

I

General Introduction

Paul Emmelkamp

University of Amsterdam, the Netherlands

Thomas Ehring

University of Münster, Germany

Overview of the Handbook

The aim of this two-volume handbook is to provide a comprehensive overview of the current knowledge on the phenomenology, classification, epidemiology, etiology, and clinical management of anxiety disorders. Whereas Volume 1 focuses on theory and research, Volume 2 covers assessment and treatment issues. For the most part, the different chapters of this handbook focus on the state of the art of theory, research, and treatment. However, as the field of anxiety disorders is a very vibrant one with a considerable amount of theoretical, empirical, and clinical innovation and refinement, all chapters additionally cover current developments and future directions in their respective fields. In addition, the handbook concludes with two chapters explicitly focusing on future perspectives from a psychological and psychiatric perspective respectively.

Some months before the publication of this handbook, the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) was introduced (APA, 2013). In the new DSM-5 – and also the ICD-11, which is currently in preparation – the definition of anxiety disorders has changed considerably in comparison to the DSM-IV-TR (APA, 2000). Most importantly, obsessive-compulsive disorders (OCD) and posttraumatic stress disorder (PTSD) are now no longer classified as anxiety disorders. Based on this recent development, one may have decided to publish a considerably slimmer book focusing on anxiety disorders according to the DSM-5 only. However, instead we decided to include OCD and PTSD that have formerly been classified in this category and certainly show a close relationship with anxiety disorders in the stricter sense. In addition, a number of supplementary anxiety-related disorders and problems are covered, including Illness Anxiety, Body Dysmorphic Disorder, Sexual Anxiety, and Test Anxiety.

As a lead-up to the specialized chapters in this handbook, this introductory chapter will give a brief overview, providing basic information regarding the definition, prevalence, etiology, and treatment of anxiety and related disorders. Throughout the

introduction, we will refer to the different chapters of this handbook for more detailed information.

Prevalence, Course, and Consequences

Anxiety disorders are the most prevalent group of psychiatric disorders, being more than twice as frequent as mood disorders (Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012). Lifetime and 12-month prevalence rates are highest for social phobia and specific phobias, and lower for panic disorder, agoraphobia, and obsessive-compulsive disorder (see Chapter 3, this volume). However, nearly all studies have been conducted in North America and Western Europe, so it is unclear whether these results also apply to other continents (see Chapter 6, this volume).

Anxiety disorders often begin at an early age, are typically quite persistent throughout the life course, and are associated with considerable developmental, psychosocial, and psychopathologic complications. Comorbidity with other Axis I and Axis II disorders is the rule rather than the exception, whereby anxiety disorders usually precede comorbid disorders (see Chapter 3, this volume). Prospective studies found that having an anxiety disorder in adolescence increases the risk for a subsequent depressive disorder and suicide attempts (Sareen et al., 2005a).

There is extensive evidence showing that anxiety disorders carry considerable costs at an individual and societal level and are related to high levels of disability (see Chapter 4, this volume). There is also an increased risk of somatic disorders such as asthma (Scott, 2009), diabetes (Grigsby, Anderson, Freedland, Clouse, & Lustman, 2002), hypertension (Stein, Scott, & Von Korff, 2009), and heart disease (Burger, 2009). Panic disorder and agoraphobia and posttraumatic stress disorder have been found more often to be associated with specific physical disorders than simple phobia, social anxiety disorder, or generalized anxiety disorder (Cafarella, Effing, Usmani, & Frith, 2012; Player & Peterson, 2011; Sareen, Cox, Clara, & Asmundson, 2005b; Wu & Andersen, 2011).

Many patients do not receive psychological or psychiatric treatment despite the availability of a number of empirically supported treatments. However, studies across numerous different countries demonstrate that, after depression, anxiety disorders are the second most common mental disorder presented in general practice (see Chapter 5, this volume), but patients commonly present with somatic rather than emotional concerns.

Description of Anxiety Disorders

Specific phobias

Specific phobias are focused upon, and restricted to, fear of specific objects and situations (see Chapter 18, this volume). Typical examples are animals, heights, storms, darkness, enclosed spaces, needles, blood, or injury, but in fact specific phobias can develop in response to almost any type of object. The key feature differentiating specific phobia from agoraphobia is that, in the case of agoraphobia, the fear is due to

anticipated difficulty in escaping or getting help should a panic attack or symptoms occur.

Specific phobia is the most common of all mental disorder with a lifetime prevalence in the community of up to 10% (Emmelkamp & Wittchen, 2009). The prevalence of specific phobias varies considerably across the lifespan. Studies in childhood, adolescent, and young adult samples usually report the highest prevalence (12-month: 6–8%), whereas prevalence rates among older adults (after age 50) appear to be lower (12-month: 4–6%), and after age 65 substantially lower (12-month: 2%). In DSM-5, the core features of specific phobia remain the same, but there is no longer a requirement that individuals over age 18 years must recognize that their fear and anxiety are excessive or unreasonable, and now the phobia has to last for 6 months or more, not only for children, as in DSM-IV, but also for adults.

Social anxiety disorder

Social anxiety disorder (social phobia) is defined as fear of scrutiny by other people leading to avoidance of social situations (see Chapter 20, this volume). These may be discrete (i.e., restricted to eating in public, to public speaking, or to encounters with the opposite sex) or diffuse, involving almost all social situations. Common features of social anxiety disorder include physical symptoms of blushing, sweating, or trembling, and fears of negative evaluation. Social phobia or social anxiety disorder is a commonly occurring mental disorder with a lifetime prevalence of 7–12% in Western cultures. Social anxiety disorder prevalence has been exhibiting prominent discrepancy between different cultures. In community studies using DSM-IV criteria the rates of social anxiety disorder are much lower in East Asia (Emmelkamp, 2012).

It is now acknowledged that social phobia often occurs in a variety of social situations rather than in one specific social situation. The diagnosis requires that a person's fear or anxiety be out of proportion in frequency and/or duration to the actual situation. It is no longer required that individuals over age 18 years must recognize that their fear or anxiety is excessive or unreasonable. The symptoms must be persistent, however, lasting 6 months or longer, not only for children, as was the case in DSM-IV, but now also for adults. Further, in DSM-5 the person must suffer significant distress or impairment that interferes with his or her ordinary routine in social settings, at work or school, or during other everyday activities. As to social anxiety disorder in children, DSM-5 includes two more behaviors as characteristic for social anxiety (i.e., extreme clinging and not being able to speak in social situations) in addition to severe, prolonged crying or tantrums, becoming physically immobilized or shrinking away from other people. These behaviors can occur as a reaction to people the child knows or to a stranger.

Panic disorder and agoraphobia

Panic disorder and agoraphobia are prevalent anxiety disorders with a lifetime prevalence estimate of approximately 4–5% (see Chapter 19, this volume). They are associated with high levels of disability and high medical utilization.

Panic disorder Panic disorder is characterized by recurrent panic attacks accompanied by at least four symptoms. The essential features of panic attacks remain the same in DSM-5, but now a differentiation between unexpected and expected panic attacks is coded. Further, the presence of panic attacks can be listed as a specifier that is applicable to all DSM-5 disorders.

Agoraphobia Agoraphobia is defined as marked fear or anxiety about using public transport, being in an open space, being in enclosed spaces, standing in line, being in a crowd, or being outside of the home alone. To distinguish agoraphobia from specific phobia, fear should be present for at least two agoraphobia situations. As in social anxiety disorder, in DSM-5 the criteria for agoraphobia no longer include the requirement that individuals over age 18 years recognize that their anxiety is excessive or unreasonable. Now the anxiety must be out of proportion to the actual danger or threat and fears should be present for a duration of 6 months or more.

Panic disorder and agoraphobia Panic disorder and agoraphobia are no longer linked in DSM-5. The co-occurrence of panic disorder and agoraphobia is now coded with two diagnoses: panic disorder and agoraphobia, each with separate criteria. This change recognizes that a substantial number of individuals with agoraphobia do not experience panic symptoms (Emmelkamp & Powers, 2009).

Generalized anxiety disorder

Generalized anxiety disorder (GAD) is characterized by excessive anxiety and worry about a number of events or activities (see Chapter 21, this volume). The individual finds it difficult to control the worry and the anxiety and worry is characterized by at least three symptoms consisting of restlessness, being easily fatigued, difficulty concentrating, irritability, muscle tension, and sleep disturbance. Importantly, the anxiety, worry, or complaints cause significant distress in important areas of functioning. The 12-month prevalence of GAD is estimated to be between 2% and 5% (See Chapter 21, this volume).

New anxiety disorders

The following disorders used to be classified in other sections of DSM-IV and have now been added to the anxiety disorders section for the first time in DSM-5.

Separation anxiety disorder In DSM-IV, separation anxiety disorder was originally included in the section “Disorders Usually First Diagnosed in Infancy, Childhood, or Adolescence,” but is now classified as an anxiety disorder in DSM-5. Criteria no longer specify that age at onset must be before 18 years and the criteria have been adapted to enable coding symptoms representative of separation anxiety symptoms in adulthood. Relatively few studies have addressed separation anxiety disorder in adulthood and most studies are based on self-report questionnaires rather than on structured clinical interviews. The few studies so far suggest that separation anxiety disorder in adulthood is highly comorbid with panic disorder and agoraphobia (e.g., Pini et al.,

2010; Silove & Marnane, 2013; Silove, Marnane, Wagner, Manicavasagar, & Rees, 2010). Moreover, a recent meta-analysis of 20 studies reveals that children with childhood separation anxiety disorder were more likely to develop panic disorder in adulthood (Kossowsky et al., 2013). Although DSM-5 allows separation anxiety disorder to grow up (Marnane & Silove, 2013), future studies are needed to support the classification of separation anxiety disorder as a stand-alone disorder in adulthood (Bögels, Knappe, & Clark, 2013).

Selective mutism Selective mutism, originally also classified in the section “Disorders Usually First Diagnosed in Infancy, Childhood, or Adolescence,” is now classified as an anxiety disorder, but the diagnostic criteria are more or less the same as in DSM-IV.

Description of Anxiety-related Disorders

In DSM-5, obsessive-compulsive disorder (OCD), posttraumatic stress disorder (PTSD), and acute stress disorder are no longer included in the section on anxiety disorders, although the clinical utility of this recategorization is questionable. OCD is now part of the section “Obsessive-Compulsive and Related Disorders,” which also includes body dysmorphic disorder, hoarding, trichotillomania, and skin-picking. PTSD and acute stress disorder are now classified in the section “Trauma- and Stressor-Related Disorders,” which additionally comprises reactive attachment disorder, disinhibited social engagement disorder, adjustment disorders, and unspecified trauma- and stressor-related disorder.

Obsessive-compulsive disorder

Obsessive-compulsive disorder (OCD) is characterized by intrusive obsessions and/or compulsive behavior such as washing, cleaning, and checking or mental acts that cause significant distress, are time consuming, and interfere in normal functioning (see Chapter 24, this volume). Obsessions can consist of persistent thoughts, images, or impulses. DSM-5 introduces a number of specifiers, thus acknowledging that individuals with OCD may present with a range of insight into their disorder-related beliefs. A distinction is now made between individuals with good or fair insight, poor insight, and absent insight/delusional OCD beliefs. Importantly this change implies that OCD with the specifier absent insight/delusional beliefs no longer should be diagnosed as a schizophrenia spectrum disorder. OCD is not very common, the lifetime prevalence in population studies varying between 1% and 3% (see Chapter 24, this volume).

Hoarding disorder

Hoarding disorder is a new diagnosis in DSM-5. In DSM-IV, hoarding could be diagnosed as a variant of OCD. It is held that there is evidence for the diagnostic validity and clinical utility of a separate diagnosis of hoarding disorder (APA, 2013), but further research is needed to justify this claim.

Posttraumatic stress disorder

There have been a number of changes in DSM-5 regarding the diagnosis of PTSD (see Chapter 23, this volume). This includes the fact that the trauma criterion is now more explicitly formulated. To fulfill the trauma criterion, the person was exposed to death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence. In contrast to DSM-IV, the person has no longer to have experienced intense fear, helplessness, or horror. As in DSM-IV, core features of the DSM-5 diagnosis are that the traumatic event is persistently reexperienced and that the individual avoids trauma-related thoughts or feelings and/or trauma-related stimuli. In addition, the person can be characterized by alterations in cognitions and mood as a result of the traumatic event and by constricted affect, i.e., unable to experience positive emotions. Further, there should be evidence that the person suffers from trauma-related alterations in arousal and reactivity such as aggressive, reckless, or self-destructive behavior, sleep disturbances, or hypervigilance. As in DSM-IV, the symptoms should be present for more than 1 month. Two specifications are included in DSM-5: (1) delayed expression and (2) a dissociative subtype. Further, diagnostic thresholds have been lowered for children and adolescents. Furthermore, DSM-5 includes a new developmental subtype of PTSD called posttraumatic stress disorder in preschool children.

PTSD is highly prevalent. In the USA the lifetime prevalence of PTSD in population surveys ranges from 6% to 9%, but the prevalence in other Western countries is somewhat lower. In most studies the lifetime prevalence of PTSD is twice as high in women than in men (see Chapter 23, this volume).

Illness anxiety disorder

Hypochondriasis has been eliminated as a disorder in DSM-5. Former patients with hypochondriasis according to DSM-IV criteria are now diagnosed with either somatic symptom disorder or illness anxiety disorder (see Chapter 26, this volume). Individuals who are characterized by having significant somatic symptoms in addition to high health anxiety will now be diagnosed with *somatic symptom disorder*. Individuals with high health anxiety but without somatic symptoms will, according to DSM-5, be diagnosed with *illness anxiety disorder*, unless their health anxiety is better explained by generalized anxiety disorder.

Relationship between anxiety and mood disorders

There is growing evidence that mood and anxiety disorders have shared components (e.g., Mineka, Watson, & Clark, 1998). In preparing DSM-5, there were discussions on the question of whether mood and anxiety disorders should be collapsed into two classes: (1) “fear disorders,” which included panic disorder, agoraphobia, social anxiety disorder, and specific phobias, and (2) “internalizing disorders,” which included depression, GAD, and PTSD (see Chapter 2, this volume). However, as the DSM-5 committee felt that the existing evidence was not robust enough, it decided that DSM-5 should maintain separate sections for mood and anxiety disorders.

Etiology of Anxiety and Related Disorders

Cognitive-behavioral perspective

Numerous laboratory-based studies have investigated learning processes involved in the development of fear. In simple classical conditioning models, a single discrete conditioned stimulus is paired with a fearsome unconditioned stimulus. As early as 1920, Watson and Rayner succeeded in changing a healthy 11-month-old baby (little Albert) into an anxious one by classical conditioning. The experimental procedure consisted of pairings of a white laboratory rat (CS) with a loud sound (UCS) made by striking a hammer on a suspended steel bar. After seven joint stimulations, the rat, now presented without sound, triggered a fear response, and the fear generalized to previously neutral objects such as a dog, fur coat, and cotton wool. Unfortunately, a number of other studies failed to condition fear in infants. Given the complexity of the development of phobias in clinical patients going beyond simple classical conditioning experiences, modern laboratory studies have focused on context and inhibitory conditioning, stimulus competition, and stimulus generalization. These more complex training procedures in the laboratory show that at-risk individuals are characterized by a more chronic apprehension of danger, by a deficit in safety learning, and by fear of overgeneralization (see Chapter 7, this volume).

Other influential theories concerning the etiology of anxiety and related disorders have been proposed by cognitively oriented therapists. In their view anxiety reactions are mediated by faulty appraisal of situations. Contemporary cognitive models of anxiety and anxiety-related disorders are heavily influenced by the seminal works of Albert Ellis (1972) and Aaron T. Beck (Beck & Clark, 1997; Beck, Emery, & Greenberg, 1985). Over the last two decades, a number of studies have shown higher levels of threat appraisal in anxiety disorders and anxiety-related disorders which are triggered by maladaptive cognitive schemas (see Chapter 8, this volume). These maladaptive schemas lead to inadequate coping of anxious patients such as safety seeking (e.g., Beesdo-Baum et al., 2012) and thought suppression (e.g., Ólafsson et al., 2013), thus reinforcing these maladaptive schemas. In addition to clinical cognitive approaches, there is an extensive experimental literature investigating information-processing biases in anxiety disorders (see Chapter 9, this volume), for example attentional bias toward disorder-specific threat (e.g., Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van IJzendoorn, 2007).

In recent years, it has increasingly been argued that traditional cognitive-behavioral approaches should be complemented by a larger focus on emotional processes; in line with this view, there is now an emerging literature on the role of emotion functioning and emotion regulation in anxiety disorders (see Chapter 12, this volume).

Developmental perspective

The age of onset of anxiety disorders, especially of specific phobia and of social anxiety disorder, is much earlier than for other mental disorders and irrespective of diagnosis increases the risk of developing a mental disorder later in life. There is some evidence that there are sensitive periods during childhood to develop specific types of fears,

but this on its own does not explain which underlying mechanisms are responsible for the development of anxiety disorders (see Chapter 10, this volume). Research from a developmental perspective has focused on risk factors enhancing the likelihood of developing an anxiety disorder and protective factors enhancing resilience in at-risk children. There is robust evidence that familial transmission plays an important role in the development of anxiety disorders, which can be partly explained by genetic factors (Burt, 2009; see also Chapter 14, this volume) and partly by family factors such as parental rearing, attachment, and parental self-efficacy (see Chapters 10 and 11, this volume). Research has also addressed the issue of how attachment and anxiety are related and there is some evidence that lack of adequate emotion regulation strategies may mediate the relationship between attachment and anxiety (Ejsborn, Bender, Reinholdt-Dunne, Munck, & Ollendick, 2012; see also Chapters 11 and 12, this volume).

Personality traits

A number of studies have addressed the issue of whether personality traits are related to specific anxiety disorders. In a recent meta-analysis, results of studies investigating the relationship between anxiety disorders and the five personality factors of the “Big Five” model of personality were analyzed (Kotov, Gamez, Schmidt, & Watson, 2010). Results revealed that individuals with anxiety disorders score high on neuroticism and low on extraversion and conscientiousness. Generally, the big five traits were unrelated to specific anxiety disorders, apart from extraversion, which was strongly negatively related to social anxiety disorder. Given the cross-sectional nature of most of the studies in this area, longitudinal studies are needed to enhance our understanding of the role of personality in the etiology of anxiety and anxiety-related disorders (see Chapter 13, this volume).

Biological processes

A large number of studies on anxiety disorders have included measures of peripheral physiological activation and central nervous system measures from the electroencephalograms (EEG) of anxious patients; these studies are reviewed in Chapter 17 (this volume). Anxiety and related disorders are related to stress, which through the hypothalamic–pituitary–adrenal (HPA) axis can alter glucocorticoid (GC) levels and thereby change the structure and function of neurons in specific brain regions associated with anxiety (see Chapter 16, this volume). Further, over the past decade an increasing number of studies have examined structural and functional neural pathways in anxiety and anxiety-related disorders (see Chapter 15, this volume). Most of these studies addressed neural alterations during specific emotion-processing tasks. There is consistent evidence that the limbic-medial prefrontal neural circuit is involved in various anxiety disorders, but not in obsessive-compulsive disorder. In PTSD, not only is the limbic-medial prefrontal neural circuit involved, but so is the hippocampus as well.

Treatment

Research over the past few decades has shown that specific forms of psychotherapy are effective and highly beneficial for most anxiety and anxiety-related disorders.

For anxiety and related disorders several variants of psychotherapy have been established in clinical randomized trials as effective and are recommended first-line treatments by the American Psychological Association (APA/Division 12/Society for Science of Clinical Psychology/SSCP), Cochrane Reviews (www.cochrane.org), and the National Institute for Health and Clinical Excellence Guidelines (NICE Guidelines; <http://www.nice.org.uk>). There is considerable evidence that cognitive-behavior therapy (CBT) is effective in a variety of anxiety and related disorders such as specific phobias (see Chapter 45, Volume 2), social anxiety disorder (see Chapter 47, Volume 2), GAD (see Chapter 48, Volume 2), panic disorder and agoraphobia (see Chapter 46, Volume 2), childhood anxiety disorders (see Chapter 49, Volume 2), PTSD (see Chapter 50, Volume 2), and OCD (see Chapter 51, Volume 2). The evidence for other psychotherapies is limited, but there is emerging data suggesting that interpersonal and emotion-focused processing psychotherapy (see Chapter 41, Volume 2), metacognitive therapy (see Chapter 37, Volume 2), and mindfulness and acceptance-based behavioral therapies (see Chapter 39, Volume 2) may have some value in GAD and manualized psychodynamic therapy in GAD and social anxiety disorder (see Chapter 42, Volume 2).

There is robust evidence that pharmacotherapy is effective in treating most anxiety and anxiety-related disorders. As stated by Baldwin and Brandish (see Chapter 43, Volume 2), “The ideal pharmacological treatment would be effective in all anxiety disorders, across all symptom domains, across the range of severity, in achieving remission, in preventing relapse, and in treating comorbid conditions, would have a rapid onset of effect, and be cost-effective in clinical practice. It would be suitable for once-daily use, have no side effects, and would not interfere with daily life” (pp. 865–866). Unfortunately, this ideal drug does not exist, but there are a number of drugs for which effects have been established in specific anxiety disorders (see the respective chapters in Volume 2). Unfortunately, a substantial number of patients will experience side effects and/or will relapse. Potential markers for successful pharmacotherapy in patients with anxiety disorders, such as genetic polymorphisms, have hardly been studied and are not ready for use in routine clinical practice. A few studies have addressed the issue of whether combining CBT and pharmacotherapy is more effective than either as a stand-alone treatment. There is some evidence that such a combination treatment is more effective than pharmacotherapy alone but not more effective than CBT as a stand-alone treatment (see Chapter 44, Volume 2).

A number of studies have investigated whether cognitive enhancers augment CBT-induced learning and memory processes without having a direct anxiolytic effect. A number of clinical trials have compared exposure-based CBT plus a cognitive enhancer to exposure-based CBT plus a placebo pill. Most studies have investigated the effects of the cognitive enhancer d-cycloserine, a partial NMDA glutamate receptor agonist. Generally, the cognitive enhancer d-cycloserine enhanced the effects of exposure (Bontempo, Panza, & Bloch, 2012; see also Chapter 65, Volume 2). Two studies have tested the effect of another cognitive enhancer, yohimbine (which increases levels of noradrenaline) as an adjunct to exposure. In the first study (Powers, Smits, Otto, Sanders, & Emmelkamp, 2009), the yohimbine plus exposure group showed significantly less return of fear at one week follow-up than the placebo plus exposure group, but the superiority of yohimbine over placebo was not replicated in flight phobias (Meyerbröker, Powers, van Stegeren, & Emmelkamp, 2012).

Looking Ahead

A number of recent developments may have a profound influence on the treatment of anxiety and anxiety-related disorders in the coming years. In the past, patients with comorbid disorders were often excluded from treatment studies. However, there is now emerging research on the treatment of anxiety disorders with comorbid substance use disorder (van Dam, Ehring, Vedel, & Emmelkamp, 2013; see also Chapter 52, Volume 2), depression (see Chapter 53, Volume 2), and personality disorder (see Chapter 54, Volume 2). Other developments concern technological innovations such as treatment delivered through the Internet (Ruwaard, Lange, Schriecken, Dolan, & Emmelkamp, 2012; see also Chapter 61, Volume 2), treatment using virtual reality technology (see Chapter 63, Volume 2), and cognitive bias modification procedures (see Chapter 64, Volume 2). Treatment studies along these lines are ongoing and may eventually lead to further implementation in clinical practice. Finally, research into moderators and mediators of treatment is still in its infancy (see Chapters 40 and 56, Volume 2). There is a clear need for studies into the processes underlying evidence-based treatments to better understand the mechanisms involved and to prevent failure (see Chapter 55, Volume 2).

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