed by each subject, approximately 800 (+/- 10) were allowed to pass through the thresholds. The number of trials within each experimental condition (happiness, sadness, etc.) was not controlled, and it was assumed that the thresholding process affected each condition equally. Additionally, the EEG threshold and MEG threshold were maintained such that the first was twice the magnitude of the second. Although the two thresholds were measured in different units (femto-Telsas versus micro-Volts), this was done in an attempt to cause similar proportions of trials to be rejected in each subject's data for each type of threshold. In other words, this was done in an attempt to control the proportion of trials rejected by the EEG eyeblink channel versus the MEG channels.

Once contaminated trials were rejected, averages were created of the remaining epoched MEG data on the basis of stimulus condition. During such averaging, stimulus locked components of the signal become additive while non-stimulus-locked components do not. This common signal processing technique raises the signal-to-noise ratio of the resulting averages well beyond that of the raw data. This practice, referred to as evoked-response-potential (ERP) analysis, is commonplace in both EEG and MEG experiments. The output from this processing step was nine sets of MEG averaged data representing each subject's magnetic neural responses to happy faces, sad faces, and so forth (Figure 7).

CTF MEG systems include a noise-cancellation procedure referred to as third-gradient filtering. An additional set of magnetic sensors are located within the system's dewar but away from the subject's head. These sensors record environmental noise within the MEG enclosure which can be compensated for in the data itself during later processing stages. Although this feature is reversible in all the data processing steps prior to source localization, third-gradient filtering was used in all applicable steps within this experiment.

Output from the MRI system is comprised of a series of image slices for each subject's brain. These slices are typically viewed using an MRI viewing piece of software, which allows the brain orientation to be adjusted while selecting the axial,

Figure 7: Averaged MEG traces for the happy face (left) and swirled face (right) conditions in a single subject. The window shown extends from 50ms pre-stimulus to 250ms post-stimulus in both cases and vertical scaling is the same as well. Seen in these images are the 100ms visual response and a 160ms response including the face-specific fusiform component. Note attenuation of both responses in the swirled face versus the happy face condition.

Figure 8: A flat map (sensor space) showing the MEG (left) and EEG (right) sensor activations corresponding to the vertical cursor in the left panel of Figure 7 (170ms post-stimulus in the happy-face condition). The view is from the top of the head looking downwards, the face is towards the top of the image, and the perspective is distorted by flattening. Note the magnetic activation in the occipital and temporal regions. The right panel of the figure shows the EEG channels, all of which except the vertical eye blink channel on the face and forehead were inactive during this collection. The electrical activation towards the front of the head may reveal that the subject blinked in response to many of the stimulus trials.
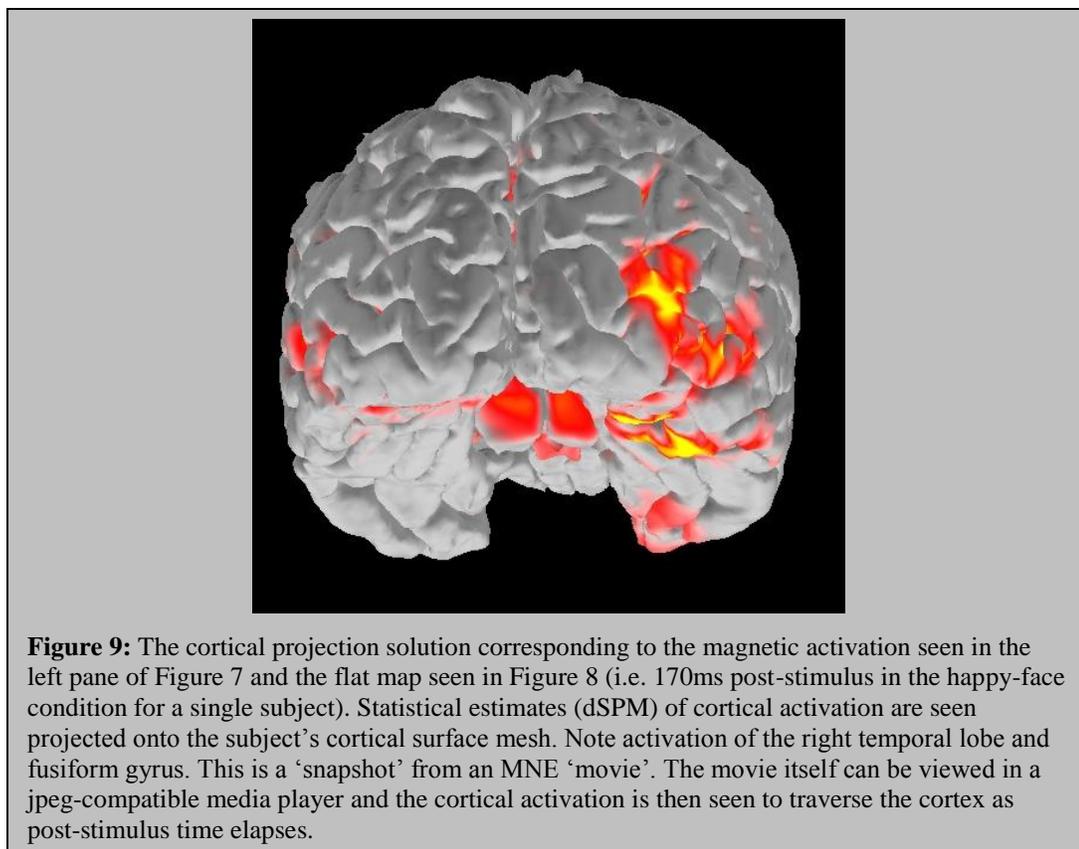
sagittal, and coronal slices of interest. Since a cortical projection technique was to be used for source localization in this experiment it was necessary to develop a model of the subjects' cortices from the MRI slice data. The combination of the Freesurfer and MNE software packages are frequently used at MRN for such analysis. Freesurfer uses the MRI output to create a mesh (a three-dimensional surface representation comprised of vertices and edges) of each subjects' cortex, comprised of approximately 60,000 vertices. As opposed to simply viewing images, this mesh is an actual digital model of the cortical surface of the subjects' brains. The creation of this mesh is a necessary precursor to cortical projection analysis, and was done for each of the subjects in this experiment.

MEG source analysis is the process of resolving magnetic activation seen by the MEG system sensors (sensor space, Figure 8) into sources within the brain of each subject (source space). This can be done using any of several techniques, but it was decided in advance that this experiment would utilize cortical projection analysis via the MNE software. As its name suggests, cortical projection limits the solution space to the

cortical surface, and thus is unsuitable for the analysis of subcortical neural sources. Although the term 'cortex' suggests only the outwardly visible, superior, lateral, anterior, and posterior surfaces of the brain, the Freesurfer-generated mesh describes the inferior surface of the brain but with the subcortical structures removed. Additionally, the two cortical hemispheres are modeled separately and thus the cortical structures of the medial walls are also accessible. Although the primary structures of interest in this experiment, the calcarine fissure and the fusiform gyrus, are indeed cortical and thus well suited for cortical projection analysis, several other structures of secondary interest, such as those of the limbic system, are not nearly so accessible. It is possible that activation of the amygdala, for example, might be seen projected onto the inferior medial walls but, in practice, MNE projection solutions perform poorly with deep sources, whether cortical or not.

Alignment of the MRI and MEG coordinate systems is a critical step in the source localization process. This is accomplished by co-registering a set of fiducial points which are known in both coordinate systems. A set of three magnetic coils, one in the nasion of the nose bridge and one just in front of each ear, are taped to the subject's face prior to MEG data collection. A multi-axial digitizer is used to record a three-dimensional set of points in order to describe the subject's head shape. These points include the location of the coils. The coils themselves are activated by the MEG system at the beginning and end of the session in order to locate the subject's head within the MEG coordinate system. In post-processing the shape data of the subject's head, including the location of the coils, is first located on the subject's head mesh (derived from Freesurfer at the same time the cortical mesh was created) and is then mated with the MEG data, which also knows the location of the coils. It is claimed that the MEG technology itself has 5 millimeter spatial resolution within the subject's brain, but this accuracy is entirely contingent upon the co-registration of the two coordinate systems. All possible precautions were taken in this experiment, but this process remains one of the greatest sources of error in MEG analysis.

Figure 9: The cortical projection solution corresponding to the magnetic activation seen in the left pane of Figure 7 and the flat map seen in Figure 8 (i.e. 170ms post-stimulus in the happy-face condition for a single subject). Statistical estimates (dSPM) of cortical activation are seen projected onto the subject's cortical surface mesh. Note activation of the right temporal lobe and fusiform gyrus. This is a 'snapshot' from an MNE 'movie'. The movie itself can be viewed in a jpeg-compatible media player and the cortical activation is then seen to traverse the cortex as post-stimulus time elapses.

Cortical projection via MNE treats each vertex on the subject's brain mesh as an individual magnetic source (commonly referred to as a 'dipole', a reference to the simplest possible unit of magnetism, which is often illustrated as a bar magnet with strength and orientation components). Various constraints can be placed on these dipoles; in this analysis the dipole orientations are required to be normal to (and outward facing from) the cortical surface. (This functionality is accomplished using the –loose 0.4 option when creating the inverse operators and --signed and --picknormalcomp when creating the movies and timecourse data). Depth weighting (using the --depth option when creating the inverse operators) was tried and specifically rejected because it creates excessive noise on the medial walls. At each dipole on the cortical surface the magnetic activation seen by the MEG sensors is explained by an electric current flowing within the cortex. This current is usually understood to be within the dendrites of neuronal populations, as opposed to their axons. The cortical projection output from MNE itself consists of movies of brain activation corresponding to the cortical activity generated by each experimental condition (happy faces, sad faces, etc.) and timecourse data for each

vertex on the cortex (i.e. the cortical response, with the above constraints applied, at that vertex for the duration of the averaged epochs, in this case -50 to 250ms). Cortical projection movies, which display hotter colors on the cortical surface mesh corresponding to the locations of greatest current flow, can be viewed on any multimedia movie viewer (Figure 9). Vertex timecourses require a few lines of Matlab code in order to be viewed as a plot of amplitude versus time (Figure 10). While movies are useful (and entertaining) for visual analysis and the suggestions they provide about which cortical regions are active in some response, this experiment, dealing with specific questions about the activities of certain regions, was more interested in timecourses.

It is often useful to combine the cortical activation solutions for multiple subjects in order to create group solutions. Movies or timecourses can be derived from these group average solutions for viewing and analysis. In order to do this either the cortical geometries of all of the subjects to be combined must themselves be averaged or a single subject must be selected onto which the other subjects' geometry is morphed. Although group average solutions were not created in this work, the subjects' brain structures were morphed onto that of a single, randomly selected subject as described. This should have no effect on the analysis presented here while retaining the option of combining groups of subjects for further analysis in the future.

MNE is able to create output in two modes, MNE and dSPM. MNE, which stands for minimum norm error, signifies that the output is given in terms of raw current and, at each vertex, the units are in nanoamperes. dSPM, standing for digital statistical parametric mapping, creates output as a t-score statistic versus prestimulus baseline. In this case the output indicates the statistical significance of post-stimulus cortical activation versus pre-stimulus. Raw current output is most appropriately used when further analysis is planned for the results (in order to avoid doing statistics on statistics), while dSPM output is appropriate for visual comparison of results between subjects or groups. Since data derived from the timecourse outputs created here are later input into SPSS for further statistical analysis, raw current, or MNE output is used. (Since there is some confusion between 'MNE', the name of the cortical projection software package, and 'MNE', the raw current estimates output from this package, 'MNE' is used to identify the software and 'raw current' to identify its output.)

In addition to creating the cortical surface mesh, Freesurfer also provides a segmentation of the brain, and the mesh is itself segmented into separate cortical regions according to the Freesurfer atlas. In this experiment the Freesurfer atlas has been used to identify the boundaries of the cortical regions of interest. Within the mesh describing the cortical surface, each of the four regions of analysis, the bilateral calcarine fissures and fusiform gyri, contained several thousand vertices. The timecourses for these vertices were output individually from the MNE software. At this point processing was handed off to a Matlab script which averaged the timecourses of the vertices within each region, for each experimental condition. The result was an average response timecourse for each of the four regions in each of the nine experimental conditions (happy, sad, angry, fearful, surprised, disgusted and neutral faces, swirled faces, and statues). In is unknown but suspected to be unlikely that the vertices of the cortical surface mesh are evenly spaced. Because of this the interpretation of the units in which the amplitudes of average timecourses are measured is difficult. Without evenly spaced vertices this amplitude cannot be interpreted as a current density (remember that this experiment used the 'raw current' output). However, since the goal of this experiment was to make comparisons between experimental conditions, rather than absolute statements about the magnitudes of current flow, this was not a critical obstacle.

Although the timecourse data output from MNE retained its sign (i.e. positive or negative) in the interest of preserving this information for future use, the absolute value was taken prior to creating each regional average timecourse. This decision was made because this experiment was deemed to be interested only in the absolute activation of each region – not in the direction of the cortical currents. In this way the analysis presented here might be considered to be, 'fMRI style'.

Due to the noisy nature of MEG data, the average regional timecourses were themselves low-pass filtered with a cutoff frequency of 25 Hz. Although such filtering at the epoch level creates artifacts within the data, as described previously, it was felt that such artifacts, occurring at the ends of the timecourses where the filter window is no longer completely filled with data, were comfortably separated from the time windows of analysis in this work (i.e. the timecourses themselves extended from 0 to 250ms, while the analysis of interest occurred between 100 and 200ms). Additionally, since this filtering was done in the very last stages of data analysis, the error introduced did not have the same opportunity to be magnified by subsequent steps as might have been the case with filtering done early in the process. The benefit of such filtering is that it became much easier to identify the relevant peaks of interest in the timecourses and thus the analysis became more reliable.
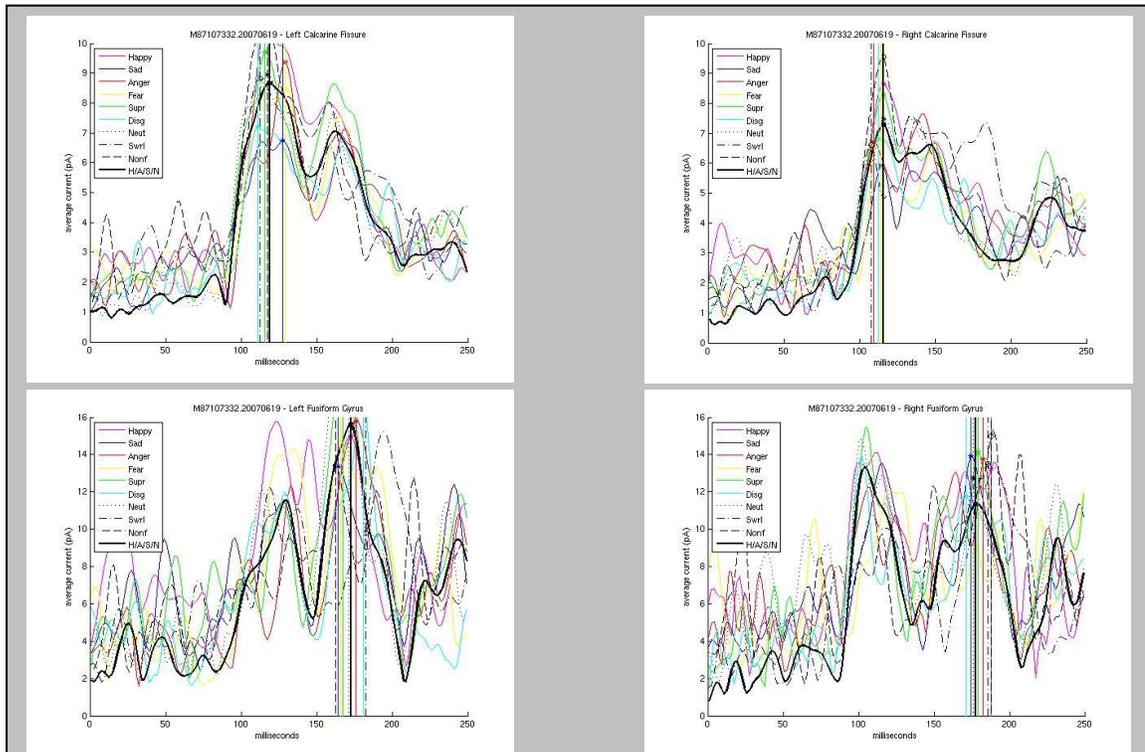
Figure 10: Timecourse data associated with the bilateral calcarine fissure and fusiform gyrus for the subject seen in Figures 7 through 9. Left and right calcarine responses are show in the upper left and right frames respectively. Fusiform regions are below. Responses for all nine experimental conditions are shown in different colors and line styles. The heavy black line represents the averaged response across the happiness, anger, surprised, and neutral conditions and, due to its relatively low noise level, is used as an aid in understanding the overall responses. The peaks that have been chosen by the automated process are demarcated by vertical lines.
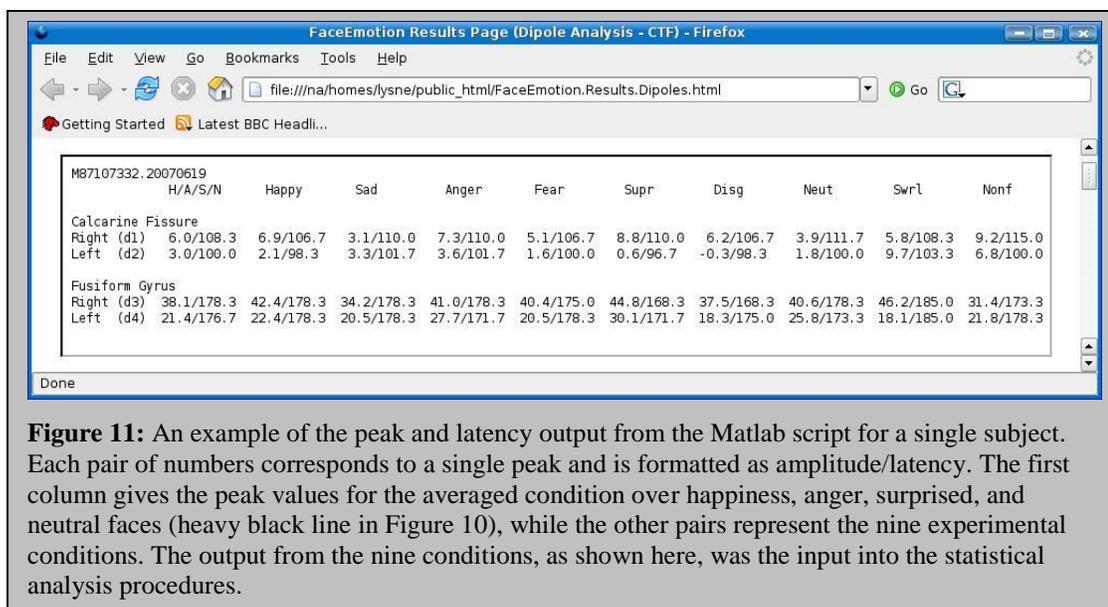
Figure 11: An example of the peak and latency output from the Matlab script for a single subject. Each pair of numbers corresponds to a single peak and is formatted as amplitude/latency. The first column gives the peak values for the averaged condition over happiness, anger, surprised, and neutral faces (heavy black line in Figure 10), while the other pairs represent the nine experimental conditions. The output from the nine conditions, as shown here, was the input into the statistical analysis procedures.

The same Matlab script which is used to create average timecourses for each region and condition also performs the function, with user input, of selecting peaks of interest within these timecourses. For each timecourse the user manually selected a window of interest within which a peak was automatically selected. The selection of timecourse peaks, however, is one of the most frustrating aspects of MEG data analysis. While approximately half of the subjects in this experiment displayed a prototypical visual response followed by a prototypical fusiform response, the other half varied widely. Personal experience with MEG analysis suggests that, while macro-scale cortical organization and responses are relatively predictable between subjects, micro-scale responses are not. For example, while all subjects in this work displayed at the macro scale the 'forward sweep' of activation described by Adolphs (2002a, 2002b) to follow the presentation of a facial stimulus, the timing and pattern of that activation was seen to vary. Individual differences are often significant at levels of analysis such as that of this work. In identifying the timecourse peaks in this experiment it was attempted to follow a set of general rules as closely as possible (note that all latencies reported in this work include the 20 millisecond visual stimulus delay measured for the MRN MEG setup.):

1. The calcarine fissure was expected to display a prominent peak within the window of 90 to 130ms after onset of visual stimulus.
2. The fusiform gyrus was expected to display a prominent peak within the

window of 140 to 180ms after onset of a facial stimulus.

3. Within a hemisphere the response of the calcarine fissure should precede that of the fusiform gyrus by at least 20ms.

4. The timing of the responses of the two hemispheres within a single subject should be similar.

5. When a peak could be identified within the designated time window, it was selected to the exclusion of other non-peaking segments of the timecourse within the window even if of greater amplitude (i.e. when the timecourse continued to increase, exceeding the amplitude of the peak, but did not form a peak at this level within the window).

6. When a peak could not be identified within the designated time window, the portion of the timecourse having the smallest (absolute value) slope was used.

7. When the timecourse increased or decreased uniformly throughout the window of interest, possessing neither a peak nor a segment of relatively small absolute slope, the window was scored manually according to the judgment of the investigator. Of greater than 1,000 peaks identified according to these rules, less than ten required manual intervention. When manual scoring was required it was done according to the trend that seemed to be suggested by the data, but also with the understanding that if an ambiguous data point were manually scored in an extreme fashion it might cast doubt upon the final results of this work.

When these rules were applied across the body of subjects, it was found that some subjects displayed a relatively early visual peak (~90-110ms), some a relatively late visual peak (~110-130ms), and some that could be interpreted as responding with both an early and a late peak. This ambiguity was resolved with a decision to choose the earlier peak in all cases. This decision was made in hopes of capturing the first, primary response of the calcarine fissure, and the results of this work may have changed if a different decision had been made.
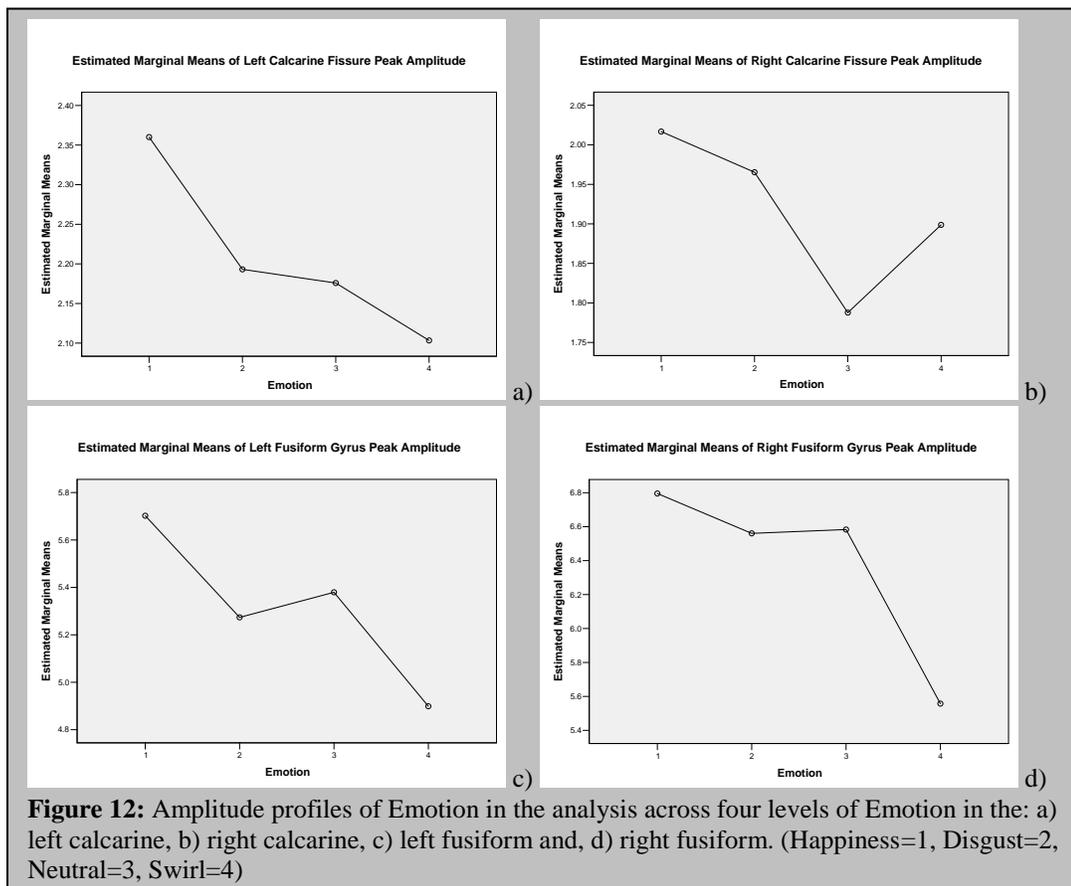
Further complicating the selection of timecourse peaks, while the responses to facial stimuli were relatively predictable, displaying calcarine and fusiform peaks roughly

corresponding to the rules described above, the non-face stimulus did not always evoke a response that could be easily interpreted. Some subjects responded to non-face stimuli in a way analogous to that of faces, while in others it was difficult to find similarities between facial and non-facial responses. In retrospect, this was predictable. The fusiform gyrus was anticipated to respond selectively to faces, begging the question of what a non-face fusiform response would look like. As stated previously, in some subjects this response was similar enough to a facial response that it could usefully be interpreted according to the same rules, while in others it could not.

In all, peaks were selected for 828 timecourses in this experiment, representing 23 subjects, four cortical regions, and nine experimental conditions. Each identified peak contributed both an amplitude and a latency value to the statistical analysis procedures described next. At this stage in the experiment it was felt that the fusiform gyrus data was quite good, while data from the calcarine fissure was somewhat uncertain.

Statistical Analysis

Statistical analysis of the data generated in this experiment was performed according to two separate designs. The first design was intended to focus specifically on the profiles of emotional responses in the bilateral calcarine fissure and fusiform gyrus. This was intended to address *Specific Aims 1 and 2, Hypotheses 1 through 4*. It was preplanned that the profile of results across the Emotion factor of the design would be interpreted separately in each region regardless of the significance of the simple main effect of Emotion in that region (i.e. regardless of the significance of the relevant omnibus test). Although it would have been possible to analyze the data from each region completely independently of the others (i.e. separate one-way ANOVAs), the advantage of a pooled variance estimate across the regions led to a larger statistical design where data from all four regions were loaded at once. Within this design Hemisphere (left/right), Region (calcarine fissure/fusiform gyrus), and Gender were treated as between-subjects factors, and Age was used as a covariate. It was preplanned to conduct all pairwise comparisons between levels of Emotion in each profile, and an appropriate

Figure 12: Amplitude profiles of Emotion in the analysis across four levels of Emotion in the: a) left calcarine, b) right calcarine, c) left fusiform and, d) right fusiform. (Happiness=1, Disgust=2, Neutral=3, Swirl=4)

Left Calcarine Fissure Peak Amplitude					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff.** **(1-2, nA/v)**	**Lower Bound** **(nA/vertex)**	**Upper Bound** **(nA/vertex)**
Happiness (1)	Neutral (3)	.048	.184	.001	.367
Happiness (1)	Swirl (4)	.012	.257	.046	.468

Right Calcarine Fissure Peak Amplitude					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff.** **(1-2, nA/v)**	**Lower Bound** **(nA/vertex)**	**Upper Bound** **(nA/vertex)**
Happiness (1)	Neutral (3)	.005	.229	.057	.401

Table 1: Significant pairwise comparisons between amplitude responses in the analysis across four levels of Emotion. The confidence interval was 95%. A Bonferroni correction for all possible comparisons was applied to the results (c=6).

Bonferroni correction was used in all cases. These will be referred to as "profile" analyses.

The second design, which will be referred to as "exploratory" analyses, was intended to investigate differential responses of the calcarine fissure and fusiform gyrus in a broad context which allowed for effects according to gender and age, hemisphere and region. This design was intended to address the questions raised by *Specific Aim 3*. It was originally intended that the statistical design used in the profile analyses described above would be able to satisfy this goal, but it quickly became apparent that the covariate Age significantly interacted with several of the other factors. Since it was difficult to interpret the interaction of a covariate with other factors in the design it was decided that Age would be blocked into a factor called "Youth". Subjects were divided according to their ages at the mean age level of 29 years, and the resulting "Youth" factor had two levels, with subjects below 29 years of age being placed in the first group and those greater than or equal to 29 years of age placed in the second. Creation of the between-subjects Youth factor made it possible to interpret the interaction between subjects' age and the other factors in the design in ways that were more easily understood. The number of subjects in each group of the Youth factor was unequal as was the age range covered by each group (younger group: 15 subjects, 7 male, 8 female, mean age 24.7, minimum age 22, maximum age 28, std. dev. 1.5; older group: 8 subjects, 3 male, 5 female, mean age 39.1, minimum age 33, maximum age 48, std. dev. 4.8), but this was secondary to the small

sample size and future research will be needed for a more comprehensive investigation of the effect of age. Youth, Hemisphere, Region, and Gender were used as between-subjects factors, and the levels of Emotion were treated as a within-subjects factor. No covariate was used for the exploratory analyses.

  Finally, the data itself suggested that several post-hoc comparisons be performed on the profiles of peak amplitude and latency. Particularly, the peak amplitude and latency responses to the six facial conditions containing an emotional expression (happiness, sadness, anger, fear, surprise, and disgust) were averaged into a single pair of variables in order to represent emotional faces in a general sense. The two non-facial conditions (swirled faces and non-face artwork) were averaged in the same way. This allowed contrasts to be run on peak amplitude and latency such that emotional faces, neutral faces, and non-facial conditions could be compared directly. These contrasts were only run in the manner of the profile analyses described above, with Region, Gender, and Hemisphere treated as between-subjects factors and Age as a covariate. Only the contrasts between the three levels of facial conditions described here were interpreted, and effects of and interactions with the between-subjects factors were ignored. Within these contrasts it was planned that all possible comparisons would be performed.

Figure 13: Latency profiles of Emotion in the analysis across four levels of Emotion in the: a) left calcarine, b) right calcarine, c) left fusiform, and d) right fusiform. (Happiness=1, Disgust=2, Neutral=3, Swirl=4)
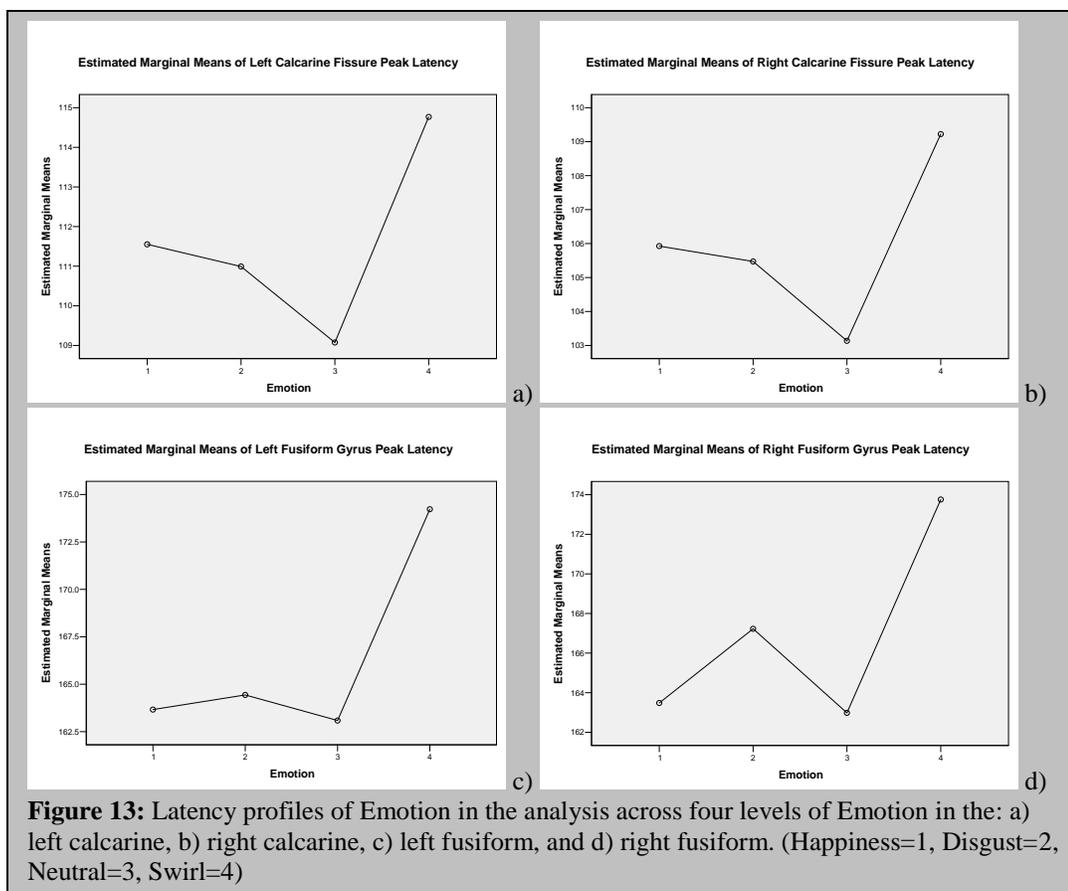
Since *Specific Aim 1* of this work was to attempt a replication of the previous results of Lewis et al (2003), ANOVA as described above were performed using the subset of emotional conditions, Happiness, Disgust, Neutral, and Swirled Face, as had been done by the previous authors. *Specific Aim 2* was meant to extend Lewis et al by expanding the group of emotional conditions to the nine described above in the Methods section. Separate ANOVA were performed on both sets of emotional conditions. Peak amplitude and peak latency were analyzed separately in both cases. The post-hoc analyses were only run on the full nine emotional conditions. To summarize, ten separate ANOVA were interpreted in the Results. Four profile analyses were performed; one for each of peak amplitude and peak latency, and separate analyses of each were conducted for the Lewis et al. subset of emotional conditions (4) as well as the extended set of emotional conditions developed for this experiment (9). The profile analyses used a mixed-model design with between-subjects factors Hemisphere, Region, and Gender, within-subjects factor Emotion, and covariate Age. Profiles of amplitude and latency

were interpreted across the Emotion factor in each region, but other effects were not.
Four exploratory analyses were performed in order to interpret the effects of Hemisphere,
Region, and Gender along with their interaction with the blocked age factor of Youth.
Once again, separate analyses were conducted for peak amplitude and latency, and for the
subset and full set of levels of Emotion. In these models Hemisphere, Region, Gender,
and Youth were between-subjects factors and Emotion was a within-subjects factors.
There was no covariate in the exploratory ANOVAs. Finally, two post-hoc analyses were
performed in a manner similar to the profile analyses previously described, but with the
emotional face conditions combined and the non-facial conditions combined.

All analyses were performed using the General Linear Model included with the
SPSS software (Version 13.0, GLM command).

Right Calcarine Fissure Peak Latency					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff. (1-2, ms)**	**Lower Bound (milliseconds)**	**Upper Bound (milliseconds)**
Swirl (4)	Neutral (3)	.042	6.088	.149	12.027

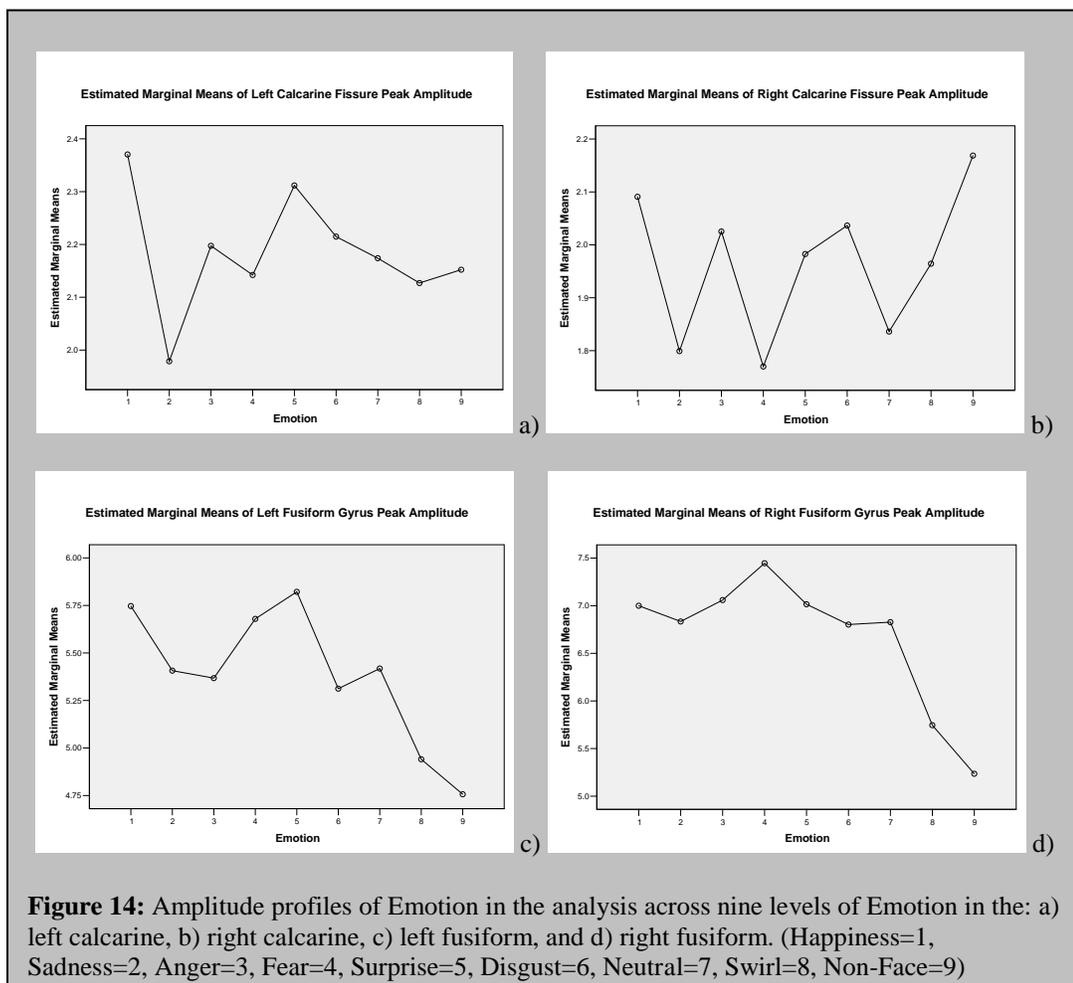| **Left Fusiform Gyrus Peak Latency**					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff. (1-2, ms)**	**Lower Bound (milliseconds)**	**Upper Bound (milliseconds)**
Swirl (4)	Happiness (1)	.005	10.561	2.675	18.447
Swirl (4)	Disgust (3)	.013	9.789	1.696	17.882
Swirl (4)	Neutral (4)	.003	11.173	3.421	18.852

Right Fusiform Gyrus Peak Latency					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff. (1-2, ms)**	**Lower Bound (milliseconds)**	**Upper Bound (milliseconds)**
Swirl (4)	Happiness (1)	.000	10.276	5.285	15.267
Swirl (4)	Disgust (2)	.008	6.529	1.389	11.668
Swirl (4)	Neutral (3)	.000	10.773	4.610	16.937
Disgust (2)	Happiness (1)	.044	3.747	.074	7.420
Disgust (2)	Neutral (3)	.003	4.245	1.279	7.210

Table 2: Significant pairwise comparisons between latency responses in the analysis across four levels of Emotion. The confidence interval was 95%. A Bonferroni correction for all possible comparisons was applied to the results (c=6).

Chapter 3: Results

Profile Analysis of Peak Amplitude with Four Levels of Emotion (Specific Aim 1: Hypotheses 1 and 2)

 The profile analysis of peak amplitude across four levels of Emotion revealed that the simple main effect of Emotion was significant in the left calcarine (F(3,17)=7.003, p=.003, partial eta sq=.553), right calcarine (F(3,17)=3.301, p=.046, partial eta sq=.368), and left fusiform (F(3,17)=6.558, p=.004, partial eta sq=.536). Significant pairwise comparisons are show in Table 1. A Bonferroni correction for all possible comparisons was applied to these results (c=6). The amplitude profiles discussed in this section are shown in Figure 12.

Figure 14: Amplitude profiles of Emotion in the analysis across nine levels of Emotion in the: a) left calcarine, b) right calcarine, c) left fusiform, and d) right fusiform. (Happiness=1, Sadness=2, Anger=3, Fear=4, Surprise=5, Disgust=6, Neutral=7, Swirl=8, Non-Face=9)

Profile Analysis of Peak Latency with Four Levels of Emotion (Specific Aim 1: Hypothesis 1 and 2)

In the profile analysis of peak latency across four levels of Emotion, the simple main effect of Emotion approached significance in the right calcarine ($F_{(3,17)}=2.961$, $p=.062$, partial eta sq$=.343$) and was significant in the left ($F_{(3,17)}=5.609$, $p=.007$, partial eta sq$=.497$) and right fusiform ($F_{(3,17)}=11.935$, $p=.000$, partial eta sq$=.678$). Multiple pairwise comparisons were significant and are shown in Table 2. A Bonferroni correction for all possible pairwise comparisons was applied to these results (c=6). The latency profiles discussed in this section are seen in Figure 13.

Profile Analysis of Peak Amplitude with Nine Levels of Emotion (Specific Aim 2: Hypotheses 3 and 4)

In the profile analysis of peak amplitude across all nine levels of Emotion the simple main effect of Emotion approached significance in the left calcarine ($F_{(8,12)}=2.716$, $p=.058$, partial eta sq$=.644$) and achieved significance in the left

Left Calcarine Fissure Peak Amplitude					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff. (1-2, nA/v)**	**Lower Bound (nA/vertex)**	**Upper Bound (nA/vertex)**
Happiness (1)	Sadness (2)	.008	.389	.070	.708

Right Calcarine Fissure Peak Amplitude					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff. (1-2, nA/v)**	**Lower Bound (nA/vertex)**	**Upper Bound (nA/vertex)**
Happiness (1)	Neutral (7)	.033	.229	.011	.447

Left Fusiform Gyrus Peak Amplitude					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff. (1-2, nA/v)**	**Lower Bound (nA/vertex)**	**Upper Bound (nA/vertex)**
Surprise (5)	Disgust (6)	.008	.497	.087	.907

Right Fusiform Gyrus Peak Amplitude					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff. (1-2, nA/v)**	**Lower Bound (nA/vertex)**	**Upper Bound (nA/vertex)**
Fear (4)	Nonface (9)	.018	2.120	.229	4.010

Table 3: Significant pairwise comparisons between amplitude responses in the analysis across nine levels of Emotion. The confidence interval was 95%. A Bonferroni correction for all possible comparisons was applied to the results (c=36).
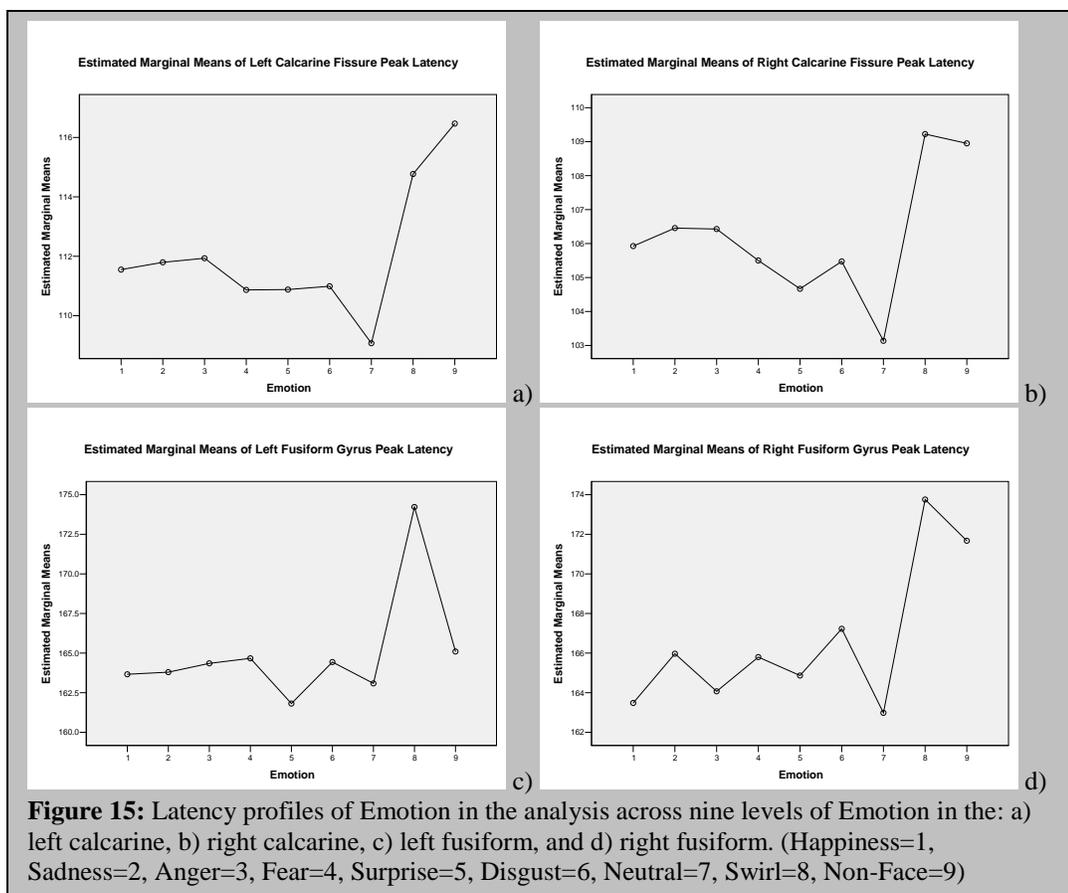
Figure 15: Latency profiles of Emotion in the analysis across nine levels of Emotion in the: a) left calcarine, b) right calcarine, c) left fusiform, and d) right fusiform. (Happiness=1, Sadness=2, Anger=3, Fear=4, Surprise=5, Disgust=6, Neutral=7, Swirl=8, Non-Face=9)

fusiform ($F(8,12)$=4.273, p=.012, partial eta sq=.740). Significant pairwise comparisons were found in all four regions and are shown in Table 3. A Bonferroni correction for all possible pairwise comparisons was applied to the results (c=36). The amplitude profiles discussed in this section are seen in Figure 14.

Profile Analysis of Peak Latency with Nine Levels of Emotion (Specific Aim 2: Hypothesis 3 and 4)

The profile analysis of peak latency across all nine levels of Emotion revealed that simple main effect of Emotion was nearly significant in the left fusiform ($F(8,12)$=2.771, p=.054, partial eta sq=.649) and was significant in the right fusiform ($F(8,12)$=4.858, p=.007, partial eta sq=.764). Significant pairwise comparisons existed in both the left and right fusiform and are seen in Table 4. A Bonferroni correction for all possible pairwise comparisons was applied to the results (c=36). The latency profiles discussed in this section are seen in Figure 15.

Exploratory Analysis of Peak Amplitude with Four Levels of Emotion (Specific Aim 3)

The exploratory analysis of peak amplitude with four levels of Emotion revealed main effects of Region (F(1,19)=51.632, p=.000, partial eta sq=.731) in which peak amplitude was greater for the fusiform gyrus than the calcarine fissure, Youth (F(1,19)=6.256, p=.022, partial eta sq=.248) in which individuals in the older group displayed greater amplitude than those in the younger group, and Gender (F(1,19)=7.279, p=0.14, partial eta sq=.277) in which females displayed greater amplitude than males. A main effect of Emotion was also present (F(3,17)=6.061, p=.005, partial eta sq=.517), and subsequent pairwise comparisons with a Bonferroni correction for all possible comparisons (c=6) showed that Happiness > Neutral (p=.004) and Happiness > Swirl (p=.025). These main effects are shown in Figure 16.

Amplitude analysis also revealed a two-way interaction between Region and Youth (F(1,19)=5.697, p=.028, partial eta sq=.231). The simple main effect of Region

Left Fusiform Gyrus Peak Latency					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff.** **(1-2, ms)**	**Lower Bound** **(milliseconds)**	**Upper Bound** **(milliseconds)**
Swirl (8)	Happiness (1)	.031	10.561	.544	20.578
Swirl (8)	Anger (3)	.020	9.874	.943	18.805
Swirl (8)	Surprise (5)	.015	12.409	1.547	23.270
Swirl (8)	Neutral (7)	.016	11.137	1.336	20.937
Swirl (8)	Nonface (9)	.004	9.123	2.142	16.104

Right Fusiform Gyrus Peak Latency					
Emotion 1	**Emotion 2**	**Sig. (p)**	**Mean Diff.** **(1-2, ms)**	**Lower Bound** **(milliseconds)**	**Upper Bound** **(milliseconds)**
Swirl (8)	Happiness (1)	.000	10.276	3.936	16.615
Swirl (8)	Sadness (2)	.013	7.787	1.075	14.499
Swirl (8)	Anger (3)	.000	9.686	3.851	15.521
Swirl (8)	Fear (4)	.041	7.958	.170	15.745
Swirl (8)	Surprise (5)	.036	8.890	.328	17.452
Swirl (8)	Disgust (6)	.050	6.629	.000	13.057
Swirl (8)	Neutral (7)	.002	10.773	2.994	18.603
Disgust (6)	Neutral (7)	.017	4.245	.477	8.012

Table 4: Significant pairwise comparisons between latency responses in the profile analysis across nine levels of Emotion. The confidence interval was 95%. A Bonferroni correction for all possible comparisons was applied to the results (c=36).

Figure 16: Significant main effects on amplitude in the analysis with four levels of Emotion; a) Region, b) Youth, c) Gender, and d) Emotion. (Region: Calcarine=1, Fusiform=2; Emotion: Happiness=1, Sadness=2, Anger=3, Fear=4, Surprise=5, Disgust=6, Neutral=7, Swirl=8, Nonface=9).
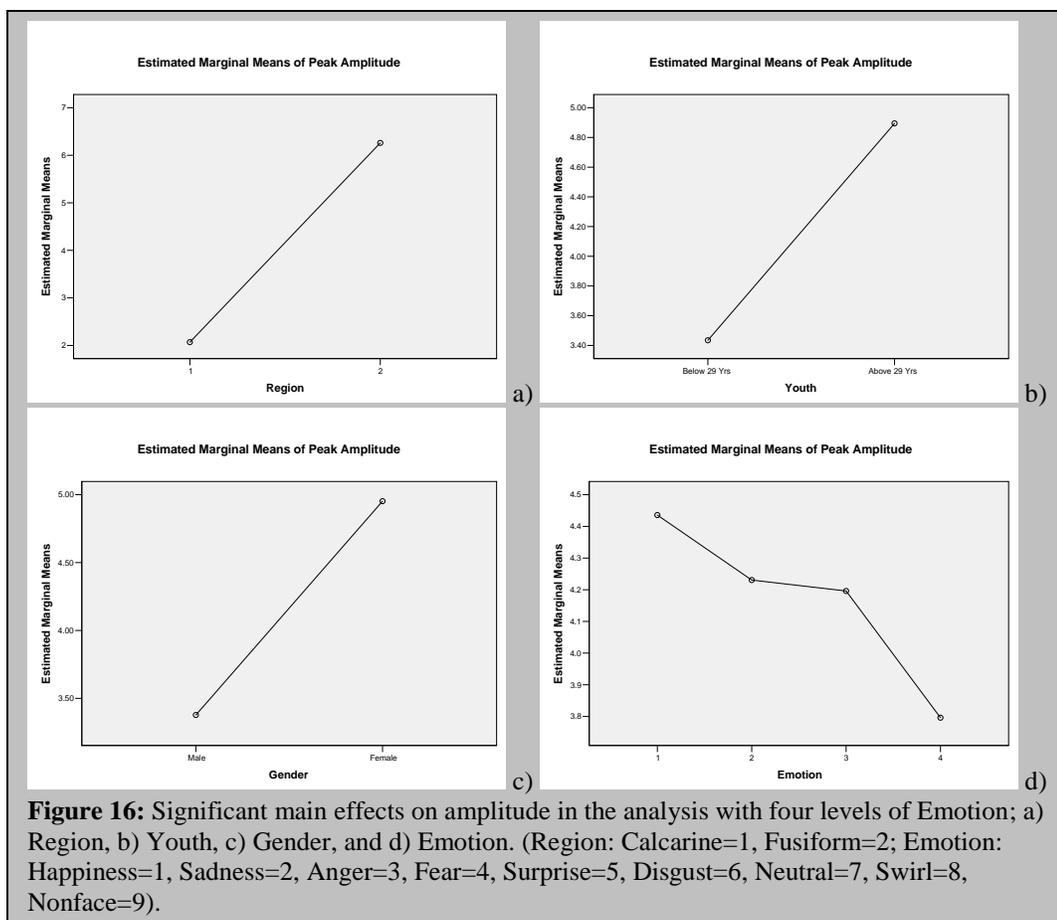
Two four-way interactions were also present in the amplitude analysis. The first, was the interaction of Emotion by Hemisphere by Region by Youth ($F(3,17)=5.431$, $p=.008$, partial eta sq=.489). In this interaction, the simple main effect of Youth was significant for all levels of Emotion in the left fusiform gyrus (Happiness: $p=.026$, Disgust: $p=.042$, Neutral: $p=.012$, Swirl: $p=.019$), with the older group always having greater amplitude. The simple main effect of Region was significant in all combinations of Emotion, Region, and Gender, with the fusiform always having greater amplitude (16 p values range from .000 to .042). The simple main effect of Hemisphere was significant in the calcarine fissure ($F(1,19)=5.612$, $p=.029$, partial eta sq=.228) of the younger group for the emotions Happiness ($p=.029$) and Neutral ($p=.011$), with left hemisphere amplitude being greater than right in both cases. The simple main effect of Emotion was significant in both the left and right calcarine for both Youth groups (left calcarine, younger group: $F(3,17)=3.808$, $p=.030$, partial eta sq=.402, left calcarine, older group: $F(3,17)=4.075$, $p=.024$, partial eta sq=.418, right calcarine, younger group:

F(3,17)=3.253, p=.048, partial eta sq=.365, right calcarine, older group: F(3,17)=3.346, p=.044, partial eta sq=.371). Of the pairwise comparisons, only the difference Happiness > Neutral (p=.024) in the right calcarine fissure for the younger group was significant. A Bonferroni correction for all possible comparisons was applied to these results (c=6) (Figure 18).

The second four-way interaction was that of Emotion by Hemisphere by Region by Gender (F(3,17)=4.283, p=.020, partial eta sq=.430). The simple main effect of Region was significant for all combinations of Emotion, Hemisphere, and Gender (16 p values range from .000 to .022), with fusiform amplitude being greater than calcarine in all cases. The simple main effect of Gender approached significance in the right calcarine fissure for the conditions Happiness (F(1,19)=4.345, p=.051, partial eta sq=.186) and Swirl (F(1,19)=4.052, p=.059, partial eta sq=.176), and was significant in the right fusiform gyrus for the conditions Disgust (F(1,19)=4.850, p=.040, partial eta sq=.203) and Neutral (F(1,19)=5.949, p=.025, partial eta sq=.238) with females displaying greater amplitude than males in all cases. The simple main effect of Emotion was significant in the left calcarine fissure for males (F(3,17)=4.282, p=.020, partial eta sq=.430) where the pairwise comparison Happiness > Swirl was significant (p=.030). The simple main effect of emotion was significant in the left calcarine fissure for females (F(3,17)=4.956, p=.012, partial eta sq=.467) where the pairwise comparison Happiness > Neutral was significant (p=.013). The simple main effect of emotion was significant in the left fusiform gyrus for females (F(3,17)=3.700, p=.032, partial eta sq=.395) although no

Figure 17: Significant interaction between Region and Youth on amplitude in analysis with four levels of Emotion. The axis and parameter variables are swapped between a) and b). (Region: Calcarine=1, Fusiform=2)

Figure 18: Significant four-way interaction between Emotion, Hemisphere, Region, and Youth on amplitude in analysis with four levels of Emotion. Emotion is on the x-axis of each plot, Hemisphere varies from left to right, and Region varies from top (Calcarine) to bottom (Fusiform). Within each frame plots are parameterized by Youth. (Hemisphere: Left=1, Right=2; Emotion: Happiness=1, Disgust=2, Neutral=3, Swirl=4)

pairwise comparisons survived the Bonferroni correction (c=6). The simple main effect of emotion was significant in the right fusiform gyrus in females (F(3,17)=10.479, p=.000, partial eta sq=.649) where the pairwise comparisons Happy > Neutral (p=.000) and Disgust > Neutral (p=.035) were significant (Figure 19).

Exploratory Analysis of Peak Latency with Four Levels of Emotion (Specific Aim 3)

The exploratory analysis of latency with four levels of Emotion revealed main effects of Region (F(1,19)=516.491, p=.000, partial eta sq=.965) where peak latency in the fusiform gyrus was greater than in the calcarine fissure, and Gender (F(1,19)=7.829, p=.011, partial eta sq=.292) where males showed greater peak latency than females. A main effect of Emotion was also present (F(3,17)=21.810, p=.000, partial eta sq=.794) which was driven by the significant pairwise comparisons of Swirl > Happiness (p=.000), Swirl > Disgust (p=.001), Swirl > Neutral (p=.000), and Disgust > Neutral (p=.028). A Bonferroni correction for all possible pairwise comparisons was applied to these results

(c=6). These main effects are seen graphically in Figure 20.

Two significant interactions were seen in the exploratory latency analysis with four levels of Emotion. The interaction of Emotion by Region (F(3,17)=3.891, p=.028, partial eta sq=.407) is seen in Figure 21. The simple main effect of Region was significant in all cases (Happiness: p=.000, Disgust: p=.000, Neutral: p=.000, Swirl: p=.000), with latency in the fusiform always being greater than the calcarine. The simple main effect of Emotion was significant in both the calcarine (F(3,17)=4.448, p=.018, partial eta sq=.440) and the fusiform (F(3,17)=16.270, p=.000, partial eta sq=.742). In the calcarine the pairwise comparison Swirl > Neutral was significant (p=.014). In the fusiform the comparisons Swirl > Happy (p=.000), Swirl > Disgust (p=.000), Swirl > Neutral (p=.000), and Disgust > Neutral (p=.007) were significant. A Bonferroni correction (c=6) was applied to all pairwise comparisons (Figure 21).

The second significant interaction, Emotion by Youth by Hemisphere

Figure 19: Significant four-way interaction between Emotion, Hemisphere, Region, and Gender on amplitude in analysis with four levels of Emotion. Emotion is on the x-axis of each plot, Hemisphere varies from left to right, and Region varies from top (Calcarine) to bottom (Fusiform). Within each frame plots are parameterized by Gender. (Hemisphere: Left=1, Right=2; Emotion: Happiness=1, Disgust=2, Neutral=3, Swirl=4)

(F(3,17)=4.452, p=.018, partial eta sq=.440) is seen in Figure 22. The simple main effect of Emotion was significant for all combinations of Hemisphere and Youth (16 p values range from .007 to .037). The simple main effect of Emotion in the left hemisphere for the younger age group (F(3,17)=5.328, p=.009, partial eta sq=.485) was driven by the significant pairwise comparisons Swirl > Happiness (p=.018), Swirl > Disgust (p=.008), and Swirl > Neutral (p=.005). The simple main effect of Emotion in the left hemisphere for the older age group was significant (F(3,17)=3.557, p=.037, partial eta sq=.386), but no pairwise comparisons were significant. The simple main effect of Emotion in the right hemisphere for the younger Youth group (F3,17)=5.607, p=.007, partial eta sq=.497), was driven by the significant pairwise comparisons Swirl > Happiness (p=.018), Swirl > Neutral (p=.005), and Disgust > Neutral (p=.037). The simple main effect of Emotion in the right hemisphere for the older age group (F(3,17)=4.227, p=.021, partial eta sq=.427), and was driven by the significant pairwise comparisons Swirl > Happiness (p=.037), Swirl > Disgust (p=.016), and Swirl > Neutral (p.=011). A Bonferroni correction for all possible comparisons was applied to these results (c=6) (Figure 22).
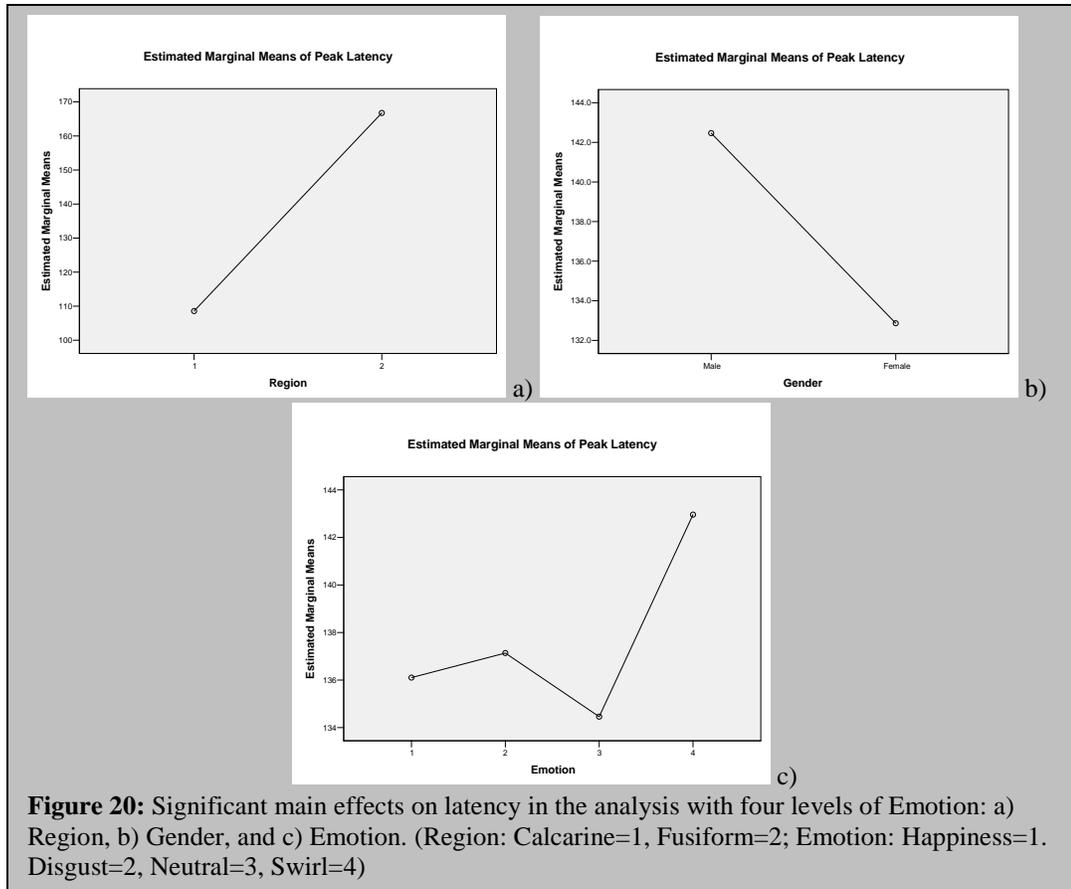
Figure 20: Significant main effects on latency in the analysis with four levels of Emotion: a) Region, b) Gender, and c) Emotion. (Region: Calcarine=1, Fusiform=2; Emotion: Happiness=1. Disgust=2, Neutral=3, Swirl=4)

Exploratory Analysis of Peak Amplitude with Nine Levels of Emotion (Specific Aim 3)

The exploratory analysis of peak amplitude with nine levels of Emotion revealed main effects of Region ($F_{(1,19)}$=52.642, p=.000, partial eta sq=.735), with amplitude in the fusiform being greater than that in the calcarine, Youth ($F_{(1,19)}$=5.576, p=.029, partial eta sq=.227), with the older age group having greater amplitude than the younger, and Gender ($F_{(1,19)}$=7.117, p=.015, partial eta sq=.273), with females having greater amplitude than males. The main effect of Emotion was nearly significant ($F_{(8,12)}$=2.838, p=.051, partial eta sq=.654) and was driven by the pairwise comparisons Happiness > Neutral (p=.027), Happiness > Nonface (p=.006), Anger > Nonface (.027), and Surprise > Nonface (.019). A Bonferroni correction for all possible comparisons was applied to these results (c=36). These main effects are shown in Figure 23.

Three interactions became significant during the exploratory amplitude analysis. The first interaction was between Region and Youth ($F_{(1,19)}$=5.377, p=.032, partial eta sq=.221). Within this interaction the simple mains effects of Region were significant for

Figure 21: Significant interaction of Emotion and Region on latency in ANOVA with four conditions of Emotion. (Region: Calcarine=1, Fusiform=2; Emotion: Happiness=1, Disgust=2, Neutral=3, Swirl=4). The axis and parameter variables are swapped between a) and b).
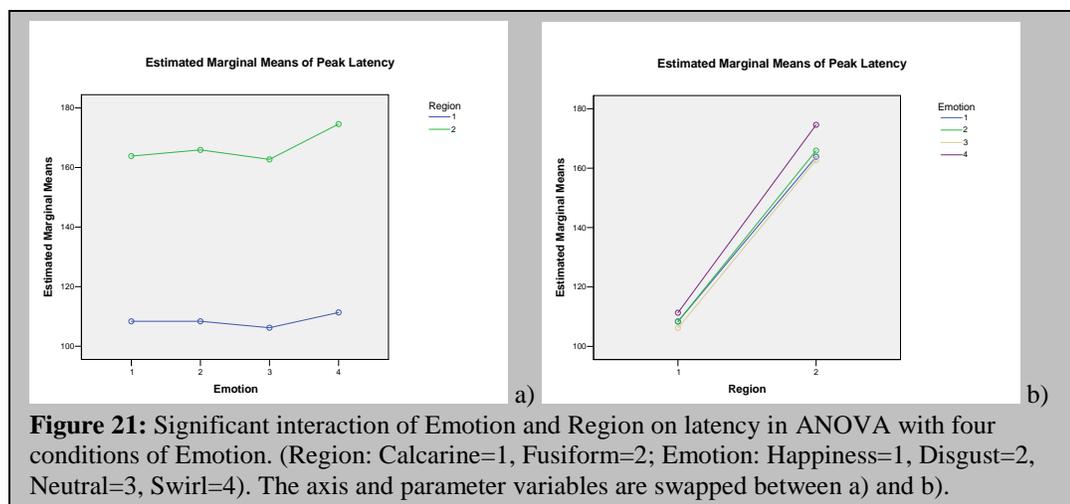
both age groups (younger: $F(1,19)=18.223$, $p=.000$, partial eta sq=.490; older $F(1,19)=34.426$, $p=.000$, partial eta sq=.644), with the older group having greater amplitude in both cases. The simple main effect of Youth was significant in the fusiform ($F(1,19)=6.189$, $p=.022$, partial eta sq=.246) with the older group showing greater amplitude than the younger, but not in the calcarine. The interaction between Region and Youth is shown in Figure 24.

The second interaction was between Emotion and Hemisphere ($F(8,12)=4.036$, $p=.015$, partial eta sq=.729). Within this interaction the simple main effect of Hemisphere was non-significant at all levels of Emotion. The simple main effect of Emotion was non-significant in the right hemisphere but was significant in the left ($F(8,12)=6.306$, $p=.002$, partial eta sq=.808). The significant simple main effect of Emotion in the left hemisphere was driven by the pairwise comparison Happiness > Nonface ($p=.039$). A Bonferroni correction for all pairwise comparisons was applied to this result (c=36). The interaction between Emotion and Hemisphere is shown in Figure 25.

The third interaction was Emotion by Hemisphere by Region by Youth ($F(8,12)=3.549$, $p=.024$, partial eta sq=.703). Within this interaction the simple main effect of Hemisphere was significant in the calcarine fissure of the younger age group for the conditions of Emotion, Happiness ($F(1,19)=5.612$, $p=.029$, partial eta sq=.228), Sadness ($F(1,19)=4.729$, $p=.043$, partial eta sq=.199), Fear ($F(1,19)=5.769$, $p=.027$, partial eta sq=.233), Surprise ($F(1,19)=5.980$, $p=.024$, partial eta sq=.239), and Neutral ($F(1,19)=7.857$, $p=.011$, partial eta sq=.293), with the left hemisphere having greater

amplitude than the right in all cases. The simple main effect of region was significant in all cases except in the left hemisphere of the younger age group for the Emotion condition of Surprise (p=.057), with the fusiform showing greater amplitude than the calcarine in all significant cases (35 p values range from .000 to .047). The simple main effect of Youth was significant in the left fusiform for Happiness (F(1,19)=5.814, p=.026, partial eta sq=.234), Anger (F(1,19)=6.140, p=.023, partial eta sq=.244), Surprise (F(1,19)=6.140, p=.023, partial eta sq=.244), Disgust (F(1,19)=4.759, p=.042, partial eta sq=.200), Neutral (F(1,19)=7.711, p=.012, partial eta sq=.289), Swirl (F(1,19)=6.591, p=.019, partial eta sq=.258), and Nonface (F(1,19)=5.157, p=.035, partial eta sq=.213), and nearly significant for Fear (F(1,19)=4.222, p=.054, partial eta sq=.182), with the older age group displaying greater amplitude in all cases. The simple main effect of Youth was also nearly significant in the right fusiform in the case of Anger (F(1,19)=4.321, p=.051, partial eta sq=.185). Finally, the simple main effect of Emotion was significant in the left fusiform for the older group (F(8,12)=4.149, p=.014, partial eta sq=.734), with the pairwise comparison Surprise > Disgust (p=.007). A Bonferroni correction for all possible comparisons was applied to this result (c=36). The four-way interaction between Emotion, Hemisphere, Region, and Youth is seen in Figure 26.

Exploratory Analysis of Peak Latency with Nine Levels of Emotion (Specific Aim 3)

The exploratory analysis of peak latency with nine all levels of emotion revealed significant main effects of Region (F(1,19)=555.364, p=.000, partial eta sq=.967), with

Figure 22: Significant three way interaction between Emotion, Youth, and Hemisphere on latency in analysis with four levels of Emotion in the a) younger group and, b) older group. (Hemisphere: Left=1, Right =2; Emotion: Happiness=1, Disgust=2, Neutral=3, Swirl=4)
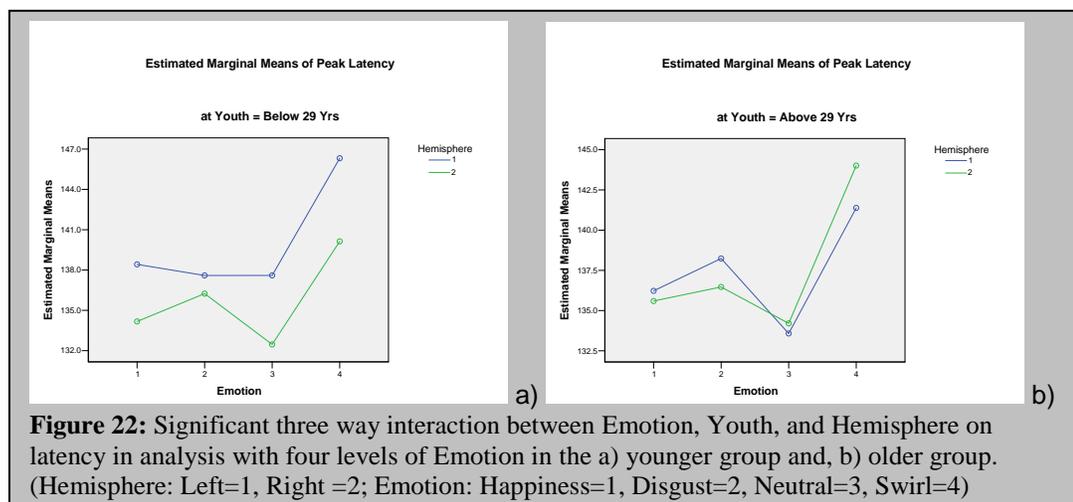
the fusiform showing greater latency than the calcarine, and Gender (F(1,19)=7.681, p=.012, partial eta sq=.288), with males displaying greater latency than females. A significant main effect Emotion was also present (F(8,12)=7.304, p=.001, partial eta sq=.830), which was driven by significant pairwise comparisons in which the Swirl condition required greater latency than all other conditions except the Nonface condition (Happiness: p=.002, Sadness: p=.000, Anger: p=.001, Fear: p=.001, Surprise: p=.001, Disgust: p=.006, Neutral: p=.000). A Bonferroni correction for all possible comparisons was applied to these results (c=36). These main effects are shown in Figure 27.Two significant interactions were present. The first was Emotion by Region (F(8,12)=4.400, p=.011, partial eta sq=.746). Within this interaction the simple main effect of Region was significant at all levels of Emotion (p=.000 in call cases), with the fusiform always displaying greater latency than the calcarine. The simple main effect of Emotion was significant in the fusiform (F(8,12)=5.738, p=.004, partial eta sq=.793), but not the calcarine. Within the fusiform this effect was driven by the pairwise comparisons in which Swirl required greater latency than all other conditions except Nonface (Happiness: p=.000, Sadness: p=.001, Anger: p=.000, Fear: p=.002, Surprise: p=.000, Disgust: p=.001, Neutral: p=.000) , and the comparison of Disgust > Neutral (=.044). A Bonferroni correction for all possible comparisons was applied to these results (c=36). The interaction of Emotion with Region is seen in Figure 28.

The second significant interaction was between Emotion, Region, and Youth ($F_{(8,12)}$=3.111, p=.038, partial eta sq=.675). Within this interaction, the simple main effect of Region was significant in all combinations of Emotion and Youth (p=.000 in all cases), with the fusiform always displaying greater latency than the calcarine. The simple main effect of Emotion was significant in the fusiform for both the younger ($F_{(8,12)}$=3.235, p=.033, partial eta sq=.683) and older ($F_{(8,12)}$=3.982, p=.016, partial eta sq=.726) age groups. In the younger group this effect was driven by the pairwise comparisons of the Emotion conditions Happy (p=.002), Anger (p=.002), Fear (p=.022), Surprise (p=.005), Disgust (p=.035), and Neutral (p=.005) having shorter latencies than the Swirl condition. The comparison Sad < Swirl was nearly significant as well (p=.056). In the older age group the pairwise comparisons between Happy (p=.015), Sad (p=.032), Anger (p=.011), Surprise (p=.038), Disgust (p=.038), and Neutral (p=.001) all showed shorter latencies than the Swirl condition. Additionally, the simple main effect of

Figure 23: Significant main effects on amplitude in analysis with nine levels of Emotion, a) Region, b) Youth, c) Gender, and d) Emotion. (Region: Calcarine=1, Fusiform=2; Emotion: Happiness=1, Sadness=2, Anger=3, Fear=4, Surprise=5, Disgust=6, Neutral=7, Swirl=8, Nonface=9)
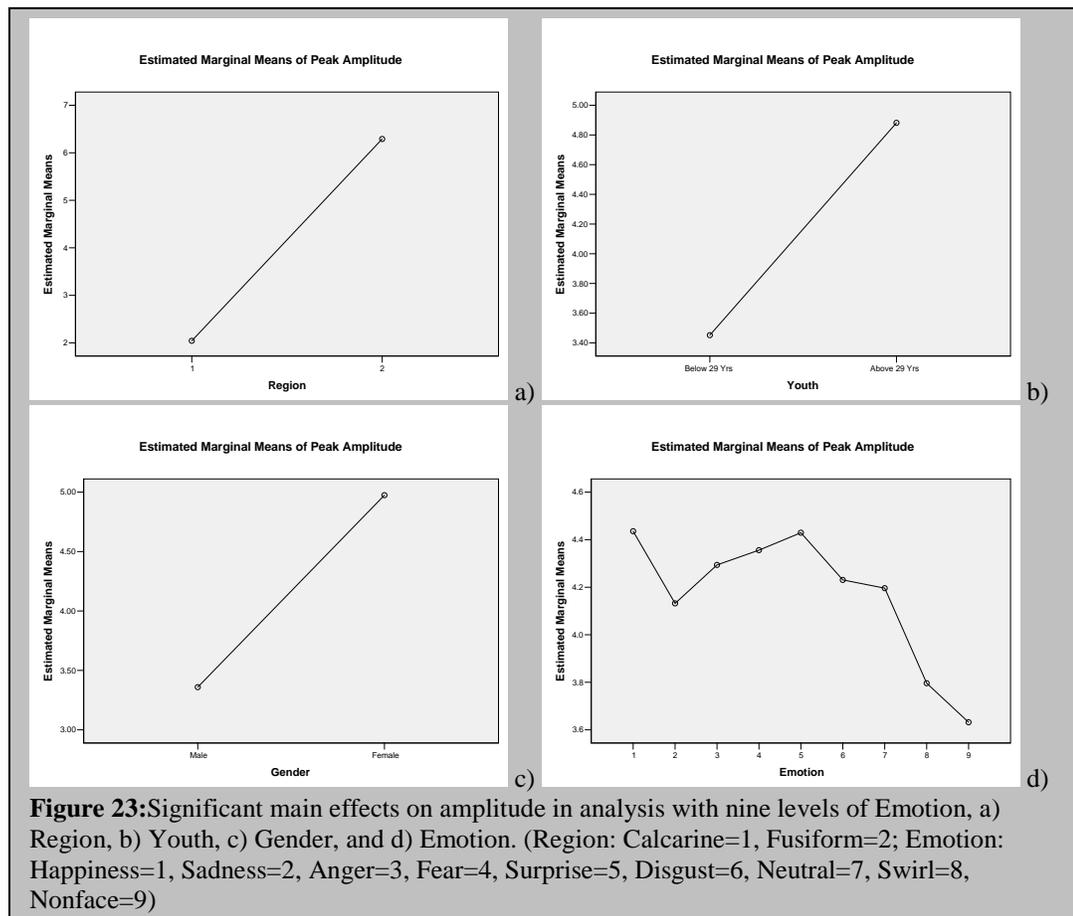
Emotion was nearly significant in the calcarine for the younger age group (F(8,12)=2.745, p=.056, partial eta sq=.647), which was driven by the significant pairwise comparison of Neutral < Swirl (p=.015). A Bonferroni correction for all pairwise comparisons was applied to these results. (c=36). The interaction of Emotion with Region and Youth is seen in Figure 29.

Post-Hoc Analysis of Peak Amplitude

The simple main effect of the contrast on peak amplitude was significant in the right fusiform (F(2,18)=5.823, p=.011, partial eta sq=.393). Also in the right fusiform, the averaged emotional face condition elicited greater amplitude than did neutral faces (p=.014), and neutral faces resulted in greater amplitude than did the averaged non-facial condition (p=.040). A Bonferroni correction for three comparisons was applied to these results. These effects are shown in Figure 30.

Post-Hoc Analysis of Peak Latency

The simple main effect of the contrast on peak latency was significant in the left calcarine (F(2,18)=5.136, p=.017, partial eta sq=.363), the right calcarine (F(2,18)=4.365, p=.028, partial eta sq=.327), the left fusiform (F(2,18)=4.016, p=.036, partial eta sq=.309), and the right fusiform (F(2,18)=13.260, p=.000, partial eta sq=.596). The comparison between neutral faces and the averaged non-face conditions was significant in the bilateral calcarine fissure and bilateral fusiform gyrus, with non-faces requiring greater latency than neutral faces in all locations (left calcarine: p=0.13, right calcarine: p=0.31, left fusiform: p=0.31, right fusiform: p=.000) In the right fusiform the averaged emotional face condition required greater latency than the neutral face condition as well (p=.033), and the averaged non-face condition required greater latency than the averaged emotional face condition (p=.000). A Bonferroni correction for three comparisons was applied to these results. These effects are shown in Figure 31.

Figure 24: Significant interaction of Youth with Region on amplitude in analysis with nine levels of Emotion. (Region: Calcarine=1, .Fusiform=2) Axis and parameter variables are swapped between a) and b).
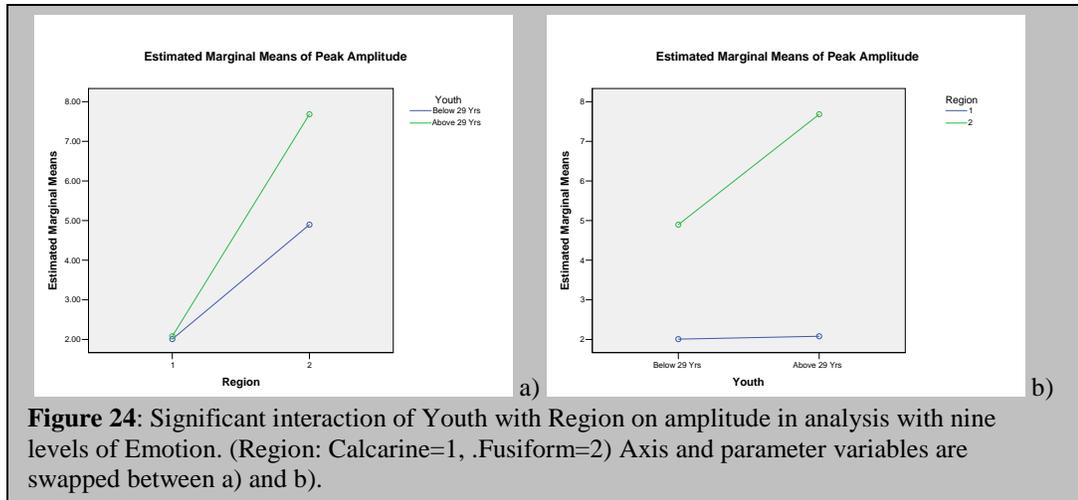
Chapter 4: Discussion

Specific Aims and Hypotheses

specific aim 1, hypothesis 1.

Despite being an attempt to prove a negative result, Hypothesis 1, pertaining to an expected lack of facial emotion-related differences in primary visual processing in the calcarine fissure, was retained in this analysis in order to provide contrast with the anticipated positive results related to Hypothesis 2 in the fusiform gyrus. It was not expected that any emotion-related effects, or even effects related to the presence or absence of a face in the stimulus would be found in this area. Results here indicate that Hypothesis 1 has been falsified, and that such differences do indeed exist in the primary visual processing region. Significant differences were found in both amplitude and latency. Analysis of the four-emotion amplitude profiles indicated that the happiness condition displayed significantly greater amplitude than the neutral condition in the bilateral calcarine fissure, and significantly greater amplitude than the swirled face condition in the left calcarine (Figure 12, Table 1). The four-emotion latency profiles showed a significantly greater latency for the swirled face condition than the neutral face condition in the right calcarine fissure (Figure 13, Table 2).

specific aim 1, hypothesis 2.

Building on the work of Lewis et al (2003), Hypothesis 2 anticipated the finding of significant facial emotion-related differences in the amplitude but not latency activations of the fusiform gyrus. It was expected that the previous finding that the amplitudes related to happy, disgusted, and neutral faces in the right fusiform would be ordered as: happiness > disgust > neutral. The four-emotion profile analysis of amplitude indicated that the amplitude-related portion of Hypotheses 2 had been falsified insofar that no significant amplitude differences were found in the bilateral fusiform gyrus (Figure 12, Table 1). The four-emotion profile analysis of latency revealed that the latency-related portion of Hypothesis 2 was also falsified in that significant differences in stimulus-related latencies were found in the bilateral fusiform (Figure 13, Table 2). Particularly, the swirled face condition demonstrated significantly longer latencies than the other three conditions in both hemispheres and, in the right fusiform, disgusted faces

showed longer latencies than happy and neutral faces.

specific aim 2, hypothesis 3.

Hypothesis 3, was again an attempt to verify a negative result in the calcarine fissure by extending the expected lack of findings in Hypothesis 1 to the entire stimulus set. The nine-emotion profile analysis of amplitude partially falsified Hypothesis 3 by again revealing stimulus-related differences in activation of the bilateral calcarine fissure (Figure 14, Table 3). Particularly, happy faces were seen to elicit greater peak amplitude than sad faces in the left calcarine, and happy faces again resulted in greater amplitude than neutral faces in the right calcarine. The nine-emotion profile analysis of latency upheld the latency-related portion of Hypothesis 3 by showing no significant stimulus-related differences (Figure 15, Table 4).

specific aim 2, hypothesis 4.

Hypothesis 4 represented the most ambitious portion of this work, hoping to demonstrate significantly different patterns of activation in the bilateral fusiform gyrus depending on the emotional content of the stimulus faces. As opposed to Hypothesis 2 which, in an attempt to replicate the previous findings of Lewis and colleagues (2003) predicted differences in amplitude but not latency, Hypothesis 4 predicted that differences would be found in both. Again it was hoped that the right fusiform amplitude ordering of happiness > disgust > neutral would be maintained and perhaps extended

Figure 25: Significant interaction of Emotion with Hemisphere on amplitude in analysis with nine levels of Emotion. (Happiness=1, Sadness=2, Anger=3, Fear=4, Surprise=5, Disgust=6, Neutral=7, Swirl=8, Nonface=9; Left=1, Right=2) The axis and parameter variables are swapped between a) and b).
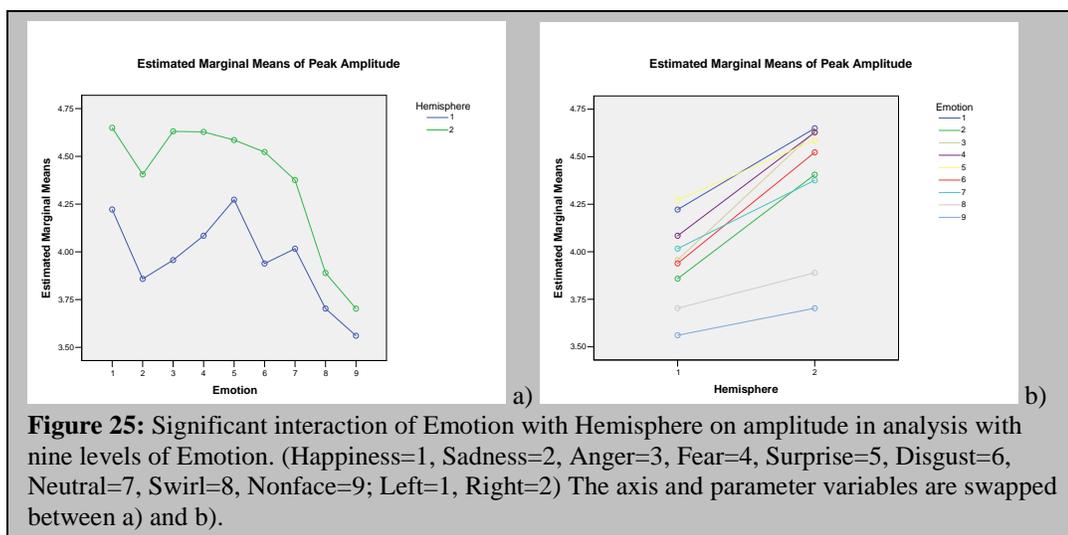
across the broadened range of emotional conditions employed here. The nine-level profile analysis of amplitude supported the amplitude-related portions of Hypothesis 4 by revealing limited but significant emotion-related differences (Figure 14, Table 3). In the left fusiform happy faces elicited greater amplitude than disgusted faces and, in the right fusiform, fearful faces resulted in greater amplitude than the non-face condition. The left fusiform finding of happiness > disgust, despite being in the left as opposed to right hemisphere, is the only significant support for the happiness > disgust > neutral fusiform amplitude hypothesis found in this work. The nine-level profile analysis of latency supported the latency-related portions of Hypothesis 4 by again demonstrating significantly longer latencies in the bilateral fusiform for the swirled face condition compared to most if not all of the other stimulus conditions. Greater latency was also seen in the right fusiform for disgusted versus neutral faces (Figure 15, Table 4).

discussion of specific aims 1-2, hypotheses 1-4.

As a group the results pertaining to Specific Aims 1 and 2, Hypotheses 1 through 4 have several implications. Prior to undertaking this work, it was expected that there would be no emotion-related differences in the response of the calcarine fissure. Several investigators have shown that the calcarine does respond differentially to some set of properties in facial and other visual stimulus, but what those properties are remains unclear (presence or absence of a face, presence of emotion and perhaps intensity of facial expression, positivity of expression, presence of face- or emotion-suggestive cues, simple visual complexity). In the current data there is significant indication that the amplitude of the calcarine response is greater to happy versus neutral faces, as is seen bilaterally in the four-level analysis (Figure 12 plots a and b, Table 1) and in the right hemisphere of the nine-level analysis (Figure 14 plot b, Table 3). Additionally, in the

Figure 26: Significant four-way interaction between Emotion, Hemisphere, Region, and Youth on amplitude in analysis with nine levels of Emotion. Emotion is on the x-axis of each plot, Hemisphere varies from left to right, and Region varies from top (Calcarine) to bottom (Fusiform). Within each frame plots are parameterized by Youth. (Hemisphere: Left=1, Right=2; Emotion: Happiness=1, Sadness=2, Anger=3, Fear=4, Surprise=5, Disgust=6, Neutral=7, Swirl=8, Nonface=9)

four-level analysis, the left calcarine is seen to respond with significantly greater amplitude to happy versus swirled faces (Figure 12 plot a, Table 1), and in the nine-level analysis the right calcarine displayed greater amplitude response to happy versus sad faces (Figure 14 plot b, Table 3). Although only a few pairwise comparisons significantly show greater calcarine amplitude for happy verses other emotional faces (sadness, neutral, and swirl), the profile plots of amplitude suggest that the response to happy faces is greater than nearly all other conditions (except non-faces in the right hemisphere of the nine-level analysis, Figure 14, plot b). This is not true for all emotions, and sadness falls below the mean amplitude of neutral faces bilaterally in the nine-level analysis as does fear in the right hemisphere (Figure 14 plots a and b, non-significant comparisons). With regard to the amplitude of calcarine response, this combination of results appears to support the positivity hypothesis, by which the calcarine fissure responds preferentially to cues of positive affect and which was seen in the results of Bayle et al. (2007) and suggested in those of Batty and Taylor (2003). The emotion/intensity hypothesis, which suggests that the presence of any 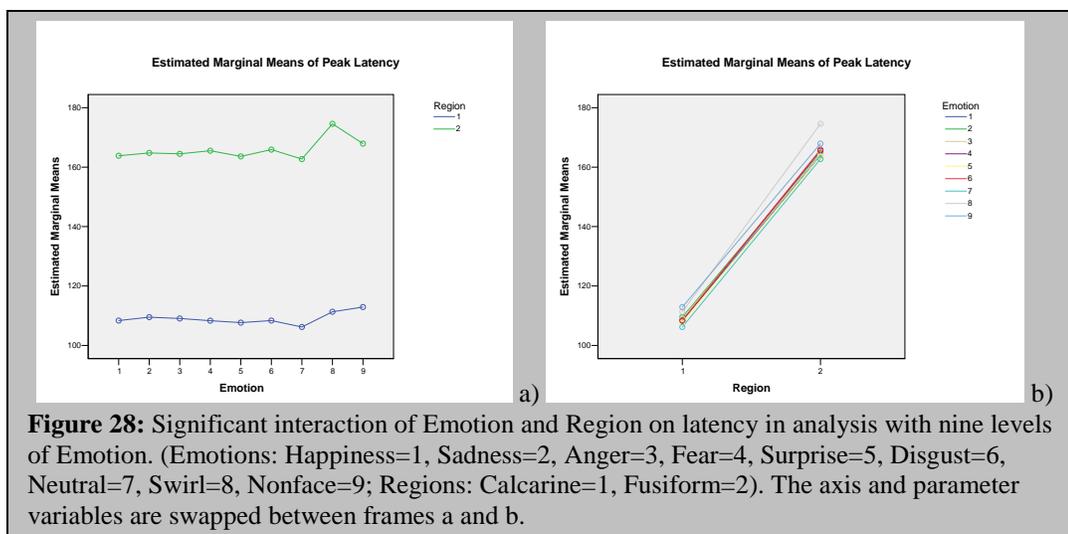emotional content on a face increases the calcarine response, is suggested to not be supported by the relatively low amplitude responses to sadness and fear. As discussed previously, it is possible that, instead of responding to the holistic emotional content of the face, the calcarine responds to some suggestive set of visual cues. Along these lines the happy faces utilized in this work all displayed open-mouthed smiles with visible teeth. Happiness was the only condition in which teeth were visible, and this is possibly the type of cue that the calcarine might be sensitive to. The calcarine is also seen to respond in approximately the same amplitude range to swirled faces as to intact faces (Figure 12 plots a and b, Figure 14 plots a and b). In the left hemisphere the response to the non-face sculpture condition appears very similar to that of the swirled face condition (Figure 14 plot a) while in the right hemisphere the non-face response shows the largest amplitude of all conditions (Figure 14 plot b). This pattern of results is difficult to interpret. In the left hemisphere the similar response to both indistinct swirled faces and identifiable sculptures suggests that there is no face-specific response in the calcarine. This is also suggested in the right hemisphere where faces are seen to generate no greater amplitude that do the control conditions (non-significant comparisons). That the visually distinct sculptures generate a greater response than any of

the facial conditions suggests that some combination of visual clarity and strong, identifiable features play a role in the right calcarine response, and that this distinction is only present in the right hemisphere suggests some type of lateral specialization.

With regard to the latency response of the calcarine fissure there exists only a single significant pairwise comparison, in the right hemisphere of the four-level analysis, where the response to swirled faces is seen to require greater time than that to neutral faces (Figure 13 plot b, Table 2). Nonetheless, across the latency profile plots of the calcarine (Figure 13 plots a and b, Figure 15 plots a and b), two observations were made. First, with regard to latency, the control conditions of swirled faces and sculptures seem to behave similarly in that both appear to require greater latency than do the facial conditions. That the visually intelligible sculptures generate a similar response to the indistinct swirls suggests that this effect is not simply one of comprehensible versus incomprehensible stimuli or differences in visual complexity. This supports the face-specific hypothesis with regard to the latency of the calcarine response. Second, the

Figure 27: Significant main effects in the exploratory analysis of peak latency with nine levels of Emotion: a) Region, b) Gender (Calcarine=1, Fusiform=2), and c) Emotion (Happiness=1, Sadness=2, Anger=3, Fear=4, Surprise=5, Disgust=6, Neutral=7, Swirl=8, Nonface=9)

Figure 28: Significant interaction of Emotion and Region on latency in analysis with nine levels of Emotion. (Emotions: Happiness=1, Sadness=2, Anger=3, Fear=4, Surprise=5, Disgust=6, Neutral=7, Swirl=8, Nonface=9; Regions: Calcarine=1, Fusiform=2). The axis and parameter variables are swapped between frames a and b.
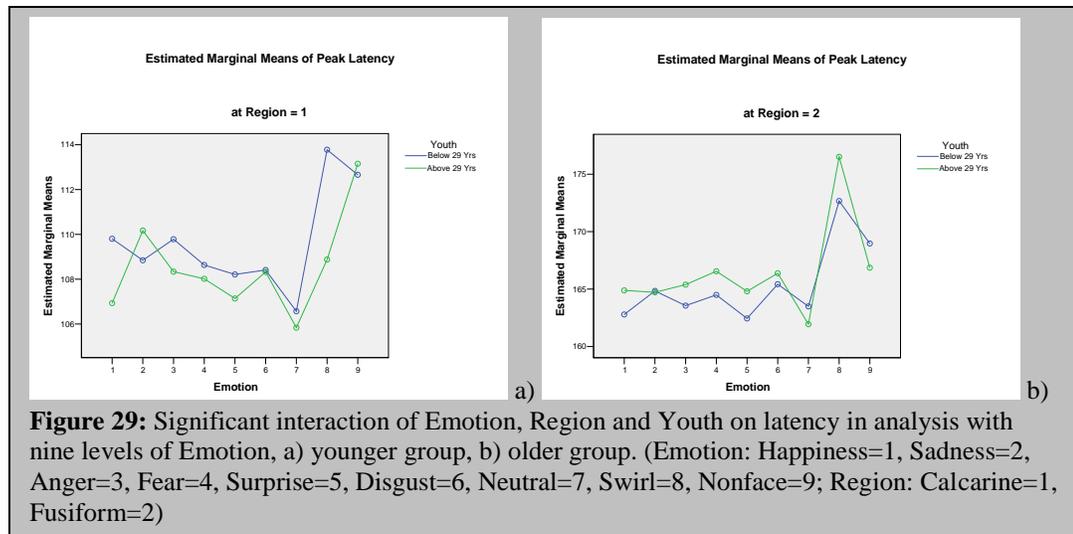
latency of the response to neutral faces is the smallest of all conditions, suggesting that, for facial stimuli, the response latency is increased when there is an emotional expression to be processed. This supports the emotion/intensity hypothesis, but only with regard to calcarine latency as opposed to calcarine amplitude.

Summarizing the responsivity of the calcarine fissure, as is supported by several significant pairwise comparisons the calcarine appears to respond with greater amplitude to happy faces versus neutral (bilateral), sad (right), and swirled faces (left). There does not appear to be an overall difference between the range of the amplitude response to comprehensible faces versus swirled faces, but the right hemisphere may respond more strongly to visually distinct non-facial conditions. Thus support is suggested for the happiness or valence hypothesis, where the amplitude response of the calcarine shows a preference for happy and/or positive emotions versus negative and/or other emotions and neutral faces. That a relatively small amplitude response is seen to sad faces (bilateral) and fearful faces (right) offers further support for the valence hypothesis. There does not appear to be a gestalt-like, explicitly face-specific response as is seen in the fusiform gyrus, and thus the face-selective hypothesis may not be supported with regard to the amplitude response of the calcarine. Finally, it appears that visually distinct control stimuli may function differently than swirled faces in the right calcarine with regard to amplitude. The calcarine appears to respond more quickly to faces than non-faces regardless of emotional expression, but neutral faces are responded to most quickly and the response appears to be delayed by emotional content being present on the face. With

regard to the latency of the calcarine response, both the face-specific and the emotion/intensity hypotheses are supported.

With regard to the amplitude response of the fusiform gyrus only two pairwise comparisons were significant. In the nine-level analysis surprised faces were seen to elicit significantly greater amplitude than disgusted faces in the left hemisphere, and fearful faces greater amplitude than the non-face condition in the right (Figure 14, plots c and d). The facial morphology of fearful and surprised expressions are quite similar, and fear could even be conceptualized as a unpleasant surprise response (with happiness or joy corresponding to the alternative of pleasant surprise). If these two significant comparisons are grouped together into a generalized fear response, then a replication of the Batty and Taylor (2003) result, of the relatively greater amplitude of the fear response in the bilateral fusiform gyrus is suggested. As opposed to the calcarine fissure, the amplitude response to happy faces in the fusiform gyrus is not notably large. Although not supported by significant comparisons, the amplitude of the response in the fusiform to both swirled faces and non-face objects does appear does appear to be notably low (Figures 12 and 14, plots c and d). This observation tends to support the well-established face-specific responsivity of the fusiform gyrus. Non-faces are seen to bilaterally generate slightly less amplitude than swirled faces in fusiform, suggesting that, as opposed to the ambiguous results seen in the right calcarine fissure, both swirls and objects represent the same functional control condition in the fusiform.

Figure 29: Significant interaction of Emotion, Region and Youth on latency in analysis with nine levels of Emotion, a) younger group, b) older group. (Emotion: Happiness=1, Sadness=2, Anger=3, Fear=4, Surprise=5, Disgust=6, Neutral=7, Swirl=8, Nonface=9; Region: Calcarine=1, Fusiform=2)
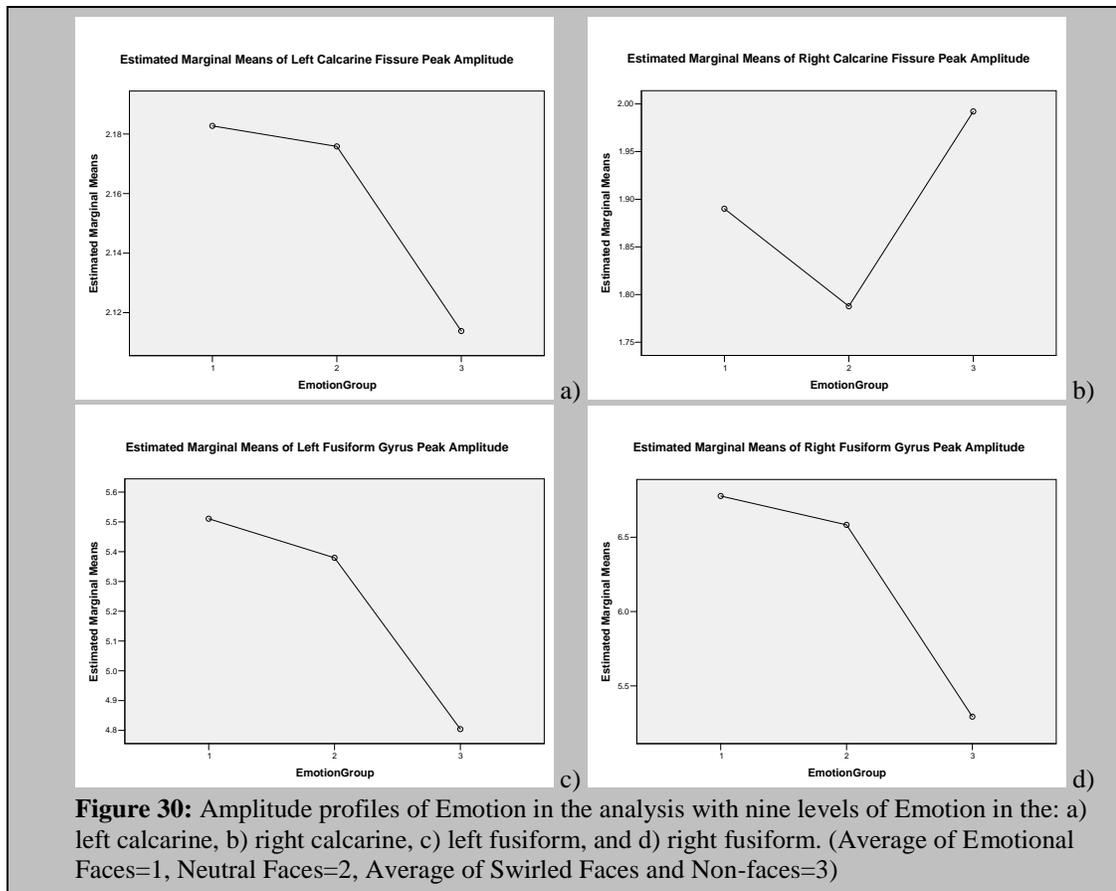
One of the most consistent and striking results seen in this work occurred in the latency response of the fusiform gyrus where multiple pairwise comparisons showed the response to swirled faces to require significantly greater time than that to almost all other facial conditions. In the right fusiform significant comparisons are seen between swirls and happy, angry, surprised and neutral faces, as well as non-face objects and, in the left, all comparisons between swirls and facial conditions but not non-face objects are significant. It is thus strongly suggested that swirled faces consistently require greater response latency than faces bearing any expression in the fusiform gyrus. Although the face-specificity of the fusiform has been demonstrated many times with regard to amplitude, this result extends such specificity to the latency of response as well. The response of the fusiform to non-face objects is ambiguous which, in the left hemisphere, appears to function similarly to faces but, in the right hemisphere, appears similar to swirls. There is a suggestion that disgusted faces also require above average latency in the fusiform. In the four-level analysis disgusted faces are seen to require significantly greater latency than happy and neutral faces in the right hemisphere and, in the nine-level analysis, disgusted faces are again seen to require greater latency than neutral in the right hemisphere (Figures 13 and 15, plots d). Batty and Taylor (2003) found sad, fearful, and disgusted faces to require greater response latency than happy and surprised faces and this result is also suggested in the current right fusiform results (Figure 15 plot d). In this profile sad, fearful, and disgusted faces are seen as three peaks, and happy, angry, surprised, and neutral faces the four valleys.

Summarizing the responsivity of the fusiform gyrus, the delayed reaction to swirled faces dominates the current results. It also seems likely, especially in the right hemisphere, that disgusted faces require greater response latency than several other emotional conditions. In terms of amplitude the face-specific nature of the fusiform response appears to have been replicated, with both swirled faces and non-face objects generating notably lesser results than facial conditions. Finally, fearful and surprised faces generated greater responses bilaterally than many other conditions.

specific aim 3.

The intention of Specific Aim 3 was to allow for a more comprehensive, free-form style of analysis of the experimental results in order to investigate potential effects related to region (calcarine versus fusiform), hemisphere, gender, age, and any other effects that may have revealed themselves. The amplitude analyses using both four and nine levels of Emotion uncovered the same group of significant main effects. It was found that the amplitude of the fusiform response was significantly greater than that of the calcarine (Figures 16 and 23 plot a), that the older group of subjects responded with greater overall amplitude than the younger group (Figures 16 and 23 plot b), and that women responded with greater amplitude than men (Figures 16 and 23 plot c). It was also found than happy faces elicited a significantly larger amplitude response than several other conditions, including neutral and swirled faces in the four-level analysis, and swirled faces and non-face objects in the nine-level analysis. Additionally, the nine-level analysis showed that angry and surprised faces produced significantly greater amplitude than non-face objects (Figures 16 and 23 plot d).
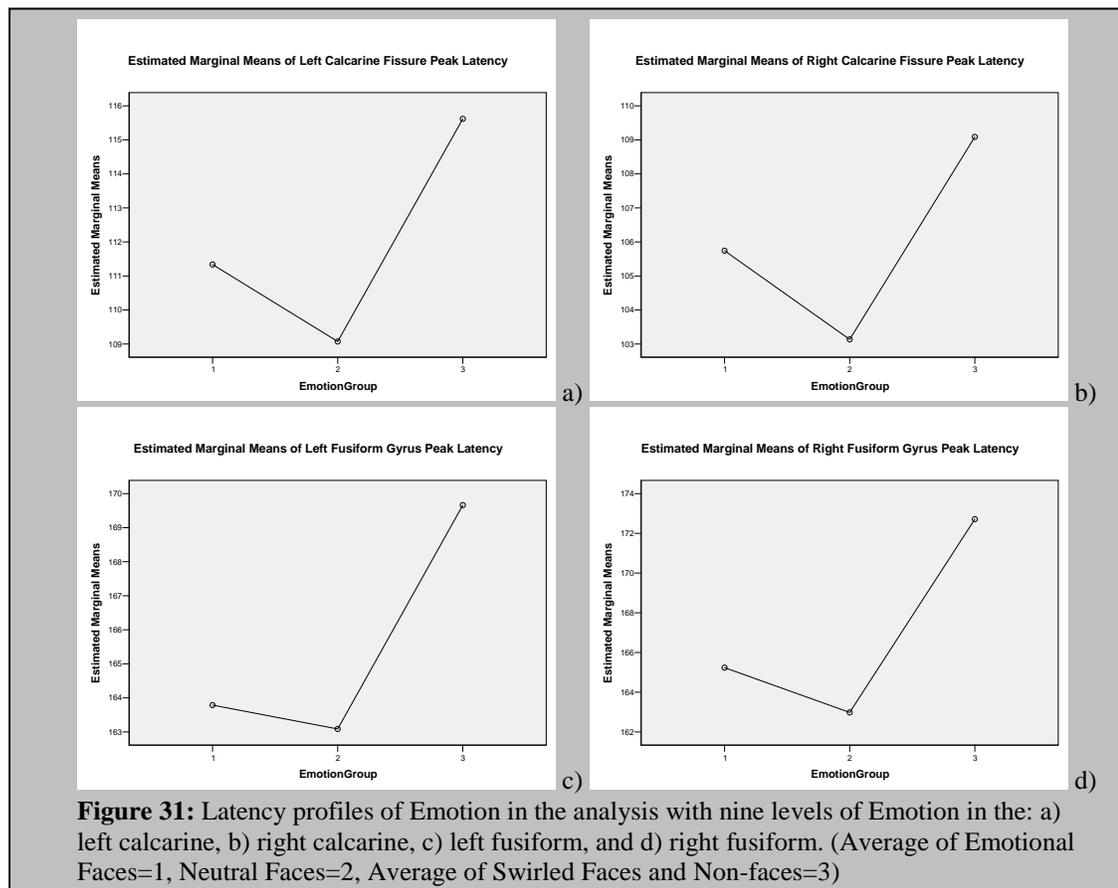
A significant interaction between age (Youth) and region was found in both the four- and nine-level amplitude analyses. Although the amplitude of the response was always greater in the fusiform than the calcarine, this difference was magnified in the older group of subjects as compared to the younger (Figures 17 and 24).

Figure 30: Amplitude profiles of Emotion in the analysis with nine levels of Emotion in the: a) left calcarine, b) right calcarine, c) left fusiform, and d) right fusiform. (Average of Emotional Faces=1, Neutral Faces=2, Average of Swirled Faces and Non-faces=3)

A significant four-way interaction between emotional condition, region, hemisphere, and age (Youth) was seen in both the four- and nine-way amplitude analyses. In three of the four regions the older age group displayed greater amplitude (Figures 18 and 26 plots b, c, and d), but this relationship is reversed in the left calcarine (Figures 18 and 26 plot a). This reversal may have accounted for the interaction of region, hemisphere and age. Analysis of the emotion profiles was inconclusive however, with the four-level analysis showing significantly greater amplitude for happy faces than for neutral faces in the right calcarine of the younger group, and the nine-level analysis showing that significantly greater amplitude for surprised versus disgusted faces in the left fusiform of the older group. Additionally, visual inspection of the emotion profiles in both analyses suggest lesser amplitude for the swirled faces and non-face objects in the fusiform but not the calcarine. Potentially this reduced response of the fusiform to stimuli that was not recognizable as a face was responsible for the introduction of emotional condition into this interaction (Figures 18 and 26).

Both the four- and nine-level latency analyses also revealed the same group of significant main effects. In both analyses the calcarine was seen to respond more quickly than the fusiform (Figures 20 and 27, plot a). This was expected since the timecourses were scored according to a set of rules which obliged the peak in the primary visual region to precede the peak in the fusiform face-responding region. Both analyses showed that women responded more quickly than men (Figures 20 and 27, plot b), and that the response to the swirled face condition took longer than all other facial conditions but not longer than the response to the non-face objects (Figures 20 and 27, plot c). Additionally the four-level analysis showed the disgusted face response to require greater latency than the neutral face response.

Both latency analyses revealed a significant interaction between emotional condition and region. As expected, the calcarine always responded more quickly than the fusiform. In the fusiform, the response to the swirled face condition was seen to lag behind the responses to all of the other facial conditions but not to the non-face objects.

Figure 31: Latency profiles of Emotion in the analysis with nine levels of Emotion in the: a) left calcarine, b) right calcarine, c) left fusiform, and d) right fusiform. (Average of Emotional Faces=1, Neutral Faces=2, Average of Swirled Faces and Non-faces=3)

Disgusted faces again elicited a slower fusiform response than neutral faces as well (Figures 21 and 28).

Several complex, multi-way interactions were significant in either the four- or nine-level analyses of either amplitude or latency, but not both. Due to the number of factors involved in these interactions and the fact that they did not appear in both the four- and nine-way analyses, less confidence was placed in them. An interaction between emotion and hemisphere was found in the nine-level amplitude analysis (Figure 25). Visually, greater amplitude was seen in the right hemisphere than in the left. It appears that this hemisphere-based amplitude differential effects the various emotional conditions to different degrees, with neutral and especially swirled faces and non-face objects demonstrating a lesser right-hemisphere bias than several other conditions, and angry faces showing a greater bias. The four-level amplitude analysis revealed a significant interaction between emotional condition, hemisphere, region, and gender (Figure 19). This interaction seems to be explained by the simple two-way interaction between emotion and gender which was only seen in the left calcarine. The four-level latency analysis showed an interaction between emotional condition, age (Youth), and hemisphere that visual inspection suggested was due to the left and right calcarine responding differently in the younger group but not the older (Figure 22). The nine-level latency analysis showed an interaction between emotional condition, age (Youth), and region, which visual inspection suggested may have been caused by the neutral face condition eliciting a slower response in the calcarine of the younger group as well as a faster response in the fusiform of the same group (Figure 29).

discussion of specific aim 3.

Taken together the findings of the exploratory analyses performed to satisfy Specific Aim 3 of this experiment suggested an interesting pattern of results. Significant effects of gender were found, with women responding with overall greater amplitude and shorter latency than men. Although it is difficult to tie these neuroimaging findings to psychological function, the fact that these results include the fusiform gyrus, a region known to respond selectively to faces, suggests some type of face perception differential between the genders. As is seen in the literature review above, numerous investigators have found behavioral evidence of an emotional recognition advantage in women

(Rahman, et al., 2004, Montagne et al., 2005, Hampson et al., 2006, Proverbio et al., 2007). In terms of neural response Proverbio et al. (2006) has shown greater amplitude of the lateral occipital P110 component in women versus men and Orozco and Ehlers (1998) showed a greater P450 component although at greater latency as well. Finally, Proverbio et al. (2007, 2009) showed that parenthood enhances both behavioral performance and the amplitude of the N2 response between 210 and 270ms in women but not in men. A number of participants in this work were parents, and thus the gender effect may be expected to be further enhanced. Overall, the gender differences found in this work confirms and extends the existing literature.

A significant effect for age was found, with the older group responding with greater amplitude than the younger. The literature review above found a general consensus that emotional recognition abilities decline in the elderly (Tessitore et al., 2005, Williams et al., 2006, Ruffman et al., 2008, Chaby and Narme, 2008). Chaby and Narme characterize these effects as beginning at 50 and accelerating after 70. Accompanying this decline is a shift in activation during emotion-related tasks away from the primary emotion-processing regions of the limbic system to frontal cortical regions (Hedden and Gabrieli, 2004). In terms of facial emotion recognition it is unclear whether this effect is related to the decreasing visual acuity which accompanies the aging process or not (Sullivan and Ruffman, 2004, Chen, 2009). With regard to neural activation, Iidaka et al. (2002) found that, despite changing patterns of neural activation over time, no region in older adults was activated to a greater extent than in younger, and Tessitore et al. (2005) found posterior fusiform activation to be reduced in older adults when processing fearful and threatening stimuli. In general, the increased amplitude found in the older subjects in the current study is not consistent with the body of published literature on this topic. On the other hand, even the oldest participant in the current work fails to meet the definition of 'elderly' used in most published studies on aging.

A significant effect of region was found, with greater amplitude being seen in the fusiform than in the calcarine and with longer latencies being seen in the fusiform as well. The difference in latency was explained by the rules used to identify the calcarine and fusiform peaks, which created a systematic difference. A true effect of amplitude was

seen however, with the fusiform demonstrating a larger response than the calcarine. As discussed in the methods section, the average timecourse used to represent the activity of the calcarine and fusiform regions in this work cannot be interpreted as a measure of current density in the cortex because the vertices (dipoles) are unlikely to be evenly distributed over the cortical surface. For this reason a region represented by a greater density of vertices in the cortical mesh would appear to produce apparently lesser average amplitude according to the methods used here because each vertex would represent a smaller patch of cortex. Since the cortical surfaces of all subjects in this work were all morphed onto that of a single subject, the question of density of cortical dipoles can be resolved simply. In the left calcarine a cortical surface area of $1811mm^2$ was represented by 2786 dipoles, and in the right calcarine an area of $1609mm^2$ required 2384 dipoles. Thus, in the left calcarine, each dipole represented an average cortical surface area of $0.65mm^2$, and in the right $0.67mm^2$. In the left fusiform $1018mm^2$ were represented by 1610 dipoles and in the right fusiform $1471mm^2$ required 2222 dipoles. In this case each dipole in the left fusiform represented an average area of $0.63mm^2$ and in the right $0.66mm^2$. Although the average area of cortical surface represented by each dipole in these regions is not identical, these areas are sufficiently similar to indicate that the difference between calcarine and fusiform amplitude seen here was not caused by the methodology of this work. Since the MEG sensors themselves were approximately evenly spaced, the greater amplitude of the second peak seen in the overlaid sensor-space traces in Figure 7 supports this conclusion as well.

An interaction between region and age was also present in the amplitude response. Both age groups showed similar amplitudes in the calcarine and, although fusiform response was seen to be greater than calcarine in both groups, this differential increased in the older group. As mentioned above, an amplitude increase in the elderly in any part of the cortex is counter-indicated by the existing literature (Iidaka et al., 2002). The mean age of the older group of participants was 39.1 years, and oldest subject in this experiment was 48-years-old at the time of participation. Although age-related effects begin to appear as early as 40 years of age it seems likely that the older group of subjects were not truly elderly and may not demonstrate the effects expected in the literature. What appears to be an age-related effect may be better explained by other age-correlated

factors. Parenthood was not controlled for in this analysis and, since older women are more likely to be mothers than younger ones, the increased amplitude shown by Proverbio et al. (2006, 2009) at a latency commensurate with later facial processing may be responsible for the effect seen here. Additionally, the participants in this experiment were not recruited randomly, and graduate students and faculty of a psychology department as well as students of engineering and physics were over-represented. The intelligence of this group is likely to be above average, and factors related to emotional perceptivity may be present as well.

Overall main effects of emotional condition on both amplitude and latency were also found, and were similar to those reported for Hypotheses 1 through 4 above. The amplitude effect was driven by significantly greater responses to happy faces as compared to neutral, swirled, and non-faces (Figures 16 and 23, plots c). In the nine-level analysis, angry and surprised faces were also seen to generate greater amplitude than non-faces. Sadness is seen to generate lesser amplitude than other emotions and neutral faces as well (non-significant comparison). Swirled and non-face conditions appear to generate similar but lesser amplitude than facial conditions. Although is it difficult to tell if swirls and non-faces functionally represented the same control condition, the fact that the visually distinct non-faces generated lesser amplitude that the indistinct swirls again suggest that portions of the visual system respond specifically to faces as opposed to some other property of the stimulus such as visual coherence or complexity. The overall amplitude results of Specific Aim 3 are similar to those for Specific Aims 1-4: first, happy faces appear to generate greater amplitude than many other facial conditions; second, sad faces tend to generate lesser amplitude than other facial conditions; and third, the two control conditions generated considerably less amplitude than did the recognizable face conditions. The latency effect was driven by significantly longer responses to swirled faces than to all of the other facial conditions but not to the non-face condition (Figures 20 and 27, plots c). The non-face condition required lesser latency that swirled faces (non-significant comparison), but longer latencies than the facial conditions (non-significant comparisons). It was indeterminate from this analysis why and to what extent the swirled face and non-face conditions functioned as similar types of control conditions. Although the calcarine and fusiform demonstrated a similar pattern of latency

results the effects appear to be considerably greater in the fusiform ((Figure 28, plot a).

Discussion of Post-Hoc Analyses

The results of the post-hoc analyses reinforce several suggestions previously made by the data in this work. First, the greater amplitude elicited by emotional and neutral faces versus non-facial conditions in the right fusiform gyrus replicates the already well-established face-preferential nature of this region. The face-specific hypothesis is supported in amplitude response of the right fusiform gyrus. Second, the greater latency required by the response to non-facial conditions versus neutral faces in the bilateral calcarine fissure and fusiform gyrus again underscores the latency effect of non-faces versus faces as discussed previously. The face-specific hypothesis is partially supported in the latency response of all four areas. Finally, the three significant comparisons in the latency response of the right fusiform gyrus allows further characterization of this region. In the right fusiform support has been found that non-facial conditions require greater latency than facial conditions, and that emotional faces require greater latency than non-emotional faces. Both the face-specific and the emotion/intensity hypotheses are supported in the right fusiform.

General Discussion

The three models of facial identity and emotion processing discussed at the beginning of this work have in common the concept of a serialized order of operations, each of which presumably are accomplished by specialized neural regions (Bruce and Young, 1986, Haxby et al., 2000, Adolphs, 2002a, 2002b). Adolph's description of a 'forward sweep of activation' over the cortex describes this conceptualization, with the earliest visual processing taking place in the occipital regions, sweeping forward over the temporal lobes, and finally reaching the frontal areas. When movies of post-stimulus cortical activity are created with the MNE software, this 'sweep' of activity is indeed seen in every subject. Adolph's insight that neural regions involved in face processing may be activated at several times is also noticeable in the movies. The example timecourses from a single subject's calcarine fissure and fusiform gyrus shown in Figure 10 reveal both regions to be activated nearly simultaneously at least twice, once around 100ms and again between 150 and 200ms. This pattern was seen universally throughout

this work. The early literature on face processing appears bound to the serial conceptualizations of the earlier models in which activation first progresses through the visual processing stages of the occipital lobe and only then propagates to the fusiform and other temporal regions. This paradigm, which is evident in the hypothesis formulated in this work as well, explains some of the surprise in recent years as investigators have begun to find suggestions of facial- and emotion-modulated processing in the calcarine, a function once thought reserved for other regions, and early activation of the fusiform taking place at latencies thought to be reserved for earlier visual processes. In a similar fashion the earliest models of Bruce and Young and Haxby et al. postulate facial identity and expression to be processed in completely separate pathways, although Young was seen to back away from this position later. Identity processing was usually assigned to the fusiform gyrus and emotion processing to the superior temporal sulcus. The present results as well as those of Lewis et al. show the fusiform response to be modulated by emotional expression. Generally speaking, the models of facial processing seen to date may not be sufficiently complex and the possibilities of repeated activations of regions and functions and of rapid propagation of information to downstream processing units may need to be introduced.

Future Directions

A number of pronounced and apparently consistent effects were found in this work, notably those of gender, age, and the interaction between region and age. These effects raise the question: what do they mean? The truly fascinating aspect of such neuroimaging results is not the effects in and of themselves, but the investigation of what they mean in the realm of the functional psychology of the individual. The gender effect of larger amplitudes and shorter latencies in women, especially in the fusiform gyrus, makes a strong suggestion that there is some gender difference in facial processing. The effect of increasing amplitude with age suggests that neural development continues into the forth decade of life and, since this effect is seen differentially in the fusiform, an age effect on facial processing is also suggested. Important future work might seek to not only replicate these effects but also to understand their significance with regard to individual psychological capacities. Many psychological disorders include a social component, and the facial emotion protocol employed here would seem to be a simple

and direct instrument by which to access basic social perception mechanisms in humans. If a correspondence could be established between the results of this protocol and some related social function, then an important avenue would be opened by which to investigate the social aspects of psychological dysfunction. If these effects do indeed suggest some capacity developing with age then perhaps a significant perspective on human maturation may be opened as well. A battery of psychological results related to anxiety and depression was collected from the subjects in this experiment and could serve as a starting point for further exploration.

This investigation limited itself to two cortical regions. Although there was good reason to focus on the calcarine and fusiform, facial perception and emotion are certainly inclusive of many other brain regions as well. Additional areas worthy of investigation might include the superior temporal sulcus, amygdala, cingulate cortex, and prefrontal regions. Since whole-head MEG data was collected in this experiment, such an investigation could be undertaken using the existing data. An analysis of the superior temporal sulcus is particularly suggested, since the Haxby, Hoffman, and Gobbini model (2000) describe this as the region where decoding of facial affect takes place.

Limitations

A number of shortcomings existed with regard to this experiment. Most importantly, the number of subjects (n=23), while being large for a pilot study in neuroimaging, may not have been sufficient to detect smaller effects. This lack of power may be responsible for the failure to uncover a more comprehensive pattern of effects related to facial emotion. Additionally, as opposed to the more rigorous process of random selection, the subjects in this experiment were chosen for their availability and familiarity with MEG data collection procedures. The second factor is likely to have resulted in higher quality experimental data being collected than would have been the case with randomly selected, untrained subjects, but is also likely to have limited the range of or even biased several important variables. The distribution of ages clearly overrepresented younger subjects and the subject population recruited heavily from students and faculty of a university psychology department. Technical specialists including engineers and computer scientists, physicists, and neuroscientists were also overrepresented. Thus the sample was likely to be biased on variables such as intelligence

and emotional perception. These factors could easily limit the ability of the experimental findings to be generalized to a wider population.

The stimulus presentation for this experiment was specifically constructed such that no difference in average luminance would be seen by the subject as the faces and other stimuli were displayed and removed. In doing so it was expected that the response of the calcarine fissure would not only be minimized, but also that the response would be limited to effects truly related to the stimulus itself as opposed to those reflecting changes in luminance level. It was suspected that this approach succeeded, because the response of the calcarine was so small as to become difficult to identify in some subjects. Additionally it was speculated that the unobtrusive nature of the stimulus may have contributed variability to the timing of the neural responses seen here. Whereas a sudden change in luminance level may have contributed an artifact to the data in some manner, a more aggressive stimulus presentation may also have led to more consistent neural responses.

The stimulus faces themselves used in this experiment were criticized by several researchers and participants for being indistinct in their emotional content. Additionally, the degree to which they expressed their intended emotions appeared to vary. As seen by Sprengelmeyer et al (2006), the intensity of affect of expression modulates the neural response of the calcarine fissure, and the failure to control for this factor is likely to be responsible for some amount of uncontrolled variance. These flaws were noted during development of the stimulus presentation software but, since this work was in large part a replication attempt of the previous findings of Lewis et al, it was determined that the previous stimulus set would be retained. Nonetheless, the confusing nature of many of the faces presented here is likely to have had some effect on the results. Likewise, data was not collected on the participants individual affective reactions to the facial stimulus, another factor seen to impact neural results (Pizzagalli, et al., 1999, 2002).

Finally, the choice of cortical projection analysis techniques in this experiment may be questioned. While cortical projection is useful in exploratory neuroimaging work because it allows the entire cortical response to be conveniently visualized, experience in this and other work suggests that it may also be less sensitive than the alternative of dipole analysis techniques. In a study such as this one, in which the responses of specific

brain regions were investigated, and particularly for regions closely related to basic sensory processing, for which simple dipole models are often sufficient to approximate neural activity, manual placement of dipoles into these regions in order to capture their responses may have yielded superior timecourse results. The calcarine fissure particularly, but the fusiform gyrus as well, are closely tied to early visual processing, and a dipole-based analysis may have improved the outcome of this work.

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