

The history of generalized anxiety disorder as a diagnostic category

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Precursors: panophobia, neurasthenia, and anxiety neurosis

The phenomenology of generalized anxiety disorder (GAD), ie, chronic free-floating anxiety accompanied with anxious apprehension or worry about many circumstances of daily life, has been described by several authors since the dawn of modern psychiatry in

From the 19th century into the 20th century, the terms used to diagnose generalized anxiety included “pantophobia” and “anxiety neurosis.” Such terms designated paroxysmal manifestations (panic attacks) as well as interparoxysmal phenomenology (the apprehensive mental state). Also, generalized anxiety was considered one of numerous symptoms of neurasthenia, a vaguely defined illness. Generalized anxiety disorder (GAD) appeared as a diagnostic category in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) in 1980, when anxiety neurosis was split into GAD and panic disorder. The distinct responses these two disorders had to imipramine therapy was one reason to distinguish between the two. Since the revised DSM-III (DSM-III-R), worry about a number of life circumstances has been gradually emphasized as the distinctive symptom of GAD. Thus, a cognitive aspect of anxiety has become the core criterion of GAD. The validity of GAD as an independent category has been questioned from DSM-III up to preparation of DSM-5. Areas of concern have included the difficulty to establish clear boundaries between GAD and (i) personality dimensions, (ii) other anxiety-spectrum disorders, and (iii) nonbipolar depression. The National Institute of Mental Health has recently proposed the Research Domain Criteria (RDoC), a framework destined to facilitate biological research into the etiology of mental symptoms. Within the RDoC framework, generalized anxiety might be studied as a dimension denominated “anxious apprehension” that would typically fit into the research domain called “negative valence systems” and the more specific construct termed “potential threat.”

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Dialogues Clin Neurosci. 2017;19:107-115.

Keywords: *anxious apprehension; DSM; DSM-5; ICD-10; ICD-11; generalized anxiety disorder; negative valence system; worry*

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the late 18th century. Early authors reported that this type of chronic anxiety could culminate in paroxysmal attacks. Thus, GAD and panic attacks were lumped together under the same illness.

In this section, we will first discuss the term “pantophobia,” a medical term in common usage until the early 20th century; we will then mention “neurasthenia,” a diagnostic term whose extreme popularity was matched by its vagueness; we will finally turn to “anxiety neurosis,” the immediate precursor of GAD and panic disorder (PD).

Panophobia

The term panophobia also appeared under related forms, such as pantaphobia, pantophobia, or panphobia. According to the Oxford English Dictionary, pan(t)ophobia was first attested to in English in 1781. The etymology is the post-classical Latin *pantōphōbōs*, from the Greek *παντοφόβος* (all-fearing), whose literal sense is “anxiety about everything.” The term “pantophobic” was first employed by the Latin-speaking physician Caelius Aurelianus (fifth century), who wrote about the etymologies of medical terms that he translated from Greek into Latin. He noted that some physicians spoke of “pantophobic” patients, who were allegedly afraid of everything.^{1,2} A frequent archetype of pan(t)ophobia or “vain fear” (Latin: *inanis metus*) quoted by classical authors is a saying by Aristotle in the Nicomachean Ethics, written in 350 BC (Book 7): “the man who is by nature apt to fear everything, even the squeak of a mouse.”³

In 1917, Devaux and Logre⁴ argued that the correct denomination should be pantophobic and not panophobic; etymologically, the latter could be understood as the “fear of the god Pan.” Interestingly, the word “panic” is derived from Pan, the Greek god of shepherds and cattle; the adjective *panikos* (*πανικός*) (“of Pan”) was used to designate panic fright because noises heard in mountains and valleys were attributed to Pan.

Boissier de Sauvages (1706-1767) wrote the first significant French medical nosology. His position at the transition from classical to modern medicine is exemplified by the fact that his work was the last major medical textbook to be written in Latin and that it was soon followed by a posthumous French translation. Boissier de Sauvages subdivided mental disorders, called *vesaniae*, into four Orders: (i) Hallucinations; (ii) Morositates,

including pica, bulimia, polydipsia, antipathia, nostalgia, panophobia, satyriasis, nymphomania, tarantism (ie, immoderate craving for dance), and hydrophobia; (iii) Deliria; and (iv) Folies anormales. The disorder mainly concerned with anxiety is panophobia.⁵ In Boissier de Sauvages’ nosology,⁶ the first form of panophobia is little more than nocturnal terror. However, other subtypes of panophobia are reminiscent of modern anxiety disorders. In *panophobia hysterica*, also called “panic terror caused by vapors,” hysterical and hypochondriac subjects experience sudden fright and react dramatically with heart racing or pallor when startled by innocuous noises or sights. This was attributed to a diathesis of exacerbated sensibility. It was reported that these subjects may additionally present with the complicating symptoms of grief or worries. In *panophobia phrontis* (from the Greek *φροντίς*: care, worry, preoccupation), also called worry (French: *souci*), the patients present with features evocative of GAD. These individuals are constantly extremely worried, and for this reason they avoid company, preferring to keep to themselves. They complain of pain and bodily tension.

According to the historian of psychiatry German E. Berrios,⁷ in 1902, Albert Pitres and Emmanuel Régis⁸ gave the best description of panophobia. Pitres (1848-1928) trained with Jean Martin Charcot, studied cortical localizations, and later became professor of psychiatry in Bordeaux. He wrote the book *Les Obsessions et les Impulsions* with Régis (1855-1918). Régis later wrote a textbook of psychiatry (*Précis de Psychiatrie*), whose successive editions were a reference in the early decades of the 20th century in France. Régis introduced in French many concepts from Kraepelin and Freud. The two authors described panophobia at a congress of psychiatry in Moscow in 1897.⁹ They quoted Théodule Ribot,¹⁰ who in turn had attributed the term panophobia to George Beard, the creator of neurasthenia. Pitres and Régis described a disorder of emotions, “a state of vague but permanent anxiety or terror that was termed panophobia or pantaphobia (Beard); it is a condition where the patient is afraid of everything, where anxiety, instead of being fixated to the same object, floats as in a dream and gets fixated only for an instant, according to random circumstances, passing from an object to the next. The most prominent symptom of the panophobic state is what Freud very rightly termed ‘anxious expectation’.” For Pitres and Régis, panophobia and Freud’s anxiety neurosis are clearly synonyms.

Neurasthenia

Beard's neurasthenia was a most successful diagnostic category. It is a very broad concept, whose meaning has evolved since Beard's original description in 1869 until its retention as a diagnostic concept (F48.0) in the tenth revision of the *International Statistical Classification of Diseases and Related Health Problems (ICD-10)*, where it must be excluded for the diagnosis of GAD (F41.1). In Beard's treatise,¹¹ "pantaphobia" [sic] is one of the many manifestations of neurasthenia ("There is a manifestation of morbid fear which is not uncommon, and to which we might perhaps give the term pantaphobia, or fear of everything").

In parallel with works on the phenomenology of GAD, clinical descriptions of PD were also published. An important figure in the history of PD is Édouard Brissaud,¹² who in 1899, identified "pure paroxysmic anxiety" (*anxiété paroxystique pure*, p 348), specifying that the condition may at times evolve toward agoraphobia.

Anxiety neurosis

Sigmund Freud first used the term "anxiety neurosis" (*angstneurose*) in German in 1895 in his article entitled "On the Grounds for Detaching a Particular Syndrome From Neurasthenia Under the Description 'Anxiety Neurosis'."¹³ Freud had also used the term "*névrose d'angoisse*" in a paper published in French in the same year.¹⁴ Freud's etiological theory—now outdated—postulated that anxiety neurosis was caused by an accumulation of sexual excitation that could not find discharge in coitus. Interestingly, Freud listed as second symptom in his clinical description of anxiety neurosis the "anxious expectation,"—a core criterion for GAD in *DSM-5*—for which he gave the following example: "A woman, for instance, who suffers from anxious expectation will think of influenza pneumonia every time her husband coughs when he has a cold, and, in her mind's eye, will see his funeral go past." The symptomatology of anxiety neurosis according to Freud is much broader than that of modern GAD. Freud lists the following classes of symptoms: (i) general irritability; (ii) anxious expectation, which, as mentioned above, approximates the worry criterion of *DSM-5*; (iii) anxiety attacks; (iv) equivalents of anxiety attacks (eg, attacks of sweating, ravenous hunger, tremor, vertigo, paresthesias); (v) *pavor nocturnus*; (vi) vertigo; (vii) typical phobias or

agoraphobia; (viii) nausea, diarrhea (in contrast to constipation in neurasthenia); (ix) paresthesias, rheumatic pains (Freud adds that several individuals known as rheumatic are in reality suffering from anxiety neurosis—is this relevant to nowadays fibromyalgia?).

In the early 20th century, French authors—eg, Francis Heckel¹⁵ in his renowned treaty on anxiety neurosis—adopted Freud's term of anxiety neurosis but refuted the sexual etiology. Heckel's treatise was completed in 1914, but the onset of World War I delayed its publication until 1917. Heckel describes in detail the paroxysmal manifestations ("*crises d'angoisse*") and the interparoxysmal symptomatology (the "mental state" of anxiety neurosis). He dismisses the validity of the psychoanalytical investigation method: "it is obvious that two psychoanalysts working with the same patient will delineate complexes and emotional syntheses that are radically different" (p 210).

Generalized anxiety disorder in modern psychiatric classifications

DSM-I and *DSM-II*

*DSM-I*¹⁶ (known as *DSM* when it was published) had a chapter termed "psychoneurotic disorders." Anxiety was supposed to be a danger signal perceived by the "conscious portion" of the personality and produced by a threat from within the personality; the various ways in which the patient attempted to handle this anxiety resulted in various types of "reactions." The concept of reaction patterns, developed by Adolf Meyer, was at that time a hallmark of American psychiatry. The category called "anxiety reaction" was diagnosed when the anxiety was diffuse and neither restricted to situations or objects (as was the case in phobic reactions) nor controlled by any specific psychological "defense mechanism" (as was the case in dissociative, conversion, obsessive-compulsive reactions). Anxiety reaction was characterized by anxious expectation and frequently associated with somatic symptomatology; it was to be differentiated from normal apprehensiveness or fear.

*DSM-II*¹⁷ renamed the reactions of *DSM-I* as "neuroses." *DSM-II* stated that anxiety was the chief characteristic of "neuroses"; anxiety could be felt directly or controlled unconsciously by various symptoms. In *DSM-II*, the diagnostic category "anxiety neurosis" was characterized by "anxious over-concern extending

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to panic and frequently associated with somatic symptoms”; thus, it encompassed both future categories denominated panic attacks and GAD.

The advent of generalized anxiety disorder in *DSM-III* and subsequent revision of criteria in *DSM-III-R* and *DSM-IV*

The splitting of *DSM-II* anxiety neurosis into (i) GAD and (ii) PD in the *DSM-III*¹⁸ in 1980 was the official birth date of GAD as a diagnostic category. In reality, as discussed by Rickels and Rynn,¹⁹ GAD was conceived of a few years earlier. Whereas the so-called Feighner Criteria²⁰ developed at Washington University in St Louis still grouped free-floating anxiety and anxiety attacks under the single diagnosis of anxiety neurosis, the Research Diagnostic Criteria—developed by Spitzer et al soon thereafter—separated GAD from PD.²¹ One major argument for the separation of spontaneous panic from anticipatory anxiety was the finding that they could be distinguished on the basis of response to medication, an approach later termed “pharmacological dissection.”²² Indeed, a double-blind placebo-controlled trial by Klein²³ had shown that patients treated with imipramine had fewer panic attacks even though their levels of anticipatory anxiety remained high. However, more recent studies have disproved this claim that PD is a specific indication for antidepressant therapy, whereas GAD is not responsive; Kahn and colleagues were the first to show results with imipramine that contradicted Klein’s observations.²⁴ It is now recognized that antidepressants are effective in the treatment of GAD.²⁵

Because of the high degree of comorbidity with other disorders, the autonomy of *DSM-III* GAD was soon questioned, and its elimination was regularly debated with each new revision of *DSM*. GAD is known for showing high comorbidity with other anxiety disorders and with depression. The criteria of GAD have been modified in successive editions of *DSM* in order to bolster the validity of this category. *Table 1* shows the evolution of the definition of GAD over succeeding editions of *DSM* and *ICD*.¹⁹

A study reported in 1984 by Anderson and colleagues²⁶ found that subjects with GAD had fewer autonomic symptoms and an earlier, more gradual onset than patients with PD, a finding that tended to support the distinction between the two categories. An important study reported in 1986 by Barlow and colleagues²⁷

produced findings that anticipated the increased emphasis on worry in the criteria of GAD. Barlow et al commented that *DSM-III* GAD was largely a residual diagnosis among the spectrum of anxiety disorders because patients diagnosed with other *DSM-III* anxiety disorders almost always met the criteria for GAD also. Notably, two forms of GAD were suggested by Barlow et al: a residual form representing the apprehensive expectations that accompany other anxiety disorders and a qualitatively different form of chronic worry that represents an independent syndrome. Early clinical studies of *DSM-III* GAD found that GAD seldom occurred in the absence of major depressive disorder (MDD). However, this comorbidity weakened as duration of GAD increased; thus, the duration requirement for GAD was increased to 6 months in *DSM-III-R* and later, *DSM-IV*.²⁸

During the transition from *DSM-III-R* to *DSM-IV*,²⁹ it was also suggested that, often, patients with GAD experience excessive anxiety from an early age and with chronicity, and that GAD might be better conceptualized as a vulnerability that should be located on axis II of the *DSM* multiaxial system for assessment. Akiskal³⁰ has suggested that GAD might be best considered as an anxious temperament. A set of somatic symptoms associated with GAD that differs substantially from those for other anxiety disorders was determined. These findings led to a reduction in the number of items in the symptom criterion, from 18 in *DSM-III-R* to six in *DSM-IV* (see *Table 1*). Another substantial revision in *DSM-IV* was greater emphasis on the uncontrollability of worry.

Generalized anxiety disorder in *DSM-5*

The high comorbidity between GAD and depressive disorders remained problematic during the preparation of *DSM-5*. This high comorbidity has been explained in various ways, including genetic pleiotropy,³¹ which means that GAD and nonbipolar depression might represent different phenotypic expression of a common etiology. Accordingly, it was proposed to merge GAD and nonbipolar depression in a spectrum of mood/anxiety disorders, by creating three subclasses of emotional disorders: (i) bipolar disorders; (ii) distress disorders (MDD, dysthymic disorder, GAD, and posttraumatic stress disorder [PTSD]); and (iii) fear disorders (PD, agoraphobia, social phobia, and specific phobia).³²

	<i>DSM-III (1980)</i>	<i>DSM-III-R (1987)</i>	<i>DSM-IV (1994)</i>	<i>DSM-5 (2013)</i>	<i>ICD-10 (1992)</i>	<i>ICD-11 Beta Draft</i>
Anxiety	Generalized, persistent anxiety.	<i>Unrealistic</i> excessive anxiety and worry (apprehensive expectation) about 2 or more life circumstances.	- Excessive anxiety and worry (apprehensive expectation) about a number of events or activities. - <i>Difficult to control the worry.</i>	- Excessive anxiety and worry (apprehensive expectation) about a number of events or activities. - Difficult to control the worry.	Generalized and persistent anxiety, not restricted to or even predominating in any environmental circumstances (ie, "free-floating").	Marked symptoms of anxiety accompanied by either <i>general apprehension</i> (ie, "free-floating anxiety") or <i>worry</i> focused on multiple everyday events (family, health, finances, school, or work).
Duration	≥ 1 month	≥ 6 months	More days than not for at least 6 months.	More days than not for at least 6 months.	Most days for at least several weeks at a time, and usually for several months.	More days than not for at least several months.
Number of symptoms	Unspecified number of symptoms from 3 of 4 categories.	At least 6 of 18 specified symptoms.	At least 3 of 6 specified symptoms.	At least 3 of 6 specified symptoms.	Unspecified number of symptoms.	Unspecified number of symptoms.
Symptoms or symptom categories	1. Motor tension. 2. Autonomic hyperactivity. 3. <i>Apprehensive expectation</i> . 4. Vigilance and scanning.	- Motor tension (n = 4). - Autonomic hyperactivity (n = 13). - Vigilance and scanning (n = 5).	1. Restlessness or feeling keyed up or on edge. 2. Being easily fatigued. 3. Difficulty concentrating or mind going blank. 4. Irritability. 5. Muscle tension. 6. Sleep disturbance.	Identical to <i>DSM-IV</i> .	- Apprehension (worries about future misfortunes, feeling "on edge", difficulty in concentrating). - Motor tension. -Autonomic overactivity.	Additional symptom such as muscular tension or motor restlessness, sympathetic autonomic overactivity, subjective experience of nervousness, difficulty maintaining concentration, irritability, or sleep disturbance.
Associated features	Mild depressive symptoms.	Mild depressive symptoms.	- Somatic symptoms, exaggerated startle response. - Frequent co-occurrence with mood disorders, other anxiety disorders, substance-related disorders, other conditions associated with stress.	Similar to <i>DSM-IV</i> . Symptoms of autonomic arousal are less prominent in GAD than in other anxiety disorders, such as panic disorder.	/	/

Table I. Evolution of the definition of generalized anxiety disorder in succeeding editions of the DSM and ICD. DSM, Diagnostic and Statistical Manual of Mental Disorders; GAD, generalized anxiety disorder; ICD, International Statistical Classification of Diseases and Related Health Problems; OCD, obsessive-compulsive disorder.

Modified and updated from reference 19: Rickels K, Rynn M. Overview and clinical presentation of generalized anxiety disorder. *Psychiatr Clin North Am.* 2001;24(1):1-17.

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However, other data still argued for some distinctions between GAD and MDD. For instance, epidemiological surveys showed differences in risk factors for GAD and MDD, arguing against the view that the two disorders are merely different manifestations of a single underlying internalizing syndrome or that GAD is merely a prodromal, residual, or severity marker of major depressive episode.³³ Another proposal³⁴ was to relabel GAD as “generalized worry disorder” in *DSM-5*, to reflect that worry is the core feature and to capture the behavioral consequences of anxious apprehension and worry by adding a criterion C (“marked avoidance of potentially negative events or activities”; “marked time and effort preparing for possible negative outcomes of events or activities”; “marked procrastination in behav-

ior or decision-making due to worries”; and “repeatedly seeking reassurance due to worries”). One rationale for this criterion C is the supposition that worry acts as a cognitive coping strategy that manifests in avoidant behaviors.

The final version of *DSM-5* did not differ much from *DSM-IV*,³⁵ GAD being defined by the following diagnostic criteria:

- A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).
- B. The individual finds it difficult to control the worry.
- C. The anxiety and worry are associated with three (or more) of the following six symptoms:

Impairment in social and occupational functioning	Rarely more than mild.	Rarely more than mild.	Significant distress and impairment.	<i>Significant distress and impairment.</i>	/	Significant distress or significant impairment in functioning.
Exclusions	Not due to another mental disorder, such as a Depressive Disorder or Schizophrenia.	Not due to an organic factor (hyperthyroidism, caffeine). Anxiety/worry unrelated to panic disorder, social phobia, OCD, or anorexia nervosa.	Not due to a substance, a general medical condition. Does not occur exclusively during a mood disorder, a psychotic disorder, or a pervasive developmental disorder.	Anxiety or worry not better explained by another mental disorder (eg, panic disorder, social anxiety disorder, OCD, separation anxiety disorder, posttraumatic stress disorder, anorexia nervosa, somatic symptom disorder, body dysmorphic disorder, illness anxiety disorder, schizophrenia, or delusional disorder).	The transient appearance of symptoms of depression does not rule out GAD as a main diagnosis. The sufferer must not meet the criteria for depressive episode, phobic anxiety disorder, panic disorder, or OCD.	/
Prevalence	Equally common in males and in females. Rare in the general population.	Not commonly diagnosed in clinical samples, where it is equally common in males and in females.	<i>Sex ratio: two-thirds female in epidemiological studies. Lifetime prevalence: 5% in community sample</i>	<i>The lifetime morbid risk is 9%. Females are twice as likely as males to experience GAD. Individuals of European descent tend to experience GAD more frequently than do individuals of non-European descent.</i>	- More common in women. - Often related to chronic environmental stress.	

Table I. Continued

1. Restlessness or feeling keyed up or on edge.
2. Being easily fatigued.
3. Difficulty concentrating or mind going blank.
4. Irritability.
5. Muscle tension.
6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep).

Criterion F in *DSM-5* makes it clear that GAD is largely an exclusion diagnosis. GAD cannot be diagnosed if the anxiety is better explained by other anxiety disorders (panic, phobic, social anxiety, or obsessive-compulsive disorder). Also, GAD cannot be caused directly by stressors or trauma, contrary to adjustment disorders and PTSD.

Generalized anxiety disorder in *ICD-10* and *ICD-11*

In *ICD-10*, GAD (F41.1) includes anxiety neurosis, anxiety reaction, and anxiety state, but excludes neurasthenia. *ICD-10* also proposes diagnostic criteria for research: (i) at least 6 months with prominent tension, worry, and feelings of apprehension about everyday events and problems; and (ii) at least four symptoms out of a list of 22 items, of which at least one item is from a list of four items of autonomic arousal (palpitations/accelerated heart rate, sweating, trembling/shaking, dry mouth).

The *ICD-11* Working Group decided to retain a categorical approach to the anxiety disorders. GAD will be included in the category of “anxiety and fear-related disorders,” distinguished from “obsessive-compulsive or related disorders” and “disorders specifically associated with stress.”³⁶ In the draft of *ICD-11*,³⁷ GAD is redefined: worry about multiple areas of everyday life has been introduced as an alternative essential feature to generalized apprehension. GAD can now co-occur with other mental and behavioral disorders.

Overview of the evolution of the concept of GAD since the second half of the 20th century and future perspectives

Prevalence, sex ratio, and the importance of worry

According to *DSM-III* and *DSM-III-R*, GAD had a low prevalence and rarely caused more than mild impairment. Starting with *DSM-IV*, it was required that GAD cause clinically significant distress or impairment; this

is because this requirement became part of the definition of a disorder in *DSM-IV*. Also in *DSM-IV*, GAD morphed from a rarely diagnosed condition into a disorder with a lifetime prevalence reaching up to 5% in a community sample. Also, the sex ratio changed dramatically. According to *DSM-5*, GAD is about twice as likely in females as in males, whereas in *DSM-III* it was supposed to be equally common in both sexes.

However, the most important evolution is that since *DSM-III-R*, general apprehensiveness or worry that are not restricted to any particular stimulus has been progressively established as the distinctive and core symptom of GAD. Worry about everyday matters is a relatively specific symptom, contrary to somatic symptoms of GAD, which are also found in other disorders. Worry is translated as “*souci*” and “*sorge*” in the French³⁸ and German³⁹ editions of *DSM-5*, respectively. The concept of worry puts the emphasis on the psychological symptomatology, specifically on the cognitive functioning. Thus, an anxious condition that, earlier, might have been considered as related to noncortical emotions and corporeal sensations is now grounded on cognitions based in the prefrontal cortex. The emphasis on the cognitive aspect of anxiety had already been made much earlier. Édouard Brissaud (1853-1909)⁴⁰ distinguished “*angoisse*” (anguish), the sensation of somatic distress, and “*anxiété*” (anxiety), the intellectual processing of anguish; this distinction still exists to some extent with corresponding word pairs in other romance languages. Worry may provide short-term relief by means of the avoidance of threatening imagery.⁴¹ Another important cognitive aspect of GAD is intolerance of uncertainty.⁴² The long-term consequences of worry include the inhibition of emotional processing and the maintenance of anxiogenic conditions.⁴³ One effect of worrying may be to suppress somatic (eg, cardiovascular) symptoms of anxiety.^{44,45} Over successive editions of *DSM*, worry displaced somatic symptoms, although the latter are still important in transcultural psychiatry (see the article by Khambaty and Parikh in this journal issue). Research has provided evidence for the dimensionality of worry. Thus, GAD, whose central feature is worry, may be quantitatively rather than qualitatively different from normal functioning. Ruscio et al⁴⁶ argued that a focus on normal and pathological extremes has constrained the study of worry phenomena and that dimensional conceptualization of worry may significantly enhance understanding of both worry and GAD. The debate

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between dimensional and categorical approaches is relevant to the Research Domain Criteria (RDoC) initiative.

Future perspectives—RDoC

The National Institute of Mental Health initiated the RDoC project,⁴⁷ a research framework designed for studying the full range of human behavior from normal to abnormal based on multiple levels of information (genes, molecules, cells, brain circuits, physiology, behavior, and self-report). Currently, the RDoC framework is organized around five basic domains of functioning: negative valence systems, positive valence systems, cognitive systems, social processes, and arousal and regulatory systems. Logically, anxiety might be explored within the negative valence system.^{48,49} The negative valence system contains several constructs, one being “potential threat (anxiety)” described as activation of a brain system in which harm may potentially occur but is distant, ambiguous, or low/uncertain in probability, characterized by a pattern of responses such as enhanced risk

assessment (vigilance). The construct of “anxiety” is distinguished from other constructs within the negative valence systems, namely “acute threat,” “sustained threat,” “loss,” and “frustrative reward.” The RDoC encourages the study of clinical dimensions rather than *DSM* clinical categories. Anxious apprehension is a dimension that could be more validly studied within the RDoC framework than a diagnostic category such as GAD. Anxious apprehension is defined by a persistent pattern of negative repetitive thinking about perceived threats. It might involve left-hemisphere activity, notably the left inferior frontal gyrus.⁵⁰ Sharp et al⁵¹ analyze how the RDoC matrix might allow a transdiagnostic dimension such as anxious apprehension to be studied in several research domains. While it could belong under the cognitive systems domain of RDoC—since it involves negative repetitive thinking and a breakdown in executive flexibility—the most obvious place for anxious apprehension in the RDoC matrix lies under the construct “potential threat” within the domain of negative valence. □

Acknowledgments/Conflict of Interest: The author has no conflicts of interest to declare.

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La historia del trastorno de ansiedad generalizada como una categoría diagnóstica

Desde el siglo XIX y hasta el siglo XX, los términos empleados para diagnosticar la ansiedad generalizada incluyeron la "pantofobia" y la "neurosis de ansiedad". Tales términos designaron manifestaciones paroxísticas (ataques de pánico) como también fenomenología interparoxística (el estado mental de aprensión). También la ansiedad generalizada fue considerada uno de los numerosos síntomas de la neurastenia, una enfermedad definida vagamente. El trastorno de ansiedad generalizada (TAG) apareció como una categoría diagnóstica en la tercera edición del Manual Diagnóstico y Estadístico de los Trastornos Mentales (DSM-III) en 1980, cuando la neurosis de ansiedad fue dividida entre el TAG y el trastorno de pánico. Una de las razones para distinguir estos dos trastornos fue la respuesta diferente que tuvieron a la terapia con imipramina. A partir de la edición revisada del DSM-III (DSM-III-R), la preocupación *People Like Us* - situaciones de vida se ha enfatizado gradualmente como el síntoma distintivo del TAG. En consecuencia, un aspecto cognitivo de la ansiedad ha llegado a ser el criterio central del TAG. La validez del TAG como una categoría independiente ha sido cuestionada desde el DSM-III hasta la preparación del DSM-5. Algunos aspectos tomados en cuenta han incluido la dificultad para establecer límites claros entre el TAG y 1) dimensiones de la personalidad, 2) otros trastornos del espectro ansioso y 3) la depresión no bipolar. Recientemente, el Instituto Nacional de Salud Mental de EE.UU. propuso los Research Domain Criteria (RDoC), un sistema destinado a facilitar la investigación biológica acerca de la etiología de los síntomas mentales. Dentro del sistema RDoC, la ansiedad generalizada podría ser estudiada como una dimensión denominada "aprensión ansiosa", la cual podría ajustar típicamente con el dominio de investigación llamado "sistemas de valencia negativa" y más específicamente con el constructo llamado "amenaza potencial".

L'histoire de l'anxiété généralisée en tant que catégorie diagnostique

Entre le XIX^e et le XX^e siècle, plusieurs termes ont été utilisés pour dénommer l'anxiété généralisée, notamment la « pantophobie » et la « névrose d'angoisse ». Ces termes désignaient à la fois des manifestations paroxystiques (les attaques de panique) ainsi que les symptômes intercritiques (l'état mental d'appréhension). D'autre part, l'anxiété généralisée était aussi considérée comme l'un des nombreux symptômes de neurasthénie, une maladie de définition imprécise. Le trouble anxieux généralisé (TAG) est apparu pour la première fois en tant que diagnostic dans la 3^e édition du manuel statistique et diagnostique des troubles mentaux (DSM-III) en 1980 quand la névrose d'angoisse a été divisée en TAG et trouble panique. Ces deux troubles ont été distingués sur la base d'une réponse différente au traitement par imipramine. À partir de la révision du DSM-III (DSM-III-R), l'inquiétude face à un certain nombre de situations de la vie courante a été conceptualisée petit à petit comme le symptôme cardinal du TAG. Ainsi, un aspect cognitif de l'anxiété est devenu le critère primordial du TAG. La validité du TAG en tant que catégorie diagnostique indépendante a été mise en doute depuis le DSM-III jusqu'à la préparation du DSM-5. Les questionnements reposaient sur la difficulté à établir des frontières claires entre le TAG et (1) les dimensions de personnalité, (2) les autres troubles du spectre de l'anxiété et (3) la dépression non-bipolaire. L'institut national de la santé mentale aux États-Unis a récemment mis en place le Research Domain Criteria [RDoC], un cadre destiné à faciliter les recherches biologiques dans le domaine de l'étiologie des troubles mentaux. Dans le cadre du RDoC, l'anxiété généralisée pourrait être étudiée comme une dimension appelée « appréhension anxieuse », qui appartiendrait typiquement au domaine de recherche dénommé « systèmes de valences négatives » et plus spécifiquement au concept dit de « menace potentielle ».