Panic Attacks as a Dimension of Psychopathology: Evidence for Associations With Onset and Course of Mental Disorders and Level of Functioning

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ABSTRACT

Objective: One of the proposed revisions for DSM-5 is to rate panic attacks as a separate dimension across all mental disorders. The idea is that panic attacks occurring outside panic disorder are a dimension predicting important clinical outcomes. The aim of this study was to validate the proposition for DSM-5 that panic attacks have predictive value for overall psychopathology onset, course, and functioning.

Method: Data were derived from the Netherlands Mental Health Survey and Incidence Study (NEMESIS), a prospective population-based study. Using the Composite International Diagnostic Interview (with classifications based on DSM-III-R), 5,571 subjects were selected who had (1) no panic history, (2) a history of panic attacks (but no panic disorder), (3) current panic attacks, or (4) current panic disorder. The impact of panic status on the prevalence of anxiety, affective, alcohol, and any mental disorders; on the onset and persistence of these disorders during 3-year follow-up; and on levels of functioning during 3-year follow-up (as assessed with the 36-Item Short-Form Health Survey) was examined.

Results: Current panic attacks outside the realm of panic disorder were associated with increased prevalence of mental disorders (χ^2_3 = 490.6; P < .001), increased onset of mental disorders (hazard ratio = 4.42; 95% CI, 2.88–6.80), persistence of mental disorders (odds ratio = 2.72; 95% CI, 1.53–4.82), and impaired functioning during 3-year follow-up (F = 69.67; P < .001). Although the impact was smaller than for panic disorder, the associations identified for panic attacks were consistent and significant and were, to a lesser extent, also found for a history of panic attacks.

Conclusions: Given the consistent impact of panic attacks on various aspects of psychopathology, the proposition to dimensionally rate panic attacks across all mental disorders may be of great value for clinical care.


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One of the proposed revisions for DSM-5 is to dimensionally rate panic attacks across all mental disorders.1,2 The idea is that panic attacks occurring outside panic disorder predict the occurrence of, persistence of, and level of functioning in other disorders. Panic attacks are highly prevalent in the general population,3–9 and high rates of comorbidity with a wide range of mental disorders have been reported.4,6,10,11 For example, 71.9% of persons with lifetime panic attacks had a lifetime DSM-IV disorder.6 Furthermore, it was shown that panic attacks significantly increase the risk of onset of mental disorders.12–17 In addition, a few studies have reported an impact of past panic attacks on psychopathology,4,12,16 suggesting that even a history of panic attacks should raise awareness among clinicians for current and future psychopathology.

However, in a review undertaken to propose changes in DSM-5, Craske and colleagues1 concluded that a more thorough understanding of the impact of panic attacks is needed. First, it is unclear to what extent associations reported for panic attacks are driven by panic disorder, because the majority of studies did not stratify analyses to compare panic attacks versus panic disorder.1 The impact of full-blown comorbid mental disorders such as panic disorder on other mental disorders is known and would be no reason to specify panic attacks alongside mental disorders. Second, insight into the contribution of a history of panic attacks is lacking. Previous studies either did not differentiate between a history of panic attacks and current panic attacks1 or reported contradictory results.12,16 Third, the impact of confounding variables has not always been taken into account, although studies that adjust for potential confounders still report evidence for the impact of panic attacks (see Craske et al1). Fourth, most previous studies relied on cross-sectional data. Prospective data would enable examining the impact of panic attacks on course trajectories. Finally, given that little attention has been paid to the impact of panic attacks on persistence of psychopathology and on course of functioning,18,19 research addressing these aspects is needed.

The present study addresses these gaps by examining the association between panic attacks and presence of a wide range of mental disorders, the predictive value of panic attacks on onset and persistence of mental disorders, and the impact of panic attacks on current and future functioning. Effect on outcomes was compared between persons with no panic history, a history of panic attacks (but no panic disorder), current panic attacks, and current panic disorder. Our aim was to thereby empirically test the proposal for DSM-5 to dimensionally rate panic attacks across mental disorders.
Panic attacks occur in a wide range of psychiatric disorders; that is, their occurrence is not limited to panic disorder or anxiety disorders.

Clinicians should be aware of the risk of onset of psychiatric disorders when patients present with panic attacks.

In patients with panic (panic disorder, panic attacks, past panic attacks), both mental functioning and physical functioning are more impaired than in those without panic.

**METHOD**

Procedures

Data were derived from the Netherlands Mental Health Survey and Incidence Study (NEMESIS), a naturalistic, prospective, general population survey (N = 7,076). Data were recorded in 3 waves: at baseline in 1996 (T0), after 12-month follow-up in 1997 (T1), and after 3 years in 1999 (T2). The mean time between T0 and T1 was 379 days (SD = 35 days) and between T1 and T2, 744 days (SD = 71 days). The sampling procedure consisted of a multistage, stratified, random sample. Procedures were approved by the ethics committee of the Netherlands Institute of Mental Health and Addiction, and informed consent was obtained according to the prevailing Dutch law of 1996. Participants were representative of the Dutch population with regard to gender, civil status, and level of urbanization. Only the 18–24 years age group was slightly underrepresented. Of the 7,076 respondents interviewed at baseline, 5,618 were followed up after 1 year (response 79.4%), and 4,848 were followed up after 3 years (response 68.5% of those participating at T0). In the current study, availability of data from the baseline assessment and at least 1 follow-up assessment was considered necessary. At both follow-up measurements, 4,796 subjects were assessed; at T0 and T1, 822 were assessed; and at T0 and T2, 52 were assessed. Those with a history of panic disorder (without current panic attacks or panic disorder) (n = 99) were excluded to prevent the possibility that associations of past panic attacks were driven by past panic disorder. This resulted in a total sample size of 5,571. Attrition between baseline and T2 was not significantly associated with any of the panic groups, after adjustment for sociodemographics and somatic disorders.

Characteristics

Baseline characteristics included gender, age, education (lower than versus equal to or higher than secondary school), and presence of somatic disorders. Somatic disorders were defined as the number of self-reported somatic disorders, out of a 32-item list used in various large-scale psychiatric cohort studies, that were treated or monitored by a doctor in the year preceding T0. This list includes the most common somatic disorders, such as chronic obstructive pulmonary disease, osteoarthritis, heart disease, stroke, peptic ulcer, and diabetes. Comparisons between self-reports of chronic physical disorders and medical records show moderate to good concordance.

Assessment of Mental Disorders

A range of mental disorders were assessed with the CIDI. Anxiety disorders consisted of 12-month agoraphobia, simple phobia, social phobia, generalized anxiety disorder, or obsessive-compulsive disorder, but not panic disorder. Affective disorder consisted of 12-month major affective disorder, dysthymic disorder, or bipolar disorder. Alcohol disorder consisted of 12-month alcohol dependence. Given the small numbers of subjects with 12-month schizophrenia (n = 11), eating disorder (n = 13), and drug disorders (n = 54),...
these disorders could not be analyzed separately. These diagnoses, as well as anxiety, affective, and alcohol disorders, were included in the category “any disorder.”

**Assessment of Functioning**

Functioning was assessed with the 36-Item Short-Form Health Survey (SF-36)\(^3\) at all 3 waves. The SF-36 is a widely applied questionnaire involving 8 subscales. Scoring was performed on a 0–100 scale, with 100 defined as maximum functioning. In this study, total scores were computed. Good reliability and validity of this instrument have been shown elsewhere.\(^3\)\(^2\) Sufficient internal reliability was also demonstrated in NEMESIS (total scores: T0, Cronbach \(\alpha = 0.83\); T1, \(\alpha = 0.82\); T2, \(\alpha = 0.81\)).

**Statistics**

The distribution of characteristics of participants across panic groups was compared using 2-tailed \(\chi^2\) statistics for categorical variables and 1-way analysis of variance statistics for continuous variables. Differences between panic groups were calculated in separate analyses.

The prevalence of psychopathology (ie, any disorder) and the prevalence of anxiety disorders, affective disorders, and alcohol disorders were compared across panic groups using 2-tailed \(\chi^2\) statistics. In addition, differences in prevalence of separate mental disorders across panic groups were calculated in separate analyses.

To examine whether panic predicts onset of psychopathology in a sample at risk, ie, without psychopathology at baseline, incidence densities were calculated, which took into account differences in sample sizes between the panic groups and possible differences in length of follow-up period. Incidence density was defined as the number of onsets per 100 observed person-years. The observation period was calculated per person. Onset of the disorder was estimated halfway between T0 and T1 if a subject fulfilled criteria for a new disorder at T1, and halfway between T1 and T2 if a subject fulfilled criteria for a new disorder at T2 only. Both first-ever incidence and recurrent incidence disorders were taken into account. Cox regression analyses were conducted to examine the association between panic groups and time to onset of psychopathology.

The association between panic groups and persistence of psychopathology during 3 years of follow-up was examined using logistic regression analyses. Persistence was defined as a 12-month diagnosis at T1 and/or any 2-year diagnosis at T2 among those with a diagnosis at baseline. Subsequently, similar analyses were conducted for the persistence of each specific disorder separately, ie, anxiety, affective, and alcohol disorders.

We adjusted both longitudinal analyses for gender, age, education, and somatic disorders. Because current mental disorders may impact upon onset or persistence of psychopathology, we additionally adjusted for current mental disorders (other than the group under consideration). Thus, when investigating onset or persistence of anxiety disorders, we additionally adjusted for current mood disorders, alcohol disorders, eating disorders, drug disorders, and schizophrenia. All analyses were conducted using SPSS version 15.0.\(^3\)\(^6\)

Finally, to examine the association of panic groups (as compared to subjects without panic) and level of functioning during 3 years of follow-up, linear mixed models were used. Estimated mean scores were calculated for the total SF-36 scores. All variables were entered in the model as fixed factors. The only random factor entered in the model was the subject. A panic-by-time interaction term was entered to investigate whether the course of functioning over the 3-year follow-up period differed between the panic groups.

**RESULTS**

**Sample**

Of the total sample (\(n = 5,571\)), a large majority, 91.9% (\(n = 5,173\)), had no current or past panic at T0 (NoPan). A history of panic attacks (HisPA) was present in 2.7% (\(n = 151\)) of the sample. Current panic attacks (PA) were present in 2.0% (\(n = 111\)) of the sample, and current panic disorder (PD) was present in 2.4% (\(n = 136\)) of the sample. The baseline characteristics of the total sample and across panic groups are displayed in Table 1.

**Panic and the Association With Psychopathology**

As illustrated in Table 2, rates of comorbid disorders were significantly higher in all panic groups compared to NoPan: 15.9% of NoPan, 35.1% of HisPA, 52.3% of PA, and 81.6% of PD had any mental disorder (other than panic disorder) (\(P < .001\)). Associations were strongest for PD, but also significant for PA and, to a lesser extent, HisPA. A higher
prevalence of comorbid disorders in PA was also found when investigating anxiety disorders and affective disorders, and in HisPA when investigating anxiety disorders, affective disorders, and alcohol disorders. Again, in general, associations were strongest for PD, followed by PA, and finally HisPA.

Panic as Predictor of Onset of Psychopathology

Of the total sample, 4,529 subjects (81.3%) had no mental disorder at baseline. Of these, 504 (11.1%) developed a disorder during follow-up. In total, 11,814.4 person-years of follow-up time were observed; hence, the incidence density was 4.27 per 100 person-years for the total sample (Table 3). In the NoPan group, the incidence density was 3.97; in HisPA, the incidence density almost doubled (7.57); and in PA and PD, it rose to 19.59 and 23.09, respectively. As shown by the hazard ratios (HRs), onset of psychopathology was associated with all panic groups. Associations could not be explained by sociodemographics and somatic disorders. Likewise, onset

Table 2. Prevalence of Psychopathology (%) in Total Sample (n = 5,571) and Across Panic Groups (no panic, history of panic attacks, current panic attacks, current panic disorder) at Baseline

| Disorder                  | Total Sample (n = 5,571) | No Panic (n = 5,173) | History of Panic Attacks (n = 151) | Current Panic Attacks (n = 111) | Current Panic Disorder (n = 136) | Overall Statistics | Comparisons Between Panic Groups
|---------------------------|--------------------------|----------------------|-----------------------------------|-------------------------------|-------------------------------|-------------------|-----------------------------
| Any disorderb (n = 1,042) | 18.7                     | 15.9                 | 35.1                              | 52.3                          | 81.6                          | 490.6 (3) < .001 | A, B, C, D, E, F          
| Anxiety disorderb (n = 676) | 12.1                     | 9.8                  | 23.2                              | 39.6                          | 67.6                          | 516.4 (3) < .001 | A, B, C, D, E, F          
| Agoraphobia               | 1.3                      | 1.0                  | 5.3                               | 12.6                          | 0.0                          | 129.7 (3) < .001 | A, B, D, E, F            
| Simple phobia             | 7.1                      | 5.7                  | 13.9                              | 19.8                          | 41.2                          | 291.4 (3) < .001 | A, B, C, E, F            
| Social phobia             | 4.5                      | 3.3                  | 7.9                               | 13.5                          | 39.7                          | 436.9 (3) < .001 | A, B, C, E, F            
| Generalized anxiety disorder | 2.5                      | 1.6                  | 4.0                               | 11.7                          | 27.9                          | 412.4 (3) < .001 | A, B, C, D, E, F         
| Obsessive-compulsive disorder | 0.5                      | 0.2                  | 2.6                               | 1.8                           | 7.4                           | 166.9 (3) < .001 | A, B, C, F               
| Affective disorder (n = 437) | 7.8                      | 5.7                  | 15.9                              | 36.0                          | 57.4                          | 629.5 (3) < .001 | A, B, C, D, E, F         
| Major depressive disorder | 5.9                      | 4.4                  | 8.6                               | 23.4                          | 46.3                          | 480.7 (3) < .001 | A, B, C, D, E, F         
| Dysphoric disorder        | 3.1                      | 2.0                  | 6.6                               | 12.6                          | 31.6                          | 426.2 (3) < .001 | A, B, C, E, F            
| Bipolar disorder          | 1.1                      | 0.7                  | 4.6                               | 9.0                           | 7.4                           | 137.0 (3) < .001 | A, B, C                   
| Alcohol disorder (n = 170) | 3.1                      | 2.8                  | 6.6                               | 3.6                           | 8.1                           | 19.4 (3) < .001 | A, C                      

aSignificant differences between panic groups (P ≤ .05): A = no panic vs history of panic attacks, B = no panic vs current panic attacks, C = no panic vs current panic disorder, D = history of panic attacks vs current panic attacks, E = history of panic attacks vs current panic disorder, F = current panic attacks vs current panic disorder.

bOther than panic disorder.

cPer definition; that is, when agoraphobia is accompanied by panic disorder, the diagnosis is panic disorder with agoraphobia, not agoraphobia.

Table 3. Associations Between Panic Groups (no panic, history of panic attacks, current panic attacks, current panic disorder) and Onset of Psychopathology in Samples at Riska

<table>
<thead>
<tr>
<th>Disorder</th>
<th>N at Risk</th>
<th>N Onset</th>
<th>Incidence Density (per 100 person-years)</th>
<th>Adjusted for Sociodemographics and Somatic Disorders Onlyb</th>
<th>Adjusted for Current Mental Disordersc</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HR 95% CI</td>
<td>HR 95% CI</td>
</tr>
<tr>
<td>Onset of any disorderd</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total sample at risk</td>
<td>4,529</td>
<td>504</td>
<td>4.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No panic</td>
<td>4,353</td>
<td>453</td>
<td>3.97</td>
<td>1.00 (ref)</td>
<td></td>
</tr>
<tr>
<td>History of panic attacks</td>
<td>98</td>
<td>18</td>
<td>7.57</td>
<td>1.70 1.06–2.73</td>
<td>2.25 1.36–3.75</td>
</tr>
<tr>
<td>Current panic attacks</td>
<td>53</td>
<td>22</td>
<td>19.59</td>
<td>4.42 2.88–6.80</td>
<td>4.95 3.08–7.94</td>
</tr>
<tr>
<td>Current panic disorder</td>
<td>25</td>
<td>11</td>
<td>23.09</td>
<td>4.85 2.66–8.82</td>
<td>3.75 2.08–6.77</td>
</tr>
<tr>
<td>Onset of anxiety disorderd</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total sample at risk</td>
<td>4,895</td>
<td>294</td>
<td>2.24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No panic</td>
<td>4,668</td>
<td>246</td>
<td>1.95</td>
<td>2.46 1.48–4.08</td>
<td>2.25 1.36–3.75</td>
</tr>
<tr>
<td>History of panic attacks</td>
<td>116</td>
<td>16</td>
<td>5.51</td>
<td>5.72 3.58–9.14</td>
<td>4.95 3.08–7.94</td>
</tr>
<tr>
<td>Current panic attacks</td>
<td>67</td>
<td>19</td>
<td>12.31</td>
<td>5.72 3.26–10.01</td>
<td>3.75 2.08–6.77</td>
</tr>
<tr>
<td>Current panic disorder</td>
<td>44</td>
<td>13</td>
<td>14.44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset of affective disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total sample at risk</td>
<td>5,134</td>
<td>381</td>
<td>2.78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No panic</td>
<td>4,878</td>
<td>342</td>
<td>2.62</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>History of panic attacks</td>
<td>127</td>
<td>13</td>
<td>3.95</td>
<td>1.38 0.80–2.41</td>
<td>1.25 0.71–2.17</td>
</tr>
<tr>
<td>Current panic attacks</td>
<td>71</td>
<td>11</td>
<td>6.24</td>
<td>2.07 1.14–3.79</td>
<td>1.71 0.93–3.14</td>
</tr>
<tr>
<td>Current panic disorder</td>
<td>58</td>
<td>15</td>
<td>11.47</td>
<td>3.43 2.04–5.80</td>
<td>2.24 1.31–3.84</td>
</tr>
<tr>
<td>Onset of alcohol disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total sample at risk</td>
<td>5,401</td>
<td>504</td>
<td>0.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No panic</td>
<td>5,028</td>
<td>42</td>
<td>0.30</td>
<td>1.00 (ref)</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>History of panic attacks</td>
<td>141</td>
<td>3</td>
<td>0.79</td>
<td>3.45 1.06–11.18</td>
<td>2.95 0.90–9.69</td>
</tr>
<tr>
<td>Current panic attacks</td>
<td>107</td>
<td>3</td>
<td>1.05</td>
<td>4.82 1.48–15.70</td>
<td>3.69 1.10–12.42</td>
</tr>
<tr>
<td>Current panic disorder</td>
<td>125</td>
<td>4</td>
<td>1.25</td>
<td>5.61 1.94–16.27</td>
<td>3.93 1.28–12.05</td>
</tr>
</tbody>
</table>

aBoldface indicates statistical significance.

bAdjusted for gender, age, education, and number of somatic disorders.

cNot applicable for “any disorder” analysis.

dOther than panic disorder.

Abbreviations: CI = confidence interval, HR = hazard ratio, ref = reference group.
of anxiety disorders, affective disorders, and alcohol disorders was increased for panic groups. Associations were least strong for those with HisPA and did not reach significance when onset of affective disorders was investigated. Although most associations were stronger for PD compared to PA, associations between PA and onset of psychopathology were quite strong, with HRs varying between 2.07 (onset of affective disorder) and 5.72 (onset of anxiety disorder). When we adjusted for current mental disorders as a potential confounder in the association between panic attacks and onset of psychopathology, HRs diminished, but remained higher as compared to HRs for those without panic. Thus, although current mental disorders had an impact on onset of psychopathology, they did not explain the reported associations for panic attacks.

**Panic as Predictor of Persistence of Psychopathology**

About half of the subjects with any disorder at baseline had any disorder at T1 and/or T2 (49.7%) (Table 4). Whereas in NoPan 45.0% of mental disorders persisted, psychopathology more often persisted across increasing levels of panic (HisPA, 52.8%; PA, 69.0%; PD, 73.0%). Associations were strongest for PD (OR = 3.30) and still fairly strong in PA (OR = 2.72). In HisPA, the association did not reach significance (OR = 1.37; 95% CI, 0.79–2.39). Anxiety disorders, affective disorders, and alcohol disorders also tended to persist in the presence of panic compared to NoPan. When we investigated persistence of any disorder and of anxiety disorders, estimates were somewhat higher for PD than for PA; when we investigated the persistence of affective disorders and of alcohol disorders, estimates were somewhat lower for PD compared to PA. ORs for HisPA did not reach significance in any of the comparisons, nor did ORs in alcohol disorders. Comorbid current mental disorders impacted upon persistence of psychopathology but could not fully explain the associations between panic groups and persistence of psychopathology.

**Impact of Panic on Level of Functioning**

Subjects with panic had significantly lower levels of functioning compared to those without panic during 3-year follow-up in analyses that were basically adjusted for sociodemographics, current mental disorders, and somatic disorders (F = 69.67, P < .001) (Figure 1). At T0, the level of functioning was lowest for PD (β = −13.1; P < .001), followed by PA (β = −8.2; P < .001) and HisPA (β = −3.2; P = .001) (NoPan = reference). Also at other timepoints, the level of functioning of all panic groups was significantly lower than that of NoPan. A post hoc analysis revealed that a lower level of functioning in panic groups

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**Table 4. Associations Between Panic Groups (no panic, history of panic attacks, current panic attacks, current panic disorder) and Persistence of Psychopathology During 3-Year Follow-Up**

<table>
<thead>
<tr>
<th>Persistence</th>
<th>Adjusted for Sociodemographics and Somatic Disorders Only</th>
<th>Adjusted for Current Mental Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>(%)</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td>Any disorder</td>
<td>49.7</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>No panic</td>
<td>45.0</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>History of panic attacks</td>
<td>52.8</td>
<td>1.37</td>
</tr>
<tr>
<td>Current panic attacks</td>
<td>69.0</td>
<td>2.72</td>
</tr>
<tr>
<td>Current panic disorder</td>
<td>73.0</td>
<td>3.30</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>41.1</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>No panic</td>
<td>34.9</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>History of panic attacks</td>
<td>45.7</td>
<td>1.66</td>
</tr>
<tr>
<td>Current panic attacks</td>
<td>54.5</td>
<td>2.26</td>
</tr>
<tr>
<td>Current panic disorder</td>
<td>67.4</td>
<td>3.40</td>
</tr>
<tr>
<td>Affective disorder at T0</td>
<td>45.3</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>No panic</td>
<td>40.0</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>History of panic attacks</td>
<td>33.3</td>
<td>0.74</td>
</tr>
<tr>
<td>Current panic attacks</td>
<td>62.5</td>
<td>2.45</td>
</tr>
<tr>
<td>Current panic disorder</td>
<td>60.3</td>
<td>2.08</td>
</tr>
<tr>
<td>Alcohol disorder (n = 170)</td>
<td>31.2</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>No panic</td>
<td>29.0</td>
<td>1.00 (ref)</td>
</tr>
<tr>
<td>History of panic attacks</td>
<td>39.0</td>
<td>1.71</td>
</tr>
<tr>
<td>Current panic attacks</td>
<td>50.0</td>
<td>2.79</td>
</tr>
<tr>
<td>Current panic disorder</td>
<td>45.5</td>
<td>1.95</td>
</tr>
</tbody>
</table>

**Figure 1. Total Scores on the 36-Item Short-Form Health Survey (SF-36) During 3 Years of Follow-Up by Baseline Panic Groups, Adjusted for Gender, Age, Education, and Number of Somatic Disorders**

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applied for both mental functioning ($F = 93.13; P < .001$) and physical functioning ($F = 21.59; P < .001$) subdomains.

During the first year of follow-up, the level of functioning of both PD and PA improved significantly more compared to NoPan, as is indicated by significant interaction with time ($PD \times time: t = 4.65, P < .001$; $PA \times time: t = 3.39, P = .001$). HisPA subjects did not show any significant improvement of functioning during the first year of follow-up. Results are similar for the 3-year follow-up ($PD \times time: t = 3.72, P < .001$; $PA \times time: t = 2.05, P = .04$; $HisPA \times time = NS$). Between T1 and T2, interaction with time was not significant, indicating that most improvement occurred during the first year of follow-up.

Additionally adjusting for comorbid mental disorders at baseline reduced beta values, but functioning remained significantly lower in all panic groups and at all timepoints compared to those without panic ($F = 30.80; P < .001$), and again this applied to both mental ($F = 43.20; P < .001$) and physical ($F = 8.34; P < .001$) subdomains (results not shown).

**DISCUSSION**

With the DSM-5 forthcoming, the nosologic status of panic attacks has gained renewed interest. In earlier times, Freud reckoned the central position of anxiety symptoms (shown). HisPA subjects did not show any significant improvement in any subdomain at baseline reduced beta values, but functioning remained significantly lower in all panic groups and at all timepoints compared to those without panic ($F = 30.80; P < .001$), and again this applied to both mental ($F = 43.20; P < .001$) and physical ($F = 8.34; P < .001$) subdomains (results not shown).

**Strengths and Limitations**

Data were derived from a large and methodologically sound general population study with a longitudinal design, allowing examination of onset, persistence, and level of functioning over a 3-year period. Moreover, the data allowed the investigation of panic attacks outside the realm of panic disorder and the investigation of a history of panic attacks. The results should be interpreted within the context of the following limitations. First, criteria for panic were derived from DSM-III-R. In DSM-III-R, panic attacks were not described separately but integrated within the criteria of panic disorder. As a result, onset of a panic attack was restricted to a “sudden onset” in our study, whereas in DSM-IV a crescendo criterion was also required to fulfill criteria of a panic attack. However, it is likely that using a more strict definition of a...
panic attack (ie, including the crescendo criterion) would only further strengthen associations between panic attacks and psychopathology.

Second, data did not allow the distinction between situationally bound panic attacks, situationally predisposed panic attacks, and spontaneous attacks. Thus, panic attacks occurring in the context of a phobic stimulus in an individual with an anxiety disorder could not be distinguished from unexpected panic attacks. This should be noted, because it can be hypothesized that only unexpected panic attacks have predictive value for course trajectories, and that anxiety responses to phobic stimuli or situations do not. However, if so, exclusion of situationally bound and predisposed panic attacks would further strengthen our findings.

Third, the total sample of the present study was large. As a result, statistical power was sufficient in most analyses. However, for specific subsamples and specific outcomes (especially regarding alcohol disorders), sample sizes were smaller, resulting in wider confidence intervals in these analyses. In these analyses, nonsignificant findings may therefore reflect insufficient statistical power, since it is important to note that risk estimates were generally increased in these smaller subgroups.

Fourth, given that part of our sample had only 1 follow-up assessment, the onset and persistence rates of disorders may be underestimated. Differential bias across panic groups is not likely, because attrition was not associated with any of the panic groups.

Fifth, the prospective associations between panic attacks and psychopathology shown in this study are useful in clinical practice. However, the reported associations may not be causal; that is, the possibility that panic attacks represent an underlying construct that causes the associations cannot be ruled out. Given that the construct of anxiety sensitivity is associated with panic attacks,\textsuperscript{12,17} it would have been worthwhile to assess anxiety sensitivity and adjust analyses for anxiety sensitivity. This was not possible, as the construct of anxiety sensitivity was not assessed in NEMESIS.

Sixth, posttraumatic stress disorder (PTSD) has not been assessed in NEMESIS. Including PTSD would have been interesting, given that in PTSD the occurrence of panic attacks is common and associated with adverse consequences.\textsuperscript{35}

**CONCLUSION**

Given the consistent impact of panic attacks, and to a lesser extent a history of panic attacks, on various aspects of psychopathology, dimensionally rating panic attacks across mental disorders may be of great value for clinical care. Further work is needed to unravel the nature of the association between panic attacks and psychopathology and to examine beneficial effects of treating panic attacks.

**Disclosure of off-label usage:** The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration-approved labeling has been presented in this article.

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**REFERENCES**


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