Anxiety Disorders Diagnosis: Some History and Controversies

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Abstract Treatment of and research on anxiety disorders depends on the adequate conceptualization and measurement of these conditions. We review the history of the nosology of anxiety disorders and note that divisions of "neurosis" have inadvertently taken attention away from what is shared among conditions now classified separately. We note the changes in the definition of agoraphobia over time and the striking differences between DSM-IV and ICD-10 definitions. We mention ongoing controversies in the diagnoses of posttraumatic stress disorder, acute stress disorder, and generalized anxiety disorder. Finally, we discuss

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controversies surrounding the proper placement of obsessive-compulsive disorder and putatively related conditions in future diagnostic classifications. We hope that reviewing controversial aspects of diagnosis is useful to clinicians and researchers interested in the neurobiology of anxiety disorders.

Keywords Anxiety disorder · Nosology · Classification · Agoraphobia · Posttraumatic stress disorder · Acute stress disorder · Generalized anxiety disorder · Obsessive-compulsive disorder

1 Introduction

In this chapter, we intend to familiarize readers with some of the historical origins of the anxiety disorders section of the Diagnostic and Statistical Manual of Mental Disorders (DSM), fourth edition (APA 1994), noting some differences between this and the similar section in the International Classification of Diseases (ICD), tenth edition (WHO 1992, 1993). We will use these foundations to discuss some ongoing nosologic controversies. We submit that an understanding of the limitations of classification is vital to clinicians and researchers interested in the neurobiology of anxiety disorders. Though we mentioned some of these issues in a previous chapter (Stein and Bienvenu, 2008), our emphasis is different here in that we focus more on individual diagnostic constructs and less on higher-order constructs and dimensions.

Before we begin, it is important to emphasize that we are all affected by our conceptualizations of psychopathology, and these conceptualizations *matter* in clinical practice and research. For example, in a group of studies conducted in the 1960s (the US/UK diagnostic project), researchers found that American psychiatrists had a relatively broad concept of schizophrenia compared with British psychiatrists, who more frequently diagnosed mood, "neurotic," and personality disorders (Cooper et al. 1969; Gurland et al. 1969; Kendell et al. 1971; Kramer 1969; Zubin 1969). Making note of such differences was important not just to clarify why so many Americans were diagnosed with schizophrenia, compared to Brits. That is, the illustration of these differences was important because reliable diagnoses are *essential* for studies of etiology, prognosis, and treatment effectiveness that inform clinical practice. Studies like these gave impetus to the development of explicit diagnostic criteria (Feigner et al. 1972; Spitzer et al. 1978) that prepared the way for DSM-III (APA 1980).

2 A Brief History of Anxiety Disorders Classification

Though anxiety itself has been discussed for millennia (McReynolds 1975), its appearance as a syndrome in the medical literature is a relatively recent phenomenon (Stone 2002). In the eighteenth century, physicians such as Boissier de Sauvages (1752), Battie (1758), Whytt (1765), and Cullen (1807) wrote of

"panophobia" (fear of everything), "praeternatural anxiety" (anxiety outside the normal range), "nervous disorders," and "neurosis," respectively (Stone 2002). Notably, by "neuroses" (nerve conditions) Cullen meant "those affections. . .which do not depend on topical affection of organs but upon general affection of the nervous system" (Knoff 1970); thus, the neuroses originally included a number of neurologic and psychiatric conditions, not just what we now call anxiety, depressive, somatoform, and dissociative disorders. Over time, the term "neurosis" has endured, though the group of phenomena it describes has narrowed, and the term has carried varying etiologic connotations (Stone 2002).

It is worth mentioning, in passing, that in the mid–late nineteenth century Beard coined the term "neurasthenia" (weakness of the nerves) (Beard 1880). This popular label was subsequently applied to what we now recognize as a broad range of anxiety and other syndromes (Stone 2002), though "neurosis" outlasted "neurasthenia" as a broad psychopathologic descriptive term [note that a much narrower definition of neurasthenia remains in ICD-10 (WHO 1992)]. Meanwhile, a number of other categories within neurosis were more or less delineated (Tyrer 1985), including agoraphobia (Westphal 1872), anxiety neurosis (Freud 1895/1962), specific and social phobias (Hartenberg 1901; Marks 1970; Ribot 1896), obsessive-compulsive neurosis (Janet 1908), milder depressive states (Lewis 1938), and panic disorder (Klein 1964). We say "more or less delineated" since most of the listed authors described relatively broad, overlapping syndromes. "Neurosis" was a broad diagnostic category in DSM until the third edition (APA 1980), and it remains a broad diagnostic category in ICD-10 (WHO 1992).

Table 1 summarizes the classification of neurotic and anxiety disorders from DSM-I through DSM-IV (APA 1952, 1968, 1980, 1987, 1994). Note that the authors of DSM-III moved somatoform and dissociative disorders to separate categories, eliminated "depressive neurosis," grouped the remaining former "neurotic" disorders as "anxiety disorders," and added posttraumatic stress disorder (PTSD) to this new category. By DSM-III, the term "neurosis" had long taken on psychoanalytic etiologic implications. DSM-III and its descendants were meant to provide atheoretical descriptions of mental disorders; this is why the term "neurosis" was phased out, despite its value and history as a descriptive term (Fava et al. 2008; Frances et al. 1993; Tyrer 1985). Table 2 summarizes the "Neurotic, stress-related, and somatoform disorders" in ICD-10 (WHO 1992).

By far, the most marked change in classification of the anxiety disorders occurred with DSM-III. All psychiatric diagnoses were defined more explicitly than before, with diagnostic criteria that facilitated clearer communication for clinical practice and research. In addition, the anxiety disorders were given substantially more attention (Frances et al. 1993), with the delineation of panic disorder and generalized anxiety disorder (GAD) from "anxiety neurosis" and the categorization of different kinds of phobias, including agoraphobia, social phobia, and simple (specific) phobia.

Notably, there are reasons to question the utility of carving neurosis into separate categories (Tyrer 1985). Long before explicit diagnostic criteria were developed, change over time and cross-sectional comorbidity among the various neurotic conditions was recognized as common (Slater and Slater 1944). This is no less

Table 1 Classification of neurotic/anxiety disorders in the American Psychiatric Association's Diagnostic and Statistical Manuals of Mental Disorders

DSM-I psychoneurotic disorders (1952)	DSM-II neuroses (1968)	DSM-III anxiety disorders (1980)	DSM-III-R anxiety disorders (1987)	DSM-IV anxiety disorders (1994)
Phobic reaction	Phobic neurosis	Agoraphobia with panic attacks	Agoraphobia without history of panic disorder	Agoraphobia without history of panic disorder
		Agoraphobia without panic attacks	Social phobia	Social phobia
		Social phobia	Simple phobia	Simple phobia
		Simple phobia		
Anxiety reaction	Anxiety neurosis	Panic disorder	Panic disorder with agoraphobia	Panic disorder with agoraphobia
		Generalized anxiety disorder	Panic disorder without agoraphobia	Panic disorder without agoraphobia
			Generalized anxiety disorder	Generalized anxiety disorder
Obsessive compulsive reaction	Obsessive compulsive neurosis	Obsessive-compulsive disorder	Obsessive-compulsive disorder	Obsessive-compulsive disorder
		Posttraumatic stress disorder	Posttraumatic stress disorder	Posttraumatic stress disorder
				Acute stress disorder
Depressive reaction	Depressive neurosis			
Conversion reaction	Hysterical neurosis			
Dissociative reaction	Neurasthenic neurosis			
	Hypochondriacal neurosis			
	Depersonalization neurosis			

Table 2 Neurotic, stress-related, and somatoform disorders in ICD-10 (1992)

Phobic anxiety disorders	Dissociative [conversion] disorders
– Agoraphobia	– Dissociative amnesia
– Social phobias	– Dissociative fugue
– Specific (isolated) phobias	– Dissociative stupor
	– Trance and possession disorders
Other anxiety disorders	– Dissociative motor disorders
– Panic disorder	– Dissociative convulsions
– Generalized anxiety disorder	– Dissociative anesthesia and sensory loss
– Mixed anxiety and depressive disorder	
	Somatoform disorders
Obsessive-compulsive disorder	– Somatization disorder
	– Hypochondriacal disorder
Reaction to severe stress, and adjustment disorders	– Somatoform autonomic dysfunction
– Acute stress reaction	– Persistent somatoform pain disorder
– Posttraumatic stress disorder	
– Adjustment disorders	Other neurotic disorders
	– Neurasthenia
	– Depersonalization-derealization syndrome

true since the introduction of explicit diagnostic criteria with DSM-III and its descendants (Andrews et al. 1990, 2002; Brown et al. 2001; Boyd et al. 1984; Creed and Barsky 2004; Freyberger and Spitzer 2005; Kessler 1995; Lieb et al. 2007; Merikangas et al. 1996). The extent of comorbidity among conditions formerly classified as neuroses has rightly turned attention toward what these conditions share, including personality correlates (Bienvenu et al. 2001; Kahn et al. 2005; Krueger et al. 2001). Factor analytic studies are consistent in finding that anxiety and depressive disorders are highly comorbid, though phobic, panic, and obsessive-compulsive disorders are particularly highly comorbid (forming a "fear factor"), and depressive, generalized anxiety, and posttraumatic stress disorders are also particularly highly comorbid (forming a "distress" or "anxious misery" factor) (Cox et al. 2002; Kendler et al. 2003; Kessler et al. 2005b; Krueger 1999; Krueger et al. 1998, 2003; Miller et al. 2008; Slade and Watson 2006; Vollebergh et al. 2001). There is also substantial evidence that anxiety and depressive disorders share a genetic basis that presumably underlies the phenotypic comorbidity patterns (Hettema 2008a; Kendler et al. 2003).

3 Controversy in Classification of Individual Anxiety Disorders

3.1 Agoraphobia Past and Present, in the United States and Elsewhere

Of all the anxiety disorders, agoraphobia's nosologic status is probably the most controversial. Westphal 1872 coined the term "agoraphobia" (fear of the

marketplace – open city squares) to describe a syndrome he encountered in his neurological/psychiatric practice. His patients had great difficulty crossing squares without extreme anxiety, though they also had difficulty in other situations – e.g., being alone on empty streets; using public transportation; being in situations like the theatre, concerts, or crowded rooms; or being in lectures and large meetings (Kuch and Swinson 1992). Westphal noted that the condition was somewhat inexplicable, though he recognized it as a condition of abnormal anxiety in particular situations with associated avoidance and resultant problems in everyday life (i.e., what we have, for many years, conceptualized as a phobia). The name "agoraphobia" has never been entirely satisfactory, as the feared situations clearly extend beyond "the marketplace"; Le Grand du Saulle 1878 preferred the term "fear of spaces" (Stone 2002). As noted by Marks 1970, the syndrome has had many other labels, including "phobic-anxiety-depersonalization syndrome," "phobic anxiety state," "locomotor anxiety," "topophobia" (fear of particular places), "kenophobia" (fear of empty spaces), and "platzangst" (place anxiety), though none of these have outlasted "agoraphobia."

As mentioned previously, categories of phobia (including agoraphobia) were not specified in the DSM until DSM-III (see Table 1). Interest in phobias appears to have increased, at least in part, due to interest in the use of behavioral therapy (Marks 1970). Also, with the delineation of panic disorder, the DSM gradually began to construe agoraphobia as strongly related to panic, even as a consequence of panic. That is, though panic and autonomic anxiety symptoms, including "fear of fear" (fear of incapacitating anxiety in certain situations), had long been noted in patients with agoraphobia (Freud 1895/1962; Westphal 1872), panic gradually became the predominant organizing symptom in the DSM (Frances et al. 1993), based largely on Klein's cogent argument that agoraphobia often developed after (and presumably as a result of) spontaneous panic attacks (Klein 1980). This influence was present in DSM-III and has increased since then (Frances et al. 1993); that is, a theory of the cause of agoraphobia has been built into the DSM definition of agoraphobia, despite the intention of DSM-III to produce an atheoretical descriptive document, and despite even Klein's observation that situational phobias (e.g., claustrophobia) often precede a first panic attack (Klein 1980). Thus, DSM-III included "agoraphobia with panic attacks" and "agoraphobia without panic attacks" (simple/specific and social phobias have never included such panic presence/absence specifiers) and stated that an agoraphobic "has marked fear of and thus avoids being alone or in public places from which escape might be difficult or help not available in case of sudden incapacitation." Restated, agoraphobia was not just fear and avoidance of specific typical situations; fear of incapacitation was built in to the definition. DSM-III-R went further, including "panic disorder with (or without) agoraphobia," as well as "agoraphobia without history of panic disorder." In "panic disorder with agoraphobia," agoraphobia was defined as "fear of being in public places or situations from which escape might be difficult (or embarrassing) or in which help might not be available in the event of a panic attack"; practioners were instructed to include "cases in which persistent avoidance behavior originated during an active phase of Panic Disorder, even if the

person does not attribute the avoidance behavior to fear of having a panic attack." Even the definition of "agoraphobia without a history of panic disorder" implied that what was feared was not the situation itself but "suddenly developing a symptom(s) that could be incapacitating or extremely embarrassing." DSM-IV went further still in the theme of agoraphobia as "fear of fear," stating that agoraphobia is "anxiety about being in places or situations in which escape might be difficult (or embarrassing) or in which help may not be available in the event of having an unexpected or situationally predisposed panic attack or panic-like symptoms." For these reasons, many modern psychiatric texts have no chapter on agoraphobia – agoraphobia is almost always discussed in chapters on panic disorder.

The DSM definition of agoraphobia stands in stark contrast to that of ICD-10. The ICD-10 definition embodies what is often referred to as the "European position," which considers agoraphobia a particularly severe phobia (Marks 1987, Fava et al. 2008), defined as a "fairly well-defined cluster of phobias embracing fears of leaving home, entering shops, crowds and public places, or travelling alone in trains, buses or planes" (WHO 1992). Thus, the focus in ICD-10 is on the fear and avoidance of the situations themselves, not on the fear of anxiety/panic in those situations. ICD-10 acknowledges the frequent accompaniment of panic, depressive, and obsessional symptoms but does not imply primacy of panic the way DSM does. ICD-10 was undoubtedly influenced by Marks 1987 and others arguments that agoraphobia should be a stand-alone diagnosis, often related to but not inextricably bound to panic. In support of this position, typical agoraphobic (situational) fears have long been noted to cluster together within individuals, separate from other types of fears (Arrindell et al. 2003, Marks 1987), and panic itself does not appear necessary for this natural clustering (Cox et al. 2003).

So, one may wonder, which definition, that in DSM or that in ICD-10, is "correct"? We submit that neither is correct in any absolute sense, since our diagnoses reflect concepts and conventions, not necessarily nature (though approximating nature as much as possible is presumably ideal). Nevertheless, it is reasonable to ask what evidence suggests panic is *causally* related to agoraphobia, as implied in DSM. In reviewing this evidence, it is important to note that definitional issues such as those outlined previously are crucial to understand and usually confusing, in part because these definitions have been a moving target. With this caveat in mind, we note several facts thoughtfully reviewed by Craske 1996 for the consideration of the DSM-IV anxiety disorders committee. [Note that, though the DSM-IV anxiety disorders committee appears to have given some consideration to the European position, they do not appear to have seriously called into question the DSM-III assumption that fear of incapacitation should define agoraphobia. We add additional context to the points reviewed by Craske]:

- Most DSM-III agoraphobics who presented to anxiety disorders clinics in 1980s American research studies did endorse panic attacks or other symptoms that could be incapacitating or embarrassing in those situations. [Since DSM-III

defined agoraphobia as fear of incapacitation, this should not be particularly surprising.]

- Early post-DSM-III epidemiologic studies, which used to measure more of an imperfect ICD-10 (fear/avoidance of situations) than DSM construct of agoraphobia, found that, though most persons with agoraphobia did not meet DSM-III panic disorder criteria, some of these respondents may have had fear of fear. [Note that this was not measured directly – i.e., the fact that respondents had autonomic anxiety symptoms, including panic attacks, in the phobic situation does not mean that respondents feared these symptoms themselves; such symptoms also occur in patients with other phobias when confronted with relevant stimuli. Also, the clinical reappraisal study by Horwath et al. 1993, which suggested epidemiologic "agoraphobia without panic" often reflected misclassification, used the DSM-III definition of agoraphobia.]
- In studies of patients with DSM panic and agoraphobia, patients often reported (retrospectively) that panic attacks preceded or began simultaneously with DSM agoraphobia. [Notably, such patients sometimes retrospectively report that agoraphobic symptoms preceded their first panic attack (e.g., Argyle and Roth 1989; Fava et al. 1988; Fava et al. 1992; Lelliott et al. 1989, Perugi et al. 1998). In addition, it is interesting that many patients with panic and agoraphobia had their first panic attack in a typical agoraphobic situation (Faravelli et al. 1992; Lelliott et al. 1989; Perugi et al. 1998)]. Craske noted that prospective longitudinal studies were nonexistent at the time of her review.
- In patients with DSM agoraphobia (usually panic disorder and agoraphobia), expectation of panic in particular situations (though not frequency, severity, or expected/cued nature of panic) predicted the degree of avoidance. Craske noted that this finding does not prove that panic is causally related to avoidance.

The authors of DSM-IV decided to continue with the "fear of fear" concept in defining agoraphobia, despite concerns raised by Craske and the definitional concerns we raise here, and despite the fact that this would conflict with the ICD-10 definition (Frances et al. 1993). Nevertheless, the authors of DSM-IV noted that the boundary between agoraphobia and situational (specific) phobia is indistinct (Craske et al. 1996). The specific feared situations overlap, and the age of onset is similar in these two putatively distinct groups.

More recent studies in community samples add credence to the notion that agoraphobia should not be defined as fear of panic (Fava et al. 2008; Hayward and Wilson 2008):

- Wittchen et al. (1998) found that many young Germans had agoraphobic syndromes (with multiple situational fears) but no history of fearful spells. These participants would meet the ICD-10 criteria for agoraphobia, though some would presumably not meet DSM criteria (e.g., persons who avoided traveling for fear of getting lost).
- Hayward et al. (2003) found that only 20% of adolescents with agoraphobic fears and avoidance had ever experienced a panic attack.

- Bienvenu et al. (2006) found that persons who had agoraphobic symptoms but no history of spontaneous fearful spells were at increased risk for a later onset of panic disorder during a 13-year follow-up period; i.e., in these persons, the DSM-implied one-way causal direction between panic and agoraphobia was backwards.

Though it is not clear how agoraphobia "should" be defined, we recognize that the DSM-IV definition has certain advantages. Specifically, compared to the definition in DSM-IV, the ICD-10 definition is relatively vague, even though it appears empirically valid. That is, in the DSM-IV definition, what is meant to be feared in typical agoraphobic situations is clear (i.e., embarrassing or incapacitating symptoms). Nevertheless, researchers, in particular, should be aware of this unresolved controversy and the lack of a clear demarcation between situational (specific) phobias and agoraphobia. In addition, researchers, in particular, should not assume that they "know" what persons with agoraphobic syndromes fear; conceptualizations do not obviate the need for a clear phenomenologic understanding.

3.2 Posttraumatic Phenomena

Though the diagnosis PTSD first appeared in DSM-III (see Table 1), the diagnosis "traumatic neurosis" (a.k.a. "shell shock," "combat fatigue," and "war neurosis") had been used for many years. Interestingly, DSM-I included a vaguely similar construct, "gross stress reaction," though this diagnosis was not carried forward into DSM-II (Andreasen 2004).

In DSM-III, PTSD was defined as a syndrome that occurred following a psychologically traumatic event that "would evoke significant symptoms of distress in almost everyone." The text noted that such events were "generally outside the range of human experience" (to differentiate this construct from common stressful experiences like simple bereavement, chronic illness, business losses, or marital conflict). In fact, this language was added to criterion A in DSM-III-R, along with examples of potential traumatic stressors (serious threats of death and injury, etc.). However, the field soon realized that many deleterious traumatic events were not outside the range of usual human experience – perhaps especially in the United States (Breslau et al. 1991; Wittchen et al. 2009), so that concept was dropped in DSM-IV. DSM-IV also expanded the definition of a potential PTSD-related trauma, including, for example, being diagnosed with a life-threatening illness. In addition, it was no longer necessary to experience the event first-hand. Thus, what was initially conceptualized as a relatively violent, immediate kind of stressor gradually changed to something substantially less well delineated. This "criterion creep" has been particularly controversial (Andreasen 2004; Breslau and Kessler 2001; McHugh and Treisman 2007; Rosen et al. 2008; Wittchen et al. 2009). Another controversial aspect of this diagnosis is that many within, and, particularly, outside the field have understood PTSD as being *caused* by the stressor in too simplistic a fashion; i.e., without consideration of

additional risk factors such as personality traits and family or personal history of psychopathology (McHugh and Treisman 2007; Rosen et al. 2008).

As noted above, the PTSD construct may be too broad and overinclusive. However, it is also arguable that the diagnostic criteria are under inclusive. For example, some studies have noted that the use of a strict PTSD definition fails to identify many persons with PTSD symptoms who have clinically significant distress and/or impairment (Marshall et al. 2001; Stein et al. 1997), though not all studies agree on the extent of impairment in subthreshold cases (Breslau et al. 2004). Notably, the DSM requirement that PTSD symptoms be spread across the three diagnostic clusters has little empirical support (Stein and Bienvenu 2008). Thus, it makes sense to consider alternate and, perhaps, easier-to-remember definitions that consider external construct validators like functional impairment (Norman et al. 2007).

The DSM-III definition of PTSD did not include a duration criterion, so patients could be diagnosed with the condition immediately after the trauma. However, depending on the nature of the trauma, many persons would be expected to have substantial symptoms immediately afterward. Thus, in DSM-III-R, a criterion was added specifying that the symptoms had to be present for at least 1 month. However, this left patients with substantial immediate PTSD symptoms and related distress and/or impairment without a diagnosis. In DSM-IV, a new diagnosis, acute stress disorder (ASD) was introduced. ASD, by definition, can only occur within 4 weeks of the trauma and can only last 4 weeks. This diagnosis emphasizes dissociative symptoms much more than PTSD does. The rationale for this emphasis was that several studies found that peritraumatic dissociative symptoms predicted later PTSD symptoms more than reexperiencing, avoidance/numbing, and hyperarousal symptoms did (Classen et al. 1998; Ehlers et al. 1998; Murray et al. 2002). Other studies, however, have not found that dissociative symptoms have unique prognostic significance (Brewin et al. 1999, 2003; Bryant et al. 2008; Harvey and Bryant 1999). In addition, many persons with PTSD apparently never met criteria for ASD, and it seems reasonable to argue that the presence of acute dissociative symptoms is simply one of several risk factors for PTSD (Marshall et al. 1999). Thus, it is unclear whether the addition of the ASD diagnosis has been particularly useful.

3.3 Generalized Anxiety Disorder

Chronic free-floating anxiety was noted by Freud 1895/1962 in his description of anxiety neurosis, and it was clear, by DSM-III, that not all patients from that category were well-characterized by the new diagnosis panic disorder. Since the introduction of GAD in DSM-III, nosologists have attempted to reliably and validly define it. Over time, the GAD construct has narrowed and may be more reliable, though many researchers have cast doubt on the validity of the narrower definitions. As noted by Hoehn-Saric et al. 2007, GAD does not appear to exist in nature as the sharply delineated condition implied in successive versions of the DSM.

In DSM-III, the duration criterion for GAD was 1 month. Similarly, in ICD-10, generalized anxiety must be present "most days for at least several weeks at a time." However, DSM-III-R (and DSM-IV) lengthened the duration requirement to 6 months, with little empirical basis (Breslau and Davis 1985). A number of community studies have used internal and external construct validators to examine whether or not the DSM duration criteria identify a unique group of individuals. These validators have included sociodemographic factors, age of onset, course, impairment, distress, severity, comorbidity, family history, and treatment for anxiety. In summary, there is little evidence that the 6-month criterion is valid in terms of describing a unique group of generalized anxiety sufferers (Angst et al. 2006; Bienvenu et al. 1998; Breslau and Davis 1985; Kessler et al. 2005a; Lee et al. 2008); shorter-duration syndromes (e.g., 1 month) appear quite similar. Importantly, generalized anxiety syndromes lasting 1 month appear as heritable as those lasting 6 months; this is inconsistent with the idea that shorter-duration generalized anxiety syndromes are purely environmentally-mediated transient stress reactions (Kendler et al. 1992a).

Since DSM-III-R, "excessive" worry "about two or more life circumstances" has been required for a GAD diagnosis, though this criterion was not present in DSM-III and is absent in ICD-10. As with the duration criterion, the nature-of-worry criteria have been examined using internal and external construct validators. Bienvenu et al. 1998 found that the DSM-III-R nature of worry criteria did not identify generally anxious persons with a particular demographic or comorbidity profile. Ruscio et al. 2005 examined the "excessive worry" criterion with regard to a broader range of construct validators and in a larger sample. The "excessiveness" criterion did identify persons with earlier-onset, more severe, and more comorbid generalized anxiety syndromes, though persons with substantial non"excessive" worry also had relatively high impairment, treatment-seeking, and comorbidity compared to persons without substantial generalized anxiety. To our knowledge, the other DSM-IV nature-of-worry criterion, "difficult to control," has not been examined using these methods.

Another DSM-IV decision is worthy of consideration here. In DSM-III and DSM-III-R, autonomic anxiety symptoms were counted as associated symptoms of GAD, and they remain so in ICD-10. However, in DSM-IV, autonomic symptoms were eliminated as associated symptoms of GAD. The rationale for excluding autonomic symptoms was that these were less frequent than hyperarousal symptoms in GAD patients in anxiety disorder specialty clinics (reviewed and examined in Marten et al. 1993). To our knowledge, this decision did not take into account the possibility that generally anxious patients presenting in primary care settings may have predominant physical symptoms, including autonomic symptoms (Rickels and Rynn 2001). To our knowledge, this issue remains unexplored.

A final controversy concerns whether GAD should be grouped with depressive disorders instead of the anxiety disorders, based on the comorbidity patterns mentioned previously (note that PTSD is also particularly highly comorbid with this group), as well as apparently overlapping genetic causes (e.g., Kendler 1996; Kendler et al. 1992b, 2006; Roy et al. 1995). Hettema (2008b) recently reviewed

the relevant literature focusing on multiple external validators of a GAD-major depression relationship, including genetics, childhood environment, demographics, personality traits and disorders, life events, biology, comorbidity, and pharmacology. He concluded that the evidence supported a close relationship between these conditions, but that this relationship was not particularly specific (i.e., other anxiety disorders are also strongly related to major depression).

3.4 OCD and Putatively Related Conditions

The most controversial issue in the nosology of OCD seems to be whether or not OCD should remain classified as an anxiety disorder, and whether putative OCD-related conditions should be classified as such in DSM-V (Hollander et al. 2008; Regier 2007). Notably, ICD-10 includes OCD in the "neurotic, stress-related, and somatoform disorders" but does not list OCD as an "anxiety disorder" (the same is true for PTSD, which is listed in the "reaction to severe stress and adjustment disorders" subsection). Additional arguments for removing OCD and grouping it with putatively related conditions include relatively distinctive phenomenology and neurocircuitry, though none of the arguments are free from controversy (Mataix-Cols et al. 2007; Stein 2008; Storch et al. 2008), and it is not clear that the remaining conditions classified as anxiety disorders are themselves homogenous in most respects. Notably, though some putative OCD-related conditions (e.g., body dysmorphic disorder) are highly comorbid in persons with OCD and appear to run in families of patients with OCD (e.g., Bienvenu et al. 2000), anxiety disorders like GAD are also common in persons with OCD and their family members (Nestadt et al. 2001).

Another controversial issue is whether compulsive hoarding (CH) should be classified within or outside of OCD. Though it has been common practice to refer to CH as an OCD symptom, some have argued that CH is a relatively discrete entity that occurs often, but not always, in the context of other OCD symptoms (Frost and Gross 1993; Steketee and Frost 2003; Wu and Watson 2005). In addition, neuropsychological and neuroimaging findings suggest some differences between those with CH and those with only other OCD symptoms (Saxena 2008). This area of research deserves further attention.

4 Summary

Anxiety disorders treatment and research depends on the adequate conceptualization and measurement of these conditions. We reviewed the history of the nosology of anxiety disorders and noted that divisions of "neurosis" have inadvertently taken attention away from what is shared among conditions now classified separately. We noted the changes in the definition of agoraphobia over time and the striking differences between DSM-IV and ICD-10 definitions. We mentioned ongoing

controversies in the diagnoses PTSD, ASD, and GAD. Finally, we discussed controversies surrounding the proper placement of OCD and putatively related conditions in future diagnostic classifications. We hope reviewing controversial aspects of diagnosis is useful to clinicians and researchers interested in the neurobiology of anxiety disorders.

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