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CME Objectives

After completing this educational activity, physicians practicing clinical psychiatry should be able to:

- Identify predictors of the development of phobic avoidance.
- Differentiate between panic as a primary event and panic due to exposure to a feared situation in patients with panic attacks.

Statement of Need and Purpose

In patients with panic disorder, the level of phobic anxiety correlates with the duration of illness and age at onset of illness, and patients with phobic avoidance are more disabled than those with panic disorder alone. Physicians responding to surveys published by Physicians Postgraduate Press have requested updated information on the diagnosis and treatment of panic disorder and associated phobias. This CME activity is designed to address these requests. There is no prerequisite for participating in this CME activity.

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Date of Original Release/Review

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Faculty Disclosure

In the spirit of full disclosure and in compliance with all ACCME Essential Areas and Policies, all faculty for this CME activity were asked to complete a full disclosure statement. The information received is as follows:

Dr. Katerndahl is a consultant for and a member of the speaker's bureau for SmithKline Beecham Pharmaceuticals.

Predictors of the Development of Phobic Avoidance

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Background: Panic disorder and agoraphobia are closely linked. There are indications that uncontrolled panic attacks often lead to the rapid development of phobic avoidance, but our ability to predict which individuals with panic will develop avoidance has been limited. The purpose of this study was to identify independent predictors of the development of phobic avoidance and the time course of that development.

Method: We conducted a secondary analysis of survey data from the community-based Panic Attack Care-Seeking Threshold Study. The presence of panic attacks was confirmed in 97 randomly selected adults from randomly selected households screened using the Structured Clinical Interview of DSM-III-R (SCID). The presence of limited and extensive phobic avoidance was measured using the SCID, while rapidity of development (lag time) was measured as the difference between onset of panic and onset of avoidance. Predictors considered included panic characteristics, psychiatric comorbidity, cognitive appraisal, family characteristics, illness attitudes, symptom perceptions, and coping style.

Results: Thirty-six subjects (37%) had at least mild phobic avoidance, with 81% (N = 29) of those developing the avoidance less than 1 year after the onset of panic attacks. The development of phobic avoidance was associated with the presence of panic disorder ($\beta = 1.36$), the number of comorbid psychiatric disorders ($\beta = 0.69$), and the number of family members and/or friends available to discuss health concerns ($\beta = 0.87$). Further progression to agoraphobia was predicted by the presence of depersonalization during panic attacks ($\beta = 0.50$). Rapid onset of avoidance (panic avoidance lag time < 1 year) was predicted by the perception that depersonalization is a life-threatening symptom ($\beta = 1.56$).

Conclusion: The development of phobic avoidance is closely linked to panic attacks and often develops soon after panic onset. Full-blown panic disorder and psychiatric comorbidity are important in this development. Depersonalization is also key to the development of avoidance and the rapidity of the development.

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Since the release of the third edition of the *Diagnostic and Statistical Manual of Mental Disorders*,[1] panic disorder and agoraphobia have been linked conceptually. Studies have supported the panic-agoraphobia relationship,[2] even across countries.[3] The level of phobic anxiety correlates with the duration of panic disorder and the subject's age at panic onset.[4]

Klein[5] proposed that these disorders were linked causally. Although some evidence suggests that avoidance can begin prior to onset of panic attacks,[6–10] the majority of the literature has found that most of those with both panic and agoraphobia report that onset of panic is the primary event.[6,7,11,12] Differentiating panic as a primary event from panic due to exposure to a feared situation is important, and this difficulty may contribute to contradictory findings. The situation in which the first panic attacks occur is an important clue in this differentiation. Even subjects who report the onset of avoidance prior to the onset of panic often state that panic attacks were a precursor to avoidance severe enough to be considered agoraphobia.[10] One study[8] suggests that if avoidance begins prior to panic disorder, the risk for development of agoraphobia is diminished. In 12% to 60% of the cases,[6–8,13] the 2 disorders begin simultaneously or within the same year.

Previous work suggests that between 8%[13] and 32%[7] of subjects developing phobic avoidance after panic attacks do so within days of the onset of panic. The presence of agoraphobia correlates with 1-year[14] and 5-year[15] outcomes, and the development of phobic avoidance has far-reaching implications for persons with panic. Patients with phobic avoidance are more disabled than those with panic disorder alone.[8,16] Their remission is less likely than is remission in patients without agoraphobia.[17] Finally, patients with agoraphobia in conjunction with panic disorder report

high levels of role impairment.[6] Global improvement in these patients correlates with improvement in phobic avoidance, but not with improvement in panic disorder.[18]

Thus, an understanding of the relationship between panic and phobic avoidance is critical to prediction of outcomes and development of interventions. The purpose of this study was to identify predictors of the development of phobic avoidance, its early onset, and its rapidity of onset after panic onset.

METHOD

Sample

This report presents a secondary analysis of survey data from the Panic Attack Care-Seeking Threshold Study.[19,20] This community-based study consisted of in-depth interviews of 97 adults with DSM-III-R panic attacks. Randomly selected individuals from randomly selected households were screened for the presence of panic attacks using the Structured Clinical Interview of the DSM-III-R (SCID).[21] Using methods similar to those of the Epidemiologic Catchment Area study, clusters of 3 households were selected at intervals of 8. The intervals started from a randomly selected intersection within 18 census tracts. Using the Kish method,[22] 1 randomly selected adult (≥ 18 years old) was selected from within each selected household.

Subjects with panic attacks completed an in-depth interview concerning panic characteristics, psychiatric comorbidity, illness attitudes, coping strategies, symptom perceptions, family characteristics, quality of life, and health care utilization. Subjects did not have to meet criteria for panic disorder to be included in the study.

Instruments

Using the panic disorder section of the SCID, subjects were classified as having "extensive phobic avoidance" (agoraphobia), "mild-moderate phobic avoidance," or "no avoidance." This article uses the term *phobic avoidance* to mean agoraphobic-type avoidance of public places or situations in which help may be unavailable. The SCID was also used to identify comorbid simple and social phobias, generalized anxiety disorder, obsessive-compulsive anxiety disorder, and major depressive episodes. The Symptom Checklist-90 (SCL-90)[23] was used to measure the severity of psychiatric symptoms. The severity of panic attacks was assessed using a modified version of the Acute Panic Inventory[24] to describe the panic symptoms experienced during the self-defined worst panic attack. Subjects were also asked what they thought was causing their panic symptoms during the worst attack. This open-ended question was encoded as "dying," "heart attack/stroke," "minor problem," "anxiety/stress," "going crazy," or no explanation.

Illness attitudes and behaviors were measured using the Illness Attitude Scales (IAS),[25] the Illness Behavior Questionnaire (IBQ),[26] the Readiness for Sick Role Index,[27] and the Health Locus of Control.[28] Perceptions were also assessed. Symptom perceptions were measured using 5 Symptom Perception Scales[29] including 12 panic-related symptoms and 12 nonpanic symptoms for each of 5 constructs (severity, embarrassment, threat to life, need for treatment, and disruption to functioning). In addition, perception of panic attacks was assessed using the Appraisal Dimension Scales.[30]

Family characteristics were assessed using the Duke Social Support and Stress Scale,[31] the Family Inventory of Life Events and Changes,[32] and the Family Adaptability and Cohesion Evaluation Scales (third edition).[33] Subjects were also asked about the number of family members and friends with whom they discuss their health. Coping strategies used were measured with the Ways of Coping Checklist.[34]

Analysis

Identification of potential predictors. Potential predictors of phobic avoidance ("agoraphobia," "mild-moderate phobic avoidance," or "no avoidance") were identified through bivariate analyses using chi-square and 1-way analysis of variance testing. Potential predictors were those variables with significant ($p \leq .05$) bivariate analyses. In subjects with at least some phobic avoidance, the age at onset of avoidance was compared with potential predictors using the Student t test and Pearson correlational analysis. The lag time between onset of panic and onset of avoidance was also noted. Because panic and avoidance frequently began during the same year ($N = 29$), lag time was considered not only as number of years, but also as immediate onset (lag time < 1 year) versus delayed onset. Bivariate analyses used with immediate versus delayed onset were the Fisher exact test and the Student t test. Because the lag time in years was skewed, a logarithmic transformation was done prior to testing with 0.01 added to lag times of "0." Bivariate analyses used the Student t test and Pearson correlation analysis with lag time in years.

Regression analysis for phobic avoidance variables. Potential predictor variables were used in regression analysis. Stepwise logistic regression was conducted with the entire sample to identify independent predictors of the presence of any phobic avoidance ("mild-moderate

Table 1. Demographic Description of the Sample[a]

Characteristic	Subjects With Phobic Avoidance (N = 36)	Subjects Without Phobic Avoidance (N = 61)
Gender (female)	29 (81)	47 (77)
Ethnicity		
Hispanic	20 (56)	34 (56)
Non-Hispanic white	12 (33)	17 (28)
African American	4 (11)	10 (16)
Age, mean ± SD, y	38.5 ± 11.0	40.6 ± 16.2
Socioeconomic status,[b] mean ± SD	62.6 ± 18.8	62.4 ± 19.9
Marital status[c]		
Single	11 (31)	15 (25)
Married	15 (42)	32 (53)
Marital loss[d]	10 (28)	13 (22)

[a]All values shown as N (%) unless otherwise specified.
[b]Measured by Hollingshead scale.[35]
[c]Data missing for 1 patient without phobic avoidance.
[d]Divorced, separated, or widowed.

Table 2. Subjects' Explanation for Worst Panic Attack[a]

Explanation	Total	Phobic Avoidance: None[b]	Phobic Avoidance: Mild-Moderate	Phobic Avoidance: Agoraphobia
"Dying"	9 (9)	4 (44)	0 (0)	5 (56)
"Heart attack/stroke"	21 (22)	12 (57)	3 (14)	6 (29)
"Minor problem"	9 (9)	7 (78)	1 (11)	1 (11)
"Anxiety/stress"	30 (31)	21 (70)	5 (17)	4 (13)
"Going crazy"	16 (16)	10 (62)	1 (6)	5 (31)
No explanation	10 (10)	5 (50)	1 (10)	4 (40)

[a]All values shown as N (%). Percentages in the Total column are percentages of the total sample (N = 97); percentages in the Phobic Avoidance columns are percentages of the Ns shown in the Total column.
[b]Data missing for 2 patients in this subgroup.

Table 3. Predictors of Development of Agoraphobia[a]

Predictor	Some Phobic Avoidance (N = 97)	Agoraphobia (N = 36)
Panic disorder	1.36	...
No. of comorbid disorders	0.69	...
No. of family/friends available	0.87	...
Depersonalization during panic	...	0.50

[a]Values shown are beta coefficients.

phobic avoidance" + "agoraphobia"). Using only subjects with some phobic avoidance, stepwise logistic regressions were performed with the presence of agoraphobia and with immediate versus delayed onset. Multiple linear regressions were performed with age at onset of avoidance and lag time (the time between onset of panic and onset of avoidance) in years. Power analysis suggests that there was a power of 62% for detecting a large effect size at the $p \leq .1$ level using subjects with phobic avoidance. Statistical significance was set at $p \leq .1$ because of the exploratory nature of this study.

RESULTS

Table 1 presents the demographic description of the sample, and compares those with and those without phobic avoidance. Fifty-four subjects (56%) were Hispanic. Of the 36 subjects with phobic avoidance, 25 (69%) had agoraphobia. The mean ± SD age at onset of avoidance was 28.5 ± 13.0 years; thus, the mean ± SD duration of avoidance at the time of interview was 10.0 ± 9.4 years. Although the mean ± SD lag time between onset of panic and onset of avoidance was 2.4 ± 7.6 years, 29 subjects (81%) reported that avoidance began during the same year as the panic.

Predictors of Phobic Avoidance

In 2 areas—severity of psychiatric symptoms and depersonalized symptom perception—results suggested a connection to mild-to-moderate phobic avoidance and agoraphobia. In comparing the 25 subjects with agoraphobia with the rest of the sample, there were significant differences for 6 of the 9 SCL-90 scales measuring severity of psychiatric symptoms. Additionally, 3 of the 5 Symptom Perception Scales concerning symptoms of depersonalization reflected significant differences.

The subject's perception of what was causing the panic attack was also a strong indicator of development of phobic avoidance. As reflected in Table 2, of those subjects who interpreted their worst panic attack as a sign of "dying" or "going crazy" or assigned no explanation, 88% (14/16) with any phobic avoidance had agoraphobia. Data also indicated a relationship between subjects who so interpreted the cause of their attacks and 2 factors: the number of family members and/or friends available ("yes," mean = 2.34; "no," mean = 1.52; $t = 1.94$, $p = .061$) and readiness for sick role ("yes," mean = 18.3; "no," mean = 8.9; $t = 4.01$, $p < .001$). In addition, 94% of subjects (10/16) with such an interpretation of the cause of their panic attacks showed depersonalization during attacks, which may explain why cognitive appraisal was not an independent predictor. There was no connection between scores on the Appraisal Dimension Scales and phobic avoidance.

Table 3 presents the results of 2 logistic regressions: (1) predicting any phobic avoidance and (2) predicting agoraphobia. It depicts those factors that independently predict each step in the development of agoraphobia: comorbid psychiatric disorders and the presence of depersonalization during panic attacks. Neither severity of psy-

Table 4. Predictors of Avoidance Characteristics (N = 36)[a]

Predictor	Panic-Avoidance Lag: Immediate Onset (< 1 y)	Panic-Avoidance Lag: Lag Time (≥ 1 y)	Age at Avoidance Onset
Depersonalization is life threatening	1.56	...	...
Panic course			
Duration of panic	...	0.53	...
Age at panic onset	...	...	0.72
Attitudes			
Disease phobia	...	0.30	...
Readiness for sick role	...	...	0.23

[a]Values shown are beta coefficients ($p \leq .05$).

chiatric symptoms nor any of the 5 symptom perception constructs (severity, embarrassment, threat to life, need for treatment, or disruption to functioning) predicted the development of agoraphobia.

One predictor—readiness for sick role—was significant for all 3 remaining phobic avoidance variables. In each case, the more ready the subject was to assume a sick role, the later the onset of avoidance. Furthermore, as illustrated in Table 4, readiness for sick role is also a factor, along with age at onset of panic, in determining the subject's age at onset of avoidance.

Indicators of Lag Time Between Onset of Panic and Onset of Avoidance

The lag time in years was associated with 3 SCL-90 scales. Subjects with no explanation for their worst attack had shorter lag times (explanation, mean = 2.8 years; no explanation, mean = 0.2 years; $t = 1.23$, $p = .09$). Regression analysis found 2 independent predictors: the duration of panic and the degree of disease phobia.

However, dichotomizing lag time into immediate versus delayed onset produced different results. The significant factors on bivariate analyses were symptom perceptions, with 19 of 30 subscales yielding significant differences. This proved especially true for perceptions of embarrassment and need for treatment and for symptoms of depersonalization and fear. Logistic regression found only 1 independent predictor: the perception that depersonalization is life threatening.

DISCUSSION

The most surprising finding was that availability of a support group of family and friends is a predictor of the development of phobic avoidance. While previous reports linked panic and phobic avoidance, this study indicated a close association between the 2 and supports the rapid development of avoidance after onset of panic. While previous reports have discussed the role of depersonalization, this study alone linked progression from mild to extensive avoidance with presence of depersonalization during panic attacks.

Development of Phobic Avoidance

This study supports the close association between panic attacks and phobic avoidance. It further supports the often rapid development of phobic avoidance after the onset of panic attacks. Not only did all subjects with phobic avoidance report its onset as associated with the onset of panic, but the majority reported onset as simultaneous or within the same year as that of the panic attacks. Panic attacks that meet criteria for panic disorder predict development of phobic avoidance. That finding further supports a causal relationship, an association that has been found previously.[8,36] In addition, 2 findings further indicate the rapid development of avoidance after panic onset; age at panic onset predicts age at avoidance onset, and duration of panic predicts lag time in years.

The number of comorbid psychiatric disorders and availability of a support group of family members and/or friends to discuss health problems were also predictors of the development of phobic avoidance. Psychiatric comorbidity, especially depression, has been found previously to be a predictor of agoraphobia,[2,6,8,16,37–40] but the availability of family and friends to discuss health problems has not been examined previously. This finding suggests 2 relationships to avoidance: that people with more personal support develop avoidance because more personal support enables avoidance or that family and friends contribute to a catastrophic interpretation. Previous work has found that cognitions and concerns are important to the development of agoraphobia.[38,39,41]

Other predictors of avoidance have been studied. The role of fear during panic attacks is controversial.[42,43] Although some studies have found that age at panic onset,[8,16] panic duration,[16,43] and panic symptomatology[10,38,44,45] are important in the development of phobic avoidance, not every study agrees on the importance of panic characteristics.[39] Previous work has reported that hypochondriasis,[38] interpersonal sensitivity,[13] and gender[2,13,38] are also predictors; this study, however, did not find these variables to be predictors.

The roles of cognitions, interpersonal sensitivity, and availability of family and friends in the onset of phobic avoidance may be intermingled. Fears of collapse (54%), death (33%), and causing a scene (32%) during panic attacks are common in people with agoraphobia.[46] Because

people with panic disorder are interpersonally sensitive and have the dependent personality typical of agoraphobics,[47] the availability of family and friends and their opinions about health concerns might be important to those developing phobic avoidance. The importance of family and friends to agoraphobics is evident; they report that being with their spouse (85%), being with friends (60%), and talking about problems with friends (62%) often make them feel better. Conversely, 87% of people with agoraphobia report that domestic stress and arguments make their agoraphobia worse.[46] This indication of reliance upon others, coupled with psychiatric comorbidity, makes agoraphobics vulnerable to catastrophic interpretations made by others and themselves. Such catastrophic cognitions in this population are not short-lived; 40% retain strong convictions in these cognitions. Fears about mental and social dangers are retained longer than those about physical dangers.[48] Hence, these individuals are particularly vulnerable to the development of phobic avoidance.

We found that the progression from mild to extensive avoidance (agoraphobia) was solely dependent upon the presence of depersonalization during panic attacks. In addition, the perception that depersonalization is life threatening was the sole predictor of rapid development of avoidance. The identification of depersonalization as a predictor of the development of agoraphobia is not new,[44,49] and depersonalization is associated with anticipatory anxiety.[10] Depersonalization may contribute to the fear of losing control (14%) or becoming mentally ill (13%).[46]

In terms of the subject's age at onset of avoidance, 2 predictors—age at onset of panic and readiness for sick role—were identified in this study. This relationship with age at panic onset emphasizes the close relationship between panic onset and avoidance onset. Again, the relationship with readiness for sick role may attest to the importance of cognitions. People who are amenable to being ill are less vulnerable to the onset of avoidance because they may more readily accept the catastrophic implications of their panic attacks. This interpretation is supported by the relationship between avoidance onset, cognitive appraisal of the first panic attack,[12] and a high degree of neuroticism.[50]

Those people who develop phobic avoidance often do so rapidly after onset of panic. This tendency may be related to subjects' frequent statements that the first month after panic onset is the worst.[36] In this study, the panic-avoidance lag time was predicted by duration of panic disorder and the severity of disease phobia. Again, the link to the duration of panic disorder emphasizes the link between panic onset and avoidance onset. Disease phobia may result in resistance to avoiding activities; thus, these people force themselves to continue exposure to anxiety-provoking situations, delaying onset of avoidance. The only previous study of predictors of lag time found that severity of panic attacks, panic symptomatology, and the presence of depression predicted a shorter lag time.[45]

Limitations

This study has several limitations. The sample size limitation compromised the statistical power in analyses. Numerous bivariate analyses were performed, which would inflate the experimentwise alpha level. However, these were performed only as a way of reducing the number of independent variables used in regression analyses. The only bivariate analyses involved cognitive appraisal and were used to help in the interpretation of the regression results. In addition, many of the instruments used have not been validated in studies of Hispanic subjects.

As with any study, the representativeness of the sample is also a concern. Although our probability sample took race into account, the sample was not representative of San Antonio in terms of ethnicity. Even so, the sample statistics in this study are consistent with those in the literature, suggesting that these findings are generalizable. A previous community study found that 21% of subjects with panic attacks had agoraphobia[36] as opposed to 25% in this study. The sample in this study was 81% female (63%–90% in the literature[46]), reported a mean age at avoidance onset of 28.5 years (19–32 years in the literature[6,10,46]), and reported a mean panic-avoidance lag time of 2.4 years (1.9 years in the literature[10]). Thus, sample statistics in this study are consistent with those in the literature, suggesting that these findings are generalizable.

CONCLUSION

Our findings confirm the close link between panic attacks and agoraphobia, further suggesting that panic attacks lead to phobic avoidance, often rapidly. The availability of friends and family to discuss health problems, readiness for sick role, and depersonalization were important predictors of phobic avoidance.

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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1. Which of the following is *not* true about panic due to exposure to a feared situation?
a. The situation in which the first panic attack occurred is important.
b. Even when avoidance occurs prior to the onset of panic, panic still precedes full-blown agoraphobia.
c. Panic and avoidance often begin simultaneously.
d. If avoidance begins prior to panic, the risk of agoraphobia is greater.

2. The development of agoraphobia is important in panic disorder for all of the following reasons *except*:
a. Global improvement correlates more with improvement in avoidance than in panic.
b. Those with phobic avoidance are less disabled than those with panic disorder alone.
c. Presence of agoraphobia correlates with one- and five-year outcomes.
d. Remission is less likely in patients with agoraphobia.

3. People with agoraphobia are less likely to believe that their worst panic attack indicates:
a. A minor health problem
b. That they are dying
c. That they are going crazy
d. That there is no explanation for the attack

4. Independent predictors of the transition between no avoidance to mild-moderate avoidance include which of the following?
a. Limited symptom attacks
b. The availability of family and friends to discuss health concerns
c. The presence of dysthymia
d. The severity of panic symptoms

5. Evidence of a close temporal panic-agoraphobia relationship includes all of the following *except*:
a. Association between duration of panic disorder and lag time between panic and avoidance onsets
b. Association between ages at onset of panic and avoidance
c. Both disorders begin in young adulthood
d. Both disorders often begin within the same year

6. Previous work failed to find the following as predictors of phobic avoidance:
a. Gender
b. Interpersonal sensitivity
c. Coping process
d. Hypochondriasis

7. A possible reason that the availability of family and friends is a predictor in the development of avoidance is that:
a. Family members may increase the patients' level of stress.
b. Family and friends may reinforce the belief that the patient is having a stroke.
c. The presence of friends often makes the patient feel worse.
d. Family and friends may support avoidant behavior.

Answers to the February 2000 CME posttest

1. b 2. a 3. c 4. a 5. d 6. c 7. b

Circle the one correct answer for each question.

1.	a	b	c	d
2.	a	b	c	d
3.	a	b	c	d
4.	a	b	c	d
5.	a	b	c	d
6.	a	b	c	d
7.	a	b	c	d

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1. Was the educational content relevant to the stated educational objectives? ❑ Yes ❑ No
2. Did this activity provide information that is useful in your clinical practice? ❑ Yes ❑ No
3. Was the format of this activity appropriate for the content being presented? ❑ Yes ❑ No
4. Did the method of presentation hold your interest and make the material easy to understand? ❑ Yes ❑ No
5. Achievement of educational objectives:
   A. Enabled me to identify predictors of the development of phobic avoidance. ❑ Yes ❑ No
   B. Enabled me to differentiate between panic as a primary event and panic due to exposure to a feared situation in patients with panic attacks. ❑ Yes ❑ No
6. Did this CME activity provide a balanced, scientifically rigorous presentation of therapeutic options related to the topic, without commercial bias? ❑ Yes ❑ No
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