



Longitudinal course of panic disorder with and without agoraphobia using the national epidemiologic survey on alcohol and related conditions (NESARC)



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ABSTRACT

Few naturalistic, longitudinal studies of panic disorder with and without agoraphobia (PD/PDA) exist, limiting our knowledge of the temporal rates of incidence, relapse, and chronicity, or the factors that predict category transition. Data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) wave 1 ($n=43,093$) and wave 2 ($n=34,653$) were utilized to determine transitional rates, and predictors of category transitions, over a 3-year period. Analyses revealed very high 3-year remission rates for PD and PDA (75% and 67%, respectively), although relapse also was relatively frequent (PD=12%; PDA=21%). Logistic regression revealed previous history of panic attacks, generalized anxiety disorder/major depression (GAD/MDD), nicotine dependence, female sex, younger age, and major financial crises to be reliable predictors of incidence and relapse. The direction and magnitude of association of many predictor variables were similar for PD and PDA, with notable exceptions for social anxiety and romantic relationship factors. Clinicians should be aware of the relapsing–remitting nature of PD and PDA and, thus, take caution to not reduce or eliminate effective treatments prematurely. Similarly, the current study suggests clinicians pay particular attention to concurrent factors relevant to relapse in PD/PDA that may also be clinically addressed (e.g., co-morbid MDD/GAD and nicotine dependence).

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1. Introduction

Panic disorder (PD) and panic disorder with agoraphobia (PDA) are anxiety disorders of moderately high lifetime prevalence in the general population (1–2% 1-year prevalence rates, American Psychiatric Association, 2000; Grant et al., 2006; lifetime prevalence of 4.8%, Kessler et al., 2006). The scientific basis for the understanding of PD, PDA, and the phenomena of agoraphobia has evolved significantly over many years, as is reflected in DSM revisions. At present, there are few prospective, naturalistic follow-up studies of the course of PD and PDA that apply the most recent diagnostic criteria (DSM-IV/DSM-IV-TR; APA, 1994, 2000). Such studies have substantial scientific and clinical value as they reveal the natural course of this syndrome with respect to incidence, remission, relapse, chronicity, and severity.

Several studies examining the temporal course of PD/PDA exist, however these studies are arguably limited in their generalizability due to a number of methodological shortcomings. These methodological issues include use of outdated diagnostic nomenclature and

older assessment devices, lack of direct comparisons between PD and PDA, reliance on relatively small sample sizes, reliance on exclusively treatment-seeking clinical samples, and/or limited evidence or report of diagnostic reliability (Andersch and Hetta, 2003; Faravalli et al., 1995; Swoboda et al., 2003). Although the methodological limitations of these studies raise caution in interpretation, they generally indicate that most patients improve over time in terms of symptomatic functioning and ability to cope and function, though few patients reach complete recovery (e.g., 18% meet recovery criteria over 15 year follow-up in Andersch and Hetta, 2003; 12% in 12–60 month follow-up, Faravalli et al., 1995; and 33% over 11 years, Swoboda et al., 2003). When significant improvement was observed, it generally occurred within the first 2 years after initially seeking treatment (Andersch and Hetta, 2003; Faravalli et al., 1995). In each study, few individuals continued to meet full diagnostic status on follow up (18% at 15 year follow up, Andersch and Hetta, 2003; 12.5% on 11 year follow up, Swoboda et al., 2003), and functional impairment was lessened over the follow-up period. The meaning of this temporal improvement, however, is difficult to discern given most patients in these studies had continual or episodic medication management and/or psychotherapy over the course of follow-up. These outcomes suggest PD/PDA patients experienced fairly chronic need for symptomatic management.

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A 12-year follow-up report of the Harvard/Brown Anxiety Disorders Program (HARP) study, a study of treatment-seeking individuals, presents data differentially for PD and PDA (Bruce et al., 2005). The results of this study revealed a relatively low cumulative 0.48 probability of remission for PDA over this long time course (Bruce et al., 2005). This estimate contrasts with a relatively high cumulative 12-year probability of recovery for PD (0.82). It is important, however, to resist the temptation to interpret the recovery numbers for PD as suggesting it is a disorder of typically brief duration or of only modest severity. Indeed, HARP data suggests relapse or recurrence is quite high for both PD (0.56) and PDA (0.58).

One earlier community-based (not treatment-seeking) longitudinal study from the Baltimore section of the Epidemiological Catchment Area Study (ECA; Eaton et al., 1998) also examined the course and predictors of PD/PDA. The investigators report incidence of 1.43 per 1000 per year, with nearly twice as many emergent cases of PDA than PD. Looking at risk factors for PD/PDA development, the Baltimore ECA revealed an overall pattern for significant symptoms of anxiety to be present before PD/PDA criteria were met, either in the form of panic attacks/limited-symptom attacks, or chronic symptoms of generalized anxiety. Analyses revealed younger age (< 30), female sex, and Caucasian racial identity as identifiable risk factors in this population. Female sex as a risk for relapse (in PD only, as PDA tended to be more stable) also was found in the HARP data (Yonkers et al., 2003), where females exhibited a three-fold greater risk during 8-year follow-up as compared to men.

Because there are few naturalistic, epidemiological/community-based longitudinal investigations of PD/PDA, the degree of knowledge and expected generalizability of the specific predictors of disease course, including predictors of transitions from disorder status, is limited. The present study utilizes data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Grant and Dawson, 2006) Waves 1 (W1) and Waves 2 (W2) to provide independent naturalistic, longitudinal data on the course of PD and PDA in a general population sample (vs. a treatment seeking sample). Stability of diagnostic status was first examined by determining probabilities of transition from one diagnostic category to another (e.g., PD at W1 to No PD/PDA at W2).

Cases of incidence, relapse, and chronicity were then further examined by looking at potential risk factors for transition over the NESARC interviewing periods. These include variables that have been associated with new incidence and/or recurrence in past research, such as younger age, female sex, and presence of comorbid psychopathology (Eaton et al., 1998; Yonkers et al., 2003), and specific psychosocial stressors. A recent review has suggested both cumulative and class-specific (e.g., interpersonal, health-related, etc.) effects of psychosocial stressors on risk for panic (Klauke et al., 2010). The potential predictors that were examined included the presence of psychopathology (i.e. major depression [MDD], generalized anxiety disorder [GAD], social phobia [SoPh], and alcohol and/or nicotine dependence), socio-demographic variables (i.e. sex, age, and marital/relationship status), features of PD (i.e. age of onset, duration of longest episode, number of episodes, medication, therapy, and panic attack in the past year), and psychosocial stressors (i.e. loss of employment, death of a family member, change in romantic relationship, and major financial crisis).

2. Methods

2.1. Participants

The NESARC is a longitudinal survey, with its first wave of interviews fielded between 2001 and 2002 and a second wave of interviews collected between 2004 and 2005. The NESARC is a representative sample of individuals 18 years and older

Table 1

Demographics of NESARC respondents from W1 and W1 respondents who completed W2.

	W1, n=43,093	W2, n=34,653
Sex (% female)	57	58
Age (M years (S.D.))	46.4 (18.18)	49.1 (17.30)
Education (%)		
Less than high school	18.2	16.6
High school graduate/GED	29.1	28.7
Some college, no degree	20.6	21.2
Associate's degree	8.8	9.1
Bachelor's degree	12.2	12.7
Graduate degree	11.1	11.8
Marital status (%)		
Married	48.2	41.3
Domestic partnership	3.0	2.5
Widowed	9.9	7.9
Divorced	12.5	10.7
Separated	3.4	2.6
Never married	23.0	15.4
Race (%)		
White, not hispanic	56.9	58.2
Black, not hispanic	19.1	19.0
American Indian/Alaskan Native, Not Hispanic	1.6	1.7
Asian/Native Hawaiian, Pacific Islander	3.1	2.8
Hispanic or Latino	19.3	18.3
Psychopathology (% yes)		
Major depression, lifetime		19.0
Generalized anxiety disorder, lifetime		4.7
Social phobia, lifetime		5.1
Alcohol dependence, lifetime		11.4
Nicotine dependence, lifetime		16.4
Panic features (M (S.D.) or % yes)		
Age of onset		33.6
Duration of longest episode (years)		25.7
Number of episodes		13.24
Medication for panic		36.6
Therapy for panic		44.1
Panic attack in the past year		2.1
Psychosocial stressors (% yes)		
Loss of employment		6.2
Death of family member		32.6
Change in romantic relationship		6.6
Major financial crisis		11.8

Note. W1=Wave 1; W2=Wave 2. Demographics of participants who completed waves 1 and 2.

living in the United States. In addition, it also representatively sampled persons living in non-institutionalized households including boarding houses, rooming houses, non-transient hotels and motels, shelters, facilities for housing workers, college dormitories, and group homes (described in detail in Grant and Dawson, 2006). NESARC response rate was 81% (Grant and Dawson, 2006).

Efforts were made to re-interview all 43,093 respondents from W1 in W2, with 80.4% (n=34,653) participating in W1 and W2. Of persons with PD (with or without Agoraphobia) in W1 (n=2294), 84.5% (n=1939) participated in W2. Table 1 presents demographic information for the sample.

2.2. Measure

The interview instrument used to diagnose all disorders was the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule, DSM-IV version (AUDADIS-IV; Grant et al., 2003; Ruan et al., 2008). Within the PD section, respondents were asked three questions including: (1) "Have you ever had a panic attack, when all of a sudden you felt frightened, overwhelmed or nervous, almost as if you were in great danger, but really weren't?" (2) "Were you ever very surprised by a panic attack that happened totally out-of-the-blue, for no real reason, or in a situation where you didn't expect to be frightened?" (3) "Did you ever think you were having a heart attack, but the doctor said it was just nerves or you were having a panic attack?" If the interviewee responded in the positive to at least one of the three questions, they were queried about the presence of the 13 DSM-IV panic attack symptoms. They also were asked additional diagnostically relevant questions (e.g., interference in functioning, change in behavior) to help determine presence/absence of PD. Agoraphobia was assessed by asking

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