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23

TESTING EVOLUTIONARY HYPOTHESES ABOUT MENTAL DISORDERS

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Do mental disorders differ from other medical disorders because they are 'mental'? Not at all. The capacities for grief and anxiety were shaped by natural selection no less than the capacities for nausea and physical pain. The continuity between normal and abnormal anxiety is no different from normal and abnormal blood sugar. Mental and other medical disorders arise from the same kinds of vulnerabilities, and the evolutionary approach applies equally well to both. Because psychiatry is beset by conceptual difficulties even beyond those faced by the rest of medicine, it may benefit even more.

Most people find it hard to grasp the extent of morbidity and mortality caused by mental disorders. According to WHO data from 1990, a single psychiatric disease, unipolar depression, accounts for more disability-adjusted lost years (DALYs) in the world population than all but three other causes (pneumonia, diarrhoea, and perinatal causes) and several times more than HIV, war, and malnutrition (Murray and Lopez 1996: Fig. 23.1). By the year 2020 it

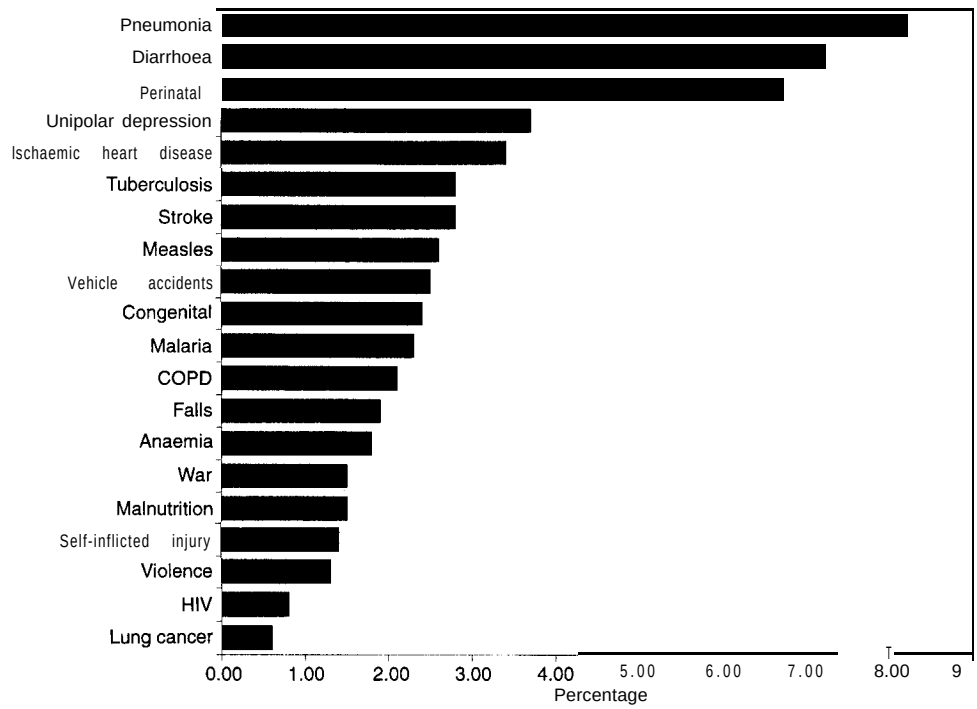

Fig. 23.1 Leading causes of world DALYS 1990 (from Murray and Lopez (WHO) 1996. Science 274: 741.)

is predicted to be the second most significant health problem, after myocardial infarction. Current estimates for women of reproductive age in developed countries are astounding. In this group, unipolar depression accounts for 19 per cent of all DALYs, three times higher than the next most severe causes: schizophrenia, traffic accidents, bipolar disorder, obsessive compulsive disorder, alcoholism, osteoarthritis, chlamydia, and self-inflicted injuries. Mental disorders cause a high proportion of all human suffering, disability, and death, and should be a high priority for Darwinian medicine.

PSYCHIATRIC DISORDERS

This chapter shows how hypotheses can be formulated and tested about how natural selection can give rise to vulnerabilities that result in specific mental disorders. Several major psychiatric disorders are considered in terms of the eight kinds of vulnerabilities outlined in Chapter 2 (Table 23.1). This exercise is useful on two counts. First, it illustrates the main point of Chapter 2-that each kind of vulnerability requires substantially different kinds of hypotheses and tests. Second, it outlines what we do not know about the origins of mental disorder, a sort of 'encyclopaedia of ignorance'. It does not summarize the many recent contributions to evolutionary psychiatry reviewed elsewhere in articles, (McGuire et al. 1992; Nesse, in press) and books (Wenegrat 1990; Stevens and Price 1996; McGuire and Troisi 1997). Instead of providing another review, this chapter focuses on specific psychopathological syndromes, the evolutionary origins of our vulnerabilities to these disorders, and, for each kind of vulnerability, the kinds of hypotheses and studies that are especially likely to advance our knowledge.

Table 23.1 Categories of evolutionary explanation for vulnerability to disease

1. Defence-what we think is disease or defect is actually an adaptation
2. Infection and other coevolving aspects of the biological environment
3. Novel aspects of the physical environment
4. Genetic quirks that are harmful only in a novel environment
5. Design trade-offs at the level of the gene
6. Design trade-offs at the level of the trait
7. Path dependence
8. Random factors

Anxiety disorders

Anxiety, like cough, fever, and pain, is a defence elicited and useful in the presence of certain dangers. Anxiety disorders result from dysregulation of the normal system (Barlow 1988). The question of why so many people have anxiety that seems excessive can be addressed only after we know when it is normal, and we cannot know when it is normal until we understand its function and regulation.

Most people readily acknowledge the utility of some anxiety, so it might be thought unnecessary to conduct formal tests of the hypothesis. However, an attempt to define adequate tests reveals how little we really know and offers a model for studying other more problematic emotions like sadness, grief, guilt, suspicion, jealousy, and boredom. Tests are based on the same approaches used to study other possibly protective mechanisms like allergic responses, fever, nausea during pregnancy, menstrual bleeding, and blood iron depletion during infection.

The methods for testing the hypothesis that anxiety is an evolved defence are based on the nine kinds of predictions about defences listed in Chapter 2. The first is that individual differences in anxiety responses should influence the degree of protection against a threat. Some individuals have hypofunctional anxiety systems, whether from genetic, traumatic, or toxin-induced defects that prevent anxiety expression, from drugs that block anxiety, or simply from being at the low end of the anxiety distribution. They should show decreased ability to avoid and escape dangers and increased rates of death and harm. Conversely, individuals who readily experience anxiety should be relatively protected from dangers. The evidence

for these predictions is remarkably skimpy (Wilson et al. 1994).

Second, the form of anxiety should match its function. Almost every aspect of the 'fight-flight response'-increased heart rate, glucose, clotting, sweating, and breathing-matches what is needed in the face of serious danger (Cannon 1929). These reactions are sometimes neglected by modern psychiatrists who study them as 'panic attacks'. One solid line of thought proposes that panic is designed to protect against suffocation. While I am not convinced that this is the primary function of panic, some evidence supports the idea (Klein 1996). Third, the characteristics of subtypes of anxiety should be different from global anxiety in ways that better meet certain kinds of threats. Fear of heights does seem to cause a response, freezing, that is probably adaptive in high places, but systematic data are lacking. Panic attacks occur initially in most patients where they would be helpful-away from home (Lelliott et al. 1989). The fear of blood is the only anxiety associated with fainting, and this may well be an adaptation (Marks 1988). The correspondence between the atheoretical categories of anxiety disorders in the *Diagnostic and statistical manual of mental disorders* of the American Psychiatric Association (1994) and the dangers people faced in the ancestral environment (Marks and Nesse 1994) is remarkable, but more work could be done to assess the match between the responses characteristic of each kind of anxiety, and the utility of those responses in the face of a particular danger.

Fourth, proximate mechanisms should match expectations concerning the function of the defence. If, for instance, the high heart rate in anxiety was an epiphenomenon resulting from skin vasodilation, this would argue against its functional significance. In fact, the high heart rate associated with anxiety results from coordinated actions of sympathetic innervation on the heart and vessels to increase blood flow to muscles. Adrenal cortical hormone secretion in the face of danger adjusts the body for energy expenditure-breaking down glycogen in the liver, increasing the availability of glucose and its ability to be utilized by muscles, and decreasing its entry into cells involved in digestion and repair. Much has been made of high cortisol secretion in the face of psychological stress (Mason 1975). It remains unclear if this secretion is an adaptation, a mistake, or if, for our ancestors, such stress was routinely accompanied by the need for action (Sapolsky 1992). Considerable evidence suggests that cortisol is designed to protect against tissue damage caused by other aspects of the stress syndrome (Munck et al. 1984). Many components of the primary stress system should be harmful to tissues or expensive or disruptive of routine activity, otherwise they would be expressed all the time instead of packaged and tightly controlled.

The fifth and sixth predictions can be tested with comparative studies. A species should not show fear of heights if it is never endangered by heights, either because trees are its usual habitat like gibbons, or because they hardly ever encounter high places, like muskrats. Baboons, who often spend time on cliffs, might well benefit from experiencing more fear in high places compared with other primates. A comparative test of such predictions would be welcome.

The seventh and eighth predictions, about regulation of a defence, are the most important for understanding the relationship between normal and abnormal anxiety. Is anxiety expressed when it is useful? Do dangerous situations reliably arouse anxiety? How these responses are regulated remains unclear, as do the differences between normal people and people with anxiety disorders. People with anxiety disorders do not misjudge the likelihood of danger, they seem instead to overreact to cues of danger. Like normal people, they consistently underestimate the likelihood of common dangers and, also, like other people, they believe that they are less likely to suffer harm than the average person (Nesse and Klaas 1994).

Are fears of snakes and spiders 'innate' or 'learned'? Experiments show that the question is too simple. Vervet monkeys do not show fear on initial exposure to a snake, but after a single observation of another monkey's fearful

response, an enduring fear is created, one that cannot be created to other novel stimuli like flowers (Mineka et al. 1984). Human studies show that fear responses are more readily conditioned to cues of objects that were dangerous in the ancestral environment, like snakes, than to objects dangerous only now, like guns (Öhman et al. 1985; Cook *et al*. 1986). There are trade-offs. Systems that express innate fear at first contact with the object protect an isolated individual on first exposure to a danger, but are of little help with novel dangers. Systems that require experience do not protect initially but offer better protection against new dangers, at the cost of learning to fear some stimuli that are not dangerous (Staddon 1983).

Why are people more often more anxious than seems useful? The encounter with any potentially dangerous stimulus poses a signal detection problem. For a given signal, will expressing the defence yield a net benefit or a net cost? If anxiety is inexpensive, and a lack of response is costly or fatal, natural selection will shape regulation mechanisms to a hair trigger with many resulting false alarms (Nesse and Williams 1995). On a more human level, social threats invisible to an observer, and perhaps not noticed consciously by the individual, can arouse profound subjective anxiety, making clinical psychiatry challenging indeed (Slavin and Kriegman 1992).

Finally, why are anxiety disorders so common? Each of the evolutionary origins of vulnerability contributes. Much anxiety that seems pathological is, in fact, a normal defence. There are also trade-offs: too little anxiety is as disadvantageous as too much. In a population distribution, some people will be at the maladapted extremes. Genetic variation is probably maintained because environments, especially social ones, differ in their dangerousness and the particular dangers they pose. In addition, novel dangers create new anxiety disorders, such as an unrealistic fear of AIDS in some people, and too little fear of AIDS in others. A full evolutionary explanation of anxiety disorders would address, for each specific kind of anxiety: normal functions, regulation, and how dysregulation can arise from novel aspects of the environment; trade-offs at the level of the trait and the gene; and historical constraints and random factors. We are a long way from this goal.

Depression

Like anxiety, depression seems to be an exaggeration of a normal response. Unlike anxiety, the utility of ordinary sadness and grief is not obvious. Anxiety precedes a danger and induces action, so it is easy to see how it can prevent harm, while low mood usually follows a loss and induces lack of action, so its value is more difficult to see. None the less, ordinary sadness and grief are so reliably aroused by the same kinds of losses in almost everyone that they must have some utility. Low mood must somehow influence future behaviour to increase reproductive success. There are many possibilities. Low mood can motivate avoidance of a situation that may cause further losses, it can facilitate changes in strategy that are necessary after a loss, it can facilitate submissive behaviour after a loss of status. These hypotheses need testing. To understand depression, we will need to understand the evolutionary functions and regulation of normal mood. We are far from such an understanding.

One way to investigate the functions of mood would be to find people who lack a capacity for low mood and identify the disadvantages they experience. However, it is hard to distinguish those people who have little capacity for low mood from people who are simply fortunate. We know that tendencies to low mood are strongly influenced by genetic factors and, when the specific genes are identified, it will be much easier to address this question.

In the meanwhile, we should consider the possibility that depression is a growing worldwide epidemic created by some novel aspect of our environment. This is supported by the extraordinary frequency, morbidity, and mortality for depression (Kessler *et* al. 1994) and by cohort data that indicate rapid rises in prevalence (Klerman and Weissman 1989; Cross-National Collaborative Group 1992). To answer this question, of great public health significance, we urgently need epidemiological studies

to determine the rates of depression in different kinds of cultures, especially primitive horticulturists and hunter-gatherers.

Manic depressive illness

Manic depressive illness appears to be a genetic disorder with heritability over 50 per cent. A review of seven studies found 69 per cent concordance rates for monozygotic twins reared together, 67 per cent for monozygotic twins reared apart, and 13 per cent for dizygotic twins (Rush et al. 1991). How can genes persist that cause an illness that severely interferes with function and is fatal in at least 20 per cent of cases (Goodwin and Jamison 1990)? The main possibilities are: (i) the genes are recent mutations, (ii) they are quirks that cause illness only in modern populations, and (iii) they somehow give an advantage that outweighs the disadvantage. The first and second possibilities are unlikely in view of the long recognition of this disorder in many societies and the strong selection against it (Goodwin and Jamison 1990). The third possibility has been considered in some detail because of the high rates of manic depressive illness in successful creative people (Jamison 1993). Mood disorders are more frequent both in accomplished writers and in their relatives (Andreasen 1987). Preliminary results also suggest that relatives of patients with manic depressive illness score high for creativity (Richards et al. 1988). If this is confirmed, the next step would be to determine the effects of creativity and manic depressive illness on fitness, preferably in premodern societies. Several routes to increased reproductive success seem possible. Creative accomplishment seems to increase sexual attractiveness, and it has been suggested that creativity is a product of sexual selection (Miller 1994). Another route to reproductive success could be via the social success of people with manic depressive illness or their relatives. When specific genes for manic depressive illness are identified, it will become much easier to study advantages that may counterbalance the high mortality rate.

If genes for manic depressive illness conferred a selective advantage that was not frequency dependent, we would all have the manic depressive illness phenotype. Would we still recognize it as a disease, or would we identify as diseased those rare people who lack wide mood fluctuations? This illustrates how natural selection could result in 'universal diseases'-syndromes like ageing that decrease everyone's health but none the less persist because they give an overall reproductive advantage. The 'young male syndrome'-risk taking and violent competition arising from sexual competition in men-may be an example (Wilson and Daly 1985).

Eating disorders

Eating disorders (bulimia and anorexia nervosa) are essentially unknown in traditional cultures, were rare in modern societies until this century, recently affected nearly 10 per cent of college females, and are now decreasing somewhat (Pate et al. 1992). They seem to be caused by novel features of our environment. What are these novel factors, and how do they interact with the evolved mechanisms that regulate eating? The selective forces that shaped mechanisms to limit excessive weight gain probably were feeble compared with those designed to prevent starvation, so it is not surprising that the ready availability, at any time with little effort, of a variety of tasty high-calorie foods has caused an increase in the frequency of obesity.

Serious eating disorders almost always begin with an attempt to lose weight by restricting food intake. The predictable adaptive response is aroused-overwhelming impulses to consume any available source of calories. At some point these impulses overcome will-power just as certainly as any attempt to hold one's breath ends with a deep inspiration. This bingeing causes a profound sense of loss of control that makes dieters even more fearful that their eating will make them obese. So they try even harder to diet, and an escalating feedback cycle ensues. Studies with volunteers show that a very low calorie diet itself induces profound psychological and behavioural changes (Keys 1950). If food is available, most dieters cannot resist their impulses and binge. However, a few

people, by will-power, exercise, laxatives, vomiting, and a profoundly distorted self-image, can limit their food intake and stay thin. The required discipline absorbs much of their energy, and if their self-image is distorted enough, they believe they are obese even as they die of starvation.

This simplified perspective on eating disorders explains only why they arise in a modern environment, not why some people get them and others do not. Knowledge of the mechanisms that regulate eating is already impressive and growing larger; it includes information on the genetic, psychological, and social factors that make some people especially vulnerable to eating disorders. It should soon be possible to integrate these perspectives. Many aspects may fit together: the much higher frequency of these disorders in women, the onset of eating disorders at sexual maturity, their rarity after menopause, the finding that men may be designed to seek mates with a waist/hip ratio of 0.7 (Singh and Young 1995), and the increase of these disorders in cultures where women must attract their own mates and where media constantly display visual images of exaggerated female forms (Pate *et al.* 1992). We may soon find out what happens when new drugs make it possible to adjust weight to any level desired. Evolutionary analysis should help us assess the likelihood of two outcomes. Will the availability of such agents prevent the cycles of weight gain and dieting that result in eating disorders, or will people use them to achieve extraordinary thinness in an arms race that will be fatal for some? The frequency of plastic surgery and breast augmentation suggest that we should prepare for the latter.

Substance abuse

An evolutionary approach to substance abuse follows the same lines as for eating disorders, but substance abuse is more common and seems to be a product not just of the very recent modern environment, but of any environment where drugs or alcohol are available. Hunter-gatherer cultures use drugs and alcohol, and to excess, but supplies are erratic, impure, and limited in amount and methods of use. Only modern societies have the organizational and economic structures providing the steady supplies that foster alcoholism and other addictions.

Current research emphasizes brain mechanisms of addiction, and social and genetic differences that explain why some people abuse substances and others do not. However, all these factors may merely influence which individuals succumb to the effects of novel factors acting on brain mechanisms we all share, mechanisms that were not evolved to cope with such exogenous chemicals. Chemicals are involved in neurotransmission, and drugs can act directly on the mechanisms that regulate behaviour, so consuming them can easily come to dominate life (Pomerleau 1997). The mystery is why so few people become dependent on substances. This perspective undercuts the hope that drug use is a problem mainly for people with certain deficits or mainly in certain disadvantaged or stressful environments, and suggests instead that substance abuse is a universal problem for smart organisms with access to pure chemicals (Nesse 1994, Nesse and Berridge 1997).

Child abuse

Child protection workers have long laboured to discover why people would hurt their own children, but it took two ethologists to suggest that people might not be hurting their own children. Daly and Wilson checked the rates of fatal abuse for children living with two genetic parents, as compared with those living with at least one step-parent. Having a step-parent in the home increased the fatality rate for children from birth to the age of 2 years, not by a factor of two or three, but by at least 50 times (Daly and Wilson 1987; Gelles and Lancaster 1987). This does not explain why these children are killed, nor does it mean that such murders are an adaptation, but it does demonstrate the protection that comes from living with both biological parents and it illustrates the utility of an evolutionary approach.

Schizophrenia

Schizophrenia is strongly influenced by genetic factors (Kendler 1983) yet it substantially

decreases fitness (MacSorley 1964). Evolutionary hypotheses must account for this mystery. The prevalence is relatively constant worldwide at about 1 per cent of most populations (Jablensky *et al.* 1992), making it unlikely that the frequency could be accounted for by recent mutations and drift unless many genes are involved. The genes responsible for this disease may also give a selective advantage (Crow 1995). Most hypotheses assume that the advantages are in the cognitive/emotional system and that the advantages accrue to people with the disorder. It seems more likely that any benefits accrue to people with the genes but no disorder; the benefits may have nothing to do with mental life-they might protect against some infection, for example. The test, of course, is to examine relatives of people with schizophrenia for traits that would have given a selective advantage in the paleolithic. If the selection force no longer exists, that would remind us that some evolutionary questions may have answers that we cannot find. If the genes that cause schizophrenia are in mutation-selection balance, then the eighth source of vulnerability, random factors, would be the closest we can get to an explanation. At present, this final possibility seems the most likely explanation, but the alternative cannot be ruled out. The discovery of specific genes for schizophrenia would help us assess these hypotheses.

Normality

The psychiatric condition that may be most illuminated by an evolutionary perspective is normality. Long the subject of controversy, normality has proved an elusive concept. A leading psychiatric textbook previously included a chapter with a dozen different definitions, based on statistical norms, social expectations, or subjective experience. The WHO definition of health is optimistic: 'Health is a state of complete physical, mental and social well-being and not merely the absence of disease and infirmity'. A Darwinian perspective suggests that there is no one answer to this question. The effect of a condition on reproductive success gives important information on its likely evolutionary status, but we do not call normal many behaviours that increase reproductive success, and we do not call abnormal many that decrease reproductive success, such as birth control. So, a Darwinian approach does not define normality, but it helps to explain why the search for a definition has proved so difficult. Much suffering and conflict arises from normal operations of normal evolved systems, but medical or social intervention is none the less often justified. Far from oversimplifying, an evolutionary approach reveals the manifold complexities of mental disorders.

SUMMARY

From an evolutionary perspective, explaining mental disorders is no different from explaining other medical disorders, and the categories of causes, and kinds of hypotheses and tests, apply equally well to both kinds of disorders. Anxiety is a defence like pain, and dysregulation can result in disorders characterized by too little as well as too much anxiety, illustrating the trade-offs involved. Sadness and grief are almost certainly also defences, but until studies are conducted to help us better understand their functions, we will have a hard time understanding whether depression is a defence, an overshoot of a defence, or a trade-off. Manic depressive illness results from genetic variation that may offer fitness advantages as well as disadvantages, and the same might be true for schizophrenia, although it is more likely that mutation-selection balance is the correct explanation. Eating disorders are caused by novel factors in the modern environment interacting with nutrition regulation mechanisms that evolved to solve very different problems. Alcoholism and substance abuse are, at root, a product of our brains encountering environmental novelties. Explicitly stating such hypotheses, with attention to the different kinds of tests needed depending on the postulated origins of vulnerability, may facilitate studies that will help us better understand the origins of mental disorders and how to treat them.