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Predictors of the Course of Anxiety Disorders in Adolescents and Young Adults

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Abstract Anxiety disorders belong to the most frequent mental disorders and are often characterized by an early onset and a progressive, persistent/chronic, or recurrent course. Several individual, familial, and environmental risk factors for adverse course characteristics of anxiety disorders (including higher persistence, lower probability of remission, and increased risk of recurrence) have been identified, and previous research suggests that clinical features of anxiety (e.g., higher severity, duration, and avoidance) as well as comorbid other mental disorders are particularly useful for predicting an unfavorable course of anxiety disorders. However, additional studies are needed to identify risk factors for individual course trajectories of anxiety disorders in general as well as specific diagnoses. Doing so is essential in order to more precisely identify individuals with anxiety disorders who are at increased risk for adverse long-term outcomes and might thus particularly profit from targeted early interventions.

Keywords Anxiety · Adolescence · Course · Persistence · Chronicity · Remission · Recurrence · Predictor · Risk factor · Individual · Familial · Environmental

Introduction

The timeframe of childhood, adolescence, and young adulthood constitutes a core high-risk period for the development of several forms of psychopathology, particularly anxiety disorders [1, 2, 3•, 4]. Initially transient and circumscribed neurobiological, cognitive, affective, and behavioral dysfunctions during this sensitive phase are likely to generalize and escalate with time, thus leading to severe and persistent psychopathology associated with impairment and disability in several areas of life [5, 6]. However, specific fears and anxieties often manifest as part of typical development in childhood and adolescence, which impedes an identification (especially of initial stages) of psychopathological anxiety [7–9]. In contrast to normative fears and anxieties, clinically relevant forms of anxiety are generally more persistent and excessive and associated with substantial distress and impairment to the affected individual [10]. The individual anxiety disorders share several clinical features, e.g., extensive anxiety, bodily symptoms, avoidance behavior, and/or considerable distress/impairment [10–13]. Nonetheless, the diagnostic class of anxiety disorders represents a phenotypically highly heterogeneous group of disorders, and specific anxiety disorders often differ from each other with respect to symptomatology, onset, course, risk factors, and clinical correlates [2, 3•, 14].

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Prevalence

Anxiety disorders represent the most frequent of all mental disorders with (cumulative) lifetime prevalences of up to 30 % in adolescent and young adult samples [3•, 4, 15, 16, 17••]. Regarding specific anxiety disorders, prevalence rates are highest for specific phobia, social anxiety disorder (SAD), and separation anxiety disorder and lower for panic disorder, agoraphobia, and generalized anxiety disorder (GAD) [3•, 4, 16, 18]. For instance, within the National Comorbidity Survey Adolescent Supplement (NCS-A), lifetime prevalences were 31.9 % for any anxiety disorder, 19.3 % for specific phobia, 9.1 % for SAD, 7.6 % for separation anxiety disorder, 2.3 % for panic disorder, 2.4 % for agoraphobia, and 2.2 % for GAD in adolescents aged 13–18 years [4]. Moreover, prevalence

rates are two to three times higher in females than in males [3•, 4, 15, 16, 19]. Though, concrete prevalence estimates partially vary across studies, which is presumably primarily due to methodological differences (e.g., inconsistencies with respect to age groups, assessment measures, source of information, diagnostic systems, method of data aggregation, number and types of diagnoses referred to as anxiety disorder, and strictness in application of diagnostic criteria) [14, 20].

Onset

Anxiety disorders typically have an early onset rooted in childhood or adolescence [1, 2, 4, 14, 21]. The earliest age of onset has clearly been found for separation anxiety disorder and individual subtypes of specific phobias, which in most cases is before the age of 12 [1, 21, 22]. Incidence rates for SAD are highest in late childhood and throughout adolescence, while panic disorder, agoraphobia, and GAD typically begin in late adolescence or early adulthood [1, 2, 21]. However, there is also evidence that subthreshold forms of anxiety disorders (e.g., fearful spells) often manifest considerably earlier in childhood or early adolescence [23–25].

Impairment and Disability

Anxiety disorders are associated with substantial impairment and disability, reduced psychosocial functioning, increased suicidality, and adverse developmental long-term consequences [3•, 17••, 26, 27]. For instance, using data from the Oregon Adolescent Depression Project (OADP), a large-scaled prospective-longitudinal study among adolescents, Essau et al. [17••] revealed that anxiety disorders in adolescence predicted lower total/work adjustment, more familial problems, lower life satisfaction, lower coping skills, and higher chronic stress at age 30; moreover, these associations were partially mediated by psychopathology in adulthood. Previous findings suggest that particularly those with higher levels of impairment and disability are at elevated risk of developing secondary other mental disorders, especially depression [28–30].

The Course of Anxiety Disorders

Findings from clinical [31, 32] and cross-sectional [33••] studies suggest that anxiety disorders are highly persistent, chronic conditions. For instance, Kessler et al. [33••] indirectly assessed disorder persistence via prevalence ratios within the NCS-A and found considerably higher persistence estimates for anxiety disorders than for mood and substance use disorders. Except for separation anxiety disorder (12-month to lifetime ratio 20.9 %), which mainly occurs in childhood, 12-month to lifetime ratios for individual anxiety disorders were high, ranging from 51.2 % for GAD to 90.9 % for SAD. Moreover, 12-month to lifetime ratios were higher than 30-day to 12-month ratios (except for separation anxiety disorder), suggesting disorder persistence to be rather due to recurrence than to chronicity.

However, retrospectively assessed information on onset and course in cross-sectional studies may be subject to recall and memory biases, leading to an overestimation of stability [5, 34–36]. Thus, prospective epidemiological studies are indispensable to inform on the course of anxiety disorders, as they are less susceptible towards biases. Prospective-longitudinal research consistently found that anxiety disorders in childhood or adolescence strongly predicted the presence of the same condition (homotypic continuity) [26, 37••, 38–41] as well as other mental disorders (heterotypic continuity) [26, 28, 37••, 38, 40–42] later in life, although, however, it has to be noted that often only a minority of individuals was found being diagnosed with the same disorder across several time points [43–46, 47•]. For example, within the Great Smoky Mountains Study, a large-scaled population-based study that prospectively followed up children from the U.S. into adulthood, anxiety disorders in childhood or adolescence were shown to strongly predict later anxiety, depressive, and/or substance use disorders in adolescence or adulthood [38, 40]. Except for specific phobias, each individual anxiety disorder showed homotypic continuity, and continuity of specific phobia, SAD, and GAD was more pronounced in girls than in boys [40]. Within the Early Developmental Stages of Psychopathology Study (EDSP), a prospective-longitudinal community study among adolescents and young adults from Germany, course characteristics of specific phobia were examined and high rates of homotypic and heterotypic continuity were found [48]: Of those with specific phobia at baseline, 41 % retained the same diagnosis at follow-up and this rate increased to 73 % when other anxiety disorders and depression at follow-up were included. Merely 10 % did not meet criteria for any DSM-IV disorder at follow-up.

With respect to heterotypic continuity, particularly strong associations were found for anxiety disorders and subsequent depression [28, 30, 38, 40]. For instance, within the EDSP, any anxiety disorder as well as each of the examined specific anxiety disorder(s) (specific phobia, SAD, agoraphobia, panic disorder, and GAD) predicted subsequent depression [28]. Clinical characteristics of anxiety that were strongly associated with the onset of depression included having two or more anxiety disorders, higher impairment, and experiencing panic attacks.

A specific example for homotypic and heterotypic continuity are panic attacks, as they were found to strongly increase the risk of developing full-threshold panic pathology as well as other anxiety, depressive, somatoform, and substance use

disorders [49–54]. Also milder forms of panic pathology such as fearful spells were shown to elevate the risk of panic disorder and other forms of psychopathology [25, 49, 55].

In recent years, a series of research prospectively examined distinct developmental trajectory classes of anxiety symptoms or disorders across several time points in adolescence: Olino et al. [56••] prospectively followed-up N=1,635 adolescents until young adulthood and identified 6 trajectory groups of anxiety and depressive disorders: (1) consistently low anxiety and depression (65.1 %), (2) initially high but declining anxiety (5.5 %), (3) increasing depression (22.8 %), (4) increasing depression and late onset anxiety (3.7 %), (5) persistent anxiety (2.1 %), and (6) persistent depression (1.3 %). The authors further examined associations with sex, parental psychopathology, and childhood abuse and found that initially high but declining anxiety was predicted by female sex, parental substance use, and childhood abuse; increasing depression was predicted by female sex, parental depression, and childhood abuse; increasing depression and late onset anxiety was predicted by female sex and parental anxiety; persistent anxiety was predicted by parental anxiety and childhood abuse; and persistent depression was predicted by parental depression and childhood abuse.

Using data of the Medical Research Council National Survey of Health and Development, a large-scaled epidemiological study in which individuals born in 1946 were followed-up over 21 assessment waves until the age of 56, Colman et al. [57] revealed the following developmental trajectories of anxiety and depressive symptoms from early adolescence to middle adulthood: (a) no symptoms (44.8 %), (2) adult-onset moderate symptoms (11.3 %), (3) repeated moderate symptoms (33.6 %), (4) adolescent symptoms with good adult outcome (5.8 %), (5) adult-onset severe symptoms (2.9 %), and (6) repeated severe symptoms (1.7 %). These trajectory groups differed with respect to core developmental markers in early childhood in a way that those with no symptoms had the highest birth weight and lowest age at first standing and walking, while those with repeated severe symptoms had the lowest birth weight and highest age at first standing and walking.

Another large-scaled prospective-longitudinal study among adolescents from the Netherlands (Tracking Adolescents' Individual Lives Survey (TRAILS)) showed that anxiety symptoms decreased from early to middle adolescence and slightly increased from middle to late adolescence [58]. Developmental trajectories were similar for symptoms of GAD, panic disorder, SAD, separation anxiety disorder, and obsessive-compulsive disorder, and females had consistently higher levels of anxiety (except for obsessive-compulsive disorder) as well as less decreasing symptoms of anxiety from early to middle adolescents (except for separation anxiety disorder). Several individual, familial, and environmental risk factors at baseline were associated with either an increased risk of anxiety throughout adolescence (frustration, effortful control, lower parental emotional warmth, parenting stress, current parental stress, anxiety, and depressive symptoms, lifetime parental internalizing symptoms, familial health problems, family dysfunction, lower income, and being the perpetrator or victim of bullying) or an initially high but declining risk of anxiety over time (low self-esteem/competence, parental rejection and overprotection, as well as being both the perpetrator and victim of bullying) [59••].

Predictors of an Unfavorable Course

Predictors of incident anxiety disorders have been extensively studied, and several individual, familial, and environmental variables were identified as risk factors for anxiety (for comprehensive review, see [14, 60]) However, as anxiety disorders often take a progressive, persistent, or recurrent course, it is required to examine not only risk factors for disorder onset but also predictors for unfavorable course trajectories of anxiety in order to specify high-risk individuals for developmental complications who might particularly profit from targeted early interventions at initial stages of anxiety. Unfortunately, only a few large-scaled prospective-longitudinal studies so far have systematically examined and compared the role of multiple (individual, familial, and environmental) risk factors for unfavorable course trajectories of anxiety disorders in adolescent or young adult samples. However, several studies (cross-sectional or longitudinal, among adolescents or adults) focused on individual variables and their associations with specific course characteristics of anxiety disorders such as persistence/chronicity, remission, or recurrence. Respective findings are summarized below.

Sex

There is some evidence that females may be at elevated risk not only for disorder onset but also unfavorable course characteristics of anxiety [33••, 57, 59••, 61, 62]. For instance, levels of anxiety in girls were found to be consistently higher and to less strongly decrease over the course of adolescence compared to boys [58, 62]. Some studies also obtained higher prevalence ratios in females, suggesting higher levels of recurrence and/or persistence of anxiety disorders in girls and women [33••, 61]. However, other research found no sex differences respecting longitudinal patterns of anxiety from childhood to adulthood [57] or revealed that adolescent girls were more often affected by fluctuating anxiety and/or depressive symptomatology, but not persistent anxiety/depressive disorders [56••]. Studies in the area of panic pathology found that both remission and recurrence were more frequent in women or that men spent a higher proportion of time in panic episodes [63–65].

Age

Preliminary findings suggest that the course of anxiety disorders may be particularly unfavorable in younger individuals [33••, 65] and those with disorder onset early in life [47•, 66]. For instance, an earlier onset was associated with higher persistence of SAD [47•] and an elevated risk of recurrence of panic disorder with agoraphobia [66]. However, there are also studies that found anxiety disorders to be more persistent in older than in younger adolescents [67]. An older age might be especially associated with an unfavorable course of fears and anxiety typically occurring later in life; e.g., persistence of fear of falling was shown to be more likely among older individuals [68].

Other Demographic Variables

Besides, demographic characteristics such as lower socioeconomic status, lower education, lower income, unemployment, being unmarried, or having no children were shown to be associated with unfavorable course trajectories of anxiety/depression [57, 69], higher persistence [33••], lower probability of remission [64, 70], or higher risk of recurrence of anxiety [71•].

Characteristics of Anxiety Symptomatology

Several studies suggest that clinical features of anxiety symptomatology (e.g., higher severity and persistence) may be particularly useful to inform on the course of anxiety disorders [47•, 63, 64, 69, 71•, 72–75, 76•, 77]. For example, using data of the Netherlands Study of Depression and Anxiety (NESDA), a large prospective-longitudinal cohort study among adults with anxiety and/or depressive disorders and healthy controls, Hendriks et al. [72] revealed that higher severity and duration of anxiety arousal and avoidance in those with current anxiety disorder(s) at baseline predicted lower probability of remission and increased risk of persistence until 2-year follow-up. Among participants with past but not current anxiety disorder(s) of the same study, higher persistence and severity of anxiety and avoidance symptoms prior to/at baseline predicted an increased risk of recurrence until 2-year follow-up [71•]. Within the Netherlands Mental Health and Incidence Study, a prospective study of adults from the community, higher severity of panic and agoraphobia predicted higher persistence of panic pathology [63], while higher frequency of panic attacks predicted lower probability of remission [64]. Within the EDSP, specific characteristics of initial panic symptomatology (such as consumption of alcohol/drugs/medication and feelings of anxiety/depression as perceived reasons and consequences of initial panic symptomatology, negative appraisal, and subsequent avoidance) were associated with the development of full-blown panic attacks and panic disorder [74]. In line with these findings, several other studies found that higher levels of anxiety-related avoidance behavior [47•, 72, 75, 76•], catastrophic anxiety cognitions [47•], or higher impairment/disability due to anxiety [47•, 71•, 77] were associated with higher persistence, lower chance of remission, or increased risk of recurrence of anxiety disorders.

Comorbidity

Moreover, previous research consistently revealed that comorbid other mental disorders (e.g., past or current other anxiety, depressive, somatoform, substance use, or personality disorder(s); presence of panic attacks) and somatic diseases were associated with more unfavorable course characteristics of anxiety disorders [31, 47•, 63, 65, 67, 69, 70, 71•, 76•, 77–82]. For example, within the Harvard/Brown Anxiety Disorders Research Program, a prospective study among adults with past or current anxiety disorder, Bruce et al. [31] found that comorbid anxiety, depressive, and/or substance use disorders predicted lower probability of remission and elevated risk of recurrence of anxiety disorders over 12 years. Using large-scaled, prospective-longitudinal data, Ansell et al. [79] examined associations of personality disorders with onset, remission, and relapse of individual anxiety disorders over a time period of 7 years and showed that schizotypal, avoidant, and/or obsessive-compulsive personality disorders were associated with a more unfavorable course of SAD, panic disorder, GAD, posttraumatic stress disorder, and/or obsessive-compulsive disorder.

Personality, Temperament, and Other Individual Characteristics

In addition, there is evidence for specific temperamental and personality traits to predispose for an unfavorable course of anxiety disorders [64, 70, 71•, 83]: For instance, elevated anxiety sensitivity and neuroticism were revealed to be associated with recurrence of anxiety disorders [71•] as well as with lower probability of remission from panic pathology (subthreshold or threshold panic disorder) [64] or SAD [70]. Higher persistence, lower probability of remission, and increased risk of recurrence of anxiety disorders were further related to other individual characteristics such as lower levels of self-worth, self-esteem, mastery, or life satisfaction [62–64, 71•, 78].

Early Adversities

In the area of environmental risk factors, especially early adversities such as childhood abuse and neglect, violence, unfavorable parental rearing, and family dysfunction seem to increase the risk for an unfavorable course of anxiety disorders

[56••, 71•, 84•, 85, 86], particularly in combination with other risk factors such as familial liability [85]. For examples, within the EDSP, family dysfunctioning (dysfunctional communication, affective overinvolvement, and general dysfunction) but not unfavorable parental rearing was associated with higher persistence of SAD. Both family dysfunctioning and unfavorable parental rearing interacted with parental psychopathology on predicting persistence of SAD in a way that (a) parental overprotection only predicted higher persistence of SAD in those with parental SAD and (b) dysfunctional problem solving only predicted higher persistence of SAD in those with any parental disorder [85].

Stressful Life Events and Daily Hassles

Also major and minor stressors were found to elevate the risk for an unfavorable course of anxiety disorders. For instance, previous research revealed that a higher number of negative life events was associated with higher persistence of anxiety disorders [67], that lacking positive life events, ongoing difficulties, and stressors regarding family, friends, and household were related to higher persistence or lower probability of remission from panic pathology [63, 64], and that higher levels of daily hassles were associated with reduced chance of remission from SAD [70].

Conclusions

Anxiety disorders are common, associated with substantial impairment and disability, and strongly increase the risk for developmental complications and secondary other mental disorders. They typically have an early onset in childhood and are often characterized by a progressive, persistent/chronic, or recurrent course. This emphasizes the need for preventive and early treatment interventions in high-risk individuals and those at initial stages of anxiety disorders who are predisposed for unfavorable course trajectories and developmental complications. Thus, it is required to examine not only risk factors for onset but also predictors of the course of anxiety disorders.

Several risk factors for unfavorable course characteristics of anxiety disorders (including persistence, lower probability of remission, and increased risk of recurrence) have been identified, and previous research suggests that particularly clinical features of previous/current anxiety symptomatology (e.g., longer duration, higher severity, and higher impairment) as well as the existence of comorbid other conditions are useful as predictors of an unfavorable course. Nonetheless, far more studies focused on risk factors for incident anxiety, and merely a few prospective-longitudinal studies to date investigated and compared the role of multiple (individual, familial, and environmental) variables for an unfavorable course of anxiety disorders (or individual course trajectories, e.g., persistent vs. "waxing and waning symptomatology"). Moreover, little is known on whether predictors for an unfavorable course differ from those for onset or vary with respect to individual anxiety disorders. Also, previous research sparsely examined complex interactive effects between individual, familial, and/or environmental variables on predicting persistence or recurrence of anxiety disorders.

Thus, future research in this field is essential in order to more precisely identify individuals with subthreshold or initial anxiety disorders who are at increased risk for progressive, persistent, or recurrent symptomatology and might therefore especially profit from targeted preventive and early treatment interventions.

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Ethical Standards The manuscript does not contain clinical studies or patient data.

Compliance with Ethics Guidelines

Conflict of Interest Eva Asselmann and Katja Beesdo-Baum declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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