A Double Dissociation in the Affective Modulation of Startle in Humans: Effects of Unilateral Temporal Lobectomy

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Abstract

■ In the present study we report a double dissociation between right and left medial temporal lobe damage in the modulation of fear responses to different types of stimuli. We found that right unilateral temporal lobectomy (RTL) patients, in contrast to control subjects and left temporal lobectomy (LTL) patients, failed to show potentiated startle while viewing negative pictures. However, the opposite pattern of impairment was observed during a stimulus that patients had been told signaled the possibility of shock. Control subjects and RTL patients showed potentiated startle while LTL patients failed to show potentiated startle. We hypothesize that the right medial temporal lobe modulates fear responses while viewing emotional pictures, which involves exposure to (emotional) visual information and is consistent with the emotional processing traditionally ascribed to the right hemisphere. In contrast, the left medial temporal lobe modulates fear responses when those responses are the result of a linguistic/cognitive representation acquired through language, which, like other verbally mediated material, generally involves the left hemisphere. Additional evidence from case studies suggests that, within the medial temporal lobe, the amygdala is responsible for this modulation. ■

INTRODUCTION

Recent evidence implicates the amygdala in the acquisition and expression of fear in animals (LeDoux, 1996; Davis, 1992; Kapp, Pascoe, & Bixler, 1984) and humans (LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998; LaBar, LeDoux, Spencer, & Phelps, 1995; Bechara et al., 1995). However, a majority of these studies have utilized classical fear conditioning, in which a neutral stimulus acquires emotional properties by being paired with an aversive event, as a model of emotional learning. Classical conditioning models experiential learning in which the subject learns through a direct encounter with the reinforcer. Although this paradigm provides an opportunity to compare learning across species, humans may gain knowledge about the emotional nature of stimuli through means other than direct experience.

Both humans and animals can learn by observing the actions of others. For example, kittens are more likely to press a lever to obtain food if they saw their mothers performing the same action (Chesler, 1969). In what is likely the most well-known demonstration of observational learning in humans, Bandura, Ross, and Ross (1961, 1963a) found that children who watched an adult model interact with a "bobo" doll in an aggressive manner, either in person or on video, were more likely to act aggressively toward a "bobo" doll when given the opportunity, especially if the model had been rewarded for the aggressive actions (Bandura, Ross, & Ross, 1963b). In addition, humans can learn through verbal communication, being told about a stimulus without having to experience or encounter it. For example, you may be told to avoid a particular neighborhood because it is prone to violent crime. You learn about the neighborhood without having been a victim of crime yourself. In other words, a person may judge a picture of an armed robbery as fear-inducing or can fear a gun without ever having had personal experience with guns. Knowledge in this case can be acquired through various forms of communication, such as by observing scenes in which guns are associated with danger or being told of the dangers associated with guns.

There are obviously other ways in which humans learn, but examining these two means of learning, observation and communication, broadens our models of emotional learning. In the present study we examine the role of the medial temporal lobe, especially the amygdala, in the modulation of behavioral fear responses acquired through means other than tradi-

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tional fear conditioning. The viewing of emotional pictures taps into many kinds of learning, such as observation, while the instructed fear paradigm models learning through verbal communication. Evidence from neuroimaging studies suggests that the amygdala is more active when emotion is aroused through viewing pictures (Lane et al., 1997; Irwin et al., 1996); the amygdala is also active during emotional learning when learning occurs through verbal communication (Phelps et al., 2001). However, observed activation of the amygdala does not indicate its precise role.

To investigate the role of the medial temporal lobe, including the amygdala, in the affective modulation of startle under circumstances more representative of the way in which humans learn about the emotional nature of stimuli, healthy subjects and unilateral temporal lobectomy patients were tested in two paradigms: (1) viewing emotional pictures and (2) instructed fear. Startle eyeblink, which is the first component of the human startle reflex (Lang, Bradley, & Cuthbert, 1990), was used as the dependent measure. An increase in startle eyeblink is referred to as potentiated startle and is taken as an index of fear (e.g., Brown, Kalish, & Farber, 1951). Before presenting our results, we will review previous studies utilizing these two paradigms.

Emotional Picture Viewing

Researchers have found that emotions evoked by viewing (Bradley, Cuthbert, & Lang, 1990) or imagining (Vrana & Lang, 1990) a negative scene will potentiate the startle reflex in humans. Lang et al. (1990) have proposed a theory to account for this modulation. They argue that emotional behavior is organized biphasically with most behaviors able to be classified as appetitive or defensive. The hypothesis states that reflexes are enhanced to the extent that the emotion of the context matches the emotion of the reflex. Reflexes are attenuated when the emotion of the context and the reflex are mismatched. For example, startle, a defensive reflex, is increased during viewing of negative pictures, a negative emotional context. On the other hand, startle is decreased during positive pictures, a positive emotional context. Based on research utilizing monaural startle probes, Lang et al. hypothesize that the right hemisphere is responsible for this modulation but are silent as to which structures in particular may be differentially involved in the modulation of startle. Supporting the proposed right hemisphere bias in processing emotional pictures, greater right hemisphere activation has been observed using fMRI (Lang et al., 1998; Lane et al., 1997; Irwin et al., 1996). Given the role of the amygdala in the modulation of startle during fear conditioning (e.g., Davis, 1992), it is reasonable to expect the amygdala might also be involved in the modulation of startle during the perception of negative scenes.

Instructed Fear

Instructed fear, also referred to as anticipatory anxiety, is a paradigm in which subjects are told when an aversive event is possible (e.g., Grillon, Ameli, Woods, Merikangas, & Davis, 1991). In this paradigm, subjects form a cognitive representation of the aversive nature of the stimulus through (verbally mediated) awareness of the relationship between a stimulus and an aversive event without necessarily having to experience that event. This cognitive representation is sufficient to elicit behavioral fear responses typically observed in traditional fear conditioning. Hugdahl (1978) and Hugdahl and Öhman (1977) told subjects that they would receive a shock during a particular stimulus and observed a fear response, as measured by skin conductance, comparable to that displayed by a group who underwent traditional fear conditioning without the verbal instruction. Grillon et al. (1991) observed potentiated startle in subjects during a stimulus signaling the possibility of shock, even though no shock was delivered.

The role played by awareness of the relationship between stimulus and event in the acquisition and expression of fear responses in classical conditioning has been of interest for some time. Bechara et al. (1995) observed that awareness of the relationship between cue and an aversive noise and physiological (skin conductance) evidence of conditioned fear dissociate along the lines of hippocampal versus amygdala damage. Bilateral amygdala damage did not preclude awareness of the cue–noise relationship but did result in a failure to exhibit conditioned fear responses. Bilateral hippocampal damage, on the other hand, prevented awareness of the cue–noise relationship but did not block expression of conditioned fear. Previous research in our laboratory has shown that patients who have undergone unilateral temporal lobectomy (UTL), which includes resection of the amygdala, fail to exhibit conditioned fear as measured by skin conductance (LaBar et al., 1995). They are, however, able to verbalize the cue-shock contingency, indicating awareness of the aversive nature of the cue. In instructed fear, awareness of the relationship between stimulus and event is what the subject learns and is the basis of the expression of fear responses.

Earlier studies of instructed fear in normal subjects have suggested that there may be a hemisphere bias in this task. Grillon and Davis (1995) found greater startle potentiation during instructed fear when monaural acoustic probes were delivered to the right ear/left hemisphere compared to the left ear/right hemisphere. Based on certain assumptions about the neural circuitry that mediates the startle reflex, these results were interpreted to mean greater involvement of the left amygdala during instructed fear. Consistent with this hemisphere bias, Phelps et al. (in press) found left amygdala activation using fMRI during the same instructed fear paradigm.

The monaural startle probe and neuroimaging studies during viewing of emotional pictures and using the instructed fear paradigm suggest that the right and left amygdala, respectively, are involved in these tasks. However, they do not offer direct evidence of the precise role of the amygdala. In the present studies, we offer an extension of these monaural startle and neuroimaging studies. Monaural startle studies provide a clue to hemispheric biases in startle modulation but do not locate areas within a hemisphere where modulation of the response is occurring. Neuroimaging studies, on the other hand, demonstrate that the amygdala is active during these paradigms, but do not provide information as to whether it is critically involved in the task. By observing the performance of patients with specific hemispheric damage we may be able to determine if the amygdala is involved in these tasks.

RESULTS

Emotional Picture Viewing

During the emotional picture paradigm, normal control subjects and right temporal lobectomy (RTL) and left temporal lobectomy (LTL) patients were shown positive, negative, and neutral pictures. Startle eyeblink was recorded, as were subjective ratings of the pictures. Based on previous research, it is expected that control subjects will show potentiated startle during the negative pictures and a slight attenuation of startle during the positive pictures (see Lang et al., 1990, for review).

Arousal Ratings

All groups rated negative and positive pictures as more arousing than neutral pictures. Negative and positive pictures were rated as equally arousing. A 3 × 3 ANOVA was conducted with valence (negative, neutral, positive) and group (control, LTL, RTL) as factors. There was a significant effect of arousal, $F(2,42) = 21.99$, $p < .001$, but no interaction with group, $F < 1$, indicating that controls and patients rated pictures equivalently. A planned repeated measures ANOVA conducted on each group's data showed a significant main effect of valence for all groups, $F(2,22) = 8.73$, $p < .01$, $F(2,10) = 7.93$, $p < .01$, and $F(2,10) = 8.97$, $p < .01$ for the control group, LTL group, and RTL group, respectively. A contrast analysis on each group's ratings also showed a significant quadratic trend indicating that all groups rated negative and positive pictures as more arousing than neutral pictures. Mean arousal ratings are shown in Table 1.

Table 1. Mean Arousal Ratings

	Negative Pictures	*Neutral Pictures*	*Positive Pictures*
Control	3.11 (1.48)	2.00 (0.83)	3.34 (0.74)
LTL	3.88 (1.06)	1.98 (0.69)	3.88 (0.90)
RTL	3.85 (1.05)	1.92 (0.77)	3.55 (0.77)

All groups rated negative and positive pictures as more arousing than neutral pictures. LTL = left temporal lobectomy; RTL = right temporal lobectomy.

Table 2. Mean Pleasantness Ratings

	Negative Pictures	*Neutral Pictures*	*Positive Pictures*
Control	1.37 (0.28)	3.00 (0.34)	3.91 (0.41)
LTL	1.20 (0.14)	3.00 (0.18)	4.05 (0.30)
RTL	1.17 (0.10)	2.87 (0.40)	4.33 (0.34)

All groups rated positive pictures as more pleasant than neutral pictures and neutral pictures as more positive than negative pictures. LTL = left temporal lobectomy; RTL = right temporal lobectomy.

Pleasantness Ratings

All groups rated positive pictures as more pleasant than either neutral or negative pictures and neutral pictures as more pleasant than negative pictures. A 3 × 3 ANOVA was conducted with valence (negative, neutral, positive) and group (control, LTL, RTL) as factors. There was a significant effect of pleasantness, $F(2,42) = 356.42$, $p < .001$, but no interaction with group, $F < 1$, indicating that controls and patients rated pictures in a similar manner. A planned repeated measures ANOVA on each group's data with valence as a factor indicated a significant main effect of valence for all groups, $F(2,22) = 134.03$, $p < .001$, $F(2,10) = 210.62$, $p < .001$, and $F(2,10) = 129.72$, $p < .001$ for the control group, LTL group, and RTL group, respectively. A contrast analysis on each group's ratings also showed a significant linear trend indicating that all groups rated positive pictures as more pleasant than neutral pictures and neutral pictures as more pleasant than negative pictures. Mean pleasantness ratings are shown in Table 2.

Startle Eyeblink

The control and LTL groups showed potentiated startle during negative pictures. The RTL group, however, did not show potentiated startle during negative pictures. A slight attenuation of startle during positive pictures was observed in all groups, although this only reached significance in the LTL group. A 3 × 3 ANOVA was conducted with valence (negative, neutral, positive)

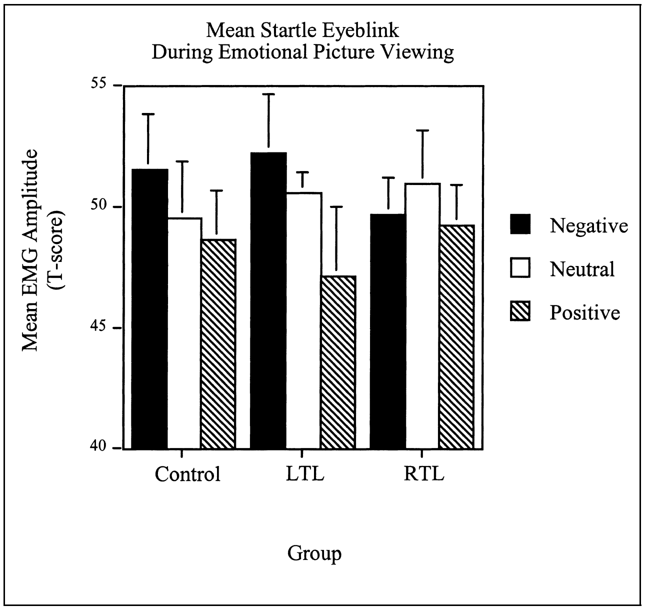

Figure 1. Mean startle eyeblink during viewing of negative, neutral, and positive pictures. Control subjects and LTL patients showed potentiated startle during negative pictures. RTL patients showed no effect of valence on startle.

and group (control, LTL, RTL) as factors. There was a significant main effect for valence, $F(2,44) = 6.16$, $p < .01$, but there was no effect of group, $F < 1$, and no interaction, $F(4,44) = 1.47$, $p > .05$. Planned repeated measures ANOVAs conducted on each group's data with valence as a factor showed a significant main effect for valence in the control group, $F(2,22) = 3.99$, $p < .05$, and LTL group, $F(2,10) = 5.551$, $p < .05$. There was no effect of valence in RTL subjects, $F < 1$. In control subjects, startle during negative scenes was significantly greater than startle during positive scenes, $t(11) = 3.04$, $p < .05$. LTL subjects showed greater startle during negative compared to positive scenes, $t(5) = 2.406$, $p < .05$, and during neutral compared to positive scenes, $t(5) = 2.42$, $p < .05$. Mean startle eyeblink is presented in Figure 1.

Instructed Fear

During instructed fear, normal control subjects, RTL, and LTL patients, and one bilateral amygdala patient (SP) saw two colored squares. They were told that one color signaled the possibility of receiving a shock (threat stimulus) while there was no chance of receiving a shock during the other (safe stimulus). Startle eyeblink was used as the measure of fear responding. Based on previous research, it is expected that control subjects will show potentiated startle during the threat stimulus relative to the safe stimulus (Grillon et al., 1991).

The control group and RTL group showed potentiated startle during the threat stimulus. However, the LTL group did not show potentiated startle during the threat stimulus. Baseline startle amplitude and the rate of habituation were similar across trials for each of the groups. To examine the effect of threat on the startle eyeblink response a 2 × 3 ANOVA was conducted with stimulus type (threat, safe) and group (control, RTL, and LTL) as factors. There was a significant main effect of stimulus type, $F(1,25) = 8.447$, $p < .01$, indicating potentiated startle during threat compared to safe stimuli. There was also a significant Stimulus type × Group interaction, $F(2,25) = 9.683$, $p < .001$. Post hoc simple effect analyses on this interaction revealed significant potentiated startle during threat compared to safe trials in control subjects, $F(1,13) = 20.894$, $p < .001$, and RTL patients, $F(1,7) = 14.435$, $p < .01$. There was no facilitation of startle eyeblink during threat trials in LTL patients, $F(1,5) = 5.177$, $p > .05$. If anything, LTL patients showed the reverse pattern with startle during safe trials greater than during threat trials. However, this was likely due to asymmetrical counterbalancing. When the data were reexamined by removing two LTL patients in order to control for stimulus presentation order, this slight trend was no longer present, $F(1,3) = 2.474$, $p > .2$ (mean threat = 47.34; mean safe = 49.95). Patient SP, with bilateral amygdala damage, showed no difference in startle eyeblink amplitude during threat and safe periods. Figure 2 shows mean startle eyeblink amplitude for each group and Patient SP.

Double Dissociation in Startle Eyeblink in RTL and LTL Patients

RTL patients did not demonstrate potentiated startle during emotional picture viewing but did demonstrate

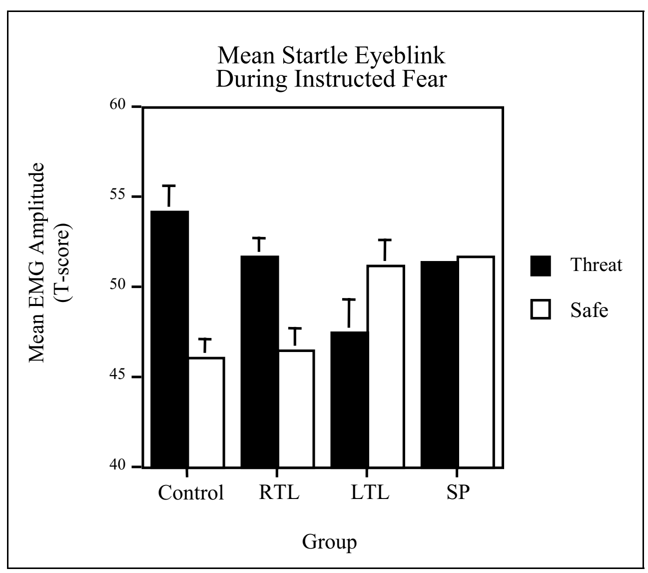

Figure 2. Mean EMG amplitude during threat and safe trials. The control and RTL groups show potentiated startle during threat compared to safe trials. The LTL group shows a trend for potentiated startle during safe trials. Patient SP shows no difference between threat and safe trials.

potentiated startle during instructed fear, while LTL patients demonstrated the opposite pattern of impairment, suggesting an interaction between patient group, task, and stimulus type. Ten patients were tested in both paradigms, 5 RTL and 5 LTL. Examining data from these patients, a 2 × 2 × 2 repeated measures ANOVA was conducted with stimulus type (negative, positive), task (picture viewing, instructed fear), and group (RTL, LTL) as factors. For the purposes of this analysis, the threat stimulus during instructed fear and the negative pictures during emotional picture viewing were termed negative stimuli, and the safe stimulus during instructed fear and the positive pictures during emotional picture viewing were termed positive stimuli. There were no main effects for stimulus, task, or group. The only significant interaction was that between stimulus type, task, and group, $F(1,8) = 12.1$, $p < 01$. The double dissociation suggested by this interaction will be addressed in the Discussion.

DISCUSSION

Control subjects and LTL patients demonstrated an increase in startle during viewing of negative pictures. RTL patients, in contrast, did not show this increase. This is consistent with previous studies suggesting a right hemisphere bias in the modulation of startle during viewing of affective pictures (Bradley, Cuthbert, & Lang, 1991, 1996a). This impairment in RTL patients is not due to a difference in the perceived unpleasantness or arousing nature of the pictures since all groups rated the negative pictures the same.

Consistent with previous studies of instructed fear (Grillon et al., 1991), control subjects and RTL patients demonstrated potentiated startle during instructed fear, which suggests that the right medial temporal lobe, including the amygdala, is not necessary for modulating responses based on verbal instruction. Left unilateral temporal lobe damage, however, does impair modulation of fear responding during instructed fear. This impairment for LTL subjects is consistent with other studies suggesting a left hemisphere bias in processing aversive stimuli when the aversive nature is learned through verbal instruction (see Introduction).

Although the lesions of the RTL and LTL patients in this study are limited to the medial temporal lobe (MTL), a number of structures within the MTL structures, in addition to the amygdala, are damaged. Therefore, our data with unilateral temporal lobectomy patients do not directly address whether it is damage to the amygdala or surrounding cortical areas that leads to the deficit in the modulation of startle eyeblink in the present study. However, considering also the data of Angrilli et al. (1996) and our results with Patient SP, it is likely that the amygdala is responsible for the present results. Angrilli et al. tested a patient with selective right unilateral amygdala damage in a similar paradigm using negative and neutral pictures. They also observed an impairment in potentiated startle during negative pictures. This result suggests that it is the amygdala within MTL that modulates startle in emotional picture viewing and that it is damage to the amygdala in our RTL patients that leads to the observed impairment in potentiated startle. Likewise, Patient SP's performance during instructed fear supports the assumption that it is damage to the left amygdala rather than to surrounding regions that is responsible for the impairment in LTL patients during instructed fear. Her right amygdala damage is the result of a unilateral temporal lobectomy, the identical surgery our RTL patients underwent. The results obtained from RTL patients suggest that unilateral damage to these surrounding structures is insufficient to lead to the impairment in instructed fear. SP's left amygdala damage is the product of gliosis specific to the amygdala and supports the conclusion that it is damage to the left amygdala within the medial temporal lobe that leads to the observed impairment in potentiated startle.

A limitation of the present study is the fact that startle eyeblink was recorded only from the left eye of participants. Given that our patients had unilateral damage and that the eye from which startle was recorded was not always contralateral to the damage, one concern might be that the results are due to a failure to detect potentiation in startle rather than an impairment in our patients' ability to demonstrate potentiated startle. We believe the observed impairments are due to a failure to demonstrate potentiated startle under different circumstances. First, muscles in the upper half of the face are bilaterally innervated and since the startle probe was presented binaurally, it is unlikely that the simple fact of unilateral damage would result in the observed impairments. Second, our patients are able to demonstrate potentiated startle, RTL patients during instructed fear and LTL patients during emotional picture viewing.

Issues of Laterality

The present report demonstrates a double dissociation in the modulation of startle eyeblink. RTL patients do not show potentiated startle during viewing of emotional pictures but do show potentiated startle during instructed fear, while LTL patients show the opposite pattern of impairment. These data suggest that the medial temporal lobe, including the amygdala, is involved in the modulation of behavioral fear responses when learning occurs through means other than traditional classical conditioning. Learning theorists such as Tolman (1955) make a distinction between learning and performance (see Hilgard & Marquis, 1961, revised by Kimble, 1961, for a discussion of this point), and here it is important to make a similar distinction between emotional learning and emotional expression. As was demonstrated in the subjective ratings of the emotional pictures by both RTL and LTL patients, the perception and rating of emotion are intact. Both patient groups also reported that they were aware when the shock was possible during instructed fear. Therefore, the medial temporal lobe, unilaterally, is not necessary for acquiring knowledge of the emotional nature of stimuli nor for expression of that knowledge through ratings or verbal report. However, the medial temporal lobe is necessary for the modulation of behavioral fear responses.

The issue of laterality of function has been of interest for some time (e.g., Hailman & Bauers, 1990; Davidson, 2000). One of the first theories of hemispheric asymmetry in emotional learning that must be addressed is that formulated by Hugdahl (1995), which posits that associative learning, especially when emotional stimuli are involved, such as in classical fear conditioning, is represented in the right hemisphere. Intuitively instructed fear is more similar to classical fear conditioning than is viewing emotional pictures. During instructed fear, as in classical fear conditioning, a subject expects an aversive event cued by a particular stimulus; although unpleasant at times, there is no expectancy of an aversive event during viewing of emotional pictures. This being the case, one might expect that RTL patients would be impaired in instructed fear rather than LTL patients; however, the opposite pattern of results was found. Other data would predict an impairment in both LTL and RTL patients. LaBar et al. (1995) found that unilateral temporal lobectomy patients, regardless of side of lesion, do not show fear conditioning as measured by skin conductance. Therefore, it is interesting that side of lesion did have differing effects in the present study, but not in a way predicted by Hugdahl's hypothesis or by the LaBar et al. study.

Another hypothesis of hemispheric asymmetry that focuses on the amygdala's role in emotional learning is that of Morris, Öhman, and Dolan (1998) in which they investigated the role of the amygdala in fear conditioning using PET. In their study, subjects were presented with 4 faces, 2 of which had angry expressions and 2 had neutral expressions. One of the angry faces, designated the CS+, was followed by presentation of the unconditioned stimulus, a loud white noise. During scanning, subjects were shown masked presentations of both the angry and neutral faces. Masked presentations consisted of a 30-msec presentation of the face followed by a 45-msec presentation of a mask to prevent conscious awareness of the stimulus. The faces served as both stimulus and mask. The critical comparison was amygdala activity during trials in which the CS+ was masked by a neutral face, and so was not consciously perceived, versus trials in which the CS+ served as the mask and was consciously perceived. They found that the right amygdala was active during trials in which presentations of the CS+ were masked. The left amygdala was active during trials in which the CS+ served as the mask. The authors suggest that the amygdala is able to discriminate the learned emotional significance of stimuli that are not consciously perceived. They argue that the observed right amygdala activity might be related to the right hemisphere advantage in processing emotional faces, while conscious perception of the face produces left amygdala activity because processes related to conscious perception, such as verbal labeling, inhibit activity of the right amygdala. The impairment in LTL patients in instructed fear corresponds to their finding of left amygdala activation during viewing of an angry face previously paired with white noise. This would suggest that the left amygdala is involved when a consciously perceived stimulus acquires emotional salience.

However, in a second formulation, Dolan and Morris (2000) report that the right amygdala is activated when a stimulus acquires salience through conditioning and the left amygdala is activated when the stimulus is innately fearful. Since all presentations were supraliminal, this contradicts their earlier finding (Morris et al., 1998) that consciously perceived presentations of a face previously paired with a loud noise activated the left amygdala and not the right. The inconsistency of their results may be due to the type of stimuli used. They used pictures of faces in their studies while we used colored squares in instructed fear and pictures of scenes. Although our results are in accord with their earlier findings, the present report does not support their most recent conceptualization of the amygdala's lateralized role in emotional processing. The amygdala is known to play a role in the processing of faces (see Aggleton & Young, 2000, for review), and it may be that their results are more indicative of face rather than emotional processing.

Gazzaniga and colleagues (Gazzaniga, 1981; Baynes & Gazzaniga, 1997; Gazzaniga & LeDoux, 1978) conceive of the left hemisphere as an "interpreter" that examines the behavior and emotion of the individual in order to create rationales or theories to explain the world. This view of the left hemisphere complements the view of Gainotti (1997) and Gainotti, Caltagirone, and Zoccolotti (1993) who argue that the left hemisphere is responsible for intentional actions such as the expression of emotion, and that the right hemisphere is involved in basic and automatic aspects of emotion such as emotional arousal. Our results correspond with these conceptions of the left and right hemispheres. Although subjects are not performing some action that must be explained to him/herself, there is interpretation of the instructions during instructed fear. The subject must exert effortful processing in that the instructions must be intentionally recalled in order to determine which is the "threatening" stimulus. Our results with RTL patients are in accord with the view of the right hemisphere as being involved in automatic aspects of emotion. While viewing the pictures in the emotional picture paradigm, subjects did not have to recall instructions or process the pictures in an effortful manner in order to rate them. Subjective judgements were made automatically.

Finally, although the previously mentioned theories of hemispheric specialization in emotional processing are, by and large, consistent with our results, Kolb and Taylor (1990) have perhaps the most appropriate conceptualization. They argue that emotion is not lateralized in an all-or-none fashion. Rather, the left hemisphere is involved in the verbal components of emotion. This is consistent with our findings of an impairment in LTL patients in instructed fear. They argue that the right hemisphere is involved in nonverbal components of emotion. The impairment in RTL patients in the emotional picture viewing paradigm can be seen as an impairment due to nonverbal emotional processing.

The double dissociation demonstrated in the present study can be viewed in two ways. First, it can be seen as a double dissociation based on the physical characteristics of the stimuli, simple colored squares whose emotional qualities are verbally encoded, versus complex pictures of scenes that are nonverbal in nature. The second manner in which the dissociation can be viewed is in terms of the processing required when presented with the stimuli. The simple squares used in the instructed fear paradigm required effortful processing. The instructions had to be intentionally recalled and brought to mind to interpret the emotional significance of the stimulus. The pictures used for viewing likely required little effortful processing. Rather, these pictures consisted of vivid scenes whose emotional content was immediately salient, resulting in noneffortful, automatic processing. These two approaches (i.e., stimulus properties vs. processing demands) are not mutually exclusive explanations of the dissociation. The colored squares used in the instructed fear paradigm had verbally encoded emotional properties and required more intentional and effortful processing. The pictures of emotional scenes were visual in nature and brought about more automatic processing. As discussed above, there are several hypotheses of hemispheric asymmetry with which the present results are in accord. In the present study we have refined and have extended these earlier descriptions of hemispheric laterality to include the amygdala's modulation of emotional responses as measured by the potentiation of the eyeblink startle reflex.

METHODS

Unilateral Temporal Lobectomy Characteristics

Patients with medically refractory complex partial seizures of medial temporal lobe origin were studied at least 2 years following unilateral anteromedial en bloc temporal lobe resection. A majority of patients were medication-free at the time of testing. An approximate 3.5-cm resection of the anterior middle and inferior temporal gyri was made. This allowed access to the temporal horn and was followed by dissection of the occipito-temporal fasciculus and subsequent removal of 70–80% of the amygdala and all of the hippocampus, parahippocampus, and projection fibers to their posterior extent at the atrium of the lateral ventricle (Spencer & Spencer, 1985; Spencer, Spencer, Mattson, Williamson, & Novelly, 1984). The extent of the lesion is standard and does not vary greatly between subjects, regardless of side of lesion.

Eyeblink Measurement

The eyeblink component of subjects' startle response was measured by electromyogram (EMG) (BioPac Systems) and stored off-line for later analysis. Berg and Balaban (1999) state that ''which eye is selected is a matter of convenience and preference'' (pp. 36), and researchers utilizing the paradigms employed in this study have chosen to record from either the left (e.g., Grillon et al., 1991; Bradley et al., 1990) or right eye (e.g., Grillon, Ameli, Merikangas, Woods, & Davis, 1993). The left eye was chosen in this study for convenience. Two Ag–AgCl electrodes were placed on the orbicularis oculi muscle under subjects' left eye. A ground electrode was place behind subjects' left ear.

Prior to analysis, the raw EMG signal was filtered using a 50-Hz high pass filter then fully rectified and integrated. An eyeblink was defined as the difference between the preblink baseline, taken as the mean EMG activity in the 50 msec prior to the startle probe, and the peak amplitude occurring in the 120 msec following the startle probe. Subjects' EMG amplitudes were standardized (T scores = $z(10) + 50$) before analysis due to large between-subject differences in baseline eyeblink amplitude.

Emotional Picture Viewing

Participants

Twelve patients were studied 2–6 years following unilateral anteromedial en bloc temporal lobe resection. A majority of patients were also tested in the instructed fear paradigm. Six left (LTL) and six right (RTL) unilateral temporal lobectomy patients participated (mean age = 37.67 ± 10.07 years; mean education = 14.54 ± 3.56 years). The control group consisted of 12 nonepileptic adult subjects matched for age and education (mean age = 37.58 ± 8.73 years; mean education = 15.17 ± 3.56). They did not have a history of epilepsy or other neurological impairment.

Materials

Sixty color pictures depicting 20 positive, 20 negative, and 20 neutral scenes were created. All the negative pictures and most of the positive pictures were selected from the International Affective Picture System (Lang, Öhman, & Vaitl, 1988). All of the neutral pictures and some of the positive pictures were selected from other sources in order to equate the presence of people in all pictures. The pictures were presented for 4.5 sec on a computer screen (Apple Multiple Scan Display). An average of 7 sec separated picture presentations. There was a minimum interval of 15 sec between startle stimulus presentations. The startle probe was a 40-msec, 100-dB burst of white noise presented binaurally through headphones (Koss TD/60).

Procedure

Recording electrodes were attached once consent was obtained. During presentation of 36 of the pictures, a startle probe was delivered such that 12 pictures of each valence were probed. Participants then rated all pictures, first for arousal, explained as emotional strength or intensity, and then for pleasantness. Each rating was made on a 5-point scale with 1 being low and 5 being high and subjects were instructed to not compare pictures when making their ratings.

Instructed Fear

Participants

Eight right (RTL) and six left (LTL) unilateral temporal lobectomy patients participated (mean age = 39.07 ± 9.97 years; mean education = 14.46 ± 3.55 years). A majority of the patients had also been tested in the emotional picture viewing paradigm. The control group consisted of 14 adult subjects matched for age and education (mean age = 37.93 ± 8.83 years; mean education 14.75 ± 2.79 years) without a history of epilepsy or other neurological impairment. One patient with bilateral amygdala damage, SP, was also tested. Patient SP is a 55-year-old female with 14 years of education. She has gliosis of the left amygdala and a right hemisphere temporal lobectomy (Phelps et al., 1998).

Materials

Yellow and blue blocks were presented on a computer screen (Apple Multiple Scan Display). Each block was presented for 30 sec with a countdown timer imbedded in each block. During habituation and rest trials, the word "REST" appeared on the screen. Startle eyeblink was elicited by a 40-msec, 100-dB burst of white noise presented binaurally through headphones (Koss TD/60). The 50-msec shock stimulus was delivered through an SD9 Square Pulse Stimulator (Grass Instrument Company) to the median nerve of subjects' left wrist.

Procedure

Participants gave informed consent before testing began. Participants were told that during the course of the experiment they would receive at least one, but not more than three, shocks to the wrist. The shock would occur during, for example, the blue block (threat stimulus) but never during the yellow block (safe stimulus) or during rest periods. Assignment of threat and safe to the two colors was counterbalanced across subjects.

Once the recording electrodes were attached, but before the shock electrode was connected, participants were given six trials of habituation to the startle probes, with 30 ± 2 sec between startle stimulus presentations. Following this habituation procedure, they were reminded of the instructions and the shock electrode was secured to their wrist. Additional six habituation trials to the noise were given that lead directly into the experiment proper. Two blocks consisting of three presentations of each color followed by a 3-min rest period were administered. Colors were presented in strict alternation. First stimulus, threat or safe, was counterbalanced across subjects. After the second rest period, the shock electrode was removed and another 3-min rest period ensued. Only one shock was delivered during the final presentation of the threat stimulus. One startle probe was presented during each presentation of Threat and safe stimuli. The startle probe occurred in the final 8 sec of the stimulus with a minimum of 22 sec between startle probe presentations. Three startle probes were presented during each rest period.

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