

QnAs with Joseph LeDoux

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In his 1933 inaugural address to the American people, President Franklin Roosevelt attempted to rouse the nation out of the stultifying Depression with his famous aphorism on fear as a self-fulfilling end. Decades later, a scientific understanding of fear continues to remain elusive, despite the unraveling of brain circuits triggered when people respond to a raft of dangers. That is, in part, because neuroscientists often ignore the distinction between the defensive response to danger and the conscious experience of fear, says New York University neuroscientist Joseph LeDoux. A member of the National Academy of Sciences, LeDoux has long explored the neural basis of emotions. Through pellucid accounts in scholarly literature and popular tomes, he has expounded the argument that baroque wiring diagrams that purport to show how the brain experiences complex emotions such as fear fail to capture the whole picture. Whether it is the timorous feeling before a test, the widespread dread of snakes, or the crippling worry of sexual incapacity, fear, says LeDoux, involves additional circuits beyond those involved in defensive responses. In his Inaugural Article (1), LeDoux explains why a deceptively trivial semantic distinction might have serious implications for understanding emotions and treating psychiatric conditions, including phobias, obsessive-compulsive disorder, and post-traumatic stress disorder.

PNAS: In your Inaugural Article, you argue that the term “fear system,” as used in the past for the brain circuitry that processes and responds to danger, is a misnomer. Why?

LeDoux: We know something about how the brain responds to threats from animal studies. For example, we have mapped out the neural pathways that allow a conditioned threat stimulus to control an animal’s defensive response to the stimulus, and we can detect hormonal and autonomic nervous system changes tied to the response. We can show through imaging studies that similar pathways operate in humans during responses to danger. We can also directly ask people how they experienced the stimulus while responding to it, and many studies have found that the human brain can respond

to threat stimuli without any corresponding conscious awareness of the stimuli and without feeling fear. So the conscious experience of fear is not necessarily in the sequence of events involved in detecting and responding to danger.

PNAS: Are there clinical implications to conflating nonconscious threat processing with the conscious state of fear, the brow-knitting feeling that envelops people when they break into a cold sweat?

LeDoux: People with anxiety disorders are bothered by the fear and anxiety that they consciously experience. If we claim we are studying human feelings of fear or anxiety when we measure defense responses in rats, we are giving a false impression. Still, what we researchers do has significant implications for psychiatry that should be specified. For example, a number of treatments for people with fear and anxiety disorders are the result of animal work. These treatments change the way implicit systems operate, and only indirectly affect conscious feelings. It may sound subtle, but the difference is important. These findings from animal studies are more relevant to behaviorally based therapies than to talk therapies. Moreover, this distinction is consistent with a National Institute of Mental Health initiative that emphasizes basic brain mechanisms that contribute to psychiatric problems over abstract conceptions of psychological states and diagnoses.

PNAS: To distinguish between threat processing and conscious fear, you propose the term “defensive organismic state” for responses to danger. Can you explain the term?

LeDoux: The defensive organismic state is the end result of turning on a defensive survival circuit. For example, when animals face danger, the amygdala is turned on, physiological responses ensue in the brain and body, and feedback is sent to the brain from the body. A fruit fly, worm, or sea slug can detect threats and respond in a way that mobilizes resources to deal with the threats. That’s a defensive organismic state. But only organisms that can be conscious that this is happening can experience fear.

PNAS: Why do you take issue with the popular characterization of the amygdala (a



Joseph LeDoux. Photo courtesy Diemut Strebe.

brain region implicated in threat processing) as the seat of fear in the brain?

LeDoux: The amygdala contributes to fear, but simply activating this brain region is not sufficient to create a feeling of fear. Such feelings are not hardwired in the amygdala or other subcortical brain areas, as some people think. Fear is a cognitive awareness of danger, and that experience might involve the activation of the amygdala (in the case of a snake at your feet) or may not involve the amygdala (in the case of existential fears, such as a fear of not leading a meaningful life).

PNAS: You decry the practice of anthropomorphizing animal brain states. Why do you think the search for evolutionary similarities among animals in psychological constructs like fear is misguided?

LeDoux: Searching for evolutionary commonality in high-level, conscious brain states, such as fear is—in my opinion—taking the wrong tack, partly because fear depends on introspection, language, and culture for its elaboration. We don’t know if other animals experience conscious fear, but if they do it’s likely to be different from our own experience because the neocortical circuits involved

This is a QnAs with a recently elected member of the National Academy of Sciences to accompany the member’s Inaugural Article on page 2871.

in these cognitive processes that create conscious states in humans are either absent in or different from those of other animals (language, for example, changes the cognitive brain). That said, defense responses elicited by threats via subcortical circuits

are highly conserved in humans and other species, and make important—albeit indirect—contributions to conscious fear. This is why we should turn the approach on its head and, instead of looking for human emotions in other animals, ask what is in

the brain of other animals that is also found in ours, and what it means.

1 LeDoux JE (2014) Coming to terms with fear. *Proc Natl Acad Sci USA* 111:2871–2878.