

# Freeze, Flight, Fight, Fright, Faint: Adaptationist Perspectives on the Acute Stress Response Spectrum

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## FOCUS POINTS

- Threat-induced fainting (flaccid immobility), which often presents as blood-injection-injury type specific phobia, may have evolved as a defense response during human intragroup and intergroup warfare, rather than as a pan-mammalian defense reaction, as is currently assumed.
- Fainting can be added to the known biologically determined sequence of responses (freeze, flight, fight, fright) that humans may exhibit during acute stress.
- This reconceptualization of blood-injection-injury phobia has clinical, health services, and basic research implications.

## ABSTRACT

This article reviews the existing evolutionary perspectives on the acute stress response habitual faintness and blood-injection-injury type-specific phobia (BIITS phobia). In this article, an alternative evolutionary perspective, based on recent advances in evolutionary psychology, is proposed. Specifically, that fear-induced faintness (eg, fainting following the sight of a syringe, blood, or following a trivial skin injury) is a distinct *Homo sapiens*-specific extreme-stress survival response to an inescapable threat. The article suggests that faintness evolved in response to middle paleolithic intra-group and inter-group violence (of con-specifics) rather than as a pan-mammalian defense response, as is presently assumed. Based on recent literature, freeze, flight, fight, fright, faint provides a more complete description of the human acute stress

response sequence than current descriptions. Faintness, one of three primary physiological reactions involved in BIITS phobia, is extremely rare in other phobias. Since heritability estimates are higher for faintness than for fears or phobias, the author suggests that trait-faintness may be a useful complement to trait-anxiety as an endophenotype in research on the human fear circuitry. Some implications for the forthcoming Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition as well as for clinical, health services, and transcriptomic research are briefly discussed.

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## INTRODUCTION

### **Freeze (Hypervigilance), Flight, Fight, Fright, (Tonic Immobility)**

A coherent sequence of four fear responses that escalate as a function of proximity to danger has been well established by ethologists working with non-human primates. The sequence, originally described by Gray,<sup>1,2</sup> begins with what ethologists call “the freeze response” or “freezing,” a term corresponding to what clinicians typically call hypervigilance (being on guard, watchful, alert).<sup>1,2</sup> This initial freeze response is the “stop, look, and listen” action tendency associated with fear. Prey that remain “frozen” during threat are more likely to avoid capture, because the visual cortex and the retina of mammalian carnivores (and, to a lesser degree, of male *Homo sapiens*) evolved primarily for detecting moving objects and not color.<sup>3,4</sup> This initial freeze response is followed by attempts to flee, and then by attempts to fight; in that order (thus “flight or fight”

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would have been a more accurate term than the original term coined by Cannon<sup>5</sup> in 1929).

The next step in this sequence of responses is tonic immobility during direct physical contact with the carnivore (or the human predator). Tonic immobility was referred to as “playing dead” in the early literature. In the posttraumatic stress disorder (PTSD) literature tonic immobility has been referred to as peritraumatic “panic-like” symptoms. A widely used European term for tonic immobility, which may be more specific, is “fright.” The French term is “effroi.”<sup>6,7</sup> Fright is closest to the German (and Kraepelinaean) concept of “schreck” as in “schreckneurosen.”<sup>8</sup> Unfortunately, in child psychology, fright (tonic immobility, schreck, effroi) has also been referred to as “freezing.” This atypical use of the term “freezing” to denote “fright” has created much confusion (especially since the ethological term closely resembles the meaning of “freeze” in military and police parlance).

The tonic immobility (fright) defense response is pan-mammalian (like the freeze, flight, and fight responses which precede it). Tonic immobility is most useful when a slow-moving vulnerable organism (eg, the opossum) is confronted with a life-threatening situation involving mobile large predators.<sup>9,10</sup> A captured prey that becomes tonically immobile rather than struggling and fighting may increase its chance of escaping if the predator temporarily loosens its grip under the assumption that its prey is indeed dead. Tonic immobility may enhance survival and is therefore adaptive when there is no perceived possibility of escaping or winning a fight.<sup>11,12</sup> The tonic immobility survival response may be the best explanation for the behavior of some rape victims during the assault.

### **OVERVIEW OF FAINTNESS IN BLOOD-INJECTION-INJURY TYPE SPECIFIC PHOBIA**

There are three primary reactions in blood-injection-injury type specific phobia (BIITS phobia). Two are shared with other phobias: the emotional response (fear) and the behavioral response (avoidance). The third response is fainting (syncope) or faintness (pre-syncope). This syncopal (flaccid immobility) response is not shared with any other phobic disorder.<sup>13-16</sup> Marks and colleagues<sup>9</sup> were the first to draw attention to the specificity of fainting when they found that fainting was reported by only 0.02% of their sample of “mixed phobias”, and by 100% of their sample of BIITS phobia patients.

This unique feature is noted in the *Diagnostic and Statistical Manual-Fourth Edition-Text Revision (DSM-IV-TR)*<sup>16</sup>:

*“A vasovagal fainting response is characteristic of BIITS phobia; ~75% of such individuals report a history of fainting in such situations. The physiological response is characterized by an initial brief acceleration of heart rate and elevation in blood pressure followed by a deceleration of heart rate and a drop in blood pressure, which contrasts with the usual acceleration of heart rate and elevation in blood pressure in other specific phobias.”*

In the Baltimore Epidemiological Catchment Area (ECA) study, Bienvenu and Eaton<sup>17</sup> found that while subjects with BIITS phobia avoid indicated needle sticks, they do not appear to avoid medical doctors, outpatient health centers, or hospitals. Unfortunately, some otherwise excellent studies of phobia have clustered doctor phobia, hospital phobia, acquired immunodeficiency syndrome phobia, cancer phobia, dentist phobia, and social phobia together with BIITS phobia. Faintness, however, rarely occurs in response to these stimuli. Instead, arousal, vasoconstriction, and tachycardia are the typical responses.<sup>16</sup> Thus, other phobias are more similar to other anxiety disorders than to BIITS phobia. Research by Page and Martin<sup>18</sup> clearly indicates that habitual fainting precedes the appearance of BIITS phobia in many subjects. The authors argue that the tendency to faint around blood may be the key inherited individual difference, with subsequent blood avoidance developing via conditioned learning. This model is similar to an inherited disposition toward panic with subsequent learned agoraphobia.

This unique third aspect of BIITS phobia, fainting, is often neglected. This article will argue that faintness can be added to the list of four known biologically determined responses (freeze, flight, fight, fright) that a particular individual may exhibit in fear-inducing contexts.

Both genetic and clinical research on anxiety disorders are often facilitated by a “lumper mentality” (versus “splitter mentality”).<sup>3,19,20</sup> Vasodepressor (vasovagal, neurocardiovascular) syncope and pre-syncope greatly overlap with *DSM-IV-TR* BIITS phobia.<sup>13,16</sup> “Lumpers” may be able to argue that whether these symptoms are diagnosed as BIITS phobia or as vasovagal syncope depends predominantly on whether the first clinician to evaluate the patient is a mental health provider or an internist. More recent critical reviews, beginning with Kaloupek and colleagues,<sup>13</sup> have used vasovagal syncope synonymously with BIITS phobia.

In the largest epidemiological study using modern diagnostic criteria of this spectrum of behaviors in a non-clinical sample, Bienvenu and Eaton<sup>17</sup> examined

1,920 subjects in the Baltimore ECA study. They concluded that over 3% of the United States population, 4.4% of women and 1.8% of men, suffer from clinically significant BIITS phobia at some point in life. The median age of onset was 5.5 years, and 78% of the subjects reported experiencing symptoms within the last 6 months. Epidemiological studies have uniformly shown a significantly higher prevalence of blood phobia and threat-induced faintness in women compared with men.<sup>21,22</sup>

Repeated syncope or pre-syncope among young otherwise healthy persons following a trivial skin injury, a vaccination, an injection, or the sight of a syringe or blood, is a common and often frustrating symptom encountered in primary care but also in cardiology, pediatrics, adolescent medicine, neurology, and in some active duty military personnel.<sup>9,23,24</sup> Especially perplexing to cardiologists, neurologists, and to blood banks is the finding that persons with BIITS phobia often faint while in a sitting position.<sup>23</sup> The cardiological literature describes the sequence of autonomic nervous system responses observed in vasovagal syncope (above-normal early tachycardia followed by hypotension due primarily to massive vasodilatation in lower limb muscles) as hemodynamically “paradoxical.”<sup>23</sup> Cardiologists also find the asystole that often precedes fainting in young adults puzzling. However, from a neuropsychiatric perspective, the asystole may be easily conceptualized as extreme heart rate variability.

Reviews consistently note that fainters are more anxious prior to blood drawing than non-fainters, but also manifest a robust parasympathetic activation in association with stimuli related to blood drawing.<sup>13,14,23</sup> Attempts to divide fainters into subgroups, depending on whether they faint at the sight of the syringe or only after blood is drawn have met with limited success. Attempts to divide fainters into subgroups depending on whether they actually faint or just experience faintness have also failed.<sup>10,25,26</sup> This over-categorization has been rejected based on both nosological<sup>17</sup> and genetic reasoning.<sup>27</sup>

It should be noted that heritability estimates are higher for faintness than for fears or phobias.<sup>26</sup> Anywhere from two thirds to three fourths of patients with BIITS phobia have at least one first-degree relative affected with BIITS phobia. The familiarity of faintness was originally attributed by Marks and others solely to learning within a shared household environment.<sup>9</sup> Recent research suggests, however, that the role of learning in BIITS phobia is minor. A significant genetic contribution to the etiology of BIITS phobia, and particularly fainting,

was noted in a recent, twin study.<sup>18</sup> As Page<sup>4</sup> has also noted, “confidence in a genetic interpretation can be drawn from the observation that fainting subjects are not able to reliably identify whether their parents have fainted in response to blood and injury.” Kleinknecht<sup>26</sup> reached a similar conclusion. Page and Martin<sup>18</sup> recommended that future behavioral research on BIITS phobia should “focus on the mechanisms whereby genes associated with fainting can give rise to blood fears.”

### **IS BLOOD-INDUCED FAINTING A PAN-MAMMALIAN DEFENSE BEHAVIOR?**

Recent advances in evolutionary psychology have put into question some of the existing adaptationist hypotheses regarding faintness. These are based on blood-loss minimization or on disgust sensitivity. These existing evolutionary biological hypotheses regarding fainting are pan-mammalian; they argue that a tendency towards blood-induced faintness evolved prior to the emergence of the genus *Homo* and is common to all mammals.

#### ***Minimizing Blood Loss***

It is not surprising that the earliest adaptationist hypothesis of BIITS phobia in the psychological literature was that blood-induced fainting increases the probability of survival because a radical drop in blood pressure minimizes blood loss or cardiovascular shock, serving an adaptive function in the case of injury.<sup>10,25</sup> As Page<sup>4</sup> pointed out, however, this hypothesis does not explain fainting provoked by an injection or by trivial skin injuries, neither of which involve blood loss. Furthermore, cardiovascular research has consistently found that vasoconstriction and tachycardia are the initial responses to blood loss, whereas faintness or fainting is not experienced until there is a 30% drop in blood volume.<sup>28,29</sup>

#### ***High Disgust Sensitivity***

The second evolutionary explanation of BIITS phobia was that blood-induced syncope is controlled by the same pan-mammalian physiological mechanism that regulates disgust.<sup>4,9</sup> Early theorists hypothesized that in some individuals the sight of one's own blood might induce a disgust reaction.<sup>9</sup> However, disgust (and the associated phenomena of nausea and vomiting) is thought to have evolved to protect all mammalian omnivores from the risk of ingesting pathogen-laden food.<sup>9</sup> It is difficult to imagine the adaptive benefit of fainting next to pathogen-laden food, when withdrawal and avoidance seem more likely to increase survival

rates. More recent careful studies by Merckelbach and colleagues<sup>30</sup> failed to find a strong association between BIITS phobia and disgust sensitivity.<sup>31-33</sup>

### **Atypical Form of Fright**

Another conceivable pan-mammalian explanation is the pan-mammalian tonic immobility, discussed above. However, while tonic immobility closely resembles fright, it does not resemble faintness. An organism in tonic immobility is immobile but is markedly tachycardic, vasoconstricted, hyperalert, and prepared to flee in a moment of opportunity. In contrast, the vasodilatation and extreme bradycardia in fainting typically render an organism unconscious or incapacitated and, therefore, incapable of taking advantage of a lapse in the predator's grip.<sup>4</sup>

### **RELEVANT RECENT ADVANCES IN EVOLUTIONARY PSYCHOLOGY**

A discussion of relevant recent advances in evolutionary psychology may be useful. Some evolutionary psychologists (as recently as the mid 1990s) have argued that important traits (adaptations) should be characterized by low, heritability estimates, low phenotypic variance, low genotypic variance, universality across individuals, and universality across cultures (recently reviewed by Miller<sup>34-36</sup>). The rationale originally proposed was that natural selection should diminish variance, thereby driving the trait to fixation, as evinced by low h-squared. Reviews of new research<sup>34,37,38</sup> strongly suggest that while this line of reasoning makes sense for adaptations shaped by selection for survival utility, it is inappropriate for adaptations shaped by what Darwin in 1871 termed "sexual selection" (also known as mate selection).<sup>39</sup>

Miller<sup>36</sup> argues that "If some psychological adaptations evolved as sexually selected fitness indicators... we should expect them to violate many standard criteria used by evolutionary psychology to distinguish adaptations from non-adaptations." These conclusions are to a great degree based on recent work by anthropologists and primatologists who bring a female perspective to evolution, such as Jane Goodall, Carol Gould, Anne Campbell, Helen Fisher, Avishag Zehavi, Sarah Hrdy, Helena Cronin, Jeanne Altmann, Alison Jolly, Lynn Margulis, Meredith Small, and others.<sup>34,36-38</sup> New developments in animal signaling theory and game theory suggest that there are two distinct kinds of human psychological adaptations: naturally selected survival mechanisms and sexually selected fitness indicators. Behavioral traits that are more common in one sex

but not the other usually result from sexual selection (through mate choice). Miller states: "...sex differences are highly diagnostic of sexual selection."<sup>34</sup>

Although Darwin dedicated a substantial portion of *Descent of Man, and Selection in Relation to Sex*<sup>39</sup> to human sexual selection, it was not until the mid 1990s that evolutionary psychologists revived Darwin's ideas regarding sexual selection of behavioral traits. Miller<sup>34</sup> suggests that one reason for this neglect is that natural (non-sexual) selection, which is primarily pan-mammalian, was more acceptable to Victorian and early 20th century evolutionary biologists, most of whom were male and were less comfortable with discussing female sexuality and female-specific survival strategies.

### **A NEW HUMAN-SPECIFIC ADAPTATIONIST PROPOSAL FOR FAINTNESS**

Darwin's sexual selection theory was out of favor when pioneering thinkers, such as Isaac Marks,<sup>9</sup> did much of their writing about phobias. The literature reviewed above lends considerable support to the alternate view that distress-related fainting, and other habitual faintness may be mediated by more recent, *Homo sapiens*-specific adaptations arising from sexual selection.

It was until recently assumed that the origins of human warfare are in the neolithic (holocene). However, careful newer research has documented extensive *Homo sapiens* intragroup warfare in the middle paleolithic (the period in which *Homo sapiens* was predominantly pre-verbal).<sup>40-46</sup> A recurrent cause of death among paleolithic humans was wounding by a sharp object penetrating the skin. As recently as medieval times, inadequate capacity to treat infection meant that receiving a non-lethal wound during combat was almost as dangerous as receiving a fatal combat wound.<sup>47-49</sup> Thus, it could reasonably be argued that throughout the paleolithic environment of evolutionary adaptedness (EEA), the sight of blood during an antagonistic encounter with con-specifics was consistently associated with life-threatening danger. Fainting in response to the sight of blood may have evolved as an alternate distress reaction, or adaptation, that aided the survival of non-combatants in some EEA combat situations.

While fainting clearly involves a marked and abrupt increase in vagal tone (parasympathetic activation), the initial physiological response during *Homo sapiens* combat undisputedly included a markedly diminished vagal tone.<sup>50-52</sup> However, consider a sympathetically activated non-combatant on the losing side of a paleolithic conflict. In these circumstances, observing an approaching sharp object,

experiencing skin-penetration by that object, or witnessing fresh blood on oneself (or on a fellow group member) is a crucial turning point. From this point on, continued sympathetic arousal may be an ineffective survival response (eg, adversaries have moved from posturing to actually killing members of one's group). In addition, it is possible that sympathetic activation has been at least partially exhausted.<sup>10,25</sup>

It is unlikely that most non-combatants (females and prepubertal children) could outrun a young male adversary. Hence, the few non-combatants who inherited the polymorphism for the "paradoxical" fainting response to the first sight of a sharp object or blood now possess a survival advantage. In a non-combatant, a genetic polymorphism to "reverse gears," abruptly increase vagal tone and collapse flaccidly to the ground rather than flee or fight, could have been selected.

While fainting is not part of the acute stress reaction sequence for most individuals, neither is fright.<sup>12</sup> The primary function of fear-induced fainting may have been to non-verbally communicate to equally preverbal adversaries that one was not an immediate threat and could be safely ignored. It is likely that such a polymorphism increased a non-combatant's chance of surviving violent conflicts during the EEA and hence that trait was selected. The *Homo sapiens*-specific hypothesis presented here predicts that the syncopal response induced by the sight of blood was more common among individuals who were non-combatants during the EEA. For these individuals, the strategies of flight or fight might have been less effective survival responses than immediate fainting at the sight of blood.

Both inter-group and intra-group violence would have primarily occurred between males, with females and children serving as objects of competition rather than as immediate targets. Recent investigations of female lineages through mitochondrial DNA and of male lineages through the Y chromosome, provide strong evidence that when past human populations experienced violent inter-group confrontation, invaders typically killed the post-pubertal males<sup>62</sup> and took females and most prepubertal individuals captive.<sup>63</sup> Thus, during the paleolithic EEA fainting was most likely highly maladaptive in a post-pubertal male engaged in combat (resulting in death or resulting in a drop in social hierarchy—a key fitness indicator).

In contrast, fainting may have been adaptive for all others, since it preserved their lives. All epidemiological data on contemporary populations suggests that a syncopal response to blood, injec-

tion, and injury is significantly less common among post-pubertal males. This gender and age pattern is clearly noted in the *DSM-IV-TR*.<sup>16</sup>

The evolutionary perspective proposed here can explain many seemingly paradoxical aspects of BIITS phobia. For example, Kaloupek and colleagues<sup>13</sup> found that contrary to expectations, blood donors were found to faint more frequently with experienced phlebotomists than with inexperienced phlebotomists. This observation is consistent with the evolutionary explanation presented here. As Kaloupek and colleagues<sup>13</sup> note, the inexperienced phlebotomist is "slow and communicative" while the experienced phlebotomist is "rapid and non-communicative." A sharp object held by a rapidly moving noncommunicative stranger shares enough stimulus properties with a life-threatening middle paleolithic assault to elicit a response appropriate to a lethal stimulus. Thus, it is the experienced phlebotomist who shares more stimulus characteristics with a violent middle paleolithic adversary.

Finally, studies by Shalev and colleagues<sup>53</sup> and Shalev and colleagues<sup>54</sup> which were recently supported by Bryant and colleagues,<sup>55-58</sup> Vaiva and colleagues<sup>6</sup> and Vaiva and colleagues<sup>7</sup> and other researchers,<sup>51,52,59-61</sup> all suggest that prolonged episodes of tachycardic fright may have immediate consequences in terms of subsequent PTSD. One may argue that a rapid early switch from a tachycardic fright to a bradycardic faint during overwhelming psychosocial stress might have been adaptive in certain EEA circumstances. Differently stated, an early switch from fright to faint may have diminished over-learning or "searing" of psychological trauma memories.

#### **CLINICAL, RESEARCH, AND HEALTH SERVICES IMPLICATIONS**

In the US, fainting triggered by a trivial injury routinely leads to costly and often invasive cardiological and neurological workups in both adults and children.<sup>17,64</sup> Cost estimates are not available; hence, health services research on habitual fainting may be warranted.

While none of the BIITS phobia patients in the Baltimore ECA study had sought mental health treatment specifically for phobia, half of them were in psychiatric treatment for an unrelated disorder.<sup>17</sup> Therefore, clinical psychiatrists may want to routinely query patients about BIITS phobia.

Ample clinical research demonstrates the effectiveness of exposure and cognitive restructuring in treating some highly heritable phobic symptoms, including BIITS phobia. However, this effectiveness

speaks more to the clinically relevant question of maintenance factors than to neurobiological and the forthcoming *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (taxonomic) relevant question of etiology. Unconstrained adaptive speculation is likely to yield little that will enhance our understanding of these phenomena; however, a systematic effort that brings to bear the known evidence regarding the origin and function of anxiety symptoms in early *Homo sapiens* and across the zoologic spectrum is bound to lead to useful hypotheses at the very least. A research focus on distal (ultimate) causation is fully compatible with and complementary to the standard psychiatric research focus on proximal causation. For reviews on testing evolutionary hypotheses about behavioral disorders, see Nesse<sup>65</sup> and McColl and colleagues<sup>66</sup>. Several new testable and falsifiable research hypotheses can be generated by the *Homo sapiens*-specific sexual selection adaptationist view of faintness proposed in this article.

Neurobiologically, one may hypothesize that at the transcriptome level, BIITS phobia involves a developmentally sensitive gene expression mechanism that, in males, is turned off at puberty by androgens such as testosterone and dehydroepiandrosterone and that BIITS phobia may often spontaneously remit circa menopause.

As noted above, heritability estimates are much higher for habitual faintness than for fears or phobias.<sup>26</sup> Based on the literature reviewed here, the author suggests that trait-faintness may be a useful complement to trait-anxiety as an endophenotype in research on stress-related disorders including PTSD.

Finally, research designed for specific culture-bound genomes can be a useful approach in stress-related disorders.<sup>67-71</sup> With regard to BIITS phobia, one may hypothesize that if it is based on *Homo sapiens*-specific (non pan-mammalian) sexual selection, then BIITS phobia is likely to vary across ethnic groups.

## CONCLUSION

The author proposes a revised adaptationist framework for conceptualizing habitual faintness and BIITS phobia, which may have implications for the forthcoming *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. Specifically, the author proposes that faintness in response to stimuli associated with bloodletting might have been a *Homo sapiens*-specific survival response in paleolithic non-combatants. Syncope associated with BIITS phobia in contemporary contexts may be elicited by stimuli that are similar enough to middle paleolithic threats that signaled life-threatening danger.

Finally, freeze, flight, fight, fright, faint might provide a more complete description of the human acute stress response sequence than current descriptions. **CNS**

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