Chapter 6

Why Do Mental Disorders Persist?
Evolutionary Foundations for Psychiatry

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Abstract

Discovering why natural selection has left humans vulnerable to mental disorders will make psychiatry more sensible and effective, but defining the appropriate objects and kinds of explanation remains challenging. Asking how a disorder increases fitness is a mistake; disorders are not adaptations and they do not have evolutionary explanations. The correct objects of explanation are the traits that make all members of a species vulnerable to a disorder. Task 1 is to describe the evolutionary origins and functions of the traits involved. Task 2 is to describe the proximate processes that result in the disorder. Task 3 is to discover why natural selection left the traits vulnerable to malfunction. Five main kinds of explanation need to be considered: stochasticity, path dependence, mismatch, trade-offs that benefit the individual and traits that benefit gene transmission at a cost to the individual. Depression, addiction, eating disorders, autism and schizophrenia are used to illustrate the opportunities and challenges of framing and testing hypotheses about vulnerability. Multiple explanations are often needed for a single disorder, frustrating the wish for simplicity. However, recognising the fundamental differences between organic and designed systems offers opportunities for resolving – or at least understanding – some enduring controversies in psychiatry.

Keywords

adaptationism, evolutionary biology, evolutionary medicine, evolutionary psychiatry, mental disorders, methodology, psychiatry

6.1 Introduction

Mental disorders don't have to exist. Natural selection could have eliminated the genetic variations that make us vulnerable to schizophrenia, autism and bipolar disorder. It could have shaped organisms that cooperate reliably without conflict. It could have made us capable of controlling our emotions and our impulses to eat and drink. But it didn't.

Genetic variations that cause mental disorders persist. Relationship conflicts arouse anger, jealousy, depression and wishes for spiteful revenge. And the belief that we can use willpower to reliably control our emotions, eating and drinking is an illusion. Mental disorders not only persist, they are the greatest and least tractable health problems facing our species. Explaining why they persist in the face of natural selection will provide a missing scientific foundation that can make psychiatry more sensible, more effective and more like the rest of medicine.

Reaching agreement on the best evolutionary explanations for vulnerability to mental disorders will be challenging, however. Even for non-psychiatric diseases (see Chapter 2 for the differences between conditions, illness, disease and disorder, etc.), methods for framing and testing evolutionary hypotheses are still developing (Nesse, 2011). Applying those methods to mental disorders poses additional challenges. Observable tissue pathology is usually absent. Information-processing systems have failure modes that are different from those of physiological and anatomical systems. Behaviour and emotions are not shaped directly but via selection on genes that influence brain variations that interact with

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environments to yield actions that vary in their effects on fitness. And selection forces emerge from and vary depending on culture. I Challenges also arise from cognitive tendencies. Humans are fascinated by function and seduced by simplicity. These tendencies are major obstacles to progress in evolutionary psychiatry. It is tempting to view disorders as if they are adaptations and to look for possible benefits that could provide simple explanations. But disorders in themselves are not adaptations shaped by natural selection. They do not give net fitness benefits. They do not have evolutionary explanations. The correct objects of explanation are traits that make organisms vulnerable to disorders.

Considerations of function are, however, fundamental and of enormous value. Studying emotional disorders without knowing their evolutionary origins and functions encourages viewing symptoms as if they are diseases. The result is continual controversy about psychiatric diagnosis (see Chapter 2) and slow progress in research on emotional disorders. Looking for the brain abnormalities causing mental disorders without understanding normal function is like looking for the heart abnormalities causing heart failure without knowing what the heart is for.

Adding evolutionary considerations of function transformed ethology into the theoretical and experimental science of behavioural ecology (Westneat and Fox, 2010). Evolutionary psychology describes the evolutionary origins and fitness consequences of human behavioural and emotional traits (Buss, 2020; Lewis et al., 2017; Welling and Shackelford, 2019). Evolutionary medicine provides tools for framing and testing hypotheses about why natural selection has left us vulnerable to diseases (Gluckman et al., 2009; Nesse and Williams, 1994; Perlman, 2005; Stearns and Medzhitov, 2016; Williams and Nesse, 1991). Evolutionary psychiatry is now applying principles of evolutionary medicine to mental disorders (Abed and St. John Smith, 2016, 2022; Adriaens and De Block, 2011; Brüne, 2016; Crespi, 2020; Kennair, 2003; McGuire and Troisi, 1998; McGuire et al., 1992; Nesse, 1984, 2019; Wenegrat, 1990).

Conceptual confusions still obstruct progress, however. Some arise from a failure to grasp that proximate and evolutionary explanations are different and that both are essential (see Chapters 1 and 2). Controversy also continues about how best to frame and test hypotheses about behaviour (Buller, 2005; Buss and von Hippel, 2018). That evolutionary explanations are essential is now widely accepted, but controversies persist. Gould and Lewontin's critique of adaptationist explanations offered no guidance about how to actually go about testing evolutionary hypotheses (Gould and Lewontin, 1979). That omission and the article's clever rhetoric have left many scientists still thinking – decades later – that all hypotheses about function are untestable 'just-so stories'. Global debates about adaptation have now mostly been supplanted by the assessment of specific hypotheses with specific evidence (Pigliucci and Kaplan, 2000), but many scientists and doctors remain out of the loop.

Another obstacle is the tendency for simple, attractive explanations to persist because people pay attention only to confirming information (Staw, 1976). Conflicting views become the enemy, and the resulting debates are rarely resolved. The combination of commitment, confirmation bias, and preference for simplicity helps to explain the persistence of global debates about group selection, life history theory, adaptationism, nature versus nurture and genetic drift versus natural selection. Evolutionary psychiatry will progress faster if such global debates can be minimised by systematic consideration of all possible explanations for specific hypotheses. This makes it worthwhile to describe the proper objects and kinds of explanation in some detail.

6.2 The Objects of Explanation

Proposals abound for possible fitness benefits thought to explain depression, eating disorders, addiction, attention deficit hyperactivity disorder (ADHD), autism and even schizophrenia. One reason why this mistake is common is that some conditions frequently considered to be disorders or diseases are actually adaptations; pain, anxiety and low mood are examples. Another reason is that individuals at the tails of trait distributions where diseases become likely experience benefits as well as costs. A third reason is that explanations that propose a possible function for a disease often make good memes that spread fast irrespective of their veracity.

Mood disorders that reduce fitness are not adaptations, they are harmful products of

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dysfunctions in evolved mechanisms (Wakefield, 1992). They do not have evolutionary explanations in terms of their functions. However, the capacity for having and regulating mood is an adaptation. Understanding its evolutionary origins and functions is essential. Why the system is vulnerable to dysfunction is, however, a fundamentally different question.

Substance use and abuse have often been viewed as adaptive, but the appropriate objects of explanation are chemically mediated motivation and learning mechanisms. Understanding how those mechanisms give advantages is a different question from that of why they make us vulnerable to addiction. Why some individuals are more vulnerable than others is a third question. Discovering why the genetic differences that increase the risk of substance abuse persist will offer part of an answer. It will also be important to further test the hypothesis that natural selection shaped preferences for altered states or certain substances, especially alcohol and nicotine (Hagen et al., 2013; Slingerland, 2021). Such a confirmation would explain substance use but would not fully explain vulnerability to addiction and substance abuse that harms fitness.

Eating disorders have often been interpreted as adaptations, usually as extreme eating patterns that give advantages in special situations (Brüne, 2018; Mayhew et al., 2018). For instance, it has been proposed that when food sources are insufficient to sustain childbearing, restrictive dieting can stop reproductive cycling and prevent a useless pregnancy. However, starvation turns off cycling all by itself, and additional caloric restriction is likely to be fatal. The tendency of people with anorexia nervosa to engage in extreme exercise inspired the hypothesis that food scarcity may generate motivations to run that take starving people to places with more food. But anorexics exercise not to find food but to lose weight. The sexual competition hypothesis suggests that women are vulnerable to eating disorders because modern media augment the natural motivation for having a desirable body in order to get better mates (Abed, 1998). This explains why so many women use extreme caloric restriction in intense efforts to be attractive, but it does not by itself explain anorexia nervosa and bulimia (see Chapter 11 for a review and alternative perspective on eating disorders). That requires also considering the adaptive response to starvation that induces gorging and increasing the body weight set point. Starvation from whatever cause in either sex sets off this response. The resulting out-of-control eating creates increasing fear of obesity and more intense efforts to restrict food intake in a vicious positive-feedback cycle that explains the connection between anorexia and bulimia (Nesse, 2017).

For autism, it is much harder to specify the trait that accounts for vulnerability, but the extremes of a dimension from systematising to empathising (Greenberg et al., 2018) and from autism to schizophrenia (Crespi and Dinsdale, 2019) may be important. Dysfunctions in capacities for social relationships that may reflect sex differences are involved, but pathology in autism ranges widely and can include excess sensitivity to stimuli, inability to inhibit repetitive behaviours, language and intellectual disabilities and epileptic seizures. The special abilities of some individuals with autism offer intriguing clues, but they are not universal traits shaped by selection and they do not increase Darwinian fitness. They may give clues to possible relevant modules and selection forces, but they cannot explain the persistence of the responsible genes.

After ascertaining that a condition is actually a disorder and not an adaptation, the search for an evolutionary explanation proceeds in three steps. Step 1 is to identify the trait(s) that make all individuals in a species vulnerable to the disorder. Step 2 is to understand the proximate mechanisms – genetic, physiological and psychological – that result in malfunction. Step 3 is to determine what combination of evolutionary explanations makes the trait vulnerable to failure. Five categories of potential explanation deserve detailed description.

6.3 Categories of Explanations for Vulnerability

Evolutionary questions about why natural selection left us vulnerable to mental disorders are specialised versions of evolutionary medicine questions about why we are vulnerable to disease in general (Gluckman et al., 2009; Nesse, 2005a; Nesse and Williams, 1994; Perlman, 2005; Stearns and Medzhitov, 2016). Table 6.1 provides a list of possible evolutionary explanations for vulnerability, a mapping to categories used previously in

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Table 6.1. Evolutionary explanations for vulnerability

Categories	Previous categories	*Cui bono*
(0) Adaptations that can seem like disorders (Section 6.3.1)	Defences	The individual
(1) Stochasticity (Section 6.3.2.1)		No benefits
(2) Path dependence and major transitions (Section 6.3.2.2)	Constraints	No benefits
(3) Selection is slow/mismatch (Section 6.3.2.3)	Mismatch	No benefits now
	Fast pathogen evolution	No benefits
(4) Trade-offs and intrinsically vulnerable traits (Section 6.3.2.4)	Trade-offs	The individual
(5) Traits and trade-offs that benefit gene transmission at a cost to the individual (Section 6.3.2.5)	Traits that increase reproductive success at a cost to the individual	Genes

evolutionary medicine and information about who benefits (*cui bono*).

6.3.1 Adaptations That Can Seem Like Disorders: Negative Emotions

'Adaptations that can seem like disorders' is listed as item (0) in Table 6.1 because it is a crucial consideration that is not an explanation for vulnerability. Recognising negative emotions as adaptations is a major contribution of evolutionary psychiatry. They are usually symptoms, not diseases. Five major implications follow. First, recognition of emotions as symptoms encourages searching for life situations that might be arousing them. Second, determining whether an emotion is pathological depends on the presence or absence of the relevant situation. Third, normal emotions are often useless in the individual instance. Fourth, deficits of negative emotion and excesses of positive emotion are under-recognised disorders. Finally, an evolutionary perspective calls attention to the need to consider disorders of all emotions, not just anxiety and depression.

Specific functions have often been proposed for specific emotions. However, different emotions correspond not to different functions but to the different situations that have shaped them (Nesse, 1990; Plutchik, 1980; Wierzbicka, 1992). If one insists on defining an emotion in terms of its function, the function can be framed as: 'The function of Emotion E is to adjust physiology, expression, memory, cognition, facial expression and behaviour in ways that improve the ability to cope with the adaptive challenges in Situation S.' Sophisticated treatments for these issues are available (Al-Shawaf et al., 2016; Averill et al., 1994; Griffiths, 1997; Izard, 2010; Tooby and Cosmides, 1990; Wierzbicka, 1992).

The tendency to view different emotions as separate parts of a designed machine reflects a tacit creationism that is prevalent throughout biology (Nesse, 2020). Decades of debate about basic emotions continue because of trying to view emotions as distinct parts of a machine. However, emotions are suites of settings that evolved from precursor emotions with overlapping characteristics that were shaped to cope with somewhat overlapping situations. This explains why the symptoms of depression and anxiety disorders cannot be fully separated. Situations that threaten loss are highly associated with situations in which loss occurs, so anxiety and mood disorders have high comorbidity and many overlapping features.

The word 'depression' implies pathology to many people; the phrase 'low mood' allows description of symptoms that are usually – but not necessarily – products of intact mood-regulation systems. Most evolutionary explanations for low mood or depression describe possible functions. Those include soliciting aid, manipulating others, inhibiting effort in unpropitious times, conserving calories during winter or famine, avoiding attacks after losing a status competition, motivating contributions to a group when exclusion is a risk, inhibiting activity during infection and curtailing effort to free up time to solve a problem (Durisko et al., 2015; Hagen,

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2011; Nesse, 2009; Rottenberg, 2014). Many authors advocate for the primacy of the function they think is most important. Unproductive debates ensue.

Progress will come by stepping back from attempts to pin a function on low mood and instead searching for the situations in which it is useful. In general terms, low mood is useful in unpropitious situations where efforts will be wasted or harmful (Nesse, 2000). The situation of failing efforts to make progress towards a goal is slightly less general (Carver and Scheier, 2014; Heckhausen, 2000; Klinger, 1975). However, these global situations do little to account for guilt, crying, low self-worth, rumination and hopelessness. More specific situations have shaped more specific kinds of low mood (Cheung et al., 2004; Gilbert, 2006; Monroe and Hadjiyannakis, 2002; Watson and Andrews, 2002). Loss of a status competition and being trapped in a subservient role seem especially salient in many cases of depression (Price and Sloman, 1987). Situations influencing status in a group also are especially potent influences on mood. However, non-social situations, such as inflammation, can also arouse appropriate low mood (Raison et al., 2006). Subtypes of low mood that arise in different situations are, however, not as distinct as we might like; they are overlapping states that evolved from common precursors. Investigating how different situations give rise to different symptom patterns is a crucial unfinished project (Keller and Nesse, 2006; see also Chapter 8 of this volume).

It will be essential to distinguish evolutionary explanations for the mood system from explanations for why it is vulnerable to dysfunction. Are cases of depression seen in psychiatric clinics mostly normal, useful low mood or mostly pathological depression? My impression after experience with thousands of depressed patients is about the same as that reported a century ago by Aubrey Lewis, the inaugural chair of the London Institute of Psychiatry: about a third of patients have low mood somewhat appropriate to their situation, about a third have grossly excessive responses to a life situation and about a third have fundamentally abnormal mood-regulation mechanisms (Lewis, 1934). However, studies using modern methods have yet to address the question systematically.

Why did natural selection leave mood-regulation mechanisms vulnerable to dysfunction? That question is fundamentally different from the question of why the capacity for normal low mood exists at all. All five evolutionary reasons are relevant. Before considering them, it is worthwhile to recognise that normal regulation mechanisms often give rise to useless emotions.

6.3.1.1 Why Most Experiences of Negative Emotion Are Useless but Normal

It seems obvious that normal emotions from normal mechanisms should be reliably useful and that useless emotions should be products of abnormal regulation mechanisms, but both statements are false. Many experiences of negative emotion are useless products of normal emotion regulation mechanisms. They are, in Wakefield's valuable nomenclature, harmful conditions that are not dysfunctions (Wakefield, 1992). Five different processes can result in normal mechanisms giving rise to useless or harmful emotions.

The smoke detector principle explains why false alarms and excessive defensive responses are normal and necessary (Nesse, 2005b). To ensure an early warning from every fire, smoke detectors are designed to go off when toast is burnt. The many annoying false alarms are worth it to ensure early warning about every real fire. Signal detection theory describes the optimal response threshold. The principle has been expanded to explain cognitive distortions as error management theory (Haselton and Nettle, 2006).

Adaptive sensitisation is a second reason why negative emotions are usually normal but useless. Repeated experiences of pain indicate that the mild cues of nociception have been insufficient to provide protection against tissue damage (Williams, 2016). Such experiences adaptively sensitise nociception and pain systems, so they go off more easily (Crook et al., 2014). Such self-sensitising systems are inherently vulnerable to runaway positive feedback, a possible evolutionary explanation for chronic pain that is equally relevant for anxiety disorders (Nesse and Schulkin, 2019).

A happenstance sequence of unlucky events is a third reason why normal mechanisms often give rise to useless experiences of negative emotion. One model considers an organism deciding, on each move, whether to forage or wait (Trimmer et al., 2015). Foraging brings rewards in 'good'

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environments but costs in 'bad' environments; the valence for the environment often reverses. Happenstance sequences of non-reward can result in giving up when rewards are available. A related model analyses the decision a fox must make about digging in holes that might contain tasty rabbits or dangerous badgers. When rabbits are more common than badgers, digging is worth it. But even when rabbits predominate, an unlucky sequence would cause a fox to give up on foraging. This illustrates how 'adaptive behaviour might lead to self-reinforcing pessimism' (Meacham and Bergstrom, 2016: 3). Depression researchers use the metaphor of 'kindling' to describe how previous episodes increase the risk of depression. Whether the phenomenon is pathology or an adaptive response remains uncertain.

Mismatch between ancient brains and modern environments is a fourth reason why normal mechanisms give rise to useless emotional responses (Griffiths and Bourrat, 2021). Mechanisms shaped to manage social life in small kin groups cause enormous problems when they are aroused by the exigencies of subservient roles in a modern bureaucracy. More details about this are given in Section 6.3.2.3 (also see Chapter 1).

Emotion regulation systems were shaped to maximise gene transmission, not individual health or happiness. We are inordinately distressed by our children's problems, even when there is nothing we can do to help, and emotions aroused in mating competitions often benefit our genes at a big cost to us. More details about this are given in Section 6.3.2.5.

6.3.1.2 Implications from Recognising That Some Apparent Disorders Are Adaptations

Recognising that negative emotions are often useless products of normal systems changes the approach for researchers, clinicians and patients. It encourages attending to the possible usefulness of symptoms, while also supporting the use of any safe means to dispatch useless suffering. It also suggests that most medications relieve negative emotions not by replacing deficient neurotransmitters but by blocking normal response systems, in the same way that analgesics block pain.

6.3.2 Things Natural Selection Cannot Do

Five reasons why natural selection leaves us vulnerable to disease are summarised briefly in this section. It would satisfy our wish for simplicity if vulnerability to each disorder could be attributed to just one reason, but most disorders require multiple explanations.

6.3.2.1 Stochasticity

Genetic drift is the null hypothesis for molecular evolution. Deleterious and advantageous genetic variants can be lost or go to fixation due to stochastic effects alone (Lynch et al., 2016). Fixation of mildly deleterious alleles is especially common in small populations, but their role in disease vulnerability is hard to assess because lack of variability makes them hard to identify. More obvious vulnerabilities arise from mutations that are generated constantly but selected out only slowly and from previously neutral alleles that become pathogenic in novel environments. Also, the process of brain development, while tightly canalised, is subject to unavoidable stochastic variations. Stochasticity is a powerful explanation for disease vulnerabilities.

Mutation–selection balance is the natural major candidate to explain disease-associated alleles (Keller and Miller, 2006; Kendler, 2013). The sequencing of the human genome brought hope that we would soon find the responsible alleles. Studies of candidate genes brought further hope, but almost none could be replicated. Genome-wide association studies (GWASs) expanded the data massively to discover that no common alleles have a substantial effect on the risk for major mental disorders (Kendler, 2013). Ever-larger studies have discovered that the effect size of an allele is inversely proportional to its prevalence, so each contributing allele explains about the same tiny proportion of variance. For schizophrenia, that amount is 0.04%, or 4 parts in 10,000 (Keller 2018). This is consistent with natural selection eliminating deleterious mutations with a speed proportional to their deleterious effect on fitness.

A third conclusion is also surprising: the responsible alleles are not specific to one disorder (Baselmans et al., 2021; Liu et al., 2020; Taylor et al., 2018). Also, the vast majority of relevant genetic variants are in non-coding regions. For simplicity, I use the word 'alleles' to describe all genetic variants. Massive overlap is found for alleles contributing to anxiety and depression, as well as for those contributing to bipolar disorder and schizophrenia. Polygenic risk scores use all

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data from all loci to predict risk. Polygenic risk scores for schizophrenia are significantly associated with autism, bipolar disorder and depression but are not associated with ADHD (Mistry et al., 2018). Intriguingly, the genetic risk for schizophrenia and autism have also been associated with creativity and educational attainment. This suggests a research strategy. If alleles that confer risk also confer benefits, then individuals in the decile with the *lowest* risk for a major mental disorder should have deficits in some areas. This is the most interesting research idea that emerged from my review of psychiatric genetics in preparation for this chapter.

6.3.2.2 Path Dependence/Major Transitions

The inability to redesign a trait from scratch makes organic systems fundamentally different from machines. The nerves and vessels in the eye come between the light and the retina, but they can never be rerouted because the transition would require thousands of generations in a fitness valley. Path dependence also imposes substantial constraints on robustness at the genetic level. We tend to think about the fitness effects of new alleles in isolation, but they enter networks of massively pleiotropic genes that each interact with thousands of others (Haig, 2020).

Major transitions to a new niche leave organisms vulnerable because of path dependence and the slowness of natural selection. For instance, the transition to an upright posture has left us vulnerable to hernias, haemorrhoids, foot pain, back pain, pregnancy problems and varicose veins. Our ancestors must have suffered terribly during the transition to bipedalism 4 million years ago. The transition to the social-cognitive niche is more recent but at least as wrenching (Hrdy and Burkart, 2020; Whiten and Erdal, 2012; also see Chapters 1, 3 and 4 of this volume). In just the past few hundred thousand years, our ancestors became capable of trade and complex society. Language capabilities may have developed within the past 50,000 years (see Chapter 4 for a discussion on the evolution of language). Settled living and agricultural surpluses in just the past 20,000 years made possible new means of social control, new kinds of hierarchies, new social roles, changed mating and parenting patterns, and cities. Our brains are evolving to cope with these changes but not fast enough to ensure robustness. The development of language has been cited as a specific explanation for vulnerability to schizophrenia (Crow, 1997), but many other factors are likely involved (Brüne, 2016; Del Giudice, 2018).

Our limited ability to inhibit impulses is another example. Getting long-term gains in a complex social context often requires inhibiting impulses to take short-term rewards. Inhibiting self-interested behaviour is crucial for social success, but this ability is limited in many people. Capacities for empathy and intuiting others' motives are also crucial to maximising social benefits, but they too still remain crude.

6.3.2.3 Mismatch and the Slowness of Natural Selection

Natural selection is slow compared to rates of environmental change, and it is far slower than the evolution of pathogens and the arrival of new mutations. Vulnerabilities result.

The slow pace of purging deleterious mutations is an obvious cause of disease. Selection is also slow to control selfish genetic elements that insert and replicate themselves in the genome despite the costs to individuals (Ågren and Clark, 2018). It is amazing that selection has managed to sufficiently reduce mutation rates and control selfish elements to maintain a stable genome – if, indeed, it has.

Mismatch of phenotypes with modern environments is inevitable given the slowness of natural selection (Gluckman and Hanson, 2006; Griffiths and Bourrat, 2021). Everyone knows that the environments we have created to satisfy our wishes for sweets, salt, fat and leisure have resulted in epidemics of chronic disease. Obesity and eating disorders are prime examples, but alcoholism and drug addiction are also made possible by ready access to substances and means of administration that have only recently become available. Lack of selection until recent times against these often fatal disorders is an essential part of any evolutionary explanation.

What about emotional and relationship problems? Are they far more common now than a few decades ago? How about compared to a few hundred years ago? What about before the rise of agriculture? Every generation thinks that things were better for previous generations, but that is mostly an illusion resulting from the saliency of problems now and the fading of painful memories with time.

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Epidemiological studies using randomly chosen subjects do not show major increases in mental disorders in recent decades (Bebbington and McManus, 2020), although there is some evidence for increases in depression across longer intervals (Hidaka, 2012). However, social media now seem poised to harm our mental health as much as fast food harms our physical health. We can't resist its pull despite the anxiety, depression and feelings of social inadequacy that are aroused by unprecedented social comparisons (Vogel et al., 2014). While apparently rapid increases in rates of autism and ADHD could reflect changing diagnostic patterns, it remains possible that these rates are being increased by environmental factors or assortative mating of individuals who carry vulnerability alleles.

Discovering the prevalence of mental disorders in hunter-gatherers is an important opportunity that is fading fast. There are good reasons why it has not been done. Samples of thousands are required for accurate epidemiological studies, but most hunter-gatherer groups contain only scores of people. Diagnostic instruments have limited reliability even in modern societies; their performance in other settings would be questionable. Nonetheless, we should gather as much data as we can from as many populations as possible before it is too late (Konner, 2002).

Valuable generalisations can be extracted from the cross-cultural data collected by the International Consortium for Psychiatric Epidemiology using standardised diagnostic criteria and random sampling methods (Kessler et al., 2014). Rates of schizophrenia, autism and obsessive-compulsive disorder (OCD) vary somewhat between countries but not dramatically. Behavioural disorders such as eating disorders and addiction have long been present at low rates, but they are increased and show moderate variations in developed societies. Rates of emotional disorders, by contrast, vary by more than eightfold in different countries (Kessler and Bromet, 2013). This does not implicate modern environments specifically, but it indicates that rates are strongly influenced by factors that differ between countries.

The role of mismatch is important for ADHD (Swanepoel et al., 2017; also see Chapter 14 of this volume). The simplest proposal is that a short attention span imposed no costs for ancestral humans, so it should not be considered a disorder, but we don't know if it imposes costs in other cultures. Some authors ask how ADHD gives advantages; this illustrates the mistake of viewing the extreme of a trait as an adaptation. Fitness in ancestral environments should peak near the population average value of a trait. The strongly male-skewed sex ratio of ADHD is consistent worldwide (Fayyad et al., 2017). This encourages asking whether higher levels of activity and faster task switching give advantages for males or if their increased vulnerability reflects a system more prone to dysfunction. Low Apgar scores are the single best predictor of ADHD, being present in twice as many boys with ADHD as controls (Hanć et al., 2018). However, a recent review failed to confirm the role of most prenatal factors (Sciberras et al., 2017), increasing uncertainty about the possibility that some cases of ADHD are, as it was previously called, minimal brain dysfunction.

Extensive research on the developmental origins of health and disease has examined how capacities for plasticity can yield maladaptive outcomes in modern environments (Nettle et al., 2013). For instance, the tendency for low-birthweight infants to later become obese, diabetic and hypertensive has been attributed to a mechanism that could have evolved to adjust metabolism to cope with harsh environments predicted by experience *in utero* (Gluckman et al., 2019). Primate studies have not confirmed fitness benefits from such plasticity (Tung et al., 2016), but the genomic imprinting mechanism that mediates the effect is quite specific and powerful. A related mechanism increases the responsiveness of the stress system to early adversity (Meaney and Szyf, 2005). These changes could be epiphenomena, but even if they are adaptations they might well impose costs greater than benefits in relatively safe and well-provisioned modern environments.

The slowness of natural selection relative to pathogen evolution is less relevant for psychiatry than in the rest of medicine, but caudate damage induced by antibodies to streptococci accounts for some cases of OCD (Swedo et al., 2004). Also, some cases of schizophrenia are caused by *Toxoplasma gondii*, parasites with the clever strategy of inducing fearlessness in mice that that gets the parasite reliably into its cat host (Burgdorf et al., 2019). More generally, inflammation is responsible for some depression (Miller and Raison, 2016), and it is central to the

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pathophysiology of Alzheimer's disease (Heneka et al., 2015). The pathognomonic plaques in Alzheimer's disease are composed of amyloid beta. This has often been assumed to be a toxic by-product of brain metabolism; however, drugs that disrupt amyloid beta do not slow progression. A different approach might have been pursued if the antimicrobial function of amyloid beta had been recognised earlier (Soscia et al., 2010). Similarly, the *APOE e4* allele, which is strongly associated with Alzheimer's disease, is viewed as pathological, but it helps to defend against pathogens; this is likely why it slows cognitive decline in horticulturalists (Trumble et al., 2017; see also Chapter 17 of this volume). Alzheimer's disease research may offer an unfortunate case study of how the lack of an evolutionary perspective can slow progress.

Considering mismatch and the slowness of natural selection is useful. Knowing that natural selection has not protected us from addiction helps patients to feel less defective and more respectful of their foe. It could also help young people to recognise the risks of drug experimentation. Understanding the starvation protection response helps eating disorder patients understand why restrictive dieting doesn't work. Understanding the trade-offs in mechanisms that protect against brain infection can advance our understanding of Alzheimer's disease. And discovering the factors that account for the eightfold national differences in rates of depression could do more to relieve depression than all current treatment efforts. The difficulty, of course, is in finding the responsible causes in the midst of massive variations in media exposure, diet, exercise, workplaces, religion and family structure and the likelihood that multiple factors are responsible. Getting comparison data from hunter-gatherer communities should be a high priority.

6.3.2.4 Trade-Offs That Benefit the Individual

Trade-offs are inherent to every system, whether evolved or designed. Cars that get better gas mileage have reduced acceleration and vice versa, so most cars have acceleration and gas mileage in the middle range. Those at the extremes reveal the costs of the trade-offs. Slow, efficient cars sometimes get into accidents because they can't merge easily into fast traffic; fast cars sometimes get into accidents because they are fast.

Trade-offs are also illustrated by the problems experienced by individuals at diametric extremes (Badcock, 2019; Crespi and Dinsdale, 2019; Crespi and Go, 2015; Del Giudice and Crespi, 2018). Individuals with heavier body weight are more likely to survive a famine but less likely to escape from a predator. Greater than average anxiety increases safety at the cost of lost opportunities. Greater than average low mood reduces useless efforts at the cost of lost opportunities. A tendency to persist increases success at some tasks, but rapidly shifting attention is superior for others. A tendency to make causal connections readily results in more theories that can predict events but more superstitions and false beliefs. Gregariousness increases the number of social connections, but introversion increases their depth. The reduced fitness experienced by individuals with trait values at the tails creates stabilising selection; it narrows the distribution but rarely enough to protect everyone.

Some trade-offs are more likely than others to result in vulnerability to disorders. Much depends on the shape of the fitness function. If it is flat and broader than the trait distribution, the trait value should not strongly influence fitness and few individuals should experience vulnerability. However, narrow fitness functions with steep slopes cause problems for individuals whose values diverge only modestly from the mean and even for those at the mean. Steep, narrow fitness functions are often products of arms races. The possibility of death from infection selects strongly against even moderate deficiencies in immune response, while the risks of autoimmune disease and faster ageing select against stronger immune responses. Even at the optimum trait value, vulnerabilities from infection and excess immune responses persist (Graham, 2013).

Selection that maximises performance can also result in vulnerability, especially when winner-take-all competitions shape cliff-edged fitness functions. Race cars are stripped down to a lean edge where a high risk of catastrophic failure is the price for having a chance to win. Breeding horses for speed results in long, thin leg bones that are vulnerable to fracture. Selection for high cognitive performance may have shaped cliff-edged fitness functions that make humans vulnerable to major disorders such as schizophrenia (Nesse, 2004).

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Legacies of the major transition to the human socio-cognitive niche (Hrdy and Burkart, 2020; Pinker, 2010; Whiten and Erdal, 2012) may account for vulnerabilities more generally. Strong selection on path-dependent systems could account for some mental disorders. The challenge will be knowing where to look. It could be that trade-offs at the trait level are a good place to start. For instance, abilities to create theories of causation could overshoot and result in vulnerability to paranoia and delusions. However, problems can arise from lower levels. If neuronal pruning in childhood (Sellgren et al., 2019) maximises some cognitive ability, overshooting in some individuals could have implications for schizophrenia. If the advantages of a large brain are associated with fast brain growth in the first year of life, this could outpace the control capacity of canalisation mechanisms with implications for autism, where exceptionally fast early brain growth is typical. In summary, 'Many psychotic symptoms and syndromes may be considered trade-offs, primarily manifesting themselves in domains related to the evolution of our "social brain"' (Brüne, 2004: 49). Variations in brain development or neuronal pruning could, of course, cause disorders even if they are not associated with performance advantages.

The socio-cognitive niche creates and is created by the social selection that has made humans wonderfully cooperative at the cost of much distress and vulnerability. Partner choices are selection forces. Tendencies to choose sexual partners with certain characteristics shape extreme traits like peacock tails that maximise reproduction at the expense of the individual's health and longevity. Tendencies to choose the best possible social partners can also shape extreme traits with major benefits and costs to individuals (Frank, 2006; Hrdy and Burkart, 2020; Nesse, 2007; West-Eberhard, 1979). People prefer social partners who are honest, empathic, wealthy and generous, so individuals with those characteristics get the best partners and associated fitness benefits. This creates strong selection for prosocial traits and for preferences for partners with those traits. The result is a species with unparalleled capacities for cooperation, commitment, relationships and morality that come at the cost of vast distress from guilt, social anxiety, low self-esteem and extreme concern about reputation. Prosocial traits benefit groups, but they are shaped because they increase the inclusive fitness of individuals who are preferred as partners.

Cybernetic analysis of control systems also suggests a source of special vulnerability (DeYoung and Krueger, 2018; Nesse, 2021). Positive feedback is ubiquitous in optimal control systems. It switches a process all the way on or off. Many actions, once begun, are best continued. For instance, starting to eat initiates a positive-feedback loop that motivates continuing until satiation or until the food is gone. If the off mechanism fails, an eating binge results. Mood systems are especially vulnerable to positive feedback. Failure lowers motivation, encouraging more failure. Success in pursuing a goal, especially a status goal, indicates a propitious situation in which additional investments will likely pay off. This can initiate runaway increases in mood of the sort seen in a manic episode. Most people experience a decline in mood shortly after a major success. This apparently senseless mood reduction may well be an adaptation that protects against a positive-feedback cycle of escalating mood (Nesse, 2019). Or it may just be an epiphenomenon of neurochemical systems recovering after recent strong activity.

6.3.2.5 Trade-Offs That Benefit Genes at a Fitness Cost to Individuals

Natural selection doesn't give a fig about our happiness; it just maximises gene transmission, often at the expense of health, welfare and longevity. Several kinds of selection shape traits that benefit genes at our expense.

Sexual selection shapes traits that increase reproductive success at a cost to the individual. Men get a larger fitness pay off than women for abilities to compete for mates, and they pay the price of threefold higher mortality rate in early adulthood and a much shorter lifespan (Kruger and Nesse, 2006; Lemaître et al., 2020). The costs of traits that increase mating success for women are harder to identify because of the lack of a comparison group. An extraordinary proportion of life problems and resulting mental disorders arise from mating conflicts (Buss, 1988). Unrequited love, the pain of being rejected, the fear of being left, being stalked, being harassed, jealousy and being trapped in an abusive relationship are common precipitants of mental

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disorders. In stable relationships, infertility causes much distress.

Sexual selection also shapes traits that impose risks related to childbearing and parenting (Hrdy, 1999; Strassmann, 1981). The costs and risks of pregnancy are borne mainly by women, but both partners can be consumed by the travails of parenting, and concern for the welfare of grown children wreaks havoc on many lives. These problems result from traits shaped to benefit gene transmission even at the cost of individual health.

Kin selection shapes tendencies to make sacrifices that benefit family members who share genes identical by descent (Griffin and West, 2003). The costs of such sacrifices are highest and most satisfying for children and siblings, but problems experienced by extended family members can nonetheless cause great distress. Traits costly to individuals were once thought to evolve because of their benefits to groups, but this works only if group members are kin who share genes identical by descent. Alleles that result in an individual having lower inclusive fitness than other group members will be selected out even if they benefit the group (West et al., 2021). While selection for benefits to the group is not a viable explanation, selection by the group is powerful. Social selection shapes prosocial traits whose benefits to the group are wonderful side effects of their benefits for maximising the transmission of an individual's genes. These prosocial traits make culture possible, and culture creates emergent selection forces that further advance the process.

Cultural group selection describes how groups with stronger norms succeed at the expense of other groups. Those norms also create emergent forces of natural selection that shape human emotional and behavioural tendencies (Richerson et al., 2015). They promote cooperation but at the cost of neurosis and social anxiety. And while cooperation that benefits the group sounds nice, it can also be a product of ruthless punishment imposed by a despot to control and exploit subordinates.

Competitions between paternal and maternal genomes are also implicated. As David Haig has pointed out, alleles from the paternal line get advantages from inducing more maternal investment in a pregnancy, while those from the maternal line benefit more from reserving resources for future reproduction (Haig, 2020). Subtle mechanisms that imprint genes from the father differently from those of the mother seem well suited to advancing the interests of each genome and causing problems (Haig, 2008).

Sexually antagonistic selection offers yet another example of how selection can benefit genes at the expense of individuals. Alleles with different benefits and costs to males and females can be maintained despite increasing the vulnerability of one sex. Wonderful complexity ensues (Frank and Crespi, 2011).

Antagonistic pleiotropy can explain the persistence of genes that increase the individual's Darwinian fitness at one life phase or situation with costs later or in other situations. The classic example is a gene that causes ageing but is selected for because it offers benefits early in life when selection is stronger (Williams, 1957). When such alleles are fixed, their effects will not show up in genetic studies. Other fixed alleles can persist because their costs are outweighed by benefits that are manifest only in certain environments. A hypothetical example is a tendency to carry extra fat stores that imposes costs in most generations but might be life-saving in a generation that faces starvation.

Balancing selection maintains polymorphisms because different alleles give benefits in different environments (Power et al., 2015). Sometimes the benefits are to the individual, but sometimes benefits are to gene transmission at a cost to the individual. The sickle cell allele (Hb-S) is the classic example. Heterozygotes do better than homozygous individuals in environments where malaria is present. However, frequency-dependent selection also influences the polymorphism prevalence: Hb-S gives advantages when rare, but as it becomes common the proportion of homozygous individuals with sickle cell disease increases, so selection turns against the allele. Heterozygote advantage has often been suggested as a possible mechanism maintaining polymorphisms for mental disorders, but it is viable only for alleles with large effects and therefore is unlikely to account for mental disorders.

The more general possibility that alleles causing mental disorders persist in the genome because they give fitness benefits remains under consideration. For instance, some studies find schizophrenia to be associated with creativity (Nettle and Clegg, 2006), and others find indicators of positive selection on autism single-nucleotide polymorphisms (SNPs) (Polimanti and Gelernter, 2017). However, increasingly large

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GWASs find no evidence for positive selection for SNPs associated with schizophrenia and good evidence for strong background selection eliminating deleterious variants in areas enriched with schizophrenia-associated SNPs (Smeland et al., 2020). Plain old mutation-selection balance looks increasingly like the main explanation for highly heritable serious mental disorders (Keller, 2018).

The unanswered question is why syndromes like autism and schizophrenia have relatively consistent characteristics. Why are these the failure modes? Why are they influenced by so many variants with tiny effects? I think we will eventually discover that some systems have been shaped to performance peaks adjacent to fitness cliffs that make them intrinsically vulnerable to certain kinds of failure, and that the genetic variants that influence these risks include mutations being selected out and alleles that are beneficial, harmful or neutral depending on the genetic background and the environment.

6.4 Conclusion

Mental disorders need evolutionary explanations, but viewing disorders as adaptations is a mistake. The correct objects of explanation are traits that leave all members of a species vulnerable to a disorder. Most explanations are based on a combination of five main reasons why natural selection has left us vulnerable:

- *The inherent stochasticity of natural selection and development* that limits optimality is responsible for much vulnerability, especially for serious, highly heritable disorders.
- *Path dependence* is also responsible for vulnerability, especially after major transitions such as the human shift to the socio-cognitive niche.
- *The slowness of natural selection* results in mismatch with fast-changing environments that contributes to the vulnerability to some disorders, especially addiction and eating disorders, but mismatch does not offer a global explanation for all mental disorders.
- *Trade-offs* combine with stochasticity to leave some individuals at maladaptive trait extremes, but the risk depends on the shape and spread of the fitness function.
- Finally, vulnerability can result from *traits that maximise gene transmission at a cost to health*.

The fact that more than one factor influences our vulnerability to a single disorder frustrates our natural wish for simplicity. However, considering all factors systematically will eventually provide solid evolutionary answers to the question of why natural selection left us so vulnerable to so many mental disorders, and those answers will provide a new foundation that will make psychiatry more sensible, more effective and much more like the rest of medicine.

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