Emotion, Motivation, and Anxiety: Brain Mechanisms and Psychophysiology

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The organization of response systems in emotion is founded on two basic motive systems, appetitive and defensive. The subcortical and deep cortical structures that determine primary motivated behavior are similar across mammalian species. Animal research has illuminated these neural systems and defined their reflex outputs. Although motivated behavior is more complex and varied in humans, the simpler underlying response patterns persist in affective expression. These basic phenomena are elucidated here in the context of affective perception. Thus, the research examines human beings watching uniquely human stimuli—primarily picture media (but also words and sounds) that prompt emotional arousal—showing how the underlying motivational structure is apparent in the organization of visceral and behavioral responses, in the priming of simple reflexes, and in the reentrant processing of these symbolic representations in the sensory cortex. Implications of the work for understanding pathological emotional states are discussed, emphasizing research on psychopathy and the anxiety disorders. Biol Psychiatry 1998;44:1248–1263 © *1998 Society of Biological Psychiatry*

Key Words: Emotion, anxiety, brain mechanisms, motivation, fear

Introduction

The aims of this paper are twofold. First, a theoretical model of emotion is presented that is founded on basic experiments from both the animal and human research laboratories. In this view, emotions are held to be products of Darwinian evolution. Expressed emotions developed from primitive actions that facilitated the survival of species and individuals. In man, the evolved affects are best characterized as motivationally tuned states of readiness. The second aim of this paper is to show how this approach generates a useful technology, facilitating particularly the study of human anxiety disorders. Applications are described that can aid in the differential diagnosis of anxiety. Research is presented, showing that psychophysiological analyses conducted during initial patient evaluation can help predict success in therapy.

The Motivational Organization of Emotion

Patterns of emotional expression are highly varied. Theorists have compiled categorical lists that include as many as eight (Plutchik 1962) or 10 (Izard 1977) so-called primary affective states, augmented by various blends. Verbal reports of affects can have a great richness and subtlety of discrimination, with hundreds of emotionally descriptive words available in natural language lexicons. It is proposed here, however, that the evolutionary foundation of emotion has a simpler, two-factor motivational organization. That is, affects are organized by brain systems that adaptively respond to two basic types of stimulation, appetitive or aversive. This biphasic organization of emotion has been proposed by many theorists. Konorski (1967), for example, developed a model based on a typology of unconditioned reflexes and their biological, motivational roles. Exteroceptive reflexes were either preservative (e.g., ingestion, copulation, nurture of progeny) or protective (e.g., withdrawal from or rejection of noxious agents). Preservative emotions include such affects as sexual passion, joy, and nurturance; fear and anger are representative of protective affects. Dickinson and Dearing (1979) further developed Konorski's dichotomy into two opponent motivational systems, aversive and attractive, each activated by a different, but equally wide range of unconditioned stimuli, determining perceptual–motor patterns and the course of learning.

The view that affects might be organized by overarching motivational factors has also been suggested by researchers studying subjective reports of emotion, beginning with Wundt's (Wundt 1896) "mental chemistry." Contemporary studies of natural language categories (Shaver et al, 1987; Ortony et al 1988) suggest that emotional knowledge is hierarchically organized, and that the superordinate division is between positivity (pleasant states: love, joy) and negativity (unpleasant states: anger, sadness, fear). Osgood and his associates (e.g., Osgood et

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al 1957), using the semantic differential, earlier showed that emotional descriptors were primarily distributed along a bipolar dimension of affective valence—ranging from attraction and pleasure to aversion and displeasure. A dimension of activation—from calm to aroused—also accounted for substantial variance. Similar conclusions have been drawn by other investigators based on verbal reports (e.g., Mehrabian and Russell 1974; Russell 1980; Tellegen 1985), as well as facial expressions (Schlosberg 1952).

The view taken here merges these lines of theoretical development. It is postulated that two motivational systems exist in the brain, appetitive and defensive, and that each can vary in terms of activation or arousal. That is, arousal is not viewed here as having a separate substrate, but rather as representing intensity of activation (metabolic and neural) of either the appetitive or aversive system, or the coactivation of both systems (see also Cacioppo and Bernston 1994). The varying emotional states, observed and reported, reflect these basic motive systems. That is, the motive system determines the general behavioral *strategy*, defense or appetitive acquisition. The specific somatic and autonomic patterns of affective responding are *tactical*, in that they are formed by the behavioral context. To give an example from the observation of animals, if a caged rat is subjected to electric shock on the foot pads, the defense system is engaged. It is then likely to 1) flee if an exit is available ("fear"), or 2) attack a cagemate if one is present ("anger"). If shocks are repeated randomly and uncontrollably it will 3) first cower helplessly and then become dull and unresponsive ("depression"). Although emotions may come in many forms, shaped by genetics and learning to fit the demands of local context, their fundamental organization is motivational. Thus, their primary description is in terms of affective valence (i.e., appetitive or aversive) and arousal (intensity of activation).

Patterns of Human Emotion

The behavior of very primitive organisms can be wholly characterized by two responses: direct approach to appetitive stimuli and withdrawal from aversive stimuli (see Schneirla 1959). This modest behavioral repertoire cannot, however, implement the many subgoals of human beings nor effectively deal with the perceptually rich, complex environment in which we live. Elaborate instrumental acts, behavioral delay, and response inhibition have evolved, complicating the path of simple bidirectional goal-related behavior. Thus, emotional behaviors in humans are more adaptive and creative, and less predictable than those of less evolved species.

In human beings, the presumed indices of emotional expression include responses in three reactive systems (Lang 1978): 1) expressive and evaluative language; 2) physiological changes mediated by the somatic and autonomic systems; and 3) behavioral sequelae, such as patterns of avoidance or performance deficits. This is the database of emotion, and a theory of emotion has to cope with its breadth and diversity. The task is not simple. Correlations among emotion indices, within and between systems, are generally quite modest (e.g., Lang 1968; Mandler et al 1961), and the patterns of response can vary considerably within subjects and across different contexts of stimulation (Lacey 1958; Lacey and Lacey 1970). Analysis is further complicated by the fact that, whereas human emotions appear to have derived from primitive actions, the defining response may never actually occur; the boss's insult may incite hostility, but the angry blow is withheld. In this sense, emotions are often dispositions to action, with an accompanying physiology of preparation that is not discharged.

As noted previously, affective expression is in great part a tactical response to contextual demands. Thus, response patterns in emotion have often proven unreliable, reflecting variability in stimuli and methods across experiments. If procedures are held constant, however, and standard emotional stimuli are used, tactical features can be specified and emotion's underlying strategic framework of appetite and defense should be highlighted. We have extensively tested this hypothesis in such a standard context—viewing emotional pictures—as a method for investigating emotion in the laboratory.

Emotion and Perception

Over the past 10 years, we have developed a set of calibrated picture stimuli to use in the scientific study of emotion. There are currently over 600 pictures in the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1997), which includes normative ratings of the pleasure and arousal associated with each picture, obtained from groups of naive subjects. A representative sample of IAPS pictures, distributed in the two-dimensional affective space formed by covarying pleasure and arousal ratings, is presented in Figure 1. The overall boomerang-shaped distribution of these picture stimuli indicates two arms that extend from a common calm, nonaffective base toward either the high-arousal pleasant or the high-arousal unpleasant quadrant. This organization is consistent with an underlying bimotivational structure: two systems of appetitive and aversive motivation that each vary along a dimension of arousal. Despite considerable effort to fill gaps in this affective space (e.g., in the unpleasant–low arousal quadrant) and force a circumplex model, this pattern has remained relatively stable, and is

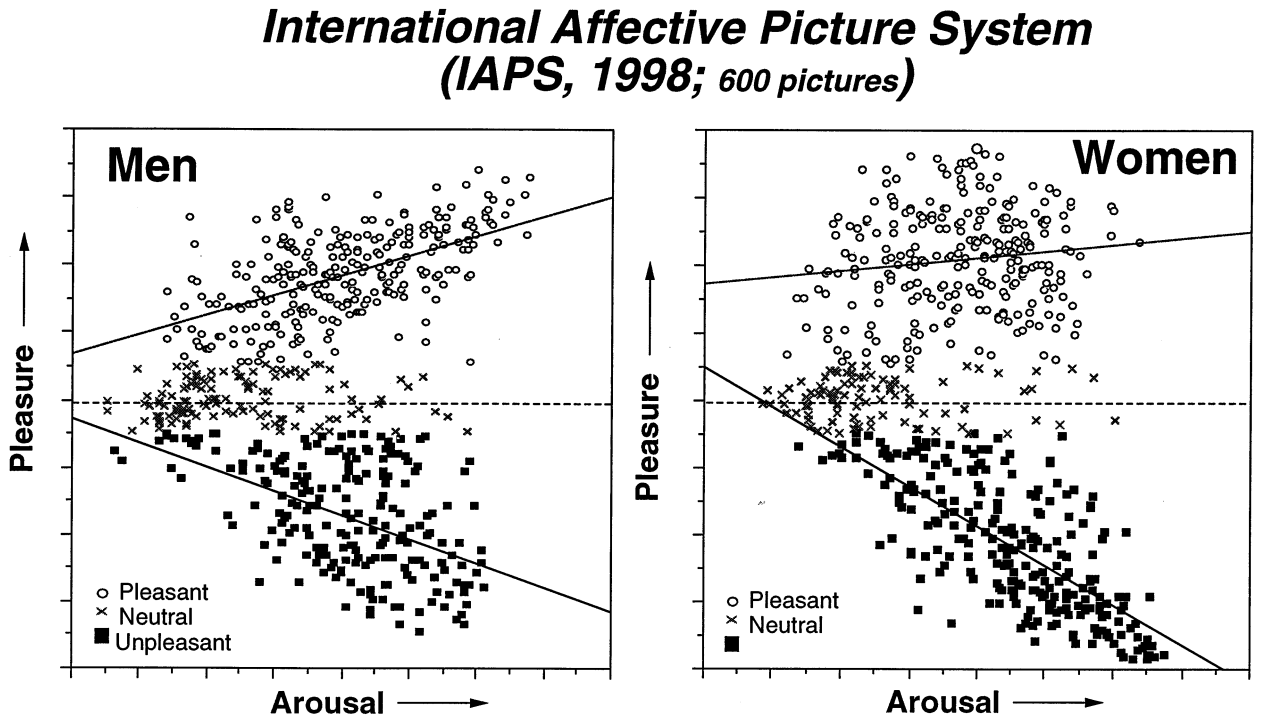

Figure 1. Distribution of pictures from the IAPS standardization sample of men and women, plotted in a two-dimensional affective space, defined by the mean ratings of pleasure (y-axis) and arousal (x-axis) for each stimulus. The separate limbs of the overall boomerang-shaped distributions are consistent with the hypothesis that emotional reactivity is organized by two underlying neural systems—appetitive and defensive—that each vary in arousal.

very similar for collections of acoustic stimuli [International Affective Digitized Sounds (IADS); Bradley et al 1998] as well as verbal materials [Affective Norms for English Words (ANEW); Bradley et al 1998] (see Figure 1).

The Psychophysiology of Picture Processing

Research has demonstrated that these photographic images evoke a broad range of emotional reactions, varying in intensity, and involving both pleasant and unpleasant affect (e.g., Greenwald et al 1989; Lang et al 1993). As Figure 2 illustrates, a number of physiological systems covary significantly with pleasure or arousal, as defined by evaluative judgments. When valence ratings are ranked from the most to the least unpleasant for each subject, facial muscle activity during picture viewing is strongly related to differences in affective valence; corrugator ("frown") electromyographic (EMG) activity increases linearly as pictures are rated as more unpleasant; conversely, zygomatic ("smile") EMG activity increases with judged pleasantness. Heart rate is also responsive to differences in affective valence; unpleasant pictures generally prompt marked deceleration during viewing, whereas greater acceleration is obtained when viewing pleasant pictures.

Other evoked responses vary with changes in rated arousal, rather than affective valence. Skin conductance activity covaries positively with judged arousal, increasing monotonically with increases in rated arousal, regardless of picture valence. The slow cortical response evoked directly by the picture stimuli is also directly correlated with stimulus arousal; both pleasant and unpleasant arousing pictures prompt a marked positive-going slow wave (Cuthbert et al in submission). This positive slow wave is sustained for nearly the entire viewing period, whereas the slow-wave response to neutral pictures is distinctly more negative. These measures, then, index the intensity or activation level of the current motivational state, rather than its direction (i.e., appetitive or defensive).

Behaviors elicited in the context of emotional picture perception also covary with motivational parameters. When first exposed to a new picture, reaction time responses to probes are significantly slower for emotionally arousing, compared to calm, pictures (Bradley et al 1992). These data suggest that new activating images may require more attentional resources at encoding. Choice viewing behavior also covaries with arousal. When normal

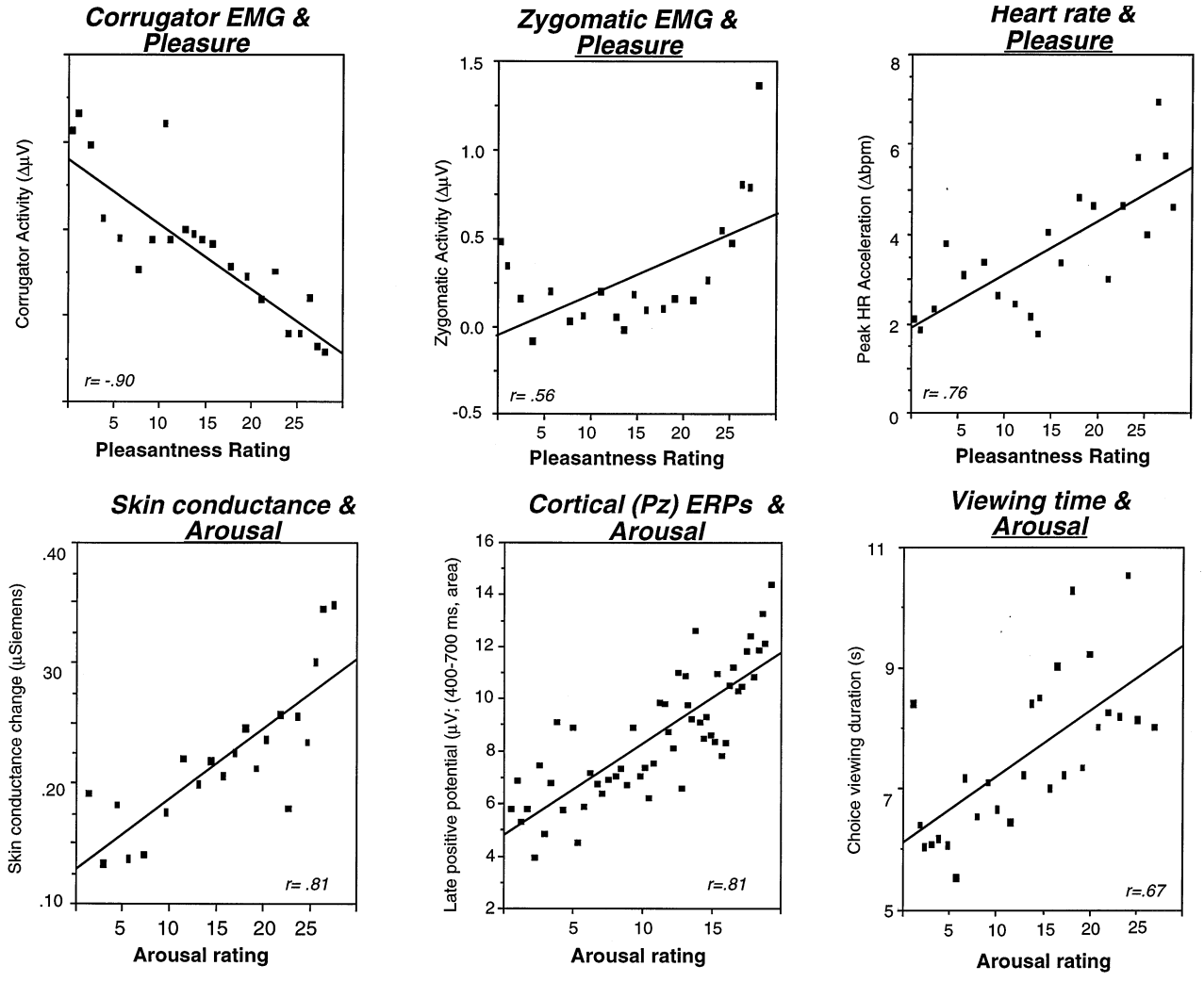

Figure 2. Covariation of affective judgments of pleasure (top row) or arousal (bottom row) with physiological and behavioral responses to picture stimuli. Corrugator EMG (top left), zygomatic EMG (top middle), and heart rate (HR) (top right) each vary consistently with differences in rated pleasure. On the other hand, skin conductance (bottom left), cortical event-related potentials (ERPs) (bottom middle), and viewing time (bottom right) vary consistently with differences in arousal ratings. In each plot, affective judgments are rank ordered for each subject; the graphs depict the mean responses at each rank across subjects.

subjects are placed in a free-viewing context, unpleasant pictures are viewed as long as pleasant pictures, and both are viewed for a longer duration than unarousing, neutral pictures. As might be inferred from the popularity of "slasher" movies, or the habitual slowing of traffic at a roadside accident, normal subjects allocate more processing time to arousing, intense images, regardless of valence. This relationship does not occur if pictures evoke very high levels of distress; when phobics view pictures specific to their fear, a palpable reduction in viewing time is found, consistent with their general avoidant behavior pattern (see Hamm et al 1997).

As the phobia data imply, relationships between specific measures can vary widely for individuals, and to some extent between particular groups. Gender effects are clear. For example, pleasantness ratings covary more closely with facial muscle activity in female than male subjects; on the other hand, skin conductance changes are more closely correlated with arousal ratings in male than in female subjects (Lang et al 1993). Overall, however, motivational variables of affective valence and arousal predominate in organizing the picture perception data. A factor analysis (see Tables 1 and 2) of various affect self-report, physiological, and behavioral measures resulted in a strong two-factor solution, with pleasantness ratings, heart rate, and facial muscles loading on a first, valence factor and arousal and interest ratings, viewing time, skin conductance, and cortical slow-wave electroen-

Table 1. Factor Analyses of Measures of Emotional Picture Processing

Measure	Factor 1 (valence)	Factor 2 (arousal)
Valence ratings	**.86**	−.00
Corrugator muscle[a]	**−.85**	.19
Heart rate	**.79**	−.14
Zygomatic muscle[a]	**.58**	.29
Arousal ratings	.15	**.83**
Interest ratings	.45	**.77**
Viewing time	−.27	**.76**
Skin conductance	−.37	**.74**

Lang et al 1993. [a]Bioelectric potentials from muscles that mediate facial expression.

cephalographic (EEG) activity loading highly on a second, arousal factor. The cross-loadings for all measures are very low. Thus, affects are built around motivational determinants. The motivational states elicited by these affective cues (and the somatic, cortical, and autonomic substrates of their perception) are assumed to be fundamentally similar to those occurring when organisms stop, look, and listen, sifting through the environmental buzz for cues of danger, social meaning, and incentives to appetite.

Neural Imaging: Motivation in the Visual Cortex

Using positron emission tomography (PET), Lane et al (1997) examined regions of brain activity in a group of female subjects, viewing pleasant, neutral, and unpleasant pictures from the IAPS set. The largest blood oxygenation level dependent (BOLD) effects were found for unpleasant pictures—in the thalamus and in Brodmann's visual areas 18 and 19 of the occipital cortex (when activity occasioned by neutral pictures was subtracted out). Unexpectedly, the activity prompted by pleasant pictures was not much different from that for neutral stimuli. This finding was consistent, however, with skin conductance recordings taken coincident with the PET measurement. That is, for this sample of 10 female subjects, pleasant pictures led to significantly less electrodermal activity than unpleasant materials.

Table 2. Sorted Loadings of Dependent Measures on Principal Components

Measure	Factor 1 (valence)	Factor 2 (arousal)
Valence ratings	**.89**	.07
Corrugator muscle[a]	**−.83**	−.10
Heart rate	**.73**	−.02
Arousal ratings	−.11	**.89**
Cortical slow wave	−.06	**−.79**
Skin conductance	.19	**.77**

Cuthbert et al in submission.
[a]Bioelectric potentials from muscles that mediate facial expression.

We recently extended our exploration of brain activity during emotional picture processing, utilizing functional magnetic resonance imaging (fMRI; Lang et al 1998). In this experiment, functional brain activity was monitored in both female ($n = 8$) and male ($n = 12$) subjects. Data were collected while subjects processed pleasant, neutral, and unpleasant pictures. Results again indicated more extensive activity in occipital cortex when viewing both pleasant and unpleasant picture viewing, relative to viewing neutral pictures (Figure 3, upper panel). In general, a larger area of activation was found in the right than in the left visual cortex. Although all stimulus contents activated area 17 in the calcarine fissure, areas specific to emotional stimuli were apparent in Brodmann's areas 18 and 19, in the fusiform gyrus, and at parietal sites. Echoing the PET data, significantly more right hemisphere activation was found in female than male subjects, specifically for unpleasant stimuli (see Figure 3, lower panel). Male subjects, on the other hand, tended to have a larger area of activation for pleasant pictures.

The fMRI data suggest that emotional inputs undergo more processing than nonaffective stimuli at a very early stage in cortical afferent analysis. One explanation is based on research findings with animal subjects by Amaral et al (1992). These investigators suggest that reentrant projections from the amygdala feed back to primary visual cortex. The PET experiment results (Lane et al 1997) are not inconsistent with this view, in that activity temporally coincident with occipital activation was apparent in the left ventral temporal stream, including the region of the amygdala. An alternative view has been offered by Posner (1996). He proposed that projections from cingulate cortex determine attentional priming of the visual area. These different anatomical hypotheses are testable using functional images of the whole brain during picture processing. That is, presumed connections between neural structures can be assessed by covariance methods that assess interacting regions of BOLD activity (e.g., Horwitz 1994).

Motivational Circuits in the Brain

The psychophysiological reactions, patterns of regional blood flow in occipital cortex, and behavioral responses that are all evoked by picture viewing reflect (in their organization) the engagement of neural structures in appetitive or defensive motivation systems. What we know about the brain's motivational systems comes primarily from animal research, particularly behavioral neurophysiology studies of rodents. An outline of the rat's defense motivation system, with its efferent output paths, is illustrated in Figure 4.

Input normally passes from the sense organs to the sensory cortex and then from sensory-specific nuclei of

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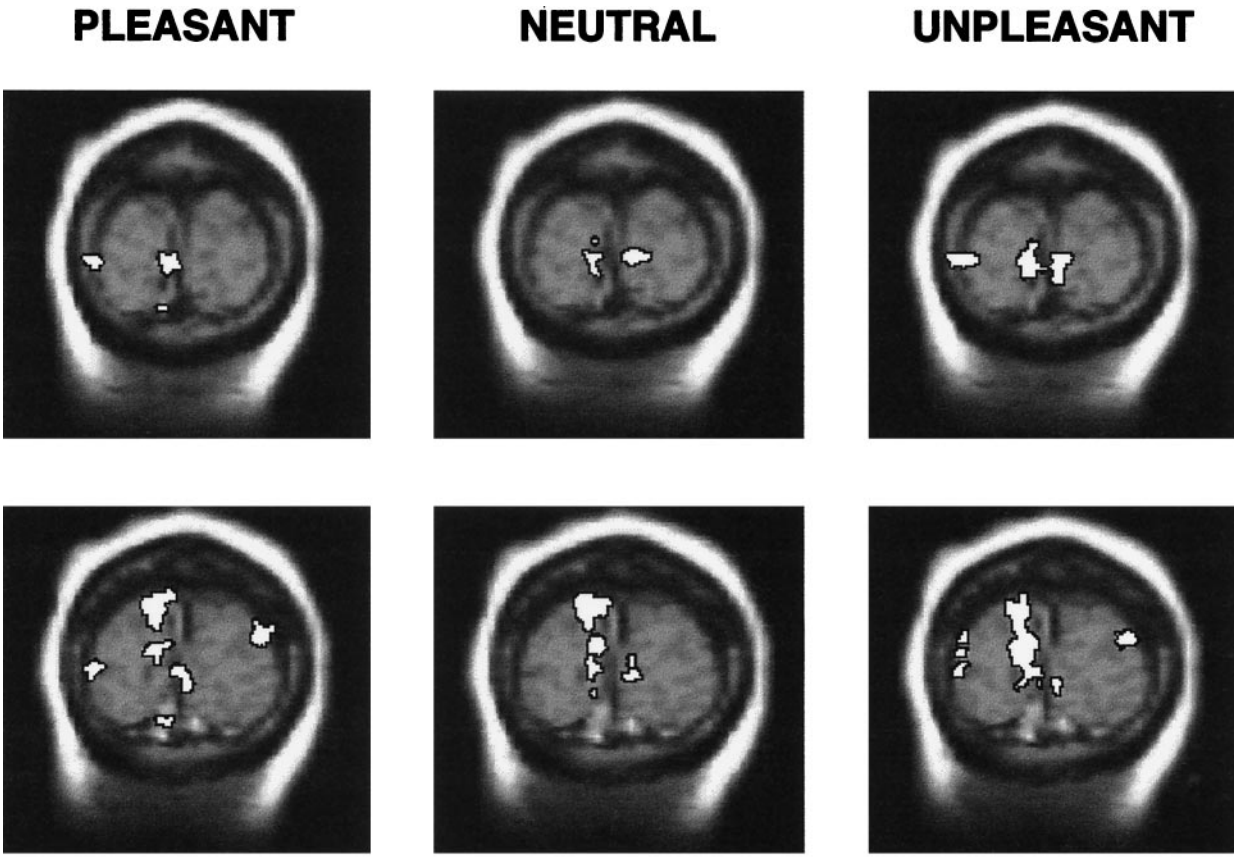

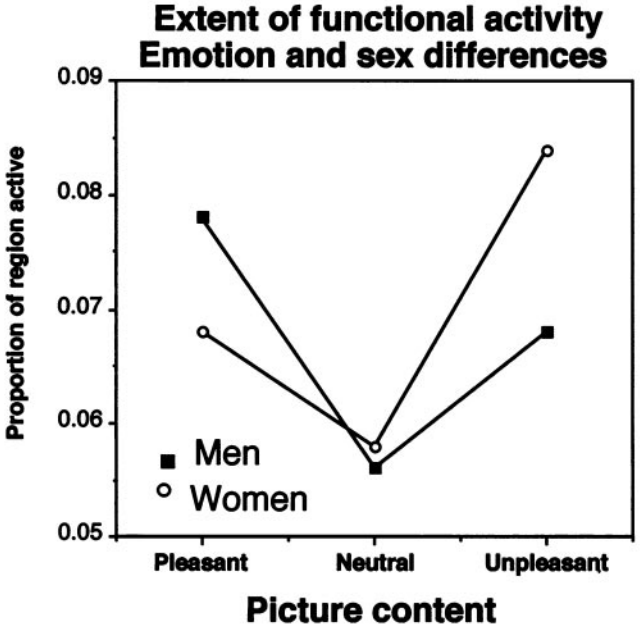

Figure 3. Top: Sites of functional activity during processing of pleasant (left column), neutral (center column), and unpleasant (right column) pictures, compared to no picture processing, as determined from averaging functional maps across subjects. Pixel clusters meeting criteria are depicted in outlined white, located on two successive coronal slices 5 mm thick, with the most anterior slice approximately 10 mm from the occipital pole. Top row: In this most anterior slice, all stimulus picture contents show activity centered on the calcarine fissure; only emotional pictures are beginning to show activity in the right occipital gyrus (MRI view, i.e., from an anterior perspective). Second row: All picture contents continue to show activity centered on the calcarine fissure, as well as in a portion of Area 18 directly above the calcarine fissure. Only emotional pictures show bilateral activity in the occipital gyrus (Lang et al, 1998). Bottom: Functional activity in the right posterior occipital cortex during processing of emotional and neutral pictures for men and women. Women show significantly more activation for unpleasant than pleasant pictures; men tend to show an opposite effect, greater activation for pleasant than unpleasant stimuli.

the thalamus to the amygdala. Efferent to the amygdala, the aversion circuit branches, with each path apparently governing separate response outputs. Direct projections to the nucleus reticularus pontis caudalis modulate the startle response, potentiating the reflex in the context of nociceptive and fear-conditioned stimuli (e.g., Davis 1989, 1997; Davis et al 1987; Fendt et al 1994). Autonomic response (e.g., blood pressure change) is dependent on an intact

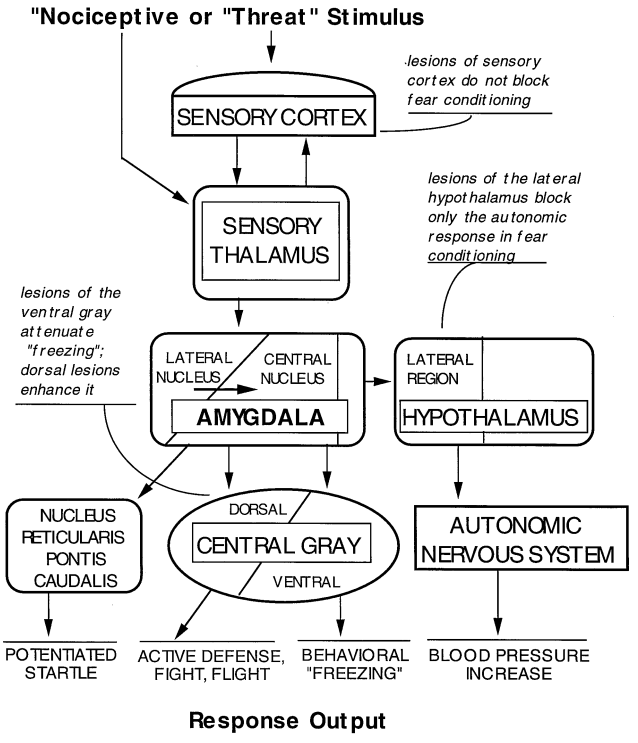

Figure 4. Defense motivation system. Unconditioned and conditioned aversive stimuli proceed from sense receptors to sensory cortex and/or sensory thalamus (see Le Doux 1990). The lateral nucleus of the amygdala receives input signals from the thalamus, transmitting them to the amygdala's central nucleus. There are three important connections efferent to the amygdala: a) a projection from the central amygdala to the lateral hypothalamic area that mediates the autonomic emotional response; b) projections to the midbrain central gray region, which mediates coping behaviors (see Fanselow et al 1995); and c) a direct projection to the nucleus reticularis pontis caudalis, which modulates the startle circuit (see Davis 1989, 1997 for details).

pathway through the hypothalamus (LeDoux 1990), whereas somatic components require an intact midbrain (i.e., periaqueductal central gray). Furthermore, the ventral central gray is the fear "freezing" path, whereas the dorsal gray is a critical part of the fight/flight action circuit (see the data and discussion of Fanselow et al 1995, and the papers edited by Depaulis and Bandler 1991). Taken together, the neurophysiological findings suggest that the amygdala is a key site in the defensive motivational system; structures "downstream" from the amygdala are implicated in the different types of defense behaviors.

Some of these same neural structures are active in appetitive motivation; other nuclei are specific to the appetitive system, mediating different outputs or inhibiting defense responses. The startle reflex, for example, is exaggerated in defensively motivated rats. It is, however, reduced in the context of signals that specifically indicate the animal is safe from painful shock (Falls and Davis 1995). Other work shows that startle is reduced in the presence of a stimulus that has previously been paired with a primary reward (Schmid 1995). Neither startle reduction in "safe" environments nor the inhibition found in the context of reward require amygdala activation. "Pleasure-attenuated startle" does depend, however, on an intact nucleus accumbens (Koch et al 1996). "The finding that the mesolimbic dopamine system is involved in this phenomenon suggests that other parts of the complex limbic–striatal–pallidal circuitry that governs reward-related behavior . . . might also be relevant for the reduction of the ASR (acoustic startle response) in the presence of a stimulus that predicts reward" (Koch and Schnitzler 1997, p 45; see also Robbins and Everitt 1996).

The Emotional Priming Model

In addition to organizing responding to specific affect-eliciting input, the active motivational system exerts a modulatory effect on other processing operations in the brain. This means that memory associations, action programs, and other representations that are linked to the engaged motivational system are specially "primed." That is, they are preset for activation; they have a higher probability of being accessed than other information in the brain (and have a greater potential output strength). Reciprocally, memories and action programs linked to the nonengaged system have a reduced probability and strength of activation. To provide a cognitive example: if we give a subject the category prime "baked goods," his first association to the word "roll" might well be "bread." Conversely, the associations "wagon" or "skates" would be much less likely, and perhaps even actively inhibited. A quite different result would be expected, of course, if the category prime was "toys" or "playthings." Priming is an automatic process (McKoon and Ratcliff 1980). It can take place outside awareness, e.g., when priming stimuli are presented rapidly, below recognition threshold. This mechanism may explain why negative, unpleasant associations are more probable in depressed individuals, or why anxious patients respond more rapidly to "threat" cues.

The most primitive and fundamental motivational priming is at the level of unconditioned exteroceptive reflexes. It will be recalled that reflexes can be sorted (Konorski 1967) according to the primary reinforcement properties of their unconditioned stimuli, either appetitive or aversive, and the consummatory or defensive function of the reflex itself. In the priming view, responses to unconditioned stimuli are modulated depending upon the relationship between: 1) the motivational, biological role of the reflex—appetitive as in salivation or defensive as in pain

withdrawal; and 2) the currently active motivational state, appetitive or defensive, in the neural circuits of the subcortex. An independently evoked defensive reflex should be augmented when the organism is already reacting to an aversive foreground stimulus (i.e., is in a defensive state); this same reflex will be reduced in amplitude when the organism is processing an appetitive foreground. Finally, both these priming effects—potentiation and diminution of responding—are expected to be enhanced according to the level of affective drive or activation.

Startle Modulation

The startle response has proven to be a convenient defensive reflex for testing the above hypotheses. In most mammals, an abrupt sensory event will prompt a chained series of rapid flexor movements that cascade throughout the body (Landis and Hunt 1939). This startle reaction appears to be a primitive defensive reflex that serves a protective function, avoiding organ injury (as in the eyeblink), and acting as a behavioral interrupt (Graham 1979), clearing processors to deal with possible threat. Abruptness is the key to startle elicitation; the risetime of the eliciting stimulus should be instantaneous. In human subjects, sudden closure of the eyelids is one of the first, fastest (occurring within 25–40 msec after startle stimulus onset), and most stable elements in the reflex sequence, and this blink component is measured in the studies reported here. Electromyograph electrodes placed just beneath the eye (see Anthony 1985; Lang et al 1990) sense the bioelectric potentials produced by orbicularis oculi contraction, allowing one to measure the onset latency and magnitude of this muscle activity. Although strong stimuli generate larger and more reliable reflexes, high stimulus intensity is not necessary to evoke a reaction.

According to the motivational priming hypothesis, the defensive startle reflex should be of significantly greater amplitude (and faster) when the aversive motivational system is active, e.g., as in a fear state. Alternatively, if appetitive system activation predominates, as in states of pleasure, the startle reflex should be attenuated (see Figure 5). Evidence for defense system priming of the startle reflex has been found in both animal and human studies of fear conditioning. This was first examined systematically by Brown et al (1951), who compared reflex responses to startle probes (shots from a toy pistol) presented to male rats during neutral or shock-conditioned stimuli at extinction. Results conformed to expectation; animals did indeed react more forcefully when the startle stimuli were presented during fear-conditioned signals (see also Ross 1961; Spence and Runquist 1958). As already noted, appetitive priming of the startle reflex in animals has also been

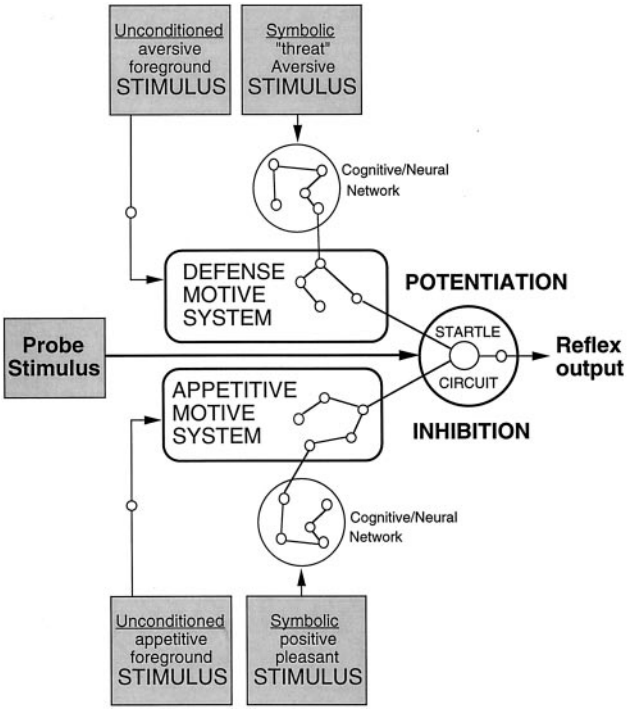

Figure 5. Startle reflex priming. Probe stimuli (acoustic, auditory, or tactile) activate the pontine startle circuit, resulting in startle reflex output. When previous aversive unconditioned or symbolic stimuli activate the defense motive system, its direct projections to the startle circuit potentiate (augment) this reflex response. Alternatively, when the appetitive motive system is active, its projections to the startle circuit result in reflex inhibition.

demonstrated, i.e., probe reflex responses are attenuated both during "safety" signals and in the presence of stimuli associated with reward (e.g., Koch and Schnitzler 1997).

Several studies have confirmed reliable potentiation of the blink response in humans following simple shock exposure or as a function of learned associations that parallel the modulatory patterns previously obtained with rats (Greenwald et al in submission; Hamm et al 1993; Grillon and Davis 1995). In brief, the blink response to a startle probe is generally larger after subjects experience electric shock, and selectively larger to startle probes presented during exposure to a shock-conditioned stimulus than to probes presented during exposure to an unshocked control stimulus. Wide use has been made of startle probes in the assessment of human attention.

Probing Emotional Perception

As mentioned earlier, picture viewing is an observational, intake task in which—like a "freezing" rat or an attentive predator—subjects are generally immobile, with sensory processors engaged. When startle probes are administered

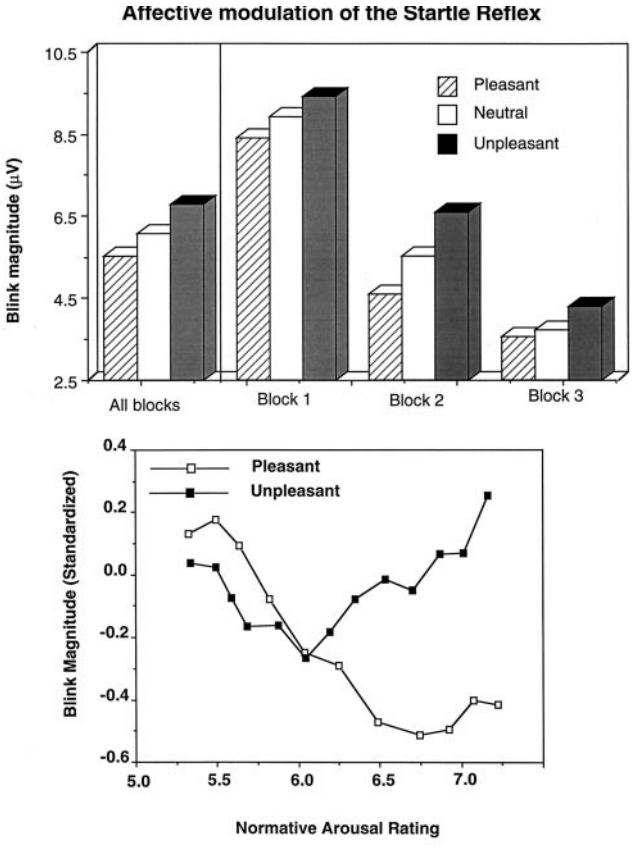

Figure 6. The startle reflex is clearly modulated by affective valence, with blinks elicited when viewing unpleasant pictures potentiated, and blinks evoked when viewing pleasant pictures inhibited, compared to neutral stimuli. Although the overall magnitude of the blink reflex decreases (i.e., habituates) with repeated presentation, affective modulation of the startle reflex continues to occur both when pictures are repeated within a session (top panel, Bradley et al, 1993) and between sessions (bottom panel, Cuthbert et al, 1996).

in this context, results have consistently conformed to the motivational priming hypothesis as Figure 6 illustrates, there is a startle inhibition during pleasant stimuli and strong potentiation when pictures were judged to be unpleasant; the largest startle blink responses occurred during unpleasant content and the smallest during pleasant pictures (e.g., Lang et al 1990; Vrana et al 1988; see Bradley et al in press for a recent review).

These emotional–perceptual effects seem ubiquitous. Balaban (1995) found affective picture modulation of startle probe responses in 5-month-old infants. Jansen and Frijda (1994), using evocative video film clips, and Hamm et al (1990), using IAPS pictures, having obtained the affect–startle effect in European subjects. Interestingly, emotional modulation of the reflex does not seem to depend on novelty. It persists even with repeated presentation of the same picture stimuli. That is, although there is an overall diminution of the startle reflex over blocks of trials with the same pictures, affective potentiation and inhibition remain to the last trial block (Bradley et al 1993). Similarly, affective modulation persists when the same set of pictures is viewed in separate experimental sessions (Bradley et al 1995).

INTENSITY AND MODALITY. Probe studies of picture perception have generally employed binaural startle stimuli in the range of 90–100 dB; however, lower intensities (sufficient to reliably evoke startle) also produce affective startle modulation (Cuthbert et al 1996). Furthermore, significant affective modulation has been shown with monaural acoustic probes. In the monaural case, emotional pictures appear to be differentiated most reliably by probes presented to the left (presumably conferring an advantage in right brain processing) compared to the right ear (Bradley et al 1991, 1996).

Affective modulation of startle is observed for picture stimuli regardless of whether the startle probe is visual, acoustic, or tactile (e.g., Bradley et al 1990; Hawk and Cook 1997), suggesting that modality-specific processes are not primary in these modulatory effects. Furthermore, affective modulation is not confined to visual percepts; when the foreground stimuli consist of short, 6-sec sound clips of various affective events (e.g., sounds of lovemaking; babies crying; bombs bursting), and the startle probe is a visual light flash, the same affect–reflex effect is obtained (Bradley et al 1994). Other researchers have found startle potentiation in subjects smelling unpleasant odors (Miltner et al 1994; Ehrlichman et al 1995), supporting the view that affective reflex modulation is broadly motivational and thus consistent across affective foregrounds of differing stimulus modality.

Psychophysiology and Psychopathology

Consistent with the motivational priming hypothesis, modulatory effects on the startle reflex appear to increase with greater activation in each motive system. Probe startle potentiation is largest for unpleasant pictures that are rated most arousing, whereas conversely, the most arousing pleasant pictures prompt the greatest probe startle inhibition (Cuthbert et al 1996). Thus, individuals with specific phobia, looking at pictures of the phobic object (e.g., snakes or spiders) show startle potentiation well beyond that routinely seen in normal subjects (Hamm et al 1997). The potentiation is, however, clearly selective; that is, these same phobics show the normal reflex inhibition to startle probes when looking at arousing pleasant stimuli (See Figure 7, Sabatinelli et al 1996).

Probe reflex inhibition reflects attentional engagement

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(Graham 1992), as well as an appetitive motive state. Consistent with this view, probes presented during less arousing, unpleasant stimuli—pictures of sad events, pollution, ill people—tend to prompt some reflex inhibition. Strong potentiation is found mainly during viewing of highly arousing stimuli (Cuthbert et al 1996). Interestingly, incarcerated psychopaths show reflex inhibition (relative to neutral pictures) to both arousing pleasant and arousing unpleasant picture stimuli (see Figure 8, Patrick et al 1993). This probe effect is not reflected in the subjective reports of psychopaths; they rate the unpleasant pictures negatively, in the same way as normal subjects. Furthermore, when a subsample of the psychopath group is selected, based on Hare's checklist (Hare 1991), who are high on measures of emotional detachment (e.g., showing blunted affect and no remorse for criminal acts), this reflex inhibition to unpleasant stimuli is further accentuated. These findings are dramatically different from what is seen in the normal population, and the exact opposite of those found in phobic patients. They support the view that psychopaths may have a deficit in the aversive motivational system (see Lykken 1957).

Anxiety Disorders

The model of emotion outlined here has also guided research on the anxiety disorders. Two current lines of research are of particular clinical relevance. The first approach may help to sharpen differential diagnosis, with implications for the development of more effective treatment plans; the second line of inquiry may prove useful in improving prognosis.

FEAR AND ANXIETY. Cook et al (1988) studied the psychophysiological responses of three groups of anxiety patients—simple phobia, social phobia, and panic disorder with agoraphobia—all of whom participated in an assessment of their emotional imagery prior to treatment.

In the imagery procedure, texts were presented (over earphones) that describe neutral or fearful situations, which patients were instructed to use as prompts to an imagined, personal experience of events. Some of the fear scripts described dangerous encounters that are generally fear evoking (e.g., an auto accident, an intruder in the house); other scripts were developed after interview and were specific to individual patients. These latter texts focus on individual clinical problems in an effort to activate patients' specific pathological fear. The scripts of panic patients, for example, would emphasize themes of panic, physiological distress, entrapment, or loss of control, taking place in the supermarket, workplace, or on the highway. During this imagery, heart rate and skin conductance were recorded. Afterwards patients rate their experience of each image for affective valence, feelings of dominance/control, and intensity of arousal.

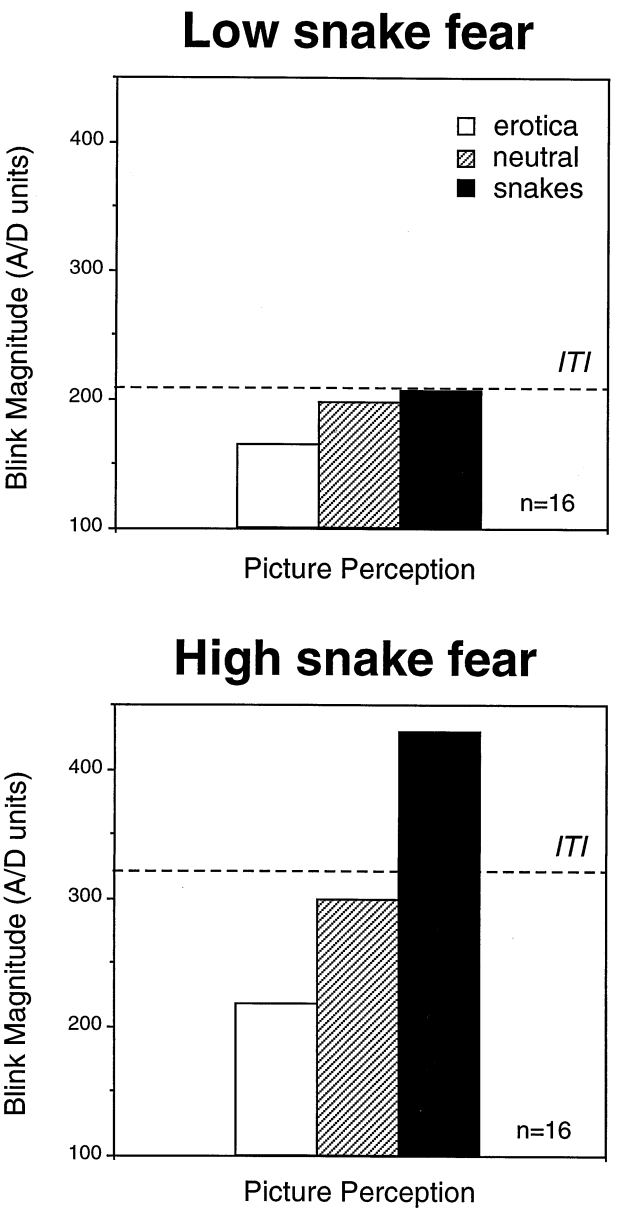

Figure 7. Startle reflex blinks evoked by probes presented during viewing of pleasant erotic pictures, emotionally neutral pictures, and pictures of snakes. Individuals high and low in snake phobia are compared. For snake phobics, startle potentiation during snake pictures clearly exceeds both that found for neutral pictures and for probe stimuli presented during the nonpicture, intertrial intervals (Sabatinelli et al 1996). Startle is in analogue to digital units. Startle magnitude during intertrial interval (ITI) represented by dotted line.

In the overall results of an initial study (n = 133), patients generally showed strong activation of autonomic responses during fear imagery, relative to neutral imagery, and reacted with particular intensity to the phobia-related content. Furthermore, no difference be-

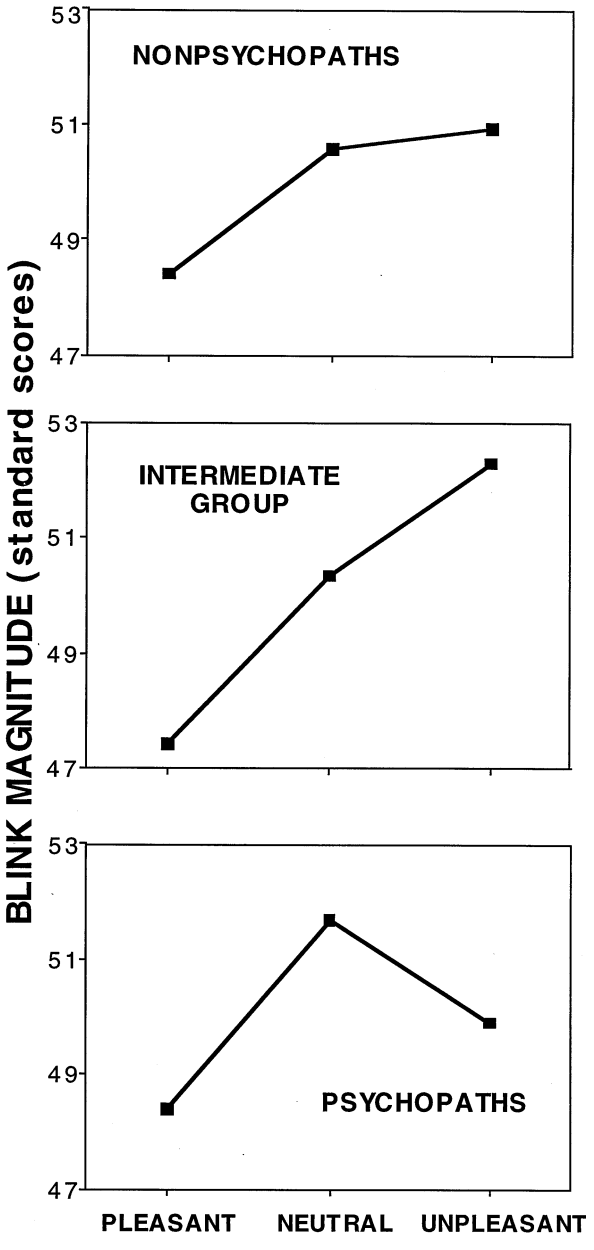

Figure 8. Mean blink response magnitudes for startles presented during viewing of pleasant, neutral, and unpleasant slides, by diagnostic group: top panel = nonpsychopaths; middle panel = mixed group (an intermediate group with some psychopathic features); bottom panel = psychopaths; n = 18 per group. Group assignment was determined by Hare's Revised Psychopathy Checklist (Hare 1991). Startle magnitude is expressed in standard score units (mean = 17; SD = 10) obtained by normalizing raw blink magnitude scores within subjects; onset latency is expressed in raw units (msec) (Patrick et al, 1993).

tween groups was found in their reported fear experience; regardless of diagnosis, patients all rated their personal fear images as very arousing and highly unpleasant.

When autonomic responses were examined, however, a significant group difference emerged in both heart rate and skin conductance reactivity; simple phobics showed the largest overall reactivity to their clinical fear content, and panic patients, the smallest. That is, despite verbal reports of fear that were equal in intensity across groups, the panic patients were minimally responsive physiologically, relative to the robust reactions of simple phobics. At the time, the data were difficult to interpret. In many ways, the patients with panic and agoraphobia could be seen as having a more severe, more generalized disorder. The findings suggested, however, that the distress of panic patients might be less focused, less well organized around specific cues, than is the case with simple phobics.

Recent research with animals provides an interesting perspective on the above clinical experiment. Phillips and LeDoux (1992) and Kim and Fanselow (1992) have reported a significant neurophysiological difference between cue-explicit fear (fear behavior in the presence of an auditory stimulus that has been reliably followed by electric shock) and a more generalized fear of the context in which shock occurs (e.g., the experimental chamber). Both cue and context prompt fearful freezing in the rat; however, whereas hippocampal lesions significantly reduced context freezing, they do not affect the incidence of freezing to an explicit shock cue. A further distinction between cue-explicit and more generalized fear has been made by Michael Davis and colleagues. As already noted (see Figure 4), potentiated startle that normally occurs in the presence of fear cues is eliminated by lesions of the central nucleus of the amygdala. Potentiated startle is also observed after corticotropin-releasing hormone (CRH) is injected into the cerebral ventricles of the rat, inducing a generalized state of arousal, resembling anxiety. Unlike cue-conditioned fear, however, CRH potentiated startle is not eliminated by lesions of the amygdala's central nucleus. Instead, this anxietylike, CRH-driven potentiated startle appears to depend on a different structure, the bed nucleus of the stria terminalis (Lee and Davis 1997). This same bed nucleus (and not the amygdala's central nucleus) is also critical to potentiated startle occurring when rats (naturally light-avoidant animals) are exposed to a brightly lit experimental chamber (Walker and Davis 1997). In brief, the defense system neurophysiological circuit for unconditioned anxietylike reactions appears to involve a different pathway from that engaged by explicit, conditioned fear cues. The failure of human panic patients to show clear cue-specific autonomic nervous system reactivity (e.g., to text-prompted memory imagery), despite clear evidence of high anxiety, may similarly indicate that a different circuit is active in these patients than the one mediating defense reactions to explicit phobic stimuli.

In a new study of 116 patients and control subjects, the

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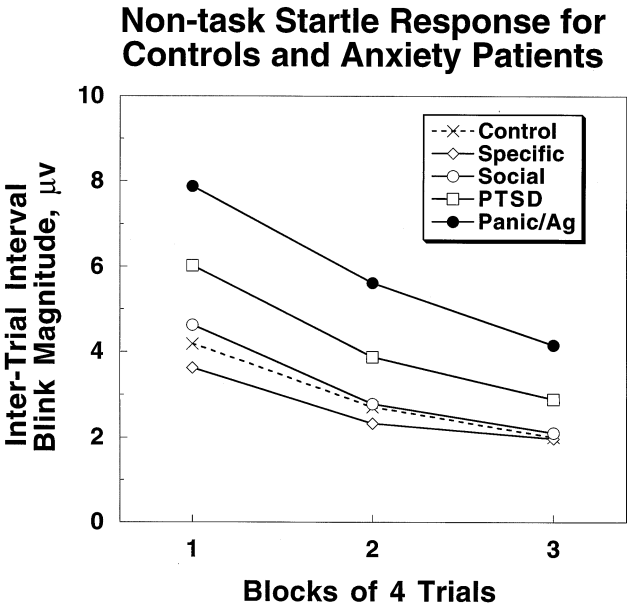

Figure 9. Anxiety group differences in blink reflex magnitude to startle probes administered during three sequential blocks of four rest trials (i.e., during intertrial intervals between imagery cues). Ag, agoraphobia.

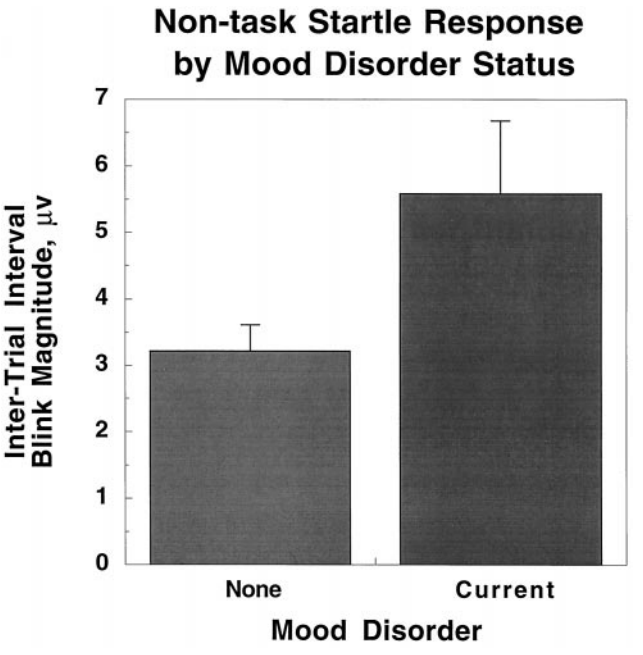

Figure 10. Differences in blink reflex magnitude (during rest trials) between anxiety research subjects with no current comorbid mood disorder and subjects satisfying DSM-IV criteria for a current mood disorder.

startle probe reflex was added to the physiological measures being recorded. As previously observed, heart rate increase during personal fear imagery was again smaller for panic patients, relative to other diagnoses. Furthermore, panic patients also showed the least reflex potentiation to startle probes presented during these images (relative to their neutral scene response). On the other hand, the absolute magnitude of startle reflexes was actually largest for panic disorder. As can be seen in Figure 9, the panic group (along with a newly added posttraumatic stress disorder (PTSD) group) showed significantly larger base startle reactions over trials than other phobic patients. Thus, although panic patients were relatively less reactive than other diagnoses to the specific distress cues specified at interview, the startle findings suggest that—like the light-avoidant rat—they were significantly more activated by the general context (i.e., the novel, perhaps threatening context of psychological test and evaluation).

Startle sensitivity may characterize patients high in negative affect, a temperamental disposition defined by Watson et al (1988). In addition to larger reflexes, the panic patients (along with the PTSD group) had higher scores than simple and social phobics on questionnaire measures of generalized anxiety and depression (all p values $<.01$). In a further exploration of these phenomena, we studied the effects of comorbid mood disorder (DSM-IV diagnosis) on startle magnitude. As can be seen in Figure 10, those in the sample who were also depressed showed significantly larger base startle reflexes than those without this comorbidity. Although these are general phenomena, across diagnoses, it is worth noting that the incidence of mood disorder and the base startle potentiation effect were greatest in the panic disorder group.

IMAGERY AND PROGNOSIS. In an early study of desensitization, Lang et al (1970) recorded heart rate during treatment of snake-phobic subjects. Fear images reported to be maximally frightening—images so distressing that the subject was temporarily unable to proceed—were compared across subjects. The degree of heart rate acceleration evoked by these images was found to be significantly related to measures of therapeutic outcome (averaged behavior test, observer reports, and self-ratings: $r = .75$, $p < .05$). A parallel covariation was found between improvement on these measures of treatment outcome and the degree of heart rate reduction found with repeated fear image exposure ($r = .91$, $p < .05$).

Some years later (Lang 1985), we analyzed data from anxiety-disordered patients who had been seen in the Psychology Department Clinic at the University of Wisconsin. They had all been administered an emotional imagery battery prior to treatment, during which heart rate was recorded, and were subsequently treated with some variant of cognitive or behavior therapy. Therapists' re-

ports and case notes were used to distinguish patients who had been successfully treated from those terminating treatment prior to the resolution of their distress. When these two groups were compared, successful patients again showed faster heart rates during personal fear imagery than were found for unsuccessful cases (Levin et al 1982).

At the University of Florida Fear and Anxiety Disorders Research Clinic, we continue to assess the imagery responses of anxiety-disordered patients prior to treatment. Recently, we analyzed the data from 87 patients whose treatment had been terminated—patients variously diagnosed as simple phobia, social phobia, or panic disorder who either completed or failed to successfully complete cognitive–behavioral therapy. In a discriminant function analysis of the cardiac data, successful patients again showed significantly higher heart rates in anticipation of, and during fear imagery, than did the noncompleters [$R^2 = .19$, $F(2,37) = 4.36$, $p < .05$]. Furthermore, in a larger analysis (including demographic variables, distance from the clinic, diagnosis, questionnaire responses, and physiological reactivity), the heart rate response in imagery was the second best predictor of successful treatment, second only to pay structure (income and insurance), and ahead of the third best predictor, education.

Summary and Conclusions

In the view presented here, emotions are considered to be action dispositions. It is held that affects evolved from reflexive, overt reactions to appetitive or aversive stimulation that served immediate survival functions (e.g., nurturance, sexual approach, fight, flight). The neural mechanisms for these functions are preserved in the human brain in subcortical and deep cortical structures, and are the foundation of human emotion. Anxiety and fear are states in which the defensive components of the motivation circuit are active, and related primitive autonomic and somatic reflexes are engaged. Thus, human emotional arousal can be measured bioelectrically as activity (often subovert) in muscles and glands.

We have tried to show experimentally that these physiological data can importantly elucidate the valence and arousal characteristics of emotion, and can be of significant value to the diagnostician and the therapist. Psychopaths show a clear deficit in defense responding, reacting with probe startle inhibition during stimulation that normal subjects find fearful and excitatory. Anxiety diagnoses differ importantly in patterns of emotional processing, perhaps reflecting neurophysiological circuit variants currently being elucidated in animal research. Thus, simple phobia is a cue-specific disorder, with defense responses readily activated by explicit phobic imagery; panic disorder appears to be less tied to explicit cues, characterized by a more general hyperreactivity that suggests a temperamental sensitivity of the defense system. Finally, it is proposed that the degree to which defense responding is activated by memory imagery may predict subsequent therapeutic success. Patients showing strong heart rate acceleration to phobic cues are more likely than low responders to have completed treatment with a successful outcome.

Overall, the approach described here underlines the importance of animal research in providing a neurophysiological foundation for study of human emotion and anxiety. Psychophysiological measurement (including neural imaging) is clearly the fundamental bridging tool, connecting these advances in basic science to research in psychopathology. The work implies that clinical analysis will need to go beyond traditional interview and testing, integrating behavioral and physiological data into a new conception of emotional disorder, with the goal of explicating pathological affects and devising more effective treatments for anxiety.

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