Commentary

Fear and Anxiety—Distinct or "Kindred" Phenomena?

Katharina Domschke

In his central philosophical work "Being and Time" (1), the German phenomenologist Martin Heidegger clearly differentiates fear from anxiety. Fear, according to Heidegger, is directed to something threatening rooted within the world, something particular, distinct, and determinate: "That in the face of which we fear, the 'fearsome' is in every case something that we encounter within-the-world and which may have either readiness-to-hand, presence-at-hand, or Dasein-with as its kind of Being…shrinking back in the face of what fear discloses—in the face of something threatening—is founded upon fear…[that] which we fear is a detrimental entity within-the-world which comes from some definite region but is close by and is bringing itself close, and yet might stay away, and…anything 'fearsome' is always encountered as an entity within-the-world" (1).

Anxiety, in contrast, is indeterminate and elicited by nothing in particular, but is experienced in the face of being-in-the-world per se: "…we must recall that in the face of which one has anxiety…is being-in-the-world as such…not an entity within-the-world…which is completely indefinite…which…cannot bring itself close from a definite direction within what is close by; it is already 'there' and yet nowhere; it is so close that it is oppressive and stifles one's breath, and yet it is nowhere…. In anxiety one does not encounter this thing or that thing which, as something threatening, must have an involvement…. It is rather the possibility of the ready-to-hand in general" (1).

This distinction between fear and anxiety has been proposed not only by Heidegger but by many others, including Søren Kierkegaard (2), Sigmund Freud (3), and, more recently, LeDoux and Pine (4), who suggested a "two systems" view of fear and anxiety. Also, modern nosological systems in psychiatry and psychology, i.e., the DSM-5 or ICD-10, attribute fear to the group of phobic disorders (i.e., specific phobias, social anxiety disorder/social phobia and agoraphobia), which are related to the immediate or imminent presence of a discrete aversive object or situation. Anxiety, however, relates to the group of "other anxiety disorders," i.e., panic disorder and generalized anxiety disorder, which are characterized by a more free-floating anxiety resulting from a sustained expectation that an unpredictable, diffuse aversive event is likely to occur. Also, within the negative valence systems domain of the Research Domain Criteria, a distinction between fear, represented by acute threat, and anxiety, represented by potential threat, is suggested. However, the validity of this concept has been debated based on research findings not unequivocally supporting a clear-cut dichotomy between fear and anxiety.

In the current issue of *Biological Psychiatry: Global Open Science*, Daniel-Watanabe and Fletcher (5) address this pressing taxonomic issue by reviewing selective evidence from the published literature on if and how fear and anxiety actually constitute separate entities, which is of utmost relevance not only clinically but also for basic research.

The authors exemplarily highlight rodent and human studies providing evidence for a neuronal activity-based distinction between fear on one hand, involving activity of the central nucleus of the amygdala, and eliciting phasic responses and anxiety on the other hand, depending on activity of the bed nucleus of the stria terminalis (BNST) and resulting in a sustained response. However, Daniel-Watanabe and Fletcher (5) also identified studies not supporting a clear-cut distinction between neurocircuits underlying fear and anxiety, respectively. Indeed, highly complex amygdala–BNST interactions and the organization of the amygdala and the BNST in functional subregions suggest that the BNST not only shapes anxiety-related responses to diffuse threats but also governs reactions to discrete threatening stimuli. The amygdala seems to drive not only fear-related behavior but also anxiety-related behavior (6). On a physiological level, most studies reviewed by the authors point to a distinction between fear and anxiety responses as mirrored by differential physiological reactions (e.g., startle response, heart rate) during the no-shock, predictable-shock, unpredictable-shock task or while imagining threatening scenarios. However, their findings do not unequivocally support a clear dichotomy but instead point to a spectrum-like pattern (5). Furthermore, the authors spotlight observable behaviors in rodent and human models, such as the Mouse Defense Test Battery and its human analog, the Joystick Operated Runway Task, and mental imagery of threat scenarios. These experiments have yielded evidence mostly for a distinction between fear- and anxiety-related behavior, with some inconsistencies across studies (5). Molecular studies investigating potentially differential genetic underpinnings of fear- and anxiety-related disorders were not reviewed by the authors. While there is some evidence for risk genes potentially specific to anxiety/arousal [e.g., *NPSR1* (7)], both clinical and molecular genetic studies increasingly point to a shared genetic component between anxiety disorders that is larger than the unique contributions to any one disorder and that transcends diagnostic boundaries (8).

As major limitations in attempts to explore distinct or shared characteristics between fear and anxiety, Daniel-Watanabe and Fletcher (5) discuss the partly restricted face and construct validity and thus finite translatability of animal models [for a comprehensive review, see (9)], constraints in the

SEE CORRESPONDING ARTICLE ON PAGE 341

© 2022 THE AUTHORS. Published by Elsevier Inc on behalf of the Society of Biological Psychiatry. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). https://doi.org/10.1016/j.bpsgos.2022.07.001

sensitivity of available measurement devices, such as the limited spatial and temporal resolution of functional magnetic resonance imaging, and the questionable discriminatory power of tasks modeling phasic and sustained fear.

Daniel-Watanabe and Fletcher's review (5) reignites the long-standing scientific and clinical discussion on how to elucidate common or potentially differential pathways underlying fear- and anxiety-related phenotypes in the most valid and reliable ways. It seems that—in analogy to the linguistically highly sophisticated philosophical take on fear and anxiety as cited above—psychiatric/psychological phenomenology should be revisited, striving toward a more precise verbal terminology and clinical definition of fear- and anxiety-related phenotypes in the complex human system rather than in oversimplified animal models. This should include complementing standard measures of behavior by extensive assessments of conscious subjective experience [also see (10)]. The discussion is further complicated by the fact that, according to Heidegger, there are "further variations of fear, which we know as timidity, shyness, misgiving, [or] becoming startled" (1) or, according to Daniel-Watanabe and Fletcher (5), "other aspects of the experience of anxiety, such as uncertainty and avoidance." Along these lines, it is a matter of debate whether the terms "fear" and "anxiety" are sufficient to represent the broad and often mixed spectrum of emotions, cognitions, and behaviors related to this wide semantic and clinical field. It is also debatable as to whether they appropriately capture the nosological entities of separation anxiety disorder and selective mutism, which in the DSM-5 are now also comprised in the anxiety disorders chapter. A more precise phenomenological definition might aid in disentangling the complex taxonomic tree of anxiety disorders, with potentially pleiotropic effects stemming from a common biological trunk, but distinct mechanisms influencing phenotypic differentiation when branching out. This intricate multilevel investigation could be facilitated by systems biology approaches supported by artificial intelligence. A more detailed insight into the molecular, neuronal network, physiological and behavioral characteristics of the anxiety and fear-related spectrum is eventually expected to aid in identifying persons at risk for anxiety disorders amenable to targeted preventive interventions and to inform more personalized treatment options in an individualized precision psychiatry/psychotherapy approach.

In summary, Daniel-Watanabe and Fletcher (5) conclude that while fear and anxiety are most certainly not to be used interchangeably, in humans they might not be as clearly distinct as suggested by animal models. Fear and anxiety seem to represent closely interrelated diagnostic constructs remaining to be further interrogated for their shared and unique molecular, neuronal, physiological, and behavioral substrates—quite in accordance with Martin Heidegger's reconciling notion: "Of course it still remains obscure how [anxiety] is connected ontologically with fear. Obviously these are kindred phenomena" (1).

References

1. Heidegger M (1962): Being and Time. Oxford, UK: Basil Blackwell Publisher Ltd.
2. Kierkegaard S (2015): The Concept of Anxiety: A Simple Psychologically Orienting Deliberation on the Dogmatic Issue of Hereditary Sin (Kierkegaard's Writings, VIII). New York: W.W. Norton & Co.
3. Freud S (2012): General Introduction to Psychoanalysis, Part Three: General Theory of the Neuroses, XXV. Fear and Anxiety. Stansted, UK: Wordsworth Editions.
4. LeDoux JE, Pine DS (2016): Using neuroscience to help understand fear and anxiety: A two-system framework. Am J Psychiatry 173:1083–1093.
5. Daniel-Watanabe L, Fletcher PC (2022): Are fear and anxiety truly distinct? Biol Psychiatry Glob Open Sci 2:341–349.
6. Gungor NZ, Paré D (2016): Functional heterogeneity in the bed nucleus of the stria terminalis. J Neurosci 36:8038–8049.
7. Gottschalk MG, Domschke K (2016): Novel developments in genetic and epigenetic mechanisms of anxiety. Curr Opin Psychiatry 29:32–38.
8. Purves KL, Coleman JRI, Meier SM, Rayner C, Davis KAS, Cheesman R, et al. (2020): A major role for common genetic variation in anxiety disorders. Mol Psychiatry 25:3292–3303.
9. Bach DR (2022): Cross-species anxiety tests in psychiatry: Pitfalls and promises. Mol Psychiatry 27:154–163.
10. Taschereau-Dumouchel V, Michel M, Lau H, Hofmann SG, LeDoux JE (2022): Putting the "mental" back in "mental disorders": A perspective from research on fear and anxiety. Mol Psychiatry 27:1322–1330.