

On Including Pain as an Integral Part of the Fight-or-Flight Response

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We propose that pain should be included as an integral part of fight-or-flight response in publications, presentations, teaching materials, and clinical practice.

In 1915, W.B. Cannon described two “instincts” that occur in animals in the context of “emotional excitement”.¹ That work is best remembered for establishing the concept, now known as *flight or fight* response (F/F). In essence, F/F consists of automatically activated defensive behaviors to deal with threats.² Subsequent work, now known as “predatory imminence continuum theory”,³ identifies and differentiates defensive behaviors in F/F into three sequential aspects or states: *pre-encounter* (recognized threat, but at a distance), *post-encounter* (threat within closing distance), and *circa-strike* (imminent or actual attack). Each state relates to the progressive degree of threat and corresponds to progressive states of anxiety, fear, and panic.³ Specific brain regions are associated with each defensive state,⁴ and brain-region -“switching” to active defense (F/F) occurs as the threat progresses.⁵

Pain is not important as a survival message in the pre- or post-encounter states but would be in the circa-strike state, that is, the actual attack. The neuroanatomical connection between pain and F/F involves the descending pain-modulating pathways.⁶ Switching during progressive danger imminence, which requires active F/F behavior, has been shown to occur in the midbrain periaqueductal gray (PAG), a region involved in descending pain modulation.^{7–9} In mice, distinct coding characteristics in the PAG are manifested during flight vs “freezing” defensive responses to threat;¹⁰ in rats, studies using early gene (*c-fos*) expression revealed that the pattern of pain activation within the PAG “reflected a quality more akin to the ‘behavioral significance’ of the noxious event”, that is, an “escapability dimension” involving “the emotional strategy (active or passive) used by the animal to cope with the noxious event”.¹¹ The shift in threat imminence also occurs in humans. Using functional magnetic resonance imaging (fMRI) and an active avoidance paradigm, in which volunteers were virtually pursued through a maze by a predator endowed with the ability to chase, capture, and inflict pain, brain activity shifted from planning avoidance strategies in the ventromedial prefrontal cortex to the PAG as the predator grew closer.¹²

Our proposal to include pain as an integral part of the fight-or-flight response has been anticipated by many publications and presentations that start out by stating that pain is beneficial since it alerts to impending tissue damage, the recount of Dr. Livingstone’s attack by a lion, “he shook me as a terrier dog does a rat. The shock produced a stupor similar to that felt by a mouse after the first shake of a cat. It caused a sort of dreaminess, in which there was no sense of pain or feeling of terror, though quite conscious of all that was happening”,¹³ and even Freud’s conjecture that human psychological defense against internal threat evolved from animal defense against external predatory threat.¹⁴ However, to our knowledge, this is the first explicit proposal that pain is always included in descriptions of the physiological components of the fight-or-flight response.

Disclosure

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