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Evolutionary Explanations for Mood and Mood Disorders

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Evolution and Behavior

The evolutionary principles that have made possible major advances in the understanding of animal behavior (Alcock 1997) are just now being applied to the challenge of understanding human emotions and affects (Barkow et al. 1992; Buss 1995; Konner 2002; Plutchik 1980; E. O. Wilson 1978). In this chapter, I summarize some of those advances and some attempts to use them to better understand mood and its disorders.

Much of the opportunity, and much of the difficulty, arises because evolutionary questions about behavior and emotions are fundamentally different from proximate questions (Mayr 1983). Most medical research is about how the body's mechanisms work, how they go awry, and why some individuals become sick and others do not. Evolutionary questions, by contrast, do not ask about how the body works but instead ask why it is the way it is in all members of a species—what historical sequences, selective advantages, and other evolutionary forces account for traits being the way they are and why they fail in the ways they fail (G.W. Williams and Nesse 1991). Methods for test-

ing postulated answers can only sometimes use the familiar experimental method; they much more often use the comparative method or assessments of design features in the light of hypothesized functions (Reeve and Sherman 1993; Rose and Lauder 1996).

Although most of the recent work on mood is at the preliminary stage of attempting to formulate the correct questions and suggest possible answers, enough specific proposals have now been made and assessed to provide the rudiments of an understanding of why natural selection shaped a capacity for mood at all and why it is so likely to cause problems (Morris 1992). Before moving to those issues, a very brief overview of some recent advances in animal behavior will provide a basis for the discussion.

Two generations ago, the field of animal behavior was mostly descriptive, but it has been transformed by an evolutionary approach (Alcock 2001; Krebs and Davies 1997). The most fundamental advance is recognition that all biological traits need not only explanations of their proximate mechanisms (ranging from molecules to perceptual stimuli and cognitive and emotional mechanisms) but also evolutionary explanations of the selection forces that shaped those mechanisms. These are not alternatives

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but complementary components of a complete explanation (Tinbergen 1963). For instance, previous studies of bird song were only descriptive, perhaps with some attention to development and possible functions. Now, researchers not only correlate the duration, quality, and volume of songs with characteristics of the singers but also try to determine if the singing serves to defend territories or advertise for mating partners or both.

The study of animal behavior also has been transformed by the demise of naïve group selection theories and recognition of the roles of kin selection (Hamilton 1964a, 1964b) and reciprocity (Trivers 1985) in shaping social behaviors. Behavioral traits must be explained in terms of how they increase the frequency of genes that code for them, not in terms of the benefit to the species (G.C. Williams 1966). This is not the place to provide full explanations of these advances or to describe the many other ways that considerations of evolutionary function have transformed the field of animal behavior into a theoretically based quantitative science (Alcock 1997). Recognizing this transformation is essential, however, because it has been the inspiration for attempts to use the same principles to understand human psychopathology (McGuire and Troisi 1998; McGuire et al. 1992).

These attempts to use the same principles have aroused great interest but much accompanying misunderstanding and unnecessary controversy (Buss et al. 1998; Queller 1995; Segerstråle 2000). The sociobiology wars are mostly over, and evolutionary studies of human behavior are now thriving despite their difficulties (Barrett et al. 2002). Most everyone involved recognizes that natural selection shaped human behavior-regulation mechanisms but that the human niche is distinctive and that much work remains to show how the forces of natural selection shaped the brain mechanisms that result in emergent social forces and the complexity and diversity of human behaviors (Barkow 1989; Buss 1995). Furthermore, the previous tendency to conflate behavioral genetics and evolutionary approaches to behavior is a mistake now made only rarely, and recognition is growing that a functional approach to behavior is not just not reductionistic; it is the strongest scientific antidote for reductionism. A functional approach studies the regulation of behavior at high levels of organization, relying heavily on facultative mechanisms that adjust behavior to changing circumstances. Neuroscience unravels pathways and their molecular mediators, whereas evolutionary approaches examine how those mechanisms give a selective advantage by making it possible for organisms to gather and process information that adapts their behavior to rapidly changing environments (Krebs and Davies 1984). To offer a single example, a junco given the choice to forage at a feeder that provides

three or four seeds every visit or at a feeder that provides the same mean with much more variability will choose the low-risk feeder in usual circumstances. However, if the temperature decreases from room temperature to freezing, the juncos instead prefer the more risky choice. Why? At freezing temperatures, the rate of caloric gain at the less risky feeder is too slow for them to survive the night, whereas the risky strategy offers at least some chance of survival (Caraco et al. 1990).

Evolutionary Explanations of Disorders

The other major roadblock to applying evolutionary ideas to depression has been the difficulty of seeing how selection can help to account for a disease. It seems obvious that natural selection can explain adaptive mechanisms but not defects in design. The solution to this difficulty is recognizing that although selection does not shape diseases directly, it is responsible for leaving bodies with vulnerabilities that result in diseases (Nesse and Williams 1994). From this perspective, the question becomes, for each disease, why natural selection did not design the body to be more resilient and resistant to disease. Why do we have wisdom teeth and an appendix? Why has selection not shaped better immune defenses and more effective ways of eliminating cancerous cells? Why are our bones and backs not stronger? Why do so many people experience debilitating episodes of depression?

A systematic approach to questions about the body's vulnerabilities has proved useful in the rest of medicine (Stearns 1998) and may prove even more useful in psychiatry (McGuire and Troisi 1998). In simplified outline, there are six reasons that natural selection might leave an aspect of the body vulnerable to disease (Nesse and Williams 1994). First, we live in an environment substantially different from the environment in which we evolved, and many diseases, including most chronic diseases such as addictions, obesity, and atherosclerosis, result from this mismatch (Eaton et al. 1988; Trevathan et al. 1999). Second, we remain susceptible to infection because pathogens evolve so much faster than we do (Ewald 1994). Both of these initial evolutionary explanations for disease arise because natural selection is a slow process.

The third reason for vulnerability is that no trait in the body can be perfect—all are tradeoffs. For example, if the radius and ulna were thicker, they would break less readily, but we would lose the invaluable ability to rotate our wrists. The fourth reason is that natural selection is subject to many limitations. It is subject to random happenstances that may increase the frequency of deleterious genes, and it also can never start over to correct a mistake; it works only by gradual increments. Like our poorly laid

out QWERTY keyboards, our bodies are stuck with many suboptimal designs resulting from path dependence, such as our inside-out eyeballs with vessels that come between the light and the retina.

The fifth explanation is that we misunderstand what natural selection shapes. Many people imagine that it shapes bodies for health, longevity, or even happiness, but, alas, only reproductive success influences the frequency of genes in the next generation. As a result, we have many behavioral tendencies that advance the interests of our genes even as they harm our own lives, such as the notable and too often fatal bravado of young men (M. Wilson and Daly 1985). Also, the desperate goal pursuits associated with some depressions are likely ones that may benefit the individual's genes at great cost to the individual.

Finally, many responses that superficially appear to be diseases, such as fever and cough, are actually sophisticated mechanisms that help to protect us in certain circumstances. It is obvious to most people that pain can be useful, but less well known is that people born with no capacity for pain usually die by age 35 (Sternbach 1963). The utility of coughing and vomiting to clear foreign materials and toxins is obvious, but there is less recognition that the aversiveness of these experiences is a part of their design. Although the utility of anxiety is widely recognized, no one has yet systematically looked for people who have the psychiatric disorder of deficient anxiety (Marks and Nesse 1994).

Evolutionary Questions About Depression

This brief background about evolutionary approaches to behavior and to medical disorders provides a framework for formulating the evolutionary questions about depression. The global question is why depression exists at all. Each of the six evolutionary reasons for disease deserves consideration, but the last possibility is most fundamental and must be considered first. Does depression arise, like cancer and stroke, from a defect in the body's machinery; or is it, like fever and pain, a protective defensive response; or is it, like chronic pain or febrile seizures, a complication or maladaptive extreme of a useful response? The lack of agreement on an answer to this question accounts for much of the confusion that surrounds depression research. An answer, even if tentative and supported mainly by circumstantial evidence, would provide a framework for integrating our knowledge about depression and for posing new research questions.

On cursory examination, the answer seems clear. Depression is so disabling and so often fatal that it seems obvious that it must arise from a defect. As many who have

had severe depression testify, the depths of melancholic depression are so physical and pervasive that any suggestion that the condition could have utility seems risible (Wolpert 1999). In my view, this is indeed sufficient evidence that severe depression is a pathological state without adaptive utility. Not all agree, however, and there are reasons for caution in accepting any conclusion on the matter too readily. Normal severe physical pain can make people completely unable to function. Even the fever, cough, fatigue, and malaise of the normal inflammatory reaction to influenza cause disability equal to all but the most severe depressions. The simple fact of intense suffering and disability is not in itself adequate evidence that depression has no useful function.

The closely related relevant question is whether the capacity for mood variation within the normal range is an adaptation or an epiphenomenon. It is certainly possible that depression has no specific function but is an epiphenomenon (Akiskal 2001). There are, however, several reasons that some believe that low mood is a useful response: it is universal, it is regulated by important and consistent aspects of the environment, it influences behavior in tangible ways, and major disruptions of the system (i.e., mood disorders) compromise function and decrease fitness (Morris 1992). Because *depression* is so often defined as a pathological state, the more generic phrase *low mood* will be used here to refer to a range of depression-like states that range from clearly normal to the possibly pathological.

Epidemiology

Several epidemiological facts about depression appear fresh in an evolutionary perspective. First, its vast prevalence, so high that it will soon be the greatest cause of disability-adjusted lost years in modern societies (Murray and Lopez 1997), argues strongly against its arising from some bodily defect, unless, like atherosclerosis, it results from living in an environment to which we are poorly suited (Eaton et al. 1988). Given the extraordinary near-perfection of most physiological systems, from renal physiology to the immune responses and our cognitive capacities, it would be most unlikely for a disorder as severe and prevalent as depression to arise simply from poor design.

Second, and even more striking, the age at onset is at the prime of life. Some cases start in childhood and some late in life, but the incidence of new onsets peaks in early adulthood when selection is the strongest (Weissman et al. 1996). This makes depression epidemiology quite dif-

ferent from that of almost all medical diseases. Although a few medical disorders have their peak rates of onset early in life, the incidence of most diseases rises steadily in adulthood. This is because of the good evolutionary reason that reproductive value is highest at sexual maturity, and therefore selection is strongest at this age (G. C. Williams 1957). Over the course of evolution, this has resulted in selection for modifier genes that push the expression of deleterious effects of genes and related disease onsets to later (and occasionally earlier) in the life span. The mystery of why depression tends to have its onset at just the age when everything else in the body is at its functional peak may be explained by the conflicts associated with the coincident peak of competition for mates and status.

The third epidemiological factor cast in a new light is the overwhelming influence of adverse life events on depression onset. This is often conceptualized in a model in which stressors act on mechanisms with preexisting vulnerability to cause damage and failure (Brown et al. 1986; Kessler 1997). In an alternative model, however, low mood could be, like pain, a normal and useful response to certain kinds of threats. The prevalence of mild depressive symptoms (Kessler et al. 2003), the role of certain adverse life events in precipitating or worsening these symptoms (Monroe et al. 2001), the continuous distribution of depression severity with no zone of rarity that separates pathological from more mild depression (Ruscio and Ruscio 2002), and the superior performance of models based on continua instead of categories (Angst and Merikangas 2001; Judd et al. 1998) all weigh toward considering the possibility that depression, or at least low mood, serves some defensive reaction (Morris 1992).

Evolution and Emotions

A general evolutionary framework for understanding emotions and affects is essential for considering low mood, and depression in particular. As is the case with the field of animal behavior, emotions research is now routinely based on evolutionary biology (Oatley and Jenkins 1996; Plutchik and Kellerman 1989). Work continues on just how many basic emotions there are and how they are shaped in the course of development (Ekman and Davidson 1994), but now general agreement is that the generic emotional capacities of human and animal emotions were shaped by natural selection (Oatley and Jenkins 1996). Although some approaches still try to identify the function or functions of each emotion, there is growing agreement that the organizing factor for each emotion is not its

function but the situation in which it gives a selective advantage (Nesse 1990; Tooby and Cosmides 1990). In this perspective, there is no need to argue about which aspect of an emotion is primary; cognitive, physiological, behavioral, expressive, and subjective aspects of emotions are all components of a coordinated suite of changes that helps the organism cope with the adaptive challenges of a situation that has recurred over evolutionary history. Likewise, there is no need to look for a single function; an emotion's many aspects may serve multiple functions to meet the several challenges that are associated with a situation. In panic, for instance, the physiological arousal, tendency to freeze, preoccupation with finding routes of escape, and subjective anxiety are all useful in situations that involve life-threatening danger. The positive or negative valence of emotions is expected because emotions would not be shaped for neutral situations but only for those that involve opportunities or threats. The fact that related emotional states are only partially differentiated from one another is likewise expected, and this makes it unnecessary to insist on a sharp distinction between emotions and longer-duration affects and moods (Oatley and Bolton 1985). Emotions and affects need to be understood in terms of the situations in which they are useful, the adaptive challenges of those situations, and how the characteristics of the emotion or affect help to meet those challenges (Clark 1992).

This view implies that it is a mistake to think that some emotions are inherently more useful than others. All are useful in certain circumstances and harmful in other circumstances. There is a pervasive tendency, so prevalent that it has been called "the clinician's illusion," to think of aversive states as problems instead of solutions. In medicine, this has been manifest in reflexive tendencies to prescribe drugs to block pain, fever, diarrhea, nausea, vomiting, and cough without pausing to consider their utility. This habit does little harm only because natural selection has shaped both redundant defenses and regulation mechanisms that express inexpensive defenses, such as cough and fever, according to the "smoke detector principle"—in which many false alarms are justified to be sure of responding to each actual incident of genuine threat (Nesse 2005). In psychology, a welcome turn to positive psychology has tended to seek evidence that positive feelings are generally beneficial (Seligman and Csikszentmihalyi 2000) and has attempted to understand why they are elusive (Buss 2000; Nesse 2004). Positive feelings certainly are preferable, and in the safe setting of most technological societies, they tend to be more beneficial than negative feelings. However, the core fact remains that whether an expression of an emotion is useful or harmful depends entirely on the situation.

In What Situations Is Low Mood Useful?

This background about emotions makes it possible to pose the question about low mood and depression more exactly. That is: In what situations that recurred over evolutionary history would the characteristics of low mood or depression have offered a selective advantage? Nearly a dozen partially overlapping answers have been suggested. Some were originally phrased in terms of functions, but transforming them to hypotheses about situations in which these states would be useful makes them more comparable. This is the core of current work on evolution and depression.

Situations that cause low mood are most generically associated with loss. The loss can be of property, relationships, status, health, or any other resource. Sadness caused by loss shares many features with low mood and depression, but if the loss is discrete and life can go on, then sadness is quite different from depression. It does not have the hopelessness, the global lack of motivation, or the low self-esteem and tendencies toward guilt that typify depression. Can sadness have any useful function? Certainly, losing resources is an important situation that has recurred in the lives of every one of our ancestors. Those who had a special reaction would have several possible advantages. Among the ways that sadness can be useful are

- Motivation to regain the lost resource
- Motivation to replace the lost resource
- Avoidance of situations similar to the one that resulted in the loss
- Thinking of ways to protect other resources
- Adjustment of strategies that cannot go forward in the same way without the resource
- Thinking about the situation that led to the loss to find ways to prevent future losses
- Making reparations if the loss was caused by violating a norm or a relationship partner's expectations

The exemplar of loss is the experience of infants who are separated from their mothers as studied by John Bowlby and Harry Harlow (Bowlby 1973; Harlow and Harlow 1962). Bowlby's seminal contribution was to interpret this situation in an evolutionary context in which the infant's and mother's reactions made adaptive sense. In particular, the initial protest was seen as an attempt to signal location and need to the mother, whereas the more passive "despair" phase was seen as a way to avoid predation and conserve resources if the mother was away for an

extended period. The apparently abnormal kinds of attachment he and others described (Ainsworth et al. 1978) have now been themselves reconsidered in evolutionary terms as possible facultative adaptations that infants may make to mothers with different tendencies and abilities to provide care (Belsky 1999; Chisholm 1996). The utility of passivity in situations in which resources are scarce gave rise to the phrase *conservation-withdrawal*, with emphasis again on the situation of the infant (Engel and Schmale 1972; Schmale and Engel 1975).

Loss of a relationship in adulthood usually has been interpreted in the context of attachment, with grief as the exemplar (Wortman et al. 1993). It is crucial to determine whether grief is a response shaped to cope with the loss of a loved one or an epiphenomenon of attachment. The most extensive treatment is by John Archer, who concluded that grief seems too maladaptive and too closely connected to attachment to be useful (Archer 1999). It could well be that attachments are so constrained that loss necessarily means grief or that the pain of anticipated loss is essential to the functions of attachments. However, there does not seem to be any reason that individuals could not be shaped to provide deep altruism and affection to kin who are alive and to move on without great disability after they die. Furthermore, the profound pain of grief may itself have utility to prevent future losses and to cope with the situation of having to make fundamental adjustments in life. The question is unanswered (Nesse 2000b).

A more general situation in which depression might be useful is any circumstance in which help is needed. This is consistent with crying and other low mood signals that could bring help. Aubrey Lewis (1934) emphasized this function, and it is also central in more recent treatments (Sloman et al. 1994; Watson and Andrews 2002). The general irritability of depressed patients and the wish of most people to avoid them weigh against this as a main function (Coyne et al. 1987), but data are not yet available to determine whether mild depression usually elicits help from others. The demise of extended family groups in recent decades makes the social environment fundamentally different in ways that may change the utility of pleas for help.

Perhaps the best-developed proposal is that depression is useful after loss of a status conflict. John Price (1967) originally put the hypothesis forward on the basis of animal and clinical observations that continued striving after a loss led to brutal attacks, whereas "involuntary yielding" signaled submission and ended the battle. He further developed this position in collaboration with several colleagues who have reported studies in which unwillingness to yield was associated with depression and yielding was associated with remission (Price et al. 1994;

Sloman and Price 1987; Stevens and Price 1996). This is supported by some data showing superior social judgment capacity after a low mood induction (Badcock and Allen 2003). The strength of this position is that it helps to explain the low self-esteem and lack of striving in depressed patients; exactly these traits would protect against attack, and they are the most difficult to account for otherwise. In a related vein, Hartung (1988) suggested that especially capable people often may need to conceal their abilities from their superiors to avoid attack, thus explaining some cases of depression and the self-handicapping so characteristic of neurosis.

A more general framework treats striving for status as one of many goals whose pursuit can lead to depression if there is no way to succeed but also no way to disengage (Nesse 1999, 2000a). Hamburg et al. (1975) provided an early elaborated biological model:

A feeling of sadness and discouragement sets in [when] the subject estimates the probability of effective action is low.... Depressive responses can be viewed as adaptive...in a medium range of intensity. Feelings of sadness and discouragement may be a useful stimulus to consider changing [the] situation...sadness may elicit heightened interest and sympathetic consideration on the part of significant other people. (p. 240)

In psychology, Klinger (1975) offered the most comprehensive early treatment. Since then, the model has been elaborated and further developed by many others (Brickman 1987; Diener and Fujita 1995; Emmons 1996; Higgins et al. 1997; Janoff-Bulman and Brickman 1982; Palys and Little 1983; Pyszczynski and Greenberg 1987). The importance of this work has received little recognition in psychiatry, however. Carver and Scheier's (1990, 1998) research showed that mood is influenced not by the degree of goal attainment but by the rate of approach compared with the expected rate of approach. Moving toward a goal faster than expected raises mood, whereas evidence that reaching the goal will take more time or effort than expected lowers mood. Persisting in the pursuit of a goal despite the low mood's signaling the need to disengage arouses increasingly strong and eventually pathological depression. This was at the heart of Bibring's (1953) long-admired psychoanalytic paper on depression that emphasized the central role of highly cathected desires that could not be fulfilled. A very similar focus on the role of goal pursuit is at the heart of McGuire and Troisi's (1987, 1998) recognition of the role of unrealistic wishes in depression. In a reanalysis of the best-detailed life events data available, Brown et al. (1995) found that the risk of depression is not increased equally by all severe life events; situations that involve humiliation or entrapment

are much more likely to result in depression. This was interpreted as being consistent with the involuntary yielding functions of low mood, but it provides equal support for a broader view of the importance of inescapable but unreachable goals.

All of these authors recognized that there must be a mechanism for maintaining persistence in goal pursuit despite obstacles, but there also must be some mechanism for disengaging motivation from a goal when it is clear that the goal is unobtainable. Most of the research has been done on college students, but the perspective is even more powerful in the clinic. One woman's depression is precipitated by the realization that her efforts to help her daughter escape from drug addiction and likely death are futile. Another cannot stop her husband's binges but will not give up on the marriage. Some graduate students get halfway through a rigorous program, only to realize that others are doing better, no amount of work can compensate, and no other career path seems viable. In addition, millions of workers, laid off in midlife, only gradually realize that their efforts to attain comparable positions will never succeed.

This perspective also offers a possible explanation for sex differences in vulnerability to depression (Wenegrat 1995) and for why rates of depression are so high in certain modern environments (Weissman et al. 1996). Globally, media exposure and mass society increase the reference group and the range and grandeur of possible goals and possible selves to the point at which none of us can succeed, even aside from the fact that the images we see are increasingly realistic media-created fantasies (Sloman and Gilbert 2000). On a more personal level, the life goals of ordinary people are now larger and longer in duration than they were in past generations, with required investments so huge and prolonged that failure leaves few viable alternatives. This perspective also offers a framework for considering mechanisms by which personality traits may contribute to depression; intense ambition, strong attachments, fear of being alone, and a tendency to put all of life's meaning on one large goal are all traits that make it more likely that a person will find himself or herself trapped in pursuit of an unreachable goal.

Closely related is the suggestion that the capacity for mood was shaped to allocate resources and effort among various environments and strategies that vary in their propitiousness (Nesse 1999, 2000a). A situation that offers temporarily rich rewards for little effort deserves the intense effort and risk-taking made possible by high mood. Unpropitious situations, in which efforts are more expensive than gains, are best escaped or avoided. If one is stuck in such a situation, it is best to exert little effort and take few risks. If the overall life circumstance offers

no current strategy in which the effort or risk is greater than the cost, the best thing to do is...nothing. The model is based on foraging theory, in which an optimally foraging animal moves to a new patch when that is worthwhile despite the time and effort of finding a new patch (Charnov 1976). When the cost of finding a new patch exceeds the overall mean rate of return, further foraging exerts a net cost and should stop until the situation becomes more propitious.

Human foraging patterns seem to follow these principles, but the resources that humans mainly strive for are not calories, but relationships, status, and the welfare of children and kin. The categories of effort used by behavioral ecologists are helpful in looking at the tradeoffs that bedevil human lives (Krebs and Davies 1997):

1. Somatic effort
 - Obtaining resources to grow and develop
 - Defending against predators, pathogens, and loss of resources
2. Reproductive effort
 - Mating
 - Parenting and helping kin
3. Social effort
 - Building relationships and alliances
 - Striving for status and power

As with every other species, humans must allocate effort among these different tasks, and every allocation to one detracts from the others (Heckhausen and Schultz 1995; Little 1999). A person who works 80 hours a week has little time or energy for taking care of children, or even taking care of self. Someone who is enmeshed in status striving will have little time and energy left for finding a mate, whereas preoccupation with making oneself an attractive mate can undermine other pursuits. However, this issue is even more complex. Different strategies in pursuit of different goals will pay off in some situations but not in others. It is essential to allocate effort to what is paying off here and now. More specifically, we should expect organisms to allocate effort according to what I call the “central Darwinian algorithm”: optimal allocation of resources and effort to different enterprises requires taking whatever possible current action will give the greatest marginal gain in reproduction-limiting resources. Developmental aspects of this principle are intuitively obvious: people invest in status displays when groups are forming, they look for mates at sexual maturity, they invest enormous effort in family when they have young children, and they become generative later in life. However, from day to day and month to month, some

pursuits will be viable but others will not. A mechanism to disengage motivation from unproductive pursuits fosters reallocation to more productive strategies and enterprises (Klinger 1975; Wrosch et al. 2003). When essential investments in one area fatally deprive another area, the resulting stress should be no surprise. Most so-called life crises arise from precisely this kind of Hobson’s choice. For instance, the single working mother of a chronically ill child may face the impossible choice of either keeping her job or caring for her child.

Although everyday mood variations reallocate effort among various enterprises according to what is and is not working, the same mechanism is relevant to global mood variations that reflect the productivity of efforts in all domains. When all available avenues in life appear to offer few rewards, a global pullback from habitual efforts may be warranted to avoid wasted effort and risks and to have a chance to consider possible alternative directions (Gut 1989). When such withdrawal leads to a fundamental new direction in life, depression often remits.

Situations in which efforts appear to be futile are the basis for the influential “learned helplessness” perspective on depression (Seligman 1972). Dogs that experience inescapable shock will, when a barrier is removed, stay in the shock chamber, even though they could escape. This has been used as a model for humans with depression who remain in bad situations that they could escape. The central message has been that many depressed people are far more pessimistic about their plight than is justified and far less helpless than they think they are (Seligman et al. 1979). This perspective has led to helpful interventions designed to give people a sense of increased efficacy (Peterson et al. 1993). The same perspective is found in cognitive therapy, which seeks and finds evidence of cognitive distortion and unjustified pessimism that can be corrected with systematic cognitive retraining (Beck 1976).

What has been somewhat absent from the learned helplessness literature, however, is attention to the origins of the mechanisms that result in dogs staying where they are shocked. The stimulus is so unnatural that it is difficult to tell what is actually going on. Does the pain arouse systems shaped to cope with loss of a hierarchy battle? Have dogs that persisted in the face of related natural situations fared even worse?

A clue is offered by the Porsolt test, which measures the duration of active swimming for rats dropped in a beaker of water. Drugs that prolong swimming time often have proved to be effective antidepressants in this model (Porsolt et al. 1978). A closer, ecological analysis found something different, however (Nadeau 1999). When the rats stop swimming, they do not just drown; they float

quietly, with just their noses above the water. This is not a pathological helpless response but a useful adaptation for a rat swept into deep water when there is no quick way out. Rats that swim too vigorously for too long will certainly drown sooner. This makes a sobering prediction: in a natural situation, and likely even in a beaker in a laboratory, rats given antidepressants will drown sooner than those given placebo.

Attempts to bring the literature about self-esteem into an evolutionary framework have begun. Sociometry theories suggest that self-esteem is designed to indicate one's position in a group, with low self-esteem signaling the need to invest more in the group or to consider giving up on the group (Leary and Baumeister 2000). Further research suggests that people whose self-esteem is contingent on achieving goals set by others, or contingent on rising in a hierarchy, are vulnerable to depression as compared with those who pursue more "noble goals" or personal goals that do not involve social comparison (Crocker and Wolfe 2001). An explicitly evolutionary perspective recognizes competition everywhere and sees the task of adapting to it as central to life (Gilbert 1997; Gilbert et al. 1995), with depression playing an essential role in coping with status loss. In an elaboration and variation, Allen and Badcock (2003) suggested that people carefully monitor their social investment potential; when they perceive it as low and are at risk of being excluded from the group, a state of depression offers protection by inhibiting risk-taking and increasing monitoring of others' assessments. A different slant on related phenomena notes the prevalence of guilt and, especially, survivor guilt as vulnerability factors for depression and the social utility of capacity for guilt (O'Connor et al. 2002).

In situations characterized by a nonviable central life goal or strategy, it may be best to quit striving and to invest effort and time instead in mulling over the situation in preparation for possible major changes. Emmy Gut (1989) has written particularly well about these benefits of low mood when a fundamental reappraisal is needed. The benefits of pulling back and reconsidering all options without being distracted by constant pressures and striving are also central to many other presentations about the utility of depression. In particular, the social navigation hypothesis proposed by Watson and Andrews (2002) emphasizes the utility, in the face of social damage, of experiencing an emotion akin to physical pain and of sending honest signals to kin that the current situation is unworkable. They summarized evidence that depressive thinking is in some respects more realistic, but whether this is really an adaptation or simply a move toward accuracy from the usual rose-colored view (Sedikides 1993) is not certain. Neither is it clear that depression actually motivates

others to help more (Coyne et al. 1987), although Hagen (2002) provided some evidence that postpartum depression does engage helping and improves some outcomes.

Watson and Andrews (2002) have supported Hagen's (2002) suggestion that depression may have been shaped specifically to manipulate others into providing help, either after childbirth or in any social situation in which a person can influence others only by going "on strike." These ideas fit well with certain themes in behavioral ecology in which all animal communications are seen as manipulations (Krebs and Dawkins 1984) and in which the honesty of such signals is guaranteed only by high costs (Zahavi and Zahavi 1997) of the sort that are present in depression. The possibility that depression could have such a manipulation or extortion function is odious to those who are striving to remove stigma from depression, and the main evidence in favor of it is the otherwise explainable data that depression is more common in people who are in untoward circumstances. A critique of the social navigation hypothesis and adaptationist hypotheses in general suggests that wide trait variation offers a simpler explanation (Nettle 2004). The test will be whether others really do respond to these signals with predicted help that is greater than the huge costs of being depressed and with more help than they would offer to a different kind of request for aid.

Assessment of Functions of Low Mood and Depression

Despite the variety of hypotheses proposed for possible functions of low mood and depression, the main possibilities refer to just a few situations: loss of position in a hierarchy, changes in propitiousness of goal pursuit more generally, and communication with and manipulation of others by signaling a need for help or by failing to contribute to essential tasks. As noted earlier, testing evolutionary hypotheses about the selective forces that shaped a trait is quite a different and more difficult enterprise than testing proximate hypotheses about structures and mechanisms. The main differences encountered in testing evolutionary, as compared with proximate, hypotheses are that evolutionary hypotheses are not mutually exclusive, so evidence against one hypothesis is not strong evidence for alternative hypotheses. The difficulties of finding and using comparative data mean that the assessment often comes down to whether a trait's characteristics sufficiently match those expected to justify support for the hypothesis. Although such methods do not offer the strong inference that is so often available in testing proximate hypotheses (O'Donohue and Buchanan 2001; Platt

1964), the complications do not mean that the questions are impossible to answer—only that they are difficult and that hypothesis assessment requires considerable judgment in addition to relevant data.

The universal experience of low mood and its close regulation by circumstances involving unrewarded efforts or absence or loss of crucial resources or rank in a hierarchy offer support for the hypothesis that it has some adaptive function related to regulation of behavior. Nonetheless, investigators are just beginning to determine the exact circumstances that arouse normal low mood, what adaptive challenges they contain, and how some characteristics of low mood could help to meet those challenges. A closely related protective response, anxiety, seems to have been differentiated into a cluster of partially overlapping subtypes, each shaped to cope with a specific kind of danger (Marks and Nesse 1994). Thus, animal phobias, social phobias, and panic disorder show differences as well as overlapping symptoms, and people vulnerable to one kind of anxiety are often also vulnerable to others (Barlow 1988). This idea is just now being applied to depression, but preliminary studies suggest that the symptoms of depression arising from failure are different from those arising from loss or lack of a crucial resource (Keller and Nesse 2005). More detailed data allowing comparison of depression symptoms for cases with different precipitants may help to resolve the question.

Another major unanswered question is whether these findings about ordinary low mood and mild depression have anything to do with serious depression. They could be as little associated as the muscle stiffness after exercise and the muscle stiffness encountered in parkinsonism. The question is difficult, but the possibilities are clear. Depression could itself be 1) an adaptation to certain situations (akin to fever), 2) a pathological extreme of a normal response (akin to chronic pain), 3) a pathological complication (akin to the dehydration that can result from diarrhea), or 4) pathology unrelated to normal mood and its regulation (akin to Parkinson's disease). The position taken here is that answering the question about the situations in which low mood is helpful is a necessary but incomplete precursor to questions about full-fledged depression. Furthermore, there may well be subtypes of low mood, each shaped to cope with different situations.

Differences in Vulnerability to Depression

Explaining why individuals differ in their vulnerability to depression is an entirely different question from the ques-

tion of why all humans have a capacity for low mood. An evolutionary perspective does offer useful directions regarding this question, however. The high heritability of vulnerability to depression is well recognized (Wallace et al. 2002). The evolutionary question is whether the responsible genes are simply mutations not yet selected out or whether their prevalence is maintained for some reason (Houle 1998). In addition, variation in vulnerability results from differences in early experiences. In this case, the question is whether the effects are best understood as effects of facultative mechanisms that adjust the organism to its environment or as the results of experiences that damage brain mechanisms. I consider genetic differences first.

Genetic Differences

At first blush, it seems as if genes that make individuals vulnerable to depression must be defective mutations that selection has not yet been able to eliminate. Even aside from the severe selective effect of suicide, the disability and social costs associated with recurrent depression must have decreased reproductive success, even in Paleolithic times. However, extensive efforts have thus far failed to find single genes that account for more than 5% of the variation in the risk for depression. Geneticists are increasingly cautioning that depression appears to be a polygenic disease whose risk may depend on dozens of genes, in which case the force of selection becomes so tiny that mutations can persist for many generations and even drift to higher frequencies, despite some small negative effect of selection (Risch and Merikangas 1996). Furthermore, massive epigenetic effects may mean that the effects of a gene on phenotype may vary considerably from individual to individual, thus helping to explain the persistence of considerable genetic and associated phenotypic diversity. This all seems quite likely.

Trait Variation and Selection

However, considering the functions of low mood and related regulation mechanisms suggests possibilities beyond the simple notion of genetic mutation and the limited power of selection. If low mood can be a useful response in certain situations, then genetic variations will influence the threshold and intensity of the response, with maximum fitness at some intermediate level. The perils of excessive low mood are obvious, but deficits in capacity for low mood also should reduce Darwinian fitness. Furthermore, the fitness of different degrees of responsiveness may change dramatically with changes in the environment. Optimistic investors did well in the late

1990s but lost their gains and more in the early years of the new millennium, while pessimists reaped profits from bonds. Likewise, in secure environments of plenty, a deficient tendency to low mood may be optimal, but at times of famine, political unrest, and rigid hierarchies, those who lack a capacity for low mood may be at a serious disadvantage. In practical terms, it would be extremely difficult to differentiate individuals who lack a normal capacity for low mood from those who have simply been fortunate in life. However, if new antidepressants ever become both reliably effective and free from most side effects, tests of this idea will be carried out, whether wittingly or unwittingly, as we observe the lives of those who lack the normal capacity for low mood.

The optimal baseline level of mood and the optimal mood change in response to unpropitious circumstances are two distinct traits shaped by different selection forces. The optimal level of general stable mood will vary depending on the nature of the long-term environment, but if the main value of the capacity for mood is to adjust behavior so that investments and risk-taking are increased or decreased in concert with changes in propitiousness, the absolute level of mood may have relatively little influence on fitness; more will depend on the ability to change behavior in the right direction at the right time. If this is correct, then selection may act only weakly on the absolute level of baseline mood compared with its actions on the responsiveness of mood to environmental variations.

Much attention has been paid to the possibility that it may be difficult to identify genes for mental disorders because the heritable factors may differ in different lineages; less attention has been paid to the possibility that genes can lead to depression via their effects on intermediate states. The evidence that exposure to life events is heritable is striking but is obvious in retrospect, given what we know about genetic influences on sensation seeking and other personality traits that correlate with experiencing many life events (Kendler and Karkowski-Shuman 1997). Less obvious is the possibility that genes may increase vulnerability to depression by influence on temperament (Ono et al. 2002), which makes it more likely that certain people will get themselves into situations where they cannot disengage from the pursuit of unreachable goals. As already noted, several routes often lead to such situations. Extreme ambition, of the sort sometimes associated with neuroticism, makes it likely that an individual will constantly feel inadequate and unable to accomplish what seem to be essential life goals. A tendency to make very strong attachments is likely to result in continuing a relationship and trying vainly to improve it, despite abuse or lack of love. A tendency to have only a few attachments, or only one big life goal, provides fewer options when

things go badly. Extreme moral compunctions also are often associated with situations that make it difficult to escape from exploitation. General fearfulness also inhibits individuals from taking the risks necessary to get out of bad situations, as may a general lack of self-esteem. Most general of all, a tendency to see one's life in terms of one overpoweringly important central goal makes it more likely that the person will find himself or herself trapped in a nonviable overall life situation.

These ideas are somewhat theoretical but have important implications not only for the general view of genetic effects on mood but also for specific research strategies. In particular, they suggest the need to conduct phenotyping that goes beyond mere enumeration of symptoms and episodes. An ecologically based phenotyping would incorporate the relation of specific symptoms to not only the number of severe life events but also the nature of those life events; the individual's temperament, values, and life goals; and how the life events influence assessments of ability to progress toward those goals. It is conceivable that it will be possible to identify different routes to depression associated with specific genes that increase depression vulnerability—a degree of gene–environment interaction that may be essential to consider despite its complexity.

Balancing Selection

Yet another possibility is that genes that cause depression give a selective advantage either via pleiotropic effects or by benefits that accrue only in certain environments or in combination with certain other genes. This has been proposed most specifically in the case of bipolar disorder, for which the costs of illness are even more horrendous than they are for unipolar depression and in which some potential benefits are obvious (Jamison 1993; D.R. Wilson 1998). The grand creativity, sexual attractiveness, and disinhibition of people in the throes of mania give a clear route to short-term reproductive success. The more moderate but sustained productivity of those with hypomania offers another route (Akiskal 2003), but if higher mood reliably offered a fitness benefit, it already should have spread unless there were significant tradeoffs. Even aside from the advantages and disadvantages associated with clinical syndromes, close relatives of those with bipolar disorder might experience benefits without the costs associated with clinical disorders. There is ample evidence for increased creativity of people with manic depression, and some convincing evidence shows that their relatives also are more creative than average (Andreasen 1987; Richards et al. 1988). Whether they are especially sexually attractive or successful is another unanswered question.

Genes for bipolar disorder could be selected for if the creativity associated with mania benefits the group to an extent that outweighs the costs to the individual. It is certainly plausible that groups with more creative individuals tend to succeed and displace those without such inspiration. However, one of the main recent advances in evolutionary biology has been recognition that the power of selection acting at the level of the group is too weak to counteract any but the tiniest deleterious effects on individuals. While lemming groups might well do better if many of their members drown themselves when there is too little food, there will always be variation in the tendency to commit suicide for the good of the group, and genes that incline individuals against such self-sacrifice will soon take over despite the dire effects of uncontrolled population growth.

A control systems view suggests examination of mood as a trait regulated in the same way as body temperature or hemoglobin concentration. Values that are above or below a reference value initiate homeostatic mechanisms that restore the baseline value (Cziko 2000). In certain conditions, however, different levels give an advantage, and rheostatic mechanisms adjust the set point accordingly (Mrosovsky 1990). In infections, a higher body temperature helps to fight the pathogens. When individuals live at high altitude, low oxygen tension stimulates erythropoietin, which raises hemoglobin concentration to an appropriate level.

In any feedback-regulated system, cyclic oscillations are expected. If a thermostat turns on a furnace whenever the temperature drops below a set point, then the furnace will still be pouring out heat when the set point is reached, so the temperature will overshoot the optimal level. To minimize the range of these variations, most modern thermostats use anticipation mechanisms that turn on the furnace just before the set point as the temperature falls and turn it off just before the set point as the heat from the furnace raises the temperature. The cycles in cyclothymic disorder match what one would expect if there were a defect in the anticipation mechanism, with wide swings precipitated by small perturbations. The more severe extremes of manic depression are better characterized by uncontrolled positive feedback that leads to extremes of effort, energy expenditure, and lack of sleep that escalate until a shutdown mechanism sends the system crashing into depression. The characteristic sudden switch from mania to depression matches this pattern. Note that these principles do not depend on what brain mechanisms actually instantiate them, any more than it matters whether a furnace thermostat mechanism uses a bimetal strip or a digital detector.

Although these ideas about bipolar disorder are important to pursue, no concrete evidence so far indicates

that bipolar genes give any selective advantage. It seems likely that they are simply defects that interfere with the evolved mechanisms that normally regulate mood. Nonetheless, epidemiological studies have not yet addressed systematically the possibility that selection maintains the frequency of the responsible genes.

Adjustment of Mood Mechanisms as a Function of Life Experience

Extensive evidence documents the effects of early life events on vulnerability to depression (Lin et al. 1986). Attachment difficulties and lack of parental love lead to problematic relationships and increased risks for depression (Beatson and Taryan 2003; Sloman et al. 2003). Other early childhood adversity, especially sexual abuse, increases the risk for depression (Harkness and Monroe 2002). Although some studies have not controlled for possible genetic mediation of the effects, it seems clear that some experiences do influence rates of depression. The question posed by an evolutionary view is whether these effects are best interpreted as damage from abnormal experiences or whether they result from properly functioning facultative mechanisms that monitor certain aspects of the environment and adjust mood mechanisms adaptively.

The exemplar is the relation between disorders of attachment and later depression. Early work treated secure attachment as normal and other kinds of attachment as pathological results of faulty parenting. Newer approaches consider the additional possibility that variation in family conditions over the course of human history made anxious and ambivalent attachment styles advantageous in certain circumstances (Belsky 1999; Chisholm 1996). This hypothesis is difficult to test but is supported by the prevalence of insecure attachment styles, their association with parental difficulty or ambivalence, and the surprising lack of heritability of attachment styles.

The best-documented and strongest risk factor for depression is previous low mood or depression (Kessler et al. 2003), and the stimulus required to set off depression seems to decrease with each subsequent episode so that the onset of depression becomes increasingly autonomous from life events (Kendler 1998). This has been interpreted as akin to the "kindling" phenomenon that makes neurons increasingly vulnerable to seizures after repeated stimulation (Post and Weiss 1998). Whether or not neural kindling is the responsible proximate mechanism, an evolutionary view asks if the change in threshold results simply from damage, or if repeated exposure to certain situations engages a mechanism that adjusts the low mood threshold accordingly and adaptively.

Certainly, other response thresholds are adjusted in light of experience, the most notable being the reduction in panic threshold after a life-threatening experience (or even after a “spontaneous” panic attack).

Population Differences in Vulnerability

Extensive evidence documents the substantial differences in rates of depression in different populations (Brown et al. 1996; Weissman et al. 1996). Some of these differences may arise from variations in reporting and cultural differences in the expression of depressive symptoms (Kleinman and Good 1985), but increasing standardization of methods allows confidence that rates do vary enormously in different groups. The simplest explanation is that differing social conditions expose people in some groups to more severe life events than others. Although differences in rates of severe life events are correlated with rates of depression, no one has examined whether systematic differences in the motivational structures of people’s lives in different societies might provide an even more powerful explanation for different rates of depression. Resource allocation/goal disengagement theory predicts that depression should be more prevalent in populations where many people make enormous investments in just a few major life goals that have an uncertain payoff and no ready alternatives. Conversely, depression should be less common in groups where people pursue more limited and more relationship-related goals that offer more social support and more options if efforts to reach one particular goal fail.

The more salient population variations from an evolutionary perspective are those between ancestral and modern populations. Some studies looking for changes in depression rates in recent decades have reported positive findings (Klerman and Weissman 1989) and some have not (Murphy et al. 2000). However, the evolutionary question is whether novel aspects of the environment have increased vulnerability to depression in the same way that the ready availability of fatty and sweet foods has increased rates of atherosclerosis. Unfortunately, no reliable evidence regarding these rates is available, not even evidence on rates of depression in surviving groups of hunter-gatherers. Although methodological obstacles are high, including small group sizes and different languages, data on rates of depression in these groups may prove as crucial as the data showing that hunter-gatherers have very low rates of hypertension, obesity, and atherosclerosis. Social differences are especially salient, but many other factors could adversely influence brain mechanisms in modern environments, including artificial light, abnormal sleep patterns, dietary deficiencies of omega 3 relative to omega 6 fatty acids, and low levels of exercise.

Although gene–environment interactions in the causes of depression are now widely appreciated (Caspi et al. 2003; Kendler 1997), their implications for the effects of novel environments are still being recognized. When essentially all members of a population are exposed to evolutionarily novel environmental factors, much of the within-population variation in rates of pathology will arise from genetic differences that had no significant effects on ancestral conditions. It is thus incorrect to call these genes “defects.” They are better recognized as “quirks” that become significant only when they interact with a novel environment. Many genes that predispose to atherosclerosis are examples. Variation in traits such as nearsightedness or atherosclerosis in a modern population might well be overwhelmingly genetic in origin, even though the pathogenesis requires exposure to an environmental factor, such as abnormalities in diet or early exposure to small print.

Whether genetic differences exist between groups that might influence rates of depression is unknown. Recent findings of population differences that influence the rates of other diseases offer examples, and group differences in the prevalence of the short genotype for the serotonin promoter transporter allele are interesting, but no solid evidence shows that genetic differences explain different rates of depression. The case of seasonal affective disorder offers a particularly intriguing test. If seasonal affective disorder is a defect, then populations that have lived in extreme northern or southern latitudes gradually would have been shaped to resist the syndrome as compared with populations from areas where light levels are more stable, unless it simply reflects the slowness of selection (Sher 2000). If, however, the seasonal changes in mood are useful adaptations in areas with extreme seasonal climate variations, then populations that evolved in extreme latitudes should have increased tendencies to experience winter depression.

Research Implications

An evolutionary perspective on depression has two main implications for research. The first is the need to seriously consider and test hypotheses about the evolutionary origins and functions of low mood and its possible relation to clinical depression. The second is to call attention to the possibility that we have been studying all cases of major depression as if they represent the same condition, when different individuals may get depressed by very different routes (Akiskal and McKinney 1973). Closely related is the possibility that selection has partially differ-

entiated subtypes of depression to deal with different kinds of situations that have recurred over evolutionary history. If this is the case, then it will be essential to define depression subtypes on the basis of contributing etiological factors and to further subtype cases of depression on the basis of the nature of the precipitating life situation.

An evolutionary perspective has further implications for brain studies. Such studies seem to be moving from models based on presumed brain defects to models based on mechanisms that regulate normal and abnormal mood. However, if low mood is useful, then it seems possible that many of the brain changes associated with depression are not themselves pathological but may represent the activation of an adaptive defense mechanism. The anatomical localization of areas of increased activity in states of depression (Davidson et al. 2003) tends to support this position. If depression involves mechanisms that adaptively inhibit motivation, then effective drugs and physical treatments would not be expected to work at just one site. Instead, disruption of the low mood system at any of several points should lead to improvement, in the same way that pain can be relieved by drugs that disrupt cytokine systems at several different points or that act on opiate receptors. Furthermore, the genetic differences in vulnerability to depression may be similar to individual differences in tendency to get fever with a cold or variations in tendency to vomit in response to chemotherapy or other toxins.

Clinical Implications

Despite attempts to find ways that evolutionary views might make psychotherapy more effective (Gilbert and Bailey 2000; Weisfeld 1977), an evolutionary perspective does not specify a particular kind of treatment for depression. Its attention to the normal functions of low mood should, however, offer a useful foundation for clinical psychiatric practice in the same way that an understanding of the functions and causes of cough, fever, and vomiting provide a foundation for the practice of general medicine. Unfortunately, we are not yet in a position to offer this kind of basic science functional knowledge for the clinical practice of psychiatry. Our understanding of the proximate mechanisms involved with depression has far outstripped our understanding of what those mechanisms might be for, with much resulting confusion.

A central issue among members of the lay public is whether depression is really a disease or whether it is a normal response to certain situations. We can confidently answer the question in the case of severe, recurrent de-

pression, but we still lack the kind of understanding that would allow us to address the question scientifically for a wide range of moods and situations. This has important implications for the psychiatric diagnosis in general and for planning for DSM-V in particular. Although the exclusion of contextual factors from diagnostic criteria fosters reliability, it makes the DSM criteria incapable of distinguishing responses that are excessive from those that are normal and useful (Nesse 2001; Wakefield 1992, 1997). An evolutionary perspective offers a solid foundation for diagnosis, one only now being appreciated (Cosmides and Tooby 1999; Wakefield 1999). If pain disorders were diagnosed in the same way, the diagnosis of chronic pain would depend on only the duration and intensity of symptoms, not on the presence or absence of a cause for the pain. The exclusion of ordinary grief already protects against some false-positive diagnoses of depression. As we develop a more confident and refined understanding of the normal functions and regulation of low mood, it should be possible to differentiate aversive but normal responses from pathological conditions with criteria more scientifically based than merely severity and duration.

The evolutionary insight with the most direct clinical utility, prefigured by many clinicians, may be the normal role of low mood in disengaging individuals from goals they cannot reach. This principle does not need to be derived from evolutionary principles; it has been developed, elaborated, and confirmed by psychologists over the past four decades. So far, however, it is little appreciated in psychiatry and has not been applied to clinical populations. From Bibring to Beck and forward, expert clinicians often have focused on what people are trying to do in their lives, why they persist in trying to please others who cannot be pleased, why they try to impress others who will not be impressed, and why they persist in unrequited love. Although it usually turns out to be difficult to help people to reassess such situations and their options, this perspective has shown enduring usefulness that could be augmented by a growing evolutionary sophistication in understanding its origins and significance and the broader framework of goals that people pursue. It could also help to unite apparently diverse therapeutic approaches, each of which intervenes at one or another point in the systems that maintain depression. As with any powerful tool, however, careless application will cause harm. There is no justification for crudely analyzing a person's main life efforts and advising him or her to change. The clinical challenge is the same as it has always been—trying to understand people and their relationships, goals, and feelings in order to understand, and help them understand, why they do what they do and why they feel what they feel. That, in

combination with new diagnostic tests, genomic findings, and effective new drugs that block depression, will offer a bright future for treating depression.

References

- Ainsworth MD, Blehar MC, Waters E, et al: Patterns of Attachment: A Psychological Study of the Strange Situation. Hillsdale, NJ, Lawrence Erlbaum, 1978
- Akiskal HS: Dysthymia and cyclothymia in psychiatric practice a century after Kraepelin. *J Affect Disord* 62:17–31, 2001
- Akiskal HS: The evolutionary significance of affective temperaments. CME article presented at the 156th annual meeting of the American Psychiatric Association, San Francisco, CA, May 17–22, 2003. Available at: <http://www.medscape.com/viewarticle/457152>.
- Akiskal HS, McKinney WTJ: Depressive disorders: toward a unified hypothesis. *Science* 182:20–29, 1973
- Alcock J: *Animal Behavior: An Evolutionary Approach*. Sunderland, MA, Sinauer, 1997
- Alcock J: *The Triumph of Sociobiology*. New York, Oxford University Press, 2001
- Allen NB, Badcock PBT: The social risk hypothesis of depressed mood: evolutionary, psychosocial and neurobiological perspectives. *Psychol Bull* 129:887–913, 2003
- Andreasen NC: Creativity and mental illness: prevalence rates in writers and their first-degree relatives. *Am J Psychiatry* 144:1288–1292, 1987
- Angst J, Merikangas KR: Multi-dimensional criteria for the diagnosis of depression. *J Affect Disord* 62:7–15, 2001
- Archer J: *The Nature of Grief*. New York, Oxford University Press, 1999
- Badcock PBT, Allen NB: Adaptive social reasoning in depressed mood and depressive vulnerability. *Cognition and Emotion* 17:647–670, 2003
- Barkow JH: Darwin, Sex, and Status: Biological Approaches to Mind and Culture. Toronto, Ontario, University of Toronto Press, 1989
- Barkow J, Cosmides L, Tooby J (eds): *The Adapted Mind*. New York, Oxford University Press, 1992
- Barlow DH: *Anxiety and Its Disorders*. New York, Guilford, 1988
- Barrett L, Dunbar RIM, Lycett J: *Human Evolutionary Psychology*. Basingstoke, UK, Palgrave, 2002
- Beatson J, Taryan S: Predisposition to depression: the role of attachment. *Aust N Z J Psychiatry* 37:219–225, 2003
- Beck AT: *Cognitive Therapy and the Emotional Disorders*. New York, International Universities Press, 1976
- Belsky J: Modern evolutionary theory and patterns of attachment, in *Handbook of Attachment: Theory, Research, and Clinical Applications*. Edited by Cassidy J, Shaver PR. New York, Guilford, 1999, pp 141–161
- Bibring E: The mechanisms of depression, in *Affective Disorders*. Edited by Greenacre P. New York, International Universities Press, 1953, pp 13–48
- Bowlby J: *Separation: Anxiety and Anger*. New York, Basic Books, 1973
- Brickman P: *Commitment, Conflict, and Caring*. Englewood Cliffs, NJ, Prentice-Hall, 1987
- Brown GW, Bifulco A, Harris T, et al: Life stress, chronic sub-clinical symptoms and vulnerability to clinical depression. *J Affect Disord* 11:1–19, 1986
- Brown GW, Harris TO, Hepworth C: Loss, humiliation and entrapment among women developing depression: a patient and non-patient comparison. *Psychol Med* 25:7–21, 1995
- Brown GW, Harris TO, Eales MJ: Social factors and comorbidity of depressive and anxiety disorders. *Br J Psychiatry Suppl* 30:50–57, 1996
- Buss DM: Evolutionary psychology: a new paradigm for psychological science. *Psychological Inquiry* 6:1–30, 1995
- Buss DM: The evolution of happiness. *Am Psychol* 55:15–23, 2000
- Buss DM, Haselton MG, Shackelford TK, et al: Adaptations, exaptations, and spandrels. *Am Psychol* 53:533–548, 1998
- Caraco T, Blanckenhorn B, Gregory G, et al: Risk sensitivity: ambient temperature affects foraging choice. *Anim Behav* 39:338–345, 1990
- Carver CS, Scheier MF: Origins and functions of positive and negative affect: a control-process view. *Psychol Rev* 97:19–35, 1990
- Carver CS, Scheier MF: *On the Self-Regulation of Behavior*. New York, Cambridge University Press, 1998
- Caspi A, Sugden K, Moffitt TE, et al: Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. *Science* 301:386–389, 2003
- Charnov EL: Optimal foraging: the marginal value theorem. *Theor Popul Biol* 9:129–136, 1976
- Chisholm J: The evolutionary ecology of human attachment organization. *Hum Nat* 7:1–38, 1996
- Clark MS: *Emotion*. Newbury Park, CA, Sage Publications, 1992
- Cosmides L, Tooby J: Toward an evolutionary taxonomy of treatable conditions. *J Abnorm Psychol* 108:453–464, 1999
- Coyne JC, Kessler RC, Tal M, et al: Living with a depressed person. *J Consult Clin Psychol* 55:347–352, 1987
- Crocker J, Wolfe CT: Contingencies of self-worth. *Psychol Rev* 108:593–623, 2001
- Cziko G: *The Things We Do*. Cambridge, MA, MIT Press, 2000
- Davidson RJ, Irwin W, Anderle MJ, et al: The neural substrates of affective processing in depressed patients treated with venlafaxine. *Am J Psychiatry* 160:64–75, 2003
- Diener E, Fujita F: Resources, personal strivings, and subjective well-being: a nomothetic ideographic approach. *J Pers Soc Psychol* 68:926–935, 1995
- Eaton SB, Konner M, Shostak M: Stone agers in the fast lane: chronic degenerative diseases in evolutionary perspective. *Am J Med* 84:739–749, 1988
- Ekman P, Davidson RJ (eds): *The Nature of Emotion: Fundamental Questions*. New York, Oxford University Press, 1994

- Emmons RA: Striving and feeling: personal goals and subjective well-being, in *The Psychology of Action: Linking Cognition and Motivation to Behavior*. Edited by Gollwitzer PM. New York, Guilford, 1996, pp 313–337
- Engel G, Schmale A: Conservation-withdrawal: a primary regulatory process for organismic homeostasis, in *Physiology, Emotion, and Psychosomatic Illness*, Vol 8 (N.S.). Edited by Porter R, Night J. Amsterdam, CIBA, 1972, pp 57–85
- Ewald P: *Evolution of Infectious Disease*. New York, Oxford University Press, 1994
- Gilbert P: The evolution of social attractiveness and its role in shame, humiliation, guilt and therapy. *Br J Med Psychol* 70:112–147, 1997
- Gilbert P, Bailey KG: *Genes on the Couch: Explorations in Evolutionary Psychotherapy*. East Sussex, UK, Brunner/Routledge, 2000
- Gilbert P, Price J, Allen S: Social comparison, social attractiveness and evolution: how might they be related? *New Ideas in Psychology* 13:149–165, 1995
- Gut E: *Productive and Unproductive Depression*. New York, Basic Books, 1989
- Hagen EH: Depression as bargaining: the case postpartum. *Evol Hum Behav* 23:323–336, 2002
- Hamburg DA, Hamburg BA, Barchas JD: Anger and depression in perspective of behavioral biology, in *Emotions: Their Parameters and Measurement*. Edited by Levi L. New York, Raven, 1975, pp 235–278
- Hamilton WD: The genetical evolution of social behaviour, I. *J Theor Biol* 7:1–16, 1964a
- Hamilton WD: The genetical evolution of social behaviour, II. *J Theor Biol* 7:17–52, 1964b
- Harkness KL, Monroe SM: Childhood adversity and the endogenous versus nonendogenous distinction in women with major depression. *Am J Psychiatry* 159:387–393, 2002
- Harlow HF, Harlow MK: Social deprivation in monkeys. *Sci Am* 207:136–146, 1962
- Hartung J: Deceiving down, in *Self Deception: An Adaptive Mechanism?* Edited by Lockard JS, Paulhus D. Englewood Cliffs, NJ, Prentice-Hall, 1988, pp 170–185
- Heckhausen J, Schultz R: A life-span theory of control. *Psychol Rev* 102:284–304, 1995
- Higgins ET, Shah J, Friedman R: Emotional responses to goal attainment: strength of regulatory focus as moderator. *J Pers Soc Psychol* 72:515–525, 1997
- Houle D: How should we explain variation in the genetic variance of traits? *Genetica* 102/103:241–253, 1998
- Jamison KR: *Touched With Fire: Manic-Depressive Illness and the Artistic Temperament*. New York, Free Press, 1993
- Janoff-Bulman R, Brickman P: Expectations and what people learn from failure, in *Expectations and Action*. Edited by Feather NT. Hillsdale, NJ, Lawrence Erlbaum, 1982, pp 207–237
- Judd LL, Akiskal HS, Maser JD, et al: Major depressive disorder: a prospective study of residual subthreshold depressive symptoms as predictor of rapid relapse. *J Affect Disord* 50:97–108, 1998
- Keller MB, Nesse RM: Is low mood an adaptation? Evidence for sub-types with symptoms that match precipitants. *J Affect Disord* 86:27–35, 2005
- Kendler KS: The genetic epidemiology of psychiatric disorders: a current perspective. *Soc Psychiatry Psychiatr Epidemiol* 32:5–11, 1997
- Kendler KS: Major depression and the environment: a psychiatric genetic perspective. *Pharmacopsychiatry* 31:5–9, 1998
- Kendler KS, Karkowski-Shuman L: Stressful life events and genetic liability to major depression: genetic control of exposure to the environment? *Psychol Med* 27:539–547, 1997
- Kessler RC: The effects of stressful life events on depression. *Annu Rev Psychol* 48:191–214, 1997
- Kessler RC, Berglund P, Demler O, et al: The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA* 289:3095–3105, 2003
- Kleinman A, Good B: *Culture and Depression: Studies in the Anthropology and Cross-Cultural Psychiatry of Affect and Disorder*. Berkeley, University of California Press, 1985
- Klerman G, Weissman M: Increasing rates of depression. *JAMA* 261:2229–2235, 1989
- Klinger E: Consequences of commitment to and disengagement from incentives. *Psychol Rev* 82:1–25, 1975
- Konner M: *The Tangled Wing: Biological Constraints on the Human Spirit*. New York, Times Books, 2002
- Krebs JR, Davies NB (eds): *Behavioral Ecology: An Evolutionary Approach*. Sunderland, MA, Sinauer, 1984
- Krebs JR, Davies NB: *Behavioral Ecology: An Evolutionary Approach*. Oxford, England, Blackwell Science, 1997
- Krebs J, Dawkins R: Animal signals: mind-reading and manipulation, in *Behavioral Ecology: An Evolutionary Approach*. Edited by Krebs JR, Davies NB. Sunderland, MA, Sinauer, 1984, pp 380–402
- Leary MR, Baumeister RF: The nature and function of self-esteem: sociometer theory, in *Advances in Experimental Social Psychology*, Vol 32. Edited by Zanna MP. San Diego, CA, Academic Press, 2000, pp 2–51
- Lewis AJ: Melancholia: a clinical survey of depressive states. *J Ment Sci* 80:1–43, 1934
- Lin N, Dean A, Ensel WM: *Social Support, Life Events, and Depression*. New York, Academic Press, 1986
- Little BR: Personal projects and social ecology: themes and variation across the life span, in *Action and Self Development: Theory and Research Through the Life Span*. Edited by Brandtstadter J, Lerner RM. Thousand Oaks, CA, Sage Publications, 1999, pp 79–87
- Marks IM, Nesse RM: Fear and fitness: an evolutionary analysis of anxiety disorders. *Ethol Sociobiol* 15:247–261, 1994
- Mayr E: How to carry out the adaptationist program? *American Naturalist* 121(March):324–333, 1983
- McGuire MT, Troisi A: Unrealistic wishes and physiological change: an overview. *Psychother Psychosom* 47:82–94, 1987
- McGuire MT, Troisi A: *Darwinian Psychiatry*. Cambridge, MA, Harvard University Press, 1998

- McGuire M, Marks I, Nesse R, et al: Evolutionary biology: a basic science for psychiatry. *Acta Psychiatr Scand* 86:89–96, 1992
- Monroe SM, Harkness K, Simons AD, et al: Life stress and the symptoms of major depression. *J Nerv Ment Dis* 189:168–175, 2001
- Morris WN: A functional analysis of the role of mood in affective systems. *Review of Personality and Social Psychology* 21:736–746, 1992
- Mrosovsky N: *Rheostasis*. New York, Oxford University Press, 1990
- Murphy JM, Laird NM, Monson RR, et al: A 40-year perspective on the prevalence of depression: the Stirling County Study. *Arch Gen Psychiatry* 57:209–215, 2000
- Murray CJ, Lopez AD: Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet* 349(9063):1436–1442, 1997
- Nadeau B: The forced swim test: an empirical and rational analysis of immobility and its reduction by antidepressants. Unpublished doctoral thesis, Department of Psychology, Simon Fraser University, Vancouver, BC, 1999
- Nesse RM: Evolutionary explanations of emotions. *Hum Nat* 1:261–289, 1990
- Nesse RM: The evolution of hope and despair. *J Soc Issues* 66:429–469, 1999
- Nesse RM: Is depression an adaptation? *Arch Gen Psychiatry* 57:14–20, 2000a
- Nesse RM: Is grief really maladaptive? Review of *The Nature of Grief*, by John Archer. *Evol Hum Behav* 21:59–61, 2000b
- Nesse RM: On the difficulty of defining disease: a Darwinian perspective. *Med Health Care Philos* 4:37–46, 2001
- Nesse RM: A signal detection analysis of the smoke detector principle. *Evol Hum Behav* 26:88–105, 2005
- Nesse RM: Natural selection and the elusiveness of happiness. *Philos Trans R Soc Lond B Biol Sci* 359:1333–1347, 2004
- Nesse RM, Williams GC: *Why We Get Sick: The New Science of Darwinian Medicine*. New York, Vintage, 1994
- Nettle D: Evolutionary origins of depression: a review and reformulation. *J Affect Disord* 81:91–102, 2004
- Oatley K, Bolton W: A social-cognitive theory of depression in reaction to life events. *Psychol Rev* 92:372–388, 1985
- Oatley K, Jenkins JM: *Understanding Emotions*. Cambridge, MA, Blackwell, 1996
- O'Connor LE, Berry JW, Weiss J, et al: Guilt, fear, submission, and empathy in depression. *J Affect Disord* 71:19–27, 2002
- O'Donohue W, Buchanan JA: The weakness of strong inference. *Behavior and Philosophy* 29:1–20, 2001
- Ono Y, Ando J, Onoda N, et al: Dimensions of temperament as vulnerability factors in depression. *Mol Psychiatry* 7:948–953, 2002
- Palys TS, Little BR: Perceived life satisfaction and the organization of personal project systems. *J Pers Soc Psychol* 44:1221–1230, 1983
- Peterson C, Maier SF, Seligman MEP: *Learned Helplessness*. New York, Oxford University Press, 1993
- Platt JR: Strong inference. *Science* 146:347–353, 1964
- Plutchik R: *Emotion: A Psychoevolutionary Synthesis*. New York, Harper & Row, 1980
- Plutchik R, Kellerman H (eds): *Emotion: Theory, Research, and Experience*. New York, Academic Press, 1989
- Porsolt RD, Anton G, Blavet N, et al: Behavioral despair in rats: a new model sensitive to antidepressant treatments. *Eur J Pharmacol* 47:379–391, 1978
- Post RM, Weiss SR: Sensitization and kindling phenomena in mood, anxiety, and obsessive-compulsive disorders: the role of serotonergic mechanisms in illness progression. *Biol Psychiatry* 44:193–206, 1998
- Price JS: The dominance hierarchy and the evolution of mental illness. *Lancet* 2:243–246, 1967
- Price J, Sloman L, Gardner R, et al: The social competition hypothesis of depression. *Br J Psychiatry* 164:309–315, 1994
- Pyszczynski T, Greenberg J: Self-regulatory perseveration and the depressive self-focusing style: a self-awareness theory of reactive depression. *Psychol Bull* 102:122–138, 1987
- Queller DC: The spaniels of St. Marx and the Panglossian paradox: a critique of a rhetorical programme. *Q Rev Biol* 70:485–489, 1995
- Reeve HK, Sherman PW: Adaptation and the goals of evolutionary research. *Q Rev Biol* 68:1–32, 1993
- Richards RL, Kinner DK, Lunde I, et al: Creativity in manic-depressives, cyclothymes and their normal first-degree relatives: a preliminary report. *J Abnorm Psychol* 97:281–288, 1988
- Risch N, Merikangas K: The future of genetic studies of complex human diseases. *Science* 273:1516–1517, 1996
- Rose MR, Lauder GV (eds): *Adaptation*. San Diego, CA, Academic Press, 1996
- Ruscio J, Ruscio A: A structure-based approach to psychological assessment: matching measurement models to latent structure. *Assessment* 9:4–16, 2002
- Schmale A, Engel GL: The role of conservation-withdrawal in depressive reactions, in *Depression and Human Existence*. Edited by Benedek T, Anthony EJ. Boston, MA, Little, Brown, 1975, pp 83–198
- Sedikides C: Assessment, enhancement, and verification determinants of the self-evaluation process. *J Pers Soc Psychol* 65:317–338, 1993
- Seegerstråle UCO: *Defenders of the Truth*. New York, Oxford University Press, 2000
- Seligman ME: Learned helplessness. *Annu Rev Med* 23:407–412, 1972
- Seligman ME, Csikszentmihalyi M: Positive psychology: an introduction. *Am Psychol* 55:5–14, 2000
- Seligman ME, Abramson LY, Semmel A, et al: Depressive attributional style. *J Abnorm Psychol* 88:242–247, 1979
- Sher L: The role of genetic factors in the etiology of seasonality and seasonal affective disorder: an evolutionary approach. *Med Hypotheses* 54:704–707, 2000
- Sloman L, Gilbert P: *Subordination and Defeat: An Evolutionary Approach to Mood Disorders*. Mahwah, NJ, Lawrence Erlbaum, 2000

- Sloman L, Price JS: Losing behavior (yielding subroutine) and human depression: proximate and selective mechanisms. *Ethol Sociobiol* 8 (3 suppl):99–109, 1987
- Sloman L, Price J, Gilbert P, et al: Adaptive function of depression: psychotherapeutic implications. *Am J Psychother* 48:1–16, 1994
- Sloman L, Gilbert P, Hasey G: Evolved mechanisms in depression: the role and interaction of attachment and social rank in depression. *J Affect Disord* 74:107–121, 2003
- Stearns S (ed): *Evolution in Health and Disease*. Oxford, England, Oxford University Press, 1998
- Sternbach RA: Congenital insensitivity to pain. *Psychol Bull* 60:252–264, 1963
- Stevens A, Price J: *Evolutionary Psychiatry: A New Beginning*. London, Routledge, 1996
- Tinbergen N: On the aims and methods of ethology. *Z Tierpsychol* 20:410–463, 1963
- Tooby J, Cosmides L: The past explains the present: emotional adaptations and the structure of ancestral environments. *Ethol Sociobiol* 11:375–424, 1990
- Trevathan WR, McKenna JJ, Smith EO (eds): *Evolutionary Medicine*. New York, Oxford University Press, 1999
- Trivers RL: *Social Evolution*. Menlo Park, CA, Benjamin/Cummings, 1985
- Wakefield JC: Disorder as harmful dysfunction: a conceptual critique of DSM-III R's definition of mental disorder. *Psychol Rev* 99:232–247, 1992
- Wakefield JC: Diagnosing DSM-IV—part I: DSM-IV and the concept of disorder. *Behav Res Ther* 35:633–649, 1997
- Wakefield JC: Evolutionary versus prototype analyses of the concept of disorder. *J Abnorm Psychol* 108:374–399, 1999
- Wallace J, Schneider T, McGuffin P: Genetics of depression, in *Handbook of Depression*. Edited by Gotlib IH, Hammen CL. New York, Guilford, 2002, pp 169–191
- Watson PJ, Andrews PW: Toward a revised evolutionary adaptationist analysis of depression: the social navigation hypothesis. *J Affect Disord* 72:1–14, 2002
- Weisfeld GE: *A Sociobiological Basis for Psychotherapy*. New York, Grune & Stratton, 1977
- Weissman MM, Bland RC, Canino GJ: Cross-national epidemiology of major depression and bipolar disorder. *JAMA* 276:293–296, 1996
- Wenegrat B: *Illness and Power*. New York, New York University Press, 1995
- Williams GC: Pleiotropy, natural selection, and the evolution of senescence. *Evolution* 11:398–411, 1957
- Williams GC: *Adaptation and Natural Selection: A Critique of Some Current Evolutionary Thought*. Princeton, NJ, Princeton University Press, 1966
- Williams GW, Nesse RM: The dawn of Darwinian medicine. *Q Rev Biol* 66:1–22, 1991
- Wilson DR: Evolutionary epidemiology and manic depression. *Br J Med Psychol* 71:375–395, 1998
- Wilson EO: *On Human Nature*. Cambridge, MA, Harvard University Press, 1978
- Wilson M, Daly M: Competitiveness, risk taking, and violence: the young male syndrome. *Ethol Sociobiol* 6:59–73, 1985
- Wolpert L: *Malignant Sadness: The Anatomy of Depression*. New York, Free Press, 1999
- Wortman CB, Silver RC, Kessler RC: The meaning of loss and adjustment to bereavement, in *Handbook of Bereavement*. Edited by Stroebe MS, Stroebe W, Hansson RO. Cambridge, UK, Cambridge University Press, 1993, pp 349–366
- Wrosch C, Scheier MF, Miller GE: Adaptive self-regulation of unattainable goals: goal disengagement, goal reengagement, and subjective well-being. *Pers Soc Psychol Bull* 29:1494–1508, 2003
- Zahavi A, Zahavi A: *The Handicap Principle: A Missing Piece of Darwin's Puzzle*. New York, Oxford University Press, 1997