Chapter 7

Anxiety Disorders in Evolutionary Perspective

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Abstract

Anxiety disorders make sense only in the evolutionary context of the origins and functions of normal anxiety. Anxiety is an adaptation that adjusts diverse aspects of individuals in ways that increase fitness in dangerous situations. Subtypes were partially differentiated by different dangers. Anxiety is not fully differentiated from other aversive emotions, especially low mood. Anxiety disorders result when regulation systems fail. Explaining them requires considering five possible reasons for vulnerability. However, much harmful anxiety arises from normal mechanisms. These insights are valuable in the clinic, and they suggest new research initiatives.

Keywords

anxiety disorders, emotions, evolutionary medicine, evolutionary psychiatry, fear, panic

Key Points

- Natural selection partially differentiated subtypes of anxiety that increase the ability to cope with different kinds of dangers.
- Useless or harmful anxiety often arises from normal mechanisms.
- Explaining the utility of anxiety and the role of vicious cycles is often very helpful for patients engaged in behaviour therapy.

7.1 What Evolution Offers

It is possible to provide effective treatment for anxiety disorders without an evolutionary perspective. I did that full-time for a decade, before I finally recognised how useful evolutionary principles could be for psychiatry (Nesse, 1984). Understanding the origins and function of normal anxiety transformed my treatment of anxiety disorders and improved clinical outcomes. The improvement didn't come from doing some special evolutionary kind of therapy; it came from a fundamental reframing of what anxiety is and what anxiety disorders are. Instead of asking only what is wrong with people who have disorders, I began asking the two evolutionary questions that need answers to understand any disorder. The first is the origins and adaptive significance of the traits that causes the vulnerability. For anxiety disorders that is easy: the capacity for the anxiety and the system that regulates its expression increase fitness in dangerous situations. The second question is why the systems are vulnerable to malfunction. It was soon obvious that this question needed to be answered for all diseases, and that evolutionary medicine more generally needed to be developed before the subfield of evolutionary psychiatry (Williams and Nesse, 1991).

Much of my interest in evolutionary approaches came about because I was appalled by the vast prevalence of anxiety and depression. It seemed to me that whoever designed the organism must have been incompetent or malevolent. However, working with George Williams soon made it clear that there are several reasons why natural selection leaves us vulnerable to so many medical problems (Nesse, 2005a; Nesse and Williams, 1994). It is severely constrained by stochasticity, which limits the ability to find solutions, steadily degrades the genome and limits canalisation. Natural selection cannot start over to correct a suboptimal design. It is too slow to keep up with fast-changing environments and fast-evolving pathogens. It cannot create traits free from the trade-offs that leave them vulnerable. And natural selection maximises gene transmission, often at

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the expense of health (see Chapter 6). These categories have proved valuable for understanding why some traits leave us vulnerable to diseases.

Despite George's reluctance, we added one more category: defences that often seem like diseases. Pain, fever and cough are exemplars. They are protective responses expressed in situations where they are useful: tissue damage, infection and foreign matter in the respiratory tree, respectively. Only gradually have I come to understand George's reluctance. Defences are fundamentally different from the other categories: they are adaptations, not explanations for why natural selection has left us vulnerable. Their aversiveness and their associated costs can make even normal defensive responses seem like diseases. Also, they are prone to dysregulation, which can make them become real diseases (e.g. chronic pain). Most significant of all, defensive responses that arise from normal regulation mechanisms are often useless or harmful. An evolutionary analysis of anxiety and its disorders seems simple but turns out to illustrate the challenges as well as the opportunities for evolutionary psychiatry.

7.2 Normal Anxiety

Anxiety and fear are emotions. Emotions exist only because they have given selective advantages. This makes it tempting to try to define different emotions in terms of their functions. Fear protects against present danger, anxiety against possible dangers. However, defining emotions in terms of their functions risks tacit creationism: the tendency to view bodies as if they are machines (Nesse, 2020). Machines have distinct parts with specific functions connected in sensible ways by an engineer with a plan. Bodies are very different. Functions are often carried out by multiple interacting parts with blurry boundaries and infernally complex connections that defy our wishes for simplicity. Fear and anxiety are not completely separate so I will use the term 'anxiety' to describe both.

An explicitly evolutionary approach looks for the structure of emotions in the evolutionary history that shaped them. Instead of sharply distinct basic emotions envisioned by an engineer, natural selection has shaped overlapping suites of changes that increase fitness in situations that have recurred often over evolutionary time (Al-Shawaf et al., 2016; Del Giudice, 2021; Keltner, 2019; Ketelaar, 2015; Nesse, 1990; Nesse and Ellsworth, 2009; Plutchik, 1970; Tooby and Cosmides, 2000). Thus, different emotions correspond not to different functions, but to different situations and the adaptive challenges of those situations.

A complete evolutionary explanation of any trait requires answers to all of Tinbergen's four questions (Natterson-Horowitz, 2019; Nesse, 2013; Pfaff et al., 2019; Tinbergen, 1963). What is the mechanism? What is its ontogeny? What is its phylogeny? What is its adaptive significance? Answers to the first two questions provide proximate explanation (see Chapters 1 and 2). Answers to the latter two questions provide an evolutionary explanation.

The *mechanisms* of anxiety have been the focus of intense study for decades. Psychological mechanisms for learning and generalisation of anxiety are well described. Brain mechanisms that mediate these responses are increasingly well understood (Kalin et al., 2005). Many sources are available, so mechanisms will not be further elaborated here except to note that there is partial but not complete differentiation of the brain loci, neurotransmitters and pathways that mediate anxiety. Also of special significance is the discovery that an older neural pathway for fast transmission of signals about danger has been overlaid with a second slower pathway that incorporates more knowledge about context and prior experience (LeDoux, 2000).

The *ontogeny* of anxiety has likewise been well studied (Barlow, 2000; Costello et al., 2005). The pioneer of evolutionary psychiatry, John Bowlby, observed the fear infants experience on separation from their mothers (Bowlby, 1973). The field of attachment research is based on the functional significance of fears that help individuals cope with a particular situation at a particular time of life (Simpson, 1999; Troisi, 2020). Infants across different cultures develop a fear of strangers that is likely to be adaptive (Konner, 1972). Nightmares concerning animals under the bed are very common and easy to interpret in an evolutionary context where there were many wild animals but no houses. When children begin social life in groups, fears of being rejected or abandoned emerge in a process that elaborates into the extraordinary richness and complexity of social life (Brosnan et al., 2017). This sequence of different fears appearing at different times in

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development matches the phases in which they would be useful.

The *phylogeny* of anxiety goes back as far as behaviour (LeDoux, 2012). Even bacteria detect risky situations and swim away from them (Lyon et al., 2021; Tagkopoulos et al., 2008). Direct escape from a present danger is usually thought of as fear, while anxiety is the associated emotion that facilitates avoidance of dangerous situations. Anxiety is akin to the nociceptive responses that prevent tissue damage, while fear is akin to immediate anticipation of damage, and sadness is akin to pain that occurs when tissue is being damaged.

Anxiety is often equated with stress. Walter Cannon gave the name 'stress' to the emergency system associated with the adrenal medulla response (Cannon, 1929), but it was Hans Selye who recognised the role of the adrenal cortex in the 'general adaptation syndrome' (Selye, 1936); Selye resisted calling it 'stress' until 1946. The common view that the hypothalamic–pituitary–adrenal system is activated mostly by danger is incorrect. It is aroused by situations that require vigorous activity for effective coping – especially threats, but also opportunties. It is not aroused reliably by situations that cause psychological anxiety. The stress response allocates extra metabolic and behavioural resources in situations where the benefits are greater than the costs (McEwen, 2019; Nesse et al., 2016; Sapolsky, 2000). The sympathetic nervous system accomplishes the same ends on a shorter timescale. The parasympathetic nervous system shifts resources to storage and repair when situations permit.

Adaptive significance, the focus of Tinbergen's fourth question, is more subtle than it seems. Anxiety adjusts many different parameters that increase fitness when expressed in situations associated with danger. Different adjustments are useful for different kinds of danger. This has differentiated generic anxiety into partially differentiated subtypes, each of which corresponds to a different danger and, interestingly, a different corresponding anxiety disorder (Nesse and Marks, 1994). The human wish for simplicity encourages thinking about them as different essentialised diseases, but they evolved from common precursor emotions to cope with situations that are not entirely distinct. The resulting anxiety subtypes are not crisply differentiated, and path dependence and mismatch result in characteristics that can be poorly suited to the situation. For instance, muscle tension is useful in preparation for flight, but in social anxiety it causes useless or harmful trembling.

Each anxiety subtype induces changes in physiology, attention, motivation, behaviour, facial expression, posture and vocal characteristics. Those suites of responses evolve in conjunction with mechanisms that monitor for the presence of the relevant situation and regulate anxiety expression accordingly. But how do organisms detect the relevant situation? Are anxiety responses innate or learned? The answer to the latter question is 'both', of course, but a full answer is much more interesting.

The cues that arouse anxiety innately differ from species to species, but for mammals there is moderate consistency in unconditioned fear being aroused by sudden loud noises, rapidly moving looming objects, pain, screams and being alone in a strange place. For humans, being the object of unsmiling attention from a group of strangers may also qualify.

What about fear of snakes? Is it innate? A wonderful series of experiments conducted by Susan Mineka and colleagues showed that lab-reared infant monkeys are quite happy to reach across a toy snake to get a piece of banana. However, a single viewing of a video in which another monkey express fear of snakes suffices to establish an enduring fear response (Mineka et al., 1984). Watching a similar video of another monkey expressing fear of a flower does not create a comparable response. This is a classic example of prepared learning (Seligman, 1971).

We need to revisit tacit creationism. Imagine for a moment how natural selection shaped anxiety-regulation mechanisms. There is no essentialised image of a snake in the system, nor is there a specific circuit to anxiety centres. Selection acted on tiny heritable variations in brain structure that influence connections between cues and anxiety-regulation mechanisms. Any cue that has been associated with a danger across evolutionary time can be recruited to connect readily to anxiety. Connections that increase fitness become more frequent; those that don't are selected out. The result is nothing like perfection. Irrelevant cues may be incorporated, and cues that might be useful might never get incorporated. Responses that are not useful may persist as part of a network of responding. Nonetheless, the system does a reasonable job of arousing

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appropriate anxiety responses in situations where they could be useful.

So far, we have covered only normal anxiety. What about anxiety disorders? Individuals that we see in anxiety disorder clinics all are characterised by anxiety excessive for the situation. Whether an anxiety response is excessive or not depends entirely on the situation, and understanding the relevant situations requires an evolutionary perspective. That perspective immediately calls attention to a class of unrecognised anxiety disorders. Individuals with deficient anxiety responses (i.e. hypophobia) have a disorder at least as serious as those who have excessive anxiety (Marks and Nesse, 1994). People with hypophobia do not request treatment, however, and their disorders are not treated or even recognised.

Even with knowledge of the situations that arouse anxiety normally it is hard to distinguish normal from abnormal responses. Diagnostic criteria rely on the frequency, severity and inappropriateness of responses, but the line they draw between normal and abnormal anxiety is artificially sharp. Therefore, some people who don't reach diagnostic criteria nonetheless want and would benefit from treatment, while some who do reach diagnostic criteria have anxiety that seems to arise from normal regulation mechanisms. An evolutionary perspective does not solve the dilemma of diagnostic criteria for anxiety disorders, but it can explain why the problem has been impossible to resolve.

7.3 Explaining Vulnerability to Anxiety Disorders

Anxiety-regulation mechanisms are prone to dysfunction. It is tempting to try to explain disorders by looking for associated selective advantages, but that is a mistake. Disorders are not adaptations. They do not have net fitness benefits. They are not products of natural selection. They are not appropriate objects of evolutionary explanation. Instead, the appropriate objects of explanation are traits that leave us vulnerable to disorders. In this case, the traits are the evolved mechanisms that regulate anxiety. There are five main kinds of possible explanation for why a trait might be vulnerable to malfunction (see Chapter 6 for details).

Stochasticity, which is inherent to natural selection, is the main explanation for vulnerability to anxiety disorders. Genetic variations leave some individuals with excessive anxiety responses and others with deficient responses. Developmental stochasticity and differences in life experiences further increase the variance. The breadth of anxiety sensitivity is remarkably wide, ranging from vastly too much to vastly too little. This suggests that stabilising selection has been limited because the fitness function is relatively flat or because prior environments have varied substantially in the degree of risk. The distribution seems to skew towards excessive anxiety, but the lack of data correlating the degree of anxiety with fitness in ancestral environments makes it hard to tell what would be optimal.

Path dependence makes it impossible for natural selection to start afresh to correct a suboptimal design. In the case of anxiety disorders, this is reflected in the somewhat separate fast and slow pathways to arousing anxiety and the lack of integration of information from higher centres. This is why logical explanations about the lack of danger posed by a snake or a spider do nothing to reduce anxiety. Path dependence also accounts for the shared characteristics of anxiety that are unhelpful in a particular situation, such as sweating while giving a public presentation.

Mismatch between bodies and modern environments accounts better for deficient anxiety responses than excessive ones. We would be better off with more fear of guns, dirty needles, driving fast and electrical wires. Perhaps another 10,000 years of natural selection will provide us with better such protection. Mismatch can also help to explain some anxiety excesses.

Trade-offs are inherent to all responses. People with a great tendency to anxiety get protection at the expense of missed opportunities. People with deficient anxiety can take risks that bring benefits at the cost of damage and loss.

Traits that benefit genes at the expense of the individual are not as relevant to anxiety as they are to some other disorders, although parents sometimes are consumed by fears about their children's welfare – a perfectly natural response that nonetheless benefits genes more than the individuals experiencing the anxiety.

Each of these five reasons for vulnerability needs consideration for each anxiety disorder. However, it is difficult to tell where normal ends and where disorder begins (Faucher and Forest, 2021; Horwitz and Wakefield, 2012; Stein, 2013;

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Wakefield, 1992). With that in mind, it is useful to recognise that bad feelings are often useless or harmful products of normal mechanisms.

7.4 Why Bad Feelings Are Often Useless but Normal

It seems obvious that anxiety produced by normal regulation mechanisms should be reliably useful and that useless anxiety should be a product of abnormal regulation mechanisms. Neither assumption is correct. The assumption that useless anxiety usually arises from defective regulation mechanisms has spurred enormous efforts to find brain abnormalities that don't exist. The assumption that all expressions of normal emotion should be useful has spurred wild speculations about the possible fitness benefits of disorders. Debates about the disease status of 'harmful dysfunctions' continue to be intense (Faucher and Forest, 2021; Wakefield, 2020). An evolutionary framework helps by calling attention to five reasons why useless or harmful anxiety is produced by intact regulation mechanisms. These are different from the five reasons for vulnerability to disorder, but there is some overlap.

The smoke detector principal is the most important explanation for useless anxiety (Nesse, 2005b; Nesse and Williams, 1994; also see Chapters 1 and 6 of this volume). The presence of a danger is often uncertain. Whether or not a defensive response should be expressed depends on the likelihood that the danger is actually present, the cost of a protective response and the average cost if no response is expressed but the danger turns out to be actually present. The optimal response threshold is illustrated by considering the costs of expressing or not expressing a panic attack when a predator might be present. The utility of the panic response was recognised by Walter Cannon in his description of the fight-or-flight response (Cannon, 1939). In the face of life-threatening danger, massive physiological arousal, muscle tension and a strong motivation to flee are all potentially life-saving. If a false alarm in that system costs 100 calories but failing to express the response when a predator is actually present costs 100,000 calories, then it is optimal to express a response whenever the probability of the predator being present is greater than 1 in 1,000. This means – and I couldn't believe it when I first did this calculation – that 999 panic episodes out of 1,000 will be false alarms that are perfectly normal products of an optimal regulation system. Signal detection theory provides more sophisticated analyses of such trade-offs (Bateson et al., 2011; Green and Swets, 1966). But the brain does not need to do calculus; it simply expresses, on average across many people in many situations, responses that maximise fitness.

The capacity for adjusting the anxiety threshold as a function of experience is a secondary anxiety-regulation mechanism with great benefits and substantial risks. For tissue damage, proprioception provides protection. Only when that fails does tissue damage occur, arousing pain. Repeated arousal of pain means that dangers have not been adequately protected against and that increased sensitivity of the proprioception and pain systems will be beneficial. This runs the risk of initiating a positive-feedback loop that creates chronic pain (Nesse and Schulkin, 2019; Williams, 2016). For other dangers and losses, anxiety mediates avoidance of the danger, but if it fails, fear and possible loss result. Repeated experiences of fear indicate a dangerous environment where increased anxiety can be beneficial despite its costs. Here, too, the system comes with an inherent risk of initiating a vicious cycle. More on this is discussed in Section 7.5.3.

Mismatch results in normal mechanisms expressing useless anxiety. We have far too much fear of harmless snakes and insects. In cultures where experiences with such organisms are common, social transmission provides individuals with knowledge about which snakes, spiders and insects are dangerous and which are harmless. In modern environments, most people never have experiences that allow such learning. Thus, most of my patients with snake phobias had never encountered a snake in the wild and I don't recall even one who had experienced a snake bite. I am feeling slightly apprehensive at this very moment. A webcam mounted on a gooseneck stand is bent in an arc, bringing it close to my face and causing a tiny bit of anxiety that is relieved by bending it into an upright, less snake-like position.

However, mismatch mostly accounts for deficient anxiety responses. People have nowhere near enough fear of guns, dirty needles, driving, drugs and electrical wires. Perhaps we will in 10,000 years. For now, hypophobia is rampant.

Happenstance unfortunate sequences of events can interact with normal mechanisms to give maladaptive responses. Modelling demonstrates

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how such maladaptations can persist (Greggor et al., 2019; Meacham and Bergstrom, 2016; Trimmer et al., 2015)

Benefits to genes at a cost to the individual can cause anxiety that is useless for the individual but useful for the individual's genes in children and other kin. Many parents twist themselves in knots with worries about the dangers faced by their children; this completely natural anxiety benefits genes at a cost to the individual.

7.5 Anxiety Disorders

7.5.1 Epidemiology

Anxiety disorders are the most common mental disorders; epidemiological data describe the details (Kessler et al., 2010; Michael et al., 2007). In Western countries, lifetime prevalence rates of any anxiety disorder range from 14% to 29%. Panic disorder, agoraphobia, generalised anxiety disorder (GAD) and obsessive-compulsive disorder (OCD) have lifetime prevalence rates mostly in the range of 1–4%, while simple phobias and social phobias are more common, with estimates in the range of 2–14%. Specific and social phobias usually have their onsets in childhood, while GAD, panic disorder and agoraphobia tend to begin in late adolescence or early adulthood. Comorbidity among anxiety disorders is high; 74% of individuals with one anxiety disorder also have another. The rate is over 90% for those with GAD or panic disorder, and individuals with GAD are 12.3 times more likely to have panic disorder than individuals without GAD. The average odds ratio for an individual with one anxiety disorder having a second anxiety disorder is 6.6. Rates of anxiety disorders in non-Western countries tend to be substantially lower, with 12-month prevalence rates being about half of those in Western countries and with substantially lower rates for specific phobias, social phobias and GAD (Michael et al., 2007).

Anxiety disorders have major overlaps with other mental disorders, especially depression. Data from the National Comorbidity Study Replication show that the lifetime risk of any mood disorder is increased by factors ranging from 3.45 for phobias to 5.83 for GAD (Merikangas and Swanson, 2010). Interestingly, the genetic variations that predispose individuals to major depression are mostly the same as those that predispose individuals to GAD (Kendler et al., 1992; Middeldorp et al., 2005; Taylor et al., 2019).

Anxiety disorders have moderate heritabilities, in the range of 30–40%. Women have twice the risk for most anxiety disorders as men, with the exception being OCD where differences are small. The risk is lower for married individuals and those who have higher levels of education, employment and income. A history of physical, emotional or sexual abuse was found in 35% of subjects with major depression and panic disorder (Young et al., 1997); most likely these are the lasting effects of family conflict, but it is hard to control for genetic factors. Children with three or more early stressful experiences are considerably more likely to develop depression or GAD in response to military training (Bandoli et al., 2017).

The disorders recognised by clinicians and described in official diagnostic nomenclatures map remarkably well to different subtypes of normal anxiety and the dangers they map onto (see Table 7.1).

7.5.2 Phobias

In Western countries, about 12% of people have had a specific phobia severe enough to reach diagnostic criteria at sometime in their life, and in any given year the rate is about 9%. Many are phobias of insects and small animals. The brain shows responses to such images even before they reach consciousness (Ohman et al., 2007). Most people with simple phobias cannot recall a precipitating incident and many say they have had the problem for as long as they can remember (Poulton and Menzies, 2002). Also, individuals who fear heights as teenagers were *less* likely than others to have been injured in a childhood fall, presumably because those who were injured had – and still have – hypophobia (Poulton et al., 1998). However, such studies have severe methodological limitations (Mineka and Öhman, 2002). A model that incorporates innate tendencies and preparedness to learn anxiety offers an explanation for why some things are much more likely to cause phobias than others (Mineka and Zinbarg, 2006).

Generalisations do not do justice to the diversity one sees in the clinic. One of my patients recalled, while being treated for a fear of small insects, being suddenly whisked out the back door

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Table 7.1. Anxiety disorders and corresponding dangers

Disorder	Danger
Small animal phobia	Harm from small animals
Height phobia	Falling
Blood, illness, injury phobia	Bleeding, tissue damage
Agoraphobia	Vulnerability in open places
Claustrophobia	Vulnerability in closed places
Post-traumatic stress disorder	Life-threatening danger
Panic disorder	Predators and dire dangers
Illness anxiety disorder	Undiagnosed disease
Somatic symptoms disorder	Undiagnosed disease
Separation anxiety disorder	Isolation from kin and friends
Social anxiety disorder	Rejection or attack by a social group
Body dysmorphic disorder	Being viewed as unattractive
Obsessive-compulsive disorder	Dire consequences from an oversight
Hoarding disorder	Shortages of vital resources
Generalised anxiety disorder	Dangers of all kinds

of a paediatrician's office at age 7 to a polio ward, where she lay alone and paralysed watching insects crawl up the wall next to her. A woman with a snake phobia recalled stopping with her father on a rural road where he chopped a snake into pieces, put them in a Mason jar and had her hold it between her legs for the rest of the journey. My psychoanalytic supervisors were delighted, but they were astounded to learn that an hour of exposure therapy cured her. Most patients with phobias, however, have no idea what caused their disorders.

Treatment for phobias is reliably effective if it's possible to get the phobic person to maintain close contact with the phobic object for an extended period (Eaton et al., 2018). The challenge is often great, given that such therapy fights the natural urge to escape from danger. What works best is to have the patient stay close to the phobic object until the anxiety reduces somewhat, even from 90 to 80 on a 100-point scale. Once patients realise that progress is possible, they are motivated to continue with treatment that is usually effective. The benefit seems not to be from unlearning; instead, new inhibitory impulses are created.

The traits that account for vulnerability to phobias are the preparedness of some cues to be associated with anxiety and the capacity for learning. The main evolutionary explanation for vulnerability to phobias is the stochasticity of brain variations – inherited and acquired – that result in some people developing phobias. They are genuine disorders, not adaptations. Mismatch may also contribute, especially because of a lack of experience and a lack of cultural knowledge.

Discussing the evolutionary reasons for vulnerability to phobias helps patients to realise that their symptoms are simply an exaggeration of a useful response, not a disease that means that they have an abnormal brain. Furthermore, explaining that natural selection shaped a mechanism to reduce anxiety after extended exposures helps many to complete behaviour therapy.

7.5.3 Panic Disorder and Agoraphobia

Panic disorder offers a good example of how evolutionary thinking can be helpful in the clinic. For the first decade of practice in an anxiety clinic, I explained to patients that their panic attacks were a product of a mental disorder and that a combination of medication and behaviour therapy could help. Many said they knew their condition was not mental because they could feel their heart pounding. When I mentioned genetic predispositions, many interpreted this to mean they could not be helped. When I shifted to explaining that panic attacks are a normal, useful response to extreme danger and that panic disorder results from false alarms in that system, patients immediately appreciated the evolutionary context even without hearing the 'e-word'. This explanation made sense of their symptoms, so they no longer needed to attribute them to cardiac or neurological disease. In particular, the overwhelming mental focus on escape and the wish to flee became coherent, allowing them to complete behaviour therapy exercises that otherwise would have been impossible.

An evolutionary perspective also revealed a clinical phenomenon I had not previously

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recognised. I knew that freezing is an essential part of the panic response for other animals, but I had never heard about this response from any of the scores of patients with panic disorder I had seen. When I began asking, I found – to my amazement – that about half of patients reported feeling unable to move for a moment at the onset of panic.

About half of patients with panic attacks have agoraphobia, and most patients with agoraphobia have experienced panic attacks or some similar sudden episodes associated with fear. The nature of this connection has been explored with neurological and psychodynamic theories. However, from an evolutionary point of view the connection is straightforward. If you have repeatedly encountered a predator or other life-threatening danger on recent forays away from camp, it is smart to stay home if possible, to venture out only with comrades and to be ready to flee at the merest hint of danger. This explanation is enormously helpful to patients. They still need to follow through with often distressing exposure exercises, but the protocol now makes more sense to them. They realise that wide open spaces were indeed a situation of vulnerability for our ancestors. Patients with claustrophobia realise that enclosed spaces were also especially dangerous. The setting where humans in general feel most at peace is an open park-like setting with little underbrush and small, climbable trees (Kaplan, 1987). This is no surprise.

Why does natural selection leave us vulnerable to panic disorder and agoraphobia? The smoke detector principal offers part of an explanation, but panic disorder is not a normal adaptive response – it is a crippling disease. Like other anxiety disorders, it is heritable, and it is influenced by early adverse experiences and current stressors. Repeated exposure to big risks adaptively adjusts the system to greater sensitivity. However, the crucial pathological process involves a positive-feedback cycle that is set in motion when symptoms of panic are themselves viewed as dangerous, as they often are after patients hear from an emergency room physician, 'It does not seem to be your heart, but you should be very careful and come back immediately if your symptoms return.' Patients begin monitoring for rapid heartbeat and shortness of breath, which inevitably occur, spurring mounting fear, whose symptoms soon spiral into another attack. Patients find this explanation helpful.

They also find an evolutionary explanation helpful for grasping how medications work. Learning that benzodiazepines and alcohol offer only temporary relief at the price of more fear later is helpful for reducing their use. Antidepressants, however, block full-blown panic attacks quite nicely in most patients. Patients often ask if the drug is simply covering over symptoms. They appreciate learning that using medication for some months to stop panic attacks helps the system to become less sensitive, thus making long-term improvement likely even after the medication is discontinued. Telling patients that they likely will continue to have 'mini-attacks' for some weeks helps to alleviate concern about such experiences.

Vulnerability to panic attacks and agoraphobia runs strongly in families, members of which presumably have superior protection from dangers at the cost of a higher risk of experiencing panic disorder. Panic attacks are also more common in individuals who have experienced early adversity, which is no surprise because this often reflects a dangerous environment. Initial attacks are often set off by being in a strange town, being jet-lagged, drinking in the evening and having several cups of coffee in the morning. Interpreting the resulting panic attack as a possible heart attack initiates a vicious cycle. However, physicians who understand this can effectively prevent the creation of an iatrogenic disorder.

7.5.4 Post-traumatic Stress Disorder

A single experience of life-threatening danger is enough to set off an acute stress disorder and, in many people, post-traumatic stress disorder (PTSD) (Breslau et al., 1995; Yehuda et al., 2015). Watching someone else be killed can have equal or greater repercussions. Patients with PTSD ruminate about the danger and become hypersensitive to cues that indicate even the merest possibility that it may be recurring. Several authors have considered the possibility that such responses are an evolved adaptation, with even a minuscule chance of life-threatening danger justifying an intense protective response (Cantor, 2009). If this was an adaptation, however, most people would have such a response to a

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traumatic event, and these responses would increase their fitness. Neither seems to be correct. Epidemiological studies show that a majority of people have had an intensely traumatic experience, but only a minority develop PTSD. Vulnerability factors include genetics, sex and previous experiences of trauma, anxiety or depression (Breslau et al., 1995). New data from the Turkana in Africa show that symptoms of arousal are associated with the experience of danger, but symptoms of depression are more closely associated with the 'moral injury' of moral violations (Zefferman and Mathew, 2020). The meaning of warfare and social support for warriors in the Turkana may explain why they experience less depression than soldiers in Western countries.

The utility of a short-term response to trauma seems obvious, especially if the danger may still be present. However, the enduring symptoms of PTSD are more likely to be pathological manifestations of a system pushed beyond its normal range of functioning (Liberzon and Abelson, 2016). PTSD is an example of a disorder that is more likely for people at the tail end of a distribution. What that distribution is remains uncertain. Does the risk of PTSD mainly result from a low threshold for responding or a high intensity of response, or from failure to moderate the responses in the weeks after the trauma? These are good questions.

7.5.5 Hypochondria

Excess concern about health is now diagnosed as 'illness anxiety disorder' for those with general concerns and 'somatic symptoms disorder' for those who cannot be reassured about specific symptoms (Furer et al., 2007). The relevant danger is, of course, disease. The fear arises from a conviction that something dire is wrong and an inability to accept medical reassurance. Specifying the traits responsible for vulnerability is difficult, but confirmation bias is prominent in sustaining the belief despite contrary evidence. The origins of beliefs that one has an undiagnosed disease are products of social learning and sometimes psychodynamic mechanisms. It is tempting to attribute vulnerability mainly to novel technological environments in which sophisticated tests can reveal hidden illnesses and treatments can sometimes cure serious diseases. But preoccupation with symptoms and the desire to find explanations seem to be prevalent everywhere. It has been suggested that symptoms of illness have evolved to serve signalling functions and that this opens up opportunities for communication and manipulation (Tiokhin, 2016) that can result in positive attention that encourages additional experience or communication of symptoms (Wenegrat, 1995).

7.5.6 Separation Anxiety Disorder

The utility of separation anxiety early in life is now obvious thanks to John Bowlby's pioneering work (Bowlby, 1973). Our clinic saw many newly arrived university students who could not function because of separation anxiety disorder, although they called it homesickness (Silove et al., 2010). Being separated from parents for the first time and exposed to new sorts of social and academic competition, as well as new opportunities for drug use and sexual adventures, can set the scene for intense separation anxiety. Most such patients reported previous difficulties going to summer camps and other childhood activities away from family. If the student can be integrated into campus life with friends and successful activities and studies, the problem usually fades quickly. Sometimes, however, it escalates and interferes with social life and academic performance, requiring a move home that can be devastating. Intense treatment is appropriate to prevent such a feedback cycle from developing.

Separation anxiety disorder is a classic example of a disorder resulting from the failure of anxiety to fade after its normal expression early in development. It is probably best attributed to being at the tail end of the distribution of separation fear, but it could also represent a defect in the system that usually tempers such fear in the process of maturation.

7.5.7 Body Dysmorphic Disorder

The belief that one is unattractive can be as intractable as the belief that one has an undiagnosed disease (Stein, 2017; Veale and Gilbert, 2014). It's often present in people who are, to other people's perceptions, very attractive indeed. However, once the belief in one's unattractiveness gets established it can be used to account for all manner of experiences, such as being rejected by a date. The normal trait related to this disorder is wanting to be attractive. In the usual range, this is almost certainly useful. In a modern society with extraordinarily attractive images on billboards

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and screens and the availability of enhancing surgery, intense competition can lead to morbid preoccupation. Plastic surgeons often sent prospective patients to our clinic to ask if we thought psychological treatment might be more helpful than surgery. We often said yes, but we rarely convinced the patients. A different version of the same problem is experienced by patients who believe – despite all reassurance – that they smell bad. These syndromes all reflect the extraordinary degree to which people care about what other people think about them, a tendency that is deeply ingrained for good evolutionary reasons.

7.5.8 Social Anxiety Disorder

Social anxiety is so overwhelmingly common it is hard to say what is normal and what is pathological. The criteria defining social anxiety disorder are set so that only about 5% of people qualify for a lifetime diagnosis (Stein et al., 2017); however, most people feel considerable discomfort when in front of a crowd in an evaluative situation, and 13% of young adults report strong social fears (Fehm et al., 2008). The risks in such situations are many and considerable. Saying something that appears stupid can harm one's reputation. Revealing covert hostile feelings can ruin relationships. Even success can prove problematic if it threatens the status of others in the group who are likely to retaliate. Worst of all, simply appearing nervous in front of a group can reduce social status, causing fears that one will appear nervous – a perfect set-up for a nasty positive-feedback cycle.

While being the centre of social attention does involve risks, they are not nearly as great as most people assume – a finding possibly explained by the smoke detector principle. Treatments that try to help people avoid errors in public presentations can help, but reducing the fear of making mistakes requires making mistakes. Doing and saying silly things are difficult at first, but soon most patients realise that most people don't notice, and if they do notice they don't care very much, and even if they do care they generally forget them by the next day.

Social fears can be extremely intense. Some of our patients had no social contacts whatsoever and were incapable of writing a cheque at the grocery store or of going to a bank. Some dropped out of school and some were unemployed, while one man stayed alone in his trailer at the end of a dead-end road. These are serious disorders, but they are responsive to treatment. Such treatment goes better if the several routes to social anxiety can be investigated carefully and discussions with the patient can consider the role of positive-feedback cycles in perpetuating the disorder.

The trait that makes us vulnerable to social anxiety disorders is caring a lot about what others think about us. This almost certainly has been shaped by natural selection (Brosnan et al., 2017; Gilbert, 2014; Leary and Kowalski, 1995; Stein and Vythilingum, 2007; Tone et al., 2019). Maintaining a good reputation is essential for maximising benefits in exchange relationships. However, capacities for extreme prosocial tendencies including guilt and embarrassment seem likely to have been shaped by social selection (Frank, 2006; Hammerstein and Noë, 2016; Nesse, 2007; West-Eberhard, 1975; Westneat, 2012). Sexual selection is the familiar process in which competition to be chosen as a mate results in extreme traits. Social selection is the more general category in which social choices shape traits. Choices of social partners influence fitness strongly. Having partners with resources and tendencies to share them gives big advantages. To get such partners, people must demonstrate those traits themselves. This results in intense competition – possibly even runaway competition – to have and display desirable social traits such as honesty, generosity and the ability to sense what others want. The pairing process creates a hierarchy, with substantial benefits going to those who are – and who have – the best partners. Those who are perceived as poor partners do badly. This creates strong selection to avoid being perceived as lacking in resources, generosity, trustworthiness or loyalty to partners. It also creates constant monitoring of how others respond to every word and gesture. The miracle is that we can at times relax with friends.

7.5.9 Obsessive-Compulsive Disorder

Most of the repeated thoughts and behaviours of people with OCD are attempts to prevent possible dire outcomes from a minor misstep (Brüne, 2006; Robbins et al., 2019; Stein, 2002). The concern is more often about fear of accidentally harming others than it is about being harmed oneself. In this sense, it is the converse of

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paranoid fears of being harmed by others. So people with OCD wash their hands until they are raw, clean surfaces until they are burnished and ruminate for hours about whether the door was locked to protect others as well as themselves.

What trait makes us vulnerable to OCD? It does not seem to be carefulness in general, which is more characteristic of obsessive-compulsive personality, an entirely different condition that mostly involves conscientiousness and contempt for those who are careless. The anxiety associated with OCD escalates as the person considers stopping some protective behaviour such as washing or cleaning. What if some toxin or pathogen is still on the doorknob? My child could touch it and get sick and die. What if I left the hair-curling iron turned on? It could start a fire that burns down the house and kills my dog. What if I hit someone while driving and didn't notice? I should circle around the block and check. But what if the person I hit was already taken to the hospital? I should circle the block again and call the hospital to check.

One could make a case that a system for keeping hostile impulses unconscious has failed and the obsessions are a secondary defence. But after seeing hundreds of patients with OCD, I think they are aware of many impulses that other people don't notice, but their levels of hostility only rarely struck me as excessive.

The trait that accounts for vulnerability to repeated checking is the mechanism that normally turns off protective behaviours when they have been completed sufficiently. Most of us wash our hands cursorily; if we know our hands are contaminated, we wash until they seem clean, then concern is swept out of mind. This is a variant of the mechanism that makes decisions possible. We weigh options, decide and then convince ourselves that we made the right decision – a tendency that makes it possible to move on. Psychological tendencies towards confirmation bias and dissonance reduction are useful in this respect. People with schizophrenia often lack this useful cognitive distortion, so every decision is wracked by interminable ambivalence and second-guessing. For people with OCD, the inability to reach a comfortable decision is mainly due to concerns about how much safety behaviour is enough.

Neurological findings associated with OCD further suggest that OCD is not just the extreme of a trait but a pattern of symptoms that can result from damage to the head of the caudate nucleus. Evidence for this includes precipitation of OCD by stroke in the basal ganglia or by autoimmune responses to streptococcal infection in childhood, as well as symptom relief from surgical disruption of adjacent circuits (Robbins et al., 2019). Further evidence is provided by OCD's comorbidity with Tourette's syndrome, which involves an inability to inhibit movements and gesticulations that is associated with caudate nucleus damage (Hirschtritt et al., 2015). OCD can also be an enduring complication of taking atypical antipsychotic drugs (Lykouras et al., 2003).

Taken together, these findings suggest that OCD may not result from the extreme of any trait; it may instead be a pattern of symptoms that results from damage to the caudate nucleus, very much like the syndrome of hyperextension of the lower extremities and contraction of the arm muscles that results from spinal cord transection. In this model, no evolutionary explanation is needed, except perhaps for the reasons why the caudate is especially vulnerable to damage. Of course, OCD vulnerability could result from anatomical damage in some individuals and from being at the extreme end of harm avoidance for others.

7.5.10 General Anxiety Disorder

GAD is characterised by preoccupation with worries of all sorts (Brown et al., 1994; Wittchen and Hoyer, 2001). Will my spouse have an accident on the way home? Will my children catch Lyme disease from playing in the yard? Will my medical insurance be cancelled because I didn't pay my doctor's bill on time? Such concerns may seem minor, but when I ask GAD patients, 'What percentage of your time and effort goes to preventing bad things from happening?' the answer is usually over 80%, and often over 95%.

Psychologists identify two motivational global states: promotion and prevention (Higgins and Spiegel, 2007). Individuals in a promotion state put efforts towards getting something or accomplishing something. Individuals in a prevention state put efforts towards preventing loss, harm or damage. From this perspective, patients with GAD are at the prevention end of the promotion–prevention distribution. The most likely explanation for vulnerability is simply stochasticity. Stabilising selection has not sufficiently

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narrowed the distribution to protect people at the extremes. But could local anatomical or physiological abnormalities like those that cause OCD be responsible? Yes, but the evidence for such lesions is sparse, while the evidence for a dimension ranging from promotion to prevention is strong.

As is the case for other disorders arising from trait extremes, GAD calls attention to the other extreme: hypophobia. People who spend 95% of their efforts on promotion and 5% on prevention should be prone to accidents and mistakes of all causes, but their condition has not yet been recognised as a mental disorder.

The genetics of GAD are of especial interest. The responsible loci seem to be the same as those that predispose individuals to major depression (Kendler et al., 1992). This suggests that both traits may have evolved from common precursor states that protect against loss. Low mood protects against wasted effort, while anxiety protects against other losses. It's possible that modern societies initiate enough new worries to shift many people into the pathological category. As for trade-offs, those at either end of the distribution do badly.

7.6 Conclusions

Anxiety and its disorders illustrate the value of systematically considering all possible explanations for vulnerability. Recognising that the capacity for anxiety is an adaptation is the place to start, but this does not justify viewing disorders as adaptations. Instead, it suggests that stochasticity limits the ability of stabilising selection to narrow the distribution sufficiently to protect everyone in a population from disorder. Mismatch is relevant for some anxiety disorders, but additional data are needed to assess its role. Trade-offs are inherent for any dimensional trait, but the advantages for individuals with high levels of anxiety are not sufficient to compensate for the disadvantages. Individuals with low levels of anxiety have different advantages and disadvantages. Individuals in the middle range are assumed to do best, or at least to have done so in ancestral environments. Some syndromes, however, such as OCD, may not be extremes of any adaptive trait, but instead may reflect patterns of dysfunction that result from neural damage.

While an evolutionary perspective does not constitute a new kind of therapy, it does fundamentally transform the schema for understanding anxiety disorders. In particular, it challenges the assumption that useless anxiety arises mainly from defective brain mechanisms; normal mechanisms seem more often to be responsible. This should shift the neuroscientific approach to anxiety disorders from searching only for specific abnormalities to instead searching for the many factors likely to influence an individual's trait value on the distribution. It also should encourage much more attention being paid to systems thinking and the prominent role of positive feedback in creating and maintaining severe anxiety disorders.

As noted already, patients often deeply appreciate recognising that their symptoms are not simply manifestations of pathology, but instead are useful responses that have overshot the mark. They also especially value recognising how runaway systems can maintain their symptoms. This often makes it possible for them to complete behaviour therapy exercises that would otherwise have been even more difficult for them.

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