PANIC DISORDER AND RIGHT-HEMISPHERE RELIANCE

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Panic patients \((n = 22)\) and normal controls \((n = 26)\) completed the Preference Test (PT) and a Conjugate Lateral Eye Movements (CLEMs) task as measures of hemisphere reliance. Furthermore, they completed the Spielberger State-Trait Anxiety Inventory (STAI) and the Anxiety Sensitivity Index (ASI) as indices of self-reported anxiety. While panic patients and controls did not differ with regard to the PT, panic patients displayed significantly more left lateral eye movements than controls. Additionally, across both groups, significant positive correlations were found between right-hemisphere activation (as indexed by CLEM scores) and ASI, suggesting that stronger right-hemisphere reliance is related to greater interoceptive fear. Thus, some indications were found for a relative right-hemisphere overactivation in panic disorders.

Keywords: Panic disorder; Right hemisphere; Lateral eye movements; Cognitive styles

Panic disorder is a prevalent psychiatric illness with poor prognosis (Wittchen, 1988). The syndrome is characterized by recurrent, unexpected attacks of intense anxiety in the absence of an external frightening stimulus (DSM-IV; American Psychiatric Association, 1994). Typically, panic patients complain about a number of bodily sensations (e.g., palpitations, dyspnea, paresthesias) that they experience during panic attacks. Several authors have argued that panic attacks

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originate from a cognitive predisposition to interpret bodily arousal symptoms as highly threatening (e.g., Clark, 1986). What is the source of this cognitive misinterpretation?

One could argue that both panic patients and controls have the same amount of bodily sensations, but that panic patients tend to misinterpret them in a catastrophic fashion (Clark, 1986). Alternatively, it is possible that panic patients have a better interoceptive perception than normals (Ehlers, Breuer, Dohn, & Fiegenbaum, 1995). In both cases, it would be interesting to examine whether the right hemisphere plays a special role in panic. Germone to this issue are two separate lines of research. The first line concerns the differential involvement of the two hemispheres in emotions. While the details are still a matter of some debate (see Gainotti, Caltagirone, & Zoccoiotti, 1993), there is growing evidence for the claim that left cortical areas are critically involved in approach behavior and positive affect, while right cortical areas play a special role in avoidance behavior and negative affect (e.g., Davidson, 1992). Accordingly, a relative hypoactivation of the left hemisphere and/or a hyperactivation of the right hemisphere would contribute to anxious feelings.

Following this line of reasoning, several authors have proposed that certain anxiety symptoms may be related to a habitual right-hemisphere overactivation (e.g., Heller, Etienne, & Miller, 1995). Indeed, Merckelbach and colleagues (De Jong, Merckelbach, & Nijman, 1995; Merckelbach, Muris & De Jong, 1990) found evidence to suggest that persons who prefer a right-hemisphere thinking style (e.g. an imaginal and holistic mode of thinking) report more anxiety symptoms than do persons with a left-hemisphere thinking style (i.e., a verbal and analytic thinking mode). Their studies relied on the Preference Test (PT), a paper-and-pencil task that presumably measures hemisphere-linked cognitive styles (Zenhausern, 1978). While this task provides a rather indirect approach to hemisphere processes, there are strong indications that, at least in undergraduate students, PT scores correspond to asymmetries in background EEG activity (Merckelbach, Muris, Pool, & De Jong, 1996).

The second line of research emphasizes individual differences in autonomic self-perception. It is a well-established fact that compared to normal control subjects, panic patients perform superior on autonomic perception tasks (e.g., heartbeat perception; Ehlers et al., 1995).
Interestingly, there are reasons to believe that the right hemisphere is involved in the perception of interoceptive signals. For example, several studies reported that persons with a strong right-hemisphere activation perform better on heartbeat perception tasks than persons with a strong left-hemisphere activation (Katkin, 1985; Weisz, Balazs, Lang, & Adam, 1990). As an index of hemisphere activation, these studies relied on conjugate lateral eye movements (CLEMs), i.e., involuntary left- or right-sided shifts of individuals' gaze that usually occur immediately following the end of a question requiring reflective thought. CLEMs are often interpreted as an index of cerebral hemisphere activation contralateral to the direction of the eye movement (e.g., Kinsbourne, 1972). Moreover, as the direction of such eye movements is fairly consistent for a given individual, predominant lateral eye movements to the left or to the right are thought to reflect habitual contralateral activation of the right or the left hemisphere, respectively. While the validity of CLEMs as an index of hemisphere activation has been challenged by some authors (e.g., Raine, 1991), EEG studies (Newlin, Rohrbaugh, & Varner, 1982) and regional cerebral bloodflow studies (Gur & Reivich, 1980) provide support for the idea that CLEMs represent a useful hemispheric activation measure. With these two lines of research in mind, it seems intuitively plausible to argue that panic disorder is accompanied by a relatively strong reliance on or overactivation of the right hemisphere. A connection between panic disorder and the right hemisphere could evolve in either of two ways. To begin with, there are straightforward differences in cognitive functioning between the two hemispheres. Most researchers agree that the left hemisphere is involved in verbal and analytic processes, whereas the right hemisphere sustains an imaginal and holistic mode of information processing (e.g., Zemhauern, 1978). It has been argued that a left-hemisphere mode of reasoning may inhibit emotional reactions, whereas a right-hemisphere mode of reasoning may intensify emotional reactions (e.g., Tucker & Newman, 1981). By this view, a predominant reliance on right-hemisphere thinking processes could contribute to neurotic complaints such as panic disorder. Secondly, given the special role of the right hemisphere in negative emotions (Davidson, 1992), the initiation of emotional responses (e.g., Wittling & Pfluger, 1990), and the perception of bodily arousal symptoms (Katkin, 1985), one would expect that a chronic
overactivation of the right hemisphere contributes to a heightened sensitivity for interoceptive fear and eventually panic symptoms.

The present study examined the connection between panic disorder on the one hand and hemisphere thinking style and hemisphere activation on the other hand. More specifically, it was tested whether panic patients have a stronger preference for a right-hemisphere mode of thinking (as indexed by the PT) and/or display a stronger right-hemisphere activation (as indexed by CLEM) than normal control subjects.

METHOD

Participants

Twenty-two patients (14 women) who met DSM-IV criteria (APA, 1994) for panic disorder with or without agoraphobia were included. Their mean age was 38.9 (SD = 9.5). Patients were diagnosed by a team of clinicians at the Academic Anxiety Centre Maastricht, using standardized protocols. Five patients had comorbid depression and four others had comorbid dysthymia. Seven patients were on medication, while the other 15 were medication-free. Three patients were left-handed, while 19 patients were right-handed.

Twenty-six healthy control subjects (20 women) were recruited through advertisements in a local newspaper. Their mean age was 38.8 (SD = 15.1). Controls were included after extensive screening on psychiatric morbidity and substance abuse. Six control subjects were left-handed, while 20 were right-handed. Control subjects were paid for their participation in the current study. A chi-square test for gender (\(\chi^2 = 1.0; N = 48; p = .31\)) and a Fisher's Exact test for handedness (\(p = .48;\) two-tailed) revealed no significant differences between patients and controls. Also, the groups did not differ with respect to age [\(t(46) < 1.0\)].

Assessment

All subjects were tested individually. The following instruments were used: the Preference Test (PT; Zenhausern, 1981), the Conjugate
Lateral Eye Movements test (CLEM-test; De Jong, Merckelbach, & Muris, 1990), the State-Trait-Anxiety Inventory (STAI; Spielberger, Gorsuch, & Lushene, 1970), and the Anxiety Sensitivity Index (ASI; Peterson & Reiss, 1987). Assessment took place in a silent and stimulus poor room. The PT is a 20-item self-rating scale which asks the subject to indicate to what extent they prefer an analytical, verbal versus an intuitive, non-verbal style of reasoning. Ten items presumably address a left-hemisphere mode of thinking (e.g., “How good is your ability to think of synonyms for words?”) and 10 items presumably address a right-hemisphere mode of thinking (e.g., “Do you like using symbols and/or images in solving problems?”). Items are rated on 10-point scales (ranging from 0 = not at all/never to 10 = very much/always). To obtain a total PT score, the mean score on the right-hemisphere items is subtracted from the mean score on the left-hemisphere items. Consequently, a positive difference score reflects a relative preference for a left-hemisphere mode of thinking, whereas a negative difference score reflects a relative preference for a right-hemisphere mode of thinking. The PT has good test-retest stability and internal consistency, and previous studies have found that PT scores are related to EEG measures of hemisphericity (e.g., Merckelbach et al., 1996). The CLEM test (De Jong et al., 1990) is a 20-item task based on the phenomenon of CLEMs. The task consists of ten verbal and ten spatial questions, designed to elicit lateral eye movements. The questions are posed by an interviewer facing the subject. Immediately after each question, the experimenter records the direction of the first gaze shift as either “left” (CLEML), “right” (CLEMR) or “not scorable”. The total CLEM score is calculated as follows: CLEM = CLEML/(CLEML + CLEM). Consequently, CLEM scores range between 0 (of all scorable eye movements, none was leftward) to 1 (all scorable eye movements were leftward). There are indications that CLEMs reflect contralateral activation (Newlin et al., 1982). Thus, the higher the total CLEM score, the stronger a subject’s right-hemisphere activation.

The STAI (Spielberger et al., 1970) is a widely used paper-and-pencil questionnaire with good psychometric properties. It contains two subscales: one that measures state anxiety (e.g., “I am nervous”; STAI-state) and another measuring trait anxiety (e.g., “I am a quiet person”; STAI-trait). The range of the subscale scores is 20–80, with
higher values indicating more anxiety. The ASI (Peterson & Reiss, 1987) is a 16-item self-report instrument that measures fear of anxiety sensations. Subjects indicate on five-point scales to what extent they are concerned with the possible aversive consequences of anxiety symptoms (e.g., “When I notice that my stomach is upset, I worry that I might be seriously ill”). Total scores range from 16 to 80, with higher scores indicating higher fear of anxiety symptoms. The ASI has acceptable test-retest stability and has good construct validity (e.g., Donnell & McNally, 1990). For example, persons with high ASI-scores are very sensitive to panic induction procedures (Rapee & Medoro, 1992).

Tests were administered in the following order: CLEM, PT, ASI, and STAI. Panic patients were tested before or during the early phase of their treatment.

Data Analyses

Due to a procedural error, the ASI data of six panic patients and the STAI-trait data of three patients were unusable. Employing separate t tests, group differences in PT, CLEMs, STAI, and ASI were evaluated. For PT and CLEMs, a set of follow-up t tests were carried out to control for the influence of potential confounding factors. In these follow-up t tests, patients with comorbid depression, patients with medication or left-handed subjects were excluded from the analyses. Additionally, for the whole sample (i.e., patients and controls with complete data records; n = 42), Pearson product-moment correlations were calculated between anxiety indices (ASI; STAI) and hemisphericity measures (PT; CLEM).

RESULTS

Anxiety Measures

Mean STAI, ASI, PT, and CLEM scores of both groups are presented in Table I. As expected, patients scored significantly higher on all anxiety measures than controls: STAI-state t(46) = 10.1, p < .001; STAI-trait, t(43) = 12.3, p < .001; ASI, t(40) = 8.2, p < .001.
TABLE 1  Mean STAI-State, STAI-Trait, ASI, PT, and CLEM Scores of Panic Patients and Normal Controls (Standard Deviations in Parentheses)

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
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<tbody>
<tr>
<td></td>
<td>(n = 22)</td>
<td>(n = 26)</td>
</tr>
<tr>
<td>STAI-state</td>
<td>53.8 (13.4)</td>
<td>25.3 (4.8)</td>
</tr>
<tr>
<td>STAI-trait*</td>
<td>57.2 (11.7)</td>
<td>26.5 (4.6)</td>
</tr>
<tr>
<td>ASI b</td>
<td>43.6 (13.8)</td>
<td>20.0 (4.1)</td>
</tr>
<tr>
<td>PT</td>
<td>0.40 (1.4)</td>
<td>0.63 (1.2)</td>
</tr>
<tr>
<td>CLEM</td>
<td>0.86 (0.15)</td>
<td>0.61 (0.29)</td>
</tr>
</tbody>
</table>

Notes: a Missing data for 3 panic patients. b Missing data for 6 panic patients; STAI = Spielberger State-Trait Anxiety Inventory, ASI = Anxiety Sensitivity Index, PT = Preference Test, CLEM = Conjugate Lateral Eye Movements.

Hemisphericity Measures

Mean PT scores of patients and controls were .40 (SD = 1.4) and .63 (SD = 1.2), respectively. This difference did not attain significance (t[46] < 1.0). Statistical tests were repeated after exclusion of possible confounding factors (comorbid depression, medication, or left-handedness), but again, no significant differences between patients and controls emerged.

Mean CLEM scores of the patients and controls were .86 (SD = .15) and .61 (SD = .29), respectively. This difference was significant (t[46] = 3.7; p < .001). Thus, panic patients displayed more left-sided lateral eye movements (i.e., more right-hemisphere activation) than normal subjects. Follow-up t tests after exclusion of possible confounding factors revealed similar significant differences.

Pearson Correlations

Correlations among the anxiety measures (STAI-state, STAI-trait, and ASI) were all high and significant (all rs > .82, ps < .001). Table II shows correlations between PT, CLEM, STAI, and ASI scores. No significant associations were found between PT, on the one hand, and anxiety measures (STAI-state; STAI-trait; ASI), on the other hand, although correlations were in the right direction and approached borderline significance (all rs > -.23, ps < .07, one-tailed). Furthermore, PT was not associated with CLEM, indicating that
TABLE II  Pearson correlations between anxiety measures (STAI, ASI) and hemisphericity measures (PT, CLEM) for the combined sample (n = 42)

<table>
<thead>
<tr>
<th></th>
<th>CLEM</th>
<th>STAI-state</th>
<th>STAI-trait</th>
<th>ASI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT</td>
<td>.15</td>
<td>-.23</td>
<td>-.24</td>
<td>-.24</td>
</tr>
<tr>
<td>CLEM</td>
<td></td>
<td>.38*</td>
<td>.41*</td>
<td>.38*</td>
</tr>
</tbody>
</table>

Notes. Only relevant correlations are presented. *p < .01. STAI = Spielberger State-Trait Anxiety Inventory, ASI = Anxiety Sensitivity Index, PT = Preference Test, CLEM = Conjugate Lateral Eye Movements.

both measures of hemisphericity were unrelated. However, positive correlations were found between CLEM and STAI-state and between CLEM and STAI-trait. Also, a positive correlation emerged between CLEM and ASI. That is, leftward eye movements (i.e., right-hemisphere activation) were associated with heightened levels of subjective anxiety.

DISCUSSION

The main results of the present study can be summarized as follows. Firstly, no evidence was found to suggest that panic patients and normal controls differ with regard to verbal and analytic versus imaginal and global thinking styles. That is to say, the current PT findings do not support the idea that panic disorder is characterized by a right-hemisphere mode of thinking. Secondly, panic patients and normal controls did differ with regard to CLEMs in that patients exhibited more leftward eye movements compared to normal controls. To the extent that a relative predominance of leftward eye movements reflects right-hemisphere overactivation, this finding supports the idea that panic disorder is characterized by right-hemisphere overreliance. Thirdly, across the whole sample, only marginally significant associations were found between PT defined thinking styles and anxiety measures. Fourthly, CLEMs were correlated with self-reported state anxiety, trait anxiety, and fear of anxiety sensations (ASI).

The present study's failure to find differences between patients and controls in hemisphere-related thinking styles deserves some comment. Earlier studies have found that there is a positive correlation between a right-hemisphere thinking style as indexed by the PT and self-reported
anxiety (e.g., De Jong et al., 1995). Furthermore, recent studies indicate that the PT has good psychometric properties and is correlated with EEG asymmetry profiles (e.g., Merckelbach et al., 1996) However, most of this work is based on undergraduate samples, and it may well be the case that the PT is not a valid and stable index in other samples. Note that for subjects with a limited education, some PT items (e.g., “Do you like using symbols and/or images in solving problems”) might be difficult to understand. The majority of the subjects in the present study had a limited education and this may have undermined the validity of the PT measure. Another explanation for the failure to obtain PT differences between panic patients and normal controls might be that, unlike the CLEM task, the PT taps an aspect of hemisphere asymmetry that is less relevant to panic disorder. The absence of a correlation between PT and CLEM supports such an interpretation. Perhaps, then, not only left–right differences, but also anterior–posterior differences might be important to evaluate the role of hemisphere reliance in panic disorder.

While panic patients and normal subjects did not differ with regard to the PT, there were convincing differences between the two groups with regard to CLEMs. The fact that panic patients exhibited more leftward eye movements than controls suggests that panic patients are characterized by a right-hemisphere overactivation. Assuming that the right hemisphere plays a pivotal role in the perception of interoceptive signals and in the initiation of negative emotions, this finding fits well with panic patients’ superior performance on heartbeat perception tasks (Ehlers et al., 1995). Yet, it should be noted that the present study did not include a psychiatric control group. Consequently, it remains to be seen whether a high frequency of leftward eye movements is specific for panic disorder or is a general characteristic of various psychopathological conditions. Note in passing that there is little reason to suspect a right-hemisphere involvement in all anxiety conditions. For example, Carter, Johnson, and Borkovec (1986) have pointed to the prominent role of the left frontal areas in anxiety states that are characterized by worrying.

The validity of eye movements as an index of hemisphere activation is in dispute. Some authors have claimed that CLEMs do reflect contralateral hemisphere activation (Gur & Reivich, 1980; Newlin et al., 1982). Others have argued that CLEMs may tap transient hemisphere
asymmetries, but not habitual differences in hemisphere overactivation (Raine, 1991). However that may be, the extensive work of Katkin (1985) demonstrates that there is a strong connection between leftward CLEMs and superior performance on heartbeat detection tasks. Note also that there are more direct indications that panic patients show an increased regional cerebral blood flow in the right hemisphere (De Cristofaro, Sessarego, Pupi, Biondi, & Faravelli, 1993). These results as well as the findings of the present study warrant further research. Future studies should preferably employ direct indices of anterior and posterior hemisphere activation (e.g., EEG) in panic patients and should also include psychiatric control samples. This type of study is important because it could elucidate why autonomic perception is a good predictor of relapse and maintenance of panic disorder and panic attacks (Ehlers, 1995).

References


