



## The sad, the angry, and the asymmetrical brain: Dichotic Listening studies of negative affect and depression

Marien Gadea<sup>a,\*</sup>, Raul Espert<sup>a</sup>, Alicia Salvador<sup>a</sup>, Luis Martí-Bonmatí<sup>b</sup>

<sup>a</sup>Departamento de Psicobiología, Facultad de Psicología, València, Spain

<sup>b</sup>Servicio de Radiología, Hospital Quirón, València, Spain

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### ABSTRACT

Dichotic Listening (DL) is a valuable tool to study emotional brain lateralization. Regarding the perception of sadness and anger through affective prosody, the main finding has been a left ear advantage (LEA) for the sad but contradictory data for the anger prosody. Regarding an induced mood in the laboratory, its consequences upon DL were a diminished right ear advantage (REA) for the induction of sadness and an increased REA for the induction of anger. The global results fit with the approach-withdrawal motivational model of emotional processing, pointing to sadness as a right hemisphere emotion but anger processed bilaterally or even in the left hemisphere, depending on the subject's preferred mode of expression. On the other hand, the study of DL in clinically depressed patients found an abnormally larger REA in verbal DL tasks which was predictive of therapeutic pharmacological response. However, the mobilization of the available left hemisphere resources in these responders (reflected in a higher REA) would indicate a remission of the episode but would not assure the absence of new relapses.

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### 1. Introduction: models of emotional processing

The modern conceptualizations of the neurocircuitry of emotion put emphasis in subcortical areas, the so called limbic system, with prevalence for the amygdala and hippocampus, and also part of the basal ganglia (ventral striatum and pallidum), medial thalamus, the hypothalamus, and some parts of the brainstem as well (e.g. periaqueductal gray). The emotional network also includes as a central key some cortical areas (e.g. prefrontal cortex, parietal cortex) linked to emotional processing, with the connection of both the subcortical and cortical systems being object of an actual and extensive research (Price & Drevets, 2010). Moreover, it has been proposed the existence of a set of neural mechanisms triggered specifically by unpleasant or negative stimuli, when dangerous, harmful or repugnant (Carretié, Albert, López-Martín, & Tapia, 2009) whose main feature is to be capable of coping danger events with urgent utility at the cost of some precision. Indeed, a set of neural circuits responding to positive events has been described (Burgdorf & Panksepp, 2006). On the other hand and for practical purposes, the researcher should note the difference between the perception of an emotion and its expression or communication. A third category would be the real phenomenological experience of an emotion (described by the subject usually as a “feeling”).

Moreover, the emotional experience has three main channels to do an effective expression: facial affect, affective prosody, and emotional lexicon, as well as three components or dimensions: valence (ranging from positive or pleasant to negative or unpleasant), arousal (ranging from calming to arousing), and motor activation (ranging from to approach and to avoid, or neither) (Borod, 1992; Heilman, 1997). It is also important to consider the difference between emotional states, being restricted to the present moment; and emotional traits, more stable along lifespan.

Many studies on hemispheric asymmetries have focused on emotional processing, explaining the results of their experiments by means of a different type or process between the right and left cortex. In general, the link between emotion processing and the right hemisphere is an old issue (Mills, 1912) but the consensus today is that the right hemisphere's preferred participation is conditioned by the emotional dimensions noted above (valence, arousal, etc.). So, taking into account the sometimes conflicting findings, several models of brain lateralization for emotional processing have been proposed to date. First, the commented right hemisphere hypothesis: a classical view founded in the earlier observations of the presence of a unilateral right-sided lesion often associated with inappropriately indifference or even manic reactions (Gainotti, 1969), which posits a right hemisphere specialization for the perception, expression, and experience of emotion, regardless of valence (Borod, Bloom, Brickman, Nakhutina, & Curko, 2002; Tucker, 1981). Accumulative data from subsequent brain damage studies found hemispheric differences as a function

\* Corresponding author. Address: Departamento de Psicobiología, Facultad de Psicología (Universitat de València), Avda. Blasco Ibañez 21, 46010 València, Spain. Fax: +34 96 3864668.

E-mail address: [Marien.Gadea@uv.es](mailto:Marien.Gadea@uv.es) (M. Gadea).

of positive versus negative emotions (e.g. Adolphs, Damasio, Tranel, & Damasio, 1996) and led to the second model, the valence hypothesis, which postulates that the left frontal brain region is involved in the *experience* and *expression* of positive emotions and the right frontal brain region is that in the negative ones (Jansary, Tranel, & Adolphs, 2000; Silberman & Weingartner, 1986), with the note of some authors who added that the *perceptual* processing of both positive and negative affects would be still solely a right cerebral function (Ley & Bryden, 1982). The valence hypothesis has been subsumed by another: a motivational directional proposal known as the approach-withdrawal model, which posits emotions associated with approach and withdrawal behaviors are processed within the left- and right-anterior brain regions, respectively (Davidson, 1992; Harmon-Jones & Allen, 1998; Maxwell & Davidson, 2007). The overlap between the two last models is extensive, due to most negative emotions (e.g. fear, disgust) eliciting withdrawal behavior and most positive behaviors (e.g. happiness, amusement) eliciting approach behavior. Conversely, the study of frontal asymmetries associated with feelings of anger – a negative emotion that elicits approach behavior – has provided a great amount of data supporting the approach-withdrawal model, in correlating anger with left frontal activation (Carver & Harmon Jones, 2009; Harmon-Jones, 2003), suggesting that the approach-withdrawal model is not only a theoretical construct but also a better fit for the experience of emotion. Additionally, some of the contradictory findings may be explained under the framework of another proposal: the behavioral inhibition versus behavioral activation systems (BIS/BAS) model (Gray, 1990), because for this model the behavioral activation (BAS) would be the emotion itself but also the active control of that emotion (e.g. repression of anger), whereas the behavioral inhibition (BIS) would represent passive avoidance or emotional extinction (Hewig, Hagemann, Seifert, Naumann, & Bartussek, 2004). Finally, Demaree, Everhart, Youngstrom, and Harrison (2005) suggested a model that includes an emotional dimension called “dominance” that refers basically to feelings of control (dominance) versus being controlled (submission) by circumstances, and would be also attributable to patterns of left and right frontal activity asymmetry, respectively.

Dichotic Listening (DL), as one of the most reliable non-invasive experimental procedures to investigate hemispheric asymmetries behaviorally (Voyer, 1998), has been also applied to the study of emotional processing. In the next sections this review will focus in three main areas of research where DL has been used as a valuable tool to study the lateralization of emotions: first, the perception of negative emotions in language by means of affective prosody; second, the experience in the laboratory of an induced negative affect and its consequences upon dichotic listening scores; and three, dichotic listening performance in clinically depressed patients, as a form to investigate the extreme, pathologic, form of negative affect.

## 2. Dichotic listening and the perception of negative affect by prosody

The word “prosody” refers to the rhythm, stress, and intonation of speech, which reflects language features that may not be encoded by grammar or simple vocabulary. In general, linguistic prosody gives information about whether the utterance is a statement, a question, or a command, while emotional prosody represents the patterns of pitch, loudness, and length that signal and communicate the emotional state and intentions of the speaker. According to the dynamic dual pathway model of auditory language comprehension, syntactic and semantic information is primarily processed in a left hemisphere temporal-frontal pathway whereas sentence level prosody is processed in a right hemisphere

temporal-frontal pathway (Friederici & Alter, 2004), with the interplay for the coordination and integration of local syntactic and prosodic features during auditory speech comprehension via the posterior part of the corpus callosum (Sammler, Kotz, Eckstein, Ott, & Friederici, 2010). Studies of brain damage and neuroimage indicate a primary role for the right hemisphere in the comprehension of emotional prosody (Borod, Zgaljardic, Tabert, & Koff, 2001), although this lateralization should be viewed as a relative rather than an absolute dominance given some data showing bilateral processing (Kotz et al., 2003). Pell (2006) suggested that emotional prosody is usually examined in the context of words, and interpreting prosody in a semantic context would require some left hemisphere involvement, thereby leading to findings of bilateral processing. Additionally, it has been stressed the importance of methodological factors in the outcome of lateralization of emotional prosody specially for the neuroimage research (Kotz, Meyer, & Paulmann, 2006).

In the Dichotic Listening method, subjects are presented with two different sounds, one to each ear simultaneously, and asked to identify what they heard. The brain is provided in a moment with more information than it is capable of conscious analysis so the results are believed to reflect the basic and preferred mode of processing of each hemisphere. When verbal material is applied a right ear advantage (REA) usually appears, which indicates, due to the preponderance of the contralateral auditory pathways under dichotic stimulation, the superiority of the left hemisphere for linguistic processing (Bryden, 1988; Hugdahl, 2000; Kimura, 1967). Regarding emotional prosody and dichotic listening, early reports presented emotionally intoned sentences (manipulating basic emotions to form a happy, sad, or angry voice tone) paired with monotone sentences, and found a left ear advantage (LEA) for the emotional intonation and a simultaneous REA for the verbal content of the sentences (Ley & Bryden, 1982; Shipley-Brown, Dingwall, Berlin, Yeni-Komshian, & Gordon-Salant, 1988). The LEA for emotional prosody was also found simultaneously with the REA for neutral words, for instance the word “tower” spoken in a happy tone of voice (Bryden & MacRae, 1989; Bulman-Fleming & Bryden, 1994) regardless of response procedure (crossing out face drawings versus circling the correspondent word; Voyer, Bowes, & Soraggi, 2009), and with a relatively high level of test-retest reliability for the laterality effect (Voyer & Rodgers, 2002). The LEA was also demonstrated for phrases of nonsense words spoken in happy, sad, angry or fearful prosody (McNeely & Netley, 1998) and even for emotional prosody joined to nonsense syllables e.g. ba, pa, thus without verbal content paired (Erhan, Borod, Tenke, & Bruder, 1998). This LEA points to right hemisphere processing of emotional prosody, however, in keeping with Pell’s (2006) hypothesized left hemisphere involvement, the magnitude of the LEA for emotions was generally smaller than the REA for words. The earlier studies did not observe differences between emotions, so it was postulated a right hemisphere involvement in emotional prosody regardless of valence (Ley & Bryden, 1982). In a step forwarded study Grimshaw, Kwasny, Covell, and Johnson (2003) presented dichotically two words spoken in either a neutral or a sad prosody, asking only about the target word while ignoring the emotion, to find a robust REA for the neutral condition but a diminished REA for the sad prosody condition; apparently, the presence of the sad emotional prosody activated the right hemisphere sufficiently to facilitate right linguistic processing of the verbal content of the words, thus diminishing the REA. In a subsequent work (Grimshaw, Seguin, & Godfrey, 2009) the experiment was extended to happy and angry prosody, to find only a significant REA than did not interact with prosody. The authors suggested the results fitted better with the motivational approach-withdrawal model of emotional lateralization, with sadness associated to the right hemisphere and happiness and anger to the left one, although an

alternative explanation in terms of acoustic properties of the stimuli used was also offered. The angry prosody has been extensively studied by Aue, Cuny, Sander, and Grandjean (2010) varying both the focus of attention to it and the laterality (ear) of presentation, and measuring its effects on peripheral nervous system. They observed a pattern of responses related to angry prosody being capable of attracting attention but also capable of provoking physiological changes without voluntary attention, and not supportive of the idea of a general right hemisphere advantage for the processing of this type of prosody. In a different line of experiments, Grimshaw (1998), Techentin and Voyer (2007), and Techentin, Voyer, and Klein (2009) presented words in a congruent or incongruent emotional tone (e.g. the word “sad” spoken in a happy tone of voice) with the aim of studying the cognitive processes involved in the integration of conflicting semantic and emotional prosodic information. Results showed a stronger LEA for the detection of target emotional tones when the word and the emotional tone were incongruent than when they were congruent, suggesting that, rather than simply facilitating the processing of the word, an incongruent emotional tone can enhance the quality of the emotional information beyond the word or statement alone. An interesting example of how to study conflicting semantic versus prosodic information was the work of Voyer, Bowes, and Techentin (2008), where the subjects were asked to localize sincere or sarcastic statements presented dichotically. In keeping with the definition of sarcasm as an insult or negative remark via an indirect statement that is pronounced in a particular prosody, the authors hypothesized, and confirmed, a LEA for the detection of sarcastic phrases and a REA for the sincere ones.

### 3. Bad feelings in the lab: negative affect and its outcome upon dichotic listening

In contrast with the experiments commented above, centered on the *perception* of emotions, other research has devoted to the emotional *experience*, and developed methods to induce an emotion in the laboratory to explore the normal human feelings in real time. Indeed, a relatively small amount of experiments focused on hemispheric emotional asymmetries and applied these mood induction procedures, some of them in combination with DL. The range of laboratory methods for inducing temporary mood states is quite broad although they can be subsumed in few categories: to ask for autobiographical recall of emotional memories, to arrange the subjects for listening to music pieces or seeing film clips selected to elicit target moods, or to reading aloud some self-referent statements progressing from relative neutral to a target mood, technique known as the Velten Mood Induction Procedure (Velten, 1968) (for a comprehensive review of mood induction procedures see Gilet, 2008). Since the pioneer study of Schachter and Singer (1962) – where a combination of an adrenaline injection and two conditions of tasks designed to amuse or to annoy the subjects served the authors to argue for the labeling of arousal according to the available cognitions – and from time to time, some doubts have arisen about the effectiveness and validity of these methods, mainly around the question whether a sufficient intensity of mood is produced, the duration of the mood, or the question of demand effects, most likely to occur with self-statement techniques when subjects are explicitly instructed to try to enter a specific mood state. However, in general it seems that the various procedures are capable to elicit true changes of moods in up to 50–75% of the subjects (Jallais & Gilet, 2010), with an individual variability depending on factors like experience with recent negative events or basal symptoms of anxiety prior to the mood induction task (Scherrer and Dobson (2009)). The commented procedures are a little bit different from tasks designed to elicit a stress response,

like cognitive, physical, or social stressors. Anyway, one must note that a laboratory stressor, for instance physical pain or a public exposure, is supposed to be accompanied by a sensation of discomfort or even a negative affect, apart from the higher arousal that it is designed to elicit (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002).

In this mood induction experiments a dual task paradigm can be applied, where the subject performs a verbal DL test as the primary task, known to be preferentially processed by the left hemisphere, before and after any mood induction secondary task. The logic points to whether the inducted emotional experience changes the balance between the two hemispheres we could see a correlated consequence in the performance of the primary DL task. In this line, Asbjornsen, Hugdahl, and Bryden (1992) manipulated the subjects' level of arousal under high (shock) versus low (noise) punishment as aversive stimuli in 36 females. They found that the baseline REA lost its significance under the acute stress of electric shock threat for DL errors. The elimination of REA was caused by both an increase in correct LE reports and a drop in correct RE reports, and was explained by arguing a right hemisphere dominance for aversive emotional processing in DL. In another study al'Absi, Hugdahl and Lavallo (2002) applied a mental arithmetic and public speaking stressor to 40 right handed male, and divided the sample between low and high cortisol responders to the stressor, measuring their performance in a DL test after the stressor. Cortisol is a hormone associated to negative affect and depression (Hellhammer, Wüst, & Kudielka, 2009) and so the high responders reported a significant greater negative mood in the Profile of Mood States (POMS) scores after the stressor. When analyzing the DL scores for the free test condition (DL without explicit attentional instructions), the authors found a non-significant higher mean for left ear items in the high cortisol group after the stressor, suggesting again a link between negative affect, as measured by the POMS, and right hemisphere arousal. In a study conducted in our laboratory (Gadea, Gómez, González-Bono, Espert, & Salvador, 2005), we applied the Velten Mood Induction Procedure to generate neutral or negative affect, measured subjectively throughout the PANAS scales, in 44 healthy subjects (half men). Salivary cortisol and a Consonant–Vowel (CV) DL test were taken also pre and post mood induction. For the inducted negative affect condition, the PANAS scores confirmed greater self-reported depressed mood and the activation of the adrenal axis was observed by means of a significant increase in cortisol levels. Finally, the inducted depressed mood produced on DL a significant increase in left ear items and a significant decrease in right ear items, interpreted in line with the hypothesis of right hemisphere dominance for the processing of negative or depressed affect, with a higher right hemisphere arousal from baseline to sadness and an attentional bias toward the left ear. Note that the commented studies manipulated emotions like fear, threat, anxiety, depression, fatigue, or sadness. On the other hand, some other researchers manipulated anger and/or hostility, to observe its consequences on DL, with controversial results. In the study of Demaree and Harrison (1997) fifty subjects were divided into high or low-hostility using a standardized measure of hostility and were submitted to a physical stressor (cold-pressor paradigm). Their hypothesis was that high-hostility subjects will show an increased left ear advantage in the subsequent DL test post stressor than low-hostility subjects, indicating heightened right cerebral arousal. A closer examination of the results for the free DL test condition showed an unexpected higher REA for the whole group after the stressor (which could indicate higher arousal for the left hemisphere), but then a significant interaction with the level of hostility showed in fact a diminished REA, due to higher left ear items, for the group of high-hostility subjects. Thus, this study linked *trait* hostility to higher right hemisphere arousal under a stress and painful situation. The study of Shenal and Harrison (2003)

replicated the latter results in a sample of thirty right-handed male divided into high and low-hostility subjects, with an emotional linguistic cognitive stressor (affective auditory verbal learning test, AAVLT). However, in a more recently study, Mitchell and Harrison (2010) found a reduction in lateralization of emotion perception and activation of the left hemisphere in response to the cold-pressor pain in high hostile men. It must be noted that, although these experiments took into account the high and low hostility of the participants, they did not use a real method for inducing anger in the laboratory, but a stressor. The work of Engebretson, Sirota, Niaura, Edwards, and Brown (1999) facilitated the experimental study of anger with the development of an anger induction (AI) task similar in format to the Velten Mood Induction Procedure for depression, which involves the reading, recalling and evoking a series of descriptors of anger experience. In our laboratory we recently accomplished an experiment applying this AI method to induce an emotional state of anger in 30 right-handed men (Herrero, Gadea, Rodríguez-Alarcón, Espert, & Salvador, 2010). In a pre and post-anger induction design, the PANAS scales and the anger-hostility subscale of the POMS were used to assess self-reported mood, as well as heart rate and systolic (SBP) and diastolic (DBP) blood pressure were measured to assess cardiovascular reactivity to anger, and salivary levels of testosterone (T) and cortisol (c) to assess endocrine changes. Self-reported mood assessment showed that participants felt subjectively angry and, congruent with the hypothesis tested, a significant increase in T levels and a decrease in C levels were seen, as well as the expected pattern of cardiovascular reactivity: increases in HR and DBP (Sinha, Lovallo, & Parsons, 1992). All these measures were confident to indicate an emotional experience of anger in the subjects. The consequence of the anger mood on the DL test with respect to a baseline was an enhanced REA after anger due exclusively to an increase in right ear items, which suggested greater left asymmetrical brain activity. It is noteworthy to comment that from other sources of research (mainly EEG and neuroimage) there has been some support for a preferential relative left anterior cortical activation associated with anger in line with the predictions made by the motivational approach-withdrawal model, although there appears to be at least marginal support for the suggestion that resting right hemisphere asymmetry may be associated with trait anger (for a revision see Cox & Harrison, 2008). Waldstein et al. (2000), after showing anger induction associated with bilateral frontal EEG activation, suggested that anger can produce either approach or withdrawal behavior and that production may be related to an individual's preferred mode of anger expression. In any case the scarcity of studies limits conclusions but encourages carrying on with new experiments.

#### 4. When negative affects reach the limit of illness: dichotic listening and depression

The relationship between lateralization and negative affect experience in healthy subjects raises the question about what this could imply for the issue of affective illness. A recent revision (Hescht, 2010) states, based in a broad number of EEG recording, neuroimaging, neurochemical, and even neuroendocrine data, that clinical depression is associated with an inter-hemispheric imbalance: a physiologically hyperactive right-hemisphere together with a relative hypoactive left-hemisphere, remaining elusive the underlying mechanisms responsible for that imbalance. As a part of this field, there has been a growing interest in a putative perceptual asymmetry dysfunction as measured with DL in depressed patients. In a large series of experiments, Bruder and coworkers have found that melancholic depressed patients, especially if they were women and had no comorbid anxiety, exhibited an abnormally larger REA in verbal DL tasks which was predictive of therapeutic

response to the SSRI fluoxetine compared to *both* the scores of non-responder patients (whose REA diminished) and normal controls (Bruder, Schneier, Stewart, McGrath, & Quitkin, 2004a; Bruder, Wexler, Stewart, Price, & Quitkin, 1999; Bruder et al., 1996, 2001). There was no change in perceptual asymmetries following pharmacologic treatment, which suggests that these laterality differences between fluoxetine responders and nonresponders represent stable, state-independent characteristics (Bruder, 2003). Interestingly, this large REA was also exhibited by those patients who responded subsequently to bupropion therapy (Bruder, Stewart, Schaller, & McGrath, 2007), suggesting that their left hemisphere advantage for dichotic words was not enough to respond to fluoxetine, but was enough to respond to bupropion. Since fluoxetine covers mainly serotonin and bupropion covers mainly dopamine, one possible explanation for these findings is that neurotransmitter systems affected by each antidepressant may be asymmetrically disturbed in treatment responsive or nonresponsive subtypes of depression. Moreover, an enhanced REA for dichotic consonant vowels has been showed also among imipramine responders compared with nonresponders, placebo responders and controls (Stewart, Quitkin, McGrath, & Bruder, 1999). Other authors have reported additional data such as the enhanced REA was associated with higher basal cortisol levels in depressed outpatients (Otto, Fava, Rosenbaum, & Murphy, 1991) or that the increased REA was also found in depressed adolescents (Pine et al., 2000). Otherwise, it is important to note that there are studies that have not found such differences in depressed patients (Moscovitch, Strauss, & Olds, 1981; Wale & Carr, 1990) even when testing comparable samples (Hugdahl et al., 2003). On the other hand, there is evidence that more anxious syndromes may be associated with the opposite pattern of advantage, since patients with an early-onset atypical depression (Stewart, Bruder, McGrath, & Quitkin, 2003) or suffering from social phobia with or without a comorbid depressive disorder (Bruder, Stewart, McGrath, Deliyannides, & Quitkin, 2004b) have shown a diminished REA in verbal DL tests, thus resembling more to non-responders depressed patients. The observation of a larger REA related to responsiveness to antidepressants is valuable as a clinical marker for identifying the patients who will most benefit from pharmacologic treatment but regarding its explanation in terms of brain function it seems to be in conflict (apparently) with physiological data. Rotenberg (2008) has proposed a model to integrate the findings in which the right frontal lobe region is physiologically hyperactivated in depression along with being functionally hypoactive and insufficient. Some patients would display a compensatory overactivation of the left hemisphere functions that corresponds with a positive response to antidepressant treatment (reflected in larger REA). At the same time, non-responders would display an inappropriate attempt to compensate the right hemisphere deficiency by increasing (more) the right hemisphere irrelevant overactivation (reflected in diminished REA). As a psychological level, and according to Rotenberg (2004, 2008), the left hemisphere activation would be responsible for the goal-oriented behavior that includes search activity as a state opposite to depression (that would represent a state of renunciation of search), accounting for a remission of the depressive relapse, but representing a palliative solution because the core reason for depression would be the inability of the right hemisphere to correspond to the demands of the polydimensional context. This proposal is interesting and resembles to other more cognitive explanations of depression that point to the elaboration of negative schemas (by the right hemisphere) along with the decreased (left hemisphere) ability to monitor the feelings they generate, with the remission achieved by normalization of monitoring processes despite remaining the negative schemas (Sheppard & Teasdale, 2004). Thus, the atypical pattern of lateralization seen in non-responders more likely reflects stable trait differences in



the sense of their biological vulnerability to depression due to abnormalities of the right hemisphere. In the case of responders the mobilization of the available left hemisphere resources would indicate a remission of the episode but would not assure the absence of new relapses. Anyway, some questions stay unsolved such as why the spectrum of anxiety disorders including social phobia is associated with decreased REA, or why some depressed patients can manage with left hemisphere resources and others do not. An additional problem is that the majority of the cited studies offer their results as an index of perceptual asymmetry combined from the raw scores of right and left ears, making obscure the link between peripheral responses (ears) and central activation (hemispheres) responsible for them (e.g. an increased REA could be the result of higher right ear or lesser left ear scores or both effects) so limiting the inferences.

## 5. Conclusions

Taken as a whole, the reviewed DL data suggest the following conclusions: (a) the right hemisphere has a relative advantage in the perception of sad prosody and in the processing of negative affect, especially when the affect involves avoidance motivation (e.g. fear), (b) angry prosody, as well as anger experience, are processed more bilaterally or even in the left hemisphere depending on the subject's response in terms of withdrawal or approaching tendencies, (c) DL tests could be routinely used to identify depressed patients who will respond to pharmacological treatment, and (d) a clinical depression is characterized by a functional and physiological imbalance between the hemispheres that needs further investigation.

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