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978-0-521-15399-7 - Stahl's Illustrated: Anxiety, Stress, and PTSD

Stephen M. Stahl and Meghan M. Grady and Nancy Muntner

Excerpt

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Stahl's Illustrated

Chapter 1

Neurobiology of Stress and Anxiety

Anxiety is a normal emotional and neurophysiological reaction to a perceived threat, and serves the purpose of preparing one to “freeze, take flight, or fight.” Such a reaction is obviously an appropriate and even adaptive survival mechanism in the presence of actual threats, allowing one both to escape the current threat and to avoid future ones through conditioned fear learning. When the reaction occurs in the absence of a realistic threat, however—whether because the threat itself is unlikely or because harm from the perceived threat is unlikely—then it serves no useful purpose and instead can significantly disrupt one’s ability to function, thus constituting an anxiety disorder.

There are several anxiety disorders, as defined in the *Diagnostic and Statistical Manual of Mental Disorders (DSM) IV-TR*, each with distinct characteristics, criteria, and symptoms, but all sharing the common core symptoms of excessive fear and worry. The neurobiological circuits underlying these core symptoms may thus be involved in all anxiety disorders, with the different phenotypes reflecting not unique circuitry but rather divergent malfunctioning within those circuits.

This chapter covers the neurobiology of normal fear and worry and how genetic and environmental factors may interact to affect these circuits and increase risk for psychiatric illnesses such as posttraumatic stress disorders (PTSD), which is the focus of this book.

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SECTION ONE

The Core Symptoms of Anxiety Disorders: Fear and Worry

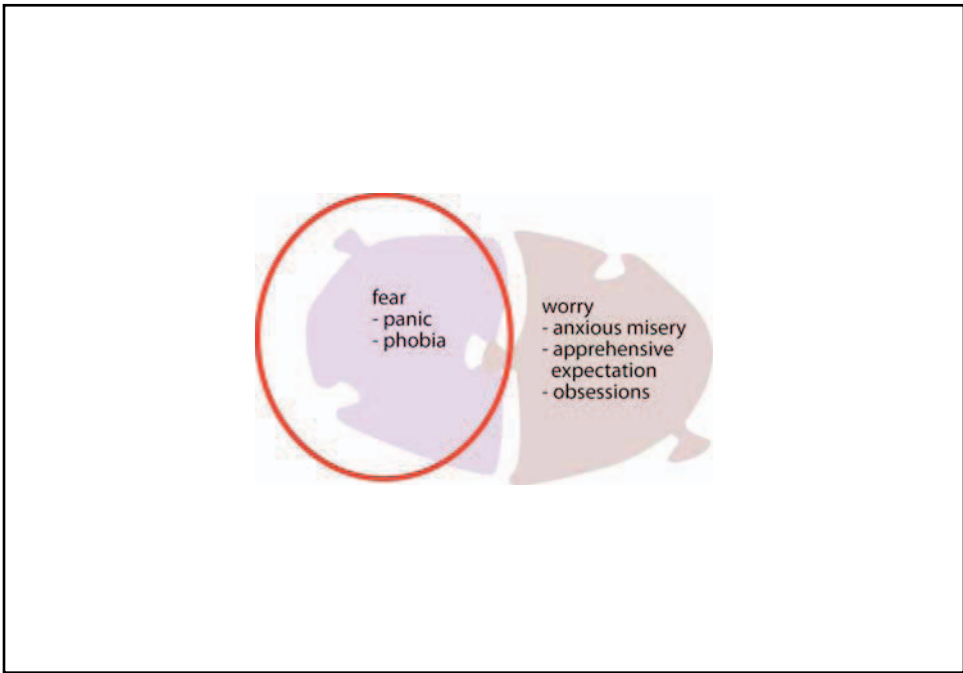
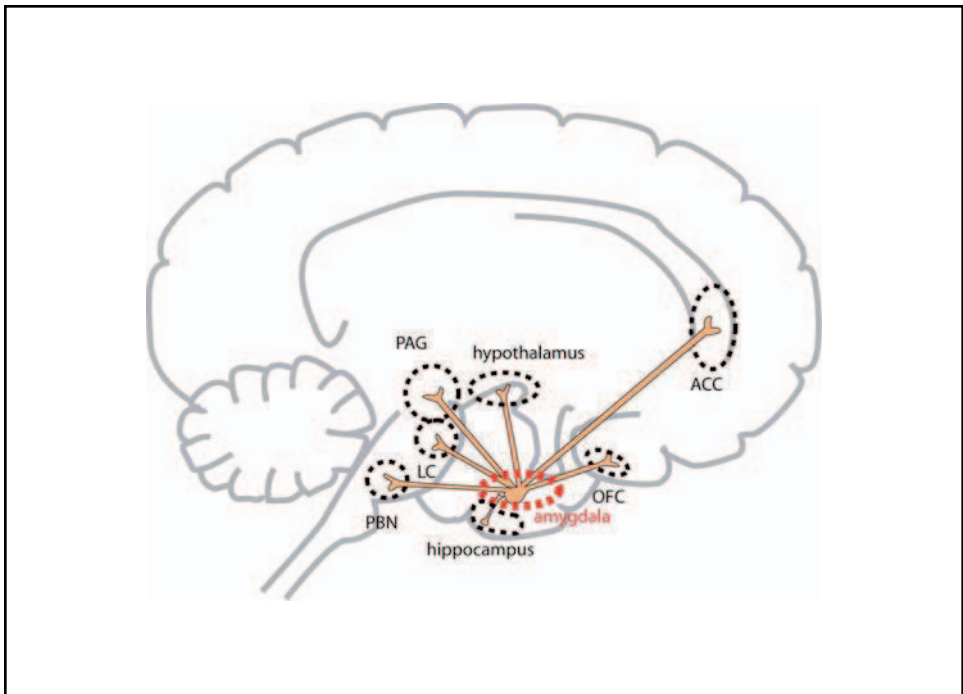


FIGURE 1.1. The two core symptoms shared by all anxiety disorders are anxiety or fear coupled with some form of worry. The circuitry mediating these two features is different, and will be addressed in turn, beginning with anxiety/fear.

The Amygdala's Role in Fear and Anxiety



PAG: periaqueductal grey. LC: locus coeruleus. PBN: parabrachial nucleus. OFC: orbitofrontal cortex. ACC: anterior cingulate cortex.

FIGURE 1.2. Anxiety is a state that encompasses both an internal “feeling” of fear and the physiological expression of that fear. Although separate circuits mediate these different aspects of anxiety, they share in common a central role of the amygdala, an almond-shaped limbic structure with widespread reciprocal connections with both higher and lower brain regions. As shown in Figures 1.3 through 1.9, the amygdala both regulates and is regulated by these other brain regions in order to produce (or suppress) a fear response.

Fear vs. Anxiety

TABLE 1.1.

	DESCRIPTION	ANATOMICAL LOCALIZATION
fear	Short-term, stimulus-specific response	Basolateral, central, and medial nuclei of amygdala
anxiety	Sustained response influencing behavior after the stimulus is removed	Basolateral amygdala projections to bed nucleus of stria terminalis

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The Amygdala and the Feeling of Fear

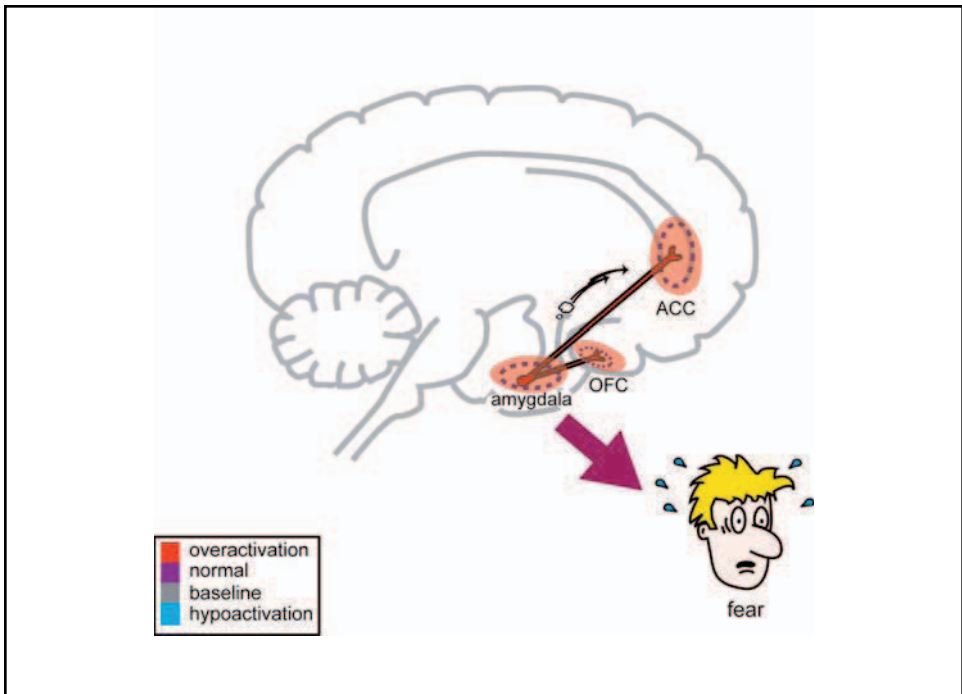


FIGURE 1.3. The emotional aspect of fear is regulated by connections between the amygdala and key areas of the prefrontal cortex, specifically the orbitofrontal cortex (OFC) and the anterior cingulate cortex (ACC).

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The Amygdala and the Physiology of Fear: Autonomic Output

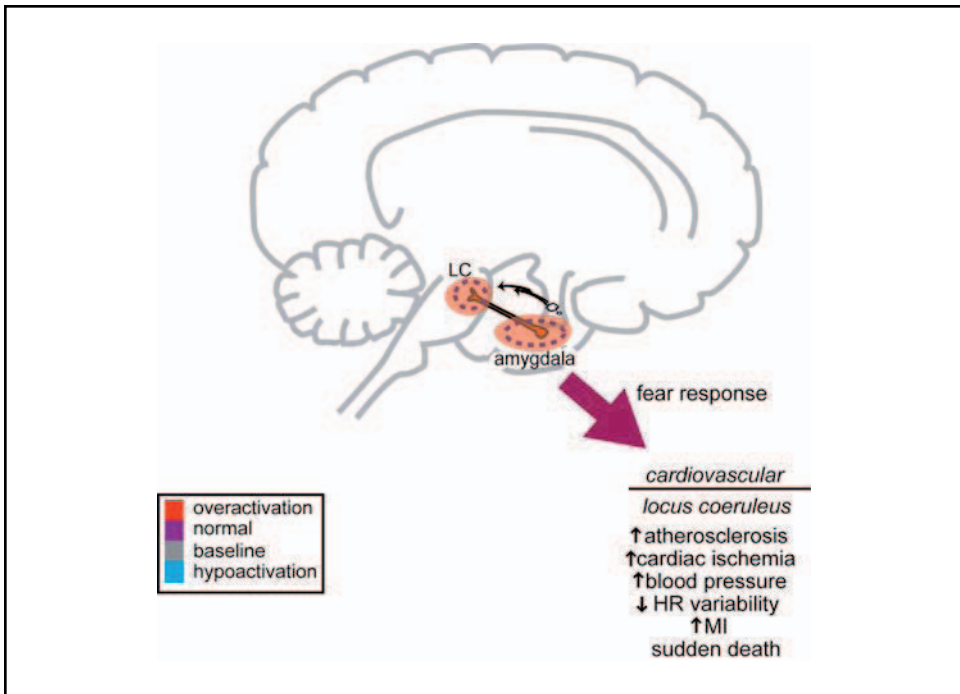


FIGURE 1.4. The physiological reaction to a fearful stimulus involves activation of multiple systems, including the autonomic system, as shown here. Activation of this system is regulated by connections between the amygdala and the locus coeruleus (LC), and leads to an increase in heart rate (HR) and blood pressure that is necessary for a fight/flight reaction.

Although acute activation of the autonomic nervous system is important for survival in response to real threats, chronic activation as part of an anxiety disorder can lead to increased risk of cardiovascular issues such as atherosclerosis, cardiac ischemia, hypertension, myocardial infarction (MI), or even sudden death.

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The Amygdala and the Physiology of Fear: Endocrine Output

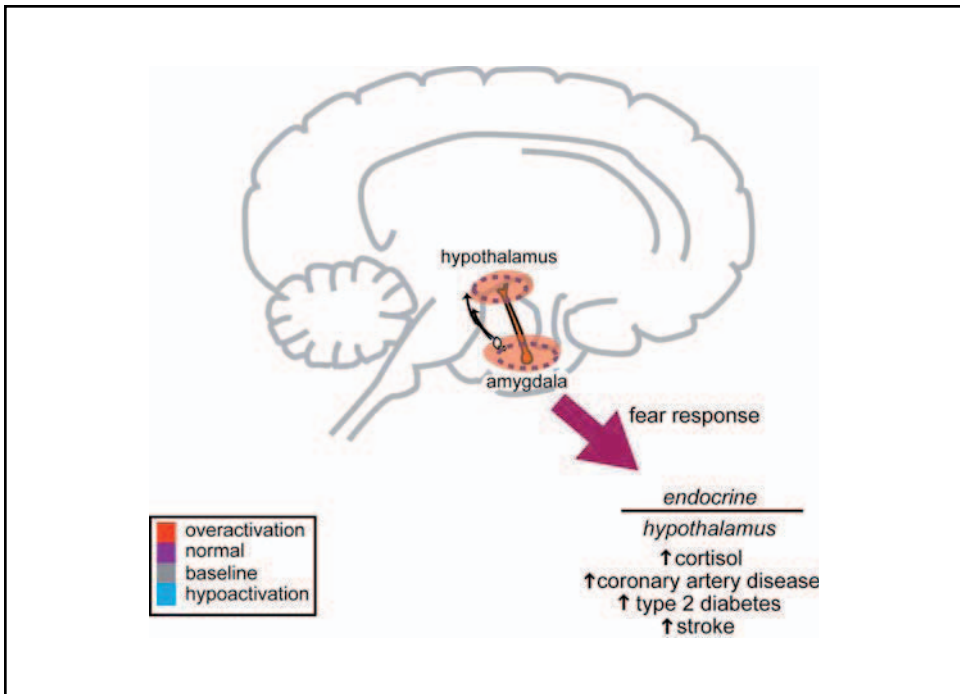


FIGURE 1.5. The hypothalamic pituitary adrenal (HPA) axis is responsible for endocrine output during the fear/stress response, and is regulated by the amygdala via reciprocal connections with the hypothalamus. During acute stress, such as exposure to a fearful stimulus, HPA activation increases the release of glucocorticoids such as cortisol, but only for a short time, until the perceived danger is gone. An abnormal stress response may occur due to chronic, unrelenting stress and/or due to stress during critical developmental periods, and can be associated with increased rates of medical complications such as coronary artery disease, type 2 diabetes, and stroke.

The role of the HPA axis in anxiety disorders is discussed in more detail in Figure 1.6 as well as in Figures 2.6 and 2.7.

The HPA Axis

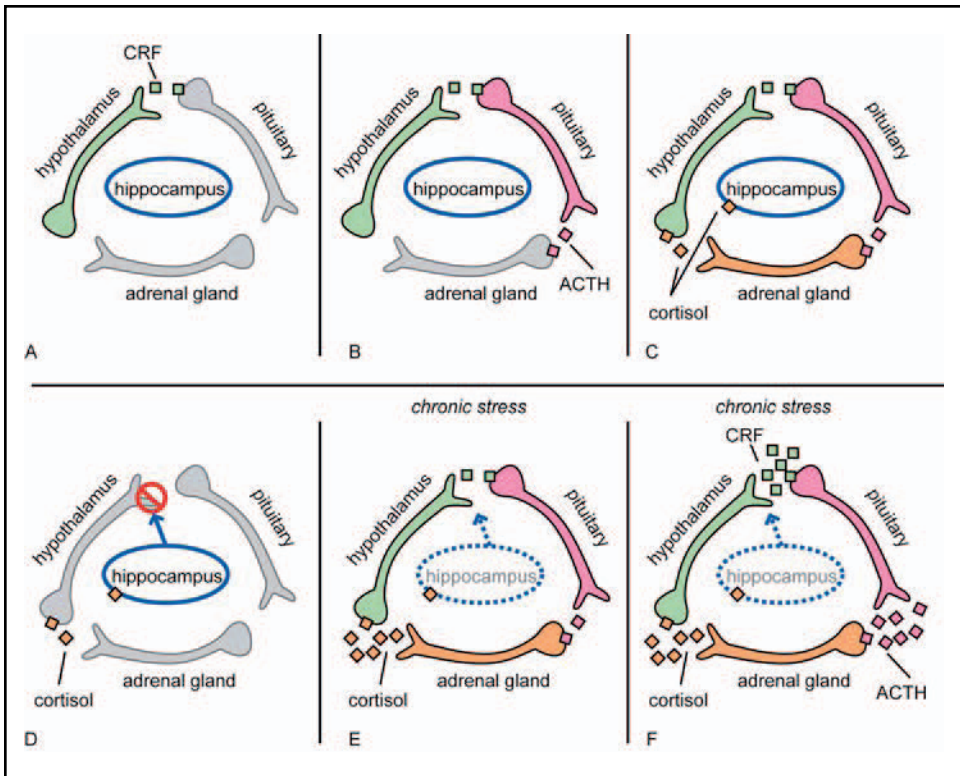


FIGURE 1.6. The central role of the HPA axis in stress processing makes it logical that it would be involved in the risk for anxiety disorders. The normal stress response involves activation of the hypothalamus and a resultant increase in corticotrophin releasing factor (CRF) (A), which in turn stimulates the release of adrenocorticotrophic hormone (ACTH) from the pituitary gland (B). ACTH causes glucocorticoid release (cortisol in humans) from the adrenal gland, which binds to receptors in the hypothalamus, pituitary, and hippocampus (C). Glucocorticoid binding in the hypothalamus inhibits CRF release, ending the stress response (D). In addition, the hippocampus plays a role in inhibiting the stress response (D).

In situations of chronic stress, excessive glucocorticoid release may eventually lead to hippocampal atrophy, thus preventing it from inhibiting the HPA axis (E). This could contribute to chronic activation of the HPA axis (F) and increase risk for an anxiety disorder.

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The Amygdala and the Physiology of Fear: Breathing Output

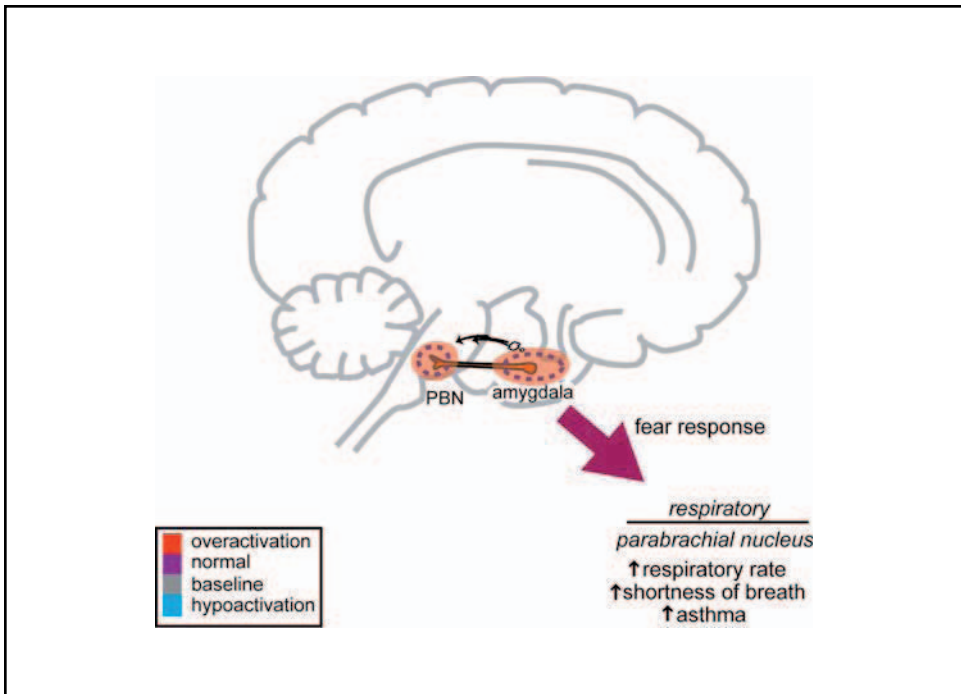


FIGURE 1.7. Increases in respiration rate are also an important part of a fear response and are regulated by connections between the amygdala and the parabrachial nucleus (PBN). However, when excessive activation occurs, this can cause shortness of breath, exacerbation of asthma, or a sense of being smothered—all of which are symptoms of a panic attack.

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The Amygdala and the Behavior of Fear

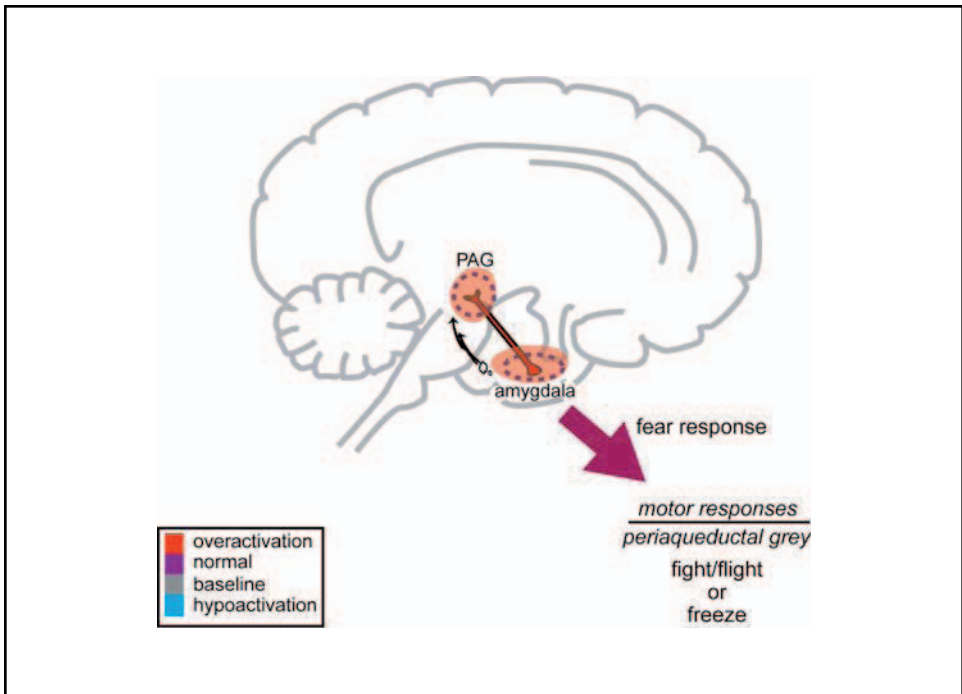


FIGURE 1.8. The emotional and physiological responses to a threat prepare one to take action in order to escape or combat that threat. The actual motor response taken—whether fight, flight, or freeze—is regulated in part through connections between the amygdala and the periaqueductal grey (PAG).