



Evolutionary Psychiatry

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Abstract

Evolutionary biology is now the foundation for scientific studies of behavior and emotion, but it is only starting to be applied in psychiatry. It asks new questions that provide a framework for integrating otherwise separate perspectives.

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The first two questions are about the evolutionary history of a trait and how it gives selective advantages. Answers provide evolutionary explanations of behavior and emotions that synergize with explanations that describe mechanisms and ontogeny. A third question asks why natural selection left us with traits that make us vulnerable to disease. In addition to mutations and environmental exposures, evolutionary psychiatry considers mismatch with modern environments, tradeoffs, and traits that increase gene transmission at the cost of host health. Answers to this question encourage a medical approach to aversive emotions as useful responses. Evolutionary psychiatry is not a method of treatment, but the basic science it brings to psychiatry has practical applications for clinical care, research, and public health that can increase psychiatry's effectiveness and its recognition as a medical specialty.

Keywords

Evolutionary biology · Natural selection · Adaptation · Maladaptation · Evolutionary medicine · Evolutionary psychology · Evolutionary psychiatry · Fitness · Emotions · Genetics · Biopsychosocial model · Tinbergen · Ethology

Introduction

Medical curricula largely focus on the anatomy, physiology, and biochemistry of bodily function and pathology, including the neuroanatomy, neurophysiology, and neurochemistry of brain and mental function and pathology. Evolutionary biology adds a focus on natural selection that provides additional insights about the functions of physical and mental traits and why some are vulnerable to malfunction. This chapter argues that evolutionary biology provides a foundation for an integrative framework that brings together otherwise disjunct aspects of psychiatry. The chapter begins by describing why an integrative framework in psychiatry is needed and three features of

evolutionary psychiatry that can help connect otherwise disparate aspects of the field.

Psychiatry in the twentieth century was characterized by different “schools” that provided contrasting theoretical frameworks for understanding the pathogenesis of mental disorders, each emphasizing different mechanisms (Luhmann, 2000). Perhaps the most divergent were psychoanalysis and biological psychiatry, with their very different models of pathogenesis and strategies for treatment. Lack of an integrative framework generated much unproductive controversy. While a “biopsychosocial” approach has long been advocated, it has not had sufficient granularity to synthesize contemporary biological, psychological, and social knowledge about mental disorders (Ghaemi, 2010).

Clinical neuroscience emphasizes the neuroanatomical, neurophysiological, and neurochemical mechanisms involved in mental disorders. It has several attractive features that make it the main focus of academic psychiatry (Insel & Quirion, 2005). The Research Domain Criteria (RDoC), for example, provides a scaffolding for organizing information and directing translational neuroscience research on mental disorders (Insel et al., 2010). Translational neuroscience has, in turn, used laboratory findings about fear conditioning and extinction, for example, to provide insights into the psychobiology of human anxiety (Ressler, 2020).

Nevertheless, biological psychiatry has often disappointed. Despite huge progress in understanding how brains work, specific brain abnormalities that cause specific mental disorders have yet to be found (Weinberger & Radulescu, 2016). This has left DSM diagnostic categories in limbo, useful in the clinic and epidemiology, but abandoned by neuroscience researchers who continue to search for brain pathologies that they hope will define mental disorders (Akil et al., 2010). Global mental researchers have emphasized the persistence of the treatment gap for mental disorders and the need for new approaches (Susser & Patel, 2014).

The principles of evolutionary biology are not new; they have provided a foundation for studies

of animal behavior ever since they transformed that field 60 years ago (Alcock & Sherman, 2010). The advance was made possible by recognition that a full biological explanation requires answers to both proximate questions about mechanisms and evolutionary questions about origins and functions (Mayr, 1993). Instead of asking only about how mechanisms worked, scientist also began asking how behaviors influence Darwinian fitness. For instance, scientists had long known that seagulls carry egg fragments away from the nest (the mechanism), but it took experiments by the Nobelist Nikolaas Tinbergen to demonstrate that this behavior decreased predation of chicks by other birds (the adaptive function).

Evolutionary medicine grew from recognition that a comprehensive explanation of clinical symptoms and disorders requires both mechanistic (or proximal) and evolutionary (or distal) kinds of explanation (Nesse & Williams, 1994; Williams & Nesse, 1991). For instance, a full explanation for the cough reflex requires describing not only the medullary cough center and its connections via the phrenic nerve to the diaphragm but also how the cough reflex gives a selective advantage. Physicians know that individuals whose cough reflex is absent or suppressed are vulnerable to pneumonia. This has practical implications in the clinic; cough suppressants should only be prescribed after the underlying mechanistic cause has been determined.

A first key feature of evolutionary medicine and psychiatry, then, is the value of integrating mechanistic and evolutionary explanations. In psychiatry, for example, a full explanation of anxiety symptoms requires understanding not only the frontal-amygdala circuitry involved in fear conditioning and extinction but also how anxiety responses provide a selective advantage (Marks & Nesse, 1994; Stein & Bouwer, 1997). Why this is crucial for a comprehensive evaluation of a patient with anxiety and how it can help in formulating a treatment plan will be discussed later in the chapter.

A second key feature of evolutionary medicine is recognition that it is a mistake to seek

evolutionary explanations for diseases, but sensible and important to ask why natural selection left us with so many traits that make us vulnerable to disease (Gluckman et al., 2009; Griffiths & Matthewson, 2018; Nesse, 2011; Stearns & Medzhitov, 2016). Why is the birth canal narrow? Why do wisdom teeth persist? Why does low mood exist? Why do neurogenetic variations that contribute to schizophrenia and autism persist? Some answers to such questions will be discussed in a later section.

A third key feature of evolutionary medicine and psychiatry is that its underlying framework is based on well-established biology. It proceeds using the standard scientific approach of using theory to pose viable hypotheses and discarding those that are inconsistent with data. Novel approaches in many areas of psychiatry have been prone to overenthusiasm about speculative hypotheses (Buller, 2005), but the fields of ethology and behavioral ecology have developed sophisticated methods for framing and testing hypotheses about evolution and behavior (Alcock, 2013; Confer et al., 2010; Mace et al., 2003), as has evolutionary medicine (Nesse, 2011).

It is noteworthy that these three key features of evolutionary medicine and psychiatry not only provide an integrative framework for psychiatry but also facilitate the integration of psychiatry with the rest of medicine. The same key principles are used to approach both somatic and mental symptoms and disorders. Each requires the integration of several different kinds of explanation, each of which benefits from a conceptual framework for approaching symptoms and disorders that is based on understanding our vulnerability to disease, and each advances by using both theory-derived hypotheses and empirical investigation.

This chapter provides an overview of the new field of evolutionary psychiatry, emphasizing how it provides an integrative framework for psychiatry that is both scientifically robust and clinically useful. The chapter begins by summarizing some relevant core evolutionary principles and some common misconceptions.

Core Evolutionary Principles and Some Key Misconceptions

Darwin made two related but distinct discoveries. The first is that all organisms have common ancestors. This single phylogeny for all of life explains why the mechanisms underlying behavior, cognition, and emotion are similar across diverse species. For instance, the dopaminergic neurotransmitter system is central to rodent and human motivation. It evolved from the closely related octopamine system which regulates mollusk and worm behavior. While such similarities are profound, there are also crucial differences. Human and chimpanzee DNA overlap by more than 98%, but small genetic differences create brains with major architectural differences. Translational neuroscience is premised on overlap in mechanisms, but such differences also impose limitations, such as the difficulty in establishing valid animal models of schizophrenia.

Darwin's second discovery was natural selection and how it shapes traits well suited to their functions (Bergstrom & Dugatkin, 2012; Dunbar, 2020). His observations of pigeon breeding made it clear that a species could change drastically over just a few generations. On his voyage to the Galapagos Islands, he observed that different bird species have shapes and sizes of beaks well suited to their different food sources. Years later, back in England, he realized that the environment could make selections similar to those made by breeders, thus shaping traits that make a species well adapted to its environment. His profound insight, shared by Wallace, was that variations among individuals within a species could influence numbers of offspring and this would, over generations, change the species. This is natural selection. It is a process that occurs necessarily whenever heritable traits influence reproductive success. Across generations, it makes the average member of a species more like the individuals who have the most offspring.

In retrospect, it is remarkable that natural selection was not recognized clearly long before Darwin and Wallace. The human tendency to think of all members of a species as if they are identical posed, and still poses, major difficulties for grasping natural selection (Barnes et al., 2017). The

inability of human intuition to grasp durations of millions of years poses additional difficulty. Finally, there is the apparent miracle of natural selection's products. When we consider how unicellular organisms evolved into multicellular organisms with specialized cells, and how this in turn led to an eye that can see and a brain that can learn, we can only gasp in astonishment at the grandeur that natural selection has created. Some traits, such as human capacities for memory and speech, are so extraordinary that many people find an evolutionary explanation hard to grasp. Many traits seem to be designed or products of some plan unfolding with a culminating goal, such as the emergence of humans. But genetic variations are random, selection is mindless, and the process of evolution has no set sequence or endpoint. It continues wherever genetic variations influence Darwinian fitness, that is, wherever there is life.

The tendency to teach evolution as sequences of traits or species ever-better adapted to their environments makes it seem as if the process is mostly about change, but selection far more often acts to keep traits the same. Cactus finches with beaks longer or shorter than average will get less food and have fewer chicks than average, thus stabilizing the trait in a middle range. Likewise, birds and humans with too much or too little anxiety will have fewer offspring than average, thus stabilizing anxiety in a middle range.

Could extreme vigilance in a few individuals be selected for because groups with a few such individuals do better than other groups? Only if those individuals have as many offspring as others in the group. If they have fewer, then their genes and individuals with extreme vigilance will become less frequent in every generation, even if their presence would benefit the group. Group selection can maintain the frequency of alleles that decrease individual fitness only in extremely limited circumstances.

The phrase "survival of the fittest" also fosters misconceptions. How long an individual survives is of no consequence in evolution except insofar as it influences reproduction. An individual who produces four surviving offspring and then dies at age 30 contributes more to the gene pool than one who has two offspring and lives until 90. A gene

or trait that increases reproduction will be selected for even if it causes suffering, increases the risk of disease, or shortens life. For instance, some genes that cause aging are selected for because they increase vigor and reproduction early in life that increases fitness more than the costs of a shorter life reduce fitness (Austad & Hoffman, 2018). That said, it is noteworthy that *Homo sapiens* are the only primates to live far beyond menopause, suggesting that grandparenting provides grandchildren with selective advantages, although the evidence for this is conflicting (Takahashi et al., 2017).

The lifespan for men is about 7 years shorter than that for women on average. Proximate explanations include more risky behavior and inflammation. But the evolutionary explanation is, in part, because men can have far more widely varying numbers of children than women, so investment in competition for mates gives big reproductive payoffs to a few men of a sort that are not available to women (Kruger & Nesse, 2006). This hypothesis is tested by the comparative method and data that confirm the prediction that differences in lifespan should be proportional to the intensity of male competition for males.

Anxiety is a tremendously useful adaptation, but as emphasized later, it necessarily entails suffering from false alarms. Consequently, anxiety disorders are the most prevalent of the mental disorders (Kessler et al., 2009), and they contribute substantially to the global burden of disease (Whiteford et al., 2013). Freud early on spoke about “ordinary suffering”; evolutionary biology provides a scientific framework for fully appreciating that natural selection does not give a fig about our happiness; it shapes capacities for pain and suffering because they increase Darwinian fitness (Buss, 2000; Nesse, 2004b), an insight with profound clinical implications. It may also, according to a recent suggestion, have shaped tendencies to avoid using suicide to avoid pain (Soper, 2019).

Many people have the notion that evolution is over for humans because most people who are born are now able to live to adulthood and to reproduce. Decreased child mortality has drastically reduced the force of selection, but evolution

will continue so long as individuals with certain genes and traits have more children than others. A few people are not interested in sex, and others just do not want to have children. Genetic variations that contribute to such tendencies will be eliminated in just a few generations.

The notion persists that behavior is somehow different from other traits or that learning is an alternative to evolutionary explanations. However, learning and other behavior regulation mechanisms are shaped by natural selection, just like all other traits. More exactly, selection shapes brain systems that monitor and interact with environments to give rise to behaviors that maximize inclusive fitness. Learning, memory, and emotions are such systems. An evolutionary view implies neither that behavior is rigidly determined nor that all individuals are identical. Instead, natural selection shapes systems that integrate data from external and internal environments with the individual’s social situation and strategies to give rise to extraordinarily flexible and sophisticated actions. The idea that evolutionary perspectives imply some kind of “genetic determinism” is simply a mistake. On the contrary, evolutionary biology provides an integrative framework for fully understanding the flexibility of individual behavior and the importance of both genetic (nature) and social (nurture) determinants in shaping such behavior.

The word “fitness” generates confusion. Physical fitness is relevant, but “Darwinian fitness” means the number of surviving and reproducing offspring and relatives as compared to others in the group. Why mention relatives? Because of kin selection. William Hamilton recognized in the 1960s that a genetic variation that decreases an individual’s reproduction could nonetheless be selected *for* if it sufficiently increases the reproduction of relatives (Hamilton, 1964). His famous formula $C < B \times r$ says that an individual should do something that harms its own fitness but benefits kin whenever the cost “C” to the actor is less than benefit “B” to kin who share “r” proportion of genes with the actor. In the apocryphal example, it is not worth sacrificing one’s life for one’s brother ($r = 1/2$), but the sacrifice is worthwhile to save the lives of eight cousins ($r = 1/8 \times 8$). This

principle of “kin selection” revolutionized the study of social behavior and provides a missing scientific framework for understanding family dynamics. The term “inclusive fitness” includes both the direct fitness from an individual’s reproduction and indirect fitness from the reproduction of kin who share genes that are identical by descent.

Herbert Spencer’s phrase “survival of the fittest” unfortunately inspired “social Darwinism,” the idea that groups benefit from competition that “weeds out” weaker individuals (Ruse, 2017). Such thinking was used to support laissez-faire capitalism, eugenics, and genocide. To counter this sort of misconception, it is helpful to think instead about “survival of the best nurtured” (Cozolino, 2014; Lakoff & Johnson, 2010). This phrase helps emphasize how natural selection shapes phenomena such as attachment and kin altruism; it may be useful in the clinic in discussing relationships and how to negotiate them.

The bottom line is that natural selection shapes brains in ways that make inevitable a powerful general principle: *Organisms tend to act in ways that maximize transmission of their genes to future generations* (Alcock, 2001; Buss, 2015; Krebs & Davies, 1993; McGuire et al., 1981; Westneat & Fox, 2010; Williams, 1966). This is the null hypothesis for studies of behavior. Behaviors and traits that do not maximize inclusive fitness need special explanation, usually in terms of individual pathology, exposure to an evolutionarily novel environment, or benefits to gene transmission. As the chapter proceeds, the implications of this general principle for psychiatry will be increasingly drawn out.

Progress in Applying Evolutionary Principles in Psychiatry

The utility of evolutionary principles for psychiatry was recognized by Charles Darwin. For instance, he noted that “Pain or suffering of any kind, if long continued, causes depression and lessens the power of action; yet it is well adapted to make a creature guard itself against any great

sudden evil (Darwin & Darwin, 1887, pp. 51–52).”

In the early years of the twentieth century, Darwin’s discoveries were little appreciated because of the limitations of his blending theory of inheritance and excessive respect for physicist Lord Kelvin’s conclusion that the earth could not be more than a few thousand years old because its heat would have radiated away. In this context, evolutionary insights relevant to medicine sputtered in the first half of the twentieth century, with various speculations about supposed “degeneration” (Zampieri, 2009). By midcentury, the modern synthesis with genetics inspired the rapid growth of evolutionary biology, and in the final third of the century, evolutionary principles became the accepted foundation for studies of animal behavior and emotion.

Some of the earliest and most influential work relevant to evolutionary psychiatry was that of Harry Harlow. He demonstrated that monkey infants were more motivated to cling to a mother substitute than to a source of milk, and he described how maternal separation led to aberrations in infant behavior (Harlow & Harlow, 1962). John Bowlby’s work on the adaptive functions of attachment, inspired by his conversations with Konrad Lorenz, further elaborated on how variations in maternal-infant attachment had sustained effects on an individual’s behavior (Bowlby, 1969).

Work by the British psychiatrist John Price on how mood states help chickens and vervet monkeys negotiate status hierarchies (Price, 1967) inspired much subsequent work, including reanalysis of data from the famous Islington studies by Brown and Harris showing that life events involving status loss are, as predicted, especially prone to precipitate depression (Finlay-Jones & Brown, 1981). Michael McGuire, a UCLA psychiatrist, laid the groundwork for evolutionary psychiatry with his early publications (McGuire, 1976; McGuire & Fairbanks, 1977) and his editorship of the journal *Ethology and Sociobiology*, now titled *Evolution and Human Behavior*. Other psychiatrists were soon applying evolutionary principles to psychiatry more generally (Abed, 2000; Konner, 1983; MacLean, 1985; McGuire

et al., 1992; McGuire & Fairbanks, 1977; McGuire & Troisi, 1987; Nesse, 1984; Stein, 2006b; Wenegrat, 1984).

The fast growth of evolutionary psychology has also provided insights relevant to mental disorders (Barkow et al., 1992; Buss, 1995; Cosmides & Tooby, 1987; Daly & Wilson, 1983; Kennair et al., 2018; Murphy et al., 2000; Dominic Murphy & Stich, 2011; Shackelford & Zeigler-Hill, 2017; Siegert & Ward, 2002; Syme & Hagen, 2020). Especially important are advances in understanding emotions and mating strategies and the origins of human cooperation.

The development of evolutionary medicine in the 1990s encouraged explicit analysis of why natural selection left organisms vulnerable to diseases. It has flourished since the turn of the millennium, with courses on the topic now offered in most universities (Grunspan et al., 2019), a new scientific society and journal, and many books documenting progress (Alvergne et al., 2016; Brüne & Schiefenhövel, 2019; Gluckman et al., 2009; Nesse & Williams, 1994; Painter et al., 2021; Perlman, 2013; Schulkin & Power, 2019; Stearns & Medzhitov, 2016; Williams & Nesse, 1991). Many early attempts incorrectly interpreted diseases as adaptations and speculated about how they offered selective advantages. Now widely recognized as a mistake, this approach has been mostly replaced by efforts to find evolutionary explanations for traits that make us vulnerable to mental disorders.

Evolutionary approaches to neuroscience were developing somewhat separately. While Maclean's concept of the triune brain has not proved enduring (MacLean, 1990), it was inspiring to many. Panksepp offered a more comprehensive view of how brain evolution influenced and was influenced by fitness (Panksepp, 1998). Michael Gazzaniga and Paul MacLean emphasized the value of evolutionary insights for neuroscience (Cory, 2002; Gazzaniga, 1992), and evolutionary neuroscience is now a thriving field (Kaas, 2020; Shepherd, 2017; Striedter, 2020). The lead from these and other scientists has inspired much more work than can be mentioned here. Even taken together, however, all efforts to date are only a bare beginning of the project to

understand the brain and behavior in evolutionary terms.

A decade ago, a group of noted experts proposed that evolutionary biology offered a solution to "the crisis of psychiatry" (Brüne et al., 2012). In subsequent years, explicit efforts to develop evolutionary psychiatry have proceeded rapidly, with several international meetings, scores of articles, and many new books (Abrams, 2020; Baron-Cohen, 1997; Brüne, 2015; Gilbert & Bailey, 2000; Nesse, 2019a, 2023; Shackelford & Zeigler-Hill, 2017), and a Royal College of Psychiatry Evolutionary Psychiatry Special Interest Group ([EPSIG.org](https://www.epsig.org)) on the topic has more than 1500 members (Abed & St John-Smith, 2016).

The first major edited volume on evolutionary psychiatry was published recently (Abed & St. John Smith, 2022). Despite this progress, and calls for education (Abed et al., 2019), no psychiatry training program yet provides education in depth about evolution and behavior, and major research agencies are still putting almost all their resources into proximate research.

Evolutionary psychiatry is still in its infancy, so this chapter cannot provide an overview of an established field. Instead, it offers an invitation to join in the effort to discover how evolutionary principles can help us understand mental disorders. The eventual goal is better prevention and treatment, but evolutionary psychiatry is not a method of treatment; rather, it brings the scientific foundation for all of biology to bear on the challenge of understanding mental disorders.

Evolutionary and Proximate Explanations

Animal behavior research was revolutionized in the middle of the twentieth century when scientists started asking a new question. Instead of trying only to describe behavior and its mediating mechanisms, they began also asking how traits give selective advantages that shaped them. Recognition that all traits need both mechanistic (proximal) and evolutionary (distal or ultimate) explanations is now universal, and most animal behavior textbooks are advertised as providing

“an evolutionary approach” (Alcock, 2013; Dugatkin, 1997). Psychology textbooks increasingly have major sections on evolutionary approaches, and courses on evolutionary psychology are now widely available. The developing knowledge in these fields is ripe for application in psychiatry. It offers insights about specific disorders and ways to settle some long-standing controversies, but most importantly, it provides an integrative framework for a biopsychosocial model that grounds biological psychiatry in both halves of biology.

Ernst Mayr showed that both proximate and evolutionary questions are needed for a biological explanation (Mayr, 1961). Nikolaas Tinbergen, the father of modern ethology, expanded the dichotomy by suggesting that a complete understanding of any biological trait requires answers to four questions; see Table 1 (Tinbergen, 1963). Darwin’s two discoveries form the basis for the two evolutionary questions: What is the evolutionary history of the trait across species? How has the trait influenced fitness? The other two questions are “proximate” ones, asking how mechanisms work and how they develop ontogenetically. This is consistent with calls from philosophers since Aristotle for a range of causal explanations; contemporary philosophers of psychiatry have similarly stressed the importance of explanatory pluralism (Ghaemi, 2010; Stein, 2011; Kendler, 2012). Answers to all four of Tinbergen’s questions are needed for a full explanation (Brüne, 2014; Natterson-Horowitz, 2019; Nesse, 2019b; Pfaff et al., 2019; Tinbergen, 1963). Schools of psychiatry have tended to focus on one or another kind of explanation, generating much useless controversy. Considering all four together offers an integrative framework. The four kinds of explanation can be organized into a 2×2 table (Nesse, 2013).

Anxiety: Four Kinds of Explanation

Mechanistic Explanations

Anxiety needs to be considered from all four perspectives (Bateson et al., 2011; Nesse, 1999; Price, 2013; Stein & Bouwer, 1997; Willers et al., 2013). Proximate explanations of brain mechanisms are well advanced. The responsible brain mechanisms have been described in detail by contemporary biological psychiatry studies of neuroanatomy and neurochemistry. Those studies often describe specific loci and neurotransmitters as having specific functions. For instance, the amygdala is sometimes described as the anxiety center, but it has many other functions, and anxiety is mediated by activity in many other pathways. The tendency to view the body as if it was a designed machine with specific parts that have specific functions has been described as “tacit creationism” (Nesse, 2020).

While biologists may hanker after finding a periodic table which provides necessary and sufficient criteria to define traits and differentiate them based on their underlying structures, the fuzziness of behavioral traits and the complexity of biological mechanisms mean that no such table is possible. If brains had been designed, they would have, like machines, discrete parts each with a specific function. But such tacit creationism fails to grasp the fundamental differences between designed and organic complexity. For instance, while the amygdala and serotonin play an important role in fear conditioning, the amygdala is involved in a range of different affects, and the serotonergic system influences a range of different processes, including sleep maintenance, vascular tone, and mood regulation. Different emotions correspond, not to different adaptive functions, but rather to different situations in which their multiple overlapping aspects are useful.

Table 1 Four kinds of explanations in biology (Nesse, 2013, 2019b)

	Static (synchronic)	Dynamic (diachronic)
Proximate explanation (mechanism)	Mechanism (causation) How the trait works	Ontogeny (development) How the trait develops in an individual
Evolutionary explanation (distal or ultimate)	Adaptive value (function) How the trait influences fitness	Phylogeny (evolution) How the trait evolved

Developmental Explanations

The ontogenetic development of anxiety mechanisms in individuals has also been well described at levels from brain to behavior. Normal human infants have separation anxiety and stranger anxiety, children have phobias of small animals, and adolescents develop social anxiety (Beesdo et al., 2009); natural selection has made different sorts of threats especially pertinent at different ages.

Ontogenetic explanations of anxiety mechanisms are clearly relevant to psychiatry. They help explain why different anxiety symptoms develop at different ages and provide insight into explaining what occurs when there are key traumatic events at different ages. It is known from the original work of Harlow on non-human primates and from studies in Romania of orphans, for example, that there are major neurodevelopmental sequelae of disrupted early attachment (Pine, 2007). And extensive studies have shown that certain stimuli, such as snakes, are pre-programmed to arouse anxiety after social learning.

Phylogenetic Explanations

Phylogenetically, avoidance of threat is seen across a wide range of species going all the way back to single-celled organisms. In the sea snail *Aplysia*, repeated exposure to danger results in faster withdrawal (Carew et al., 1983). Commonalities of mechanisms across phyla reflect their common origins and common challenges; differences result from natural selection and genetic drift. Eric Kandel received a Nobel Prize for his studies of the molecular basis of fear sensitization in *Aplysia*, work that remains relevant to understanding anxiety disorders (Kandel et al., 2000).

Anxiety is an evolved response that is similar in a wide range of species, where it plays a key role in threat avoidance (LeDoux, 2012b). Darwin's initial work on the expression of emotions across species remains inspirational (Darwin, 1998; Ekman, 2003). It also provides an important foundation for a great deal of work in contemporary psychobiology, for example, the use of standardized facial expression analysis in neuroimaging work (Ekman & Friesen, 1986).

However, one must be cautious in the interpretation of laboratory data and wary of overly simplifying this complex emotion (LeDoux, 2012a).

Explanations Based on a Trait's Adaptive Significance

The adaptive value of anxiety is generally recognized, but an evolutionary perspective provokes many questions (Bateson et al., 2011; Kennair, 2007; Marks & Nesse, 1994; Stein & Bouwer, 1997). Has natural selection shaped distinct varieties of anxiety to cope with different kinds of dangers? How are they related to each other? To what extent is each kind of fear innate or a product of prepared learning, social learning, or personal experience? Do individuals with more anxiety better avoid dangers? What price do their inhibitions impose? What about individuals with less anxiety than average? Do some have so little that they have a pathological condition of "hypophobia" that harms their fitness?

The smoke detector principle provides one of several evolutionary explanations for the prevalence of excess anxiety arising from normal brain mechanisms (Nesse, 2005c). Just as the annoyance from false alarms is a small price to pay for the benefit of early warning of any real fire, unnecessary anxiety can also be well worth it to protect against small risk of a big danger. Explaining this smoke detector principle is useful in the clinic. For some patients, the explanation provides a cure; for others, it provides a basis for encouraging exposure to perceived threats, in line with the principles of cognitive-behavioral therapy (Stein, 2006a). The subsequent section on emotions describes four other reasons why useless emotions are often normal.

Clinical Implications

Addressing all of Tinbergen's questions has several clinical implications. First, given the adaptive value of avoiding dangers, we can expect that anxiety will be one of the most common complaints in the clinic. The smoke detector principle formalizes this point and explains the prevalence of false alarms. Second, because anxiety is

necessarily aversive; we can expect that people with anxiety will suffer enormous distress and physiological changes that motivate and make possible rapid escape. The prevalence and aversiveness of such alarms help to explain why anxiety makes such a huge contribution to the global burden of disease. Third, given that different threats emerge during the life course, we can expect to see different sorts of anxiety at different life stages. A good clinician will be aware of this and will adapt screening questions and clinical foci accordingly. Fourth, given that fear modulation is governed by similar mechanisms across species and is an important adaptation, we can expect that molecules that target these mechanisms exist and that they are useful for anxiolysis across many species, justifying translational neuroscience approaches. Indeed, GABAergic anxiolytic mechanisms exist across species, and benzodiazepines that bind to these receptors diminish anxiety in many. Dampening the anxiety system offers clinical advantages (fewer false alarms) along with matching disadvantages (decreased protection, etc.). Fifth, in evaluating the anxious patient, it is important to understand both real and perceived threats and to evaluate the individual's resources for addressing anxiety. Treatment may involve not only judicious use of anxiolytic agents but also strengthening of internal and external resources for successfully facing and coping with dangers and the anxiety they arouse. Relatedly, in treating the anxious patient, we should be thinking about maintaining appropriate anxiety rather than entirely removing anxiety.

Reward Mechanisms: Four Kinds of Explanation

Systems that regulate getting resources cause as many problems as those that protect against losses. Excesses mediate addiction and gambling, deficiencies mediate depression, and dysregulation causes bipolar disorder. Integrating all four kinds of explanation can help to resolve otherwise intractable controversies.

Mechanistic Explanations

The proximal causal mechanisms underlying reward have been studied in great detail (Volkow, Koob, Baler chapter). James Olds showed that rats prefer stimulation of the nucleus accumbens to receiving food (Olds, 1958). Stimuli associated with reward become more salient, thanks to increased activity of dopaminergic neurons in cortico-amygdala-striatum circuits (Kringelbach & Berridge, 2016). Exposure to such stimuli arouses “wanting” and pursuit of the reward; these mechanisms mediate addiction. Reward consumption arouses the hedonic response of “liking” (Berridge, 1996); this response is conspicuously absent in depressed patients with anhedonia. Notably, these circuits are aroused mainly not by the magnitude of reward, but rather by its size relative to expectations and by its value in the context of needs and other opportunities and threats (Carver & Scheier, 1990). Classically, the “marshmallow test” has been thought to assess impulse control in children; but choosing a smaller reward available sooner is adaptive for individuals in environments with erratic rewards or shortened lifespan; this may explain the tendency of children with a history of socioeconomic adversity to choose a smaller faster reward. Reward mechanisms are extraordinarily sophisticated fitness maximizers, but they leave us on a “hedonic treadmill” where satisfaction is soon displaced by new desires, increasing vulnerability to addiction (Diener et al., 2006; Nesse & Berridge, 1997).

Developmental Explanations

Ontogenetically, different stimuli are rewarding at different ages. Early in life, it is important that infants find milk rewarding and that they do whatever they can to engage their mothers. In mid-childhood, social cues become salient and sought after. With adolescence, the pursuit of sex and status becomes dominant so risk-taking gives greater benefits (Natterson-Horowitz & Bowers, 2019). In adulthood, the simultaneous pursuit of status, occupation, childcare, abilities, income, and love arouses inevitable stresses and conflicts. These shifts in motivational states make sense as

strategies for maximizing fitness at different stages of life. Individuals whose brains change appropriately at different stages get selective advantages (Bjorklund & Pellegrini, 2002).

Phylogenetic Explanations

Phylogenetically, reward systems are similar across species. This explains the value of rodent models in studying the neurobiology of substance use disorders; rodents and humans both respond to sugar with hedonia (liking) and to dopaminergic agents with salience motivation (wanting) (Berridge, 1996). It turns out that these mechanisms mediate substance use in some animals in the wild (Ahmed, 2018; Dudley, 2002; Hill & Newlin, 2002; Sullivan & Hagen, 2002; van Staaden et al., 2018). The commonalities among motivational systems across species are remarkable. The central role of octopamine and its successor dopamine has endured over hundreds of millions of years, with pathways gradually modified to maximize fitness in each species.

Explanations Based on a Trait's Adaptive Significance

The adaptive value of reward systems is clear: to induce behavior that finds and gets resources such as food, shelter, health, knowledge, status, mates, and offspring. Time and effort are limited, so the system must adjust the effort and timing of pursuing conflicting needs and opportunities, all while considering possible risks. The classic approach-avoidance experiments that require rats to risk shock to get food have explored these tradeoffs in detail. In the clinic, the conflict between pursuing major goals and associated risks, such as demanding a promotion at the risk of losing a job, often causes clinical symptoms. At the same time, work on providing reward to fear-conditioned animals was instrumental in developing some of the earliest techniques of behavioral therapy (Wolpe, 1961).

Mechanisms that regulate foraging strategies are particularly important. How long should an individual stay at this bush or patch before looking for another one? It depends on how long it takes to find a new bush and the current (and declining) rate of return at the current patch. Eric

Charnov's marginal value theorem describes the optimal strategy: start looking for a new patch when the current rate of return declines below the average rate of return across many patches (Charnov, 1976). The same mechanisms regulate the rhythms of our daily lives, resulting in bouts of activity that tend to average between 1 and 2 h. Individuals within a species may, however, have different thresholds for moving to a new patch. As with every trait, pathology can result from too much or too little. ADHD is characterized by jumping too fast to the next task; those who tend to persist too long at the current task also have a disorder. Dopaminergic drugs that increase persistence are helpful for ADHD.

The reward motivation system adjusts an individual's effort and risk-taking depending on the propitiousness of current situation. In propitious situations that offer big rewards with little effort, the system shifts to high mood to take full advantage of what may be a temporary opportunity. In unpropitious situations, however, low mood inhibits efforts that would waste calories and incur risks. Recognizing the utility of low mood is a major missing foundation for understanding depression (Carver & Scheier, 1990; Klinger, 1975; Nesse, 2000).

Deciding when low mood is useful is challenging because we humans mainly pursue social resources such as relationships and status that are much harder to observe and quantify than berries on a bush. Clinicians may choose to alter mood by targeting neurotransmitters or negative thoughts, but the possibility that low mood is appropriate signaling that a new life strategy is required should also be considered. More on depression is in a later section.

All species tend to discount future rewards to some degree because the duration of the individual's future lifespan is never certain (Vanderveldt et al., 2016). Many species also have systems that adjust discounting to cope with different conditions. Harsh conditions likely to shorten life tend to shift the motivation system toward increased pursuit of early reproduction and short-term rewards, even in plants (Takeno, 2016). Many annuals shift to earlier flowering and seed set when dry conditions indicate that further growth

may be impossible. The adaptive benefit of such shifts helps to make sense of the connection between early abuse and disorders on the externalizing spectrum such as sociopathy and addiction (Ellis & Del Giudice, 2014; Gelles & Lancaster, 1987). Tendencies to inhibited goal pursuit characterize problems on the internalizing spectrum, such as anxiety and obsessiveness. Twin studies suggest that this global dichotomy between internalizing and externalizing maps to two routes to depression (Kendler et al., 1996), and some authors have suggested that fast and slow life history trajectories provide a general framework for organizing mental disorders (Del Giudice, 2016) or specific disorders (Brüne, 2016).

Clinical Implications

Understanding reward from these four perspectives has important clinical implications. First, given how adaptive approach to reward is, and the mismatch between rewards in the EEA and the contemporary availability of rewards, we can expect that substance and behavioral addictions will be among the most common problems seen in the clinic (St John-Smith et al., 2013). The ready availability of carbohydrates has given rise to an epidemic of obesity, and the availability of a range of online rewards (e.g., gambling, gaming, porn) may lead additional epidemics of “lifestyle” illnesses. Second, given that the “wanting” of addiction differs from the “liking” obtained from a reward, we can expect that people with addiction will suffer enormous distress. The addicted individual is constantly striving to obtain rewards, whose consumption has rapidly diminishing hedonic value (e.g., rewards from social media). Thus, the global burden of disease due to substances and behavioral addictions is massive. Third, given that different rewards are particularly important at different stages of life, we can expect to see different sorts of reward-based problems at different life stages. A good clinician will be aware of this and will adapt screening questions and clinical focus accordingly. Fourth, a key aspect treatment of addictive disorders involves re-learning how to manage temptations and the development of new and healthier habits. Fifth, in evaluating the addicted patient, it is important to evaluate the particular

resources for re-learning and for developing new habits. Relatedly, in treating the addicted patient, we should be thinking about healthier ways to obtaining hedonic reward rather than aiming at absolute abstinence. Finally, the rewards system downregulates in certain situations and is also vulnerable to malfunction for several reasons. More about this is in the section about depression.

Attachment: Four Kinds of Explanation

Evolutionary psychiatry got its start with John Bowlby’s recognition that mother-infant attachment is an adaptive trait, one whose disruption is responsible for much pathology later in life. Integrating all four kinds of explanation is an ongoing project.

Proximate Explanations

There is a growing understanding of the neuroanatomy and neurocircuitry of attachment (Insel, 2000). Neuroimaging studies have, for example, demonstrated that hearing the sound of one’s infant crying leads to functional activation of specific brain regions (Strathearn et al., 2009). Neuroendocrine studies have explored the role of specific neuropeptides in facilitating maternal-infant attachment (Galbally et al., 2011) although it is increasingly clear that the effects of oxytocin are far more complex than simply mediating attachment (Szymanska et al., 2017). Disruption of maternal-infant attachment has also shed light on the relevant neurocircuitry and neuroendocrinology of attachment (Teicher & Samson, 2016).

Developmental Explanations

The ontogeny of attachment has been the object of detailed studies that describe typical ages of onset and offset for various attachment phenomena and factors that influence their intensity and duration (Main, 2000). In the first months of life, constant contact is in the interests of mother and infant. As locomotion becomes possible, motivation for the infant to stay close to the mother becomes useful, as does stranger anxiety. The interests of infants and mothers diverge after a few years when continuing to nurse is in the child’s interest but not the mother’s (Dettwyler, 1995). Such experiences vary

depending on available resources, mother's temperament, and the presence of siblings. As noted earlier, Harlow's work on non-human primates and studies of institutionalized orphans have demonstrated the major neurodevelopmental and behavioral sequelae of disrupted early attachment. Early on, separated infants demonstrate agitation and then withdrawal; later in life, they tend to have unstable relationships (Harlow & Harlow, 1962).

Phylogenetic Explanations

The phylogeny of attachment has been studied in a variety of primates, with variations tending to map to ecological differences (Fraleigh et al., 2005). For instance, human infants remain immobile for an extended period, while baboon infants gradually increase roaming distance from their mother in the first weeks of life (Rowell et al., 2009). Indeed, attempts to provide any one kind of explanatory account are informed by attempts to provide the other three types of explanation.

Explanations Based on a Trait's Adaptive Significance

John Bowlby pioneered evolutionary psychiatry with his recognition that attachment gives selective advantages, ensuring that a range of harms are avoided (Bowlby, 1969). Dangers from wild animals and harm from other humans are key threats to infants. Simply being left on the ground instead of being held risks damage from infection, insects, and exposure. The general tendency for babies to cry when left alone is useful, and its aversiveness motivates mothers to do what is needed to comfort the baby (Zeifman, 2001).

While anxious and avoidant attachment styles have been viewed as abnormal, contemporary behavioral ecologists have considered the possibility that those styles of attachment are actually strategies that babies use to get care from parents who might otherwise put their efforts elsewhere (Belsky, 1999; Chisholm, 1996; Simpson, 1999). Is that correct? Does it work? Do such tendencies persist into adulthood? Much depends on understanding the adaptive significance of attachment in general and different styles of attachment in particular.

Variations in parental behavior arising from differences in genetic relatedness have inspired

extremely salient evolutionary studies by evolutionary psychologists Daly and Wilson (Daly & Wilson, 1981, 1988b). An evolutionary perspective inspired them to ask if rates of child homicide were higher in families that include a stepparent; they were 70 times higher (Daly & Wilson, 1988a). This does not mean that human parents have the same evolved adaptation that motivates some other primate to kill unrelated offspring (Driscoll, 2005), but it does call attention to how kinship influences attachment and behavior.

Clinical Implications

Understanding attachment from these four perspectives has important clinical implications. First, under different circumstances, different kinds of attachment may be advantageous. Under resource-constrained conditions, infants may need to be independent earlier; those who can do so have been termed "dandelions." Mothers in such situations may withdraw resources from the infant, with consequences for future life that often need detailed analysis in psychotherapy (Sieff, 2019). Under resource-rich conditions, longer and more intense attachments may facilitate growth; individuals who thrive under such conditions have been termed "orchids" (Lionetti et al., 2018). Second, a range of maternal-infant and sib-sib conflicts can be predicted. Mothers and other siblings are advantaged by earlier weaning but infants are advantaged by later weaning so conflict is inevitable (Trivers, 1974). Weaning conflicts begin when it becomes in the interest of the mother's genes to reproduce again. They end when it becomes in the interest of the offspring's genes to stop nursing and allow the mother to produce another sibling who will share half of its genes. These conflicts are intrinsic for mammals even though we may not be conscious of them. Empirical data also suggest that children receive more food from their biological mothers than from their stepmothers and that children with grandparents survive better than those without. Third, the idea that family dynamics can be explained on the basis of children having an unconscious sexual wish toward their parents doesn't make biological sense, although seemingly seductive behavior might manipulate

parents. Empirical data show that individuals raised in well-functioning nuclear or extended families (e.g., on kibbutzim) do not become sexually attracted to one another in adulthood, but instead prefer sexual partners who they meet for the first time as adults (Erickson, 1993; Rantala & Marcinkowska, 2011; Shepher, 1971; Westermarck, 1922). Lack of early contact helps to explain incest and related impulses that are important for understanding conflicts in reconstituted families (Lieberman et al., 2003). Fourth, the psychobiology of infant-maternal separation is likely to have mechanisms in common with those that underpin symptoms of depression and anxiety; agents that diminish the response to maternal-infant separation are likely to be useful in the treatment of mood and anxiety disorders (Marais et al., 2006). Fifth, clinical symptoms and personality traits may have origins in early attachment patterns and family dynamics (Mikulincer & Shaver, 2012); these patterns and dynamics may influence psychotherapeutic relationships.

Evolutionary Medicine: Why Does Vulnerability to Disease Persist?

If traits have evolutionary in addition to proximate explanations, what about diseases? Were they too shaped by natural selection? If anxiety gives a selective advantage, what about schizophrenia? The average psychiatrist, asked about how evolutionary theory can help psychiatry, might well mention theories linking schizophrenia with creativity and the idea that extreme creativity in some individuals benefits the species. However, such attempts to find adaptive functions for diseases are a serious mistake.

Diseases are not adaptations. They are not traits shaped by natural selection. *Viewing diseases as adaptations is a mistake that is as common as it is serious.* Diseases happen to only some individuals; they are not traits shared by all members of a species. They can influence fitness (negatively), but they do not have evolutionary explanations based on their adaptive value (Nesse, 2011, 2023).

Traits that cause vulnerability to disease are another matter entirely. Most are universal in a

species. They are shaped by natural selection, so they need evolutionary explanations. The birth canal is narrow. Our abilities to resist cancer and infection are limited. Epilepsy has many causes. Pain is useful, but chronic useless pain is common. Anxiety and mood disorders are overwhelmingly common. Schizophrenia and autism occur worldwide. Why did natural selection leave us vulnerable to so many diseases? Evolutionary medicine takes such questions seriously, and it looks for possible answers (Williams & Nesse, 1991).

Until recent decades, disease was attributed mainly to proximate causes such as genetic mutations, exposure to pathogens or toxins, or aging. Evolution, on the other hand, was thought to mainly explain why traits work so remarkably well. Evolutionary medicine grew out of recognition that traits that leave a species vulnerable to disease can have several kinds of evolutionary explanations; different authors have recommended slightly different ways to categorize them (Crespi, 2000; Ewald, 2018; Grunspan et al., 2018; Nesse, 2005d; Perlman, 2005). Six reasons for vulnerability are cited most often: constraints on selection, tradeoffs, fast pathogen evolution, mismatch with environments, reproduction at the cost of health, and defenses such as pain and cough (Nesse, 2005d). Below are expanded categories that emphasize the contrast between vulnerabilities that result from the limits of natural selection and vulnerabilities that result from traits that maximize inclusive fitness at the cost of harm to individual health.

Evolutionary explanations for disease vulnerability fall broadly into three main groups: (1) things that natural selection just can't do, (2) traits that maximize gene transmission at the cost of disease vulnerability, and (3) genes that enhance their own transmission at a cost to the host's genes (Table 2).

The Limitations of Natural Selection

There are several things that natural selection simply can't do. It can't prevent or repair all mutations, nor can it select out deleterious

Table 2 Evolutionary explanations for disease vulnerability**The limitations of natural selection**

- Deleterious mutations are inevitable and are only slowly selected out
- Genetic drift can eliminate beneficial alleles or make deleterious ones universal
- Developmental stochasticity cannot be completely eliminated
- Path dependence limits major revisions of suboptimal traits
- Mismatch with changing environments results because selection is slow
- Pathogens evolve far faster than hosts
- Selfish genetic elements can harm the host's fitness

Traits that maximize gene transmission but cause health vulnerabilities

- Benefits early in life are selected for despite costs later (antagonistic pleiotropy)
- Reproductive success is maximized at the cost of health (life history tradeoffs)
- Traits maintained by kin selection can decrease direct reproduction
- Defenses are often highly aversive and intrinsically vulnerable to failure
- Maximizing performance of a trait can compromise its robustness
- Plasticity adapts systems to situations at the cost of vulnerability to dysregulation
- Sexually antagonistic selection gives benefits to one sex at a cost to the other
- Maternal vs. paternal genome competition can harm individual fitness

mutations quickly, especially recessive ones. It cannot canalize developmental pathways to ensure completely standardized outcomes from cell migrations during development. It can't provide protection against some dangers, for instance, gamma radiation. Finally, natural selection is too slow to keep up with rapid biotic or abiotic environmental changes. These are all well-recognized reasons for disease vulnerability.

Deleterious mutations are responsible for vulnerability to a range of diseases. However, the more we learn about the genetics of mental disorders, the more it is clear that there is no "gene x for mental disorder y." Although serious mental disorders, such as schizophrenia, have been associated with very rare severely damaging variants critical to synaptic function, different genes are affected in different individuals with the same condition (Gulsuner et al., 2020). Common mental disorders have a polygenic architecture, with each gene variant contributing only a tiny proportion of the variance (Kendler, 2013). Genetic variants associated with low fitness gradually disappear from the gene pool, but new harmful mutations are constantly created (Keller & Miller, 2006; van Dongen & Boomsma, 2013).

Changes in allele frequency may result as much from genetic drift as they do from natural selection (Lynch et al., 2016). Especially in small populations, genes are influenced by stochastic factors such as the accidental death of an

individual with a beneficial mutation or high reproduction by good luck for an individual with a deleterious allele. It remains to be determined which mental disorders arise from neutral alleles that cause pathology only when interacting with certain genetic or external environments.

Just as natural selection cannot prevent all mutations, it also cannot canalize development completely, so **stochastic variation in development** occasionally results in pathology even if all genes are normal and in a normal environment. Brain development seems to be especially prone to such problems; this may have special relevance for childhood-onset mental disorders such as autism.

Less well recognized are vulnerabilities that result from **path dependence**, the inability of natural selection to start from scratch to correct a vulnerable body plan. For instance, we are stuck with a windpipe that opens into the pharynx where it can be blocked by food. A machine with that kind of problem would be redesigned from scratch, but bodies can change only by small sequential modifications. Brain mechanisms too are constrained by path dependence. Pathways that transmit signals of danger fast are incompletely integrated with slower systems that bring considered appraisals of risk (LeDoux & Pine, 2016). Path-dependent constraints may also help to explain a range of human cognitive biases, including the tendency to think about causes

simplistically, and to form convictions based on scant evidence; such limitations may help explain the human vulnerability to a range of psychiatric symptoms, including delusions.

Natural selection is also too slow to prevent **mismatch with fast-changing environments**, particularly environments that provide access to chemical and non-chemical stimuli that engage our “wanting” neurocircuitry (Gluckman & Hanson, 2006). Obesity and atherosclerosis are well-recognized products of the mismatch between our evolved physiology and current environments. Substance-related and addictive disorders, such as gambling and gaming disorder, are an example of mental disorders resulting from such mismatch (Nesse & Berridge, 1997). Note, however, that while there has been much speculation about how modern environments might increase the risk for mental disorders, there is relatively little evidence for major increases in rates, with the exception of addiction (Baxter et al., 2014). Every generation views itself as uniquely stressed, and stressors of modern life do influence rates of problems, but they are unlikely to explain most cases of anxiety or mood disorders. This said, there is every reason to investigate possible malign effects of social media and the reasons why rates of depression differ so drastically in different cultures.

Natural selection cannot keep up with **rapidly evolving pathogens**. This is relevant to pediatric autoimmune disorders (such as the onset of obsessive-compulsive symptoms after streptococcal infection) (see Laje, chapter ▶ “[Neurobiology of Neuroimmune Encephalitic Disorders](#)”) and to understanding the role of inflammation in depression. There is also a growing appreciation of the gut-brain axis; our microbiome appears to play a substantive role in governing some aspects of brain function.

Traits That Maximize Gene Transmission at the Cost of Disease Vulnerability

Antagonistic pleiotropy refers to genes with multiple effects that are opposite to each other,

usually beneficial early in life when selection is strong and deleterious late in life when selection is weak. Recognition of the role of antagonistic pleiotropy has revolutionized the study of aging (Austad & Hoffman, 2018; Turke, 2008). Many such genes are fixed so no variation is observed. However, variations that influence the rate of aging cannot be assumed to be deleterious mutations; they might give benefits earlier in life. For instance, women with the ApoE4 allele are likely to develop atherosclerotic and neurodegenerative disease earlier than other women, but they have increased progesterone levels which may increase fertility (Jasienska et al., 2015). ApoE4 also protects against parasites and can, in ancestral environments, improve fitness and even cognitive function (Trumble et al., 2017).

Tradeoffs between health and reproductive success are resolved by maximizing inclusive fitness. So, humans, like other organisms, invest inordinate effort and risk in competing for mates, having sex, and taking care of children. An extraordinary proportion of psychiatric symptoms arise from life situations involving reproductive competition, even though individual patients may be unaware of the association.

Kin selection explains why people make big and often risky efforts to help children and other relatives. Many people become understandably distraught about their children’s problems at the expense of their own health. The benefits of nurturing and altruistic motivations come with substantial costs.

Defensive mechanisms impose major costs and suffering, such as immune responses (which may lead to life-threatening allergic reactions) and anxiety reactions (which are associated with significant burden of disease). The benefits are essential but the costs are substantial. A range of adaptive but aversive emotions are discussed in more detail below.

The **tradeoff between peak performance and robustness** is observed in machines as well as bodies. The fastest race cars are light and fragile. Strong selection has shaped extreme human cognitive, linguistic, and social abilities, perhaps at the cost of vulnerability to some mental disorders. Although several authors have hypothesized that

schizophrenia reflects a fitness tradeoff at the extreme end of variation (Crow, 1997; Greenwood, 2016; van Dongen & Boomsma, 2013), newer genetic studies challenge this interpretation (Uricchio, 2019). Additional mechanisms may underlie the intrinsic vulnerability of some traits to failure (Crespi & Go, 2015; Del Giudice & Crespi, 2018).

Some cybernetic regulation systems are intrinsically vulnerable to failure. Positive feedback mechanisms maintain feeding once it begins, but they make the system vulnerable to out-of-control gorging. Small exposures to drugs and alcohol can precipitate binges. Self-adjusting systems are also especially vulnerable. Repeated arousal of anxiety sensitizes the system adaptively in dangerous environments, but at the risk of anxiety symptoms themselves initiating more anxiety. When nociception is insufficient to prevent repeated damage and pain, the system sensitizes, creating the risk of positive feedback causing chronic pain (Nesse & Schulkin, 2019). Early adaptive developmental plasticity to privation or abuse allows adaptive responses to different environments, with the rise of long-term adverse health consequences (Gluckman et al., 2019).

Finally, traits with a **cliff-edged fitness function** are shaped to a mean value close to the peak that maximizes gene transmission even though inevitable variation of offspring will leave many with trait values “off the cliff” and vulnerable to problems (Nesse, 2004a). The average trait value is stabilized, not at the peak, and not at the point that maximizes health for the population, but at the point that maximizes multigeneration gene transmission, resulting in poor outcomes for a few percent of the population—just what is observed for many highly heritable conditions (Nesse, 2019a).

Benefits to Genes at the Expense of the Individual’s Health

The cells in an individual’s body cooperate superbly because that is the best way for all of

them to get their genes into future generations. Such cooperation is possible, thanks to all cells in an individual starting off genetically identical, germline cells being sequestered from somatic cells, and apoptosis working to eliminate rogue cells. This is the huge and amazing evolutionary transition that made complex multicellular organisms possible (Smith & Szathmáry, 1995). Its limitations help to explain our vulnerability to cancer.

However, there are rare examples of genes that get around these controls (Burt & Trivers, 2006). Meiosis usually ensures that each copy of a gene has a 50% chance of getting into an egg or sperm. **Selfish genetic elements** that distort segregation can get themselves into more than the usual 50% of offspring. Meiotic driver genes can secrete poisons that kill off gametes that don’t include them, explaining why one such gene was named *wtf* (Bravo Núñez et al., 2018). While such phenomena are not yet known to cause specific human disorders, recognizing their existence, and why they are not more common, offers important insights into how natural selection works.

A more common example is **sexually antagonistic selection**. An allele can be maintained by the advantage it gives to one sex despite costs to the other sex. The conservation of iron associated with hemochromatosis alleles causes liver disease mainly in men, but benefits to women who lose a bit of iron with each menstrual cycle may maintain the genes. While major effects of sexually antagonistic selection are not revealed by genetic studies of humans, stronger immune responses in women and associated increased risk of autoimmune disease may be an example (Roved et al., 2017) that could be relevant for understanding sex differences in mental disorders.

Finally, a series of studies by David Haig describes **competition between paternal and maternal genomes** in mice about how much the mother should invest in the fetus: more gives an advantage to the genome of the father (who may not be the father of a subsequent offspring); less reserves a mother’s resources for investing in a future fetus. His recent book elaborates these ideas and related profound implications for behavior and philosophy (Haig, 2020).

Conceptualizing and Explaining Mental Disorder

A conceptual framework for psychiatry must address the central question in philosophy of psychiatry, “What is a mental disorder?”. This question turns out to be remarkably difficult to answer (Matthewson & Griffiths, 2017; Stein, 2013; Troisi & McGuire, 2002; Wakefield, 1992, 2007). Psychoanalysis provided a particular attractive framework in part because it proposed that all individuals had neurotic defenses, and it provided specific hypotheses about how such defenses malfunctioned. Biological psychiatry is attractive insofar as it suggests that mental disorders are characterized by specific neurobiological alterations and that sensitive and specific biomarkers of mental disorders will someday be found. As it turns out, however, psychoanalytic models of the unconscious are now dated, while the promise of sensitive and specific biomarkers has not materialized. The resulting frustration allows critics of psychiatry to argue that mental disorders are merely social constructions that are best explained by power differentials rather than underlying biology.

Evolutionary psychiatry buttresses an integrative framework for navigating between scientism and skepticism regarding the ontological status of specific mental disorders (Stein, 2013). As noted already, mental disorders are not like the chemical entities of the periodic table; they have fuzzy boundaries, and they involve multiple different mechanisms. On the other hand, mental disorders cannot be thought of as garden weeds, where the definition of a weed differs from garden to garden, from time to time, and from place to place. It has been difficult to find a framework that avoids both scientism and skepticism, but agreement is growing that evolutionary analyses of normal function are crucial to conceptualizing dysfunction and disease (First & Wakefield, 2013; Griffiths & Matthewson, 2018).

A rigorous understanding of the proximal and distal mechanisms that contribute to cognition, affect, and behavior can help us to steer a sensible course that recognizes the complexity of mental disorders and the range of factors that help us determine when to diagnose and if and how to intervene.

For instance, when distinguishing normal from pathological social anxiety, we rely not on biomarkers, but rather on assessment of symptom severity and duration, and related distress and impairment (First & Wakefield, 2013). Such diagnostic products of individual case formulation provide useful guides for communication and evidence-based treatment decisions (Stein & Vythilingum, 2007).

One of the key contributions evolutionary biology makes to nosology is a theoretical framework for distinguishing between symptoms and diseases (Nesse & Stein, 2012; Wakefield, 2023). Anxiety, low mood, and jealousy are evolved responses that, like pain and cough, are normal responses that are themselves diseases only when they arise from an abnormal regulation system. However, normal regulation mechanisms often give rise to useless emotions, for reasons discussed in the below section on emotions.

An evolutionary framework helps to explain the ongoing dissatisfaction with our current nosology, the failure to find biomarkers that define mental disorders, and the importance of taking an approach to symptoms like that taken in the rest of medicine. In general medicine, doctors recognize cough as an adaptive defense, so they look for possible causes. The possibility that the cough itself is pathological is considered only if no cause can be found. No biomarker can differentiate normal from abnormal cough. Rather, treatment decisions are based on analyzing what may be arousing an individual’s cough, symptom severity, and the pros and cons of suppressing cough. Similarly, no biomarker can differentiate normal from abnormal anxiety. It too is a normal defense, requiring similar careful consideration of possible causes and an understanding of the particular individual, the nature of the symptoms, and the relevant evidence base.

An evolutionary framework emphasizes that some disorders are products of multiple often interacting causes. Monocausal mechanisms will never define all disorders in psychiatry for the same reasons they don’t define many disorders in the rest of medicine. While some entities may reflect single etiological mechanisms (say, type 1 diabetes), many others are pragmatic kinds which reflect a system failure with many different causes

(say, heart failure). Similarly, in psychiatry, while some entities have a very specific and homogenous cause (say, cannabis-induced psychosis), most psychiatric entities are pragmatic kinds that involve multiple different causes, mechanisms, and symptoms (Griffiths & Matthewson, 2018; Kendler, 2012; Stein, 2011). This is consistent with our growing understanding of the genetic architecture of common mental disorders; genetic pleiotropy means that we will not be able to map single genes, and perhaps not even sets of genes, to single psychiatric disorders (Smoller et al., 2019).

An evolutionary framework also helps highlight and understand differences between emotional disorders, cognitive disorders, and behavioral disorders. Aversive emotions are experienced by most everyone, and they can be normal and useful. Delusions and hallucinations are experienced by only a few individuals, and they are typically abnormal and harmful. The mistake of thinking that aversive emotions are useless is matched by the mistake of thinking that delusions and hallucinations are useful. Delusions and hallucinations arise, not from dysregulations of normal defenses, but from failures of information processing systems. Some cases of high-functioning autism spectrum disorders represent a middle case in which the clinical condition is not a normal adaptive response, but instead reflects the extreme tail of a continuous distribution of the tendency to systematize (Baron-Cohen, 2000). Behavioral disorders such as addiction can be understood as products of normal learning mechanisms interacting with novel environments; this contributes to understanding why they can be conceptualized not as typical disorders where the normal sick role applies, but rather as atypical disorders in the sense that individuals must in part take responsibility for their own recovery (Stein, 2011).

In summary, an evolutionary perspective discourages both the reification of diagnostic constructs and the reductionism of monocausal approaches and its associated hope that they will define crisply separate disorders and susceptible to silver bullet treatments. It encourages accepting the reality that most mental disorders are like many other medical disorders in having blurry boundaries and many interacting causes and that

they may require multimodal interventions. An appreciation of distinctions between cognitive, emotional, and behavioral disorders further discourages oversimplified conclusions about our nosology and about treatment approaches. We can use the DSM as a practical way to communicate without derogating it because the world it describes is not as simple as we would wish.

Key Points About Emotions and Their Disorders

Most mental disorders are emotional disorders, and the vast majority of psychiatric patients seek relief from bad feelings (Kessler et al., 2009). Most research has looked for proximate explanations, often in just one cause. Evolutionary explanations of normal emotions and their regulation mechanisms instead provide an integrative framework that is appropriate for understanding the complexity of emotional disorders.

Until the middle of the twentieth century, the study of emotions consisted mostly of careful observation and description of psychological and neural proximate mechanisms, with a transition from generalizations to attention to individual differences (Griffiths, 1997; Lazarus, 1993; Wierzbicka, 2010). Recognition that natural selection shaped the capacities for emotions has transformed the field (Al-Shawaf & Shackelford, 2023; Al-Shawaf et al., 2016; Haselton & Ketelaar, 2006; Nesse, 1990; Plutchik, 1970; Tooby & Cosmides, 1990). The role of emotions for avoiding threats and pursuing rewards was earlier noted, but several additional principles provide a framework for considering pathology across the full range of emotions and for addressing the evolutionary medicine question of why emotions are so vulnerable to dysregulation (Nesse, 2005b, 2019a, 2023).

The most fundamental principle is that emotions are special states of operation shaped by natural selection to give advantages in certain **situations** (Nesse, 1990, 2019a, 2023). Sharp focus on the situation is crucial. The characteristics of each emotion were shaped by the adaptive challenges in situations experienced repeatedly by a species

during its evolution. This has several implications. Different emotions correspond to different situations. They are neither completely separate basic emotions nor mere positions in a dimensional space. Determining if an emotion is useful requires analyzing if the situation is present. Negative emotions are just as useful as positive emotions. Finally, it suggests five reasons why most instances of useless or harmful emotions are products of normal emotion regulation mechanisms (Table 3).

The subjective pain and pleasure that accompanies emotions contribute to their utility. Aversiveness motivates escaping and avoiding situations that harm fitness. Positive states motivate staying in beneficial situations and recreating them. The association of negative emotions with threats and losses fosters the illusion that they are usually harmful or abnormal. But individuals who lack negative emotions have serious disorders; hypophobics fail to protect themselves from danger. Individuals who lack a capacity for normal low mood are envied, but they also should be studied to see what price they pay. Individuals who lack jealousy are likely to have fewer children than others. People who lack disgust may be vulnerable to infection. Recognizing the utility of negative emotions encourages a medical approach to emotions as symptoms that require investigation.

Five Reasons Why Aversive Emotions Are Usually Normal but Useless

Natural selection shaped the mechanisms that regulate emotions, so it seems obvious that emotions arising from normal mechanisms should be useful and emotions that are useless or harmful must arise from abnormal mechanisms. However, most experiences of aversive emotions are normal but useless. Five reasons explain why (Nesse, 2023).

The smoke detector principle explains why false alarms are normal and common (Nesse, 2006). The optimal response threshold can be quantified using signal detection theory. For instance, if a noise indicates a chance that lion is nearby, and the cost of fleeing is 100 but the cost of staying if the lion is present is 10,000, then fleeing is worth it whenever the noise indicates

more than a 1.0% chance of a lion being present. That means that in 100 encounters with such a stimulus, 99 will be normal false alarms whose costs are worth it.

The implications for panic disorder are obvious, but the smoke detector principle is relevant for all defenses. Pain, fever, inflammation, vomiting, and cough are expressed whenever the small consistent costs of expressing the defense are lower than the huge but intermittent benefits. This explains why it is usually safe to use medications to block suffering of all kinds. It also explains why physicians must be alert for situations when the defense is essential. The smoke detector principle contradicts the wrongheaded belief that we should not disrupt normal painful emotions, even as it encourages respect for the value of defenses. It has been usefully adapted as “error management theory” to explain how selective advantages can result from cognitive distortions, such as the tendency of men to assume that ambiguous cues indicate a woman’s sexual interest (Haselton & Buss, 2000).

Self-adjusting systems also give rise to much useless suffering. As noted already, repeated tissue damage can sensitize the pain system, making it vulnerable to positive feedback and chronic pain (Nesse & Schulkin, 2019). Likewise, the repeated experience of danger indicates the need to shift the anxiety system to increased sensitivity. Such self-sensitizing systems facilitate adaptation to dangerous environments, but they are inherently vulnerable to pathological positive feedback loops. Panic disorder and post-traumatic stress disorders are examples. Discussing this vicious cycle can be profoundly useful in helping patients to complete difficult therapy assignments.

The observation that episodes of depression may “kindle” future episodes has been interpreted as a product of brain damage, but it could also be a product of a system that adjusts adaptively after repeated experiences of failure. Targeting the neural mechanisms that mediate self-adjusting systems offers opportunities for drug development.

Mismatch between our evolved physiology and our current environments gives rise to much useless emotion. Mass media offer visions of other lives that make most people feel inadequate

Table 3 Key points about emotions

Emotions were shaped because they improve coping with specific situations
• Emotions are adaptive states shaped by natural selection that increased fitness in situations that recurred during the evolution of the species
• Different emotions are neither distinctly separate, nor are they mere locations on dimensions; they evolved from precursor states useful in related situations
• The characteristics of different emotions correspond to the adaptive challenges in the situations that shaped them
• Subjective experience is only one aspect of an emotion; it is sometimes absent
• Assessing the normality of an emotional expression requires assessing the situation
• The emotional impact of information often is mediated by an individual's appraisal of the implications for progress toward personal goals
Both pain and pleasure are useful
• Emotions are positive or negative because they were shaped by situations involving gains or losses
• Negative emotions are as useful as positive emotions
• Disorders of excess and deficiency exist for both positive and negative emotions
Negative emotions are often useless products of normal mechanisms
• The smoke detector principle explains the prevalence of false alarms
• Self-adjusting thresholds are vulnerable to positive feedback dysregulation
• Novel environmental cues arouse emotions excessively or unnecessarily
• Happenstance sequences of experiences can result in regulation failure
• Benefits to genes can shape a trait despite its costs to the individual
Emotions are complex and vulnerable to failure
• Emotion regulation mechanisms are subject to failure for several reasons
• Disorders across the full range of emotions deserve consideration, not just anxiety and depression
• Different cultures describe emotions differently in ways that can change the experience and effects of emotions

and deprived. Social roles in bureaucracies leave many people deeply dissatisfied but unable to leave. Modern diets and lack of exercise foster obesity and inflammation that predispose to depression as well as physical illnesses. While novel environments undoubtedly are relevant, the tendency to attribute most mental problems to the stress of modern life is a misconception that has been prevalent ever since ancient Athens. Studies of mental disorders in hunter-gatherer populations are nonetheless urgently needed before the opportunity evaporates.

Even in normal environments, happenstance sequences of threatening or nonrewarding events can shift normal systems into a maladaptive dead end that prevents additional exploration that would more accurately reflect the environment's affordances (McNamara & Trimmer, 2019; Meacham & Bergstrom, 2016). Behavior therapy is well suited to helping patients escape from such traps.

Emotions often offer **benefits to our genes at our expense**. This is why sex causes so many

emotional problems. Sexual jealousy, unrequited love, stalking, and simple lack of sexual satisfaction give rise to many clinical problems. Sexual disorders offer another illustration of a system shaped to maximize reproduction at the cost of satisfaction. Why is premature orgasm a problem mostly for men, while delayed or absent orgasm is a problem mostly for women? It is likely because women who have orgasms fast and sometimes stop intercourse before their partners ejaculate will have fewer children than other women (Nesse, 2019a). The dyssynchronous sexual response system may maximize genetic fitness, but it also leads to a much frustration and many clinical consultations.

Why Regulation Mechanisms Are Vulnerable to Failure

Attention to the functions of emotions should not decrease respect for the prevalence of disorder arising from **abnormal regulation systems**.

Abnormalities may result from genetics, early experience, psychological or physical trauma, and any number of things that influence the brain directly. They have been the subject of massive research that will not be reviewed here because it is summarized well in other chapters (Schatzberg and Manchia, chapter ▶ “[Neurobiological Foundations of Mood Disorders](#)”; Meaney and Leonardo, chapter ▶ “[The Neurobiology of Anxiety Disorders and Obsessive-Compulsive Disorder](#)”).

The evolutionary question, only now being addressed, is why emotion regulation systems are vulnerable to dysregulation. This needs investigation using proximate and evolutionary analyses complemented by cybernetics. Possibilities include all those listed in Table 2. The most important are likely to be the limited ability of natural selection to remove mutations and the stochastic nature of brain development. Recognizing that aversive emotions often arise from normal mechanisms helps to explain why specific biomarkers for emotional disorders have proved so elusive. Primary brain causes will eventually be discovered for some disorders, but pathology may sometimes arise from conflicts in information processing systems in physiologically normal brains. Looking for specific brain causes of such conditions may be like examining a circuit board to try to explain why a computer crashes.

While all emotions are vulnerable to excess or deficiency, anxiety and depression get all the attention. An evolutionary view encourages attention to **excesses and deficiencies of all emotions** including jealousy, envy, pride, guilt, infatuation, boredom, disgust, and positive emotions such as enthusiasm, infatuation, and awe. Anxiety has already been covered, and disgust and jealousy will be briefly addressed, but first a brief summary of evolutionary approaches to depression is justified by the extensive work on the topic by evolutionary psychiatrists.

Depression causes more disability than any other mental disorder, and it is often profoundly maladaptive, even aside from the risk of suicide. Consequently, it has been the focus of extensive attempts to understand it in evolutionary terms (Andrews & Thomson, 2009; Beck & Bredemeier,

2016; Crespi, 2009; Gilbert, 1992, 2006; Hagen, 2011; Miller & Raison, 2016; Nesse, 1999, 2000, 2009; Nettle, 2004; Nettle, 2011; Price et al., 1994; Raison & Miller, 2013; Rottenberg, 2014; Sloman, 2008; Wolpert, 2008). Because “depression” now usually connotes an abnormal state, using that term in attempts to understand its function generates confusion. This can be reduced by using the term “low mood” to refer to states of depression that may or may not be adaptive.

Evolutionary explanations for depression are often framed in terms of specific adaptive functions. For instance, it has been proposed that depression can solicit aid, signal submissiveness, conserve resources, motivate problem-solving, and encourage behaviors that other group members value. All of these functions are relevant, but framing the explanation as a single function arouses confusion and controversy because low mood/depression has many functions.

A different approach instead describes the situations in which low mood has been useful over the course of evolution. At the most general, in unpropitious situations, effort and risk-taking are likely to result in costs greater than benefits (Nesse, 2000). However, many authors emphasize the utility of low mood in more specific social situations. The best developed thesis notes how “involuntary yielding” after a status loss can prevent attacks (Sloman & Price, 1987). Closely related are suggestions that low mood is useful when cues indicate possible exclusion from a group or when time and effort need to be conserved to deal with a major life problem (Andrews & Thomson, 2009; Kennair et al., 2017). Failing efforts to make progress toward a goal are a common denominator. This more general framing encourages links to basic behavioral ecology, the possibility that subtypes of low mood have evolved to deal with different situations (Keller & Nesse, 2006; Rantala et al., 2018), and the possibility that the high costs of disengage from a failing effort in modern environments can motivate persistence in useless efforts that escalate ordinary low mood into clinical depression (Heckhausen & Schultz, 1995; Wrosch & Heckhausen, 2002).

Some empirical research has examined these hypotheses. For instance, reanalysis of data from the Islington studies supported the predication that life events involving loss, humiliation, and entrapment are especially potent precipitants of depression (Bifulco et al., 1998; Brown et al., 1995). A series of studies has shown that people who can give up goals are less prone to depression (G. E. Miller & Wrosch, 2007; Wrosch et al., 2003; Wrosch & Miller, 2009). However, large-scale studies to determine the exact association of certain life situations with the onset, persistence, and offset of depression have yet to be done. Sophisticated studies of life events offer important guidance (Hammen, 2005; Kessler, 1997; Muscatell et al., 2009), but many of them collapse multiple depression symptoms into a sum score (Fried et al., 2014) and collapse diverse life situations into a global measure of “stress,” thus discarding the idiographic information that would allow tests of specific evolutionary hypotheses. An evolutionary framework encourages additional research into how changes in idiographic life situations influence specific depression symptoms and courses of illness. Studies of grief from an evolutionary perspective may be particularly informative (Archer, 2003; Nesse, 2005a).

Infection is another situation in which low mood can be useful by conserving energy to fight the pathogen (Doyle et al., 2019; Hart, 1988; Shattuck & Muehlenbein, 2015). The association of inflammatory cytokines with depression and the ability of interferon to precipitate depression in some subjects support this thesis (Miller & Raison, 2016) and suggest considering treatment with anti-inflammatory drugs. It also suggests looking for phylogenetic precursors of low mood in systems that mediate pain and inflammation. If they have shared evolutionary origins, that would explain many otherwise confusing associations.

Bipolar disorder calls attention to the need for a cybernetic analysis of mood regulation. Increasing the gain in a control system can result in it getting stuck at both extremes. But what does gain mean in the mood regulation system? The high heritability of bipolar disorder suggests it is a good candidate for finding specific brain abnormalities, but like other disorders, many alleles

with tiny effects seem to be responsible. Mood responsiveness in humans ranges widely from minimal in alexithymia to moderate in cyclothymia to more extreme in bipolar type 2 disorder, bipolar disorder, and borderline personality disorder (Akiskal, 1996; Akiskal & Akiskal, 2005; Wilson & Price, 2006). It seems likely that fitness has been similar across a wide range of mood responsiveness and that the regulation systems are inherently vulnerable to malfunction.

Disgust has been described as a neglected emotion. It is notable that there are continuities between gustatory avoidance mechanisms across species; in this sense, disgust is a negative emotion that, like anxiety, helps avoid harm (Rozin et al., 2008). It is only in humans, however, that disgust becomes integrated during the process of development with abstract concepts, so that we regard particular sorts of food, sexual relations, and other behaviors as “unclean.” Anthropology has taught us that this distinction between the clean and the unclean is a universal (Douglas, 1966). The arousal of the same brain areas by exposure to physical disgusting cues and morally disgusting information suggests the possibility that moral passions may have evolved from physical ones (Hutcherson et al., 2015).

Understanding how evolution has shaped disgust may be relevant to understanding a number of mental disorders. It is noteworthy that simple phobias are often accompanied not only by anxiety but also by disgust. In obsessive-compulsive disorder, there seem to be disruptions in perception of disgust, with concordant alterations on neuroimaging (Stein et al., 2001). An evolutionary perspective emphasizes the potential value of placing more focus on disgust, encouraging future work on disgust assessment and perhaps even on how exposure and response prevention techniques could be shaped to consider not only anxiety but also disgust.

Jealousy is a common cause of relationship problems, violence, and delusions. Work by David Buss and others has shown that sexual jealousy is particularly common in males worldwide, but jealousy about allocating resources outside a relationship is more common for women (Buss et al., 1999). Their analysis shows why men who

lack jealousy are likely to have fewer children than other men. The phylogeny of the responsible mechanisms is illustrated by alterations of oxytocin molecular mechanisms in montane and prairie voles that account for pair bonding (Insel and Young, 2001). The fact that jealousy is a cross-species and cross-cultural universal for species with certain mating patterns does not mean that the system is rigid. Human cultures and individuals show a large variation in jealous thoughts and associated distress and conflicts.

While monocausal explanations of pathological jealousy have been put forward by various “schools,” evolutionary biology provides a framework that can integrate multiple relevant explanations and “difference makers” that reflect where an individual falls on the spectrum between “normal” and delusional jealousy (Harris, 2003). This framework provides insights into different aspects of the phenomena (e.g., sex differences), and it suggests ways forward for both clinicians and researchers. In clinical practice, most jealousy should be normalized, and it may be helpful to explain obsessional jealousy in terms of normal mechanisms that can feedback in a vicious cycle. In research, it encourages a focus on shaping exposure and response techniques to be particularly responsive to putative mechanisms involved.

Deficiencies of aversive emotions are rarely recognized as problems although they can be severe. The lack of guilt in sociopathy is an exception. Deficient anxiety, hypophobia, is a disorder many would like to have, but it can be fatal. Lack of low mood can result in happily pursuing useless quests for a lifetime. Lack of disgust, envy, and jealousy are also pathological, even if they do not motivate requests for treatment.

The value of positive emotions has gotten welcome new attention in recent decades (Fredrickson, 2004) along with evidence that strategies for bolstering such emotions may be useful (Seligman & Csikszentmihalyi, 2014). **Deficits of positive emotion** are an underrecognized problem, even in the absence of negative emotions. As for problems arising from mild unjustified positive emotions, they have attracted modest attention because happy people don’t complain (Gruber, 2011). Hyperthymia and hypomania are recognized as clinically

significant, but simpler mild chronic excesses of positive affect are usually treated as good fortune, instead of as opportunities for investigation. Much remains to be done to understand the origins and significance of these phenomena in light of their adaptive significance.

In summary, an evolutionary framework supports a medical approach that recognizes negative emotions as defenses that increase fitness in relevant situations, but that are often aroused unnecessarily by normal regulation mechanisms. This perspective encourages clinicians to look carefully both for life situations that may be arousing emotions and also for reasons why a patient’s aversive emotional state may be useless or abnormal. It contradicts the notion that useless and harmful emotions always arise from brain abnormalities, but it also recognizes reasons why regulation mechanisms are vulnerable to malfunction. Finally, this integrative framework encourages extending the analysis of emotional disorder to the full range of emotions and to disorders of deficient negative emotions and excessive positive ones.

Assessing Individual Lives

The foundation of social psychology is in Kurt Lewin’s famous formula $B = f(P, S)$; behavior is a function of the person (P) in the situation (S) (Lewin, 1951). The tendency in psychiatric research has been to focus on person factors like genetics, early abuse, and personality characteristics. Hundreds of studies of factors that influence a person’s vulnerability to depression now enable a detailed summary of person factors that influence risk (Maj et al., 2020). It has turned out to be much harder to describe situations. Clinicians tend to incorporate all available information into a narrative that culminates in the current situation, but research studies, in a quest for reliable measures, instead use checklists of life events or measures of stress (Cohen et al., 1997). However, an evolutionary understanding of emotions shows that idiosyncratic aspects of an individual’s life situation are often crucial factors in symptom onset or offset.

An evolutionary approach comes down strongly on the side of the need to understand

the life situations of individuals as individuals, linking diathesis to situations. Admittedly, the situations that cause symptoms are often difficult or impossible to change. Knowing that bad feelings arise from an abusive relationship, children in trouble, or a difficult decision about whether to stay in a relationship or job can help to solve a problem. More often, the details reveal the good reasons why a problem persists. Understanding those reasons provides the foundation for a productive therapeutic relationship. And knowing that an emotion is useless despite being normal can reframe a problem in ways that encourage difficult decisions or setting aside unsolvable problems.

Behavioral ecologists analyze how animals make decisions that allocate effort to maximize three main kinds of resources: physical (material and personal), social (allies and status), and reproductive (mates and offspring). Such decisions involve inherent tradeoffs, and they tend to maximize inclusive fitness, not individual health or longevity. Expanded to accommodate the social resources so crucial for humans, these categories suggest a systematic framework. In general medicine, physicians conduct a Review of Systems to look for possible causes of symptoms. In psychiatry, a Review of Social Systems (ROSS) organizes the search for causes of mental symptoms. The acronym S.O.C.I.A.L. offers a useful mnemonic for the resources that need to be considered (Nesse, 2019a). A full assessment covers, for each resource, what a person has, what he or she wants and is trying to do, expectations for how things are working out, and threats, obstacles, and pending decisions. This provides a nomothetic biological framework for organizing information about idiographic social situations likely to be arousing symptoms.

The Review of S.O.C.I.A.L. Systems

Social resources: friends, status
 Occupation and other valued social roles
 Children and family
 Income and material resources

Abilities, appearance, health, and other personal resources

Love and sex

For each resource ask:

- Is the person satisfied with the availability of this resource?
- If not, is the problem scarcity, threats, conflicting goals, or high aspirations?
- What is the person trying to do, get, or change, and how?
- What is the person trying to escape, avoid, or prevent, and how?
- What decisions is the person considering about strategies and priorities?
- What future does the person expect in this area?

Relationship Benefits and Vicissitudes

Most psychiatric episodes are precipitated by relationship conflicts, and disorders that arise from other sources tend to cause relationship problems. Huge therapeutic efforts go into helping people maintain and repair relationships. While the reality of conflict is acknowledged, its evolutionary origins and functions often go unrecognized. Major advances made in the final third of the twentieth century are available to assist.

Before the 1960s, it was generally accepted that natural selection shaped traits for the good of the group or the species. In 1966, however, George Williams pointed out that the genes of individuals who sacrificed their fitness for the group would become less frequent with each generation, even if the group benefited (Williams, 1966). At about the same time, William Hamilton showed how kin selection could explain tendencies to make sacrifices for children and other kin (Crespi et al., 2014; Hamilton, 1964). Richard Dawkins used the metaphor of the selfish gene to communicate the new perspective (Dawkins, 1976), Robert Trivers described how the benefits

of trading favors could shape capacities for cooperation (Trivers, 1971), and Robert Axelrod provided a comprehensive study of such exchanges (Axelrod, 1997). Evolutionary science has extended and elaborated these principles into what is now a comprehensive framework for understanding cooperation and relationships that is ready for application in psychiatry (Apicella & Silk, 2019; Hammerstein, 2003).

This framework incorporates kin and non-kin relationships, but the major sacrifices people make for their friends and groups have provoked continuing controversy, perhaps because multiple factors have shaped capacities for such altruistic behavior. Groups with more cooperators do better than other groups, although this can explain the evolution of moral capacities only if the costs for individuals are exceedingly low compared to the benefits for the group. Mothers who provide alloparenting may get benefits out of proportion to their investments, creating selection for special kinds of cooperation (Hrdy, 2009). Groups that find ways to impose punishments on non-cooperators create powerful forces of cultural group selection that foster prosocial behavior, especially if there is a way to punish those who fail to punish non-cooperators (Richerson et al., 2015). Of particular importance for psychiatry are the advantages that come to individuals preferred as social partners. These advantages shape, via social selection, tendencies to be the kind of person that others prefer as a partner and enormous fears of exclusion (Nesse, 2007). Competition to display extreme altruism can result, a tendency that can be pathological (Hardy & Van Vugt, 2006). Guilt motivates reparations and repair of otherwise damaged relationships but also makes people vulnerable to manipulation, causing exploitative relationships that often generate severe symptoms.

An evolutionary perspective on social collaboration and conflict helps explain themes that often emerge during psychotherapy. People's expectations of others often cause problems. Believing that others are untrustworthy makes close relationships difficult and therapy challenging. Expectations that others will provide care without reciprocation also lead to constant

disappointment. Marriages or work relationships that are exploitative but hard to escape create social traps that generate extreme emotions and behavioral strategies including threatening suicide.

Theories focused on proximal mechanisms, such as schema theory, complement an evolutionary perspective by explaining how early family dynamics influence subsequent relationships and for targeting particular patterns during therapy (Riso et al., 2007). Thus, for example, schema theory has emphasized that early trauma may lead to a mistrust schema, in which the world is seen as threatening. In conceptualizing the psychotherapy of a person with such a schema, mistrust of the therapist is expected (the schema will be cued in many relationships), and good psychotherapy can provide some degree of reparative experience (psychotherapy is itself an important relationship).

An evolutionary perspective on relationships also has implications for how we conceptualize psychotherapy. The enduring challenge of negotiating the right therapeutic distance, for example, reflects the inherent difficulties posed by instrumental (exchange) relationships whose effectiveness requires empathy and intimate revelations that are more characteristic of a communal (committed) relationship. However, applying what biologists have learned about relationships to psychiatric problems and treatment is a project just getting started. Importantly, analysis of the fitness benefits and costs of relationships should never lose sight of the miracle of enduring human love and friendship. The mechanisms that make them possible were shaped by social selection and the other cultural and selection forces described above. We should be thankful for them, even as we continue to investigate their origins and the conflicts and symptoms they create.

Explaining the Persistence of Genes That Cause Disorders

Vulnerability to schizophrenia and autism depends overwhelmingly on a person's genes, but these disorders decrease fitness by about 50% (Power et al., 2013). This poses an obvious

evolutionary question. Why do the responsible genetic variations persist in the face of strong natural selection (Crespi, 2010; Keller, 2018; Keller & Miller, 2006; van Dongen & Boomsma, 2013)?

Before addressing this question, it is relevant to note that the focus of neurogenetics has been on proximate studies of genes associated with mental disorders. The initial hope was that specific gene variants would be found to account for specific psychiatric disorders. However, the effects of nearly all candidate genes have turned out to be false positives. Instead, most variation in risk arises from thousands of common variants that each have only tiny effects (Ohlsson & Kendler, 2020; Smoller et al., 2019). Across a wide range, the more common a genetic variation is the less influence it has on a disease. Remarkably, most variants, from rare to common, explain the same tiny proportion of variance: 0.04% (Gratten et al., 2014). Why is the proportion the same across the range of prevalence? Why aren't there common variations with larger effects? The main answer is that natural selection has eliminated variations that reduce fitness (Keller & Miller, 2006; Uricchio, 2019). But was fitness reduction from schizophrenia the only selection force?

All available genetic variations, statistically significant or not, can be incorporated into a polygenic score that predict an individual's vulnerability to a disease (Crouch & Bodmer, 2020). Individuals with polygenic scores in highest risk decile for most disorders have odds ratios several times those of individuals in the lowest deciles, but the differences are too small to be useful diagnostically, and they explain only a small percent of the total variation (Hyman, 2018; Martin et al., 2019). Furthermore, it turns out that polygenic risk scores for different mental disorders have significant overlap, further diminishing their diagnostic value (Bornovalova et al., 2020; Caspi et al., 2014). Finally, the relevant alleles differ drastically in different populations; algorithms for polygenic scores that predict schizophrenia risk in Europeans are nearly useless for African populations. In fact, the effects of ancestry are ten times larger than the differences

between patients with schizophrenia and controls (Curtis, 2018).

A consideration of all possible evolutionary explanations for the persistence of genes that create vulnerability for mental illness suggests a range of possibilities (Crespi, 2009; Keller, 2018; Uricchio, 2019; van Dongen & Boomsma, 2013). A first explanation is that mutations keep creating them as fast as natural selection can eliminate them; that is **mutation-selection balance**. This is consistent with data that with increasing paternal age, there are increased de novo mutations in offspring, as well as increased risk for schizophrenia, although it now appears that most of this effect arises from the later marriage age of men who later father children with schizophrenia (Gratten et al., 2016).

A second explanation comes from **interactions of previously neutral alleles with novel environments**. Neutral variations that vary stochastically across populations and generations can become pathogenic in novel environments. For instance, half of variation in addiction vulnerability (Li & Burmeister, 2009) is attributed to genetic variations, but those variations are harmless in the absence of reliable access to drugs and alcohol. Some argue that preferences for certain chemicals were shaped by ancestral benefits, such as the anti-helminthic actions of nicotine (Hagen et al., 2013), but this seems unlikely given that reward seeking is universal and these variants show tiny effects and massive pleiotropy (Peng et al., 2021). Such variants are **genetic quirks** rather than defects, with the possible exception of polymorphisms that disrupt aldehyde dehydrogenase and alcohol dehydrogenase and significantly lower risk of alcohol use disorders (Edenberg, 2007). These loci bear genetic signals of selection, but harm from alcohol use may be unimportant compared to other effects in diverse tissues (Polimanti & Gelernter, 2018).

Sharing knowledge about the role of genetics may help to reduce the stigma of addiction and alcoholism in some contexts, and sharing knowledge that the responsible genes are not defective mutations helps to reduce the stigma of genetic disease. It also encourages asking new research questions. How did patients with high genetic risk

for addiction behave in ancestral environments? Were their patterns of relationships different from those without genetic vulnerability to addiction? Did they use different foraging strategies from others? Do people with high and low polygenic risk scores for addiction forage differently when picking berries? Could computer games based on such methods provide a behavioral assay for addiction risk?

A third possibility is **balancing selection** that maintains genetic variations that cause disease in the gene pool because they offer benefits in other genetic or external environments. As noted earlier, the case of sickle cell anemia is often cited as a model; the allele for sickle hemoglobin persists because individuals who have it along with a normal allele are resistant to malaria. Such heterozygote advantage is appealing but unlikely to explain mental disorders (Keller, 2018; Keller & Miller, 2006; Nestic et al., 2019; Uricchio, 2019). The ability of natural selection to find better solutions with fewer costs may help to explain the paucity of examples other than those related to malaria (Asthana et al., 2005). While it has been suggested that alleles that predispose to schizophrenia and bipolar disorder also increase creativity or intelligence (Greenwood, 2016), genetic data do not offer strong support (Nestic et al., 2019). Instead, there is evidence for background negative selection on mutation-intolerant loci (Pardiñas et al., 2018).

A fourth kind of explanation is based on **tradeoffs**, with diametric diseases at opposite ends of a spectrum (Crespi & Badcock, 2008; Crespi & Dinsdale, 2019). This has been proposed to be especially relevant to autism as an extreme systematizing male brain and schizophrenia as an extreme empathizing female brain (Greenberg et al., 2018), with imprinted genes perhaps influencing brain development (Byars et al., 2014; Crespi, 2018; Skuse, 2000). For complex reasons, this hypothesis predicts higher birthweights of children who go on to become autistic vs. those who become schizophrenic; an analysis using the five million subjects in a Danish database supports the prediction (Byars et al., 2014). The concept of diametric diseases has far

broader implications for medical genetics (Crespi & Go, 2015).

Cliff-edged fitness functions offer a somewhat different possibility. Some traits give ever-increasing benefits up to a peak near a cliff edge where catastrophic failure becomes more likely (Nesse, 2004a, 2019a). For instance, breeding horses for speed increases leg length to an extreme that makes broken bones likely. Traits such as intelligence and social ability that have been under recent strong selection in humans may also be associated with vulnerabilities (Crow, 1997; Dunbar, 1993). Because all members of a species have values close to the cliff edge, all share vulnerability. Offspring of individuals at the peak will be especially vulnerable, but they may not show extraordinary abilities, perhaps explaining the mixed findings in studies of beneficial traits associated with highly heritable diseases. Genetic variations that slightly change the trait's position on the fitness function can be effectively neutral, increasing or decreasing fitness depending on differences in the genetic, developmental, or external environment. Asymmetric fitness functions seem likely to create genetic architectures like those that characterize many disorders, with thousands of variations very slightly increasing the risk of dire disorders that are manifest in about 1% of a population, but the possibility is just now being considered.

This short overview of evolutionary psychiatric genetics merely sketches the landscape and outlines areas for further research. In the meanwhile, evolutionary thinking can help to minimize misconceptions. One particularly important misconception is the tendency to assume that heritable mental disorders are genetic disorders caused by abnormal genes specific to the disorder. This "genes for" error is especially common in reports about genetic studies of common mental disorders. Conditions like eating disorders and major depression are moderately heritable, but there is little reason to think that the responsible genes are defective and even less reason to think that they are specific to the disorder. Instead, myriad genetic variations influence thousands of traits including motivations, cognitive tendencies, food preferences, risk-taking, social strategies,

sleep, inflammation, personality, and tendencies to use drugs. Variations in these traits in turn influence life situations and the risk of experiencing a disorder. It is worthwhile to continue searching for rare genes with big effects that may offer clues to pathogenic mechanisms, but most mental disorders are not “genetic disorders.”

Practical Implications

Evolutionary psychiatry brings the basic science of evolutionary biology to bear on problems in psychiatry. It is not a school or method of treatment, but its applications will, like those from genetics and neuroscience, emerge over decades. However, evolutionary biology has much to offer even now.

Applications of Evolutionary Biology in Psychiatry

1. Integrative framework for the biopsychosocial model
2. Nosological controversies
3. Clinical assessment
4. Treatment planning
5. Pharmacology
6. Psychotherapy
7. Public health
8. Psychiatry's place in medicine

The greatest contribution of evolutionary biology is the framework it provides for integrating otherwise disparate aspects of psychiatry. This framework for a biopsychosocial model connects knowledge about how mechanisms work with knowledge about why they are the way they are, and why natural selection has left some vulnerable to failure. It accepts the reality of organic complexity and the need to incorporate bottom-up, top-down, and recursive tangles of causation to understand and treat mental disorders. It explicitly values and incorporates both nomothetic and idiographic knowledge.

This conceptual framework can help to reframe controversies about the definition and classification

of mental disorders. The DSM-5 has received a great deal of criticism, particularly from neuroscience. But as many have pointed out, the problem results mainly from disappointment that neuroscience has not found specific causes that map to DSM categories. By emphasizing that biological traits often have fuzzy borders and are underpinned by multiple mechanisms, evolutionary biology helps us appreciate the value of DSM diagnoses even though their categories are nothing like different plant species or chemical elements.

Evolutionary biology also provides a useful framework for assessing patients. A Review of Social Systems, like a medical Review of Systems, is crucial for finding causes and distinguishing symptoms from diseases. This supports the efforts of clinicians to fully understand each individual as an individual in order to identify the origins of symptoms and whether they represent an adaptive defense (e.g., most anxiety), a defense that has gone awry (e.g., panic disorder), or a clear dysfunction (e.g., anxiety due to a brain tumor or delusions from schizophrenia). Evolutionary biology uses reproductive success to distinguish successful from unsuccessful traits, but distinctions along the spectrum between defenses, defense dysregulation, and dysfunction entail a range of other more subtle considerations.

An evolutionary framework assists treatment planning. For instance, observers from Freud to Skinner to Kendler have long noted that psychiatric symptoms often emerge when strong drives and intense reward pursuit encounter big risks and uncertainties. An evolutionary perspective helps to explain why, and it provides a behavioral ecological framework for analyzing and trying to resolve such situations. It contributes to understanding why mental disorders so frequently begin during adolescence. It explains why such situations generate high levels of distress, why reducing levels of anxiety is usually safe, and why clinical judgement about such matters needs careful adjudication of the personal and social costs of any particular intervention.

Evolutionary psychiatry offers a useful perspective on psychopharmacology. Instead of replacing deficient neurochemicals, most treatments disrupt normal systems that contribute to

symptoms. Animal models that focus on “chemical lesions” may be usefully supplemented by ecologically valid investigation of emotion regulation systems and their disruption by psychotropic agents. An evolutionary approach suggests looking for positive feedback loops that create and sustain disorders and investigating neurochemical mechanisms that alter response thresholds when defensive responses are repeatedly aroused (Nesse & Stein, 2019).

Evolutionary considerations also offer an important perspective on psychotherapy (Abrams, 2020; Gilbert, 1995; Gilbert & Bailey, 2000; McGuire & Troisi, 2006). Some consider psychotherapy as a technique that targets specific dysfunctional cognitions, just as a medication targets particular neurocircuitry, but both models are reductionistic. What happens in psychotherapy can be understood as the product of two primates engaged in a special kind of relationship. This has several implications. First, it’s an unusual relationship and so there must be specific kinds of boundaries, with the distance “just right.” Second, it has aspects in common with other kinds of relationships, e.g., parenting and alliance-building, which can then be used to think how interventions are experienced and why they might be powerful. Third, there is a lot going on; our standard theories likely capture only a small part of this.

Public health implications are substantial. There has been substantial debate in global mental health about the implications of the mental health paradox, with depression rates significantly higher in better-resourced countries than in lower ones. A simplistic focus on reducing the treatment gap should be replaced by a more nuanced perspective which emphasizes the spectrum from severe illness to wellness, the normality of aversive responses to distress, and the importance of addressing social determinants of illness (Patel et al., 2018; Stein et al., 2013). An evolutionary perspective may help bolster the claim that rather than educating the public about PTSD, we should focus mental health literacy efforts on the importance of resilience (Stein et al., 2007), and it may buttress the search for nudges, such as using taxes to reduce addictions, that might help to reduce mental disorders (Stein et al., 2018).

Finally, evolutionary psychiatry helps to demonstrate that psychiatry is, like all other medical specialties, based on biology. The rest of medicine already uses knowledge about evolved adaptive functions as the basic for understanding pathophysiology, and it is rapidly adopting an evolutionary framework for understanding vulnerability to disease. Taking the same biological approaches demonstrates that psychiatry, like the rest of medicine, offers a biopsychosocial approach, one that may help to reduce useless competition between “schools” of psychiatry that are characterized by simplistic or reductionist approaches that run the risk of being either brainless or mindless (Lipowsky, 1989).

This chapter is a necessarily brief overview. It does not attempt to cover important evolutionary perspectives on eating disorders, obsessive-compulsive disorder, personality disorders, ADHD, and bipolar disorder. It gives short shrift to many applications and specialized ideas about the disorders discussed. Also left out are interesting evolutionary perspectives on psychodynamics, learning theory, complex adaptive systems, cybernetics, epigenetics, the microbiome, immunology, niche construction, sex differences, cultural differences, and religion. Book length treatments and many more articles and chapters are available on those topics for those interested.

While many clinicians are enthusiastic about the future of evolutionary psychiatry, one also needs to be realistic about its prospects. While it offers an integrative framework for the field, clinicians focused on practical issues may be disappointed that it does not offer dramatically new treatments. But this is not a bad thing; in psychiatry, the tail has too often wagged the dog; the introduction of particular psychotherapy methods or pharmacotherapy agents has led to grand theories, which have come and gone. A framework grounded in basic evolutionary biology may prove more sustainable. However, much work is needed for clinicians and researchers to become familiar with methods for testing evolutionary hypotheses, many adapted from comparative primatology or anthropology (Lewis et al., 2017; Nesse, 2011). It is hoped that with new medical

curricula focused on evolutionary medicine, such methods will become more familiar.

Conclusion

Evolutionary psychiatry remains, as noted above, in its infancy. Developing its promise will require education of a new generation of physicians and researchers who are familiar with its constructs and methods, and funding to test specific hypotheses. Such work will need to go hand in hand with complementary work on the proximal mechanisms and social determinants that contribute to mental illness. It would be a serious mistake to promise too much too soon or to make unfounded claims for quick development of new cures. But the rapid progress evolutionary thinking has brought to behavioral ecology suggests that it can offer the same to psychiatry and the evolutionary foundations for understanding function in general medicine should offer comparable benefits in psychiatry. At the very least, evolutionary biology answers the call for new directions in psychiatry (Abed & St. John Smith, 2022; Nesse, 2019a, 2023).

An evolutionary view of humans is sometimes viewed as bleak. We are creatures shaped by natural selection to do what is good for our genes, even when that is bad for us and our loved ones. Conflict is inevitable, and responses that entail suffering have been naturally selected. However, natural selection also shaped us to be capable of caring and reason. Our ability to grasp and use knowledge about our evolutionary origins gives us a deeper understanding of the human plight and our patient's problems. That understanding is useful even now. In the long run, it will give us new powers to understand, prevent, and treat mental disorders.

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