Evolutionary psychiatry: foundations, progress and challenges

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Evolutionary biology provides a crucial foundation for medicine and behavioral science that has been missing from psychiatry. Its absence helps to explain slow progress; its advent promises major advances. Instead of offering a new kind of treatment, evolutionary psychiatry provides a scientific foundation useful for all kinds of treatment. It expands the search for causes from mechanistic explanations for disease in some individuals to evolutionary explanations for traits that make all members of a species vulnerable to disease. For instance, capacities for symptoms such as pain, cough, anxiety and low mood are universal because they are useful in certain situations. Failing to recognize the utility of anxiety and low mood is at the root of many problems in psychiatry. Determining if an emotion is normal and if it is useful requires understanding an individual’s life situation. Conducting a review of social systems, parallel to the review of systems in the rest of medicine, can help achieve that understanding. Coping with substance abuse is advanced by acknowledging how substances available in modern environments hijack chemically mediated learning mechanisms. Understanding why eating spirals out of control in modern environments is aided by recognizing the motivations for caloric restriction and how it arouses famine protection mechanisms that induce binge eating. Finally, explaining the persistence of alleles that cause serious mental disorders requires evolutionary explanations of why some systems are intrinsically vulnerable to failure. The thrill of finding functions for apparent diseases is evolutionary psychiatry’s greatest strength and weakness. Recognizing bad feelings as evolved adaptations corrects psychiatry’s pervasive mistake of viewing all symptoms as if they were disease manifestations. However, viewing diseases such as panic disorder, melancholia and schizophrenia as if they are adaptations is an equally serious mistake in evolutionary psychiatry. Progress will come from framing and testing specific hypotheses about why natural selection left us vulnerable to mental disorders. The efforts of many people over many years will be needed before we will know if evolutionary biology can provide a new paradigm for understanding and treating mental disorders.

Key words: Evolutionary psychiatry, natural selection, vulnerability to diseases, evolutionary medicine, depression, anxiety, substance use disorders, eating disorders, schizophrenia

Evolutionary biology provides a crucial foundation for medicine and behavioral science that has been missing from psychiatry. Its absence helps to explain slow progress; its advent promises major advances. Instead of offering a new kind of treatment, evolutionary psychiatry provides a scientific foundation useful for all kinds of treatment. It expands the search for causes from mechanistic explanations for disease in some individuals to evolutionary explanations for traits that make all members of a species vulnerable to disease. For instance, capacities for symptoms such as pain, cough, anxiety and low mood are universal because they are useful in certain situations. Failing to recognize the utility of anxiety and low mood is at the root of many problems in psychiatry. Determining if an emotion is normal and if it is useful requires understanding an individual’s life situation. Conducting a review of social systems, parallel to the review of systems in the rest of medicine, can help achieve that understanding. Coping with substance abuse is advanced by acknowledging how substances available in modern environments hijack chemically mediated learning mechanisms. Understanding why eating spirals out of control in modern environments is aided by recognizing the motivations for caloric restriction and how it arouses famine protection mechanisms that induce binge eating. Finally, explaining the persistence of alleles that cause serious mental disorders requires evolutionary explanations of why some systems are intrinsically vulnerable to failure. The thrill of finding functions for apparent diseases is evolutionary psychiatry’s greatest strength and weakness. Recognizing bad feelings as evolved adaptations corrects psychiatry’s pervasive mistake of viewing all symptoms as if they were disease manifestations. However, viewing diseases such as panic disorder, melancholia and schizophrenia as if they are adaptations is an equally serious mistake in evolutionary psychiatry. Progress will come from framing and testing specific hypotheses about why natural selection left us vulnerable to mental disorders. The efforts of many people over many years will be needed before we will know if evolutionary biology can provide a new paradigm for understanding and treating mental disorders.

Calls for new directions in psychiatry have echoed for decades, but only now is recognition growing that the field has been hobbled by using only one half of biology. Almost all effort has gone into research on mechanisms, while the rest of medicine and behavioral science have long also investigated the evolutionary origins and functions of those mechanisms. Evolutionary medicine goes further to ask why natural selection left some traits vulnerable to malfunction. Evolutionary psychiatry answers that question for mental disorders.

Research on animal behavior was transformed when it adopted an evolutionary foundation in the final decades of the 20th century. Recognition that brains are shaped by natural selection to maximize gene transmission expanded ethology from a descriptive science to one grounded in theory that predicts behavior. For instance, the assumption that birds lay as many eggs as possible was replaced when theoretically inspired studies showed that birds adjust egg laying in ways that maximize the number of surviving fledglings in the current environment. Animal behavior textbooks are now all grounded on evolutionary biology.

Medicine has long relied on knowledge about adaptive functions as well as mechanisms. Knowing the functions of the pancreas, the mitral valve, and the cough reflex is crucial for understanding their malfunctions. Internal medicine textbooks describe pathology in the context of normal physiological functions. Psychiatry textbooks, instead, describe pathology with little reference to normal functions.

Explaining traits that leave a species vulnerable to a disease poses special challenges, because most evolutionary explanations describe how traits give advantages. Webbed feet make ducks paddle faster. Sweating stabilizes body temperature. Cough clears foreign matter from the airways. So, it seems natural to try to explain mental disorders by proposing ways they could offer advantages. That approach is essential for negative emotions, to correct the pervasive error of viewing adaptations as if they were diseases. However, viewing true diseases as if they were adaptations is an even more serious error that is common in evolutionary psychiatry. It is tempting to try to explain schizophrenia, anorexia nervosa or autism by proposing ways that they might offer advantages, but such hypotheses are almost always wrong. Diseases are not adaptations shaped by natural selection. They are not universal traits. They harm fitness. Trying to explain diseases as if they were somehow useful gives rise to a conceptual fog, which will be dispelled, not by global debates about adaptationism, but by systematically considering specific hypotheses in the light of rigorous evolutionary theory.

Evolutionary medicine does not explain diseases; it explains traits that make bodies vulnerable to disease. Examples include the narrow birth canal, the windpipe opening into the pharynx, and the tendency for immune responses to attack the body’s own tissues. The usual explanation for disease vulnerability has been that natural selection cannot prevent all mutations. That is an important explanation, but several others are equally important. Natural selection is too slow to keep up with rapid environmental change or fast-evolving pathogens. It can’t start fresh to correct a suboptimal design. It increases the performance of traits at the cost of reduced robustness. It maximizes gene transmission, at the expense of health and happiness. And it shapes useful defenses such as pain and anxiety that feel awful and are prone to excessive expression. Evolutionary medicine frames and tests hypotheses based on these explanations.
Evolutionary psychiatry is the subfield of evolutionary medicine that addresses mental disorders\textsuperscript{1,2}. The term invites misunderstandings, because it sounds like a new treatment method, perhaps one that is alternative or somehow radical. But evolutionary psychiatry is simply the field that uses the principles of evolutionary biology to better understand, prevent and treat mental disorders. It brings in a missing basic science, that joins genetics, physiology, learning theory, cognitive science, neuroscience and psychodynamics, to better understand and treat mental disorders.

Evolutionary biology is, however, different from the other basic sciences. The others describe mechanisms, each one emphasizing a subset of causes and associated treatments. Learning theory looks to conditioning for causes and to behavior therapy for treatment. Cognitive science attributes problems to distorted thinking and encourages cognitive therapy. Psychodynamic theory looks for the effects of early life events and unconscious processes and recommends psychotherapy. Neuroscience attributes disorders to brain abnormalities and advocates medication treatment. Evolutionary psychiatry does not emphasize one kind of explanation for why some individuals get sick, nor does it advocate for one kind of treatment or some new kind of treatment. It instead provides a framework that can integrate knowledge from other basic sciences. It asks new questions whose answers provide new kinds of explanations for mental disorders. Instead of asking why some individuals get a disorder, it asks why natural selection left all humans vulnerable to the disorder.

This paper has two aims. The first is to provide an overview of evolutionary psychiatry encouraging interest and work in the area. The second is to provide readers with tools to assess evolutionary hypotheses. To that end, discussion of specific disorders is preceded by four brief sections on basic principles. The first summarizes some evolutionary principles and their appropriate and inappropriate applications to mental disorders. The second outlines how evolutionary medicine frames and tests hypotheses. The third provides a brief history of evolutionary applications in psychiatry. Finally, an overview of normal emotion functions sets the stage for examining their dysfunctions. Applying these principles to anxiety, depression, substance abuse, eating disorders, and schizophrenia illustrates the current utility and future promise of evolutionary psychiatry.

**WHAT EVOLUTION CAN AND CAN’T EXPLAIN**

Finding evolutionary explanations for traits that make a species vulnerable to disease is an onerous task. A brief overview of natural selection can encourage critical assessment of proposals that are unlikely to be correct, especially those that suggest that a disease is somehow useful or that traits that harm individual fitness can persist because they give benefits to a group.

Textbook examples describe natural selection adapting a species to a changed environment. In the classic example, as Victorian soot darkened tree trunks, lighter colored moths became easier prey for birds, so darker moths had more offspring and became more common over the generations\textsuperscript{17}. Such examples correctly emphasize that traits are adaptive or maladaptive only in relation to a specific environment, but they give the misimpression that natural selection is mostly about change. Far more often, instead, natural selection keeps things the same. Birds with wings too long or too short are more likely to die in storms, so selection stabilizes the average length at an intermediate value\textsuperscript{18}.

Natural selection also shapes physiological and behavioral systems that adapt organisms to cope with changing environments\textsuperscript{19-21}. These range from simple reflexes like sweating to mechanisms that mediate decisions of all kinds, from what to have for lunch to whether to continue a marriage. How many control systems are shaped by natural selection? Tens of thousands; they control the expression of every gene, the processes that regulate metabolism and replication in 200+ different kinds of cells, the development of tissues and organs, and, of course, every physiological parameter. Perhaps most important of all, they control behavior.

Behaviors themselves are not shaped by natural selection, but genetic variations cause brain variations that interact with environments to give rise to behaviors that influence fitness. This process shapes brains that induce behavior maximizing transmission of genes to future generations. This simple principle is the foundation for behavioral science. It does not mean that all behavior by all individuals maximizes genetic fitness in all environments; it applies only on average, in the natural environment, if the mechanisms are intact. However, recognizing that normal behavior has evolved to maximize the number of offspring who survive and reproduce is an essential foundation for evolutionary psychiatry.

Maximizing the number of surviving offspring requires subtle allocation of effort among several tasks: getting food and shelter, staying alive, finding mates and social partners, and mating and investing in offspring. The field of behavioral ecology studies how organisms allocate effort in ways that maximize reproductive success\textsuperscript{3,4}. Diseases of aging are an example. Genes that cause aging and death are selected for if they increase reproduction\textsuperscript{22,23}.

**The group selection mistake**

Until the 1960s it was assumed that natural selection shapes behaviors which benefit groups and species. Vivid confirmation seemed to be offered by a 1958 Walt Disney film of lemmings jumping into a fjord so that a few other lemmings could survive late winter food shortages to perpetuate the species. However, in 1966, G.C. Williams pointed out that the individuals who sacrifice the most will reproduce the least, so genetic variations that induce tendencies to sacrifice individual fitness will be selected out even if they benefit the group\textsuperscript{24-30}. This insight revolutionized the study of social behavior\textsuperscript{31}. As for the Disney video, it was faked\textsuperscript{32}; the film crew could not find lemmings jumping to their deaths, so they paid local residents to trap them and used brooms off-camera to sweep them into the sea, a fine example of manipulating evidence to support a false but attractive hypothesis.

If selection acts only to maximize gene transmission, how can
it explain traits such as honeybees suicidally stinging intruders? W.D. Hamilton recognized in 1964 that behaviors which decrease individual reproduction in bees can increase the fitness of other bees who have some of the same genes33. More exactly, a trait that reduces individual fitness will be selected for if the genetic costs to the individual are less than the genetic benefits to kin in the group. This principle of kin selection is often illustrated by W.B. Haldane’s apocryphal reply to a question about whether he would sacrifice his life for his brother: “No, not for one brother. But I would for two. Or for eight cousins”. Kin selection is an essential foundation for psychiatry. The term “inclusive fitness” describes the combined effects of direct selection that gives benefits to the individual and indirect selection that benefits kin34–38.

The cooperation of cells in a body illustrates the power of the principle. They cooperate so well because they all start off as identical twins. That is no accident; natural selection has shaped mechanisms that keep germ and somatic cells separate, and the process of meiosis and recombination minimizes the risk of selfish elements replicating at the expense of other genes and the host, although they can still sneak in, especially at the centromere39–42. Infected cells eliminate themselves by the process of apoptosis. This sacrifice can be viewed as a benefit to the host, but it increases transmission of the cell’s genes.

The principle that social traits can evolve only if they increase the representation of an individual’s genes in future generations is still widely misunderstood. The idea that helping tendencies are shaped by benefits to the individual’s genes can be morally disorienting in ways that arouse passionate objections43. However, the conclusion is inescapable. As summarized in K. Boomsma’s recent book on the topic, “No field study has proved that group selection can produce important adaptive change without being challenged by a simpler alternative explanation based on individual kin selection”44, p.683. Explanations for mental disorders based on benefits to a group should be viewed with suspicion.

Realizing that selection works at the level of individuals and their genes has led some scientists to argue that all normal behavior is ultimately selfish45. However, selfish genes can increase their representation in future generations by motivating generously cooperative behavior even with non-kin. Individuals who trade help or resources can both get advantages, but any delay in the exchange arouses the risk that one party will defect. The resulting complications arouse intense emotions. Hundreds of studies and publications describe how such exchange relationships work, and the special roles of reputation and culture45–63.

People in the close personal relationships that are especially relevant for mental health avoid calling attention to costs and benefits; they attribute instead their relationships to attachment, caring and emotional commitments. Kin selection is the most powerful explanation, but friendships with non-kin also have special value. Psychologists J. Tooby and L. Cosmides note that bankers are eager to lend when you have a collateral to guarantee a loan, but, when you are really in a jam, bankers are useless and friends are invaluable46.

The capacities for friendship and morality that are so relevant for psychiatry are shaped by natural selection in kin networks and cultural contexts that make the process extremely complex, but partner choice seems to be important46–67. Individuals preferred as partners get relationships with other superior partners to their mutual advantages, so characteristics that make individuals valuable as social partners are selected for, possibly even in a runaway process66,68–70. Those characteristics include having abundant resources and tendencies to share them generously but selectively. This process of social selection shapes competitive altruism71,72 and extreme attempts to please others, helping to explain problems involving self-esteem, guilt, and social anxiety73.

Complex social traits are sometimes attributed to learning or culture, as if there were alternatives to evolutionary explanations, but the capacities for learning and culture are themselves products of natural selection. They create new selection forces that shape subtle mechanisms which regulate complex emotional and behavioral responses, and those mechanisms give rise to the amazing diversity of human behaviors. Instead of suggesting an alternative to evolutionary explanations, that diversity reflects the flexibility of behavior arising from evolved mechanisms. How natural selection shaped human prosocial capacities may turn out to be the most important contribution of evolution to psychiatry, but there is no room here to elaborate on this large, subtle and controversial topic.

**Sexual selection**

Sexual selection shapes traits that increase gene transmission at a cost to host’s health and welfare73,74. The lovely long tails on peacocks and majestic antlers on deer are expensive hindrances for the individual, but they increase matings, so they are selected for despite their costs. Debate continues about the extent to which they are honest signals of vigor vs. products of a runaway process of signaling and preference for extreme signals; both seem to be relevant. The implication for human problems is profound. Competing for mates accounts for a substantial fraction of human behavior and a high proportion of violence and personal misery75,76. A study that quantifies the proportion of clinical problems that can be attributed to mate competition and sexual problems would be welcome.

**Individual differences**

Natural selection works because individuals with some genetic variants will have more offspring than others. Can natural selection maintain genetic subgroups within a species that thrive in specialized niches? Yes, but only in specialized cases that are unlikely to be relevant for mental disorders. In general, however, alleles and traits maximize fitness tend to become universal, so explaining the persistence of variation remains a central issue for evolutionary biology77–79. The global possibilities are subgroups that evolved in different environments, stochastic variations, balancing selection, trade-offs, and structural or behavioral types adapted to different niches. All have been proposed to explain...
mental disorders, so a brief mention of each is warranted.

Subpopulations evolving in different environments can experience different selection forces. For instance, high solar intensity shaped increased skin pigmentation that protects equatorial populations from damage to skin and folic acid deficiency, and low solar intensity shaped decreased pigmentation that protects populations in cold cloudy regions from vitamin D deficiency and rickets. Differences between populations that evolved in different locations are unlikely to be important for psychiatry.

Stochastic variations account for most individual differences. Deleterious mutations arise inevitably, and natural selection purges them only slowly. Does natural selection maintain some optimal low level of mutation to ensure that variations are available when needed? No, it minimizes mutation rates within the limits of genetic drift and the costs of repair mechanisms. Higher mutation rates might benefit a species, but mutator genes do not persist, because they decrease the fitness of individuals who have them. Systems that increase mutation rates temporarily in bacteria in stressful situations are intriguing, but unlikely to be relevant for humans.

Balancing selection can maintain variation at a genetic locus if different alleles are superior across different external or genetic environments. The persistence of the allele for sickle cell hemoglobin is the classic example of balancing selection by heterozygote advantage. When rare, sickle cell hemoglobin alleles are likely to be paired with an allele for normal hemoglobin, creating heterozygote individuals who are protected from both malaria and the severe disease experienced by individuals with two sickle cell alleles. Most other confirmed examples of heterozygote advantage are also hemoglobinopathies. Heterozygote advantage is relevant here mainly when variation at a single locus has major phenotypic effects, so it is unlikely to explain the persistence of the alleles with tiny effects that influence the risk of mental disorders.

Frequency dependent selection can maintain variation for complex traits as well as the genes that code for them. The classic example is polymorphic shells in a ground snail; predators form a search image for the most common shell pattern, giving an advantage to less common patterns. It has been suggested that sociopathy could similarly give higher than average fitness when its rarity in a population makes others gullible, and reduced fitness when it becomes more common, but the idea is controversial, to say the least.

Balancing selection in shifting environments can also maintain genetic variations. For instance, an allele that increases anxiety will be selected for when dangers are rife and against when environments are safer. This kind of balancing selection can maintain genetic variation that influences the risk of a disorder, but it does not directly explain why systems are vulnerable to failure.

Trade-offs maintain variations that are sometimes attributed to balancing selection. Individuals with values away from the mean will have lower than average fitness, but they will have benefits as well. For instance, higher than average stomach acid levels increase the risk of ulcers, but protect against infection. Individuals with high levels of social anxiety are less likely to win social competitions, but also less likely to be attacked. Individuals at the extremes of the systematizing-empathizing dimension will have lower fitness than those at the mean, but individuals at both extremes will also have advantages that can enhance reproductive success under some conditions. The advantages experienced by individuals with trait values away from the mean have been of special interest for autism, schizophrenia and attention-deficit/hyperactivity disorder (ADHD). The advantages experienced by individuals with values away from a trait mean deserve close attention to understand the relevant trade-offs, and they may help to explain a wide trait distribution. However, fitness is highest at the mean for most traits, so explanations for mental disorders based on benefits at trait extremes should not be accepted without critical assessment.

Specialized morphs that can exploit ecological niches are sometimes proposed to explain a mental disorder. Natural selection can shape multiple phenotypes in a species, such as different mating types in fish, turkeys and orangutans. But most can persist only if their mean morph-specific fitness is the same, and that usually requires negative frequency dependent selection that gives greater advantages to a morph when it becomes less common. For instance, when they are rare, smaller fish that sneak in to fertilize eggs have higher fitness than larger male fish guarding the nests, but their fitness falls when they are common. Morphs that increase adaptation to social niches may turn out to be relevant. However, mental disorders are not morphs with equal fitness maintained by frequency dependent selection.

The possibility that different personalities may get advantages in different social niches is spurring interest and controversy. Variations arising from adaptive plasticity mechanisms that detect and respond to environmental cues are more likely than genetic morphs, but it is difficult to distinguish functionally adaptive responses from epiphenomena. Increased stress sensitivity in individuals exposed to early adversity is an example relevant in psychiatry. Work in this area is interesting, but unlikely to explain variations that harm fitness.

To summarize, attempts to explain a trait that harms inclusive fitness by benefits to a group are inconsistent with evolutionary theory. Most individual differences are products of stochastic genetic variations that have small or inconsistent effects on fitness, but frequency dependent selection can also maintain variations, and research on morphs could be relevant. However, most adaptive individual variations are produced by universal facultative adaptations or adaptive plasticity. In the natural environment, most such adaptations maximize fitness at the population mean, but, because they involve trade-offs, individuals with values away from the mean will have advantages along with net disadvantages; those advantages can increase disease vulnerability by spreading the trait distribution, but they do not make the disease an adaptation.

The above brief discussions caution against uncritical acceptance of hypotheses that are likely to be inconsistent with evolutionary theory, but they should also enhance respect for the many areas of active research and discourse in basic evolutionary biol-
Vulnerability to mental disorders deserves brief comment. Some categories of explanations for disease vulnerability. Each deserves brief comment.

**Individual variations** are the predominant explanation for disease vulnerability. They result mainly from mutations and developmental stochasticity that natural selection cannot eliminate. They are akin to limitations on quality control in a manufacturing process.

Multiple deleterious mutations arise in each individual in every generation. They are selected out with a speed proportional to how much they decrease fitness. The result is a few rare variations with large effect sizes, fewer with moderate effects, and thousands with tiny effects. This is exactly what genome wide association studies (GWAS) are showing for major mental disorders. Most alleles that increase the risk of mental disorders persist because their rate of elimination by natural selection is balanced by the rate of new mutations.

Developmental variation is also unavoidable, and it increases the risk of disorders such as schizophrenia and autism. Could natural selection maintain a low level of developmental instability because that creates phenotype variations that increase reproduction for a few individuals in specialized niches despite lowering the average fitness for individuals? The possibility should not be accepted uncritically, but it is theoretically intriguing and potentially relevant.

Species-wide vulnerabilities make many traits suboptimal. Genetic drift and path dependence are both important. Genetic drift can leave a whole species vulnerable, as illustrated by our inability to synthesize vitamin C. Mildly deleterious mutations can become more common, especially in a small population, simply from the stochasticity of evolution.

Path dependence leaves some traits suboptimal because natural selection cannot redesign a trait from scratch. An automotive engineer can reroute a fuel line that is prone to cause fires, but the path of the urethra through the prostate gland cannot be changed, despite all the trouble it causes. The constraints on brain design are vastly larger, so an allele that gives an advantage by slightly altering one circuit will likely create problems for others.

**Parasites that evolve faster than hosts** are more important for the rest of medicine, but they are also relevant for psychiatry. Antibodies against streptococci with antigenic coats similar to human proteins can attack heart valves, causing rheumatic fever, as well as cells in the caudate nucleus, causing some cases of obsessive-compulsive disorder (OCD).

**Mismatch with modern environments** explains many woes. Natural selection is too slow to keep up with rapid social and environmental changes. Fat, salt and sugar were in short supply in the African savannah, so we have preferences for them and little protection against the diseases that result when they become readily available. Sanitation, immunizations and antibiotics have decreased the burden of infectious diseases, but rates of autoimmune diseases are escalating. Myopia is rare in hunter-gatherers, but common and increasing rapidly in modern societies; whether the cause is close work, lack of sun, working in closed spaces, or some combinations of factors remains unknown.

The above four factors all result from the limitations of natural selection. It cannot prevent all mutations and developmental variations, and it is too slow to protect against fast-evolving pathogens and fast-changing environments. However, some vulnerabilities result from systems optimized by natural selection.

**Trade-offs that benefit individuals** leave many traits less robust than they might be. High blood pressure causes atherosclerosis, low pressure causes fainting, so natural selection stabilizes the average at an intermediate level, with control systems that adjust the pressure to the situation. The risks of infections and autoimmune diseases stabilize the aggressiveness of immune responses at an intermediate level that nonetheless results in both infections and autoimmune diseases.

**Traits that increase reproduction** are selected for even if they reduce health and happiness. Competing for mates requires huge investments in appearance, wealth and social status. The dieting that sets off eating disorders is usually in the service of competition for mates. Reproductive competition helps to account for mortality rates three times higher in men than women in early adulthood in modern countries. The tendency for orgasm to occur sooner for males than females maximizes fitness at the cost of mutual sexual satisfaction. Pregnancy has obvious costs, and parturition is risky. Then there are all the efforts, sacrifices and worries required to raise children. Freud’s emphasis on the importance of sex was along the right lines, but no one in his time

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**Table 1** Evolutionary explanations for disease vulnerability

| 1. | Individual variations resulting from mutations and developmental instability |
| 2. | Species-wide vulnerabilities resulting from genetic drift and path dependence |
| 3. | Parasites that evolve much faster than hosts |
| 4. | Mismatch between bodies and novel environments |
| 5. | Trade-offs that increase the fitness of individuals |
| 6. | Traits that increase gene transmission at a cost to robustness |
| 7. | Defensive responses that are vulnerable to excess expression and dysregulation |

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recognized that selection shapes organisms to maximize gene transmission.

Defenses such as pain, cough, anxiety and low mood are useful responses shaped by natural selection. Their aversiveness is essential to their utility, but the resulting suffering is the bane of our lives. The mild unpleasantness of sweating and shivering motivates moving to someplace where heat generated by the body just matches heat radiated, about 20°C. The greater unpleasantness of nausea and vomiting protects against eating toxic things again. Physical pain is not some abstract signal which gently suggests stopping actions that cause tissue damage; it is an excruciating conscious feeling that motivates escaping the situation and avoiding it in the future. Anxiety and low mood provide similar protection against other dangers. These adaptive responses evolved because they protect against harm. They are aversive for good reasons, and their regulation systems are shaped to benefit our genes, sometimes at a cost to ourselves.

The above summary of evolutionary medicine is brief to the point of being telegraphic, and it does not discuss phylogenetic approaches to infectious diseases and cancer that are proving very useful. Several articles put the current field in a historical context that includes many applications before the 1990s.

Since then, evolutionary medicine has grown into a substantial field, with many textbooks and edited volumes. The International Society for Evolution Medicine and Public Health has annual meetings, and sponsors an open-access journal and other online resources. Courses on evolutionary medicine are now offered in most research universities in the US. However, despite many pleas, medical schools still provide little or no coverage of evolutionary biology as a basic science for medicine.

THE DEVELOPMENT OF EVOLUTIONARY PSYCHIATRY

The many books and papers about evolutionary approaches to mental disorders have had little influence on psychiatry. Historical context provides part of an explanation. C. Darwin said little about mental disorders, despite his connection with psychiatrist J. Crichton-Browne to get illustrations for his book on emotions. For the rest of the 19th and early 20th century, psychiatry was, along with the rest of medicine, enamored with vague notions about the degeneration of families or the species that had little to do with evolutionary biology. Subsequent evolutionary contributions to psychiatry came in three phases: first ethology, then sociobiology and evolutionary psychology, then evolutionary medicine.

Applications of ethology to psychiatry initially made little use of evolutionary biology. Everything changed in the mid-1960s. Recognition that capacities for social behaviors are shaped by kin selection and benefits from trading favors provided one foundation. The other was recognition that a full explanation for a trait requires an evolutionary explanation of its origins and functions as well as a proximate explanation of its mechanisms. E. Mayr advocated for this distinction effectively, but it became more useful as a part of Tinbergen's four questions. What is the mechanism? How does it develop? What is its phylogeny? What is its adaptive significance? The first two questions are about proximate mechanisms, the other two are about evolution. Recognition that all four questions deserve answers is now an established foundation for behavioral biology that continues to inspire commentary.

The significance of these advances was widely recognized only after the publication of Sociobiology by E.O. Wilson in 1975 and The Selfish Gene by R. Dawkins in 1976. They inspired the first applications of evolutionary ethology to psychiatry. Especially influential were a series of papers by M.T. McGuire and related articles that he welcomed as Editor of Ethology and Sociobiology (now Evolution and Human Behavior). Other early explorations of the implications for psychiatry came in books by M. Konner, and B. Wenegrat's Sociobiology and Mental Disorder. The term “evolutionary psychiatry” was first used by P.D. MacLean in an article on how a phylogenetic view of the “triune brain” could counter reductionism.

Studies by J. Bowlby and M.D. Ainsworth on the adaptive significance of infant attachment, and mental problems resulting from its disruption, were foundational for evolutionary psychiatry and have inspired continuing research. Recent reassessments have proposed that anxious and ambivalent attachment styles are not necessarily pathological; they can be strategies that infants use to get resources from mothers who might not otherwise be forthcoming. Especially clinically relevant is a recent proposal that considers how understanding maternal neglect in the light of its evolutionary origins and functions can be helpful for patients.

L. Sloman and J.S. Price also conducted early important research, first with chickens, then with vervet monkeys, to test the theory that depression can be understood as “involuntary yielding behavior” that prevents attacks after losing a status battle. An early paper envisioning a wide range of evolutionary applications in psychiatry inspired a falsified but sadly ignored plea to avoid speculating about how diseases might be useful to a species.

Evolutionary medicine emphasized mental disorders from its origins. In 1998, psychiatrists M.T. McGuire and A. Trevis published Darwinian Psychiatry, the first book using evolutionary medicine principles to understand mental disorders. Since then, a steady stream of books and papers have further developed the field, now called “evolutionary psychiatry” to expand acceptance by those put off by anything “Darwinian” Progress has been especially fast in the UK, where the Special Interest Group on Evolutionary Psychiatry of the Royal College of Psychiatrists has now over 2,000 members. Two leaders of that group, R.T. Abed and P. St. John-Smith, recently edited the first multiauthor overview of evolutionary psychiatry.

The field of evolutionary psychology has grown in parallel, making major contributions for understanding psychopathology. This field initially emphasized research on mating strategies, because they influence reproduction so directly. A 1988
meeting established the Human Behavior and Evolution Society, and encouraged development of evolutionary psychology as a broad field that inspired many papers, books, courses and controversies, many of which had a political flavor. Several major publications from evolutionary psychology focus on mental disorders.

The fifty years of advances in understanding behavior and mental disorders summarized above have had little influence on psychiatric research and practice. Identifying the obstacles that have slowed adoption of evolutionary biology as a basic science for psychiatry may help to overcome them. The education gap is a major impediment. Few psychiatrists get a chance to learn how evolutionary principles explain behavior. Many do not even know that evolutionary explanations are needed, and few know how to frame and test evolutionary hypotheses. Elementary errors result, even in books on the topic. For instance, many who are curious about evolutionary psychiatry are likely to turn to a book by that title which presented some intriguing Jungian ideas in a mishmash of speculation about diseases as if they were adaptations evolving because they benefit groups. The book aroused justified skepticism.

Wariness about evolution in general is also an obstacle, especially in the US, where some religious groups deny that evolution has had any role in shaping humans. Hesitation among scientists arises from perceptions that evolutionary psychology is somehow controversial. While work in all fields deserves critique, sensible scientists all recognize that natural selection shaped the brain, and the importance of understanding the adaptive significance of behavior is increasingly acknowledged across the breadth of psychology.

The largest obstacle, however, is uncertainty about what evolutionary biology has to offer. Mental health clinicians need better ways to help their patients now. So, advances in basic behavioral biology can seem abstract. However, evolutionary psychiatry can improve clinical care now by providing sensible explanations that support all kinds of therapy, as well as new ways to frame disorders that patients can understand and appreciate. Each section below emphasizes such practical applications.

**EMOTIONS AND THEIR DISORDERS**

Negative emotions are, like pain and cough, symptoms that exist because they have given selective advantages. They have evolved in conjunction with control systems that express them in the situations where they are useful. Those systems express false alarms even when functioning normally, and they are prone to malfunctions that cause disorders. Usually, however, anxiety and low mood are symptoms that indicate a problem, not disorders produced by malfunctioning control systems.

Psychiatry textbooks have long chapters about emotional disorders, but little or nothing about normal emotions. How we can regulate our emotions is the topic of many books and papers, but how our emotions regulate us gets little attention. Controversies about the nature of mood and anxiety disorders persist despite the efforts of expert committees. Decades of research have not found the expected specific brain or genetic abnormalities. Medication treatments are somewhat effective, but when to use them is the topic of vigorous public debate. News articles suggest that tsunamis of emotional problems are sweeping over whole populations. And, while mental health clinicians and researchers do what they can to stem the tide, it will never be enough. The situation arouses appropriate emotions: confusion and frustration.

The standard approach asks why some people have emotional problems and others do not. The responsible factors have been studied in exhaustive detail: individual differences in genetic make-up, early experiences, drug use, cognitive biases, relationships, family dynamics, and larger social factors. Thousands of papers and textbooks describe why some individuals experience emotional disorders and others do not.

An evolutionary medicine approach asks different questions: Why do we all have capacities for negative emotions? How are they useful? How is their expression regulated? Why are their control systems vulnerable to malfunction? Answers to these questions provide a biological foundation for understanding and treating emotional disorders in the context of normal emotions.

Recent research progress has led to a consensus that emotions are adaptive states shaped by natural selection. However, this progress is obstructed by a tendency to tacit creationism that describes emotions as if they were distinct products of a designer’s vision, each with a specific mechanism that carries out a specific function. For instance, anger is said to serve the function of signaling an imminent attack. Or threatening the end of a relationship. Or expressing dominance. Emotions do serve functions, but one emotion can serve many functions, and one function is advanced by many emotions. So, trying to map specific emotions to specific functions generates complexity and controversies.

The obstacle can be overcome by a definition of emotions based on the situations that shaped them. Emotions are special states that adjust physiology, arousal, cognition, facial expression, motivation, memory, behavior, and subjective experience in ways that gave selective advantages when expressed in situations that occurred and influenced reproductive success over the evolutionary history of a species. Control systems process information from multiple internal and external sources to express emotions in the form and to the degree that maximizes fitness in the current situation. On average. In the natural environment. In response to always insufficient information. If the control system is intact. With variations induced by cultural and individual experiences.

Mapping emotions to situations instead of functions helps to quell some persistent controversies: How many emotions are basic and how many are secondary? Which aspects of an emotion are primary, and which are secondary? Does subjective feeling initiate physiological changes, or does perception of bodily changes give rise to the feeling? An evolutionary perspective suggests that these questions do not have specific answers. Instead, multiple aspects of an emotion are expressed somewhat concurrently, influenced by details of the situation, by each other, by expectations, by cultural learning, and by recursive feedback loops.
The driving modes of modern cars offer a useful but imperfect analogy. Setting a car for sport, normal, eco or snow mode adjusts engine timing, gear ratios, suspension firmness, torque distribution, and dashboard appearance in ways that increase the ability to cope with different situations. The analogy is imperfect, because cars come off the assembly line as identical as quality control can make them, while minds are products of slightly different genomes interacting with varying environments. Furthermore, and more importantly, organic control systems are both more jury-rigged and more adaptable, so variations in a situation can arouse different aspects of an emotion to different degrees. For instance, different kinds of unpropitious situations arouse different symptoms of low mood.

The algorithms that detect the presence of situations in which emotions would be useful are nothing like an engineer’s decision tree. They are products of a process that is like machine learning, steadily improving fitness by successively changing different parameters at different levels, and keeping whatever works. The resulting organic complexity makes reverse engineering extremely difficult. Further complexity arises because multiple overlapping situations may be present; conflicting goals may be pursued simultaneously; and individuals have different values, goals, resources, strategies, relationships, and prior experience. Emotion control systems generally work, but describing the brain mechanisms that mediate them is an onerous task.

It is easier to describe the situations that an organism encounters. Situations that influence fitness can be categorized on three dimensions: kind of resource (physical or social), valence (opportunity or threat), and the situations that arise routinely during goal pursuit. Table 2 shows 24 situations that arise in goal pursuit and their corresponding emotions. The need to deal with opportunities and threats specific to more specific kinds of resources further differentiates the states. For instance, situations that arise in getting and keeping or losing a mate have shaped capacities for romantic love, sexual arousal, caring, commitment, guilt, jealousy, and grief.

Any approach to emotional symptoms which assumes that all individuals are the same loses the most important information. General checklists of life events and levels of stress do not measure the situations that arouse emotions. Information about the individual’s life situation provides a starting point for distinguishing four categories of emotions: useful for the individual; harmful for the individual, but useful for increasing gene transmission; harmful for the individual and for fitness, but arising from normal mechanisms; and harmful products of an abnormal regulation mechanism.

Appraisal theories of emotions are especially helpful in understanding individuals. Emotions are usually aroused not directly, but by an individual’s appraisal of what new information means for his/her ability to make progress towards personal goals. Those goals can differ dramatically between individuals and even within an individual at different times. The emotional impact of a positive pregnancy test depends on whether the woman was eager to conceive or considering a divorce. One patient insisted that she should not be depressed now because she had just started a job at a brokerage firm that tripled her previous salary; she was reluctant to talk about having to give up her previous career as a struggling artist.

The implications for psychiatry are profound. General measures of stress and checklists of life events ignore many factors that influence an individual’s emotions. Diagnostic criteria based only on the number, severity and duration of symptoms are necessary to get the reliability required for epidemiology, but they are not grounded in biology. Determining if an emotion is normal requires assessing the presence or absence of a situation in the context of an individual’s values, goals, strategies, expectations and psychodynamics. Determining if an emotion is useful for the individual is a separate question. An evolutionary framework for understanding the origins, functions and regulation of normal emotions provides a foundation for understanding abnormal emotions, starting with anxiety and mood disorders.

### ANXIETY AND ITS DISORDERS

Almost all research on anxiety has focused on why some people have too much of it. An evolutionary perspective brings in the other half of biology to ask how natural selection shaped subtypes of anxiety, why normal control systems may sometimes express so much excess anxiety, and why some people have too little anxiety. This reframing of anxiety disorders can improve clinical outcomes.

#### The smoke detector principle

Normal regulation mechanisms express anxiety when the ben-
efits are greater than the costs. The presence of real danger is often uncertain, and the costs of a false alarm are often low compared to the costs of no or too little anxiety. So, false alarms are normal and expected in any optimized system. Regulation of the panic response offers a relevant example. If a panic attack false alarm costs 100 calories, but not having a panic response when a predator is present costs 100,000 calories, then the panic response is worthwhile whenever the chance of a predator being present is greater than one in 1000. Therefore, 999 out of 1000 responses from an optimized control system will be false alarms that are normal and necessary for maximizing fitness. This is called “the smoke detector principle,” because everyone knows that it is worth putting up with occasional annoying false alarms to ensure protection from a real fire.

The smoke detector principle is equally useful in the rest of medicine. Most treatments do not cure, but relieve distressing symptoms such as pain, cough or nausea. That is usually safe, because optimized control systems tend to express defenses when they are not essential and because the body has backup systems. Sometimes, however, a defensive response is necessary: giving a cough suppressant to a patient with pneumonia may be fatal. Recognizing the smoke detector principle is fundamental for making wise medical decisions.

The related concept of “error management” describes the benefits of tendencies to cognitive distortions. An example is given by the decisions that men make about whether a woman is sexually interested. The benefits of assuming “yes” are large compared to the costs of assuming “no”. So, overestimating a woman’s interest gives a selective advantage, as well as obviously causing many social problems. This example also illustrates the more general principle that natural selection shapes the mind to maximize fitness at the cost of objectivity.

Hypophobia

An evolutionary perspective calls attention to the neglected disorder of hypophobia. While many people experience too much anxiety, some experience little or none, even when it would provide vital protection. Individuals with hypophobia do not request treatment. They instead come to attention in the accident ward, unemployment lines, and court proceedings.

Hypophobia is a serious and potentially fatal condition that deserves study even though the victims do not request treatment.

Panic disorder and agoraphobia

The consistent symptoms of panic attacks and their obvious adaptive utility make evolutionary analysis relatively straightforward. Panic is an emergency response that can be lifesaving in the face of acute danger. As recognized by W.B. Cannon over a hundred years ago, the rapid heart rate, fast breathing, and shunting of blood from the skin and gut to muscles all make sense as part of a fight-flight reaction. Learning that these symptoms can be useful helps patients to recognize that they are experiencing a false alarm in a normal system, instead of a possible heart attack or stroke.

Panic attacks escalate into panic disorder due to positive feedback loops, often initiated by the tempered reassurance of an emergency room physician who says: “It doesn’t seem to be a heart attack or a pulmonary embolus, but, if it happens again, come back right away.” The patient starts monitoring, and the next experience of shortness of breath or rapid heart rate arouses anxiety that further increases heart rate and shortness of breath, causing more anxiety that spirals into a full panic episode. Fear of fear produced by the possibility that symptoms could be from a dire medical illness is a common route to full-blown panic disorder.

The self-adjusting nature of defense control systems further increases vulnerability. Repeated arousal adaptively increases the sensitivity of many defensive responses. Repeated tissue damage indicates that nociception has been insufficient, making a reduced pain threshold adaptive. Such self-adjusting control systems are intrinsically vulnerable to vicious positive feedback cycles. If the pain threshold gets low enough to cause spontaneous pain, that can initiate the terrible feedback cycle of chronic pain. Repeated panic attacks signal a dangerous environment in which a faster more intense response to smaller cues of danger will be worth it, initiating a second kind of positive feedback cycle that makes panic disorder worse.

Most cases of agoraphobia are initiated by repeated panic attacks. Many publications consider possible psychological and neurological explanations, but the coexistence of agoraphobia and panic disorder is predicted by an evolutionary perspective. Repeated experiences of life-threatening danger indicate a dangerous environment in which venturing far from home may be fatal. If you encountered a lion at the watering hole two nights in a row, it is best to stay home. If getting water is essential, it will be wise to go with friends, make the trip short, and be on alert and ready to flee at the least hint of danger.

Learning about these general pathways to panic disorder and agoraphobia helps many patients. Instead of viewing themselves as disease victims, they can instead recognize that their symptoms exist for a reason and that they give advantages as well as disadvantages. Explicitly integrating this perspective with behavior therapy and medication treatment helps even more. Patients often wonder why panic attacks continue to be precipitated in grocery stores despite repeated visits without encountering actual danger. The smoke detector principle, adaptive sensitization, and positive feedback loops all provide partial answers. But because fear of fear is often central, extended exposure to the panic symptoms themselves is often essential to effective behavior therapy, which means staying in the situation until panic symptoms fade.

Many patients are reluctant to take medication for panic disorder. Concerns about dependence and rebound are justified for benzodiazepines, but antidepressants can often stop panic attacks without such problems. Patients nonetheless often worry that the medication will “just cover over the symptoms”. Such concerns can be relieved by explaining that using medications to stop panic attacks for several months resets the system to a
sensitivity appropriate for a safe environment, making symptom return less likely when medications are stopped. Discussing these factors increases the likelihood that prescriptions are filled, pills are taken as prescribed, and side effects and minor breakthrough attacks are appropriately ignored.

Phobias

Specific phobias have long been a focus for evolutionary thinking about anxiety disorders, because snakes, spiders and storms pose risks that make anxiety responses seem innate. However, framing such symptoms as “innate” or “learned” is too simple; many are products of “prepared learning”. Studies by S. Mineka and colleagues found that young monkeys raised in a laboratory showed no fear of snakes, but a single observation of another monkey showing fear while looking at a snake was sufficient to create enduring avoidance. Observing another monkey showing fear of a flower did not create avoidance. Other seminal studies conducted by A. Öhman and colleagues showed physiological responses to subliminal images of spiders and other dangerous cues.

The nature of the response to different dangers reflects the actions of natural selection. Fear of heights creates freezing, enclosed spaces motivate escape, and social dangers arouse displays of submission or confrontation.

The challenge of behavior therapy is to convince patients to do the exercises. Helping patients to recognize that their anxiety is decreasing even a little during exposure therapy, from subjective units of distress of 90 to 85 for instance, helps to motivate continuing with difficult exercises. Reframing phobic fears as exaggerations of normal useful responses, and describing how desensitization works, helps many patients to engage actively in treatment, especially if they can be convinced that their exercises are influencing a mechanism that exists to reduce anxiety levels as a function of experience.

Generalized anxiety disorder

Psychologists study two global motivational states: promotion in situations that offer opportunities and prevention in situations that pose risks. Most people shift back and forth depending on the situation, but people with generalized anxiety disorder (GAD) put almost all their life’s energies into prevention. The human gift of foresight is turned entirely to anticipating possible harms and losses. If someone does not come home exactly on time, visions of tragic accidents arise. A possible job layoff sets off fears of having to live on the street. The mechanism that allocates effort to pursuing opportunities is blocked by constant attention to possible risks. The human tendency to generalize amplifies the problem: the one time in 100 that the fear proves grounded seems to justify fear for the next 99 times.

It is fascinating that the alleles that increase the risk of GAD are the same as those that increase the risk of major depression. Both states protect against losses, and the high genetic correlation suggests that they evolved from a common precursor.

Treatment of GAD is difficult. Sometimes antidepressants are effective and cognitive therapy can help, but the tendency to allocate effort to prevention runs deep in many people. Describing the need to seek a balance between prevention and promotion can help, but systematic cognitive therapy is more effective.

Social anxiety disorder

Attending a party seems less dangerous than balancing on a cliff or deciding if a sound was made by a lion or a monkey, but the anxiety can be just as intense. What can be lost? Everything. Human success depends on social resources – friends, allies, and membership and status in a group. They can be lost in an instant by sharing an unpopular opinion, siding with the wrong party in a dispute, or even smiling when sadness is expected. The delicacy of the matter is magnified by the need to inhibit selfish, sexual and aggressive impulses. Social anxiety is also aroused by fear of failing or fear of being attacked by a competitor or a moralist who detects a possible deviation. The risks are higher now that events can be captured on media for posterity.

The human tendency to extreme social sensitivity is a product of cultural mores and social selection that increases fitness for those who are preferred partners. The clinical implications are the same as for other anxiety disorders: discussing the utility of social sensitivity and the costs of too little social anxiety helps patients to recognize that they have advantages as well as disadvantages, but that their concern is excessive. As with performance anxiety, the fear is of making mistakes, so the best exercises require actually making mistakes.

Obsessive-compulsive disorder

OCD has been now removed from the diagnostic group of anxiety disorders, but its symptoms include fear of contamination, fear that some small misstep will harm others, fear that an aggressive impulse will be acted on, and rituals to prevent those outcomes. Some patients report driving around a block again and again to check if they might have hit someone, then calling the police later to check again. Others drive home from work to see if a hair curler is still plugged in, not just once but several times.

OCD anxiety is distinctive because fear of harming others is often more extreme than fear of being harmed. This feature has suggested that OCD may represent an extreme of a psychological immune system, or an extreme of the human ability to represent future consequences of actions. It may also reflect a dysfunction that is not related to a defense. Of course, these are not mutually exclusive possibilities.

Behavior control systems in OCD are disrupted in a peculiar way. The system that normally turns off protective behaviors fails. For most people, when a protective behavior is judged sufficient, thinking turns sharply elsewhere. Decision-making is assisted...
by the useful irrationality of concluding that the decision made was the right one. Social psychological studies demonstrate the endowment effect: people value an item more as soon as they have chosen it\textsuperscript{113}. It would be interesting to study the endowment effect in people with OCD.

However, the problem is not just an absent stop signal. Attempts to disengage from washing or other protection behavior arouse more anxiety, creating a positive feedback cycle. It is as if the ability to inhibit conscious awareness of impulses to harm has failed. Presumed strong natural selection for such inhibitions in the past 100,000 years may be relevant\textsuperscript{16}. Or it may simply be that OCD is the syndrome that arises from damage in a specific locus in the caudate nucleus, the same way that aphasia results from damage to Wernicke’s area. Different explanations may apply to different cases.

DEPRESSION AND LOW MOOD

It is hard to see anything useful about depression. Pessimism, hopelessness, lethargy, low self-esteem, and ruminating about death or suicide are worse than useless, so depression is usually assumed to be abnormal. But, like physical pain, ordinary low mood is a potentially useful response to a bad situation. Both can be expressed excessively or when they are not needed, resulting in the vast suffering. Treatments are somewhat effective, but, as is the case for anxiety, the search for causes of depression has come up short: plenty of statistically significant results, but no specific common genes, neurotransmitters or brain abnormalities have been found. Controversies and calls for new directions abound.

An evolutionary perspective suggests taking a medical approach. Not the crude “medical model” which assumes that symptoms are products of a specific abnormal mechanism, but an approach like that in the rest of medicine, where some symptoms are recognized as useful responses aroused by disease or disadvantageous situations. Progress in understanding mood disorders will come from discerning the origins, functions and regulation of normal mood. That means identifying the situations in which low mood is useful, how it is useful, how it is normally controlled, and why mood control systems are so vulnerable to malfunction.

Scores of papers propose evolutionary explanations for depression, but reading them can be frustrating. Sadness, low mood, depression symptoms, and depression syndromes are not always clearly delineated. Some articles aim to explain the capacity for ordinary mood variations, others for the symptoms of depression, some more for the syndromes of major depression, melancholia or bipolar disorder. Many proposed explanations are framed as “the function of depression,” often arguing for the importance of that function over alternatives proposed by other authors. Table 3 lists some examples. All deserve consideration, but, in full evolutionary context, they are not competitors. They are varying ways lists some kinds of situations in which aspects of low mood can be expressed excessively or when they are not needed, resulting in the vast suffering. Treatments are somewhat effective, but, as is the case for anxiety disorders, the wish for simplicity helps to explain the prevalence of black or white opinions that depression is usually a product of brain abnormalities or usually a normal response. A more encompassing evolutionary view encourages recognition that some episodes of depression are aroused by current situations, while others are excessive or distorted responses, and others are unrelated to any current situation. In his case series from 1934, A. Lewis concluded that each group comprised about a third of his patients\textsuperscript{116}. My experience has been similar, but controlled studies of population samples would be valuable. Clinicians in different settings see frames a different question. In what kinds of situations would the characteristics of low and high mood increase inclusive fitness? Low mood can be useful in unpropitious situations in which efforts are likely to be wasted or cause losses. The intense effort and risk-taking characteristic of high mood can likewise be useful in propitious situations that offer big payoffs for small investments. It is interesting to consider that time-limited situations are likely to arouse more intense emotions; if good times are likely to end soon, intense activity and risk taking will be worth it; if bad times are likely to end soon, it is best to just wait.

Natural selection has differentiated the global states of low mood into overlapping subtypes whose utility depends on the resource involved and why effort is likely to pay off\textsuperscript{270,337}. Table 4 lists some kinds of situations in which aspects of low mood can be useful and how they can have increased fitness in past generations.

This approach frames depression as extreme versions of overlapping states shaped to cope with different unpropitious situations. It provides a framework for considering them together instead of emphasizing one explanation or viewing subtypes as distinctly separate. As is the case for anxiety disorders, the wish for simplicity is undermined by the messiness of organic complexity. Notions that all situational causes for depression can be collapsed into “stress,” whose effects are mediated by the hypothalamic-pituitary-adrenal (HPA) axis, are inconsistent with an evolutionary view. The mood system is not nearly that crude. Mood symptoms are differentiated to deal with different kinds of unpropitious situations\textsuperscript{337-341}. However, that does not mean that different patterns of low mood are distinct modules; they are overlapping suites of responses whose structure is very different from anything an engineer would design.

The wish for simplicity helps to explain the prevalence of black or white opinions that depression is usually a product of brain abnormalities or usually a normal response. A more encompassing evolutionary view encourages recognition that some episodes of depression are aroused by current situations, while others are excessive or distorted responses, and others are unrelated to any current situation. In his case series from 1934, A. Lewis concluded that each group comprised about a third of his patients\textsuperscript{116}. My experience has been similar, but controlled studies of population samples would be valuable. Clinicians in different settings see

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Functions proposed for depression</th>
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<tbody>
<tr>
<td>Soliciting help (Lewis, Klerman, Hamburg)\textsuperscript{314-316}</td>
<td></td>
</tr>
<tr>
<td>Involuntary yielding (Price, Sloman, Gilbert)\textsuperscript{197,198,318}</td>
<td></td>
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<tr>
<td>Sickness behavior (Hart)\textsuperscript{319-322}</td>
<td></td>
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<tr>
<td>Conservation of resources (Engel, Beck)\textsuperscript{323,324}</td>
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<tr>
<td>Extortion of resources (Hagen)\textsuperscript{325}</td>
<td></td>
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<tr>
<td>Social navigation (Watson and Andrews)\textsuperscript{326}</td>
<td></td>
</tr>
<tr>
<td>Disengagement (Klinger, Brickman)\textsuperscript{327-329}</td>
<td></td>
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<tr>
<td>Withdrawal to consider options (Gut, Andrews and Thompson)\textsuperscript{330,331}</td>
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<tr>
<td>Adjusting effort intensity and goals (Klinger, Nesse)\textsuperscript{328,329,332-334}</td>
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<tr>
<td>Motivating behaviors to gain group acceptance (Allen, Leary)\textsuperscript{333,336}</td>
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Table 4 Some situations in which low mood can increase fitness

<table>
<thead>
<tr>
<th>Situation</th>
<th>How low mood can increase fitness</th>
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<tbody>
<tr>
<td>Infection</td>
<td>Sickness behavior conserves energy for fighting infection and avoids dangers while incapacitated</td>
</tr>
<tr>
<td>Loss of a resource</td>
<td>Sadness stops actions that resulted in loss, and motivates trying to recover or replace the lost resource, warning others about danger, and protective actions to reduce future losses</td>
</tr>
<tr>
<td>Loss of a loved one</td>
<td>Grief motivates trying to prevent similar future losses</td>
</tr>
<tr>
<td>A season of scarcity</td>
<td>Seasonal low mood conserves energy when foraging is likely to be unsuccessful or dangerous</td>
</tr>
<tr>
<td>Failing efforts to reach a goal</td>
<td>Low mood reduces wasted effort and motivates waiting, considering other strategies, or pursuing other goals</td>
</tr>
<tr>
<td>Loss of a status contest</td>
<td>Depression signals submission, thus avoiding attacks by more powerful others</td>
</tr>
<tr>
<td>Threat of exclusion from a group or relationship</td>
<td>Low self-esteem motivates doing things valued by others</td>
</tr>
<tr>
<td>Lack of crucial resources</td>
<td>Depression signals a need for help</td>
</tr>
<tr>
<td>Unable to meet all commitments</td>
<td>Stress activates increased effort but also withdraws effort from some activities</td>
</tr>
</tbody>
</table>

different proportions of patients in each group, thus explaining some differences of opinion about the causes of depression.

The above summary of current thinking about evolution and depression is telegraphic in its brevity. Many reviews and books are also available for those interested. Research to test specific proposals is needed, but difficult to carry out. It will be some years until work in this area settles down to the extent that a summary can become a routine part of psychiatric education. In the meanwhile, work in the clinic and the laboratory continues, where some applications of evolutionary thinking can be useful even now.

Mood disorders are manifestations of failed control systems, so control systems theory is needed for a full explanation. Several observers have noted the tendency for depression to induce behaviors that perpetuate and escalate symptoms in a positive feedback cycle, and new research on metacognitive therapy provides ways to disrupt the cycles. Pessimism decreases initiative that could lead to success. Low self-worth inhibits social contacts. Lethargy decreases exercise. In modern societies, people can retreat to a room alone and shut off contact with others, a perfect recipe for making depression worse. Activation therapy can break the cycle.

As noted already, the self-adjusting nature of defense control systems makes them especially prone to positive feedback cycles that cause disorders. Much depression is like chronic pain that persists because repeated arousal adjusts the response threshold to a lower level. Depression is recognized to be vulnerable to “kindling”, in which repeated episodes make further episodes more likely. Brain mechanisms are being explored, but the question of whether kindling is a defect, an epiphenomenon, or an adaptation to an unfavorable environment remains to be fully addressed.

An evolutionary control system perspective helps to make sense of the repeated finding that many people with depression have the tendency to mood fluctuations, even if they do not meet criteria for bipolar or cyclothymic disorder. All control systems are compromised by the trade-off between high gain and stability. Bipolar disorder has the characteristics of a control system with excessively high gain. The early stages of mania often ramp up as enthusiasm generates success, making the environment appear extremely propitious, so that even higher energy and investments seem justified, in a runaway vicious cycle. Most people, after a great success, experience a letdown that often seems mysterious. That tendency, a reflection of what psychologists call “opponent process”, is just the ticket for preventing mood from escalating out of control, and it seems to be missing in people with bipolar disorder.

Why did natural selection leave mood control systems vulnerable to dysregulation? The standard explanations from evolutionary medicine all apply.

Individual genetic and developmental variations leave some individuals more vulnerable than others. The set point for mood seems to be as stable as that for body mass. An individual’s mood responsiveness also tends to stay consistent over time. Both are influenced by genetic variations. There is no reason to assume that the responsible alleles are deleterious mutations. Most are probably just variations whose tiny effects would not influence fitness much, at least in ancestral environments.

Mismatches with modern environments may or may not be important; we lack adequate data to be sure and drawing firm conclusions will be difficult. Some evidence suggests that mood disorders are more common now than they were in the past. However, the belief that the incidence of mood disorders has been increasing in recent decades is distorted by the salience of current problems and the tendency to forget bad times in the past. Epidemiological studies that followed the same population over time have not consistently found substantial increases. Even the presumed increased incidence of anxiety and depression related to the COVID-19 pandemic is not confirmed by systematic epidemiological assessment.

Nonetheless, substantially different rates of mood disorders in different countries imply strong socio-cultural influences, perhaps partially mediated by physical factors as well. Concern about the influence of social media is certainly justified, even if hard to confirm. We know that mood is influenced by social comparisons, and that people display especially positive views of their lives on social media, making observers feel inadequate by comparison. However, some anthropological reports found
depression in populations far removed from such modern in- fluences. While small group sizes and rapid cultural changes make definitive studies difficult, the question is important enough to justify a major investment.

Trade-offs are important in shaping mood regulation systems. The inherent trade-off between high gain and stability has already been mentioned. The smoke detector principle may also be relevant. Large costs are likely to be incurred by foraging when no food is available or by engaging in status competitions with more powerful others. The costs of waiting, conserving resources and avoiding initiative are likely to be low. So, like other defensive responses, low mood is expressed more readily and intensely than seems sensible. This has important treatment implications. Most of medicine consists of relieving painful normal responses. Recognizing that low mood can be useful does not suggest that it should not be treated. However, it does encourage careful assessment of the situation to try to identify unpropitious situations that can be changed.

Other trade-offs arise because natural selection shape organisms to maximize reproduction at the expense of individual health and welfare. A night spent in any busy psychiatric emergency room includes plenty of cases precipitated by infidelity, divorce, abandonment, or the dilemma of whether to leave a relationship. Such relationships are so close to the center of human lives that it can seem heartless to observe that these intense feelings are in the service of reproduction at the expense of individual welfare.

How are these principles useful in the clinic? Changes in the approach to four aspects of care are useful: the clinical evaluation, how to talk with patients about depression, how to describe treatment, and how to look for new treatments.

The review of SOCIAL systems and its implications

The standard clinical evaluation asks about recent life events, but sometimes lumps them into the general concept of stress. An evolutionarily informed clinician can instead conduct a review of social systems, following the model of the medical review of systems, to identify situations that might be arousing symptoms. Behavioral ecologists use several categories of effort to study decision trade-offs: somatic effort is to stay alive and healthy and to get external resources like food and shelter; reproductive effort goes towards finding mates, mating, and parenting; social efforts go towards getting allies, group membership and status in a group. Closely related categories of human resources can be summarized using the acronym SOCIAL: Social resources, including friends, groups and social status; Occupation and other valued social roles; Children, family and relatives; Income, savings and material resources; Abilities, appearance, health, skills and other personal resources; and Love and sex.

A full clinical assessment asks about how things are going in each area: what the person has, wants, hopes for, fears, is trying to do; and obstacles, opportunities, dilemmas and pending decisions about activities in that domain. This requires clinical sensitivity. Calling attention to things a person wants but does not have can arouse useless bad feelings. But taking time to discuss the situation in each domain often reveals problems that never come up in general discussions about stressful events: a child on drugs; an obese spouse addicted to sodas; a phone call from a previous lover; a job opportunity passed up to stay with the family; a medical problem calling attention to the brevity of life; an arrest warrant that prevents socializing.

Such problems rarely have easy solutions; if they did, the person would have solved them. Many can be characterized as social traps. People make big investments to create occupations, marriages, relationships with other people, memberships in groups, and status in certain domains. When rewards fade, consideration of making a change grows, but it is unwise to impulsively give up on a major life enterprise; pessimism about options can conceivably be useful to prevent turning too quickly to look for a different job or partner. So, people stew, dealing with dissatisfaction and difficult decisions in their own ways. Clinicians who learn about such dilemmas can work with a patient to gradually try to understand why the person is trapped in the dilemma, and the costs, risks and opportunities of alternatives.

It is especially important to find out if the individual is trapped pursuing an unreachable goal, because that is the perfect depressogenic situation. Normal low mood withdraws effort from the domain and motivates waiting or considering alternatives. If no alternatives are possible, or they have been tried and failed, the system further withdraws motivation, and pessimism encourages turning effort to a more productive enterprise. However, alternatives are not always available. When the likelihood of success fades after years in trying to get a degree, become a sports professional, start a restaurant, find a better job, or convince a partner to marry, giving up too quickly is unwise. But continuing to persist in pursuing an unreachable goal escalates ordinary low mood to clinical depression, which then itself interferes with pursuing the goal. Studies of this phenomenon show that depression often fades when a major goal is truly given up, and that people capable of giving up major goals are protected against depression. It is also clear that mood is influenced not by success or failure, but by rate of progress towards a valued goal.

If the above framework is found to be relevant in an individual patient, depression can be described as an extreme of a normal response. This can encourage a more active stance towards the symptoms, one that encourages collaboration in considering possibly related life circumstances and alternatives. But in other cases this approach may be inappropriate. Some patients with “endogenous” depression are eager to attribute their symptoms to current life problems, even when the temporal association is weak. And the idea that symptoms can be useful implies for some patients that they should not be treated. That notion can usually be scotched by pointing out the safety of physical pain relief, or by going further to describe the smoke detector principle. But clinical sensitivity is essential, as well as an accurate characterization of the individual case.

Treatment options and mechanisms of action can also be de-
scribed differently. Despite sophisticated clinicians avoiding this simplistic schema, many patients view their condition as caused by a “chemical imbalance”. Instead of viewing medications as correcting an imbalance, it is often more helpful for patients to think of antidepressants as blocking mental pain the same way aspirin blocks physical pain. That helps to reassure patients who are worried about getting addicted; it helps to explain why the medications do not cause euphoria; and it helps to justify putting up with side effects.

In psychotherapy, understanding the real dilemmas a person is dealing with is essential for finding and correcting distorted thinking. Also, patients who come to see that unjustified pessimism and low self-esteem can be expected aspects of depression are more likely to cooperate with cognitive behavioral treatment instead of constantly trying to justify their distorted views.

A whole separate paper would be needed to explore the many ways that evolutionary approach can advance psychotherapy. Cognitive therapy in particular is ripe for integration with evolutionary thinking. Psychodynamics has yet to incorporate the principle that mechanisms for repression and defenses increase fitness. And modern interpersonal treatments are just starting to incorporate new findings about how relationships heal.

Finally, an evolutionary framework may help guide the search for new treatments. For instance, the standard Porsolt test, used to identify chemicals likely to reduce depression, measures how a drug influences the duration of a rat swimming in a beaker of water. Antidepressant drugs cause longer swimming. But rats that stop swimming don’t drown; they float with their noses above the water, a superior strategy in the natural environment when active struggle would cause faster drowning. Expanding the search for antidepressants to consider persistence in the face of unrewarded goals may offer new ways to identify effective medications, and evolutionary perspectives may advance psychopharmacology more generally.

Anxiety and mood disorders are only the tip of the emotional problem iceberg. Excesses and deficiencies can cause abnormalities of every emotion. Deficient negative emotions, such as hypochondria and lack of low mood, are almost completely neglected; not surprisingly, since few complain about such problems. Mild excesses of positive emotions are similarly ignored. Excess disgust limits the lives of many people. Excess boredom can be crippling. Sudden intense romantic infatuation is a desperately intense and problematic condition, while the inability to experience romantic love can wreck relationships. An evolutionary framework encourages expansion from the current focus on disorders of mood and anxiety to also consider disorders of other emotions and treatments that can help.

**SUBSTANCE USE AND ABUSE**

Most of our research and knowledge about substance abuse is about why some people succumb and others do not, and about what treatments are most effective. Those are the standard questions. However, an evolutionary perspective calls attention to several others: Why do plants make psychotropic drugs? Are human motivations to use substances an epiphenomenon of motivations shaped for other reasons, or are they adaptations shaped because taking drugs increases fitness? Why are some people much more vulnerable to addiction than others? Why are most people so confident that they can use drugs and stop whenever they choose?

Plants make psychoactive substances to discourage herbivores. Chemicals that disrupt herbivores’ nervous system are especially common, because small doses can have large effects. A mouse that eats a coffee bean will likely die; an ungulate that browses on tobacco will likely get sick and not do it again. However, an arms race ensues: selection shapes herbivores that can deal with toxins, creating selection for new toxins that can better deter herbivores and perhaps give advantages to specialists who can tolerate them. The monarch butterfly caterpillar has evolved the ability to feed on milkweed and store its toxins, making the caterpillars and the butterflies distasteful to birds. Humans are omnivores who cope with diverse toxins by routing products from the digestive tract to the liver, where enzymes destroy most toxins before nutrition is forwarded to the general circulation.

Explaining vulnerability to substance abuse starts with the observation that humans have used psychoactive drugs for thousands of years – alcohol for 5,000 years, tobacco for 2,000 years, opiates, caffeine and coca for nearly as long. Different drugs induce different states with different benefits. For caffeine it is alertness; for nicotine, calm and alertness; for alcohol, disinhibition and social connection; for cannabis, pleasure and calm; for opiates, euphoria and pain relief; for cocaine and amphetamines, pleasure and energetic concentration; for psychedelics, intense experiences of diverse types. Given this diversity of drug actions, many factors will be relevant, all within the general explanation that humans are smart and learn quickly to repeat behaviors that bring benefits; those behaviors include making and selling drugs as well as using them.

Other animals also use substances, but only humans have discovered ways to concentrate and administer chemicals in ways that increase positive emotions, decrease negative emotions, and provide experiences otherwise not possible. Some drug use is planned and instrumental; for instance, taking caffeine to stay awake and complete a task. Some is planned for pleasure, such as drinking with friends. But many psychoactive substances act on motivation and learning mechanisms to increase intake steadily in the positive feedback pattern we call addiction. Most induce positive feelings, at least at first, but the liking systems that mediate subjective pleasure are only partially congruent with the wanting systems that motivate behavior.

The reinforcement mechanisms that maintain drug taking behavior are there for good reasons: learning is an adaptation that induces repeating behaviors that increase fitness. However, the system cannot tell the difference between a real orgasm and the rush from drug stimulation of dopamine receptors.

The reward system is sufficient to maintain drug use, but with-
drawal symptoms make it harder to quit. Continued stimulation by a drug induces adaptive desensitization of receptors, so withdrawal of the drug leaves the receptor unable to activate downstream processes, causing distress ranging from the headaches of caffeine withdrawal to epileptic seizures during alcohol withdrawal.

Most people are confident that they can control their behavior. This false belief greatly increases the risk of substance abuse. When they start using drugs or alcohol, people believe that they can stop whenever they choose. Depending on the drug, many people can stop using, making the risk seem abstract. But conscious decisions have a weak influence on behavior. Many people will stop using for a time, to demonstrate their control to themselves, before slipping back into a pattern of escalating use. As for so many behavioral disorders, positive feedback loops are at the root of the problem. Increased use changes the brain in ways that lead to further increased use. On top of that, substance abuse wrecks job, family and other sources of satisfaction, so that pleasure is soon available only from substances.

In summary, the standard evolutionary explanation for substance abuse is that novel substances can hijack learning mechanisms that were never protected from the effects of drugs, because these were not reliably available during most of our evolutionary history. From this perspective, drug abuse is a product of mismatch between evolved behavioral control systems and the ready availability of substances and routes of administration that were not present regularly in our evolutionary history. It is not an adaptation; it is an epiphenomenon arising from the effects of drugs on our chemically mediated motivation mechanisms.

The alternative explanation is that natural selection has shaped systems that motivate taking certain drugs because they have given a selective advantage to our ancestors. E.H. Hagen and colleagues have long argued that individuals may have obtained selective advantages from seeking and using drugs, especially nicotine. Indeed, nicotine is an effective anthelmintic that humans may use for deworming. The interesting question is whether those benefits increased connections between nicotinic receptors and reinforcing pathways in ways that increased survival, reproduction, and the rewards of smoking.

Mutations that increased our ability to metabolize alcohol emerged about 10 million years ago, about the time when our ancestors descended from trees and began eating more overripe fruit on the ground. Those with a preference for alcohol and a better ability to metabolize it would have gained advantages, but were those advantages just extra calories? Several authors have recently suggested that alcohol use may have facilitated the rise of civilization, or at least the cementing of bonds among group members, because the release of inhibitions increases bonding. Conversations over drink may be especially useful. These interesting hypotheses are hard to confirm.

How can all of this be useful in the clinic? Teaching people that their behavior is not nearly as much under their conscious control as they think would provide strong protection, but people are loathe to give up that belief. It would be wonderful if we could prevent initial drug use by telling young people that natural selection never shaped mechanisms to protect us against addiction, but youth are notoriously resistant to advice from their elders – possibly for the good evolutionary reason of avoiding manipulation. However, an evolutionary perspective on substance abuse can help to relieve stigma and encourage cooperation with treatment. Understanding the vicious cycles that escalate addiction helps in the difficult task of finding ways to stop them.

Much research is about why some individuals are more vulnerable to substance abuse than others. The risk is inheritable in a range from 72% for cocaine, to 50% for alcohol, to 3-40% for hallucinogens and opioids. But a polygenic risk score predicts only about 3% of the variance, and individuals in the highest decile have risks not significantly different from those in adjacent deciles. There is only moderate overlap between the risks for abuse of different drugs, so the notion of a drug seeking personality is only partially supported.

Men are more vulnerable than women. It is not clear if this results from the general tendency for men to take more risks, from the risks to the fetus of taking drugs while pregnant, or something else. It has been also suggested that taking drugs and heavy drinking may be displays of vigor to impress potential mates. While this may occasionally be a proximate motive, it seems unlikely to have been a selection force increasing motivation for drug use.

The influence of environmental factors is obvious. Individuals with few sources of pleasure in their lives are more likely to turn to drugs to make up the deficit. Those suffering from social distress or physical pain can get relief from drugs. Both groups are especially likely to get trapped in a positive feedback cycle. A number of life experiences can influence these factors: early abuse, unfair treatment, deprivation, injury, or simply being in an unfortunate life situation.

Concerning genetic differences that influence vulnerability, an evolutionary perspective suggests that they are not defects, but minor variations that likely had little influence on fitness until recent generations. Those variations might, however, have influenced normal behavior in the ancestral environment, for instance by affecting foraging strategies. If this is confirmed, there may be implications in terms of development of behavioral tests aiming to predict vulnerability to substance abuse.

EATING DISORDERS

Research on eating disorders illustrates the limitations of looking only for proximate mechanisms, and the opportunities and difficulties associated with seeking evolutionary explanations. The most fatal of all mental disorders, eating disorders have substantial symptom overlap, and their incidence has been increasing in recent decades, especially in developed countries.

Some papers that argue for the primacy of genetic factors suggest that many patients simply lose interest in eating, but this is not consistent with evidence that preoccupation with thinness and dieting precedes eating disorders in most cases. A GWAS on over 70,000 individuals found eight loci with statistically significant influences on the risk of anorexia nervosa, but effect
sizes were minuscule and a polygenic score including all available genetic information accounted for only 1.7% of the variation in risk. The genetic influences on anorexia nervosa are therefore unlikely to be abnormalities; they probably result from natural variation in psychological traits such as conscientiousness and neuroticism that can mediate risk in modern environments.

The evolutionary explanations proposed for eating disorders are diverse and confusing. For instance, some papers have suggested that restrictive eating might be an evolved strategy for postponing reproduction until more physical or social resources are available. However, natural selection has shaped a much more efficient and subtle system to turn off reproductive cycling when a pregnancy would be unlikely to result in a surviving offspring. When high levels of energy expenditure are not balanced by sufficient input, the system reverts follicle stimulating hormone (FSH) and luteinizing hormone (LH) to prepubertal levels, stopping reproductive cycling even at normal body weights. That is why cycling stops in some women athletes during times of intense training. This system works fine on its own; it needs no augmentation by food restriction that is likely to be fatal in a time of famine.

The “adapted to flee famine” hypothesis argues that the high exercise levels pursued by some patients with anorexia nervosa might be an evolved strategy that motivates running away from an area of famine to other locations where food is more available. However, individuals with anorexia exercise not to find food but to keep body weight low. Exercising while starving is not an adaptation, it is an aspect of a disease. Most studies of starving people report lethargy, not intense activity.

Yet another interpretation of anorexia nervosa as an adaptation proposes that it is induced by female-female competition for status in a group. It suggests that a woman can avoid attacks from other higher-status women by losing weight and thus demonstrating that she is not competing for mates and thus is not a threat. However, there are other more direct and safer ways to signal submission.

R.T. Abed and colleagues emphasize the competition among women to have body shapes that will make them desirable. In ancestral societies, the substantial physical effort needed to get limited supplies of food kept body shape variations small. In modern environments, human food preferences have shaped industries that provide ready access to cheap foods with whatever combinations of fat, salt, sugar, protein, taste and texture that people prefer. The resulting epidemic of obesity makes appearance more important than ever in sexual competition. The effect is magnified by mass media portrayals of body shapes that are caricatures of idealized extremes. Restrictive dieting seems like an obvious strategy to get a good mate and to also gain admiration for self-control. This sexual competition hypothesis provides a convincing explanation for extreme dieting and its excess prevalence in women in modern societies, but it does not fully explain eating disorders initiated by dieting for other motives, bulimia, and why the eating control system is so vulnerable to malfunction.

The eating control system was shaped to ensure protection against starvation in a trade-off with avoiding risks from being heavy and slow. Starvation is the more potent selection force, so protection against obesity is relatively weak. However, Nettle et al. note that natural selection has shaped a system that adjusts fat storage to food availability. When sufficient food supplies are reliably available, extra caloric stores are a useless burden. When food supplies are limited or erratic, the system motivates finding food, consuming it fast, and increasing the body weight set point to provide insurance against starvation.

Severe caloric restriction arouses the famine protection response, but attempts to block its effects can initiate a positive feedback cycle that sends the system out of control. Intense efforts at caloric restriction inevitably end in out-of-control eating episodes that magnify the fear of obesity and motivate redoubled commitments to restrict intake. The increased weight setpoint amplifies the fear. This combines with more hunger experienced at higher weights than previously, to spiral the system out of control.

Most people revert to their usual eating habits and weight after a period of deviation in either direction. Some persist in the patterns of bingeing and purging that characterize bulimia. A few control their eating, or at least their weight, by restriction, purging, extreme exercise, and the preoccupation about eating and body weight that characterize anorexia nervosa.

These ideas should be helpful in preventing eating disorders, as well as in their treatment. Learning that severe caloric restriction may finally result in weight gain should be a potent antidote to behavior patterns that initiate eating disorders. However, as in the case of substance abuse, the belief that conscious resolve can control behavior makes it hard to convince people that just deciding to stop eating is not necessarily a route to persistent thinness. Once established, eating disorders are much harder to control, because they give rise to a sense of identity that is tangled with eating and body weight, a sense of superiority compared to those with less self-control, and the determination to defy parents who are desperate to get their child to eat.

THE PERSISTENCE OF DELETERIOUS GENETIC VARIATION

The persistence of disease-causing alleles in the face of natural selection has been recognized as a paradox since the origins of evolutionary genetics. Proposed explanations have inspired debate for decades, but resolution now seems within reach, thanks to newly available genetic datasets and methods. Schizophrenia is the focus of the discussion below because it is the disorder that has generated most interest and research, but the general principles are also relevant for other disorders.

As recently as the turn of the millennium, there was hope that we would soon find the genes responsible for highly heritable diseases such as schizophrenia and bipolar disorder, but these expectations have been consistently frustrated. Instead of arising from common variants with large effects that code for proteins, the majority of the risk instead arises from thousands of
non-coding alleles with tiny effects. The prevalence of variants is inversely proportional to their effect size, a pattern consistent with purifying selection eliminating mutations with larger effects faster than those with smaller effects. Instead of being localized on some chromosomes, the loci associated with schizophrenia are scattered across the genome, with numbers on each chromosome proportional to the chromosome size.

Larger sample sizes and new family methods are now looking for, and finding, rare variants with larger effects, especially copy number variants and de novo mutations. These variants are estimated to account for only about 20% of the heritability of schizophrenia, but they could identify relevant neural circuits, and possibly suggest new treatments. As progress is made to identify all variants that increase the risk of schizophrenia, it is worth asking a large question: will finding them all provide a full explanation for schizophrenia? Most probably, it will also require understanding why the mind is vulnerable to the failure mode of schizophrenia. This may simply be the syndrome that results from a certain pattern of disorganized brain development. It is also possible, however, that the vulnerability results from a trait pushed to a performance peak despite associated risks of failure.

For fitness functions with a cliff edge, natural selection will push the trait to the point close to the peak that maximizes gene transmission over multiple generations, despite the low fitness experienced by the few individuals with values over the cliff. The situation gets more interesting when you consider that oscillation is expected between the value that maximizes single generation fitness despite costs to offspring and the value that maximizes gene transmission over multiple generations.

Previous hopes that specific genetic constellations would define specific disorders have also been upended. The diagnostic distinction between schizophrenia and bipolar disorder turns out to be far less crisp than had been assumed. Their genetic correlation of 72% arises from the many alleles that increase the risk of both disorders. Genetic correlations are pervasive among all mental disorders, much more so than for neurological disorders. However, this is a fast-developing area, and current methods neglect the role of assortative mating in overestimating genetic correlations.

These findings are consistent with the hypothesis that mutation-selection balance is responsible for the persistence of most disease-causing alleles. Human individuals each have about 70 mutations that are not present in their parents, one of which, on average, is in a protein coding region. Beneficial new mutations are exceedingly rare. Deleterious ones are selected out with a speed proportional to their reduction in fitness, but new ones replace them, maintaining the balance between mutation and selection.

However, interesting evolutionary questions remain. Are some alleles maintained by selection which gives advantages in some individuals or situations balancing their costs in others? Are increased intelligence or creativity associated with some alleles for schizophrenia, autism or bipolar disorder? Do alleles with immune functions that help to shape the developing brain also protect from infection?

All these questions are of interest, but the larger evolutionary question is why certain systems are so vulnerable to failing in typical ways. Are some systems intrinsically vulnerable to failure because they have been shaped to a performance peak adjacent to a cliff edge where fitness plummets? Are some control systems shaped to high gain despite the unavoidable risk of instability? Answering these questions is an important long-term project.

Polygenic risk scores for bipolar disorder and schizophrenia can predict creativity scores, but it is very hard to tell if measures of creativity might be confounded by the kinds of jobs open to people who have severe disorders. Cognitive ability can be measured more reliably. Of 75 genomic loci jointly associated with schizophrenia and intelligence, 81% were associated with lower cognitive performance, while of 12 alleles associated with bipolar disorder and intelligence, 75% were associated with higher performance. These are intriguing clues to an unsolved mystery.

A different approach considers the possible role of rapid selection for traits that became useful during the major transition to the social cultural niche in the past few hundred thousand years. T.J. Crow wrote extensively about the possibility that psychosis could be the price we pay for the capacity for language. We are now on the verge of confirming that some health problems can be attributed to wrenching major transitions in which a new niche or strategy selects strongly for traits that make other traits vulnerable because of anatomic, physiologic or pleiotropic constraints. The exemplar is the transition to bipedality and its legacy of vulnerability to hernias, hemorrhoids, back pain, knee pain, plantar fasciitis, varicose veins, and omental torsion. It is painful to imagine how prevalent these problems must have been in the first million years of bipedality.

The wrenching transition to the cognitive social niche may have created even more severe problems, considering the path-dependent interactions of multiple alleles that influence brain development pathways. Imagine a new allele changing the chemical gradients that influence neuronal migration during brain development in ways that give a benefit, perhaps something like more expressive vocalization. If this gives a net selective advantage, the allele will be selected for, despite negative effects that slightly disrupt multiple other adaptations that evolved previously.

A recently proposed model suggests that the development of social brain, language and high-order cognitive functions transformed many neutral alleles into risk alleles for schizophrenia. Around 100,000-150,000 years ago, there was a “turning point” when the number of those alleles plateaued. A steady decline then began due to natural selection, that also increased the proportion of protective alleles. This hypothesis is supported by the evidence that older alleles are more likely to increase the risk of schizophrenia and newer ones are more likely to decrease it, and by some epidemiological evidence suggesting that the incidence of schizophrenia is declining.

CONCLUSIONS

The main conclusion of this overview is simple: evolutionary biology is a basic science that has a lot to contribute to psychiatry. It provides a scientific framework that is missing from psychia-
try but foundational for the rest of behavioral science. It is not an alternative to the search for brain mechanisms; it is a complementary framework that can integrate diverse bio-psycho-social approaches. It is not a new method of treatment, but it helps all methods of treatment by putting emotional disorders in the context of normal functioning. For patients, this reduces stigma and tendencies to self-identify as diseased persons. For clinicians, this offers new ways to describe mental disorders and how treatments work. For researchers, it offers new questions whose answers will inspire new approaches to research on brain mechanisms. These practical benefits of evolutionary psychiatry are ready for application, but a larger possible conclusion deserves consideration.

A new paradigm?

Calls for new directions in psychiatry have echoed for decades, but new data give them greater urgency. Fifty years ago, the field decided to emulate the rest of medicine and find the specific abnormalities that cause mental disorders. The DSM-III categories were expected to be replaced when the responsible brain abnormalities were found. The ensuing search has produced vast new knowledge about brain mechanisms and many statistically significant differences in the brains of patients compared to controls, but no specific abnormality has been detected that accounts for any major mental disorder, and no biological test has been developed that can diagnose any disorder. New data confirm that genes influence the risk for many mental disorders, but most influences are from common variants that increase risk by less than 1%, and their effects are not specific to one disorder. Many research leaders have acknowledged that current research strategies are failing, but most suggested new approaches continue to assume that mental disorders are caused by specific brain abnormalities that we can find and use to define specific diseases.

The search for these abnormalities has been based on a tacitly creationist view of the body as a machine with discrete parts that have specific functions and simple connections that were envisioned by a sensible designer. An evolutionary perspective suggests that the complexity of organic systems is not only greater than that of designed systems; it is different in kind. One function is distributed among many parts, one part can serve many functions, and organic control systems are integrated networks of recursive connections that make organic systems more robust than designed systems, but also vulnerable to failure because they are operating in new environments, because they are shaped to maximize fitness at the expense of health, and because they are riddled with trade-offs that increase performance at the cost of robustness. As for brains, they are jury-rigged marvels, not of design, but of natural selection, that leaves them vulnerable because each genetic variant which improves one function and overall fitness may disrupt many others.

Different brain loci have different functions, but they are not as specific as we might like. For instance, the amygdala has long been described as the source of fear, but new research shows that “the amygdala is not required for the experience of fear” and that “defining brain functions in an impactful way is not trivial and it amounts to figuring out how to measure something that we often do not yet fully understand.”

Evolutionary psychiatry may offer a new paradigm. It asks different questions, provides different kinds of explanations, and views disorders in a new way. Identifying negative emotions as adaptive symptoms that are prone to dysregulation is fundamental. It suggests that diagnostic criteria for anxiety and depression that ignore possible causes are as invalid as a diagnosis of “cough disorder” that does not look for pneumonia or allergies. It views behavioral disorders as products of control system failures instead of specific brain lesions. And it asks why some systems are especially vulnerable to failure from many different causes, in the same way that internal medicine understands the many factors that can contribute to heart failure.

This paradigm will not be welcomed quickly for several reasons. The first is that few mental health professionals or researchers know much about evolutionary biology; many still do not realize that evolutionary explanations are needed in addition to proximate explanations. The second is that work in this area is exceptionally difficult, in large part because of conceptual confusion about what are appropriate objects of evolutionary explanation. Speculations about possible benefits from diseases and traits that are present only in some individuals are often so intriguing that they spread widely despite being false.

However, a third explanation may be the most important. It is desperately disappointing to have to acknowledge that organic complexity is a tangled bank that defies description using the simple boxes and arrows that we so crave. We love science when it simplifies. But an evolutionary view of mental disorders reveals a murky world of organic complexity that lacks the sharp boundaries and specific functions that satisfy our lust for order.

Talk about paradigms may be premature for a nascent field that is just now finding its footing. To discover what evolutionary psychiatry can accomplish and how it can help will require work by many people over many decades. The next step is providing clinicians and researchers with the basic evolutionary principles that ground the rest of behavioral biology, along with strategies for applying them critically to better understand and treat mental disorders. This paper is a first step in this direction.

ACKNOWLEDGEMENTS

The author would like to thank K. Boomsma, G. Guaiana, S. Stearns, M. Maj and C. Stonnington for very helpful comments and suggestions.

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