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Emotion and Pain: A Functional Cerebral Systems Integration

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Abstract Emotion and pain are psychological constructs that have received extensive attention in neuropsychological research. However, neuropsychological models of emotional processing have made more progress in describing how brain regions interact to process emotion. Theories of emotional processing can describe inter-hemispheric and intra-hemispheric interactions during emotional processing. Due to similarities between emotion and pain, it is thought that emotional models can be applied to pain. The following review examines the neuropsychology of emotion and pain using a functional cerebral systems approach. Specific comparisons are made between pain and anger. Attention is given to differences in cerebral function and physiology that may contribute to the processing of emotion and pain. Suggestions for future research in emotion and pain are given.

Keywords Emotion · Pain · Negative emotion · Functional cerebral systems · Neuropsychology

Emotion and pain are considered multidimensional constructs that have received extensive attention in neuropsychological research. Both constructs contain motor, valence, sensory, and physiological components. Emotion and pain may interfere or enhance performance depending on the situation and/or modality tested. The differential effects that are produced as a result of emotion and pain, combined with the fact that everyone experiences emotion and pain, makes the constructs interesting and difficult to study. Research indicates that emotion influences motor (Demaree, Higgins, Williamson, & Harrison, 2002), auditory (Gadea, Gomez, Gonzalez-Bono, Espert, & Salvador, 1995), somatosensory (Herridge, Harrison, & Demaree, 1997; Lee, Meador, Loring, & Bradley, 2002), visual (Klaasen, Riedel, Deutz, & Van Praag, 2002; Coupland, Sustrik, Ting, Li, Hartfeil, et al., 2004), and cardiovascular systems (Snyder, Harrison, & Shenal, 1998; Gendolla, Abele, & Krusken, 2001). Similarly, pain produces relative changes in motor (Urban, Solinski, Best, Rolke, Hopf, et al., 2004), auditory (Demaree & Harrison, 1997), somatosensory (Valeriani, Tinazzi, Le Pera, Restuccia, De Armas, et al., 2004), visual (Herridge, Harrison, Mollet, & Shenal, 2004), and cardiovascular systems (Fillingim, Browning, Powell, & Wright, 2002).

Negative mental and physical health problems that result from disorders of emotion and pain are an additional reason that neuropsychology has devoted so much attention to them. For example, depressive patients report negative emotions such as feelings of worthlessness, guilt, and anxiety that co-occur with fatigue, aches and pain, and gastrointestinal disturbances (Delgado, 2004). Heightened levels of hostility are associated with aggression towards others (Spielberger, Johnson, Russell, Crane, Jacobs, et al., 1985), increased cardiovascular liability (Davis, Matthews, & McGrath, 2000), and the development of cardiovascular disease (Matthews, Gump, Harris, Haney, & Barefoot, 2004). Chronic pain is related to anger (Burns, Kubilus, & Bruehl, 2003), depression (Delgado, 2004), lack of activity, obesity, reports of poor health, high levels of stress, and high usage of or dependence on medication (Meana, Cho, & DesMeules, 2004). Of particular interest is that the aforementioned research indicates a connection between emotional and pain disorders. Emotion often produces pain, and pain often results in emotional changes. Given the impact that emotion and pain can have on cognitive, behavioral, and physiological functioning, it is important to examine the neuropsychology basis of both

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emotion and pain. Additionally, studying the interactions of these constructs may provide new insight and lead to better health outcomes.

Several current, influential neuropsychological models of emotion include the right hemisphere model, the valence model, and the approach/withdrawal model. Despite the similarities and connections between emotion and pain, research in pain has not produced comparable models for cerebral processing of pain. Models of pain describe pain as occurring in specific brain structures, focus on aspects of peripheral processing rather than central processing, or describe pain as a pattern of activation in several disperse cortical and subcortical regions. The models fail to address how pain processing affects integrative cerebral functioning. Additionally, they are marred with the fact that everyone has had their own experience with pain and subsequently defines and approaches the construct differently. The following review attempts to overcome the handicaps that exist in pain research through looking at cerebral processing rather than the pain construct. The review applies models of emotional processing to describe pain processing and examines how functional cerebral systems are affected by emotion and pain. Additionally, the review specifically relates anger and pain through the use of functional cerebral systems.

The review begins by defining the functional cerebral systems approach, the right hemisphere model, the valence model, and motivational models of emotion in terms of emotion and pain. The neuropsychological models are used to examine cerebral processing between different brain regions (i.e., anterior-posterior, left-right) in emotion and pain. These specific models of emotion were chosen due to their support and popularity in the emotion literature. Additionally, the review demonstrates that these emotional models are readily adaptable to describe pain processing. The review examines how emotion and pain influence functional cerebral systems. More specifically, changes in cerebral activation, arousal, and physiology (focusing on cardiovascular measures) as a result of emotion and pain are considered.

The review also examines specific relationships between negative emotion and pain. In particular, anger is an emotion that strongly interacts with pain. As will be presented, this may be due to the fact that anger and pain activate the same functional systems. Although other negative emotions, such as depression, are also closely related to pain, authors contend that the relationship of pain and anger has been neglected due to a focus on the relationship between depression and pain (Janssen, Spinhoven, & Brosschot, 2001). Furthermore, the review focuses on acute pain studies due to the fact that clinical pain produces plastic changes in the CNS (Treede, Kenshalo, Gracely, & Jones, 1999). Anger occurs more commonly from acute pain, while depression is strongly related to chronic pain (Ruoff, 1996).

While the focus of the current review is to integrate emotion and pain processing at the cortical level, this should not underscore the importance of subcortical structures. Several subcortical structures may play an important role in both emotional and pain processing. Lee, Meador, Loring, Allison, Brown, et al. (2004) found evidence supporting a role for the anterior cingulate cortex, amygdala, and the cerebellum in emotional processing. With respect to the integration of pain and emotion, the anterior cingulate cortex may be particularly important. It is hypothesized that the affective dimension of pain emerges as nociceptive input ascends from the spinal cord to brainstem and limbic areas (see Price, 2000, 2002; Rainville, 2002 for reviews). Price (2002) describes a model of pain processing whereby lower brainstem and limbic areas contribute to arousal, autonomic, and somatomotor activation during pain, while the primary role of assigning affect to nociceptive input may occur at the level of the anterior cingulate cortex. Bush, Luu, and Posner (2000) describe the anterior cingulate cortex as an area that processes sensory and emotional input. Further, the anterior cingulate cortex is involved in attention and motivational networks and has extensive connections with the prefrontal cortex (Devinsky, Morrell, & Vogt, 1995) and the parietal cortex (Posner & DiGirolamo, 1998). Continued study of the anterior cingulate cortex and its connections may prove to be particularly useful in integrating pain and emotion at the cortical level.

Functional cerebral systems approach

A "functional system" (Luria, 1973) describes the use of interconnected brain regions to complete a task. For example, it would be incorrect to talk about a specific location of the brain that is responsible for conversational speech. Rather, conversational speech requires the comprehension of speech from another individual, generation of words, a coordinated series of motor movements, and the ability to put the words together in a logical linguistic fashion. Thus, while one area may perform a function (i.e., Broca's area for speech production), a functional system arises through the integration of multiple areas (i.e., connections between Broca's area, the pre-motor strip, and Wernicke's area). In a recent review of functional systems theory, Sudakov (2004) explained that functional systems are integrative, arranged in a hierarchy, sequential, and have multiple interactions with each other. Further, activity in one functional system affects activity in other functional systems. The interactions between systems are dynamic and seek to maintain an optimal level of output (Sudakov, 2004).

Understanding how integrative brain function occurs requires recognition of the division between anterior motor functions and posterior perceptual functions, as well as the division between right and left hemispheres (Tucker & Williamson, 1984). Borod, Bloom, Brickman, Nakhutina,

and Curko (2002) described the intrahemispheric factor (frontal vs. temporal, parietal, and occipital) and the interhemispheric factor (right vs. left hemisphere) as critical divisions in brain organization that must be considered in neuropsychological investigations. Anterior or frontal functioning includes higher order executive functions such as decision making, organization and planning, goal directed behavior, inhibition, motor expression, and the regulation of mental activity and cardiovascular systems. The posterior brain (which includes the temporal, parietal, and occipital lobes) may primarily function in obtaining, processing, and storing information; in the regulation of arousal; and in the regulation of cardiovascular tone. The posterior brain includes auditory, somatosensory, and visual cortex. It is primarily concerned with perception and comprehension of sensory stimuli. Function in either the frontal lobes or posterior brain can be affected by function in the other region due to intimate anatomical connections between the frontal lobes and the rest of the brain.

Similarly, functional asymmetries exist for the right and left hemispheres. The right hemisphere is most commonly associated with processing spatial stimuli, facial recognition (Mesulam, 2000), arousal mediation (Heilman & Gilmore, 1998), and negative emotion (Borod et al., 2002). The right hemisphere is described as an integrative, Gestalt-like processor. Left hemisphere functions include verbal processing, reading comprehension (Mesulam, 2000), arousal inhibition (Heilman & Gilmore, 1998), awareness of body space (de Jong, van der Graaf, & Paans, 2001), and processing of positive emotion (Lee et al., 2002). The left hemisphere is described as processing information in a logical and sequential fashion. It is important to note that while these asymmetries are common, they are not as straightforward as is presented. Individual differences in lateralization of functions may exist based on handedness (Pauli, Wiedemann, & Nickola, 1999b), sex (Crews & Harrison, 1994), age (Alden, Harrison, Snyder, & Everhart, 1997), or personality characteristics (Compton & Weissman, 2002). Additionally, while each division is functionally different, they are intimately connected via neural fibers and pathways. These connections are responsible for information transfer between neuroanatomical divisions and have given rise to several important theories that describe how functional cerebral systems interact.

It is theorized that cerebral processing in each cerebral division is affected by the distance between them or "functional cerebral space" (Kinsbourne & Hicks, 1978). The concept of functional cerebral space describes how one task may interfere with or facilitate another task as a function of the distance between cerebral regions involved in each task. Interference occurs when two tasks are competing for the same cerebral resources. Competition produces decrements on the less important task due to increasing processing demands in a particular system (Kinsbourne & Hiscock, 1983). For example, reading out loud and tapping your right finger both require the use of the left frontal lobe. Research indicates that reading out loud while simultaneously tapping your right finger produces a disturbance in right finger tapping (Bowers, Heilman, Satz, & Altman, 1978). In contrast to the interference effect, one task may also facilitate another task. Laterality research indicates an advantage for the left hemisphere on tasks that require language processing and an advantage for the right hemisphere on tasks that require negative emotional processing. Van Strien and Heut used the facilitation effect to improve right hemisphere performance on a language task. Prior to completion of a language task the authors activated or primed the right hemisphere with threatening words and were able to demonstrate improved left visual field (right hemisphere) performance on a letter recognition task (Van Strien & Heut, 1995).

Alternate theories describe cerebral functioning as a dynamic result of activation or deactivation that occurs as result of the system attempting to "balance" itself (Tucker & Williamson, 1984). According to the model, relative activation in the left frontal lobe during speech production may lead to relative deactivation in the right frontal lobe. Deactivation may also occur in the left posterior cortex due to frontal inhibition of posterior systems (Yamaguchi & Knight, 1990). Bell and Fox suggest that there may be an inverted U-shaped function that describes how cerebral activation influences cognitive performance. A "normal" level of hemispheric arousal may be advantageous to cognitive performance, while "extreme" levels of hemispheric arousal may be disadvantageous (Bell & Fox, 2003). More recent work by Liotti and Tucker (1998) and Tucker, Derryberry, and Luu (2000) suggests that connections between cortical and subcortical systems may be important in mediating interactions between hemispheres and cerebral regions. However, due to the plethora of information that exists on activation of limbic structures in emotion and pain, the following review focuses specifically on cortical activation. When behavioral measures are used, cortical activation or deactivation is generally reported by increases or decreases in performance on tasks that are reported to tap specific cortical areas. Alpha suppression in EEG studies of affective laterality generally is referred to as cortical activation (Davidson, 1988), while increases in slow wave delta bands are generally referred to as cortical deactivation. However, others have used beta magnitudes to examine activation (i.e., Foster & Harrison, 2004). Functional magnetic resonance imaging studies (fMRI) and PET use changes in regional cerebral blood flow to determine activation or deactivation. Increases in blood flow indicate increased activation, while decreases may be indicative of deactivation.

A final component that may influence functional cerebral systems is arousal. Heilman and Gilmore define arousal with both behavioral and physiological components. Behaviorally

arousal refers to an alert, awake, and prepared organism. Physiologically, arousal is defined by the anatomical area of discussion. For example, arousal in the CNS refers to excitation of neurons or the ability of the neurons to fire when activated. However, outside the CNS, arousal usually refers to increases in the sympathetic tone or activation of the heart (Heilman & Gilmore, 1998), and is measured by changes in systolic BP, diastolic BP, and heart rate. Arousal is important in describing functional cerebral systems because it may be intimately linked to attention and our ability to process sensory information. Reduced cortical and autonomic arousal is found in patients with right hemisphere damage (Morrow, Vrtunski, Kim, & Boller, 1981; Zoccolotti, Scabini, & Violani, 1982). Additionally, arousal may play a role in motivational and goal directed behavior. These factors influence what can and will be processed.

The current review uses theories of functional cerebral space, cerebral activation, and arousal to examine how emotion and pain affect cerebral functioning across different divisions of the cerebral hemispheres. Although this approach is not new, the current paper provides an integrated and updated review of cerebral function in two constructs that have traditionally been difficult to define. Additionally, the recent surge in data from imaging studies has moved away from an integrated view of brain processing and often publications focus on specific areas of the brain that are activated during completion of a task (Raichle, 2003). Application of functional cerebral systems theory to emotion and pain processing may help account for the wide range of cognitive, behavioral, and physiological outcomes that occur as a result of emotional or painful stimuli.

Neuropsychology of emotion

Emotion includes a complex mix of cognitive, affective, behavioral, and physiological components (Thayer & Lane, 2000). Emotions promote adaptation and serve complex decision making processes (Davidson, 2003a). Heilman and Gilmore (1998) describe emotion as having valence, arousal, and motor activation components. Davidson stated that emotion contains many different subcomponents that are involved in the production of behavioral, autonomic, and subjective responses associated with emotional regulation and retrieval. Neuropsychological models that attempt to explain emotion must integrate these components into a functional network or system that can guide us through the processing and expression of emotion. Influential models in emotion include the right hemisphere model, the valence model, and the approach/withdrawal model. Each of these models provides a contribution to the understanding of the functional cerebral system for emotional processing.

Right hemisphere model

The right hemisphere model describes the right hemisphere as being specialized for all emotional processing. For several decades, literature on the neuropsychology of emotion has hypothesized that the right hemisphere is important for emotional processing. The right hemisphere was first linked to emotional processing through lesion studies (e.g., Denny-Brown, Meyer, & Horenstein, 1952). Recent work within brain damaged populations continues to support the model. Borod et al. (2002) reviewed cases of unilateral brain damage and found support for the right hemisphere model in the perception and expression of emotion across facial and prosodic communication channels. An analysis of patients with right and left hemisphere damage revealed that all participants were able to recognize happy emotions, but participants with right hemispheric damage were impaired in recognizing negative emotions (Adolphs, Damasio, Tranel, & Damasio,1996). Additional work has analyzed emotional deficits resulting from brain damage in relation to lesion location. Data indicate that right medial frontal lesions result in the inability to express emotional prosody (Heilman & Gilmore, 1998; Heilman, Leon, & Rosenbek, 2004), while temporal-parietal lesions are associated with the inability to comprehend emotional prosody (Heilman, Scholes, & Watson, 1975; Ross, Harney, deLacoste-Utamsing, & Purdy, 1981). This is in contrast to left temporal-parietal lesions that generally cause the inability to comprehend propositional speech, and left medial frontal lesions that cause a reduction in verbal fluency or the expression of propositional speech.

Empirical research in non-brain damaged populations provides additional support for the right hemisphere model. In the auditory modality, Bryden and MacRae (1989) found a left ear advantage (right hemisphere processing) for the identification of emotion. Similarly, a left ear advantage was found for the emotional quality of tonal sequences (Bryden, Ley, & Sugarman, 1982). Harrison and Gorelczenko (1990) found support for the right hemisphere model in the visual modality. Participants identified facial affect faster when faces were presented to the left visual field (right hemisphere). Facial expression of emotion may also be more dependent on the right hemisphere. Dimberg and Petterson (2000) found that facial electromyography activity in response to emotional stimuli was larger on the left side of the face, indicating a right hemisphere dominance for spontaneously evoked emotional expression. In a review of 49 studies of facial asymmetry in the expression of emotion, Borod, Haywood, and Koff (1997) concluded that the left hemiface (right hemisphere) was more involved than the right hemiface (left hemisphere) in the expression of emotion. The authors concluded that the results provided strong support for right cerebral dominance in emotional expression.

Borod (1992) suggests that right hemisphere advantage for emotion arises from the fact that emotion has many characteristics (e.g., nonverbal, spatial, integrative, and patterned) that the right hemisphere is specialized to process. Several other authors have suggested that the right hemisphere's advantage for emotional processing may be due to a greater involvement of the right hemisphere in autonomic responses and arousal (Heller, 1993; Heilman, 1997) that occur with emotion. Viewed from a functional systems perspective, relative right hemisphere activation due to autonomic reactivity and arousal mediation may lead to a relative decrease in left hemisphere activation, giving rise to right hemispheric processing of emotion.

Right hemisphere activation in emotion may also be influenced by dynamic activation between the right-anterior cerebrum and the right posterior-cerebrum. Right frontal activation may relate to valence (Heilman, 1997), while right posterior activation may relate to arousal (Heller, 1993; Heilman, 1997). Additionally, relative activation in the anterior or posterior may influence the activation in opposing region. Differential activation patterns may lead to dysfunctional emotional processing. For example, in a quantitative EEG (QEEG) investigation of a patient with anger problems, Everhart and Harrison (1995) found that episodes of anger were accompanied by an increase in delta magnitude over the right frontal lobe concurrent with increased beta magnitude over the temporal lobe. Neuropsychological models of depression also focus on anterior-posterior cerebral activation patterns that lead to depression (e.g., Heller, 1993; Tucker, 1993; Crews & Harrison, 1995; Shenal, Harrison, & Demaree, 2003).

Valence model

Although the right hemisphere model is well supported, other theories of emotional processing have been proposed that may be able to better describe processing anomalies related to emotion. Lesion studies, lateralization studies, and imaging studies have discovered functional differences between the left and right hemisphere in the processing of emotion. In an investigation of patients with unilateral cerebral damage, Adolphs, Jansari, and Tranel (2001) concluded that the perception of negative valences relies primarily on the right hemisphere, whereas positive valences are processed by both the right and the left hemispheres. Additionally, it is noted that damage to the right hemisphere produces a euphoric reaction vs. a catastrophic reaction that occurs with damage to the left hemisphere (Heilman & Gilmore, 1998). Burton and Labar (1999) stated that lesions in the left hemisphere cause a disinhibition of negative affective valences of the right hemisphere thereby causing a release of negative emotion, while right hemisphere lesions result in the expression of positive emotion through disinhibition of the left hemisphere.

Additional support for the functional differences between the left and right hemispheres in emotional processing is provided by tachistoscopic presentation of emotional faces. Reuter-Lorenz, Givis, and Moscovitch (1983) presented happy, sad, and neutral faces to normal participants. Results indicated that reaction times to happy faces in the right visual field (left hemisphere) were faster, while reaction times to sad faces were faster in the left visual field (right hemisphere). A similar design was used by Harrison and Gorelczenko (1990) who found an overall processing advantage for emotional faces when they were presented to the right hemisphere; however, the advantage was most prominent during the presentation of angry faces.

Further evidence of left hemispheric processing in positive emotion and right hemispheric is provided by imaging studies. Diego, Field, Sanders, and Hernandez-Reif (2004) found that moderate massage therapy led to a decrease in anxiety and stress, and shifts to greater left frontal EEG asymmetry. This evidence suggests that reduction in negative affect or induction of a positive affective state occurs with left frontal activation. Petruzzello, Hall, and Ekkekakis (2001) found that participants with greater left frontal EEG activation exhibited an increased positive reaction to exercise relative to participants with greater right frontal EEG activation. Blair, Morris, Frith, Perrett, and Dolan (1999) found increased right frontal glucose metabolism during the perception of angry faces. In a QEEG investigation of emotional memory and cerebral activation, Foster and Harrison (2002) found a significant positive correlation between the subjective intensity of angry memories and cerebral activation in the right frontal and right temporal cortices. Additional EEG data suggest that greater right frontal activation is associated with negative affect, while greater left frontal activation is associated with positive affect (Tomarken, Davidson, Henriques, 1990; Davidson, 1995). However, Bell and Fox (2003) failed to find baseline frontal asymmetries in groups of participants who scored high in either negative or positive affect. They hypothesized that this may be due to the broad range of emotions that can be classified as negative affect. Fox (1994) suggests that not all types of negative affect are associated with increased right frontal activation.

Despite some controversy, the cumulative data have led to the valence model of emotional processing. The model states that the right hemisphere is specialized for negative emotion, while the left hemisphere is specialized for positive emotion. Recent additions to this model propose that functional differences may also exist in the expression and perception of emotion. Borod (1992) proposed that the left and right frontal lobes are specialized for the expression of positive and negative emotion, but the right posterior cortex is dominant for the perception of emotion. The valence model is supported by characteristics of positive and negative emotion, and functional processing asymmetries between the

cerebral hemispheres. Positive emotions may be more communicative and linguistic, requiring left hemispheric processing (Borod, Koff, & Buck, 1986; Borod et al., 2002). In contrast, negative emotions are related to danger or survival and require multimodal contributions, a quick scanning system, and Gestalt right hemispheric processing (Borod et al., 2002).

Neurochemical properties of the left and right hemispheres may also account for differences in emotional processing. Dopamine, a neurochemical associated with positive affect (see Ashby, Isen, & Turken, 1999 for a review) is found at higher levels in the left hemisphere (see Tucker & Williamson, 1984; Wittling, 1995 for reviews). Alternatively, the right hemisphere uses more norepinephrine and serotonin (see Tucker & Williamson, 1984; Wittling, 1995 for reviews). Altered levels of norepinephrine and serotonin are associated with negative affect such as, hostility, aggression (Cleare & Bond, 1997), and depression (Flory, Manuck, Matthews, & Muldoon, 2004).

Motivational models

Motivational models of emotion focus on motor activation or the behavioral responses that are motivated by an emotion. Approach behaviors or states lead to greater left hemispheric activation, while withdrawal behaviors or states lead to greater right hemispheric activation in the frontal cortex (Davidson, 1993, 2000). Gray (2001) stated that the distinction between approach and withdrawal emotional states is conceptually one of the clearest and best validated distinctions in emotion. In contrast to the valence model, left frontal activation is not associated with positive valence, but rather a behavioral approach state, whereas right frontal activation is associated with a behavioral withdrawal state and not negative valence (Harmon-Jones, 2004a). This distinction is important due to the fact that certain emotions, such anger, have a negative valence but may produce behavioral approach rather than withdrawal.

Davidson's (1993) motivational model describes activation of the left frontal lobe as resulting in approach-related behavior, while activation of the right frontal lobe is associated with withdrawal-related behavior. Davidson (2003b) states that left-sided prefrontal cortex (PFC) activation is required for the initiation of behavior related to appetitive goals and that hypoactivation of the left PFC may result in depression. Alternatively, right-sided PFC activation is related to behavioral inhibition and vigilance that is associated with negative or aversive emotional states and traits.

Gray (1990) details a Behavior Activation System (BAS) and a Behavior Inhibition System (BIS) for emotion. The BAS is related to emotions such as "hope" and "happiness," while the BIS is related to emotions such as "anxiety" and "fear." Personality measures relating to the BAS and BIS significantly correlate with anterior brain asymmetry indicative of approach or withdrawal states (Harmon-Jones & Allen, 1997; Sutton & Davidson, 1997).

Heilman and Gilmore (1998) describe an approach/withdrawal system dependent on interactions between the anterior and posterior brain. The authors state that the right hemisphere has a special role in motor activation or for preparing an organism to respond to a stimulus. The frontal lobes are described as mediators of avoidance behaviors and the parietal lobes as mediators of approach behaviors. These ideas are supported by evidence from lesion studies. Lesions of the frontal lobes lead to the inability to inhibit responses, manual grasp responses, and inappropriate approach behaviors. Consequently, frontal lobe lesions produce approach behavior as a result of disinhibition of parietal lobes. The parietal lobes (which mediate approach) are normally inhibited by the frontal lobes, when the frontal lobes are lesioned or deactivated the parietal lobes become disinhibited, producing excessive approach behavior. Lesions of the parietal lobes lead to neglect, deviations of eye, head, and arm movements, inability to respond, and withdrawal behaviors (Heilman & Gilmore, 1998). This increase in withdrawal behavior may be a result of increased activation of the frontal lobe due to a decrease in parietal activation, leading to inhibition or suppression of approach behavior. Schutter, Putman, Hermans, and van Honk (2001) found support for parietal mediation of approach behavioral through measurement asymmetrical activation of EEG activity.

Incorporating the valence and motivational models of emotion has traditionally been difficult because emotions such as anger or hostility have a negative valence, but can produce approach behaviors. High trait measures of anger, hostility, and aggression and anger induction have been found to correlate with increased baseline levels of left relative to right frontal activation (Harmon-Jones & Allen, 1998; Harmon-Jones, 2004b; Harmon-Jones & Sigelman, 2001). Harmon-Jones (2004a) suggests that anger generates approach behaviors that are aimed at resolving the anger, which may lead to acts of aggression.

However, work done by Harmon-Jones is at odds with prior research indicating right hemisphere function in negative emotion (i.e., Demaree et al., 2002; Foster & Harrison, 2004; Burton & Labar, 1999; Blair et al., 1999). To overcome the discrepancies it may be necessary to look at cerebral activation in brain areas other than the frontal lobes. In two case studies of patients with hostility and anger problems, it was found that hostility resulted from deactivation of the right frontal lobe and increased activation of the right temporal lobe (Everhart & Harrison, 1995; Demaree & Harrison, 1996). These cases should be interpreted with caution as they are single subjects with extreme anger disorders. Demaree and Harrison (1997) found that high hostile participants activated the right hemisphere

in response to a pain stressor as evidenced by changes in dichotic listening. These results indicate that perhaps the right posterior cortex is important for anger. Waldstein, Kop, Schmidt, Haufler, Krantz, et al. (2000) found that negative emotion induction results in bilateral EEG activation of the frontal lobes and predominately resulted in the endorsement of anger. Waldstein et al. suggest that anger may be related to either right or left frontal activation depending on how an individual handles emotion. Anger expressors are more likely to activate the left frontal lobe as a result of outwardly expressing anger through approach behaviors. Individuals who suppress anger are more likely to activate the right frontal lobe as a result of anger suppression and withdrawal from a situation (Waldstein et al., 2000). Individual differences in emotional style may be a particularly important factor in determining cerebral activation and their presence may be a contributing factor to some of the controversy in the literature.

An incorporation of Davidson's (1993) model and Heilman and Gilmore's (1998) model may provide the most parsimonious explanation for the cerebral activation concurrent with anger. Anger produces changes in both the anterior and posterior brain that are associated with behavioral approach or withdrawal. Additionally, it would lend support to Borod's (1992) addition to the valence model, indicating the importance of both the right and left frontal lobes, and the right posterior cortex in emotion.

Other emotions may be better served through this approach to emotion as well. In accordance with Davidson's model, depression is most often associated with relative right frontal activation or left frontal hypoactivation (Baehr, Rosenfield, Baehr, & Earnest, 1998; Davidson, 1998) and produces social isolation and withdrawal behaviors. Additional evidence suggests that depression may also be concurrent with suppression of the right temporal-parietal cortex (see Heller, 1990). Incorporation of Heilman and Gilmore's (1998) model is necessary to account for noted changes in right posterior cortex during anger or hostility and depression. Further, this helps account for other behavioral correlates of depression such as decreased arousal and decreased performance on spatial tasks that require the use of the right parietal lobe (Henriques & Davidson, 1997).

The three models that are presented here offer interesting and differential views of cerebral activation in emotion and pain. Evidence supporting each model should be carefully considered in order to advance theory in this area. For example, the right hemisphere model and valence model have primarily been supported by data from patients with brain damage and/or stroke (e.g., Heilman et al., 1975; Ross et al., 1981; Adolphs et al., 1996; Adolphs et al., 2001; Borod et al., 2002; Heilman et al., 2004). On the other hand, the motivational model has primarily been investigated through the examination of anger (Harmon-Jones & Allen, 1998; Harmon-Jones, 2004b; Harmon-Jones & Sigelman, 2001), an emotion that is typically viewed as having high negative emotionality and a high arousal component. Furthermore, different methodological approaches (behavioral vs. EEG) have served each model differently. Demaree and Harrison (1997) found right hemisphere activation after stress in high hostiles using a behavioral measure, while Harmon-Jones and Allen (1998) found left frontal activation with anger using EEG.

In order to improve the validity and generalizability of the right hemisphere model or the valence model, more research should examine behavioral and neuroimaging responses in general populations. For the motivational model, it may be necessary to more closely examine positive emotions.

Neuropsychology of pain

Pain accounts for 20% of medical visits and 10% of prescription drug sales; however, only 0.6% of National Institutes of Health's funding is allotted to pain research (Max, 2003). Pain is the second most frequent reason for seeing a physician and costs the US more than $100 billion each year (AAOS Committee on Research, 2003). The decade from 2001 to 2010 has been declared a decade of pain control and research by the US Congress (Public Law 106–386, 2000). For the neuropsychologist, the pain construct is difficult to grapple because it is so multifaceted. This may stem from the fact that there is a substantial amount of literature describing pain, yet no clear cut answer as to how it is produced and processed within the brain. In contrast to other sensory modalities, stimulation of the somatosensory cortex does not produce the sensation of pain, and there are no pain receptors in the brain. Previous research has produced many models for pain processing; however, no model describes integrative brain functioning in pain. Problems with prior models include focusing on single brain structures, placing too much emphasis on peripheral pain processing, or not describing how brain regions may interact with each other to produce pain. Recent imaging technologies, including fMRI and PET, have led to models that localize pain to several cortical and subcortical structures. One of the earliest and most influential theories in pain research was Melzack and Wall's (1965) gate-theory. The theory describes a mechanism is the dorsal horn of the spinal cord that modulates nociceptive information (information from nociceptors or sensory receptors that provide information about tissue damage) that will be processed by the CNS. More recently, Melzack (2001) described a pain "neuromatrix," a neurosignature pattern of activation based on genetic and sensory influences from a "body-self neuromatrix." Treede et al. (1999) describbe a lateral and a medial pain system, composed of numerous cortical and subcortical structures and have multiple pathways for pain transmission from the

spinal cord to the specific brain structures (e.g., thalamus) and the cortex. Schnitzler and Ploner (2000) concluded that pain occurs through cooperative processing of the primary and secondary somatosenory cortex, the anterior cingulate cortex, and the insula. These more recent models move closer to a functional cerebral systems approach to pain; however, they provide no specific hypotheses as to how focal cerebral activation in different brain regions due to pain would affect other functional systems.

An alternative approach that may provide insight into the pain construct is to apply models of emotion to pain. Substantial evidence suggests that intimate interactions exist between emotion and pain. Moods and emotional states change as a result of pain (Logan, Gedney, Sheffield, Yiwen, & Starrenburg, 2003; Sherman, LeResche, Huggins, Mancl, Sage, et al., 2004) and emotion may influence several aspects of pain processing. It is generally found that negative emotion increases pain intensity, and decreases pain thresholds and tolerance (Weisenberg, Raz, & Herner, 1998; De Wied & Verbaten, 2001; Meagher, Arnau, & Rhudy 2001), while positive emotion decreases pain intensity, and increases pain threshold and tolerance (Weisenberg, et al., 1998; De Wied & Verbaten, 2001; Meagher, et al., 2001). Additionally, pain may produce negative emotion in an individual (Schiff & Gagliese, 1994) or increase memory for negative emotion (Seltzer & Yarczower, 1991).

The International Association for the Study of Pain (IASP) defines pain as an "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (IASP, 1994). Although this definition separates pain into sensory and affective components, it has been suggested that pain results from simultaneous processing in the somatosensory cortex and emotion-related cerebral systems (Chapman, Nakamura, Donaldson, Jacobson, Bradshaw, et al., 2001). Chapman et al. administered painful electrical fingertip stimuli to 100 participants at different intensities. During half of the trials participants were asked to make affective judgments about the pain and in the other half participants were asked to make sensory judgments about the pain. Results revealed that affective and sensory judgments were not differentiated by pain ratings or by psychophysiological measures of pain (pupil dilation, heart rate, respiration rate, and skin conductance response). Given the non-differentiation of affective and sensory components of pain, a promising approach to the study of pain may include the use of emotional theories. This idea is further validated by the fact that the IASP has defined pain as a negative emotional experience (IASP, 1979) and studies seeking to induce negative emotion in participants use pain as a stimulus (e.g., Rhudy & Meagher, 2000, 2003; Mollet & Harrison, in press). Feldman (2004) stated that investigations of emotion and pain have developed along separate but equivalent tracks and proposed that a fusion of the work in emotion and pain begin.

Right hemisphere model and pain

Lateralization of pain processing is a debated topic; however, disentangling the data in relation to the right hemisphere model of emotion may provide substantial clues to cerebral processing of pain. Anatomical pathways suggest that pain sensation should be similar at both the right and left side of the body (Lugo, Isturiz, Lara, Garcia, & Eblen-Zaijur, 2002). However, several previous investigations have reported evidence of increased sensitivity or vulnerability to pain at the left hemibody. Lateralized pain appears more frequently at the left side of the body. Moreover, left hemibody pain is more intense and pain thresholds at the left hemibody are lower relative to the right side (Chandramouth, Kanchan, & Ambadevi, 1993; Schiff & Gagliese, 1994; Wittling, 1995). Lower-pressure pain thresholds on the left hand were in right handed participants; however no significant differences in right and left hand pain pressure thresholds exist between left-handed participants (Pauli et al., 1999b; Ozcan, Tulum, Pinar, & Buskurt, 2004). These data suggest that hand preference plays a role in lateralization of pain. Yet, Lugo et al. (2002) reported higher ratings of pain when a noxious thermal stimulus was applied to the left hand compared to the right hand in right- and left-handed participants. Differences in the measurement and application of painful stimuli may play a role in the reported effects.

Recent imaging studies have also reported right cerebral activation in response to noxious stimuli. Coghill, Gilron, and Iadarola (2001) found right lateralized activation in the dorsolateral cortex, dorsal frontal cortex, and the inferior parietal lobe in response to a noxious thermal stimulus independent of the location of stimulation. However, the authors found no lateralization patterns when looking at pain intensity ratings. In a PET investigation of experimentally-induced cluster headache attacks, Hsieh, Hannerz, and Ingvar (1996) concluded that the right hemisphere plays a preferential role in pain processing. EEG investigations suggest that cold pressor pain results in contralateral stimulation of the parietal cortex; however, the effect lasts longer over the right hemisphere (Ferracuti, Seri, Mattia, & Cruccu, 1994). Nevertheless, numerous other studies have indicated bilateral activation in response to pain (see Peyron, Laurent, & Garcia-Larrea, 2000 for a review). Bromm (2001) proposed that bilateral activation of the secondary somatosensory cortex in response to pain is needed in order to differentiate the side of the body that is hurt from the side of the body that is unaffected. Bilateral activation of parietal cortex then may be a result of pain localization, rather than a result of pain intensity or perception.

It has been suggested that the right hemisphere's role in emotion may contribute to the lateralization of pain. Min and Lee (1997) examined somatic symptoms in patients with depressive disorders, anxiety disorders, and somatization disorders. They found that comorbid somatic symptoms, especially pain, occurred more frequently at the left hemibody. The authors speculated that the emotional disorders are associated with a right hemisphere disturbance leading to left lateralization of pain and other somatic symptoms.

Properties of the right hemisphere suggest that it may be important in processing aversive events such as pain. The right hemisphere is noradrenergic (see Tucker & Williamson, 1984; Wittling, 1995 for reviews) and increases sympathetic tone (Wittling, Block, Schweiger, & Genzel, 1998a), thus preparing the body for a fight or flight response. Additionally, the emotion literature suggests that both the anterior and posterior right hemisphere play a substantial role in emotion, particularly negative emotion or withdrawal related behavior. The strong emotional component that co-occurs with pain may cause right hemisphere activation. Intense, acute pain may also provoke a withdrawal reaction related to right anterior activation.

Valence model and pain

Despite evidence of right hemisphere lateralization for the perception of pain, the application of the valence model to pain processing may provide additional help in unraveling the mysteries of pain perception. Schiff and Gagliese (1994) reported that reactions to cold pressor stimulation at either the left or right side resulted in emotional reactions that were consistent with activation of the contralateral hemisphere. Acute left sided pain (right hemisphere) resulted in higher group scores on measures of anxiety (increased right hemisphere activation, see Heller, Nitschke, Etienne, & Miller, 1997). Schiff and Gagliese also reported that right sided pain (left hemisphere) resulted in lower anxiety group scores than in the control group. The authors speculate that the right-sided pain stimulation attenuated the emotional reaction to pain due to increased positive affect associated with left hemisphere activation. Lorenz, Minoshima, and Casey (2003) found that activation in the left and right dorsolateral prefrontal cortex (DLPFC) was correlated with activation in subcortical regions and was related to pain affect and intensity ratings. During periods of low activation in the left DLPFC pain, unpleasantness ratings were significantly higher relative to periods of high activation in the left DLPFC. Additionally, periods of high activation in the left DLPFC were correlated with decreased activation in the midbrain and the anterior cingulate cortex. Periods of decreased right DLPFC activation were correlated with increased activation of the left and right insular cortex and increases in pain unpleasantness and intensity ratings. Although the data are correlational, they suggest that the level of activation in the left and right lobes may be associated with how positive or negative the pain is perceived.

Previous work suggests that positive affect can diminish pain, while negative affect may increase pain. Pain tolerance increases while viewing positive emotional pictures and decreases while viewing negative emotional pictures (Meagher et al., 2001). This effect may be described in terms of relative activation of the cerebral hemispheres. Positive emotion activates the left hemisphere (Lee et al., 2002), which may lead to inhibition of right hemispheric pain processing. Conversely, negative emotion activates the right hemisphere (Lee et al., 2002), which may lead to intensification of pain. However, negative emotion such as anxiety and fear can lead to pain inhibition. Bolles and Fanselow (1980) argued that threatening situations produce endogenous opioids in the brain that lead to pain inhibition. Wall (1979) proposed that pain associated with negative emotion occurs in phases. In an immediate phase, pain inhibition results from the need to recuperate or as a defensive reaction. Later, pain may be intensified in order to promote treatment and recovery from injury.

The fact that negative emotion may be associated with increased or decreased pain perception suggests the importance of examining dynamic cerebral activation in response to noxious stimuli. Situational demands or emotional traits may serve to influence responses. In a population of high and low hostile men, Demaree and Harrison (1997) found that high hostiles activated the right hemisphere in response to pain, while low hostiles activated the left hemisphere in response to pain, as evidenced by changes in dichotic listening. Left hemisphere activation in response to pain may be a compensatory reaction. Activating the left hemisphere can lead to positive affect (Bassel & Schiff, 2001) and an increase in parasympathetic activity (Wittling, Block, Genzel, & Schweiger, 1998b) which may induce a relaxing state that helps to reduce pain perception.

Motivational models and pain

Behavioral responses that are evoked subsequent to painful stimuli are similar to behavioral responses that positive and negative emotion induce and can be described in terms of approach and withdrawal states. Although pain is described as a sensation, it differs from other senses in that it is immediately linked to behavioral withdrawal or approach. Sensory modalities, such as vision or hearing, are more immediately linked to environmental exploration (Janssen, 2002). It has even been suggested that pain be described as homeostatic emotion because it is more akin to motivational systems such as hunger or thirst than it is to the other sensory modalities (Craig, 2003).

Motor responses to pain suggest that initial responses to pain are based on protective behavioral withdrawal reflexes

that may be mediated by spinal pathways (Urban et al., 2004). However, when behavioral conflicts occur higher cortical functioning may be necessary to produce the appropriate behavioral response (Lorenz et al., 2003). Hsieh, Belfrage, Stone-Elander, Hansson, and Ingvar (1995) stated that the nature of intense acute pain requires that it is analyzed in terms of impending motor responses that are dependent on the perceived aversiveness of the stimuli.

Davidson's (1993) approach/withdrawal model of emotion specifically looks at hemispheric activation in the frontal lobes in relation to the behavioral response associated with positive and negative emotion. In neuroimaging studies of pain, bilateral activation (Lorenz, Cross, Minoshima, Morrow, Paulson, et al., 2002; Lorenz et al., 2003) and deactivation (Hsieh et al., 1996; Tamura, Okabeb, Ohnishic, Saitod, Araib, et al., 2004) of frontal cortex has been found. Investigations that have reported frontal activation with pain attribute the activation to the affective-motivational components of pain (Hsieh et al., 1996; Fulbright, Troche, Skudlarski, Gore, & Wexler, 2001). Positive or negative affective evaluation of a painful stimulus may influence resulting approach/withdrawal behaviors. However, given the lack of research on pain and resulting approach/withdrawal behavior this is highly speculative. Yet, the fact that pain may result in left or right frontal hemisphere activation, as well as motivational behavior (Craig, 2003) supports the application of Davidson's (1993) model to pain processing.

In contrast to the previous investigations, Tamura et al. (2004) found that deactivation in the right frontal lobe was associated with a reduction in pain. Within the approach/withdrawal model, this may indicate a decrease in withdrawal related emotions leading to decreased pain as a result of a decrease in the amount of unpleasantness associated with the pain. Hsieh et al., (1996) suggested that bilateral deactivation in the prefrontal cortex found in response to pain was related to disengagement of attentional systems. They argue that pain is intrusive and causes inhibition of cognitive planning.

Evidence from migraine patients may lend additional support to the application of the approach/withdrawal model to pain. Avnon, Nitzan, Sprecher, Rogowski, & Yarnitsky (2004) proposed that evidence from participants with unilateral migraine suggests that the side of the migraine is positively associated with the level of cerebral activation in the corresponding hemisphere, such that right lateralized migraines occur with increased right hemispheric activation, while left lateralized migraines occur with increased left hemispheric activation. Fasmer and Oedegaard (2002) used migraine patients with unipolar and bipolar depression to describe this relationship. Fasmer and Oedegaard found that in bipolar patients, who may have more left hemisphere activation, migraine was more often located on the left side of the head. In contrast, unipolar patients, with presumably more right hemisphere activation, the migraine was more often located on the right side of the head. Both unipolar and bipolar depression occur with differential behavioral patterns. Unipolar depression more often leads to social isolation and withdrawal. Bipolar depression, on the other hand, more often leads to differential periods of approach and withdrawal. The differential cerebral activation as a result of lateralized migraine may play a role in resulting affective state and motivational behavior. However, Brandt, Celentano, Stewart, Linet, and Folstein, (1990) investigated the relationship between headache laterality and personality and emotional traits, and found no significant relationships.

Aversive and appetitive conditioning paradigms can help explain how emotions become associated with pain to produce approach or withdrawal responses. Results from Pavlov's (cited in Dickinson & Pearce, 1997) laboratory indicate that aversive shocks when paired with food elicit approach responses rather than withdrawal responses in dogs. The experiment indicates that the addition of positive reinforcement can alter the reflexive withdrawal response to escape the pain. In recent work with aversive and appetitive conditioning, Wunsch, Philippot, and Plaghki (2003) found an enhanced startle reflex and higher intensity rating for pain associated with aversive stimuli. In contrast, a diminished startle reflex and lower intensity rating for pain was associated with appetitive stimuli. Previous work suggests that an enhanced startle reflex occurs during unpleasant emotional conditions, while a reduced startle response is associated with pleasant emotional conditions (Vrana, Spence, & Lang, 1988). The startle reflex is an index of defensive mobilization (Bradley, Codispoti, Sabatinelli, & Lang, 2001) with increases in the startle reflex indicative of preparation for withdrawal. Accordingly, the study by Wunsch, Philippot, and Plaghki demonstrate that pain associated with aversive stimuli produces an increase in withdrawal behaviors, while pain associated with appetitive stimuli may produce a decrease in withdrawal behaviors.

Emotion and pain: Integration of functional cerebral systems

The previously presented research addresses emotion and pain using existing neuropsychological theories of emotional processing. In order to further integrate emotion and pain it is necessary to examine the influences of emotion and pain within functional neuroanatomical divisions. This integration may account for the wide range of cognitive, behavioral, and physiological changes that occur as a result of emotion and/or pain. As mentioned above, critical factors in brain organization include divisions between the frontal lobes and the posterior brain, as well as divisions between the left and

Table 1 Articles supporting similar functional roles for specific regions in emotion and pain processing

Region	Function	Emotion	Pain
Right Frontal	Expression	Heilman & Gilmore, 1998 Borod, Haywood, & Koff, 1997 Wildgruber et al., 2004	Daum et al., 1995
	Inhibition	Shenal et al., 2003 Heller, 1993 Thayer & Friedman, 2002 Rule et al., 2002	Yamaguchi & Knight, 1990 Davis et al., 1994 Talbot et al., 1995 Lorenz et al., 2003
	Valence Evaluation	Heilman, 1997 Herridge et al., 2004	Fulbright et al., 2001
	Motor Response	Davidson, 1993, 1995, 2003	Tamura et al., 2004 Wunsch et al., 2003
Left Frontal	Expression	Wildgruber et al., 2004	Daum et al., 1995
	Inhibition	Thayer & Friedman, 2002 Rule et al., 2002	Yamaguchi & Knight, 1990 Davis et al., 1994 Talbot et al., 1995 Lorenz et al., 2003
	Valence Evaluation	Heilman, 1997 Bassel & Schiff, 2001	Fulbright et al., 2001
	Motor Response	Harmon-Jones & Allen, 1997; 1998 Harmon-Jones & Sigelman, 2001 Harmon-Jones, 2004a; 2004b	Wunsch et al., 2003
Right Posterior	Perception	Heilman, 1997 Heilman & Gilmore, 1998	Treede et al., 1999 Bushnell et al., 1999
	Arousal Mediation	Heller, 1993 Heilman, 1997 Heilman & Gilmore, 1998	
	Attention/Vigilance	Posner & Raichle, 1994 Tucker et al., 1999	Janssen et al., 2001
Left Posterior	Perception		Bromm, 2001
	Arousal Inhibition	Heilman, 1997 Heilman & Gilmore, 1998	

the right hemispheres. These divisions produce four cerebral quadrants (right frontal, left frontal, right posterior, and left posterior) that may play differential roles in emotion and/or pain processing (see Table 1 and 2). Activation or deactivation of a cerebral region (as a result of emotion and/or pain) may either increase or decrease functioning within each of the four quadrants.

It should also be noted that many regions including the anterior cingulate (Casey, Morrow, Lorenz, & Minoshima, 2001), the amygdala, the basal ganglia, the hippocampus (Bingel, Quante, Knab, Bromm, Weiller, & Buchel 2002), and the thalamus have also been implicated in pain processing. While these structures most likely play a part in functional cerebral systems processing of emotion and pain, a recent study examining cerebral response to pain indicated that cortical activation was present before subcortical activation (Casey et al., 2001). The authors suggest that cortical activation may influence subcortical processing of pain at various levels (Casey et al., 2001). Thus, understanding cortical activation to emotion and pain may prove to be vital for the advancement of neuropsychological theories of both emotion and pain. As such, the current review focuses on cortical activation. Further, detailed discussion of cortical and subcortical interactions in both emotion and pain processing is beyond the scope of this paper.

Right and left frontal function

The frontal lobes perform many higher-order executive functions, including decision making, planning, motor organization, intention, verbal fluency, and design fluency (Mesulam, 2000). In relation to the functional cerebral systems for emotion and pain, the most important functions of the frontal lobes include motor expression and inhibition, valence perception, approach/withdrawal related behaviors, and cardiovascular regulation. These functions can further be divided between the right and left frontal lobe. It is generally found that the right frontal lobe plays a role in expression of emotional prosody (Heilman & Gilmore, 1998; Heilman et al., 2004; Wildgruber et al., 2002), expression of pain related behavior (Daum, Braun, Riesch, Miltner, Ackermann, et al., 1995), inhibition (Yamaguchi & Knight, 1990),

Table 2 Experiments supporting right hemispheric activation in negative emotion and pain

Mode of Evaluation	Emotion	Pain
Self-Report		Min & Lee, 1997 Fasmer & Oedegaard, 2002
Cognitive Performance	Bartolic et al., 1999 Miller et al., 1995	Seltzer & Yarczower, 1991
Motor	Borod, et al., 1997 Dimberg & Petterson, 2000 Demaree et al., 2002 Everhart et al., 2002	
Auditory	Bryden, et al., 1982 Bryden & MacRae, 1989 Bruder et al., 1989 Demaree & Harrison, 1997 Gadea et al., 1995	Demaree & Harrison, 1997
Visual	Reuter-Lorenz et al., 1983 Harrison & Gorelczencko, 1990 Herridge et al., 2004	Weisenberg et al., 1998 Meagher et al., 2001 Herridge et al., 2004
Somatosensory	Lee et al., 2002 Herridge et al., 1997	Chandramouth et al., 1993 Schiff & Gagliese, 1994 Pauli et al., 1999 Lugo et al., 2002 Ozcan et al., 2004
Physiological	Lee et al., 2002	Avon et al., 2004
Lesion Study	Borod et al., 2002 Burton & Labar, 1999 Adolphs et al., 1996; 2001	
EEG	Heller et al., 1990, 1995, 1997 Davidson, 1995, 1998 Everhart & Harrison, 1995 Demaree & Harrison, 1996 Henriques & Davidson, 1997 Baehr et al., 1998 Foster & Harrison, 2002 Tomarken et al., 1990	Ferracuti et al., 1994
PET	Blair et al., 1999	Coghill et al., 2001 Hsieh et al., 1995, 1996

negative valence perception (Blair et al., 1999), withdrawal related behavior (Davidson, 1993, 2003b), and sympathetic regulation (Wittling et al., 1998a). In contrast the left frontal lobe is important for expression of propositional speech, inhibition (Yamaguchi & Knight, 1990), positive valence perception, approach-related behaviors (Davidson, 1993, 2003b), and parasympathetic regulation (Wittling et al., 1998b).

Accordingly, differential activation or deactivation of the right and left frontal lobes due to emotion or pain produces different outcomes for functional cerebral systems. Increased activation in the right frontal lobe should produce increased expression of emotional prosody, while deactivation of the right frontal lobe or a lesion within the right frontal may led to the inability to express emotional prosody (Heilman & Gilmore, 1998; Adolphs, Damasio, & Tranel, 2002; Heilman et al., 2004). Similarly, lesions of the frontal lobes may lead to a decrease in expression of pain. Early case studies of individuals with frontal damage report that patients displayed "asymbolia for pain" or an absence of a behavioral response to pain (Daum et al., 1995).

Due to the inhibitory role of the frontal lobes, activation or deactivation of the frontal lobes also has consequences for emotional states. Increased activation in the right frontal lobe would suggest increased inhibition of both the posterior right cortex and the left frontal lobe, while deactivation would lead to decreased inhibition. Increased right frontal activation may be closely tied to the experience of negative affect and the inhibition of arousal. While negative affect can include depression, anxiety, aggression, hostility, or worry, prior research indicates that increased right frontal activation is most closely associated with depression (Baehr et al., 1998; Davidson, 1998). Increased inhibition of arousal as a

result of right frontal inhibition of the right parietal cortex may lead to an increase of withdrawal behavior and avoidance. Indeed, emotional disorders such as depression and anxiety that lead to isolation are concurrent with increased right frontal activation or left frontal hypoactivation (Heller et al., 1997). Alternatively, decreased activation in the right frontal lobe provides decreased inhibition of the right parietal cortex and may led to increased arousal. Demaree and Harrison (1996) suggested that heightened arousal seen in hostility occurs as a result of decreased right frontal lobe inhibition of the right parietal lobe. Rule, Shimamura, and Knight (2002) proposed that the orbitofrontal cortex (OFC) plays a role in filtering neural activity associated with an arousing event. Accordingly, the OFC monitors and controls emotional responses in other brain regions. OFC should result in hyper-responsivity in other brain regions associated with emotion. Further, Rule and colleagues state that OFC lesions lead to deficits in labeling sensory events as either pleasant or unpleasant. With respect to pain, OFC function may lead to differential labeling of pain as positive or negative or differential approach/withdrawal behaviors in response to painful stimuli.

Frontal inhibition of pain is noted through studies in which the frontal lobes are compromised. Talbot, Villemure, Bushnell, and Duncan (1995) demonstrated that after damage to the frontal cortex, ratings for cold pressor pain intensity and unpleasantness were significantly lower; however, tolerance for the cold pressor was substantial shorter. Davis, Hutchinson, Lozano, and Dostrovsky (1994) concluded that the frontal cortices may act to suppress or inhibit the subjective intensity of painful hot and cold stimuli. Increased frontal cerebral activation as a result of repetitive transcranial magnetic stimulation to the motor cortex has been shown to increase thresholds for cold pain (Summers, Johnson, Pridmore, & Oberoi, 2004). Further examination of the relationship between frontal lobe function and neural responses to mild pain was conducted by Rule, Shimamura, and Knight (2002), who recorded event related potentials to mild electrical shock in patients with bilateral lesions to the OFC. Results indicated a lack of habituation to the stimulus at the Pz electrode site, indicating that frontal damage can lead to disinhibition of the parietal cortex. These results suggest an inhibitory role for the frontal lobes over posterior sensory pain processing centers.

The frontal lobes may be important for cardiovascular regulation (Wittling et al., 1998a, 1998b). Cardiovascular regulation is important to the functional systems of emotion and pain because both emotional and painful stimuli can produce changes in systolic BP, diastolic BP, and heart rate. Recent work suggests that the right frontal lobe mediates sympathetic responses (Oppenheimer, Gelb, Girvin, & Hachinski, 1992; Heller, Lindsay, Metz, & Farnum, 1990; Hachinsky, Oppenheimer, Wilson, Guiraudon, & Cechetto, 1992; Wittling et al., 1998a), while the left frontal lobe mediates parasympathetic responses (Wittling et al., 1998b). However, there is considerable controversy surrounding the lateralization of sympathetic and parasympathetic responses (see Oppenheimer 2001). Yet, current data suggest that negative emotional stimuli producing right frontal activation increase systolic BP and heart rate (Wittling et al., 1998a), while positive emotional stimuli producing left frontal activation lead to decreases in systolic BP and heart rate (Wittling et al., 1998b). Further, individuals with negative emotional traits, such as anger or hostility, (thought to indicate increased right hemispheric activation) demonstrate higher resting systolic BP and heart rate (Durel, Carver, Spitzer, Llabre, Weintraub, et al., 1989; Spicer & Chamberlain, 1996). Dual-task research also indicates changes in systolic BP that may be dependent on emotional traits and hemispheric activation. Williamson and Harrison (2003) used behavioral tasks that activate the right and left frontal lobes in high and low hostile participants. Results revealed increased systolic BP in high hostile participants in response to the right frontal task; in contrast, low hostile participants evidenced decreased systolic BP in response to the left frontal task.

Frontal activation or deactivation arising from emotion and/or pain also has implications for cognitive tasks.. For example, Bartolic, Basso, Schefft, Glauser, and Titanic-Schefft (1999) found that induction of a negative mood (right-frontal activation) in normal participants lead to increased performance on a design fluency task (right hemisphere), while induction of a positive mood (left frontal activation) lead to increased performance on a verbal fluency task (left hemisphere). In an investigation of right-handed high and low anxious men, Everhart, Harrison, Shenal, Williamson, and Wuensch (2002) found that only low anxious men displayed the expected right-hand superiority for grip strength. The authors suggest that individuals who report high levels of anxiety have increased right frontal hemispheric activation which increases performance on tasks that require right frontal resources (i.e., left hand grip strength). In a similar investigation, Demaree et al. (2002) indicated that right-handed, high-hostile men have greater left hand grip strength (right frontal task) and decreased right-hand grip strength (left frontal task) relative to right handed low hostile men. The data indicate differential patterns of cerebral activation that occur with hostility influence performance on tasks that are thought to be functions of the right and left frontal lobes. Alternatively, decreased cognitive performance on frontal functions due to emotion can be found when looking at clinical populations. Depression, which may result from heightened right frontal activation or hypoactivation of the left frontal lobe, can produce deficits on right hemisphere functioning (Miller, Fujioka, Chapman, & Chapman, 1995). Clinical levels of depression may lead

to "extreme" levels of hemispheric activation that have been hypothesized to decrease performance (Bell & Fox, 2003).

Pain is generally found to decrease performance on tasks that measure frontal lobe functioning (see Eccleston & Crombez, 1999 for a review). While pain may increase activation in the frontal lobes (Lorenz et al., 2002; Lorenz et al., 2003), the difficulty in ignoring pain allows it to interfere with concurrent cognitive activities (Casey & Lorenz, 2000). Selective processing of pain over other potential stimuli is an adaptive function that promotes survival (Van Damme, Crombez, & Eccleston, 2004). The fact that pain is preferentially processed is in line with Kinsbourne and Hiscock's (1983) hypothesis that when two tasks compete for cerebral resources, performance on the less important task suffers.

Right and left posterior function

The posterior brain plays a functionally different role than the frontal lobes. The posterior region includes auditory cortex, somatosensory cortex, and visual cortex, making it primarily important for obtaining, storing and analyzing information, perception, comprehension, and regulation of arousal. Activation of the posterior cortex is needed to comprehend emotional tone of voice and to perceive emotion and pain.

Further distinctions can be made between the right and left hemispheres. The right posterior may be linked with arousal (Heller, 1993; Heilman & Gilmore, 1998), attention or vigilance to stimuli (Posner & Raichle, 1994), spatial processing (Mesulam, 2000), and negative emotion (Borod et al., 2002). The maintenance of vigilance is important to successful processing of information (Bearden, Cassisi, & White, 2004). Lesions of the parietal lobe often lead to spatial neglect, and right parietal lesions lead to more severe neglect of the contralateral hemisphere than left parietal lesions (Tucker, Harty-Speiser, McDougal, Luu, & deGranpre, 1999). Accordingly, deactivation of the posterior right cortex associated with depression leads to deficits in attending to stimuli and spatial tasks. Bruder, Kuitkin, Stewart, Martin, Voglmaier, et al. (1989) used dichotic listening to show that depressed participants were impaired in attention to stimuli presented to the left ear (right hemisphere). Liotti and Tucker (1992) found that participants were impaired on a cued spatial orienting task after induction of a depressed mood. In a neuropsychological model of depression, Shenal et al. (2003) commented that right posterior dysfunction would lead to decreased arousal and generalized reduction in brain activation.

Alternatively, increases in right parietal activation from emotional arousal or the perception of pain should lead to increases in attention to stimuli. Anxiety, a negative emotion that may occur with increased right posterior activation (Heller et al., 1997), can cause a left hemispatial bias (right hemisphere) during the perceptual processing of faces (Heller, Etienne, & Miller, 1995). Catastrophic reactions may lead to hypervigilance to pain symptoms and increased interpretations of stimuli as harmful or threatening (Janssen, 2002). Catastrophic reactions are associated with increased levels of negative affect (Janssen, 2002), left hemisphere damage (Heilman & Gilmore, 1998), and increased reports of pain (Geisser, Robinson, & Pickren, 1992), suggesting that a catastrophic reaction may be the result of relative right hemisphere activation.

The left posterior functions in language and reading comprehension (Mesulam, 2000), and in awareness of proximal space or body space (Heilman & Rothi, 1993; de Jong et al.,2001) may be important for inhibition of arousal (Heilman & Gilmore, 1998). Although, the left posterior is important for cerebral processing, relatively little information on this region's influence in emotion and pain exists. In a recent neuropsychological review of depression, Shenal et al., (2003) were unable to make specific predictions about the left posterior's contribution to depression. However, from a functional cerebral systems perspective, one would expect that tasks that activate the left posterior cortex may help inhibit right parietal arousal and lead to decreases in negative emotional arousal and to decreases in emotional perception. In a review of the parietal lobes role in pain perception, Duncan and Albanese (2002) stated cognitive manipulations that modulate activity in the primary somatosensory cortex alter perceived pain intensity, suggesting that language or reading comprehension tasks might reduce pain. Although right lateralization of pain is evidenced, Bromm (2001) stated that pain localization requires the use of both the right and left primary somatosensory cortices. Support for Bromm's hypothesis comes from data suggesting a role of the left hemisphere in keeping track of where body parts are located in space (de Jong et al., 2001). Subsequently, tasks that require awareness of body scheme may influence localization of pain.

Anger and pain

A common association that is made in emotion and pain research is the connection between negative affect and pain. Negative affect may consist of several different emotions including depression, anxiety, fear, hostility, aggression, or anger. However, acute pain is generally more associated with anger, while depression is associated with chronic pain (Ruoff, 1996). Anger produces changes in cardiovascular reactivity and arousal level that may influence the perception of pain. Within motivational models of emotion, anger is thought to result from left frontal activation (see Harmon-Jones, 2004a), while other models predict that negative affect is associated with the right hemisphere and that episodes of increased anger occur as a result of right frontal disinhibition of right parietal cortex (Demaree & Harrison, 1996). While these models seem at odds with each other, dynamic

cerebral activation predicts that increases in left frontal lobe activation would also result in a relative decrease of right frontal cerebral activation possibly leading to disinhibition of the right posterior cortex. Both of these models are supported by substantial data and popular theoretical models of emotional processing. It is also important to note that while the data support these patterns of activation in anger, the nature of functional cerebral systems and dynamic cerebral activation suggests that anger may result from a variety of patterns. However, due to the connections between negative emotion, pain, and right hemisphere activation (see Table 2) the following will focus on right hemisphere function in anger.

Right hemisphere activation that is seen in anger may be similar to patterns of activation that are associated with pain. Pain can produce bilateral activation or deactivation in the frontal cortex (Lorenz et al., 2002; Lorenz et al., 2003; Hsieh et al., 1996; Tamura et al., 2004) and pain perception may be right lateralized (Chandramouth et al., 1993; Schiff & Gagliese, 1994).

Components of anger and pain that influence cerebral processing include arousal and cardiovascular reactivity. Evidence suggests a right hemisphere dominance for the mediation of arousal (Heilman, 1997, Heilman & Gilmore, 1998) and certain aspects of cardiovascular reactivity, including regulation of heart rate and BP (Oppenheimer et al., 1992; Heller et al., 1990; Hachinsky et al., 1992; Wittling et al., 1998a).

Pain inhibition

Anger may be associated with a decrease (Janssen et al., 2001) or an increase (Fernandez & Milburn, 1994; Burns, Bruehl, & Caceres, 2004) in pain. A proposed mechanism for the decrease in pain associated with anger is the relationship between BP and pain sensitivity. In a recent review, Bruehl and Chung (2004) concluded that functional interactions between cardiovascular and pain regulatory systems are important for pain processing and that in normal, healthy participants experiencing acute pain this may be mediated by baroreceptor activation. Bruehl and Chung describe a functional system whereby pain increases sympathetic arousal leading to increased BP and activation of baroreceptors which, in turn, activate descending pain inhibition. Additionally, research indicates that resting BP is inversely associated with pain sensitivity, such that elevated resting BP results in decreased pain sensitivity (Fillingim & Maixner, 1996; Meyers, Robinson, Riley, & Sheffield, 2001; Bruehl, Chung, Ward, Johnson, & McCubbin, 2002). Interestingly, individuals with familial risk for hypertension exhibit diminished pain responses to acute pain, regardless of BP level (al'Absi, Buchanan, & Lovallo, 1996; Page & France, 1997; see France 1999 for a review). However, these results may be flawed because many of the "at risk" participants will never go on to develop hypertension (Campbell, Ditto, Seguin, Sinray, & Tremblay, 2003).

Support for pain inhibition through physiological mechanisms is indicated through experiments in which elevated BP due to experimentally-induced anxiety or anger leads to a decrease in pain. al'Absi and Peterson (2003) found that increased BP resulting from a public-speaking task predicted a decrease in cold pressor pain. Janssen et al. (2001) found that higher BP reactivity to experimentally-induced anger prior to a cold pressor task increased pain tolerance. Caceres and Burns (1997), however, found the opposite relationship. In their experiment, BP reactivity to mental arithmetic prior to a cold pressor test was positively associated with pain sensitivity. More specifically, participants who showed high BP reactivity during mental arithmetic evidenced lower threshold and tolerance on the cold pressor task relative to participants who showed low BP reactivity during this task. In a re-analysis of the data, Burns et al. (2004) found evidence to suggest that BP reactivity and subsequent pain experience may be influenced by anger-management style. They suggest that individuals high in anger suppression are capable of experiencing stress-induced analgesia, while high-anger expressors tend not to show the same effects. Individuals who generally express their anger may evidence lower thresholds in the laboratory due to the inability to express anger as they normally do, which leads to non-compliance and avoidance of the pain stimulus.

An examination of the functional systems in anger and BP may help elucidate how anger can inhibit pain. Anger has been associated with right lateralized increases in cerebral activation (Herridge et al., 1997). Additionally, the changes in cerebral activation are associated with changes in systolic BP (Schwartz, Weinberger, & Singer, 1981; Demaree & Harrison, 1997; Demaree, Harrison, & Rhodes, 2000; Foster, 2001). Lane and Schwartz (1987) proposed a model whereby lateralized cerebral activation in response to emotion causes changes in cardiovascular reactivity due to lateralized imbalance in sympathetic input to the heart. Foster and Harrison (2004) found support for the idea that increased right cerebral activation is associated with increases in sympathetic tone and that relative differences in magnitude of cerebral asymmetries may determine overall changes in cardiovascular responses. Heightened right-frontal activation due to anger may create the inability to regulate BP, resulting in increases in BP. Within the functional cerebral systems model, increased right frontal activation would also affect pain. Increases in right frontal activation should result in increased inhibition of the somatosensory cortex leading to a decrease in pain.

Other work suggests that pain inhibition occuring with increased BP is a result of faulty affect responses to the pain. Fillingim, Maixner, Bunting, and Silva (1998) suggested that

diminished pain sensitivity found with elevated BP may be the result of a blunted affective response rather than a reduction in pain intensity. In an investigation of the relationship between elevated resting BP and emotional response, Pury, McCubbin, Helfer, Galloway, and McMullen (2004) found that increases in systolic BP are associated with more neutral ratings of positive and negative pictures. Considering functional cerebral space, regulation of the cardiovascular system and affective labeling may be a dual-task that requires competition for processing resources of the frontal lobes. It may be that regulation of the cardiovascular system produces increased demands on the frontal lobes, leading to deficits in affective labeling.

Pain sensitization

Evidence suggests that in some cases anger may lead to the exacerbation of pain. Janssen et al. (2001) stated that despite physiological inhibition of pain that occurs in anger, misattribution of physiological arousal and attention can lead to increased pain reports. Anger that is directed towards the self versus towards an external target may increase the possibility that pain-induced physiological arousal is attributed to internal body symptoms (Janssen, 2002). In support of this hypothesis, Gelkopf (1997) reported a significant and somewhat high positive correlation ($r = 0.60$) between anger-in and assessment of pain. Additionally, the right posterior cortex is hypothesized to play a role in mediating attention to stimuli. Anger that results from decreased right frontal activation and increased right temporal and parietal activation may cause increased attention to painful stimuli that subsequently leads to increased pain sensitivity.

The overlap in functional systems involved in anger and in pain (i.e., right hemisphere, see Table 2) suggests that anger should produce increases in pain as a result of the facilitation effect of functional cerebral space. Emotion literature suggests that increased negative affect can lead to increased pain. Meagher et al. (2001) presented participants with slides depicting either neutral, fearful, or disgustful scenes and found that viewing either fear or disgust before a cold pressor test decreases pain intensity and upleasantness threshold ratings. The authors stated that negative affect may decrease pain thresholds due to enhancement of attention to the noxious stimuli. A similar relationship has been found in other experiments looking at the interaction in negative emotion and pain (i.e., Schiff & Gagliese, 1994; Weisenberg et al., 1998; De Wied & Verbaten, 2001).

Given the data, anger and pain have a dynamic relationship. It appears that pain inhibition may be mostly related to physiological changes associated with anger, while pain sensitization occurs more as a result of the ability to regulate anger or emotional evaluation of the pain. As a result pain inhibition may occur when a painful stimulus is first perceived; however, after further evaluation of the pain, sensitization may occur. Wall (1979) proposed a similar hypothesis.

It is important to understand the dynamic relationship between anger and pain not only from the theoretical perspective, but also due to the clinical implications it may have. Patients with hypertension or patients with anger regulation problems may be at risk for developing pain disorders. Further, patients who exhibit pain inhibition or sensitization may be at risk for hypertension or anger regulation problems. Clinicians should consider these factors during treatment.

Research directions

The demonstrated connections between emotion and pain provide unique opportunities for future research. The functional cerebral systems approach to emotion and pain provides an opportunity to investigate each construct across modalities using a number of behavioral, physiological, and neuroimaging techniques. The relationship between emotion and pain, and specifically anger can be further examined through looking at the effects of each construct on functional cerebral systems. Emotion and pain produce similar cerebral activation that can result in behavioral approach or withdrawal, increased arousal, and dysfunctional sympathetic regulation. Resulting cerebral activation can be affected by the valence attributed to the emotion or pain, arousal produced as a result of the emotion or pain, and sympathetic response to the emotion or pain.

Future research should begin by exploring the applications of the right hemisphere model, the valence model, and the motivational models of emotion to pain. This can be achieved by implementing emotion research strategies in pain research. Research should be aimed at discovering how relative activation or deactivation of a brain region affects pain thresholds, tolerance, intensity, and affective response to painful stimuli. Dual task research may also help elucidate interactions between emotion and pain. Further, it is suggested that a majority of this work be focused on the application of the motivational model of emotion to pain since few studies have examined approach or withdrawal motivation with regard to pain. However, given the fact that behavioral motivation is intrinsic to the pain experience this model may prove to be the most useful to pain researchers. Moreover, primary support for the motivational model has been provided by the examination of anger. As previously discussed, pain and anger may have a complicated relationship. Increased understanding of the underlying components in this relationship may improve diagnosis and treatment of anger and pain disorders.

Examining frontal executive functions, the motor system, the auditory system, the somatosensory system, and/or the visual system under different emotional conditions or during painful stimulation may help discover how different

emotions and levels of pain influence functional systems. While work in emotion has been and continues to be conducted from this perspective, pain research has not fully investigated the role of different levels of acute pain on functional systems. Examination of pain on different neuropsychological measures may help understand what role different brain regions play in pain processing. In a review of functional imaging studies on pain, Peyron et al. (2000) commented that no study has specifically investigated what role the frontal cortex plays in motor preparation or inhibition during pain. Future investigations may benefit from examining this role in order to determine if motivational models of emotion are useful in describing cerebral processing of pain. Additional examination of the influences of pain on behavioral measures of posterior functioning should also be conducted.

Investigations of the influence of anger on pain responsivity suggest that anger produces significant changes in pain perception. Pain inhibition can occur through physiological mechanisms, while pain sensitization can occur through individual differences in anger management or emotion regulation. Future investigations of emotion and pain may benefit from establishing how other emotional traits or states (i.e., anxiety, depression, happiness) influence the inhibition or sensitization of pain. It may be fruitful to investigate cortical activation patterns and physiological response patterns that exist with certain emotional traits. Functional cerebral systems approach suggests that these patterns may play a role in subsequent processing of painful stimuli. The presented models of emotional processing provide a framework for future work to address an integrated view of the neuropsychology of emotion and pain.

Conclusions and implications

The current review examines emotion and pain from a functional cerebral systems perspective using the right hemisphere model, the valence model, and motivational models of emotional processing. The review examines how the frontal lobes, the posterior brain, the right hemisphere, and the left hemisphere function during the processing of emotion and pain. The review proposes that pain research can be improved and approached from an emotional standpoint. The review presents the theoretical views of emotion and then applies them to pain through the use of functional cerebral systems. Emphasis is placed on inter- and intra-hemispheric interactions that lead to the experience of emotion and pain.

The proposed approach to pain research uses theories of functional cerebral systems, functional cerebral space, arousal, and lateralization to help integrate and to better explain the vast amount of information that exists in the literature. This approach to pain highlights the similarities between negative emotion and pain. Existing data suggest a strong link between activation of the right hemisphere, anger, and pain processing. Alternatively, activation of the left hemisphere may help decrease negative emotion and pain. The functional systems examination of negative emotion and pain also suggests that frontal activation or deactivation influences cerebral functioning in the posterior brain. Increased activation of the frontal lobes can inhibit processing in the posterior brain. In contrast, decreased activation of the frontal lobes can cause an increase in posterior function. Bilateral interaction between the right and left frontal lobes may influence perception of emotional valence and motor response to emotion. Bilateral interaction between the parietal lobes changes arousal level and may influence resulting processing of emotion and/or pain. The functional interactions have specific outcomes for behavioral, cognitive, and physiological functions of each region of the cerebral cortex. These outcomes may be of particular importance to clinicians who see individuals with brain damage or a stroke that is localized to one of the four quadrants presented here. For example, recognition of deficits that are associated with right temporal damage may help a clinician identify emotional or pain problems that may be present in that individual.

Examination of physiological responses and arousal produced as a result of emotion and pain reveals a relationship between anger and pain. Anger and hostility are emotional states and traits that are associated with higher resting BP (Durel et al., 1989; Spicer & Chamberlain, 1996) and increased cardiovascular reactivity to stress (Shapiro, Sloan, Bagiella, Kuhl, Anjilvel, et al., 2000). Blood pressure is an important component in resultant pain perception and regulation. Future work should address the relationship between anger and pain inhibition and sensitization using the proposed functional systems approach.

The proposed approach to the neuropsychology of pain lends itself well to scientific research because it is based on anatomical connections between functional regions of the brain and borrows a strong theoretical framework from emotion research. Scientific methods of research that have been validated in emotion research can be applied to the investigation of pain. The influence of pain on cerebral processing can be examined through the measurement of resulting behavioral and physiological responses across modalities. Changes in cortical activation or deactivation in response to pain can also be measured via imaging techniques, such as EEG, fMRI, or PET. Neuroimaging techniques may especially important in elucidating lateralized activity in response to emotion and pain. Examination of cerebral response to emotion and cerebral response pain in the same participant may allow for direct comparison of specific regions of interest. For example, research might examine right frontal activation using fMRI before and after an emotional stimulus, and before and after a painful stimulus.

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