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Sub-threshold panic attacks and agoraphobic avoidance increase comorbidity of mental disorders: Results from an adult general population sample

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ABSTRACT

Full-blown panic attacks are frequently associated with other mental disorders. Most comorbidity analyses did not discriminate between isolated panic attacks vs. panic attacks that occurred in the context of a panic disorder and rarely evaluated the impact of comorbid agoraphobia. Moreover, there are no larger scale epidemiological studies regarding the influence of sub-threshold panic attacks. 4075 German-speaking respondents aged 18–64 were interviewed using the fully structured Munich Composite International Diagnostic Interview. Limited symptom attacks, isolated panic attacks, and panic disorder were associated with other lifetime DSM-IV disorders with monotonically increasing odds and increasing tendency for multiple comorbidities across the three groups. The presence of agoraphobia was associated with more frequent comorbidity in all panic subgroups and also in persons who never experienced panic attacks. The present study suggests that populations with isolated or limited symptom should be carefully attended to in clinical practice, especially if agoraphobia is present.

1. Introduction

Panic attacks are brief episodes of intense fear accompanied by a feeling of impending doom or catastrophe. According to diagnostic criteria of the DSM-IV (APA, 2000) panic attacks must be accompanied by at least four out of 13 key symptoms that appear unexpectedly and increase in a crescendo-like fashion peaking within 10 min. To fulfil diagnostic criteria for panic disorder recurrent panic attacks have to be followed by at least one month of persistent anxious apprehension targeted at the possibility of having additional attacks, implications and consequences of these attacks, or a significant change in behaviour related to the attacks.

Panic attacks that are not followed by such anxious apprehension or behaviour changes are sometimes defined as nonclinical (Barlow, 2002; Norton, Cox, & Malan, 1992) or isolated panic attacks (Kessler et al., 2006). Epidemiological studies using standardized interviews found a substantial variation in the lifetime prevalence of such isolated full-blown panic attacks ranging from 3% (Eaton, Kessler, Wittchen, & Magee, 1994; Reed & Wittchen, 1998; Wittchen, 1986) if only unexpected panic attacks were considered to 28.3% (Kessler et al., 2006) if cued panic attacks were also included. In addition, up to 8.7 percent of the general population (Eaton et al., 1994; Reed & Wittchen, 1998) report so called sub-threshold panic attacks, i.e., attacks that either involve less than four symptoms or lack the crescendo-like increase in fear (defined as limited symptom attacks (LSA); (APA, 2000; Norton, Zvolensky, Bonn-Miller, Cox, & Norton, 2008)), or attacks that are described by the affected persons as "attacks of fear or panic when all of a sudden [they] felt very frightened, anxious, or uneasy" but neither involve four symptoms *nor* meet the crescendo criterion (defined as fearful spells (FS); (Eaton et al., 1994)).

It has been demonstrated that panic attacks are often associated with other comorbid mental disorders, as for instance mood or anxiety disorders, somatoform disorders or substance use disorders (Alonso et al., 2004; Goodwin et al., 2004; Reed & Wittchen, 1998; Weissman et al., 1997). Most studies, however, did not discriminate between isolated panic attacks and those panic attacks that occurred in the context of a panic disorder. However, it would be of relevance to detect whether the reported association is equally

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found in those persons with panic disorder and those with isolated panic attacks. If a person with isolated panic attacks proofs to be of equal risk for comorbidity as persons with panic disorder, this group would constitute an important target group for prevention and early interventions in the health care system.

Kessler et al. (2006) were the first to analyze differences between isolated full-blown panic attacks and those that occurred in the context of a panic disorder in more detail using the database of the US National Comorbidity Survey Replication findings. Isolated panic attacks were associated with the lowest odds ratios (ORs) for other mental disorders. ORs were substantially higher if these isolated panic attacks were accompanied by comorbid agoraphobia and were even larger than those obtained for patients who suffered from panic disorder without agoraphobia. Panic disorder with comorbid agoraphobia was associated with greatest risk for comorbidity across all diagnostic categories. These data suggest that agoraphobia might be a more potent marker for severe psychopathology than isolated panic attacks, or panic attacks that occur in the context of panic disorder.

To follow up on this research in the present study panic disorder patients and persons with isolated panic attacks were compared regarding the presence of comorbid mental disorders. In parallel to Kessler et al. (2006) we included analyses to assess the impact of agoraphobic avoidance on lifetime comorbidity with other mental disorders. In addition to Kessler et al. (2006) we also included individuals with sub-threshold panic attacks in the analyses. A first smaller scale community based study by Katerndahl and Realini (1998) suggested that limited symptom panic attacks are associated with increased rates of other lifetime mental disorders. However, larger scale epidemiological studies have not yet systematically evaluated this issue.

Finally, given that full-blown panic attacks are a marker for increased rates of the presence of lifetime comorbid mental disorders we wanted to investigate the temporal relationship between panic attacks and the onset of comorbid mental disorders more closely. From the perspective of clinical intervention or prevention of mental disorders it is of high interest if the occurrence of acute panic attacks is a marker of past, present or upcoming psychopathology. Longitudinal analyses by Goodwin et al. (2004) clearly indicate that panic attacks (again this study did not discriminate between panic attacks occurring in the context of panic disorder or were isolated) are a marker for present comorbidity and predict the development of future comorbid mental disorders. Moreover, there is a large body of literature indicating that panic disorder is associated with an increased risk for developing other mental disorders such as depression, substance use disorder (Goodwin et al., 2004). However, data about past, present or future psychopathology in individuals with isolated or sub-threshold panic attacks have not yet been systematically evaluated. We therefore added an analysis separating the presence of comorbid mental disorders with regard to the age of onset of panic attacks, again discriminating persons with isolated panic attacks and persons with sub-threshold panic attacks.

2. Methods

2.1. Sample

The data analyzed in the current study were drawn from the baseline survey of the Transitions in Alcohol Consumption and Smoking (TACOS) study. A random sample of 6447 individuals aged 18–64 had been chosen from official residents registration office files of the city of Lübeck (Germany) and 46 surrounding communities with a total population of 325,107 inhabitants. All non-institutionalized persons with German nationality were included. The study followed the ethical principles of the American Psychological Association (1992) and was conducted in accordance with the Helsinki Declaration (1989). Individuals received written information on the study and were informed that they were free to participate and could withdraw from the study at any time. After consent to participate, a face-to-face interview was conducted. A total of 4093 individuals (70.2%) completed the interview between July 1996 and March 1997. Due to technical problems data sets of 18 individuals could not be analyzed, yielding to a final sample of 4075 persons that were used for the present analysis.

2.2. Diagnostic assessment

The computerized Munich Composite International Diagnostic Interview (M-CIDI), an extended and DSM-IV adapted German language version of the CIDI (Robins et al., 1988), was administered by 56 trained psychiatric lay interviewers in a face-to-face interview. The M-CIDI is designed to assess symptoms, syndromes, and full diagnostic criteria of 48 mental disorders along with information about onset, duration, recency of complaints as well as clinical and psychosocial severity. It not only allows for a detailed and comprehensive evaluation of panic attacks, panic disorder, and agoraphobia but also for the assessment of fearful spells and limited symptom attacks. Specifically, the M-CIDI in detail assesses the *worst unexpected* out of the blue panic attack that is reported by the individual. Hierarchically ordered questions ask if a person has ever experienced an "attack of fear or panic when all of a sudden [he/she] felt very frightened, anxious, or uneasy" (this question is called the "stem question"). While a no response leads to a skip of the whole panic section, a yes response to this question is followed by questions about unexpectedness of the attack, presence of a crescendo, as well as an evaluation of all symptoms listed in the DSM-IV. Afterwards, the full diagnostic criteria of panic disorder are evaluated. Diagnostic criteria for the presence of agoraphobia are assessed in a separate section of the interview. Lifetime diagnoses for all assessed mental disorders were assigned according to diagnostic hierarchy rules and organic exclusion rules as stated in the DSM-IV.

Psychometric properties of the M-CIDI have been established in a number of studies. Test–retest reliability and procedural clinical validity were examined for the M-CIDI interview in general, as well as for panic attack, panic disorder, and agoraphobia (Lachner et al., 1998; Reed et al., 1998; Wittchen, 1994; Wittchen, Lachner, Wunderlich, & Pfister, 1998). Additionally, data are provided (Wittchen et al., 1998) regarding the panic attack stem question (which refers to the fearful spells analyzed in the present manuscript). Test–retest reliability for lifetime diagnoses was $\kappa = 0.78$ for panic stem question, $\kappa = 0.57$ for panic attack, $\kappa = 1.00$ for panic disorder, $\kappa = 0.84$ for agoraphobia. Agreement with clinical consensus diagnoses was $\kappa = 0.74$ for panic disorder, $\kappa = 0.84$ for agoraphobia.

Extensive measures of quality assurance of diagnostic assessment were implemented in the TACOS study (Meyer, Rumpf, Hapke, Dilling, & John, 2000): most importantly, interviewers were extensively trained and had weekly booster sessions with WHO–CIDI trainers. The coding of every interview (including all responses to open ended questions, e.g., regarding the situation or subjective elicitors of a panic attack) was checked by a clinical psychologist, and interviewers were continuously provided with a feedback regarding the results of this process. All detected errors were corrected as described by Meyer, Rumpf, Hapke, and John (2000). Skip rules and diagnostic algorithms were applied by a computer programme, avoiding omissions of items or errors. Further details on TACOS sampling, assessment procedures and quality assurance are