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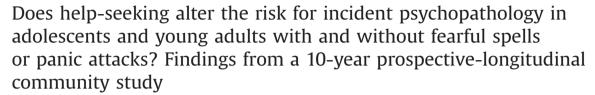
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#### Research Report





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#### ARTICLE INFO

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#### ABSTRACT

*Background:* Although fearful spells (FS) and panic attacks (PA) increase the risk for various mental disorders, few studies have examined whether help-seeking in those with FS/PA attenuates the risk for incident psychopathology.

Methods: A community sample of adolescents and young adults (N=2978, aged 14–24 at baseline) was followed up in up to 3 assessment waves over 10 years. FS, PA, psychopathology, and help-seeking were assessed using the DSM-IV/M-CIDI. Logistic regressions with interaction terms (adjusted for sex and age) were used to test interactions between FS/PA and help-seeking at baseline on predicting incident psychopathology at follow-up. Cases with panic disorder (PD) at baseline were excluded from all analyses.

Results: FS/PA at baseline predicted the onset of any disorder, any anxiety disorder, PD, agoraphobia, generalized anxiety disorder, social phobia, and depression at follow-up (Odds Ratios, OR 1.62–5.80). FS/PA and help-seeking at baseline interacted on predicting incident PD (OR=0.09) and depression (OR=0.22) at follow-up in a way that FS/PA only predicted the respective disorders in individuals not seeking help at baseline. In those with FS/PA, a higher number of panic symptoms interacted with help-seeking on predicting incident PD (OR=0.63) in a way that a higher number of panic symptoms only increased the risk for PD in those without help-seeking at baseline.

*Limitations:* Help-seeking at baseline was not restricted to panic-specific interventions, but included treatment due to other psychological problems as well.

*Conclusions*: Findings suggest that early help-seeking might modify psychopathology trajectories and prevent incident disorders in high-risk individuals with FS/PA.

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#### 1. Background

Fearful spells (FS), panic attacks (PA), and panic disorder (PD) are common and associated with substantial individual impairment and societal costs (Asselmann et al., 2014b; Eaton et al., 1994; Goodwin and Hamilton, 2001; Goodwin et al., 2005; Goodwin and Roy-Byrne, 2006; Grant et al., 2006; Kessler et al., 2006; Reed and Wittchen, 1998; Roy-Byrne et al., 2000; Rubin

et al., 2000; Warshaw et al., 1995; Wittchen et al., 2008). DSM-IV PA are defined as discrete episodes of intense fear or discomfort, in which at least 4 out of 13 panic symptoms develop abruptly and reach a peak within 10 min (crescendo) (American Psychiatric Association, 1994). The diagnosis of DSM-IV PD requires recurrent unexpected PA followed by persistent concern about additional PA, worry about implications or consequences of the PA, and/or significant change in behavior due to PA. FS are conceptualized more broadly than PA and simply describe the occurrence of distressing spells of anxiety (Eaton et al., 1994). Thus, the category of FS includes full-blown DSM-IV PA as well as milder spells associated with no or fewer panic symptoms and/or lacking crescendo in symptom onset (FS-only).

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Previous cross-sectional and longitudinal research consistently found that PA strongly increased the risk for various forms of psychopathology beyond PD, including anxiety, depressive, and substance use disorders (Asselmann et al., 2014a; Baillie and Rapee, 2005; Batelaan et al., 2012; Craske et al., 2010; Goodwin and Hamilton, 2001, 2002a, 2002b; Goodwin and Gotlib, 2004; Goodwin et al., 2004a, 2004b; Kinley et al., 2011; Reed and Wittchen, 1998; Roy-Byrne et al., 2000; Wittchen et al., 1998a; Wittchen et al., 2008). Although fewer studies examined the role of FS-only for the onset of psychopathology, prior evidence suggests that FS-only similarly elevate the risk for incident mental disorders (Asselmann et al., 2014a; Baillie and Rapee, 2005; Pine et al., 1998).

Given these findings, a series of studies tested the efficacy of early interventions in patients with PA (Dyckman et al., 1999; Febbraro, 2005; Gardenswartz and Craske, 2001; Meulenbeek et al., 2009, 2010; Nuthall and Townend, 2007; Swinson et al., 1992; Wright et al., 2000). In one study, patients consulting an emergency department due to PA (with our without PD) were either (a) reassured to suffer from PA but no severe disorder or (b) instructed to confront the situation in which the initial PA had occurred as often as possible to reduce panic symptoms (Swinson et al., 1992). Only the exposure instruction group, but not the reassurance group subsequently improved on panic, agoraphobic, and depressive symptoms. Research in students with PA (but no PD) revealed that participants attending a 1-day intervention (based on principles of cognitive behavioral therapy, CBT) were at decreased risk of developing subsequent PD and more strongly improved on panic symptoms and avoidance than wait-list controls (Gardenswartz and Craske, 2001). In individuals from the community suffering from sub-threshold or mild PD, participants attending a brief intervention program (8 2-h-sessions based on CBT principles) significantly improved on panic symptomatology compared to wait-list controls (Meulenbeek et al., 2009, 2010). Moreover, various forms of treatment in patients with PD especially CBT - were shown to effectively reduce panic pathology (Carlbring et al., 2006; Clark et al., 1999; Gloster et al., 2013; Lueken et al., 2013; Mitte, 2005; Roy-Byrne et al., 2005) and associated comorbidities (Craske et al., 2007; Emmrich et al., 2012; Tsao et al., 1998, 2002, 2005). Within the National Comorbidity Survey, a large-scaled epidemiological study among U.S. residents, individuals having received treatment due to panic or generalized anxiety disorder (GAD) were at considerably lower risk of major depression relative to those without treatment (Goodwin and Olfson, 2001; Goodwin and Gorman, 2002).

In general, high rates of help-seeking were obtained in panickers, especially in those with comorbid disorders (Boyd, 1986; Kessler et al., 2006; Leon et al., 1997; Rees et al., 1998; Roy-Byrne et al., 2000; Wang et al., 2005). A series of studies investigated predictors of help-seeking in individuals with PA or PD and found that besides demographic variables (e.g. female sex, higher age, and higher education), psychopathological characteristics such as subjective distress/impairment, more (severe) panic symptoms, and comorbidity predicted health care utilization in panickers (Angst et al., 2010; Goodwin and Andersen, 2002; Katerndahl, 2002; Realini and Katerndahl, 1993).

However, although FS and PA were consistently shown to increase the risk for various mental disorders beyond PD, previous research mainly tested the efficacy of preventive/brief interventions with respect to panic pathology and closely associated outcomes. Few studies have examined whether help-seeking in panickers decreases the risk for several forms of psychopathology, including other anxiety, depressive, and substance use disorders, although doing so may have important implications for targeted preventive and early treatment interventions.

Using data of a representative community sample of adolescents and young adults, this prospective-longitudinal study aims to

examine (a) which proportions of incident anxiety, depressive, and substance use disorders (at follow-up) could be prevented if FS/PA (at baseline, including FS-only and DSM-IV PA) were eliminated from the population (population attributable fractions) and (b) whether help-seeking attenuates the association between FS/PA and incident psychopathology. We hypothesize that FS/PA and help-seeking at baseline interact on predicting incident anxiety, depressive, and substance use disorders at follow-up in a way that the association between FS/PA and subsequent psychopathology should be stronger in individuals not seeking help than in individuals seeking help at baseline. A higher number of panic symptoms at baseline should elevate the risk for incident disorders only in panickers without help-seeking, but not in panickers with help-seeking at baseline.

#### 2. Methods

#### 2.1. Sample

Data come from the Early Developmental Stages of Psychopathology Study (EDSP), a 10-year prospective-longitudinal study among a representative community sample of adolescents and young adults with 1 baseline (T0, 1995, N=3021, response rate 70.8%) and 3 follow-up investigations (T1, 1996/97, N=1228, only younger cohort, response rate 88.0%; T2, 1998/99, N=2548, response rate 84.3%; and T3, 2003, N=2210, response rate 73.2%). The sample was drawn randomly from the Munich area (Germany); participants were aged 14-24 years at baseline and 21-34 years at last follow-up. Because the study focused on early developmental stages of psychopathology, 14-15-year-olds were sampled at twice the probability of individuals aged 16-21 years, and 22-24-year-olds were sampled at half of this probability. At T1, only the younger EDSP cohort (aged 14-17 at baseline) was examined, whereas at T0, T2, and T3, both cohorts (younger and older, aged 18-24 at baseline) were investigated. Further information on methods and design has been previously presented (Lieb et al., 2000; Wittchen et al., 1998c). The EDSP has been approved by the Ethics Committee of the Medical Faculty of the Technische Universität Dresden (No: EK-13811). After complete description of the study, all participants 18 years or older provided written informed consent; for respondents younger than 18 years, parental consent was provided.

#### 2.2. Diagnostic assessment

Diagnostic information on symptoms and disorders prior to and after baseline was assessed at each wave using the lifetime (baseline) and interval version (follow-up assessments) of the Computer-Assisted Personal Interview (CAPI) version of the Munich-Composite International Diagnostic Interview (DIA-X/ M-CIDI) (Wittchen and Pfister, 1997). The M-CIDI is an updated version of the World Health Organization's CIDI version 1.2 (World Health Organization, 1990) with additional questions to cover DSM-IV and ICD-10 criteria. The M-CIDI can be used to assess syndromes and diagnoses of 48 mental disorders with additional information on onset, duration, and clinical/psychosocial severity. Detailed descriptions of psychometric properties have been presented elsewhere (Reed et al., 1998; Wittchen et al., 1998b).

The current study focuses on follow-up incidences of anxiety, depressive, and substance use disorders. Anxiety disorders include PD, agoraphobia, GAD, and social phobia. Depression includes major depressive episodes and dysthymia. Substance use disorders include alcohol abuse/dependence, nicotine dependence, and abuse/dependence of illicit drugs. For phobias, the impairment

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