HEMISPHERIC SPECIALIZATION FOR PROSODIC EMOTIONAL PERCEPTION: TEMPORAL LOBE EPILEPSY AND THE INTRACAROTID AMOBARBITAL PROCEDURE

by

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Abstract

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Adviser: Joan C. Borod, Ph.D.

The importance of cortical and limbic structures in emotional processing has been well documented in the neuropsychological literature. Researchers have focused on performance deficits in patients with unilateral destructive lesions. Functional-anatomic correlates demonstrated that deficits in emotional perception follow damage to posterior brain regions. The purpose of this study was to extend neuropsychological understanding of brain mechanisms involved in emotional perception through analysis of the performance of unilateral temporal lobe epilepsy (TLE) patients. Our approach considered neuroanatomical and neuropsychological factors with respect to three divergent hypotheses. This paper describes the performance of preoperative epilepsy patients on an emotional prosodic perception task during the Intracarotid Amobarbital Procedure (IAP). Subjects were 22 right-focus TLE and 15 left-focus TLE right-handed males and females. Patients with limbic and neocortical foci were included. Location of seizure focus was assessed via scalp-sphenoidal video EEG. For the experimental task subjects identified the discrete emotion portrayed in tape-recordings of emotionally intoned, neutral-content sentences. Subjects received pre-IAP training to insure adequate comprehension of procedures. Standard internal carotid angiography was performed prior to injection of each hemisphere. Testing was conducted at 2 minutes post injection, and lasted for 1-2 minutes. A brief assessment of motor strength and of facial hemiplegia insured sufficient anesthetization during testing. There were no significant subject-group differences for demographic nor IAP procedural variables. Percent accuracy scores were analyzed with respect to laterality and intrahemispheric location of epileptogenic focus. The role of gender was also evaluated. Finally, the effect of variables important in prognosis and treatment of epileptic disorders (i.e., onset age, structural lesion, seizure frequency, generalized seizures) was evaluated. Overall, while impairments in identification of prosodic emotion were often observed, no systematic patterns emerged as a function of injection side or side of seizure focus. Performance effects were observed for gender; females generally performed better than males. In terms of epilepsy variables, the effect of age of seizure onset was often apparent, yet, no systematic findings emerged. Severity variables (e.g., structural lesion, generalized seizures) tended to adversely affect performance. Future research would benefit from increased numbers of baseline and experimental trials, and must consider the importance of etiological and disease variables on cognitive performance within this population.

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I. INTRODUCTION

Historically, the concept of emotion has been defined within various theoretical frameworks (e.g., evolutionary, cognitive, sociobiological). Each definition has emphasized particular aspects of emotional functioning, in so doing, implicating the specific brain systems or anatomical structures dedicated to that function as subserving emotion. Research stimulated by nineteenth century physiological theories (e.g., James, 1884; Cannon, 1927) highlighted the complexity of emotional functioning and implicated both central and peripheral nervous system components as relevant to emotional processing. Since the proposal of a brain circuit responsible for emotional functioning (Papez, 1937), extensive anatomical and physiological evidence has accumulated substantiating the role of the limbic system (e.g., LeDoux, 1986) and various subcortical structures (e.g., Weddell, 1990) in aspects of emotional behavior. More recently, research documented in the neuropsychological literature has emphasized the contributions of neocortical brain structures in the processing of emotion (see Borod, 1992, for review based on anatomical and conceptual distinctions in the neuropsychological research). Evidence from this line of research has led to the derivation of three major neuropsychological theories of emotion, which disagree in terms of both the overall degree of hemispheric involvement in emotion and the relative hemispheric dominance for different kinds of emotions.

The right hemisphere hypothesis postulates that the right cerebral hemisphere (RH) is dominant for emotional processing regardless of emotional valence (Borod, 1992; Borod, Koff, & Caron, 1983; Bryden & Ley, 1983; Buck, 1984; Heilman, Bowers, & Valenstein, 1985; Ross, 1985; Tucker & Frederick, 1989). The argument at the behavioral level is basically that emotional processing involves strategies (e.g., synthetic and holistic) and functions (e.g., spatial organization and pattern perception) for which the RH is particularly specialized (Borod, Koff, & Buck, 1986). Tucker and Williamson (1984) have suggested that the RH's greater involvement in arousal and habituation enable specialization for nonverbal (e.g., emotional) communication (Goldberg & Costa, 1981; McGuiness & Pribram, 1982). On a neuroanatomical level, research has demonstrated a greater degree of neuronal interconnectivity among right than left hemisphere (LH) regions (Gur, Packer, Hungerbuhler, et al., 1980; Tucker, Roth, & Blair, 1986), implying a greater right hemisphere capacity for multimodal integration (Goldberg & Costa, 1981). Bear and Fedio (1977; Bear, 1983) have proposed that lateralized asymmetries in the pattern of sensory cortico-limbic connections reflect functional hemispheric differences and favor RH dominance for emotional surveillance, affective reactions to stimuli, and increased autonomic responsivity.

The valence hypothesis maintains that the RH retains dominance for negative emotions while the LH is dominant for positive emotions, regardless of processing mode (Ahern & Schwartz, 1979; Dimond & Farrington, 1977; Sackeim, Greenberg, Weiman, et al., 1982; Silberman & Weingartner, 1986). Arguments supportive of this hypothesis propose that because of their inherent association with survival (e.g., escape from danger/threat), processing of negative emotions necessitates a system that is sensitive to multimodal simultaneous inputs and that is capable of rapid scanning and global situational evaluation (Borod, Koff, & Buck, 1986). These functions involve synthetic processing (RH) rather than sequential analysis (LH). Positive emotions, by contrast, may be more dominated by LH functions, since these emotions have been conceptualized as linguistic and communicative as opposed to emotional and reactive (Borod, Koff, & Buck, 1986).

Finally, a third hypothesis proposes that a dichotomy exists in terms of direction of movement, which is relevant to hemispheric dominance for emotional processing. The RH is believed to be specialized for withdrawal/avoidance emotions and the LH for approach emotions (Davidson, 1984; Davidson, Ekman, Saron, et al., 1990; Fox, 1991; Kinsbourne & Bemporod, 1984). This differentiation draws from observations of a fundamental behavioral continuum described in biological theories of emotion. It is founded on the assumption that emotions serve an evolutionary adaptive purpose. Kinsbourne's (1984) formulation of this concept is based on the biological notion that organisms at every phylogenetic level have two basic choices in every circumstance: to approach/continue ongoing activity or to stop/retreat. Over the course of evolution, as the adaptive problems faced became increasingly complex, emotions evolved and became linked with the already established approach and avoidance systems. Withdrawal/avoidance emotions are thought to be associated with the RH because of its specialization for undifferentiated automatic movement, arousal, and habituation (Borod, 1992; Davidson, 1984). Approach behaviors are believed to be LH-based due to its specialization for sequentially executed fine movement, activation, and focal attention (Borod, 1992; Davidson, 1984; Davidson, Ekman, Saron, et al., 1990).

Researchers testing these hypotheses in studies of brain-damaged subjects with unilateral destructive lesions (e.g, stroke, tumor) (e.g., Borod et al., 1990; Borod, Rorie, Haywood, et al., 1996; Bowers et al., 1987; Blonder, Bowers, & Heilman, 1991) have focused on relative performance deficits in the expression, perception, and experience of emotion. Impaired performance is most often presumed to be a direct effect of the sustained brain injury. Research using normal subjects has alternatively focused on laterality effects on performance (e.g., Bryden & Ley, 1983; Silberman & Weingartner, 1986) or regional metabolic brain activation (e.g., Gur, Skolnick, & Gur, 1994) during emotional processing tasks. To date, there is evidence from studies with normal subjects which lends support primarily to the RH hypothesis for emotional perception, but also to the valence hypothesis in terms of emotional expression. With brain-damaged patients, the literature tends to support the right hemisphere hypothesis. Functional-anatomic correlations have been demonstrated such that deficits in emotional perception follow damage to more posterior (e.g., parietal, temporal) brain regions (Borod, 1992; Gainotti, 1987; Ross, 1981).

The overall goal of the current project was to extend the neuropsychological understanding of brain mechanisms involved in the perception of emotion through specific examination of the contribution of temporal neocortical and limbic structures. Neuroanatomical, as well as neuropsychological, distinctions were evaluated with respect to hypotheses based on the current neuropsychological theories of emotion. The focus of the project was on the perceptual mode of processing emotional information within the prosodic communication modality.

We have analyzed the performance of unilateral temporal lobe epilepsy (TLE) patients on a task of emotional prosodic perception during the Intracarotid Amobarbital Procedure (IAP). The use of TLE patients provided a unique opportunity to examine alterations in perceptual aspects of emotional processing subsequent to the destructive effects of focal irritative lesions in circumscribed brain areas. With respect to the neuropsychological hypotheses tested, deficits during right hemisphere anesthetization for perception of all emotions would lend support for the right-hemisphere hypothesis. Alternatively, deficits during RH anesthetization for perception of negative emotions and deficits during LH anesthetization for positive emotions would provide support for the valence hypothesis. The inclusion of patients with epileptic foci originating in primarily limbic (mesial temporal) regions permitted us to test several alternatives relevant to the lateralization of emotional perception: (1) limbic structures function similarly to ipsilateral cortical structures; (2) functions are more diffusely organized in limbic structures leading to more bilateral representation; and (3) emotional perception is neocortically based.

It was hypothesized that (1) TLE patients with left-hemisphere language representation would exhibit relative deficits in emotional perception for all specific emotions presented during non-dominant (right) hemisphere injection. The performance of right TLE subjects, in particular, was expected to vary as a function of age at seizure onset such that (2) during RH anesthetization, RTLE patients with chronic seizure onset later in life might demonstrate greater impairment than RTLE patients with early chronic seizure onset. Overall, left TLE patients during LH injection are expected to show the least relative deficits. Results were expected to demonstrate overall support for the right hemisphere hypothesis.

II. Literature Review

Definitions and Background

Emotion

One longstanding controversy in emotion research has centered around the importance of biological and physiological processes to the understanding of the psychological constructs of emotion (Ekman & Scherer, 1984). Along this line, theories of emotion have traditionally been dichotomized into those which stress the role of cognition in emotional experience, and those which separate emotion from cognition, emphasizing underlying physiological processes (Borod, 1992; Zajonc, 1984). In recent years, however, most theorists have agreed that the role of cognitive processes in the initiation of emotion depends largely on how broadly or narrowly cognition is defined (Davidson & Ekman, 1994). As diverse as the field of emotion research has become, some consensus does exist concerning the parameters which distinguish an emotion from other affective states. For most theorists, emotion is viewed as differentiable from mood, and from affective style or temperament. While the criteria for such distinctions vary, most commonly cited are duration, precursor events, and consequent changes in behavior. Emotions are generally conceptualized as brief, lasting on the order of seconds to minutes, while moods persist for hours to days; temperament refers to enduring and consistent patterns of behavior (Ekman, 1994; Kagan, 1994). The antecedents of emotions have been described as more specific (Ekman, 1994) or object-focused (Frijda, 1994) than the precursors of moods. In addition, the consequences of emotions are theorized to modulate action (Davidson, 1994) or to alter action-readiness (Frijda, et al.,1989), while the resultant effects of moods modulate more generalized cognitive processes. Pertinent to the neuropsychological perspective of this study, the definition of emotion adopted here is borrowed from the more biologically oriented emotion theories (Ekman, 1984; Izard, 1977; Tomkins, 1980) where emotion refers to a biologically-based state involving reactions to appropriately evocative stimuli which include neurophysiological, perceptual, expressive, and subjective experiential components (Borod, 1992; Izard & Buechler, 1980; Plutchik, 1984; Tucker, 1993).

Prosody

Human speech can be divided into linguistic (propositional) and paralinguistic (suprasegmental) aspects. Linguistic or lexical components refer to quantitative, discretely organized elements which develop meaning through the rules of syntax (Van Lancker, 1980). Phonemes are the smallest segment of language in the lexical category.

The paralinguistic component consists of the qualitative or prosodic aspects of speech (e.g., melody, pauses, and intonation patterns). The acoustic correlates of prosodic speech are in the timing (duration), amplitude (intensity), and fundamental frequency (dominant pitch) of phonation (Shapiro & Danly, 1985). These features modify and add complexity to the linguistic aspects of speech by enabling us to convey attitudes and emotions, recognize familiar voices, and modify lexical meaning. Basically, these properties of speech are what makes human speech sound "human" and not computer simulated. Prosodic aspects are therefore generally considered crucial to effective communication.

Background: The Neurology of Prosody

The history of inquiry into the "neurology of prosody" began in the late 1940's with Monrad-Krohn's (1947) observations of the verbal behavior of brain damaged patients. During World War II he had occasion to observe a Norwegian patient with a Broca's aphasia, who had sustained extensive scarring in left fronto-temporo-parietal brain regions subsequent to a shrapnel wound. Although she recovered language functions well, she was left with a Germanic accent caused by a change in her distribution of stresses and pauses during speech. Based on these and other observations, Monrad-Krohn (1947) distinguished among four different types of prosody. Intrinsic prosody referred to changes in pauses, stresses, or intonation in order to alter meaning (e.g., **con** vict [n] vs. con **vict** [v]). Intellectual prosody was defined as the addition of attitudinal components via stress placement (e.g., He **is** clever vs. **He** is clever). Inarticulate prosody referred to the paralinguistic elements of speech (e.g., grunts and sighs). Emotional prosody was used to impart emotion to speech. Monrad-Krohn (1947) also described three clinical disorders of prosody which could occur subsequent to a nervous system lesion in patients with left-sided brain damage. He did not, however, describe these disorders in terms of focal damage, nor did he consider lesions of the right hemisphere.

The role of the right hemisphere in prosody only came under systematic investigation approximately two decades after Monrad-Krohn's observations, however, the implication of a relationship had existed for a long time (see Joanette, Goulet, & Hannequin, 1990, for a more comprehensive discussion of this literature).

More recently, the difficulties of RBD patients with respect to production and comprehension of emotional prosody have been described and systematically studied by Ross and his colleagues (1979, 1981). Ross and Mesulam (1979) described two patients who had suffered ischemic infarctions, verified by CT scan, involving right inferior frontal and anterior-inferior parietal regions. Both of these patients exhibited an inability to express emotional intonation in speech. By contrast, RBD patients in a prior study (Heilman et al., 1975), demonstrated marked deficits in the recognition of emotionally-intoned neutral sentences. Based on clinical evidence and isotope scans, the damaged area of the right hemisphere was thought to involve the superior-posterior temporal and inferior parietal lobes. Based on the results of these two studies, Ross and Mesulam (1979) postulated that the RH was dominant for organizing affective prosodic language components and that the functional/anatomic organization of affective language in the RH mirrored the organization of propositional language in the LH.

Further evidence in support of these hypotheses was provided by Ross (1981) in a study of 10 patients with focal RBD as a result of an infarct. Lesions were again localized by CT scan. Patients were examined at bedside in a manner similar to that used in assessing propositional language in aphasic patients. All patients with lesions bordering the right Sylvian fissure were determined to have some disorder of affective language (Ross, 1981; Gorelick & Ross, 1987). Because the prosodic deficits appeared to cluster in a manner similar to the linguistic deficits in left brain-damaged (LBD) patients, Ross termed these syndromes aprosodias -- encoding/decoding disorders of affective behavior. Functional-anatomic correlates for each aprosodic subtype were also created by mapping the CT lesions for each patient onto a RH template.

These clinical observations of brain-damaged patients, in concert with the belief of a more specialized RH role in emotion (e.g., see Borod, 1992, for a review), has led some researchers to postulate a dichotomous anatomic localization for prosodic mechanisms such that the LH's superior language capabilities should control linguistic prosody (Monrad-Krohn's [1947] intellectual & intrinsic prosodies) and the RH should control emotional prosody.

While Ross's (Ross & Mesulam,1979; Ross, 1981) studies were instrumental in drawing the attention of clinicians to systematic evaluation of prosody in RBD patients, Joanette, Goulet, and Hannequin (1990) described the conclusions as overly optimistic. Several criticisms of the studies were provided. Joanette et al. (1990) viewed the lack of validation of the examiner's clinical judgement as problematic because of the known lack of concordance between clinical judgements and acoustic speech analyses (e.g., Danly & Shapiro, 1982). They also point to the difficulty which can exist with intersubject reliability in prosodic perception procedures (e.g., Tompkins & Flowers, 1985). Joanette et al. (1990) additionally found no theoretical justification for the parallel between anatomical and clinical symptom classifications, particularly based on the small sample of patients observed. Finally, these researchers point out that prosodic disorders are temporally unstable and clearly most frequent in the first three days post injury. This suggests that reactive emotions associated with generalized neurological/medical insult could be involved without clear attributions to specific anatomical locations.

Hemispheric Specialization for Prosodic Emotional Perception

Studies with Normal Subjects

During the past 20 years there has been a considerable amount of research evaluating relative hemispheric dominance for emotional perception in neurologically-healthy, normal subjects. As described in reviews by Borod et al. (e.g., Borod, Koff, & Caron, 1983; Borod, 1992), experimental tasks are usually behavioral procedures designed to measure degree of hemispheric lateralization for a particular task. The technique most commonly employed for perception of prosodic emotion is the dichotic listening procedure in which stimuli are presented simultaneously to both ears, and ear asymmetries are analyzed. In general, subjects are required to discriminate between two emotionally-intoned stimuli or to identify the emotional intonation heard in a given stimulus (e.g., words, nonsense syllables, sentences, or speech-filtered stimuli). Given the predominantly contralateral innervation of the auditory system, a left-ear advantage (LEA) in the dichotic listening paradigm is interpreted as a right hemisphere (RH) superiority for task performance.

In 1971, Haggard and Parkinson conducted an investigation in which the dichotic listening procedure was used to present subjects with emotionally-intoned sentences. While a LEA/RH advantage was demonstrated for recognition of emotional intonation, no ear advantage was observed for recognition of the verbal content of the sentences. Using a somewhat different paradigm, Safer and Leventhal (1977) evaluated the performance of college students on a task in which sentences which contained both verbal emotional content and emotional intonation were presented monaurally to the left and right ears. Subjects were required to make judgements about the emotion heard using either verbal content or the speaker's tone of voice. These investigators found that when stimuli were presented to the left ear, most subjects based their global appreciation of emotion on the intonation heard. In contrast, when stimuli were presented to the right ear, most subjects deduced the emotion heard from the verbal content of the stimulus. In a third task, when subjects were asked to identify the emotional nature of both the content and the intonation of the stimuli, subjects hearing the stimuli in their right ear performed significantly better than when the stimuli were heard in their left ear. The authors' conclusions from this study emphasize the importance of the nature of the experimental task; the dual task favored greater left hemisphere involvement.

In another dichotic listening study, Ley and Bryden (1978) presented pairs of semantically neutral sentences in a multiple choice decision task, such that one sentence contained intonation conveying a particular emotion while the other was neutral in tone. Subjects were required to indicate both the lexicosemantic content heard as well as the emotion conveyed by the speaker's intonation. When the results were analyzed, 21 of the 31 subjects showed a REA (LH superiority) for content and a LEA (RH advantage) for intonation. Using a similar experimental design, Bryden and MacRae (1988) paired two-syllable words differing in the initial stop consonant and spoken in different emotional tones. The stimulus pairs were presented dichotically, and subjects were instructed to detect either the presence of a designated word or a designated emotion. When word targets were specified, subjects demonstrated a strong REA. By contrast, when the target was a specific emotion an overall LEA was obtained. This latter finding was strongest for negative emotions.

Shipley-Brown et al. (1988) used the dichotic listening paradigm to evaluate the RH s role in both affective and linguistic prosody in a study involving undergraduate students. Overall, while a significant LEA was demonstrated for both types of prosodic comprehension, this finding was more pronounced for the detection of emotional prosody.

Herrero and Hillix (1990) attempted to replicate earlier studies and to add various prosodies in simultaneous competition within a single task. Equal numbers of male and female college students were required to identify the emotional tone (i.e., mad, glad, or sad) in a man's voice stating a neutral-content sentence. The stimuli were initially presented monaurally until responses were 100% correct. Once the accuracy criterion had been reached, all possible stimulus combinations were dichotically presented, and subjects were asked to identify the emotional tone presented to each ear. Responses were only counted for the first ear reported. The investigators found no effect of gender on the accuracy of performance. In all cases, significantly higher identification scores were obtained for the left ear than for the right ear. Finally, Erhan et al. (1994) examined hemispheric specialization for emotional prosodic perception using a dichotic oddball paradigm. These investigators presented pairs of nonsense syllables spoken in seven different emotional tones to male and female college students. Overall, a significant LEA for detection accuracy was demonstrated; although more strongly in females than in males. Reaction time measures showed a similar trend for a subset of subjects in that responses tended to be more rapid for stimuli presented to the left ear (RH) than to the right ear (LH).

Taken together, the findings from studies with neurologically healthy subjects tend to support the RH hypothesis for the perception of prosodic emotion. The effect of gender on these findings is not, however, completely clear. In addition, evidence for RH involvement in processing non-emotional intonational speech contours has also been demonstrated using the dichotic listening technique in neurologically normal subjects (Behrens, 1985; Blumstein & Cooper, 1974; Grant & Dingwall, 1985; Shipley-Brown, Dingwall, & Berlin, 1988; Tompkins & Mateer, 1985).

Studies with Brain-Damaged Patients

Over the past two decades, systematic investigations have examined the effects of insult to various brain regions on emotional perception. Generally, patients with clearly defined unilateral cerebral lesions due to cerebrovascular accident (CVA), tumor, or surgical excision are evaluated to determine whether deficits exist in level of performance. Experimental tasks are usually designed to measure level of performance on discrimination or identification response measures (see reviews in Borod, 1992; Heilman & Bowers, 1990; Heller, 1990). Impaired performance is believed to imply that damaged brain areas are important to the processing required by the experimental task.

Early confirmation of clinical observations. Several early studies of patients with focal brain lesions have lent support to the contention that RH brain damage can impair affective aspects of prosody without disrupting the linguistic features of language. Heilman, Scholes, and Watson (1975) asked six RBD and six LBD subjects with temporoparietal lesions to identify a speaker's emotional mood (i.e., happy, sad, angry, or neutral) on tape recorded sentences by pointing to line drawings of faces depicting four possible emotions. Subjects were also asked to judge sentence content in a similar way. The results showed that while all subjects were errorless in content judgements, RBDs performed significantly worse than LBDs on emotional judgements. In a follow-up study, Tucker, Watson, and Heilman (1977) were interested in replicating and furthering the Heilman et al. (1975) findings to determine whether the observed prosodic comprehension deficit extended to discrimination, as well as to identification of emotional stimuli. Eleven RBD and seven LBD subjects with temporoparietal lesions identified/named a speaker's mood (i.e., happy, sad, angry, or neutral) in tape- recorded, neutral content sentences (e.g., "The boy went to the store."). On a second task, the same subjects were required to discriminate whether the emotional tone of voice was the same or different in pairs of otherwise identical sentences (16 matched tones, 16 different tones). These investigators found that the RBDs performed significantly worse than the LBDs on both the identification and discrimination tasks, with the RBDs performing at chance level.

While the results of these early studies appeared to validate clinical observations of impaired comprehension of emotional prosody in RBD patients, no neurologically-healthy subjects were tested as comparisons for the LBD patients. The question remained as to whether LBDs were also, perhaps to a lesser extent, impaired.

Role of the cerebral hemispheres in prosodic perception. Schlanger et al. (1976) asked three groups of subjects (RBD, LBD, and NC) to identify the emotional tone of voice in 10 semantically neutral and 10 meaningless sentences by pointing to line drawings of faces depicting one of three emotions (i.e., anger, joy, and sadness). They found that while both patient groups were impaired relative to the normal control (NC) group, the performance of the two patient groups was comparable. There was no effect of either emotion type nor of sentence content. Using a similar paradigm, Seron et al. (1982) examined the performance of four Wernicke's, nine Broca's, and four global aphasics on a prosodic identification task. The stimuli included strong emotional sentences (e.g., "My cat is dead" or "I won the big prize" presented in either a congruent or a non-congruent tone of voice. For both sentence types, LBDs performed significantly worse than NC subjects. For the aphasic subjects, the number of errors correlated with the severity of their oral comprehension deficit but not with the diagnosed aphasia type. The investigators concluded that when intonation is associated with a verbal message, aphasics fail to comprehend the emotional message well.

More recently, several groups of investigators have addressed the unresolved issue of right and left hemisphere roles in the comprehension of prosody. Results have been somewhat more equivocal. Using both the discrimination and identification paradigms, Denes, Caldognetto, Semenza, Vagges, and Zettin (1984) evaluated prosodic perception in groups of RBD, LBD, and NC subjects using five discrete emotions (i.e., happiness, sadness, fear, anger, and disgust). Brain-damaged subjects were classified according to inter- (left vs. right) and intra- (anterior vs. posterior) hemispheric location of lesion. Although RBDs demonstrated impaired performance on the discrimination task, relative to LBDs and NCs, on the identification task, RBD and posterior LBD groups were not significantly different in performance accuracy.

Heilman, Bowers, Speedie, and Coslett (1984) tested three groups of subjects (RBD, LBD, and NC) on two experimental tasks designed to determine relative hemispheric contributions to different aspects of prosodic perception. Brain-damaged patients had suffered unilateral cerebral infarcts verified by CT scan. In a non-emotional prosody condition, subjects listened to sentences spoken by a male reader (i.e., declarative, interrogative, or imperative). The tape was speech filtered so that the semantic message was unintelligible yet the prosody remained intact. Subjects identified the type of sentence from choices listed on a response card (i.e., ?, !, .) based on the intonation heard. In an emotional prosody condition, declarative sentences were heard representing three different emotional intonations (i.e., happy, sad, and angry). Again, the speech was filtered to remove semantic content. Subjects identified the emotion heard by indicating their choice on response cards depicting happy, sad, and angry face drawings. Overall, across conditions, RBDs performed significantly worse than LBDs, and LBDs performed significantly worse than NCs. This pattern was also seen in the emotional condition. In the non-emotional condition, however, although RBDs and LBDs both performed significantly worse than NCs, the two brain-damaged groups did not differ from one another. While the RBDs' performance was equally poor in both conditions, LBD subjects demonstrated significantly poorer performance on the non-emotional task than on the emotional task. Finally, the patient groups did not differ in terms of relative comprehension of different types of emotional or non-emotional prosody, demonstrating a lack of support for the valence hypothesis. Conclusions tentatively suggested were that the RH is dominant for emotional prosody, yet there is bilateral involvement for non-emotional prosody. The authors postulated that RBD patients could have a basic emotional prosodic processing deficit, while the LBDs' non-emotional prosodic deficit is attributable to the linguistic demands of the task. It was suggested that LBDs performed more poorly than NCs on the emotional task because of general brain damage or some LH involvement in emotional prosody.

In an attempt to elucidate whether a perceptual or an emotional disorder was at the heart of poor prosodic comprehension, Tompkins and Flowers (1985) conducted a discrimination task using pairs of filtered sentences with either a neutral or an emotional intonation. Intonations were unanimously rated by naive judges. RBDs performed significantly worse than both LBDs and NCs, although discrimination errors were made for both non-emotional as well as for emotional stimuli. The investigators concluded that the RBDs' problem was in the perceptual decoding of prosodic information rather than in purely emotional decoding. In a follow-up experiment, subjects were asked to identify the emotional tone in semantically neutral sentences either by selecting a word from two choices (e.g., anger, or joy) or by choosing a word from four response choices. In the two-choice condition, RBDs were significantly worse than both LBDs and NCs, yet in the four-choice condition, while both brain-damaged groups were significantly worse than NCs, the two patient groups were not significantly different from one another. On the basis of their findings from the two experiments, the authors concluded that increased task complexity shifts the emphasis from RH to LH processing.

In a study which expanded on the "processing defect" notion, Bowers, Coslett, Bauer, Speedie, and Heilman (1987) proposed that either a perceptual/comprehension deficit or an attentional deficit was the responsible mechanism underlying RBD patients' impaired comprehension of emotional prosody. These investigators designed a series of experiments pitting processing defect and distraction defect hypotheses against one another. A processing defect, defined as an impairment in perceiving and categorizing stimuli (presumably a RH-dominant function), would predict that RBDs should be equally impaired in the perception of prosodic emotion whether or not the semantic content is congruent with the emotional intonation. A distraction defect, which assumes that the (verbal) LH would be distracted by the semantic content (and thus involved to some extent in processing emotional prosody) predicts that RBD would be more impaired on **non**-congruent prosodic perception tasks.

In the initial experiment, RBDs and LBDs (with unilateral single event CVAs) and NCs were presented with recorded sentences spoken in an emotional tone (i.e., happy, sad, angry, or neutral). In half of the sentences, the semantic content and the emotional tone were congruent and in the other half, incongruent. The subjects were told to disregard content and identify the tone of voice heard. Overall, RBDs performed significantly worse than both LBD and NC groups. For both patient groups, performance in the incongruent condition was significantly worse than in the congruent condition. In both conditions, RBDs performed significantly worse than LBDs. NC subjects demonstrated no significant difference in comprehension between the two conditions. RBDs were significantly more disrupted by the incongruent semantics than LBDs. Finally, there was no significant effect for lesion site (anterior vs. posterior) and no effect of laterality of lesion on comprehension of different emotions. The authors concluded that RBDs' comprehension of emotional prosody can be affected by altering semantic content. This finding lent support to the distraction hypothesis. Alternatively, the authors postulated that perhaps the RBDs were inadvertently employing a compensation strategy of listening for semantics (a function "preferred" by the intact LH). This explanation would also account for the poorer performance with incongruent stimuli by both BD groups.

In a post-hoc analysis, Bowers et al. (1987) looked at the discrepant sentence stimuli and categorized them into **conflicting** (e.g., angry paired with sad) versus **inconsistent** (i.e., angry, sad, or joy paired with neutral).

The distraction hypothesis predicts that RBDs would perform more poorly on **conflict** versus **inconsistent sentences,** while the compensation hypothesis predicts no difference in comprehension between the two stimulus types. Further testing revealed that while the RBDs were worse on conflicting sentences, LBDs and NCs demonstrated no difference.

In a follow-up study, the investigators presented speech-filtered sentences, as well as neutral sentences, in the four emotional tones. If the distraction hypothesis held true, RBDs should be worse with the intact speech. Again, regardless of condition, RBDs were significantly worse than the other groups. Across all groups, however, performance with filtered speech was significantly poorer than performance with normal speech, supportive of the processing defect hypothesis. The overall conclusion was that RBDs have both a processing and a distraction defect contributing to their poor comprehension of emotional prosody. In general, however, when associated with a verbal message, the LH is to some degree involved in emotional prosody.

In a study of emotional expression and comprehension in acute (less than three months post onset) unilateral CVA patients, Cancelliere and Kertesz (1990) evaluated performance on a prosodic identification task. Four different emotional intonations were presented (happy, sad, angry, and neutral) in semantically neutral sentences. While the performance of both RBD and LBD subjects was worse than that of NCs, the two brain-damaged groups did not differ significantly from one another. As a primary focus of these investigators was intrahemispheric lesion location and classification of aprosodic subtype, a within hemisphere analysis was also conducted. The results failed to demonstrate support for the anterior-posterior distinctions made by Ross (1981). In this study, subcortical structures (particularly the basal ganglia) in both hemispheres appeared to play an important role in both the expression and perception of emotion.

Lalande et al. (1992) attempted to dissociate right and left hemispheric contributions to prosodic and semantic aspects of affect in sentences. Again, subjects were RH and LH unilateral stroke patients and neurologically-healthy controls. Three tasks were employed in this study incorporating a range of transcultural emotions (e.g., surprise, fear, and disgust). The first, a verbal contextual task, was designed to examine pure semantic categorization. Subjects were asked to identify the emotion corresponding to sentences containing semantic emotion but neutral tone. The second was a pure prosody task in which subjects identified the emotion conveyed in sentences intoned with humming. The final task was an emotional concordance task in which stimuli contained both prosodic and semantic content. In half of the sentences, prosodic and semantic content were concordant, in the other half, discordant. Subjects were required to discriminate whether the two stimuli heard were the same or different in terms of emotional intonation.

On the verbal contextual task, while none of the subject groups were significantly impaired, LBDs did perform more poorly than RBDs. On the pure prosody task, RBDs' performance was significantly impaired relative to that of NCs. LBDs, by contrast, did not differ significantly from NCs. RBDs, while not significantly worse than LBDs, did demonstrate the poorest performance. Finally, on the emotional concordance task, RBDs were significantly impaired relative to both LBD and NC subjects. All subject groups, particularly the RBDs, demonstrated greater difficulty with discordant stimuli. For the NCs, there was a significant correlation between performance on the emotional concordance and the pure prosody tasks, a correlation not observed for RBDs. On the basis of these findings, the authors concluded that: 1) As RBDs and LBDs did not differ on the pure prosody task, there must be some LH involvement in prosodic comprehension. 2) Since the basic ability of RBDs to categorize emotional words was intact (verbal contextual task), the deficit in prosodic perception must be at the phonetic level. 3) Since no significant correlation was observed between RBDs' performance on the pure prosody and the emotional concordance tasks, perhaps some subgroups of RBDs are differentially impaired such that a pure dysprosody might result from cortical damage while a deficit in emotional concordance likely represents neither a pure emotional nor a pure prosodic problem. The authors postulated that the latter deficit is attributable to a distraction effect, perhaps subcortically-mediated (e.g., basal ganglia or capsular territory).

Finally, Van Lanker and Sidtis (1993) extended the analysis of prosodic identification results in unilateral CVA patients to include acoustic parameters. In this study, while both RBD and LBD patients performed significantly worse than NCs, the two patient groups did not differ in the accuracy with which they identified sadness, happiness, anger or surprise in prosodic stimuli. An analysis of valence errors revealed that RBDs were significantly more likely to mislabel negative emotions (i.e., sadness, and anger) as positive (i.e., happiness and surprise). The authors explain this latter finding in terms of poor RBD use of fundamental frequency variability. They arrived at this conclusion by measuring the acoustic parameters of their prosodic stimuli and then using these parameters in a discriminant analysis to examine the relationship to the misclassification errors of the BD patients. Results demonstrated that the BD groups differed in their use of the acoustic variables to identify prosodic emotion. RBDs failed to utilize pitch information accurately, while LBDs demonstrated improper use of duration information. The authors suggest that both hemispheres contribute to the comprehension of emotional prosody, and that prosodic deficits can be accounted for by perceptual deficits rather than as a consequence of affective or other types of cognitive dysfunction.

Overall, research with brain-damaged subjects conducted over the past 10 years has qualified, to some extent, the unequivocal support for the RH hypothesis from early research and clinical observations. Questions which remain unanswered involve the nature of each hemisphere's contribution to prosodic comprehension and the extent to which the perceptual disorder common to RBDs is related to a deficit in comprehending emotional prosody.

In attempting to generate an overall conclusion based on the results of the above investigations, it is necessary to reconcile some of the differences in findings among the various studies. Variations in both methodology and subject selection may account for much of the observed inconsistency. Procedural variables which have been demonstrated to affect subject performance include: task type (e.g., identification, discrimination), stimulus type (e.g., verbal, non-verbal), semantic content (e.g., congruent, incongruent), stimulus valence (positive, negative), and task complexity. Critical subject variables appear to be length of time post brain injury, intrahemispheric location and diversity of lesion, and type and severity of aphasia.

The implication from the studies reviewed is that while the RH is clearly involved in the comprehension of emotional prosody, the LH may also, perhaps to a lesser degree, play a role in certain aspects of prosodic perception. Finally, subcortical, as well as neocortical brain regions, particularly within the right hemisphere, have been associated with deficits in the perception of prosody. Further research is warranted to discern the interrelationships between inter- and intra-hemispheric contributions to the comprehension of emotional prosody.

Epilepsy and Emotion

Hypotheses regarding functional brain asymmetry in emotional processing have also been tested in patients with various epileptic disorders. These investigations have predominantly focused on the experiential or subjective, rather than the perceptual and expressive components of emotion. Mood alterations and emotional outbursts have frequently been observed in relation to ictal events, particularly in patients with temporal lobe epilepsy (TLE) (eg., Bear, 1979). Due to the relatively greater epilepogenicity of the temporal lobe, seizures arising from this region comprise approximately 50% of focal epilepsies (Neidermeyer, 1990). The vascularity of limbic areas including the hippocampus and amygdala makes them especially vulnerable to compression, while the tissue itself is particularly sensitive to biochemical alterations as a result of hypoxia, metabolic disorders, viruses, and genetic conditions (Anderson, Hauser, Penry, Sing, 1982). While seizures arising from temporal lobe structures are not necessarily associated with structural damage, primary lesions can occur in these regions, and can often include tumors, vascular anomalies, dysgenesis, encephalitis, and sequelae of brain injury (Glaser, 1993). Complex partial, or psychomotor, seizures predominate in TLE. Complex partial seizures are characterized by automatisms, or automatic behavior, and usually partial or complete loss of consciousness (Kotagal, 1993). Approximately 75% of TLE patients also experience auras (simple partial seizures) either in isolation or as a precursor to complex partial seizures. In addition, about 50% of TLE patients experience secondarily generalized tonic, clonic, or tonic-clonic seizures (Mikati & Holmes, 1993). Ictal events are associated with increased brain activity as measured by various diagnostic techniques. Electrophysiological measures have provided evidence that epileptic neurons demonstrate increased electrical excitability and recurrent, hypersynchronous paroxysmal discharges (e.g., see Niedermeyer, 1990 for a review). Although clinical manifestations of seizures may not always accompany abnormal patterns of electrical activity, a close relationship has been established between onset of convulsions, tonic posturing, various autonomic reactions, and focal electrographic seizure activity (Penfield & Jasper, 1954). Functional imaging, particularly Positron Emission Tomography (PET), also used in intracranial diagnosis of epilepsy, has demonstrated hyper-metabolic zones in epileptic brain regions during ictal events, and hypometabolic zones interictally (e.g., Theodore, Brooks, Sato, et al., 1984). Emotional changes observed occurring during seizure activity are thus generally considered to result directly from increased brain activity within the region of epileptic focus, or disinhibition of connected brain regions.

Enhanced affective associations are also a presumed mechanism of the observed interictal psychological patterns of affective behavior seen in TLE (Bear & Fedio, 1977); seizure activity is thought to result in sensory-limbic hyperconnections within the temporal lobe (Bear, 1983). Interictal behavioral manifestations of temporal-limbic epileptogenic foci have also been observed in terms of sexual functioning in epilepsy patients. Persons with TLE commonly suffer from hyposexuality in contrast to patients with destructive temporal-limbic lesions (e.g., tumor), who often exhibit hypersexuality (see Neidermeyer, 1990, for a review). Behavioral/experiential affective changes in TLE thus appear to be in line with the exacerbating effects of irritative, as opposed to destructive lesions.

In terms of cognitive status, by contrast, neuropsychological testing has fairly consistently demonstrated impairments across a variety of functional domains in epilepsy patients. Similarly, deficits have been observed in the perception of emotional speech (Tompkins & Mateer, 1985) and in the comprehension of attitudinal meaning in written narratives (Cohen, Prather, Town, & Hynd, 1990). While these impairments, in general, appear independent of medication effects, greater deficits are associated with earlier seizure onset and duration and greater interictal EEG abnormality (Perrine, Gershengorn, & Brown, 1991; Brown, 1991). Impaired performance in various aspects of cognitive functioning thus likely appear secondary to the destructive effects of prolonged irritative epileptic activity. The effects of temporal lobe seizures on emotional behavior therefore may depend on the aspect of emotional processing under consideration (e.g., experiential or perceptual). In addition, primary locus of seizure activity is essential to consider, as both ictal EEG patterns and behavioral symptoms associated with TLE vary greatly as a function of the portion of the temporal lobe involved (e.g., hippocampus, amygdala, lateral temporal lobe) (Weisner, 1983). Primarily hippocampal seizures are often associated with strange feelings and experiential phenomena, amygdalar seizures with autonomic symptoms, and lateral temporal involvement with sensory hallucinations, language dysfunction, and confusion (Neidermeyer, 1990).

Neuropsychiatric Aspects of TLE

The psychiatric manifestations of seizure disorders have been a focus of study and treatment throughout the nineteenth and early twentieth centuries. More recently, emphasis has been on the psychological/psychiatric changes which occur in TLE. Among neurological disorders with confirmed anatomic locus, TLE has most frequently been associated with functional psychiatric disorders. Psychiatric symptomatology has been subdivided into ictal, postictal, and interictal personality changes. Complex automatic behaviors related to ictal aggression and hypersexuality in TLE patients have been described in the literature, yet appear to be relatively uncommon clinically. Postictal psychiatric manifestations have also been described in TLE patients. In such cases, patients can experience a post-epileptic delirium during which acts of violence, visual hallucinations, florid thought disorder, or extreme religious ecstasy have been reported. A presumed mechanism for this phenomenon is a breakdown in higher cortical inhibition of limbic circuitry; these outbursts are presumed to be mediated by limbic-hypothalamic structures (Niedermeyer, 1990). The primary attention in the psychiatric manifestations in TLE, however, has been devoted to interictal personality changes. The "temporal lobe personality" has been difficult to define via traditional psychiatric diagnostic categories; descriptions have generally been based on clinical observation of patients. The characteristics of commonly reported symptoms based on these observations are not believed to adequately describe the underlying neurological process inherent in TLE. Nevertheless, there are some similarities between emotional behaviors commonly displayed by TLE patients and behavioral changes seen in animal models subsequent to destruction of temporal brain regions. Animal studies have typically shown specific emotional changes (e.g., fear, anger, and hypersexuality) following destruction of anterior temporal areas. Similar alterations have been observed in humans with bilateral temporolimbic injury.

TLE patients have been described in the literature as displaying increased emotionality, over inclusiveness, hypermorality, aggressiveness, hyposexuality, humorlessness, and hyperreligiosity, among other traits (e.g.; Bear & Fedio, 1977; Blumer, 1991). Historically, emotionality and denial have been more commonly associated with RTLE patients, while ideational traits, depression, and catastrophic reactions have been linked with LTLEs. Based on the concept that temporal lobe lesions may disrupt sensory-limbic connections leading to these observed changes, Bear and Fedio (1977) attempted to characterize the effects of unilateral TLE on psychosocial behaviors, in effect to create a behavioral profile, through the use of subjective questionnaires. Discriminant profile analysis of the reported traits revealed that particular features of behavior, thought, and emotion differentiated TLEs from contrast groups. In the self-report inventories, traits best discriminating between TLE patients and non-TLE controls were circumstantiality, humorlessness, dependence, and sense of personal destiny. Among the questionnaire items endorsed by observers about the TLE patients, circumstantiality, obsessionalism, dependence, and sadness best discriminated TLEs from contrast groups. The emotional variables best differentiating TLEs were presence of mood swings, anger, and sadness. Duration of illness, but not seizure frequency, correlated with most of the behavioral parameters, suggesting that the psychological changes were more a progressive effect of the long-term illness rather than a direct consequence of seizures per se.

In terms of differences between RTLEs and LTLEs, the authors found that while foci in either hemisphere appeared to influence affective associations, the nature of the endorsed responses was suggestive of distinct hemispheric processing styles. RTLEs tended to endorse items related to externally demonstrated affect (e.g., overtly emotive, elation) as well as preoccupation with details. The LTLEs, by contrast, reported more anger and sadness, and were distinguished by intellectual and moral self-scrutiny; observers rated them as more viscous and obsessional. RTLEs also tended to describe themselves less severely with minimization of sadness while LTLEs emphasized depression and described themselves in terms of socially disapproving traits. Similar observations were reported by Perrini (1986) using the emotion profile index (EPI) and the Bear-Fedio personality inventory. Patients with left-onset complex partial seizures tended to provide a negative self-image with endorsement of paranoia, guilt, aggression, and dependence. Right-focus patients, by contrast, tended to rate themselves in a much more positive manner. In recent years, however, these distinctions have to a certain extent been challenged due to the variability in clinical observations of severity and frequency, and the lack of specificity of symptom/trait presentation (e.g., Mikati & Holmes, 1993). Overall, however, the conclusions from these studies do lend some support to the demonstrations of hemispheric emotional differences in the brain-damaged literature.

Bear and Fedio (1977) additionally suggested that awareness of self has been equated with the potential for verbal expression. The lack of awareness of deficit seen in RTLEs could therefore result from a functional disconnection between hemispheres such that the LH, in the absence of sensory/affective input from the damaged RH, confabulates a response. By contrast, LH deficits should thus be very apparent to conscious inquiry, as is manifested in the LTLEs' hyperawareness of deficit.

It is also important to note that, in addition to these well-described personality alterations, the incidence of diagnosable psychiatric disorders in TLE is reportedly higher than in non-epileptics. Although the vast majority of patients with TLE are well-adjusted, functional, and do not suffer from psychosis, there does appear to be an association between TLE and psychosis in some patients, with some lateralized findings. According to epidemiological studies (e.g., Flor-Henry, 1969), schizophrenic psychosis occurs most frequently in TLE patients with a left-sided seizure focus while manic-depressive psychosis is more common in patients with a right temporal EEG seizure onset. In a study using self-report measures of depression, LTLE patients were found to endorse a greater number of depressive symptoms than RTLEs. Of note, the higher scoring group contained a greater number of both left-handed and male patients than were represented in the RTLE group. Anxiety scores did not differ between the two groups (Altshuler, Devinsky, Post, & Theodore, 1990). Interestingly, in patients with both psychosis and TLE, the clinical symptoms of epilepsy generally improve along with normalization of EEG patterns, during times when the psychotic symptoms are most florid (see Niedermeyer, 1990). Mendez et al. (1993) retrospectively investigated the relationship of seizure variables and antiepileptic drugs (AEDs) on interictal depression in 101 epilepsy patients with clinically diagnosed depressive disorders requiring psychiatric evaluation. Among the DSMIII-R diagnoses represented were major depression, bipolar disorder with depressive symptoms, dysthymia, and depression not otherwise specified (NOS). Comparison groups included migraine patients with depression and non-depressed epilepsy patients. The authors found that the epilepsy patients with depression had fewer generalized convulsions (GTC) and more anticonvulsant drug therapy than non-depressed controls.

They suggest that non-reactive depression could occur when increased AED therapy leads to decreased generalization of epileptogenic foci. Depression was also specifically associated with epileptic foci within the mediobasal temporal limbic system, the most common region involved in complex partial seizures (CPS) and GTCS. While these investigators failed to find significant group differences with respect to laterality of seizure focus, they did note that their depressed epilepsy patients had more left-sided than right-sided foci.

Studies of Emotional Processing in TLE

Over the past 15 years, systematic investigations of various aspects of emotional processing in TLE have been undertaken following up on the documented reports of ictal and interictal personality alterations. The majority of these studies have focused on the experiential and expressive processing modes measured during ongoing seizure activity. In 1982, Sackeim and colleagues published a series of three retrospective clinical studies conducted to clarify functional asymmetries in the regulation of emotional behavior. The final study focused on ictal emotional outbursts in a patient population with predominantly temporal seizure foci. The authors found that in cases of gelastic epileptic seizures, the foci were twice as likely to have originated within the left temporal lobe. For dacrystic seizures, although the number of subjects was small, the epileptic focus was predominantly within the right hemisphere. The investigators combined these results with findings from two prior studies in which pathological crying was associated with LH damage, pathological laughing appeared more associated with RH damage, and right hemispherectomy was associated with euphoric emotional reactions. General conclusions were that regulation of positive and negative emotion was consistent across experience, perception, and expression, such that the LH subserves positive emotion and the RH subserves negative emotion.

A case study of three patients with gelastic seizures also lends at least partial support to this notion of hemispheric asymmetry for emotions of differing valence. In an attempt to gain insight into the mechanisms subserving laughter and its emotional concomitants, Arroyo et al. (1993) described three patients with gelastic seizures in whom electrical cortical stimulation elicited laughter. The initial patient described experienced laughter during seizures without the subjective experience of mirth. Magnetic resonance imaging revealed a cavernous hemangioma in the left superior mesial frontal region, and ictal EEG recordings demonstrated a left anterior cingulate gyrus seizure onset. The other two patients described experienced CPS localized to the left temporal lobe. Ictal and interictal EEG recordings revealed posterior basal and lateral temporal seizure onset in one patient and inferior temporal gyrus onset in the other patient. Seizures in both patients subsequently spread throughout the temporal lobe. In these two latter patients, electrical stimulation of the fusiform gyrus and parahippocampal gyrus produced bursts of laughter along with a subjective experience of mirth. The authors concluded that the anterior cingulate region may be involved in the facial and related motor acts associated with laughter, while the basal temporal cortex is involved in subjective processing of the emotional content in laughter.

In an effort to discern whether functional hemispheric asymmetries exist for all affective processes, Strauss, Wada, and Kosaka (1983) examined spontaneous facial expressions occurring during the onset of focal seizures in 38 left-onset and 39 right-onset epilepsy patients. This measure was chosen because facial expressions are thought to be representative of underlying emotional states, and because alterations occurring as a result of seizure activity appear to be uncontrollable. These investigators studied the incidence and type (e.g., happy, sad) of expression and evaluated whether associations existed between side of seizure onset and expression type. They recorded only the initial expression which occurred at the onset of focal EEG activity, and obtained concurrent ratings of emotion type from two judges. Analysis of results revealed differences in the frequency of expression type, such that neutral and sad expressions were the most common, followed by fear, surprise, and happiness. There was no association between side of seizure focus and type of expression displayed when discrete emotions were dichotomized by valence (i.e., positive and negative). Similar negative results were obtained when subjects' performance was separately evaluated by gender. Finally, there was no apparent relationship between intrahemispheric site of ictal discharge (e.g., frontal, parietal, or temporal), and type of expression observed. Although the authors point out that it is unclear whether these facial expressions are the direct sequelae of epileptic activity or a secondary response to an alternative ictal experience, they conclude that the two hemispheres may be similarly involved in the production of involuntary facial expressions.

In a similar study, Hiyoshi and colleagues (1989) reviewed the initial facial expressions of 98 TLE patients during 195 CPS in relationship to laterality and focality of EEG seizure onset. The results of this investigation were similar to the findings of Strauss et al. (1983) in that differences were observed in the frequency of expression type and that no relationship was found between type of facial expression and side of seizure onset. In this study, neutral expressions were most frequently observed followed by expressions of disgust, happiness, and sadness; anger, surprise, and fear were never observed. These authors additionally observed that expressions of emotion at seizure onset rarely correlated with subjective experience of emotion. It was noted, however, that patients exhibiting disgust expressions often experienced autonomic sensations (e.g., rising epigastric sensations) prior to seizure onset. Patients demonstrating happy expressions at seizure onset, by contrast, tended to experience psychic or sensory auras (e.g., deja vu) prior to seizures. Finally, for expressions of disgust and happiness, type of emotion was related to intrahemispheric site of seizure onset such that disgust expressions tended to occur with mesial temporal onset while happy expressions tended to occur with lateral temporal onset.

To a lesser extent, researchers have also investigated the perception of emotion in TLE patients. Generally these studies have, of necessity, been conducted during relatively quiescent interictal periods. In 1985, Tompkins and Mateer conducted a study to explore the ability of patients with temporal lobe seizure foci to appreciate attitudes conveyed through prosodic cues and lexical content. Their initial experiment was designed to assess the extent of RH involvement in judgement of consistency between verbal content in a paragraph and the emotional tone conveyed by the reader of the narrative. Subjects tested were 10 RTLE and 8 LTLE pre-surgical candidates with intractable epilepsy. All subjects were strongly right-handed and LH language dominant as assessed by intracarotid amobarbital testing. Analysis of accuracy data revealed that RTLEs made significantly more errors than both LTLEs and normal control subjects (NCs) overall, as well as specifically on items in which prosodic intonation matched verbal content (congruent). LTLEs, by contrast, did not differ from NCs on any measure. A second experiment was conducted to evaluate ability to comprehend linguistic indicators of attitude in written narrative form. Subjects were presented with both paragraphs in which the attitude conveyed was consistent and paragraphs in which inconsistencies existed in terms of attitudinal content. While LTLEs again did not differ from controls, RTLEs made significantly more errors than NCs but not LTLEs when responding to inferential questions about the paragraphs with inconsistent attitudinal context. All subjects made very few errors on the paragraphs conveying consistent attitudinal information. Combining the results from the two studies, the authors attempted to explain the RTLE impairment on congruent items in the prosodic task. The reasoned that since the RTLEs failed to demonstrate significant impairment on both factual and inferential questions within the congruent items of the lexical task, these subjects must have been capable of adequately comprehending the lexical information. The RTLE deficits with congruent items in the prosodic task must therefore represent a "fundamental impairment in extracting or interpreting prosodic information" (Tompkins & Mateer, 1985), since these subjects appeared not to benefit from intonational cues in judging the speaker's attitude. The authors further concluded that decreased accuracy with which the RTLEs answered inferential questions about the incongruent lexical paragraphs represented a decreased efficiency in utilizing a pragmatic approach to interpret ambiguous information.

To address developmental aspects of lateralized representation of emotional prosody, Cohen, Prather, and Town (1990) extended the investigation of prosodic perceptual ability to 6-11 year-old children with unilateral TLE. Eleven LTLEs, 12 RTLEs and 229 NCs were evaluated in three conditions. In the first condition the children were presented with a soundless video in which they were required to identify the emotion (i.e., happy, sad, and mad) conveyed by the speaker, through observation of her gestures. In the second condition, the subjects listened to an audiotape of the same speaker and were asked to identify the emotion in her tone of voice. In the final condition, subjects simultaneously viewed and heard the video and again made judgements as to which emotion was conveyed. Analyses relevant to the TLE subjects revealed that RTLEs performed significantly below the levels of same-aged NCs across all three receptive tasks. The performance of LTLE children fell in between that of the RTLEs and the NCs without being significantly different from either group. Although the authors concede that support for RH dominance for affective prosody would have been stronger had RTLEs performed significantly worse than LTLEs, they offer two possible explanations for the lack of such a finding. First, they suggest that early-onset chronic epilepsy is not as circumscribed a lesion as is typically seen in vascular injury; with epileptic lesions it is not uncommon to see spread of discharge to the unaffected hemisphere. This recruitment of epileptogenic activity could therefore have adversely affected the LTLEs performance, although likely not to the degree that RTLEs were affected. Secondly, the authors discuss their findings in relation to reports in the literature of a shift in language dominance after early onset LH lesions. They suggest that one might expect some decline in the RH's ability to process emotional prosody in order to accommodate this shift in propositional language subsequent to early LH damage. Similarly, after early RH damage, the LH might be expected to acquire some capacity for processing emotional prosody. Provided these assumptions are correct, it would logically follow that early onset chronic temporal lobe dysfunction could impair, to some extent, perception of emotional prosody, although significant impairment would only be expected following damage to the RH.

Epilepsy and the Intracarotid Amobarbital Procedure

History of the technique

The intracarotid amobarbital procedure (IAP) has been utilized extensively for over three decades for clinical analysis of cognitive functions as part of the pre-surgical evaluation of patients with intractable epilepsy. It is commonly referred to as the Wada test after Juhn Wada, the physician who initially described and implemented the procedure in animal studies and later in clinical practice (Wada, 1949; Wada & Rasmussen, 1960). The procedure, used to investigate hemispheric spread of epileptiform discharges, was observed to produce transient ipsilateral cessation of hemispheric activity without disrupting vital functions and inducing excessive sedation (Rausch, 1987). Apparently, Wada actually developed this technique to determine hemispheric language dominance in psychiatric patients to insure unilateral electroconvulsant therapy be administered to the non-dominant hemisphere (Loring, Meador, Lee, & King, 1992). The IAP subsequently became useful in guiding/modifying surgical resections to avoid postoperative language deficits in epilepsy patients (Petersen, Sharborough, & Jack, 1993). In 1962, Brenda Milner and colleagues extended the use of the IAP to include evaluation of memory functions in order to identify patients potentially at risk of incurring significant memory deficits postoperatively. The notion was that patients at risk for amnesia subsequent to unilateral mesial temporal excision would incur a transient amnesia following administration of sodium amobarbital to inactivate the hemisphere ipsilateral to the seizure focus.

To date, the preoperative IAP evaluation of language and memory functions has become widely accepted and increasingly utilized. It is apparent, however, that since no official standards or normative data exist governing amount of amytal administered, injection rate, and use of encephalographic or radiological imaging monitoring techniques, that substantial methodological variability exists between centers employing this technique (e.g., Miller & Fedio, 1988). This lack of consensus has been emphasized throughout several multicenter surveys of IAP protocol (e.g., Rausch, 1987; Snyder, Novelly, & Harris, 1990). Ongoing efforts have been initiated, however, to unify the IAP procedures among epilepsy centers conducting large-scale pre-surgical evaluations.

In recent years, the IAP has also become a research tool in the evaluation of additional cognitive functions including attention, neglect, and emotion (e.g., Huh et al., 1989; Lee et al., 1988; Meador et al., 1988; Spiers, et al., 1988). Finally, technological advances have enabled methodological refinement and increased precision in several aspects of the IAP. Functional imaging techniques are providing new methods for mapping of vascular amytal distribution (e.g., Jeffrey et al., 1991). More objective, quantified methods for monitoring the duration of amobarbital effects have been proposed (e.g., Bouwer, Jones-Gotman, & Gotman, 1993). Supraselective middle cerebral artery (MCA) and posterior cerebral artery (PCA) injections currently allow for a finer analysis of language and memory functions without some of the physiological limitations and confounding cognitive variables inherent in the standard IAP injections (e.g., Jack et al, 1988; Peterson, & Sharborough, 1991).

Procedural and pharmacologic aspects

Prior to the IAP, a cerebral angiogram is conducted to evaluate vascular anatomy and to assess the amount of crossflow between right and left hemispheres. Angiographic evaluation permits identification of potential anomalous circulatory patterns, in particular, anastamoses between carotid and vertebral/basilar arterial systems. This information is essential for patient safety, as well as for accurate interpretation of IAP results with respect to amobarbital distribution in various brain regions. Typically, a local anesthetic is utilized to introduce a catheter into the internal carotid artery through a transfemoral approach (Petersen, Sharborough, & Jack, 1993). The position of the catheter is verified by flouroscopy.

The IAP follows completion of angiography, generally with an initial injection of 100-150 mg of 5% sodium amobarbital administered over the course of several seconds. Subsequent injections may follow to produce adequate anesthetization as determined by appropriate behavioral response and/or typical patterns of EEG slowing involving high amplitude delta activity over frontal and temporal regions ipsilateral to the injection (Loring et al, 1992). Amobarbital is a di-alkyl substituted oxybarbiturate with structural formula $C_{11}H_{18}N_2O_3$. It is highly lipid soluble, readily crosses the blood/brain barrier, and depresses the activity of all excitable tissues (Rall, 1990; Rausch,et al., 1991). Complete hemispheric anesthesia during the IAP has been shown to persist between four and eleven minutes post injection, as reflected by presence of typical slow EEG waveforms (Gotman, Bouwer, & Jones-Gotman, 1992).

Current uses in epilepsy evaluation

Language testing. The initial rationale for the development of the IAP was the evaluation of language function (Wada, 1949). Despite some of its methodological limitations, the IAP is still generally considered the definitive technique for the determination of language dominance and, more specifically, the extent of each hemisphere's contribution to language function. Patients for whom the IAP evaluation of language is most essential are right- and left-focus neurosurgical candidates who demonstrate the possibility of atypical hemispheric language representation (e.g., discordant neuropsychological findings, left-handedness with familial sinistrality) or those for whom planned surgical intervention may encroach on critical language areas (e.g., see Rausch, et al., 1991 for more detailed discussion). Although IAP language assessment has not been standardized, most epilepsy centers incorporate similar features. Generally, patients are asked to count aloud or maintain rote serial speech during injection of the amobarbital. The timing of the onset of language testing has been somewhat controversial in the literature. Most institutions begin testing after a short delay following the onset of contralateral hemiparesis. Particularly with dominant hemisphere injection, the patient will typically cease speaking or wi ll demonstrate significant alteration in expressive language. The criteria for determination of language dominance have historically been a source of significant debate between centers employing the IAP (e.g., see Loring, et al., [1992] for further discussion). While specific tasks may vary from one center to another, functions typically evaluated include repetition, naming, fluency, and comprehension. Most agree that criteria for "passing or failing" the examination must be pre-determined and explicitly stated by each institution. Most centers currently evaluate multiple language functions serially, documenting course of impairment and time of recovery for each function. Patients are typically asked to execute simple one- and two-step motor commands, read and repeat single words and phrases, name pictures and/or objects, and to answer comprehension questions. Some controversy also exists in the literature as to whether the IAP adequately anesthetizes or functionally deafferents inputs to more posterior language areas. In cases where surgical intervention may involve more posterior regions within the dominant hemisphere, selective PCA injections may be considered for more precise localization (e.g., Petersen, Sharborough, & Jack, 1993).

Memory testing. In the early 1950s, Wilder Penfield at the Montreal Neurological Institute (MNI) made the initial clinical observations of significant memory impairment with bilateral temporal lobe dysfunction (Penfield & Milner, 1958). Two patients who underwent left temporal lobectomies postsurgically demonstrated substantial impairments in recent memory. Autopsy results from one of these patients revealed atrophy of the right hippocampus, supporting Penfield's hypothesis of pre-existing damage within the non-resected temporal lobe (Penfield & Mathieson, 1974). The strongest evidence for memory deficits following bilateral temporal lobe damage, however, came from Scoville's patient, H.M., who underwent bilateral temporal lobectomy for control of intractable seizures in 1953 (Scoville & Milner, 1957). This patient, extensively studied in the literature, demonstrated a severe and persistent post-surgical amnestic syndrome. In subsequent years, additional surgical patients from the MNI were reported to demonstrate varying degrees of memory impairment after unilateral temporal lobectomy (see Loring et al., [1992] for review). The primary conclusion drawn from these original studies was that the presence of contralateral temporal lobe dysfunction substantially increases the risk of post-surgical memory impairment. In an effort to predict contralateral hippocampal damage prior to surgery, Milner and colleagues (1962) reasoned that the IAP, by inducing pharmacological inactivation of the proposed surgical hemisphere, would allow assessment of memory in the contralateral hemisphere. Impaired performance could thus predict risk for postoperative amnesia (Milner, Branch, & Rasmussen, 1962). Clinical validation of the IAP as a predictor of postoperative memory deficits has come from a series of negative findings from the MNI. Milner (1972) described several patients who failed memory assessment during IAP and subsequently underwent modified surgical resections without significant memory loss.

Since memory evaluation during IAP was designed to identify patients at risk for global amnesia, the procedure is most relevant for patients expected to undergo temporal lobe resection. Many surgical centers currently use this aspect of IAP testing prior to any proposed temporal lobe surgery. Substantial variability does exist, however, between centers in terms of requirement for IAP, procedure for memory evaluation, criteria for passing the test, and use of the IAP information to modify surgical intervention (e.g., Rausch, 1987). Although no standardized protocol has been adopted, most centers have utilized an approach modified from the original MNI procedure (Jones-Gotman, 1987), in which discrete items are presented during hemispheric anesthetization and recall is tested after drug effects have worn off. In the MNI procedure, an object, a word, two line drawings, and a sentence are presented during the anesthetization period. Memory is assessed in a recognition paradigm which includes the use of foil items. Failures to recognize items are scored as errors. Studies by Loring et al. (1990) provide evidence that these criteria may be overly conservative, unnecessarily excluding patients from surgical intervention. Patients may be unable to recognize items presented immediately after injection but may meet criteria for passing memory tests when items are presented slightly later in the procedure without adverse postoperative effects. Lesser et al. (1986) investigated the timing of stimulus presentation and concluded that consciousness must be retained during the initial mute period following injection as patients could demonstrate adequate ability to recall items presented during that time. Nevertheless, it remains inconclusive as to whether failure to recall material presented represents impaired contralateral memory functions or incomplete encoding of the presented stimuli. Further limitations of IAP memory testing may be due to other cognitive factors, including confusion, inattention, and emotional reactivity. Finally, although IAP memory testing is presumed to assess hippocampal function, it is still unclear to what degree the hippocampus is affected during anesthetization as it receives vascular supply from both the internal carotid and the vertebral arterial distribution, and only MCA and ACA distributions are typically perfused during the IAP. Evidence of significant EEG slowing in the hippocampus during IAP (Jones-Gotman, 1987) and correlations between IAP memory performance and hippocampal neuronal densities (Rausch, et al., 1989; Sass, et al., 1991) do, however, lend convincing support to the validity of the procedure.

The Intracarotid Amobarbital Procedure and Emotion Expression/Experience

The earliest investigations of emotion using the IAP stemmed from observations by a group of Italian investigators who reported the occurrence of depressive/catastrophic reactions following LH amobarbital injections, and euphoric/maniacal or indifference reactions after RH amobarbital injection (Terzian & Cecotto, 1959). Similar alterations in affective state were subsequently described by other groups of investigators (e.g., [Alema & Donni, 1960; Alema & Rosadini, 1964; cited in Loring, et al., 1992]; Perria, Rosadini, & Rossi, 1961; Terzian, 1964; Rossi & Rossadini,1967, [described in Lee, Meador, & Brooks, 1990]). Generally, these studies reported the emergence of depressive reactions following anesthetization of the hemisphere dominant for language, while euphoric reactions were described as more frequent with non-dominant hemisphere anesthetization. Mood alterations were typically reported as occurring between four to six minutes post injection, and lasting between one and ten minutes. Usually, a recurrence of fast EEG activity, or complete EEG normalization was observed during the time of the emotional reaction (see Loring et al., [1992] for further discussion of this literature).

A second group of IAP studies found no significant associations between type of emotional response and inactivation of a particular hemisphere after amobarbital injection (e.g., Fedio & Weinberg, 1971; Werman, Christoff, & Anderson, 1959; Tengesdahl, 1963). Studies from the Montreal Neurological Institute in 104 epilepsy patients also contradicted the results of the early Italian observations (Milner, 1974). Milner used a five-point mood rating scale to objectify and systematize patients' emotional reactions post amobarbital injection. Forty of the 104 patients studied demonstrated identical changes in emotional reactivity following left and right hemisphere injections. Of the remaining patients, euphoria after LH injection was present in 37%, while euphoria following RH injection occurred in 24% of the patients. Depressive reactions were only seen in five cases; three of these occurred with LH injection and two with RH injection. The authors concluded that there was no association between LH injection and depressive reactions nor between RH injection and euphoric reactions. Finally, Kolb and Milner (1981) evaluated the effect of amytal injections on spontaneous facial expressions and on observations of mood changes in pre-operative epilepsy patients beginning within the first five minutes post injection and continuing for 15 minutes thereafter. Results demonstrated no evidence for lateralized amytal effects on mood or spontaneous facial expression. There was also no apparent relationship between occurrence of mood changes and side of epileptogenic lesion.

Given the equivalent number of early studies with opposite conclusions, subsequent investigations have begun to consider a number of variables which may have accounted for some of these discrepant findings. Loring et al. (1992) examined the effect of several variables in explaining the lack of concordant findings. The authors concluded that between-study differences in dosage, degree of drug crossflow to the contralateral hemisphere, etiological factors in epilepsy, and premorbid patient personality characteristics could not likely account for the differences reported in terms of lateralized IAP emotional responses. Factors which have also recently been considered in evaluating prior discrepant findings include criteria determining emotional responses/reactions, as well as dosage, timing, and duration in amobarbital administration. In recent years, systematic investigations of emotional expression during the IAP have raised additional questions and have clarified, to some extent, the nature of hemispheric involvement in emotion. In 1991, Kurthen and collaborators reported on the incidence of severe negative emotional reactions occurring during the IAP. The study included 80 epilepsy patients undergoing presurgical evaluation. In a total of 159 IAPs, only four cases of such reactions were observed. In three of these cases, the negative reactions occurred following barbiturization of the LH, and in one case, after RH anesthetization. All patients were right-handed with left cerebral language dominance. The authors conclude that while results are consistent with lateralization of negative emotional reactions, based on the one case with a right injection negative reaction, they do not suggest systematic lateralization of negative mood to the right hemisphere. Claverie and Rougier (1994) arrive at a complementary conclusion based on case reports of two right-handed patients who presented with an emotional change following sodium amytal injection. The investigators retrospectively reviewed 59 IAPs in 39 presurgical epilepsy patients. No negative emotional reactions were observed in any of the IAPs; positive reactions were observed in the two patients described. The positive affective states (e.g., giggling, smiling) occurred in both patients between six and 40 seconds after injection of amytal into the left internal carotid artery, and lasted for up to 15 minutes post injection. The authors conclude that the emotional changes observed are consistent with findings in prior IAP studies and general lateralization theories suggesting right and left hemispheric specialization for opposing emotional valence dimensions. Although these investigators argue that the onset of reactions in their patients occurred during typical unilateral depression of EEG activity, supporting disinhibition of the contralateral hemisphere, they concede that the prolonged nature of the observed emotional reactions makes them difficult to interpret as directly correlated with activity in only one hemisphere. They suggest that this dichotomy may be due to a dissociation between immediate and long-term emotional responses such that the rapid early onset reaction could be attributed to depression of one hemisphere, while long-term responses could be more dependent on the period of recovery from anesthetization. They further suggest that closer examination of the short early phase of barbiturate-induced emotional change could clarify the extent of each hemisphere's involvement in this complex emotional status.

Rey et al. (1991) conducted a retrospective study of emotional responses subsequent to bilaterally administered IAPs. Subjects were 73 patients with medically intractible focal epilepsy. In 28 patients, an emotional response was observed after at least one of the two injections. In the 20 patients demonstrating a response after only one injection, 15 were euphoric and five were catastrophic. In the eight cases where responses were observed following both left and right injections, five patients demonstrated a similarly valenced response to both injections (4 euphoric, 1 catastrophic), whereas three patients showed opposite responses during the two injections. Results of statistical analyses demonstrated that among the numerous variables analyzed (e.g., gender, side of injection, side of seizure focus, and presence of a structural lesion), only the inactivation of the speech-dominant hemisphere was associated with the presence of a catastrophic response. The authors concluded that it is doubtful that hemispheric asymmetry for emotional functions exists independent of hemispheric dominance for speech. Lee et al (1990) examined incidence and characteristics of emotional and behavioral responses to sodium amobarbital injection in 44 epilepsy surgery candidates. Of the total number of patients, 59% demonstrated emotional reactions; 44% occurred after RH injections, and 32% occurred after LH injections. While laughter and elation were more common following RH injection, LH injections were typically characterized by unresponsiveness or crying. These results are consistent with the early observations of lateralized emotional reactions (e.g., Terzian, 1964). In terms of cerebral speech dominance, positive mood changes were more frequent after non-dominant hemisphere injections, and crying was only seen after dominant hemisphere injection. The observed emotional changes were not significantly related to gender, degree of angiographic crossflow, patients' general cognitive status, amobarbital dose, or side of seizure focus. Of note, the authors point out that although differing emotional states appear to be associated with right and left hemisphere disease, it is unclear by which mechanism these changes occur. Several investigators (e.g., Flor-Henry, 1979) have suggested that expression of emotion following damage to one hemisphere reflects the intrinsic emotional characteristics of the contralateral intact hemisphere via release from the normal inhibitory mechanisms of one hemisphere on the other. Loring et al (1992) have termed this the "transcallosal inhibition" hypothesis. An alternative explanation has been proposed (e.g., Tucker, 1981) suggesting that emotional responses subsequent to unilateral brain damage can be attributed to changes in the brain functions of the damaged hemisphere itself or to release of inhibitory influences on ipsilateral subcortical/limbic functions.

Lee et al (1993) evaluated the likelihood of these two opposing theories in a study measuring the interval from drug effect to onset of emotional expression during the IAP. The hypothesis was that if emotional reactions occurred shortly after administration of amobarbital, affected brain regions could not be contributory in producing the observed responses. By contrast, if reactions occurred during the period of hemispheric recovery from anesthetization, support for the ipsilateral release hypothesis could be inferred. In this study, 20 presurgical epilepsy patients with CPS (10 RTLE, 8 LTLE, 2 bilateral onset) were evaluated during the IAP. Of the 23 emotional reactions observed, 19 were positive (e.g., laughter) and four were negative (e.g., crying). Of the 20 patients, three demonstrated positive reactions after both LH and RH injections. The majority of positive responses (63%) occurred after RH injection. In 7 of 19 patients, however, positive reactions occurred after LH injections. Overall, the right injection/positive response and the left injection/negative response relationships were statistically significant. Of the 23 emotional responses observed, 22 occurred less than four minutes after onset of drug effect. Since evidence from EEG studies (Gotman et al, 1992) reflect hemispheric anesthetization lasting from 4-11 minutes post injection, the authors concluded that ipsilateral brain regions affected by the amobarbital did not likely participate in the production of the observed emotional reactions. Brain structures subserved by MCA and ACA distributions include most of the limbic structures previously implicated in emotional expression (e.g., anterior hypothalamus, septal nuclei, orbital and mesial frontal lobe, anterior and middle cingulate gyri, insula, amygdala, and anterior hippocampus). Lee, et al. (1993) conclude that their results are supportive of the contralateral release hypothesis linking positive affect with normal LH functioning and negative affect with intrinsic RH emotional tone.

Using a different methodological approach, two studies evaluated mood/affective state changes during the IAP via direct patient self-report. Christianson et al. (1993) trained 28 presurgical epilepsy patients to use a six-point bipolar scale measuring pleasantness (happy-sad) to rate their mood state before, during, and after both left and right hemisphere sedation. During the IAP, patients were asked to provide their ratings by pointing to the appropriate level on the mood rating scale. Testing took place 5-7 minutes post injection. Analyses of results demonstrated that right and left focus patients indicated similar patterns of results during the three phases of testing. Although no differences in response ratings were observed before and after the IAP, testing during the IAP revealed a significant decline in mood rating after LH, but not after RH, inactivation. A significant interaction between side of injection and testing phase revealed a significant decrease in happiness during LH sedation. Inactivation of the RH did not produce a significant change in mood. When patients were grouped by side of focus, a greater negative mood state was observed in patients with LH foci than RH foci. Patients with RH foci showed a greater decline in mood during the IAP. The authors explain this finding in terms of the left focal patients' greater negative mood prior to injection. The greater decline in right focus patients' ratings thus simply reflects a more pronounced mood state change. The overall ratings of both groups during the IAP did not differ. The authors concluded that the right and left hemispheres mediate emotional behavior in different ways. The findings appear consistent with lesion studies showing negative emotional reactions in patients with LH damage, but do not lend support to LH specialization for positive emotion. Rather, the authors suggest a general emotion-mediating role for the RH. Strikingly similar results were obtained in a study by Ahern et al. (1994), in which changes in affective state were investigated during the IAP. Compared to baseline testing, patients rated their mood as significantly more negative during the LH injection. By contrast, no significant affective state change was reported when the RH was inactivated. The investigators interpreted their findings as consistent with a differential lateralization model of emotion in which the RH plays a primary role in mediation of salient negative emotions.

In a series of studies designed to evaluate hemispheric lateralization of affective prosody, Ross and collaborators evaluated aspects of expressive emotional prosody in surgical epilepsy patients during portions of the IAP. All subjects were LH dominant for propositional language. In the initial study of five patients (Ross et al., 1988), evaluation of affective prosody was conducted during left and right hemisphere injections during the period of amobarbital anesthetization, as evidenced by contralateral paralysis and marked ipsilateral EEG slowing. Acoustical analyses of speech samples obtained were later conducted in an effort to compare how well each patient utilized individual acoustical parameters to convey affective signals in neutral, happy, sad, angry, and surprise emotions.

Analyses of the speech samples demonstrated a flattening of affect in voice during the right-sided injection, as compared to pre- and post-baseline testing. The authors concluded support for RH modulation of the affective components of language. In a subsequent study incorporating additional subjects (N=11), Ross et al. (1994) studied amobarbital effects on verbal recall of emotional life experiences. Patients were asked to recall significant, negative affectively charged life events before, during and after a right-sided IAP. Testing took place during the period of RH anesthetization as evidenced by EEG slowing. Tests were not conducted during the LH injections due to the presence of dense non-fluent aphasia. Examination of the recall stories provided by each patient showed that 8 of 10 patients minimized the primary emotional content of their stories during the right-sided IAP as compared to both baseline stories. The authors note that the changes evidenced in emotional recall were reflective of a "socialization" of the original emotion described in the pre-IAP stories. They suggest that while the RH is associated with primary emotions of both positive and negative valence, the LH appears to be involved with "social" emotions, such that the LH inhibits the display of primary (RH) emotions and generates positive, more socially acceptable, displays (e.g., Buck & Duffy, 1980). Ross and colleagues further elaborate on the concept of a hemispheric differentiation within the cognitive component of emotion in that social emotions are considered anatomically linked to the analytic/sequential cognitive and linguistic systems within the LH, while the primary emotions are associated with the more holistic/syncretic systems within the right hemisphere. Furthermore, the authors speculated that through reciprocal anatomic connections between the amygdala and ipsilateral neocortex, the possibility exists for hemispheric neocortical influences on the affective tone within the ipsilateral temporal-limbic systems. In consideration of the overall results from IAP studies of expression/experience, however, experimental evidence to date has not provided conclusive information regarding the relative contributions of specific intrahemispheric regions in the mediation of emotional processing.

Perception

In contrast to the fairly numerous studies involving emotional expression/experience during the IAP, to our knowledge there is only one investigation in the literature which evaluated perception of emotion during unilateral hemispheric anesthetization. Ahern et al. (1991) examined the ability of 12 epilepsy patients undergoing the IAP to evaluate intensity of emotional facial expressions. Experimental stimuli were photographs of one male and one female actor displaying facial expressions of three emotions (i.e., neutral, happy, and disgust). Patients were shown the photographs and asked to rate the stimuli by directing the examiner to move an indicator on a 3-point scale, ranging from pleasant to unpleasant. All subjects were tested before, during, and after the IAP. During the IAP, patients were tested between 6 and 19 minutes post injection, from one minute before to eight minutes after disappearance of amytal-induced EEG slowing. Analysis of results revealed that in comparison with pre- and post-baseline testing, ratings obtained during non-dominant hemisphere injection were of significantly lesser value across both emotions tested. Ratings during dominant hemisphere injection did not differ significantly from baseline. Order of injection, side of lesion or side of focus did not have an effect on the observed results. The authors suggested that findings are consistent with a more essential role for the RH in perception and perhaps interpretation of emotional stimuli. Clearly further research would be required using the IAP paradigm to elucidate the contributions of both inter- and intrahemispheric factors in emotional perception.

III. METHODS

Overall Design

Epilepsy patients with right-hemisphere temporal lobe epileptic foci (RTLEs) and left-hemisphere temporal lobe epileptic foci (LTLEs) were recruited for study from the Comprehensive Epilepsy Center at the Hospital for Joint Diseases. Both male and female subjects were represented within each subject group. Within each patient group, an attempt was made to select equal numbers of subjects with epileptic foci confined to limbic brain regions and subjects with additional temporal neocortical involvement. All subjects were examined on screening measures to ensure that criteria were met with respect to demographic background, handedness, medical, neurological and psychiatric history, and general intellectual and cognitive functioning. Subjects "passing" screening criteria were also be examined on several tasks designed to control for cognitive factors which could potentially confound performance on experimental tasks. Subjects were tested on a perceptual measure of prosodic emotion. According to study protocol, subjects were asked to identify the emotion portrayed in tape recordings of emotionally-intoned sentences. Performance within each stimulus set was scored for accuracy.

Statistical design included analysis of variance (ANOVA) on the perceptual experimental dependent variables, using subject group (RTLE, LTLE) and side of injection (RINJ, LINJ) as the independent measures. Laterality of primary epileptic focus (RTLE, LTLE) was analyzed as a between-subject variable while hemisphere injected (RINJ, LINJ) was a within-subject repeated measure. In addition to the analysis of discrete emotions (happy, angry, sad), dimensional classifications of the discrete emotional stimuli, (i.e., valence [positive, negative] and motoric direction [approach, withdrawal]), were also examined on a preliminary basis. Additional ANOVAs were conducted on the data from the TLE patients, using age at seizure onset, location of epileptic focus (limbic, neocortical), presence of structural lesion, seizure frequency, and presence of secondarily generalized seizures (seizure type) as independent measures. Finally, gender was incorporated as a between-subjects variable in all of the above analyses when sample size permitted.

Hypotheses

Primary Hypotheses

1) Lateralized Neocortical Differences as a Function of Emotional Valence: The three primary hypotheses regarding relative hemispheric dominance for different kinds of emotions were tested.

   a. Right hemisphere hypothesis: The right hemisphere is dominant for emotional perception regardless of emotional valence.

   b. Valence hypothesis: The right hemisphere is dominant for perception of negative emotions while the left hemisphere is dominant for perception of positive emotions.

   c. Motoric direction hypothesis: The right hemisphere is dominant for perception of avoidance/withdrawal emotions, while the left hemisphere is dominant for perception of approach emotions.

2) Alterations in Hemispheric Specialization as a Function of Age at Seizure Onset: It was hypothesized that the performance of RTLE patients would vary as a function of age at seizure onset such that subjects with late onset epilepsy would demonstrate impaired performance relative to subjects with early onset epilepsy. The predictions for the age of onset hypothesis would vary

in accordance with whichever laterality hypotheses proves to be operative.

Exploratory Hypotheses

1) Interhemispheric Effects -- Neocortical versus Limbic Mechanisms: It was hypothesized that temporal neocortical structures are more specialized for the perception of emotion than are limbic/subcortical structures. Again, the predictions for this hypothesis would vary in accordance with the operative laterality hypotheses.

2) Alterations in Hemispheric Specialization as a Function of Presence of Structural Lesion: The neurological subject characteristics of the patient population tested during this study allowed us to explore the effects of destructive versus irritative lesions (determined by structural imaging studies) on emotional prosodic perception.

3) The relationship between seizure frequency and task performance: The variability of our subject pool in terms of frequency of epileptic seizures permitted us to explore the relationship between average number of seizures routinely experienced, laterality of seizure focus, and ability to comprehend emotional prosody. It

was hypothesized that subjects experiencing lower seizure frequency would be more likely to show a RH, Valence, or Motoric Direction effect, depending on which emotion theory is operative.

4) <u>The relationship between secondarily generalized seizures and task performance:</u> The variability of our subject pool in terms of presence of generalized epileptic seizures would permit us to explore the relationship between presence of secondarily generalized seizures, laterality of seizure focus, and ability to comprehend emotional prosody. It was hypothesized that subjects who do not experience generalized seizures would be more likely to show a RH, Valence or Motoric Direction effect, depending on which emotion theory is operative.

5) <u>The relationship between gender and task performance:</u> Previous literature has demonstrated the importance of gender considerations in neuropsychological studies. Gender was expected to interact with variables such as laterality of seizure focus and age of chronic seizure onset to influence task performance regardless of the operative laterality hypothesis. Three specific predictions were made:

   a. Females would perform with greater accuracy in the perception of prosodic emotion than would males.

   b. Females would show a greater degree of lateralization than males in their emotional accuracy scores.

c. When/if there are valence effects (by injection or lesion-side), females would demonstrate such effects more than males.

Subjects

The number of subjects to be included was determined prior to initiation of this study by using a power analysis (Ramsey & Ramsey, 1989; Bakeman, 1992). The degrees of freedom and alpha level (.05) used to determine the noncentrality variable (lambda) were obtained from a pilot study of this experimental paradigm (Santschi-Haywood, Perrine, Borod, et al., 1996). In order to obtain an acceptable power value of .80 based on the effect size obtained in that study, a minimum total of 27 subjects across the two groups would be required.

Twenty two RTLE and 15 LTLE adults served as subjects. An effort was made to include equal numbers of TLE patients with epileptic foci in neocortical (lateral temporal) and limbic (mesial temporal) areas within each group.

Informed Consent

Informed consent was obtained from each subject prior to participation in this investigation. Each participant was informed about the purpose of the research study as well as the lack of immediate individual benefit. Subjects were informed that the procedures in which they would participate were in no way intrusive and that the risks involved were at most mild frustration. It was clearly explained to all participants that any data collected would be kept completely confidential. Subjects were further apprised of their right to discontinue participation at any time during the study without adverse effect to their future medical care.

Inclusion Criteria

All subjects were right-handed without history of secondary neurological disorder, pre-morbid psychiatric disorder, or substance abuse. Patients were included for study if they had been diagnosed with temporal lobe epilepsy arising from a primarily unilateral seizure focus. Inter- and intra-hemispheric location of epileptic foci was determined using data from scalp/sphenoidal EEG, simultaneous video recording of seizure onset, and structural findings from CT or MR imaging.

An attempt was made to control subject selection such that the RTLE and LTLE groups did not differ significantly with respect to demographic (i.e., gender, education level), and neurological (i.e., age at chronic seizure onset, location of epileptogenic focus, current seizure frequency, and presence of secondarily generalized seizures) variables. As significant differences were not found between groups (via independent samples t-test or Chi square), it was not necessary to enter these variables as covariates in subsequent analyses of the resultant data. In addition, presence or absence of abnormalities/lesions on CT or MR scans was considered to determine the effect of this variable on task performance.

Table 1a. Demographic Characteristics

variable	RTLE (N=22)	LTLE(N=15)	t-value	p-value
age	31.0(10.9)*	31.9 (9.3)	.53	.601
gender	55% female	53% female		
education	13.0 (3.3)	13.2 (2.3)	.14	.887
WAIS-R FSIQ	92.6 (14.2)	89.4 (9.9)	.63	.537

* M (SD)

Table 1b. Seizure Variables

variable	level	RTLE (N)	LTLE (N)	Chi ^{2} value	p value
Lesion	Y	6	5	.091	.763
	N	16	10	1.385	.239
Location	temporal	10	9	.053	.819
	other	11	5	2.250	.134
Frequency	low	12	9	.429	.513
	high	9	5	1.143	.285
GTCs	Y	12	12	.000	1.000
	N	9	2	4.45	.035*

Screening Tasks

At the time of selection for inclusion in this research protocol, each subject was admitted to the HJD Comprehensive Epilepsy Center for extended clinical and diagnostic video-EEG evaluation of their seizure disorder. On admission, all patients were screened for medical and demographic background. Patients also underwent psychiatric screening and completed several personality questionnaires and inventories (e.g., Bear-Fedio, MMPI). During routine neuropsychological evaluation, selected WAIS-R subtests (e.g., Information, Block Design, Digit Span) were administered to ensure an adequate (subtest scaled score > 4) level of attentional and general intellectual functioning required to complete the experimental tasks.

Procedures

Subject testing took place during both left- and right-hemisphere injections of the Intracarotid Amobarbital Procedure (IAP) in the Neuroradiology Department of Tisch Hospital at NYU Medical Center. It is essential to note that subjects who underwent the IAP were epilepsy surgery candidates for whom the IAP was a routine part of clinical pre-surgical evaluation. Testing of emotional perceptual ability during this procedure was extremely brief and in no way interfered with testing routinely conducted during the IAP as it was conducted during "down" time subsequent to satisfactory completion of routine testing. The subjects who took part in this study did not incur any additional risk related to their participation in this research protocol. Any patients postictal from recent seizures were not included in the IAP procedure. For the purposes of this investigation, patients were not tested for a minimum of 24 hours subsequent to either a generalized or complex partial seizure to ensure adequate cognitive clearing. This is a conservative time frame based on generally accepted clinical protocols in the neuropsychological testing of epilepsy patients.

The Intracarotid Amobarbital Procedure

Angiography and preparation for IAP testing. Standard internal carotid angiography was performed prior to the injection of each hemisphere to identify anomalous flow patterns and persistent fetal arteries anastomosing to the posterior circulation. The IAP was performed immediately following angiography. Catheterization for both the angiogram and IAP was performed through a percutaneous transfemoral approach, with placement of the catheter tip above the bifurcation of the internal and external carotid arteries.

For the IAP, an initial bolus of sodium amobarbital (typically 100mg) was machine-injected at a rate of 1 ml/second, with additional increments as necessary to produce contralateral upper extremity hemiplegia without obtundation. The hemisphere with the presumed seizure focus was tested first, followed 30 to 60 minutes later by examination of the contralateral hemisphere.

Pre-IAP training trials. Surgical candidates who underwent the IAP procedure were typically provided with an information session during the week prior to the actual procedure to answer questions and to perform a practice run-through. At this time, subjects also received a practice emotional perception trial similar to the procedures they encounterd during the IAP to insure adequate comprehension of the experimental tasks. When necessary, a second practice trial was administered to insure 100% performance accuracy for each participant. Since language impairment during the IAP may result in confusion for the inadequately pre-trained subject, an additional practice trial was administered immediately prior to angiography on the day of the IAP. These baseline tests served as comparisons for performance during the IAP.

Prosodic emotional perception

All subjects were tested on a task of emotional perception in the prosodic channel. The task included one positive (happiness) and two negative (sadness, anger) emotions to test the hypotheses regarding emotion laterality. The emotions of happiness and sadness were chosen as the most common, easily identifiable representatives of their respective valence category. The emotion of anger was included because it is easily recognized and is classifiable as both a negative and an approach emotion (e.g., happiness, anger = approach emotions; sadness = withdrawal emotions). For each of the three emotions represented, items with the highest accuracy ratings in normal subjects (for both male and female voices), had been selected and adapted for this paradigm from prosodic stimuli developed by Borod et al. (1994). Accuracy ratings ranged from 91% to 100% ($\underline{M}$ = 94.6%) as follows:

Table 2.

IAP PROSODIC IDENTIFICATION STIMULI

Voice Gender	Emotion	% Accuracy Ratings
M	HAPPINESS	91
F	HAPPINESS	91
M	SADNESS	100
F	SADNESS	96
M	ANGER	96
F	ANGER	91

Order of stimulus presentation was randomized within the experimental task (eight randomizations). Four different orders of response-choice display were also randomized across subjects and groups. Total administration time was approximately 30-40 seconds per stimulus set.

Presentation of the initial set of three (early) trials took place at exactly 2 min. 30 sec. post injection. This time frame was chosen for two reasons: 1) to allow sufficient time for a brief initial assessment of the patient's cognitive status immediately post-injection, and 2) to insure complete hemispheric anesthetization at the time of experimental testing. The second set of three trials took place following conclusion of standard serial language testing, at approximately 5-7 minutes post injection for comparison purposes, in the event that the subject responded with less than 100% accuracy in the initial experimental trial.

During the IAP, subjects were asked to perform a prosodic identification task in which tape recordings of emotionally-intoned neutral-content sentences were presented in normal cadence. Subjects identified the correct emotion either verbally or by pointing to the correct response on a 5" x 10" white foamboard listing all possible choices. To allow for expected language impairments during dominant hemisphere injection, the three response choices were displayed both verbally and pictorially; simple circular diagrams representing happy, sad, and angry faces were arranged in a vertical display with the matching emotion word printed underneath each respective diagram. Prosodic stimuli were sentences spoken in three different emotional tones adapted from Borod et al. (1994). Four neutral sentences were used (e.g., "We saw it on T.V.", "She put it on the tray"). The task consisted of two trials, with each emotion appearing twice. Each response was scored for accuracy (1 = accurate, 0 = inaccurate).

IAP Control Measures

Control measures were included to insure that the injected hemisphere was sufficiently anesthetized at the time of experimental testing. Immediately following each set of trials of prosodic tasks, motor strength was assessed by asking the subject to tap forefinger and thumb together as quickly as possible bilaterally. Evaluation of presence or absence of contralateral deficit was made by a neurologist along with evaluation of presence or absence of facial hemiplegia.

In all cases, the above experimental tasks were not performed if they would in any way interfere with a valid IAP study or if it was determined during any IAP procedure that additional non-experimental testing was required.

Statistical Analysis

Demographic/Neurological Variables

For the purposes of this investigation, epilepsy patients were divided apriori into groups based on lateralization and location of seizure focus. RTLE and LTLE groups were separated into subjects with strictly mesial temporal (limbic) seizure foci versus those with additional neocortical involvement. The latter group was comprised of patients with both mesial and lateral temporal involvement, those with mesial, lateral, and extra-temporal involvement, and finally, those with mesial temporal plus extra-temporal involvement. Due to the small number of subjects which fell within each of these three latter categories, all subjects with anything other than strictly mesial temporal seizure foci were grouped together in all subsequent analyses.

In order to control for potential subject group differences independent samples t-tests for Group (RTLE vs. LTLE) were conducted separately for the following variables: age at time of testing, and completed years of education. Further, Chi square analyses were conducted separately for the following variables: gender, age at chronic seizure onset (early vs. late), and current seizure frequency/month (low vs. high). The dichotomizations for the latter two variables were based on general consensus in the current clinical epilepsy literature. (See Table 1b for mean values.)

Cognitive Variables

To ensure comparable subject groups in terms of baseline cognitive functioning, the screening measures of general intellectual functioning and attentional ability were analyzed across Group (RTLE vs. LTLE). Independent samples t-tests were conducted for WAIS-R Full Scale IQ (FSIQ). FSIQ scores were used due to expected performance differences between RTLE and LTLE subjects on the Verbal and Performance, subscales of the WAIS-R .

IAP Procedural Variables

In order to control for differences in procedural variables during the IAP, two two-way ANOVAs for Group (RTLE vs. LTLE) x Side of Injection (RINJ vs. LINJ) were conducted separately for total amobarbital dosage and for post-injection start time during the experimental tasks. As significant differences were not found between groups, these variables were not entered as covariates in subsequent analyses of the resultant data. (See Table 3 for mean values.)

Table 3. IAP Procedural Variables

variable	RTLE	LTLE	t-value	p-value
R inject mg	101.4 (7.3)	108.6 (29.0)	1.08	.286
L inject mg	100.5 (8.0)	101.3 (31.4)	.120	.905
R time (s)	198.3 (90.9)	161.8 (61.7)	1.30	.201
L time (s)	203.7 (86.1)	165.2 (67.8)	1.30	.203
variable	**R inject**	**L inject**	**t-value**	**p-value**
total mg	104.4 (19.4)	101.1 (20.7)	.700	.487
test time	190.3 (89.1)	179.3 (67.6)	.55	.583

Angiographic Variables

In order to anatomically evaluate the level of anesthetization during each IAP injection in terms of arterial flow patterns, the degree of opacification for the three major arteries supplying the brain (anterior cerebral (ACA), middle cerebral (MCA), and posterior cerebral (PCA)) were rated by the attending neuroradiologist on a 7-point Likert scale from "1" indicating no arterial filling to "7" indicating complete arterial filling). To control for potential differences in degree of anesthetization during the IAP, six two-way ANOVAs for Group (RTLE vs. LTLE) x Side of Injection (RINJ vs. LINJ) were conducted separately for the following variables: ipsilateral ACA, MCA, and PCA, and contralateral ACA, MCA, and PCA. Again, since no significant differences were found between groups, these variables were not entered as covariates in subsequent analyses of the resultant data.

Interhemispheric Effects (Hypothesis 1)

To examine interhemispheric differences in the perception of emotional prosody in relation to the three major neuropsychological hypotheses, percent accuracy scores were analyzed via three separate three-way mixed model ANOVAs. To examine potential differences between all emotions tested, a three-way mixed model ANOVA was conducted using discrete emotion as a within-subject variable. Since the majority of the literature on emotional prosodic perception lends support to the RH hypothesis, and because the Valence and the Motoric Direction hypotheses require different dichotomizations of the discrete emotions tested, each of the latter hypotheses was tested individually in relation to the RH hypothesis.

Discrete Analyses. A three-way ANOVA was conducted for Focus (RTLE vs. LTLE) x Injection (RINJ vs. LINJ) x Emotion (Happy vs. Angry vs. Sad), where Focus was a between-subjects variable, and Injection and Emotion were repeated measures.

Dimensional Analyses.

Valence vs. RH Hypotheses. A three-way ANOVA was conducted for Focus (RTLE vs. LTLE) x Injection (RINJ vs. LINJ) x Valence (Positive vs. Negative), where Focus was a between-subjects variable, and Injection and Valence were repeated measures. For this analysis happiness was classified as a positive emotion, while sadness and anger was classified as negative emotions.

Motoric Direction vs. RH Hypotheses. To test the motoric direction hypothesis, discrete emotions were recategorized along the approach/withdrawal dimension, such that anger was classified as an approach emotion along with happiness. Sadness was categorized as a withdrawal emotion. A third three-way ANOVA was conducted for Focus (RTLE vs. LTLE) x Injection (RINJ vs. LINJ) x Motoric Direction

(Approach vs. Withdrawal). Tables 3a and 3b depict the two potential outcomes for each of the above dimensional analyses.

Table 4a.

Possible Outcomes for Hypothesis 1 (RH vs. Valence)					
Hypothesis	**Injection**	**RTLE**		**LTLE**	
		Positive Stimuli	**Negative Stimuli**	**Positive Stimuli**	**Negative Stimuli**
Right Hemisphere	RINJ	impaired	impaired	impaired	impaired
	LINJ	intact	intact	intact	intact
Valence	RINJ	intact	impaired	intact	impaired
	LINJ	impaired	intact	impaired	intact

Table 4b.

Possible Outcomes for Hypothesis 1 (RH vs. Motoric Direction)					
Hypothesis	**Injection**	**RTLE**		**LTLE**	
		Approach Stimuli	**Withdraw Stimuli**	**Approach Stimuli**	**Withdraw Stimuli**
Right Hemisphere	RINJ	impaired	impaired	impaired	impaired
	LINJ	intact	intact	intact	intact
Motoric Direction	RINJ	intact	impaired	intact	impaired
	LINJ	impaired	intact	impaired	intact

A significant main effect for Injection, such that subjects perform worse with the RH injection, regardless of group and valence, would lend support to the right hemisphere hypothesis in both analyses. If the valence hypothesis is supported, there will be a significant interaction between Injection and Valence, such that, regardless of group, with the RH injection, subjects would be less accurate for negative emotions, and with the LH injection, subjects would be less accurate for positive emotions. Similarly, if the motoric direction hypothesis is operative, there will be a significant interaction between Injection and Motoric Direction such that, regardless of group, with the RH injection, subjects would be less accurate for withdrawal emotions, and with the LH injection, subjects would be less accurate for approach emotions.

Effects of Age at Seizure Onset (Hypothesis 2)

To evaluate the effect of age at seizure onset on hemispheric specialization for emotional prosodic perception, subjects were categorized apriori into early onset (< or = 12 years of age) versus late onset (> 12 years of age) groups. One separate four-way (2 x 2 x 2 x 3)ANOVA , and two separate four-way (2 x 2 x 2 x 2) ANOVAs were conducted on accuracy scores: 1) Injection (RINJ vs. LINJ) x Focus (RTLE vs. LTLE) x Onset (Early vs. Late) x Emotion (Happy vs. Angry vs. Sad), 2) Injection (RINJ vs. LINJ) x Focus (RTLE vs. LTLE) x Onset (Early vs. Late) x Valence

(Positive vs. Negative), and 3) Injection (RINJ vs. LINJ) x Focus (RTLE vs. LTLE) x Onset (Early vs. Late) x Motoric Direction (Approach vs. Withdrawal). Predictions varied depending on the outcome of the analysis for interhemispheric effects (see Tables 5a, 5b)

Table 5a.

Possible Outcomes for Hypothesis 2 (Valence)									
		RTLE				**LTLE**			
Hypothesis	**Injection**	**Early**		**Late**		**Early**		**Late**	
		P	**N**	**P**	**N**	**P**	**N**	**P**	**N**
Right Hemisphere	**RINJ**	+	+	-	-	+	+	+	+
	LINJ	+	+	+	+	+	+	+	+
Valence	**RINJ**	+	+	+	-	+	+	+	+
	LINJ	+	+	-	+	+	+	+	+

Note: P = positive emotions, N = negative emotions

Table 5b.

Possible Outcomes for Hypothesis 2 (Motoric Direction)									
		RTLE				**LTLE**			
Hypothesis	**Injection**	**Early**		**Late**		**Early**		**Late**	
		AP	**AV**	**AP**	**AV**	**AP**	**AV**	**AP**	**AV**
Right Hemisphere	**RINJ**	+	+	-	-	+	+	+	+
	LINJ	+	+	+	+	+	+	+	+
Motoric Direction	**RINJ**	+	+	+	-	+	+	+	+
	LINJ	+	+	-	+	+	+	+	+

Note: AP = approach emotions, AV = avoidance/withdrawal emotions

The following predictions assumed a significant effect of age at seizure onset for the RTLE group on accuracy scores. Provided the right hemisphere hypothesis is supported, all subjects would be more impaired for all emotions with the RH injection. In addition, in both analyses, there will be a significant interaction between Focus (RTLE vs. LTLE) and Age at Seizure Onset (Early vs. Late) such that, late-onset RTLEs would perform worse than early-onset RTLEs during the RH injection. Performance during the LH injection would be unimpaired, and onset would have no effect on the performance of LTLEs.

In the first analysis, support for the valence hypothesis would be demonstrated by significant interactions between Focus (RTLE vs. LTLE) and Onset (Early vs. Late) and between Focus and Valence (Positive vs. Negative), such that, during the RH injection, late-onset RTLEs would be impaired relative to other groups for negative emotions, and during the LH injection, late-onset LTLEs would be impaired relative to other groups for positive emotions. Similarly, in the second analysis, support for the motoric direction hypothesis would be demonstrated by significant interactions between Focus (RTLE vs. LTLE) and Onset (Early vs. Late) and Motoric Direction (Approach vs. Withdrawal) such that, during the RH injection, late-onset RTLEs would be impaired relative to other groups for withdrawal emotions, and during the LH injection, late-onset LTLEs would be impaired relative to other groups for approach emotions.

Gender Effects

Due to the relatively small number of subjects participating in this investigation, we had attempted to control for the effects of gender by including fairly equivalent numbers of male and female subjects in both LTLE and RTLE groups. Based on the available literature regarding the relationship between gender and emotion (e.g., LaFrance & Banaji, 1992; Hall, 1978) three predictions were made as follows:

1) Females will perform with greater accuracy in the perception of prosodic emotion.
2) Females will show a greater degree of lateralization than males in their accuracy scores for the prosodic perception task.
3) When/if there are valence hypothesis effects, females will show this effect more than males.

To test these gender hypotheses, the analyses conducted to test the two primary hypotheses (1 and 2), as well as the four experimental hypotheses (3,4,5, and 6) were run a second time with the addition of gender as a between-subjects variable when group sizes permitted such analyses.

For Hypothesis 1 -- Interhemispheric Effects, three four-way ANOVAs will be conducted:

1) Focus (RTLE vs. LTLE) x Gender (Male vs. Female) x

Injection (RINJ vs. LINJ) x Emotion (Happy vs. Angry vs. Sad),

2) Focus (RTLE vs. LTLE) x Gender (Male vs. Female) x Injection (RINJ vs. LINJ) x Valence (Positive vs. Negative), and

3) Focus (RTLE vs. LTLE) x Gender (Male vs. Female) x Injection (RINJ vs. LINJ) x Motoric Direction (Approach vs. Withdrawal).

Although outcomes will vary as a function of the operative neuropsychological theory, a significant main effect of Gender is expected such that females will demonstrate greater performance accuracy than males. Additionally, if females are more lateralized than males, significant interactions are expected:

1) Gender x Injection, if the RH hypothesis is operative.

2) Gender x Injection x Valence, if the Valence hypothesis is operative.

3) Gender x Injection x Motoric Direction, if the Motoric Direction hypothesis is supported.

For <u>Hypothesis 2 -- Effects of Age at Seizure Onset</u>, three additional five-way (2 x 2 x 2 x 2 x 2) ANOVAs were conducted on accuracy scores:

1) Focus (RTLE vs. LTLE) x Gender (Male vs. Female) x Injection (RINJ vs. LINJ) x Onset (Early vs. Late) x Emotion (Happy vs. Angry vs. Sad)

2) Focus (RTLE vs. LTLE) x Gender (Male vs. Female) x Injection (RINJ vs. LINJ) x Onset (Early vs. Late) x Valence (Positive vs. Negative)

3) Focus (RTLE vs. LTLE) x Gender (Male vs. Female) x Injection (RINJ vs. LINJ) x Onset (Early vs. Late) x Motoric Direction (Approach vs. Withdrawal).

Again, while predictions would vary depending on the outcome of the analysis for interhemispheric effects, a significant main effect of Gender on accuracy (as described above) is expected. Significant interactions are also predicted:

1) Gender x Onset x Injection (for the RH hypothesis).

2) Gender x Onset x Injection x Valence (for the Valence hypothesis).

3) Gender x Onset x Injection x Motoric Direction (for the Motoric Direction hypothesis).

Intrahemispheric Effects

Since posterior neocortical brain structures are known to be important, particularly for the perception of emotion, we investigated the effect of intrahemispheric location of seizure on the percent accuracy scores on an exploratory basis using a four-way (2 x 2 x 2 x 3) ANOVA conducted on accuracy scores: Injection (RINJ vs. LINJ) x Focus (RTLE vs. LTLE) x Location ([Neocortical + Limbic] vs. Limbic only) x Emotion (Happy vs. Angry vs. Sad). As the results of prior analyses demonstrated some effect of Valence or Motoric Direction, these variables were entered into two additional separate four-way ANOVAs (2 x 2 x 2 x 2). If limbic structures function similarly to ipsilateral neocortical structures, we would expect no significant main effect of intrahemispheric seizure focus location. If, however, functions are more diffusely organized within limbic structures, leading to more bilateral representation, or, if emotional perception is neocortically based, we would expect a significant main effect of Location. In addition, the following significant interactions would be expected:

1) Location x Injection (if the RH hypothesis is operative).
2) Location x Injection x Valence (if the Valence hypothesis is supported).
3) Location x Injection x Motoric Direction (if the Motoric Direction hypothesis is supported).

Effect of Structural Lesion

To examine the effects of destructive versus irritative lesions on task performance, presence or absence of structural abnormalities on CT or MR scans was considered in a four-way (2 x 2 x 2 x 3) ANOVA conducted on accuracy scores: Injection (RINJ vs. LINJ) x Focus (RTLE vs. LTLE) x Lesion (Structural vs. None) x Emotion (Happy vs. Angry vs. Sad). Two additional four-way (2 x 2 x 2 x 2) ANOVAs were conducted using the dimensional variables of valence and motoric direction in place of discrete emotion. Since cell group size (n>2) within the Lesion variable was large enough to permit further analysis, Gender was incorporated in one additional five-way (2 x 2 x 2 x 2 x 3) ANOVA: Injection (RINJ vs. LINJ) x Focus (RTLE vs. LTLE) x Lesion (Structural vs. None) x Gender (Male vs. Female) x Emotion (Happy vs. Angry vs. Sad). Finally, two additional five-way (2 x 2 x 2 x 2 x 2) ANOVAs were conducted using the dimensional variables of valence and motoric direction in place of discrete emotion. While we had no specific predictions regarding the effect of a structural lesion on emotional prosodic perception, this variable does represent a real difference within our subject population, and as such deserved to be examined on an exploratory basis.

Effect of Seizure Frequency

To explore the effects of high versus low seizure frequency on task performance, subjects were categorized apriori based on number of seizures per month (averaged over the past three months) into low frequency (< or = 10 seizures/month) versus high frequency (> 10 seizures/month) groups based on generally accepted clinical judgement. A four-way (2 x 2 x 2 x 3) ANOVA was conducted on accuracy scores: Injection (RINJ vs. LINJ) x Focus (RTLE vs. LTLE) x Frequency (Low vs. High) x Emotion (Happy vs. Angry vs. Sad). Again, two additional four-way (2 x 2 x 2 x 2) ANOVAs were conducted, using the dimensional variables of valence and motoric direction in place of discrete emotion. As basic epilepsy research has clearly demonstrated the damaging effects of multiple seizures on affected brain tissue, we expected that the lower seizure frequency group would be more likely to show either a RH, Valence, or Motoric Direction effect, depending on which neuropsychological theory is operative.

Effect of Secondarily Generalized Seizures (Seizure Type)

To explore the effects of secondarily generalized tonic, clonic, or tonic/clonic seizures on task performance, subjects were categorized apriori based on whether or not they experienced GTCs. A four-way (2 x 2 x 2 x 3) ANOVA was conducted on accuracy scores: Injection (RINJ vs. LINJ) x Focus (RTLE vs. LTLE) x Frequency (Low vs. High) x Emotion (Happy vs. Angry vs. Sad). Two additional four-way (2 x 2 x 2 x 2) ANOVAs were conducted using the dimensional variables of valence and motoric direction in place of discrete emotion. Basic epilepsy research has also demonstrated the damaging effects of generalized seizures on affected brain tissue (e.g., Wilkus & Dodrill, 1976). We expected that the group which did not experience secondarily generalized seizures, and therefore was likely to demonstrate greater focality of impairment, would be more likely to show either a RH, Valence, or Motoric Direction effect, depending on which neuropsychological theory is operative.

IV. RESULTS

To compare between group subject performance, total accuracy scores were converted to percent correct for each discrete emotion tested (i.e., happy, angry, and sad). For each dimensional re-categorization of the discrete emotions, valence (positive, negative), and motoric direction (approach, avoid), separate percent correct scores were calculated. Overall, there were three major components to the statistical analyses conducted. First, repeated measures Analyses of Variance (ANOVAs) were conducted with percent accuracy scores for the discrete emotions. These analyses were used to test the two primary and four exploratory hypotheses. Second, the six ANOVAs from the discrete analyses were conducted for both the valence and the motoric direction dimensional variables. Finally, gender effects were evaluated using additional ANOVAs for any discrete or dimensional analysis for which group sizes were large enough (N>=2) to permit valid interpretation of findings. Where appropriate, post-hoc analyses were conducted to evaluate significant main effects and interactions.

A. Discrete Analyses

Primary Analyses

Interhemispheric Effects. In order to evaluate the interhemispheric effects of lateralized seizure foci and unilateral amobarbital injections on perceptual accuracy for the three discrete emotions, a three-way Focus (2) by Injection (2) by Emotion (3) repeated measures ANOVA was conducted. No significant main effects or interactions were observed.

Effects of Age at Seizure Onset. To determine the effects of age at seizure onset on perceptual accuracy of the three discrete emotions, a four-way Focus (2) by Onset (2) by Injection (2) by Emotion (3) repeated measures ANOVA was conducted. No significant main effects were observed. A trend for the Onset x Emotion interaction was observed ($p=.089$), such that subjects with late onset seizures (> age 12) performed better than subjects with early onset seizures for happy and sad emotions, while the early onset subjects were more accurate when the emotion portrayed was anger. Table 6a presents the mean values for this analysis.

A significant interaction for the Focus x Onset x Injection analysis was also observed ($p=.032$). Examining the results in terms of injection side, late onset RTLEs performed more accurately with the RH injection, while late onset LTLEs performed better with the LH injection. During the right hemisphere injection, RTLEs tended to perform better than LTLEs in general, with late onset subjects in both groups outperforming early onset groups. During the left hemisphere injection, early onset RTLEs performed better than early onset LTLEs and significantly better than late onset RTLEs. Late onset LTLEs were more accurate than all other groups. (See Table 6b for mean values.)

Table 6. Effects of age at seizure onset

Table 6a. Onset x Emotion Interaction (p=.089)
(percent accuracy scores)

EMOTION	ONSET			
	early	late	F-value	p-value
happy	47.83	59.62	.557	.461
angry	52.18	35.90	1.474	.233
sad	47.83	59.94	1.303	.262

Table 6b. Focus x Onset x Injection Interaction
(F = 5.06, p=.032) (percent accuracy scores)

INJ	FOCUS			
	RTLE		LTLE	
	early	late	early	late
RIGHT	52.48	62.50	40.74	46.67
LEFT	61.91	28.57	33.33	73.33

Exploratory Analyses

Intrahemispheric Effects. To assess the effect of intrahemispheric location of epileptogenic focus on percent accuracy scores for each discrete emotion, a four-way Focus (2) by Location (2) by Injection (2) by Emotion (3) repeated measures ANOVA was conducted. No significant main effects or interactions were observed.

Effects of Structural Lesion. To evaluate the effect of the presence of a structural lesion on percent accuracy scores for the three discrete emotions, a four-way Focus (2) by Lesion (2) by Injection (2) by Emotion (3) repeated measures ANOVA was conducted. A trend was observed for the main effect of Lesion ($p=.093$). TLE subjects without a structural lesion performed better than subjects with a known structural lesion, regardless of side of seizure focus or side of amobarbital injection. (See Table 7a for mean values.)

A trend was also observed for the Focus x Injection x Emotion interaction ($p=.073$). During the RH injection, RTLEs outperformed LTLEs for the angry and sad emotions, but scored equivalently for the happy emotion. During the LH injection, RTLEs performed better than LTLEs across all three emotions. (See Table 7b for mean values.)

This interaction was modified by a significant interaction for Focus by Lesion by Injection by Emotion ($p=.037$). For all three emotions (i.e., happy, angry, and sad) for the **RH injection**, for both RTLE and LTLE subjects, subjects without structural lesions performed better than those subjects with known anatomical lesions. RTLEs without lesions performed better than LTLEs without lesions for all three emotions. RTLEs with structural lesions performed better than LTLEs with lesions for the angry emotion, but worse than LTLEs with lesions for the happy and sad emotions. For the **LH injection**, results varied across the emotion, focus, and lesion variables. When percent accuracy scores for the happy emotion were examined, RTLEs with structural lesions outperformed all other groups. LTLEs without structural lesions performed better than both LTLEs with structural lesions and RTLEs without lesions. LTLEs with structural lesions performed worse than all other groups. For both the angry and sad emotions during the LH injection, RTLEs without structural lesions outperformed all other groups. For the angry emotion, all other groups performed equivalently. For the sad emotion, LTLEs with structural lesions performed better than LTLEs without structural lesions and better than RTLEs with structural lesions. RTLEs with structural lesions performed the worst on this task. (See Table 7c for mean values.)

Table 7. Effects of Structural Lesion

Table 7a. Main effect of Lesion (F = 3.00, p=.093)

(percent accuracy scores)

Irritative lesion	Structural + Irritative lesion
56.00	36.67

Table 7b. Focus x Injection x Emotion Interaction (p=.073)

(percent accuracy scores)

Inject	Emotion	Focus		F-value	p-value
		RTLE	LTLE		
RIGHT	Happy	50.00	50.00	.000	1.00
	Angry	63.64	28.57	4.50	.041
	Sad	54.55	50.00	.067	.797
LEFT	Happy	57.14	46.67	.368	.548
	Angry	42.86	40.00	.028	.869
	Sad	52.38	46.67	.108	.744

Table 7c. *Focus x Lesion x Injection x Emotion*

(F = 3.47, p=.037) (percent accuracy scores)

EMOTION	INJECT	FOCUS			
		RTLE		LTLE	
		STRUCTURAL LESION			
		YES	NO	YES	NO
HAPPY	RIGHT	33.33	56.25	40.00	55.56
	LEFT	80.00	50.00	20.00	60.00

EMOTION	INJECT	FOCUS			
		RTLE		LTLE	
		STRUCTURAL LESION			
		YES	NO	YES	NO
ANGRY	RIGHT	33.33	75.00	0.00	44.44
	LEFT	40.00	43.75	40.00	40.00

EMOTION	INJECT	FOCUS			
		RTLE		LTLE	
		STRUCTURAL LESION			
		YES	NO	YES	NO
SAD	RIGHT	33.33	62.50	40.00	55.56
	LEFT	20.00	62.50	60.00	40.00

Effects of Seizure Frequency. In order to determine the effect of seizure frequency on percent accuracy scores for the three discrete emotions, a four-way Focus (2) by Seizure Frequency (2) by Injection (2) by Emotion (3) repeated measures ANOVA was conducted. A trend was observed for the Focus x Seizure Frequency interaction (p=.068). RTLEs with low seizure frequency (< 10/month) performed better than LTLEs with low seizure frequency. RTLEs with high seizure frequency, however, performed more poorly than LTLEs with a high frequency of seizures. While RTLEs with low seizure frequency outperformed RTLEs with high seizure frequency, high frequency LTLEs performed better than low frequency LTLEs. (See Table 8 for mean values.)

Table 8. Effect of Seizure Frequency
Focus x Seizure Frequency Interaction
(F = 3.47, p=.068) (percent accuracy scores)

FREQUENCY	**FOCUS**	
	RTLE	**LTLE**
LOW	49.11	55.56
HIGH	56.26	26.67

Effects of Generalized Seizures. To evaluate the effect of the presence of secondarily generalized seizures on discrete emotion accuracy scores, a four-way Focus (2) by Seizure Type (2) by Injection (2) by Emotion (3) repeated measures ANOVA was conducted. A trend was observed for the main effect of seizure type (p=.10). Overall, regardless of side of focus or side of injection, patients with secondarily generalized seizures performed worse than patients who experienced only non-generalized complex partial seizures. (See Table 9 for mean values.)

Table 9. Effect of Generalized Seizures

Main effect of Seizure Type ($F = 2.83$, $p = .10$)

(percent accuracy scores)

SECONDARY GENERALIZATION OF SEIZURES	
YES	**NO**
42.76	66.67

B. **Dimensional Analyses**

Valence Effects

Interhemispheric Effects. In order to evaluate the interhemispheric effects of lateralized seizure foci and unilateral amobarbital injections on perceptual accuracy of the positively- and negatively- valenced emotions, a three-way Focus (2) by Injection (2) by Valence (2) repeated-measures ANOVA was conducted. No significant main effects or interactions were observed.

Effects of Age at Seizure Onset. To determine the effects of age at seizure onset on perceptual accuracy of positive and negative emotions, a four-way Focus (2) by Onset (2) by Injection (2) by Valence (2) repeated measures ANOVA was conducted. No significant main effects were observed. A significant interaction for the Focus x Onset x Injection analysis was observed (p=.040). During the right hemisphere injection, RTLEs tended to perform better than LTLEs in general, with late onset subjects in both groups outperforming early onset groups. During the left hemisphere injection, early onset RTLEs performed better than early onset LTLEs and significantly better than late onset RTLEs. Late onset LTLEs were more accurate than all other groups. (See Table 10 for mean values.)

Table 10. Valence Analyses: Effect of Age at Seizure Onset Focus x Onset x Injection Interaction ($F = 4.59$, $p=.040$) (percent accuracy scores)

INJ	**FOCUS**			
	RTLE		**LTLE**	
	early	**late**	**early**	**late**
RIGHT	48.21	65.63	36.11	50.00
LEFT	62.50	28.13	36.11	70.00

<u>Intrahemispheric Effects</u>. To assess the effect of intrahemispheric location of epileptogenic focus on percent accuracy scores for positive and negative emotions, a four-way Focus (2) by Location (2) by Injection (2) by Valence (2) repeated-measures ANOVA was conducted. No significant

findings or trends were observed.

Effects of Structural Lesion. To evaluate the effect of the presence of a structural lesion on percent accuracy scores for the positive and negative emotions, a four-way Focus (2) by Lesion (2) by Injection (2) by Valence (2) repeated measures ANOVA was conducted. No significant main effects were observed.

A significant effect was observed for the Focus x Injection x Valence interaction (p=.053). During the RH injection, RTLEs outperformed LTLEs for the negative emotions, but scored equivalently for the positive emotion. During the LH injection, RTLEs performed better than LTLEs for both positively and negatively valenced emotions. (See Table 10a for mean values.)

This interaction was modified by a significant interaction for Focus by Lesion by Injection by Valence (p=.03). For **negative** emotions during the **RH injection**, for both RTLE and LTLE subjects, subjects without structural lesions performed better than those subjects with known anatomical lesions. RTLEs without lesions performed better than all the other groups. RTLEs with structural lesions and LTLEs without structural lesions performed equivalently. LTLEs with known anatomical lesions performed worse than all other groups. For **positive** emotions during the **RH injection,** LTLE patients without lesions outperformed all other groups. LTLEs with structural lesions performed worse than all other groups. Within the **LH injection**, results varied across the valence, focus, and lesion variables.

When percent accuracy scores for the positive emotion was examined, RTLEs with structural lesions outperformed all other groups. LTLEs without structural lesions performed better than both LTLEs with structural lesions and RTLEs without lesions. LTLEs with structural lesions performed worse than all other groups. For the negative emotions during the LH injection, RTLEs without structural lesions outperformed all other groups. RTLEs with structural lesions performed the worst on this task. (See Table 11 for mean values.)

Table 11. Valence Analyses: Effect of Structural Lesion

Table 11a. Focus x Injection x Valence Interaction (p=.053)

(percent accuracy scores)

Inject	Valence	Focus		F-value	p-value
		RTLE	LTLE		
RIGHT	+	50.00	50.00	.000	1.00
	-	59.09	39.29	1.650	.207
LEFT	+	54.55	46.67	.368	.548
	-	45.45	43.33	.076	.784

Table 11b. Focus x Lesion x Injection x Valence (F = 5.18, p = .030) (percent accuracy scores)

VALENCE	INJECT	FOCUS			
		RTLE		LTLE	
		STRUCTURAL LESION			
		YES	NO	YES	NO
POS	RIGHT	50.00	50.00	40.00	55.55
	LEFT	62.50	50.00	20.00	60.00

VALENCE	INJECT	FOCUS			
		RTLE		LTLE	
		STRUCTURAL LESION			
		YES	NO	YES	NO
NEG	RIGHT	50.00	64.29	20.00	50.00
	LEFT	18.75	60.71	50.00	40.00

Effects of Seizure Frequency. In order to determine the effect of seizure frequency on percent accuracy scores for valence, a four-way Focus (2) by Seizure Frequency (2) by Injection (2) by Valence (2) repeated measures ANOVA was conducted. A trend was observed for the Focus x Seizure Frequency interaction (p=.058). As in the discrete emotion analysis, RTLEs with low seizure frequency (< 10/month) performed better than LTLEs with low seizure frequency. RTLEs with high seizure frequency, however, performed more poorly than LTLEs with a high frequency of seizures. While RTLEs with low seizure frequency outperformed RTLEs with high seizure frequency, high frequency LTLEs performed better than low frequency LTLEs. (See Table 12 for mean values.)

Table 12. Valence Analyses: Effect of Seizure Frequency Focus x Seizure Frequency Interaction ($F = 3.89$, $p=.058$) (percent accuracy scores)

FREQUENCY	FOCUS	
	RTLE	LTLE
LOW	52.28	56.95
HIGH	56.95	25.00

Effects of Generalized Seizures. To evaluate the effect of the presence of secondarily generalized seizures on valence emotion accuracy scores, a four-way Focus (2) by Seizure Type (2) by Injection (2) by Valence (2) repeated measures ANOVA was conducted. No significant main effects or interactions were observed.

Motoric Direction Effects

Interhemispheric Effects. In order to evaluate the interhemispheric effects of lateralized seizure foci and unilateral amobarbital injections on the perceptual accuracy of approach versus avoidance emotions, a three-way Focus (2) by Injection (2) by Motoric Direction (2) repeated-measures ANOVA was conducted. No significant main effects or interactions were observed.

Effects of Age at Seizure Onset. To determine the effects of age at seizure onset on perceptual accuracy of approach and avoidance emotions, a four-way Focus (2) by Onset (2) by Injection (2) by Motoric Direction (2) repeated measures ANOVA was conducted. No significant main effects were observed. A trend for the Onset x Motoric Direction interaction was observed ($p = .058$), such that subjects with late onset seizures (> age 12) performed better than subjects with early onset seizures for avoidance emotions (e.g, sad) while the early onset subjects were more accurate for approach emotions (e.g.; anger). Table 13a presents the mean values for this analysis.

A trend was also observed for the Focus x Onset interaction ($p = .081$). Overall, LTLEs with late onset seizures outperformed all other groups and LTLEs with early onset seizures demonstrated the worst performance relative to the other groups. (See Table 13b for mean values.)

A significant interaction for the Focus x Onset x Injection analysis was also observed ($p = .021$). During the right hemisphere injection, RTLEs tended to perform better than LTLEs in general, with late onset subjects in both groups outperforming early onset groups. During the left hemisphere injection, early onset RTLEs performed significantly better than early onset LTLEs and late onset RTLEs. Late onset LTLEs were significantly more accurate than all other groups. (See Table 13c for mean values.)

Table 13. ***Motoric Direction: Effect of Age at Seizure Onset***

Table 13a. ***Onset x Motoric Direction Interaction (F = 3.88, p=.058) (percent accuracy scores)***

EMOTION	ONSET	
	early	late
approach	50.00	47.90
avoid	47.80	62.50

Table 13b. Focus x Onset Interaction (F = 3.25, p=.081) (percent accuracy scores)

ONSET	FOCUS	
	RTLE	LTLE
early	53.58	36.12
late	43.75	65.00

Table 13c. ***Focus x Onset x Injection Interaction (F = 5.89, p=.021) (percent accuracy scores)***

INJ	FOCUS			
	RTLE		LTLE	
	early	late	early	late
RIGHT	48.22	62.50	41.67	50.00
LEFT	58.93	25.00	30.56	80.00

Intrahemispheric Effects. To assess the effect of intrahemispheric location of epileptogenic focus on percent accuracy scores for motoric direction, a four-way Focus (2) by Location (2) by Injection (2) by Motoric Direction (2) repeated measures ANOVA was conducted. No significant main effects or interactions were observed.

Effects of Structural Lesion. To evaluate the effect of the presence of a structural lesion on percent accuracy scores for the approach and avoidance emotions, a four-way Focus (2) by Lesion (2) by Injection (2) by Motoric Direction (2) repeated- measures ANOVA was conducted. No significant main effects were observed. A significant effect was observed for the Focus x Lesion x Motoric Direction interaction ($p = .024$). Across both approach and avoidance dimensions, RTLEs without structural lesions outperformed all other groups. For approach emotions, patients without structural lesions performed better than patients with known anatomical lesions. LTLEs with structural lesions performed worse than all other groups. For the avoidance emotion, while RTLEs without lesions outperformed RTLEs with structural damage, LTLEs with known lesions performed better than LTLEs without lesions. For patients without lesions, RTLES tended to score better than LTLEs. For patients with anatomical lesion, however, LTLEs outperformed RTLEs. (See Table 14a for mean values.)

This interaction was modified by a significant interaction for Focus by Lesion by Injection by Motoric Direction ($p = .053$). For both approach and avoidance emotions during the **RH injection**, for both RTLE and LTLE subjects, subjects without structural lesions performed better than those subjects with known anatomical lesions. RTLEs without lesions performed better than LTLEs without lesions, and RTLEs with structural lesions tended to perform better than LTLEs with lesions. Within the **LH injection**, results varied across the motoric direction, focus, and lesion variables. When percent accuracy scores for approach emotions were examined, patients without structural lesions outperformed patients with structural lesions. LTLEs with structural lesions performed worse than all other groups. For the avoidance emotion during the LH injection, RTLEs without structural lesions outperformed all other groups. LTLEs with structural lesions performed better than LTLEs without structural lesions, and better than RTLEs with structural lesions. RTLEs with structural lesions performed the worst on this task. (See Table 14b for mean values.)

Table 14. Motoric Direction: Effect of Structural Lesion

Table 14a. Focus x Lesion x Motoric Direction

(F = 5.60, p=.024)(percent accuracy scores)

MOTORIC	FOCUS			
	RTLE		LTLE	
	LESION			
	Y	N	Y	N
APPROACH	46.88	55.36	25.00	50.00
AVOID	31.25	64.28	50.00	47.78

Table 14b. Focus x Lesion x Injection x Motoric Direction

(F = 4.05, p =.053) (percent accuracy scores)

MOTORIC	INJECT	FOCUS			
		RTLE		LTLE	
		STRUCTURAL LESION			
		YES	NO	YES	NO
APPROACH	RIGHT	50.00	60.71	20.00	50.00
	LEFT	43.75	50.00	30.00	50.00

MOTORIC	INJECT	FOCUS			
		RTLE		LTLE	
		STRUCTURAL LESION			
		YES	NO	YES	NO
AVOID	RIGHT	50.00	57.14	40.00	55.55
	LEFT	12.50	71.41	60.00	40.00

Effects of Seizure Frequency. In order to determine the effect of seizure frequency on percent accuracy scores along the motoric direction emotional dimension, a four-way Focus (2) by Seizure Frequency (2) by Injection (2) by Motoric Direction (2) repeated measures ANOVA was conducted. No significant main effects or interactions were observed.

Effects of Generalized Seizures. To evaluate the effect of the presence of secondarily generalized seizures on the approach and avoidance emotion accuracy scores, a four-way Focus (2) by Seizure Type (2) by Injection (2) by Motoric Direction (2) repeated measures ANOVA was conducted. No significant main effects or interactions were observed.

C. Gender Effects

Gender effects were evaluated using additional ANOVAs for any discrete or dimensional analysis for which group sizes were large enough (N>2) to permit valid interpretation of findings. Discrete Analyses

Interhemispheric Effects. In order to evaluate the effects of gender in conjunction with the interhemispheric effects of lateralized seizure foci and unilateral amobarbital injections on perceptual accuracy of the three discrete emotions, a four-way Focus (2) by Gender (2) by Injection (2) by Emotion (3) repeated measures ANOVA was conducted. No significant main effects or interactions were observed.

Effects of Age at Seizure Onset. Due to small group sizes within the Onset variable it was not possible to conduct additional five-way ANOVAs incorporating both the Gender and the Onset variables. As we had a theoretical rationale for exploring the combined effects of age at seizure onset and gender, however, an additional four-way Onset (2) by Gender (2) by Injection (2) by Emotion (3) repeated measures ANOVA was conducted. A trend for the main effect of Gender was observed ($p = .096$). Females performed more accurately than males regardless of side of injection, age at seizure onset, or discrete emotion presented. (See

Table 15a for mean values.)

A trend was also observed for the Onset (2) by Emotion (3) interaction ($p = .074$). Patients with late seizure onset tended to perform more accurately than early onset patients in the happy and sad conditions. When the angry emotion was presented, early onset patients outperformed late onset patients. (See Table 15b for mean values.)

The above trend was modified by a significant interaction between Onset (2), Gender (2), and Emotion (3) ($p = .025$). Results varied across the Onset, Gender, and Emotion variables. For male subjects, early onset patients outperformed late onset patients for the angry and sad emotions. The converse was true for the happy emotion; late onset patients tended to be more accurate than early onset patients. For female subjects, early onset patients tended to be more accurate than late onset patients only for the angry emotion. For happy and sad emotions, late onset patients outscored patients with an early seizure onset. When the happy emotion was presented, early onset females performed somewhat better than early onset males, although late onset males and females were equivalent in their accuracy scores. Within the angry emotion, females tended to outscore males regardless of age at seizure onset. Finally, within the sad emotion, late onset females, demonstrated the highest accuracy scores overall, scoring significantly higher than late onset males. Accuracy scores for early onset males and females were equivalent. (See Table 15c for mean values.)

Table 15. Gender Analyses: Discrete Emotion Effects

Effect of Age at Seizure Onset

Table 15a. Main Effect of Gender ($F=2.94$, $p=.096$)

(mean percent accuracy scores)

Males	Females
42.71	58.90

Table 15b. Onset x Emotion Interaction ($F=2.71$, $p=.074$)

(mean percent accuracy scores)

EMOTION	ONSET	
	early	late
happy	47.54	59.47
angry	51 89	33.66
sad	47.92	55.18

Table 15c. Onset x Gender x Emotion Interaction ($F=3.93$, $p=.025$) (mean percent accuracy scores)

EMOTION	GENDER			
	MALE		FEMALE	
	ONSET			
	early	late	early	late
happy	40.91	60.00	54.17	58.93
angry	45.46	20.00	58.33	47.32
sad	50.00	30.00	45.84	80.36

<u>Effects of Structural Lesion</u>. To evaluate the effects of gender along with the effects of the presence of a structural lesion on percent accuracy scores for the three discrete emotions, a five-way Focus (2) by Gender (2) by Lesion (2) by Injection (2) by Emotion (3) repeated-measures ANOVA was conducted. A trend was observed for the main effect of Gender ($p=.073$). Female subjects tended to perform more accurately than males regardless of side of seizure focus, side of amobarbital injection, or discrete emotion presented. (See Table 16a for mean values.)

A significan effect was observed for the main effect of lesion ($F = 4.58$, $p = .042$). A significant effect was also observed for the Gender x Lesion interaction ($p = .042$). Again, females tended to perform more accurately than males regardless of presence or absence of structural lesion. Across both genders, patients without lesions performed better than patients with structural damage. Overall, females without lesions outperformed all other groups. Males with structural lesions were the least accurate of all groups. (See Table 16b for mean values.)

A significant effect was also observed for the Focus x Injection x Emotion interaction ($p=.046$). During the RH injection, RTLEs outperformed LTLEs for the angry and sad emotions, but scored equivalently for the happy emotion. During the LH injection, RTLEs performed better than LTLEs across all three emotions. (See Table 16c for mean values.)

Table 16. *Gender Analyses: Discrete Emotion Effects*

Effect of Structural Lesion

Table 16a. *Main Effect of Gender (F=3.47, p=.073)*

(mean percent accuracy scores)

Males	Females
42.71	56.68

Table 16b. *Gender x Lesion Interaction (F=4.58, p=.042)*

(mean percent accuracy scores)

LESION	GENDER			
	Male	Female	F-value	p-value
Y	16.67	55.56	4.746	.057
N	52.53	57.14	0.014	.907

Table 16c. *Focus x Injection x Emotion Interaction*

(F=3.27, p=.046) (mean percent accuracy scores)

Inject	Emotion	Focus	
		RTLE	LTLE
RIGHT	Happy	49.17	50.00
	Angry	63.34	29.17
	Sad	53.34	50.00
LEFT	Happy	54.17	46.43
	Angry	34.17	30.95
	Sad	45.00	50.00

Dimensional Analyses

Valence Effects

Interhemispheric Effects. In order to evaluate the effects of gender in conjunction with the interhemispheric effects of lateralized seizure foci and unilateral amobarbital injections on perceptual accuracy of positive and negative emotions, a four-way Focus (2) by Gender (2) by Injection (2) by Valence (2) repeated measures ANOVA was conducted. No significant main effects or interactions were observed.

Effects of Age at Seizure Onset. Again, due to small subgroup sizes for the Onset variable, it was not possible to conduct additional five-way ANOVAs incorporating both the Gender and the Onset variables. As for the discrete analysis, we conducted an additional four-way Onset (2) by Gender (2) by Injection (2) by Valence (2) repeated measures ANOVA on an exploratory basis. No significant main effects were observed. A trend was observed for the Onset (2) by Gender (2) by Valence (2) interaction ($p = .075$). Results varied across the Onset, Gender, and Valence variables. For male subjects, early onset patients outperformed late onset patients in the negative valence condition. The converse was true for the positive condition; late onset patients tended to be more accurate than early onset patients. For female subjects, late onset patients outscored patients with an early seizure onset for both positive and negative emotions. When the positive emotion was presented, early onset females performed somewhat better than early onset males, while late onset males and females were equivalent in their accuracy scores. Within the negative valence condition, females tended to outscore males regardless of age at seizure onset. (See Table 17 for mean values.)

Table 17. Gender Analyses: Valence Effects
Onset x Gender x Valence Interaction
(F=3.41, p=.075) (mean percent accuracy scores)

Valence	GENDER			
	Male		Female	
	ONSET			
	early	late	early	late
+	40.91	60.00	52.09	58.93
-	47.73	25.00	54.17	63.84

Effects of Structural Lesion. To evaluate the effects of gender along with the effects of the presence of a structural lesion on percent accuracy scores for the two valence dimensions, a five-way Focus (2) by Gender (2) by Lesion (2) by Injection (2) by Valence (2) repeated measures ANOVA was conducted. No significant main effects were observed. A trend was observed for the main effect of Lesion (p=.061). TLE subjects without a structural lesion performed better than subjects with a known structural lesion, regardless of side of seizure focus or side of amobarbital injection. (See Table 18a for mean values.)

A trend was also observed for the Gender x Lesion interaction (p = .010). Females tended to perform more accurately than males regardless of presence or absence of structural lesion. Across both genders, patients without lesions performed better than patients with structural damage. Overall, females without lesions outperformed all other groups. Males with structural lesions were the least accurate of all groups. (See Table 18b for mean values.)

A significant effect was observed for the Focus x Injection x Valence interaction (p=.035). Overall, across injection and emotional valence, RTLEs were more accurate than LTLEs. During the RH injection, RTLEs performed better on negative versus positive emotions, while LTLEs were more accurate with positive versus negative emotions. During the LH injection, both RTLEs and LTLEs performed better when presented with positive as opposed to negative emotions. (See Table 18c for mean values.)

Table 18. ***Gender Analyses: Valence Effects***

Effect of Structural Lesion

Table 18a. ***Main Effect of Lesion (F=3.82, p=.061)***

(mean percent accuracy scores)

Structural Lesion	Irritative Lesion
37.50	56.00

Table 18b. Gender x Lesion Interaction (F=2.86, p=.10) (mean percent accuracy scores)

LESION	GENDER		post-hoc	
	Male	Female	F-value	p-value
Y	55.42	20.00	5.158	.053
N	57.14	42.05	.052	.822
post-hoc				
F-value	5.953	.021		
p-value	.029*	.886		

Table 18c. Focus x Injection x Valence Interaction (F=4.94, p=.035) (mean percent accuracy scores)

Inject	Emotion	Focus	
		RTLE	LTLE
RIGHT	+	45.00	44.38
	-	58.34	39.59
LEFT	+	54.17	46.43
	-	44.17	42.86

Motoric Direction Effects

Interhemispheric Effects. In order to evaluate the effects of gender in conjunction with the interhemispheric effects of lateralized seizure foci and unilateral amobarbital injections on perceptual accuracy of approach versus avoidance emotions, a four-way Focus (2) by Gender (2) by Injection (2) by Motoric Direction (2) repeated measures ANOVA was conducted. No significant main effects or interactions were observed.

Effects of Age at Seizure Onset. Once again, due to small group sizes within the Onset variable it was not possible to conduct an additional five-way ANOVA incorporating both the Gender and the Onset variables. As for the discrete and the valence analyses, we conducted an additional four-way Onset (2) by Gender (2) by Injection (2) by Motoric Direction (2) repeated measures ANOVA on an exploratory basis. No significant main effects were observed. A trend was observed for the main effect of Gender ($p = .068$). Again, females performed more accurately than males regardless of side of injection, age at seizure onset or discrete emotion presented. (See Table 19a for mean values.)

A significant effect was observed for the Onset (2) by Gender (2) by Motoric Direction (2) interaction ($p = .002$). Results varied across the Onset, Gender, and Valence variables. For male subjects, early onset patients tended to outperform late onset patients for the avoidance emotion. For the approach condition scores were equivalent for late and early onset patients. For female subjects, late onset patients outscored patients with an early seizure onset in the avoidance condition. Within the approach condition, accuracy scores were equivalent for early and late onset patients. Within the avoidance condition, late onset females tended to outscore all other groups. When approach emotions were presented, there were no significant differences between groups in terms of accuracy scores. (See Table 19b for mean values.)

Table 19. ***Gender Analyses: Motoric Direction Effects***

Table 19a. ***Main Effect of Gender (F=3.58, p=.068)***

(mean percent accuracy scores)

Males	Females
42.97	57.89

Table 19b. ***Onset x Gender x Motoric Direction (F=11.38, p=.002) (mean percent accuracy scores)***

Valence	GENDER			
	Male		Female	
	ONSET			
	early	late	early	late
approach	43.18	40.00	56.25	53.13
avoid	50.00	30.00	53.13	80.36

Effects of Structural Lesion. To evaluate the effects of gender along with the effects of the presence of a structural lesion on percent accuracy scores for the two motoric direction dimensions, a five-way Focus (2) by Gender (2) by Lesion (2) by Injection (2) by Motoric Direction (2) repeated-measures ANOVA was conducted. A significant main effect of Lesion was observed ($p=.049$). TLE subjects without a structural lesion performed better than subjects with a known structural lesion, regardless of side of seizure focus or side of amobarbital injection. (See Table 20a for mean values.)

A trend for the main effect of Gender was also observed ($p=.064$). Female subjects tended to perform more accurately than males regardless of side of seizure focus, side of amobarbital injection, or discrete emotion presented. (See Table 20b for mean values.)

A trend was also observed for the Gender x Lesion interaction ($p = .074$). Again, females tended to perform more accurately than males regardless of presence or absence of structural lesion. Across both genders, patients without lesions performed better than patients with structural damage. Overall, females without lesions outperformed all other groups. Males with structural lesions were the least accurate of all groups. (See Table 20c for mean values.)

Table 20. Gender Analyses: Motoric Direction Effects

Effect of Structural Lesion

Table 20a. Main Effect of Lesion (F=4.22, p=.049)

(mean percent accuracy scores)

Structural Lesion	Irritative Lesion
49.22	56.53

Table 20b. Main Effect of Gender (F=3.90, p=.058)

(mean percent accuracy scores)

Males	Females
42.97	57.89

Table 20c. Gender x Lesion Interaction (F=4.30, p=.074)

(mean percent accuracy scores)

LESION	GENDER			
	Male	Female	F-value	p-value
Y	17.50	55.42	7.211	.028*
N	52.47	58.04		.762
			.094	
post-hoc				
F-value	8.853	.001		
p-value	.010**	.973		

V. DISCUSSION

The overarching aim of this research was to extend neuropsychological understanding of the brain mechanisms involved in emotional perception. Based on current theories in the neuropsychology of emotion, and on controversy in the literature with regard to hemispheric specialization for emotion, our primary focus was on the examination of laterality effects within our paradigm in our epilepsy population. Since the majority of the literature from BD and NC studies still lends support to right hemisphere specialization for prosodic emotional perception, our main objective was to utilize the laterality variables of injection side and side of seizure focus to test the RH hypothesis.

Through the use of the Intracarotid Amobarbital Procedure, we were provided with the unique opportunity to test the abilities of each cerebral hemisphere in isolation, albeit for only a few minutes. Taking the view that administration of sodium amobarbital to one hemisphere of the brain renders it incapable of contributing in any meaningful way to behaviors observed during the circumscribed period of anesthetization, we expected to draw inferences about laterality and the comprehension of emotional prosody. Given our prediction that the RH hypothesis would be operative, we expected to find a significant main effect of Injection, such that all subjects would perform less accurately with RH as opposed to LH injection. While we did obtain some statistically significant results involving side of injection through a number of interactions, there was no systematic pattern to these findings. Significant findings or trends involving side of injection were observed in three interactions within the discrete emotion analyses. There were occasions in which RH injection produced impairment as expected (e.g., late onset LTLEs), yet there were an equal number of occasions in which LH injection produced impaired performance (e.g., late onset RTLEs). In none of these analyses, however, was there a systematic effect of injection which provided clear evidence either in support of or against the right hemisphere hypothesis.

In addition to injection side, we examined laterality of seizure focus in our patient population as an indirect means of evaluating hemispheric differences. Our expectation was that RTLEs should have performed less accurately overall, as RH damage has been shown to compromise emotional perceptual ability (e.g, Borod, 1992; Heilman & Bowers, 1990). Within our analyses, there were several instances in which side of seizure focus was an issue. Significant or trend findings involving laterality of focus were obtained in four separate interactions within the discrete emotion analyses. In two of these interactions (i.e., Focus x Onset x Injection, Focus x Injection X Emotion) the findings were not consistent with our predictions. That is, RTLEs outperformed LTLEs in three of four cases in the F x O x I interaction, and in five of six cases in the F x I x E interaction. When we examined the results separately for each discrete emotion, RTLEs performed more accurately in the angry condition in three of four instances. No systematic findings were observed for the happy and sad emotions. In an effort to explain these unexpected findings, we examined the extent of pathology across RTLE and LTLE groups. There were, however, no apparent distinctions between groups in terms of structural brain damage, duration of seizure disorder, seizure frequency, or number of subjects with secondarily generalized seizures. Another possibility which might account for the lack of expected group differences is that RTLEs and LTLEs may have differed in terms of baseline abilities in emotional perception. Although our groups were not significantly different in terms of overall cognitive abilities and all subjects were able to adequately complete the experimental task prior to IAP testing, we did not conduct additional baseline evaluations of emotional perceptual abilities. Further research is planned in which extensive baseline testing will take place incorporating multiple tasks of emotional prosodic perception. Potential performance differences between groups could then be accounted for in interpreting IAP test results.

Since posterior neocortical brain structures are known to be particularly relevant for emotional perception, we also evaluated our results in terms of intrahemispheric EEG localization of seizure focus. Patients had been categorized apriori into those with a mesial temporal seizure focus and those with additional lateral temporal or extratemporal involvement. It was our intention to assess the contributions of limbic versus neocortical brain regions to emotional prosodic perception. Although these analyses were conducted on an exploratory basis, and we had no definitive predictions with respect to intrahemispheric effects, we hypothesized that lack of a significant main effect for Location would suggest that limbic and ipsilateral neocortical regions function in a similar manner with respect to our task. For all analyses conducted incorporating Location as a variable, no significant main effects or interactions were observed. It is important to note, however, that the heterogeneity of our "extratemporal" group may have contributed to the lack of findings. All patients with EEG involvement of regions other than strictly mesial temporal were grouped together due to the relatively small sample size. Subjects included in the "extratemporal" group included those with mesial plus lateral temporal involvement, others with mesial, lateral plus extratemporal involvement, and finally those with mesial plus extratemporal involvement. Future studies are planned in which a larger sample size will enable us to make more specific comparisons between groups with more circumscribed EEG foci, thereby allowing a more realistic comparison of the relative contributions of limbic versus neocortical brain regions to emotional processing.

In light of the lack of systematic findings with respect to the lateralization and localization variables, we next turned to alternate theoretical models regarding hemispheric specialization for emotion. There continues to be a debate in the literature concerning brain localization for prosodic aspects of language (e.g., Heilman & Bowers, 1990; Van Lancker & Sidtis, 1993). Although much research suggests that the RH is predominantly involved in the expression and perception of emotional prosody (e.g., Borod, 1992; Ross, 1985), a number of other investigators have suggested that both hemispheres are implicated to varying degrees in aspects of prosodic communication (e.g., Van Lancker & Sidtis, 1993). In the current study, impairments were observed in many instances with both right and left hemisphere injections. The importance of LH involvement in prosodic perception was further underscored by the seizure focus data; overall, LTLEs performed more poorly than RTLEs in these analyses.

In spite of these findings, we elected to further examine our results in terms of the two dimensional categorizations of emotion in order to assess whether any lateralized findings had been obscured in the discrete emotion analyses. If the valence hypothesis had been operative, we would have expected to find impairment in the perception of negative emotions during the RH injection and impaired performance for positive emotions during the LH injection. This effect should have been apparent in the form of a significant Injection by Valence interaction. In terms of laterality of seizure focus, support for the valence hypothesis might have been obtained in the form of a

Focus by Valence interaction, such that RTLEs would perform more poorly on negative emotions and LTLEs would be less accurate with positive emotions. This interaction could have been modified by an interaction with injection since the effects of seizure focus could only have been observed when the affected hemisphere was not anesthetized (i.e., RTLE during LH injection, LTLE during RH injection). In our analyses, there were only two instances in which the effect of valence played a role. Although a significant interaction was observed between Focus, Injection, and Valence, there were no systematic patterns either in support of, or in opposition to, the valence hypothesis. During the RH injection, while LTLEs demonstrated the expected poorer performance with negative emotions, the RTLEs' pattern of performance was in the opposite direction. During the LH injection, all subjects were actually better with positively-valenced emotions. With respect to focus laterality, RTLEs performed less accurately with negative emotions during the LH injection as expected. LTLEs, however, performed better with positive emotions during both hemispheric injections.

Similarly, our findings were examined with respect to the approach/avoidance dimension. If the motoric direction hypothesis were operative, we would have expected to see impaired perception of avoidance/withdrawal emotions (i.e., sad) with RH injection, and decreased accuracy with approach emotions (i.e., angry, and/or happy) during LH injection. Again, a significant Injection by Motoric Direction should have been observed. Lateralized findings would also have been expected in terms of a Focus by Injection by Motoric Direction interaction such that RTLEs would perform more poorly on avoidance emotions during LH injection, and LTLEs would perform more poorly for approach emotions during the RH injection. These expected interactions were not, however, apparent from our data. In the one instance where Focus, Injection, and Motoric Direction played a role, no systematic patterns of performance were apparent. During the RH injection, in three of four cases, subjects performed more poorly with the approach emotions; during the LH injection no systematic patterns emerged. In terms of seizure focus, while LTLEs did tend to perform more poorly with approach emotions during RH anesthetization, no systematic patterns were observed for RTLEs.

Since our evaluation of both the discrete emotion and the dimensional analyses were inconclusive for the RH, as well as the valence and motoric direction hypotheses, we next turned to Gender as a potentially important variable in mediating laterality effects with respect to emotion. In the process of recruiting subjects, a concerted effort was made to control subject selection so that RTLE and LTLE groups did not differ with respect to demographic variables (e.g., gender and education level). Although females were slightly over represented in our population, gender-composition differences between right and left TLE groups were not statistically significant.

There are several conceptual reasons to expect that the role of gender might be important in research involving the lateralization of brain functions. One idea which has emerged from the language literature is that females seem to demonstrate less brain asymmetry than males with respect to language functions (e.g., McGlone, 1980). Findings from emotion research, by contrast, suggest greater hemispheric lateralization for emotion in females relative to males (e.g., Myers & Smith,1987, Safer, 1981). In thinking about gender effects from a cognitive processing perspective, studies have also demonstrated that when gender effects are observed, females tend to outperform males on tasks of emotional processing (e.g., Hall, 1978; LaFrance & Banaji, 1992). Finally, in terms of the neuropsychological theories of emotion, research has shown that when the valence hypothesis is operative, its effect is more often observed for females than for males (e.g., Borod, Koff, & Buck, 1986). When we analyzed our data with respect to gender and laterality effects, there was no evidence that TLE females were more lateralized than TLE males for prosodic emotional perception, nor were females more subject to lateralizing effects by amobarbital injection. We did, however, find some significant performance effects relative to gender. A significant main effect of Gender was observed such that females were more accurate than males regardless of side of injection, focus, or discrete emotion presented. A significant Gender by Lesion effect was also seen where females tended to outperform males regardless of presence or absence of structural lesion. Finally, in three of four instances, females were more accurate than males regardless of age at seizure onset. In sum, consistent with the literature concerning gender effects on emotional processing performance, in nearly every instance where Gender played a role, females were more accurate than males on our experimental task.

To a large extent, our knowledge about brain mechanisms important in emotional processing has come from research conducted with brain damaged (e.g., stroke, tumor) or neurologically healthy subjects. Relatively less is known regarding perception of emotion in patients with epilepsy. In the evaluation of epileptic patients, there are numerous variables which are critically important in determining prognosis, course, and treatment regimen including age at seizure onset, etiology (e.g., structural lesion), seizure type, and seizure frequency. Since we had only speculative hypotheses concerning the effect of these variables on emotional processing, and because we were unclear as to how these epilepsy variables might interact with laterality variables, we conducted analyses of each of these seizure variables on an exploratory basis. Given the lack of significant inter- and intrahemispheric main effects, we elected to re-evaluate our data with respect to 1) age at seizure onset, and 2) severity of etiology.

In terms of age at seizure onset, clinical studies evaluating treatment, course of illness, and outcome measures in the epilepsy population have generally concluded that early onset seizures can be associated with numerous deleterious long-term effects (Perrine, 1992). Along these lines, one might have expected poorer performance from early onset TLE groups relative to late onset groups. Interactions with injection side and focus would be expected, but would vary depending on whether the RH, valence or motoric direction hypothesis were operative. On the other hand, there have been frequent reports in the recovery literature which suggest that both inter and intrahemispheric compensatory reorganization of function can occur subsequent to a brain insult sustained early in development. It would therefore be reasonable to expect that some functional reorganization may have occurred during the developmental process following seizure onset in infancy or early childhood. Taking this view, we would expect patients with late seizure onset to perform more poorly than early onset patients when the task involved is mediated by brain structures affected by a focal irritative (or structural) lesion. Again, differing interactions with injection side and focus would be expected depending on which laterality hypothesis was operative.

Given these two opposing arguments regarding the potential effect of age at seizure onset on performance, we analyzed our data with respect to this variable on an exploratory basis. In our analyses there were 10 instances in which Onset played a role. A significant main effect of Onset was not, however, observed. In several instances (e.g., Onset x Emotion, Onset x Motoric Direction), Onset interacted with Emotion such that late onset patients differed from early onset patients in terms of accuracy across discrete emotion or across aspects of a dimensional variable. There were also interactions with Focus and Injection, such that late onset RTLEs tended to perform better with RH injections and late onset LTLEs were more accurate with LH injections. Late onset patients also tended to perform better than early onset patients, but only during the RH injection. Overall, findings were rather unsystematic and no clear conclusions could be drawn with respect to any of the apriori hypotheses.

Finally, we examined our data in terms of the remaining three seizure variables incorporated in our exploratory hypotheses: presence of structural lesion, secondarily generalized seizures, and seizure frequency. We conceptualized these variables to be similar in that they exist along a severity continuum and appear to demonstrate some prognostic or etiological significance. In other words, our hypotheses regarding the effect of each of these variables was that the more severe the condition, the worse the expected performance. Specifically, we hypothesized that patients with a structural brain lesion at the site of epileptogenic focus would perform less accurately than patients with only an irritative epileptogenic lesion. Similarly, patients with complex partial seizures which occasionally secondarily generalized would perform more poorly than patients with CPS only. Finally, patients with a high frequency of seizures (>10/month) would perform less well in comparison with patients experiencing fewer seizures. These effects were expected regardless of injection side or focus. Accordingly, we anticipated significant main effects for each of the "severity" variables.

In the analyses incorporating presence of structural lesion as a variable, Lesion played a role in eight instances. A trend for the main effect of Lesion was observed such that patients with structural lesions performed worse than patients with irritative lesions, regardless of side of seizure focus or side of amobarbital injection. In the seven interactions in which Lesion was involved, patients with structural lesions performed less accurately in 31 of 42 comparisons. In the analyses involving secondary generalization, a trend for the main effect of Seizure Type was observed in the discrete emotion analysis. As anticipated, irrespective of seizure focus or injection side, patients with secondarily generalized seizures performed more poorly than patients who experienced non-generalized CPS. Finally, when seizure frequency was considered, a trend for the Focus by Seizure Frequency interaction was observed in the discrete emotion analyses. This interaction reached statistical significance in the valence analyses. In both cases, as hypothesized, RTLEs with low seizure frequency performed better than RTLEs with high seizure frequency. For LTLEs, however, patients with high seizure frequency tended to perform better than those with a lower seizure frequency. While the latter finding is difficult to explain, it is possible that our dichotomization of patients into high and low frequency groups was not entirely accurate. We relied on patient self-reports of seizure frequency within the three months prior to testing. For patients who experience seizures during sleep or who may be unable to accurately recall each event, the reported incidence may be an unreliable estimate. In addition, we were unable to account for any potential anti-epileptic medication effects on seizure frequency, and may therefore have obtained estimates confounded by the efficacy of therapeutic intervention. For future reference, estimates of seizure frequency may need to be based on consensus reports from both patients and family members/caregivers. Estimates may also need to be averaged over longer periods of time. Type and dosage of anti-epileptic medication(s) should also be documented and, as well as possible, taken into account in analyses involving seizure frequency.

Conclusions and Methodological Issues

To review the findings in this study, impairments in identification of prosodic emotion were observed in several instances during both right and left hemisphere amobarbital anesthetization. From a neuropsychological perspective, these results lend some support to the notion that both cerebral hemispheres contribute to a certain extent in the perception of emotional prosody. The importance of LH involvement was underscored when the data were examined by laterality of seizure focus. Overall, in many cases, LTLEs tended to perform less accurately than RTLEs. It is essential to note, however, that there were only a few trends and significant results with respect to laterality. The relative lack of findings may have been due in part to the methodological restrictions imposed by the Intracarotid Amobarbital Procedure. An increased number of both baseline and IAP experimental trials would greatly increase the robustness of future analyses of this type. Intrahemispheric effects, although not evident from our data, remain an interesting avenue for future exploration. Larger sample sizes would enable more precise comparisons of the contributions of limbic and neocortical brain regions to emotional processing. Finally, variables within the epilepsy population, particularly age at seizure onset and presence of structural lesion, were shown to have a significant effect both directly on task performance, and indirectly through interactions with laterality variables. Future research involving epilepsy patients must take these neurological and etiological variables into serious consideration when evaluating cognitive performance within this population.

VI. References

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