Hemispheric Laterality and Memory Bias for Threat in Anxiety Disorders

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The authors examined auditory perceptual asymmetries and explicit memory biases for threat in patients with panic disorder and generalized anxiety disorder relative to healthy control subjects. They did not find a greater explicit memory bias for threat in the anxiety patients. However, explicit memory biases for threat were associated with perceptual asymmetry scores; patients with a greater right-ear (left hemisphere) advantage exhibited an explicit memory bias for threat material, whereas patients with a lower right-ear advantage displayed apparent cognitive avoidance of threat material. Memory for threat words was unrelated to perceptual asymmetry in healthy control subjects. These findings suggest that neuropsychological variables may partly determine the degree to which anxiety patients process threatening stimuli.

To elucidate cognitive disturbance in anxiety disorders, psychopathologists have tested whether anxiety patients are characterized by biases for threatening information in explicit (direct) memory tests such as cued recall, free recall, and recognition. Studies of patients with generalized anxiety disorder (GAD) have failed to document an explicit memory bias for threat-related words in free or cued recall paradigms (e.g., Mathews, Mogg, May, & Eysenck, 1989; Mogg & Mathews, 1990). In contrast, panic disorder patients exhibited an explicit memory bias for threat in two studies (Cloitre & Liebowitz, 1991; McNally, Foa, & Donnell, 1989). Accordingly, explicit memory bias for threat may be confined to panic disorder (McNally, 1990). The inconsistent pattern of results, however, makes firm conclusions premature and raises the possibility that other factors may modulate explicit memory biases.

A relatively recent approach to understanding individual differences in susceptibility to negative emotion has been the examination of relative hemispheric activation. Studies in both infants and adults have found that negative affect and depression are associated with relatively greater right hemisphere activation, particularly in the right frontal lobe (Davidson, 1984; Otto, Yeo, & Dougher, 1987; Tucker, 1981). Davidson (1984) has hypothesized that the left frontal lobe is relatively more specialized for approach functions, whereas the right frontal lobe is relatively specialized for withdrawal. The apparent link between hemispheric activation and behavioral withdrawal is illustrated by a study of behaviorally inhibited children who respond warily to novel stimuli; in three-year-old children the trait of behavioral inhibition was associated with decreased left frontal activation (Davidson, 1992). Behavioral inhibition in children is also associated with the development of childhood-onset anxiety disorders (Biederman et al., 1993). Hence, hemispheric laterality may be an important variable for understanding individual differences in processing negative affective stimuli, including threat stimuli in samples of anxious patients.

To investigate further the association between hemispheric laterality and approach and avoidance to threat stimuli, we used a dichotic listening procedure to assess hemispheric processing biases (perceptual asymmetry; PA) for a verbal task, and we assessed explicit memory bias for threat in patients with GAD and panic disorder relative to healthy control subjects. We predicted that panic patients would exhibit explicit memory biases for general-threat and, especially, panic-threat words relative to GAD patients and normal control subjects. As individual differences in PA have been associated with anxiety (Tucker, Antes, Stenslie, & Barnhardt, 1978) and with diagnostic and personality subtypes (e.g., Bruder et al., 1989; Wexler, Schwarz, Warrenburg, Servis, & Tarlatzis, 1986) as well as treatment outcome in depressed patients (Bruder et al., 1990; Otto, Fava, Rosenbaum, & Murphy, 1991), we hypothesized that PA scores may play an important role in influencing responses to threat stimuli, including memory bias for threat. We also hypothesized that anxious patients would demonstrate a greater left-ear PA relative to control subjects.

Method

Subjects

Subjects were 12 outpatients (7 of whom were women) with a primary diagnosis of panic disorder (mean age = 35.4 years; SD = 10.6), 12 outpatients (5 of whom were female) with a primary diagnosis of GAD (mean age = 40.6 years; SD = 8.1), and 12 control subjects (5 of whom were women) with no history of psychiatric illness (mean age = 33.3 years; SD = 9.5). All subjects underwent a Structured Clinical Interview for DSM-III-R (SCID-UP-R; Spitzer, Williams, Gibbon, & First, 1988) administered by an experienced clinician. Control subjects were volun-

teers who responded to a newspaper advertisement. Two subjects in the GAD group were left-handed; all other subjects were right-handed.[1] All subjects provided informed consent and received monetary compensation for their participation.

Materials and Procedures

Dichotic listening task. All subjects passed a hearing test that required them to identify sounds at 35 decibels or lower and to have less than a 20 decibel difference in hearing acuity between the left and right ears. Auditory PA was assessed with a dichotic listening task that involved fused, rhymed words as stimuli: 15 single-syllable word pairs differing only in the first consonant (e.g., *bar* and *car*). These stimuli were copies of natural speech recordings with the initial consonant spliced onto the vowel–consonant (Wexler & Halwes, 1983). Word pairs were delivered simultaneously over a Nakamichi (CR-2A) stereo cassette player on matched Telephonics (296D) headphones, one word to each ear. The word pairs fuse into a single percept, and subjects were asked to indicate the word they heard on a response sheet. Subjects were administered initial training blocks prior to four blocks of 30 trials, with word pairs counterbalanced for channel presentation. The headphones were reversed after the first and third blocks. Scores for each ear represent the number of times a word presented to that ear was identified. PA was assessed by a laterality index score, $(R - L)/(R + L) \times 100$. Positive scores indicate a right-ear bias. Subjects completed the dichotic listening task prior to the memory task.

Explicit memory task. There were 24 panic words (e.g., *suffocate*), 24 general threat words (e.g., *cancer*), 24 positive words (e.g., *creative*), and 24 neutral words (e.g., *carpet*), each having a unique three-letter stem within the study. The words were taken from previous information-processing studies on anxiety disorders (e.g., Mathews et al., 1989; McNally, Riemann, Louro, Lukach, & Kim, 1992). The word types did not differ significantly in terms of mean frequency-of-usage (Francis & Kuçera, 1982). We constructed three word sets (A, B, and C), each comprising eight words from each of the four word types. The word sets did not differ significantly in terms of frequency of usage. Each word was typed onto a 14 × 18 cm card.

Using the three parallel word sets, we prepared three versions of each memory test. Each version of the cued recall test consisted of the three-letter stems from one set of words (i.e., A, B, or C). The typed stems appeared randomly on a response sheet, but no more than two consecutive stems were of the same word type.

For the encoding task, subjects viewed a series of words consisting of all items from two sets (i.e., AB, AC, or BC). We counterbalanced sets across subjects within each group, presented words in a single random sequence, and randomly started subjects at different points within the sequence to counteract any primacy or recency effects (Mathews et al., 1989). The experimenter presented each word to the subject for 8 s, and the subject rated the word in terms of its personal emotional significance on a 7-point scale that ranged from −3 (*very negative*) to +3 (*very positive*). Subjects performed emotionality ratings on six neutral practice words before rating the 64 experimental words.

Following the encoding task, subjects performed a 5-min filler task. Describing it as the "first memory task," the experimenter asked subjects to write down the names of as many foreign countries and states in the United States as they could remember. After the filler task, subjects performed the cued recall test.[2] The experimenter handed each subject a sheet containing columns of three-letter word stems and stated that all stems could be completed with a word from the emotionality rating task. Subjects had 5 min to complete the stems in the order in which they appeared on the sheet.

Results

For each word type, we submitted the number of words recalled to a 3 (group) × 4 (word type) analysis of variance

Table 1
Cued Recall Scores as a Function of Word Type and Group

Group	Word type							
	Neutral		Positive		General-threat		Panic-threat	
	M	SD	M	SD	M	SD	M	SD
Panic	2.17	1.85	2.58	1.44	3.17	1.47	4.00	1.54
GAD	2.25	1.66	2.58	1.24	3.67	2.57	2.17	1.12
Control	1.75	1.60	3.25	1.71	3.75	1.66	3.67	1.37

Note. GAD = generalized anxiety disorder. Possible range of scores = 0 to 8.

(ANOVA). We found a significant effect for word type, $F(3, 99) = 6.79, p < .0003$, a marginally significant Group × Word Type interaction, $F(6, 99) = 1.93, p < .08$, but no effect of group (see Table 1). Newman-Keuls analyses revealed that all groups recalled panic–threat, general-threat, and positive words better than neutral words ($ps < .05$). These findings are inconsistent with the hypothesis that a recall bias for threat is uniquely associated with anxiety disorders; all groups exhibited superior recall for emotional material in general.

Auditory PA scores ranged between −9.7 and +63.2, with a grand mean score of 25.5. Greater positive scores represent a stronger right ear (left hemisphere) bias. A one-way ANOVA revealed no laterality differences among groups. Subjects with panic disorder had a mean score of 27.3 ($SD = 14.1$), subjects with GAD had a mean score of 24.5 ($SD = 24.8$), and control subjects had a mean score of 24.8 ($SD = 22.2$).

To investigate whether individual differences in hemispheric activation as assessed by auditory PA scores influence recall biases for threat stimuli, we used two measures of memory bias: the difference between memory for general-threat and neutral stimuli, and between panic-threat and neutral stimuli.[3] We ap-

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[1] Deletion of the 2 left-handed subjects did not alter the significance of the regression equations.

[2] Using the methods of Mathews et al. (1989), we used an implicit (indirect) memory test (stem completion) in counterbalanced order with the explicit cued recall test. Preliminary analyses revealed no effect of test order on memory performance. Also, we found no evidence of differential implicit memory performance as a function of word type or group. Moreover, none of the regression equations were significant for the dependent variables from the implicit memory task. Space considerations preclude discussion of these nonsignificant findings.

[3] Examination of memory biases for general- and panic-threat stimuli relative to positive stimuli were also completed and revealed significant associations between perceptual asymmetry and memory bias measures. A greater right-ear advantage was associated with a greater bias toward the threat and panic stimuli relative to positive stimuli. The overall regression equation was significant ($R = .56, p < .05$) and accounted for 31% of the variance in general-threat relative to positive words. The main effect for the perceptual asymmetry scores was the only significant, individual contributor to this equation ($t[1, 30] = 2.74, p < .01$). Similarly, the overall regression equation accounted for 30% of the variance in panic-threat relative to positive words ($R = .55, p < .05$). The perceptual asymmetry variable was the only individual contributor to this equation ($t[1, 30] = 2.04, p < .05$), although the interaction term approached significance ($p < .09$). Examination of memory biases for positive stimuli relative to neutral stimuli revealed no significant effects
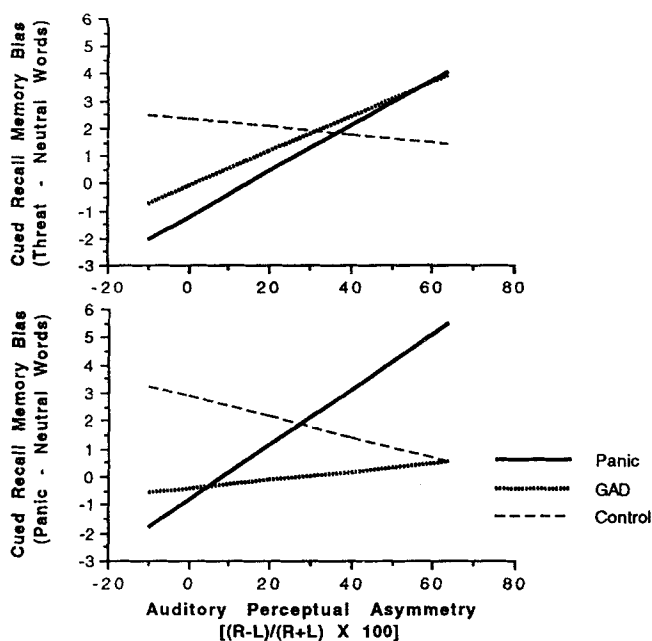
Figure 1. Relationship between cued recall memory bias for general-threat versus neutral words and panic-threat versus neutral words relative to perceptual asymmetries for each patient group. GAD = generalized anxiety disorder; R = right; L = left.

plied multiple regression techniques to examine the predictive significance of PA scores, group membership, and the interaction between PA scores and group membership. The effect of group membership was represented in the regression equation by two orthogonal contrast codes: one representing the difference between the patient groups and the control group (Contrast 1), and the other representing the difference between the GAD and panic disorder groups (Contrast 2). The interaction term between diagnostic group and PA was represented as the separate products of Contrast 1 and Contrast 2 with the PA scores. Significance was evaluated for the full multiple regression equation, followed by examination of the significance of the beta coefficients for each variable as evaluated by t tests. Results are presented in Figure 1.

For the analysis of general-threat versus neutral stimuli, the overall regression equation was significant ($R = .59$, $p < .02$) and accounted for 35% of the variance in memory bias scores. The interaction term (Contrast 1 by the PA scores; $t[1, 30] = 2.70$, $p < .02$), the main effect for the PA scores ($t[1, 30] = 2.72$, $p < .02$), and the main effect for Contrast 1 (patients vs. controls; $t[1, 30] = 3.00$, $p < .01$) were each significant contributors to this regression equation.

A similar pattern of results was obtained for the difference between panic-threat and neutral word recall. The overall regression equation was significant ($R = .55$, $p < .05$) and ac-

counted for 31% of the variance in these memory bias scores. The interaction term (Contrast 1 by the PA scores; $t [1, 30] = 2.40$, $p < .05$) and the main effect for Contrast 1 (patients vs. controls; $t[1, 30] = 2.77$, $p < .01$) were each significant contributors. The beta weight for the interaction between Contrast 2 (panic vs. GAD patients) and PA scores approached but did not reach significance ($p < .13$).

Notably, for analyses of both the general- and panic-threat word relative to neutral word recall, group membership (Contrast 1) was a significant predictor only when evaluated in the context of the full regression equation, including the PA scores and the Contrast 1 × PA Score interaction. For both of these dependent variables, analysis of the interaction term revealed a significant positive association between PA scores and memory bias for the anxious subjects, but no such association for the control subjects. For the anxious patients, a greater right-ear advantage was associated with a greater bias toward recall of general-threat and panic-threat words relative to neutral words.

Discussion

In contrast to previous research (Cloitre & Liebowitz, 1991; McNally et al., 1989), we failed to find an explicit memory bias for threat in panic disorder. Several procedural differences between the present and our previous study (McNally et al., 1989) may account for these discrepant findings. In our previous experiment, panic patients displayed an explicit memory bias for anxiety-relevant adjectives on a free recall test, especially after they had undergone an arousal induction. In contrast, the present experiment involved a cued recall test for threat-related nouns and did not involve arousal induction.

Although sample sizes were small, no trends toward mean differences between groups were evident for the PA scores. This result may indicate a genuine absence of between-group differences in PA for verbal stimuli, or it may indicate that altered PA scores in anxious individuals (Tucker et al., 1978) may be dependent on other pathologic or personality characteristics within a diagnostic group, as suggested by studies of patients with major depression (e.g., Bruder et al., 1989).

The absence of between-group differences in PA scores facilitated examination of the association between hemispheric laterality and memory bias for threat. The PA scores alone, and in interactive combination with the group membership, were significant predictors of explicit memory bias for threat. The interactions between PA and diagnostic group reflected the presumed relevance of threat stimuli for anxiety patients. PA scores were associated with the degree of explicit memory biases for general- and panic-threat for the anxious patients but not for the control subjects. In addition, a trend toward a stronger association between PA and memory bias was evident for the panic-threat stimuli for patients with panic disorder. In each case, a greater right-ear advantage was associated with a greater bias toward threat stimuli for the patient groups. At higher PA scores, memory bias for threat was greater in patients than control subjects. Patients with low PA scores demonstrated the opposite effect; memory bias scores for threat were less than those for control subjects.

Mogg, Mathews, and Weinman (1987) hypothesized that attenuated recall of threat material in GAD patients results from cognitive avoidance. Our study suggests that the apparent ten-

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($R = .34$; $p < .58$ for the full regression equation), supporting interpretations of the data in terms of threat stimuli rather than general emotional stimuli.

dency toward cognitive avoidance is associated with a lower right-ear advantage for the dichotic listening task. Previous studies have also suggested links between perceptual field advantages and cognitive style (see Heller, 1993). For example, Wexler et al. (1986) identified students as true low anxious, true high anxious, or repressors on the basis of their scores on an anxiety inventory and a social desirability scale, and assessed perceptual asymmetry with a fused, rhymed-word dichotic listening task. A lower right-ear advantage was found for the repressor group, a finding consistent with the hypothesis of greater cognitive avoidance among individuals with a lower right-ear advantage.

Nonetheless, the interpretation of our findings in terms of cognitive avoidance is speculative. Rather than reflecting cognitive style, our findings may depend on differences in verbal information-processing abilities. Individuals with greater left hemisphere laterality perform better on typical left hemisphere tasks (Banich, Elledge, & Stolar, 1992). Hence, the link between PA and memory bias for threat may reflect differences in verbal information-processing abilities. Individuals with greater left hemisphere lateralization for verbal tasks may differentially process verbal stimuli, especially those having personal emotional relevance. Relevant verbal stimuli (in this case, threat words for the anxious patients) may be extensively elaborated, and therefore be remembered especially well on cued recall tasks.

Regardless of the nature of the association, our findings have important implications for the study of memory and anxiety. Our findings of an interaction between PA scores and diagnostic group suggest that studies enrolling subjects with relatively greater right hemisphere (less left hemisphere) activation should be more likely to find evidence of impaired memory for threat for anxiety patients relative to controls. In contrast, studies enrolling patients with relatively greater left hemisphere activation should reveal memory bias for threat in these patients (see Figure 1).

In summary, this study represents the application of the study of individual differences in PA to a new area: memory bias for threat in the anxiety disorders. We obtained large effect sizes for the predictive value of PA scores alone and in interaction with diagnostic group. Our findings were obtained with relatively small samples of patients and control subjects, and warrant replication. Nonetheless, this study establishes the importance of modulating variables in determining the direction and significance of memory biases for anxiety stimuli.

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