CHAPTER 9

EVOLUTIONARY PSYCHIATRY

"Of all the tyrranies on human kind
The worst is that which persecutes the mind."

— John Dryden (1631-1700)

Mental illnesses are among the most debilitating, and the least understood, of human maladies. These disorders, with primarily behavioral symptoms, have proved resistant to conventional medical attempts at cures.

Most human diseases are the result of attacks by a vast array of microbes, parasites, and viruses, opposed by our well-developed immune systems. Mental illnesses, though, have no obvious origins in foreign organisms attacking the body—indeed, many of them have more links to genetics than to conventional pathology.

Another contrast between mental illnesses and most bodily diseases is in the nature of the symptoms. Conventional bodily diseases are accompanied by such symptoms as fever, pain, lethargy, and changes in appetite, often

caused not directly by pathogens but rather by the actions of our own immune systems in fighting infection. Fever, for instance, results from the immune system changing the internal thermostat's set point in the brain to fight bacterial infection. Other symptoms such as internal bleeding or fluid in the lungs may be due to direct effects of an illness. Both types of symptoms are outside the normal repertoire of bodily function.

Many of the symptoms of mental illnesses, in contrast, are exaggerations or distortions of normal behavioral patterns. Immune systems are helpless against them. The behavioral patterns are adapted mechanisms for dealing with life challenges, mechanisms that are universal; it is only their exaggeration and their appearance in inappropriate contexts that are pathological.

● FOUR CLASSES OF MENTAL ILLNESS

If mental illnesses are linked to genetics, we must look to evolution to understand them. Viewed in this way, the illnesses can be divided into four classes. The first class consists of those diseases that exaggerate normal, adapted behavioral schemas; examples are phobias and obsessive-compulsive disorder. Second are those illnesses that may confer a benefit under some environmental circumstances, such as depressions. Third, some illnesses such as schizophrenia reduce fitness without any clear benefit to its victims or to others. Finally, other problems such as drug addiction may not be the results of pathology at all, but rather are reactions of normal humans to environmental conditions for which evolution has not prepared them.

Using this new method of categorization, the following sections review a sampling of mental illnesses, concentrating on the roles of evolution and genetics in defining and maintaining them.

● EXAGGERATIONS OF NORMAL BEHAVIORS

Phobias

An otherwise normal teenager spots a tiny spider crawling across her desk and suddenly melts into a terrified puddle of screams and tears. She knows that her overreaction is inappropriate, but can't help herself. She has a **phobia**, an exaggerated, irrational fear of some object or situation. There are two kinds of phobias, **specific phobias** that are triggered by particular stimuli and **social phobias** to interpersonal situations that can take the form of an extreme shyness or fear of strangers.

Table 9.1 Objects of common phobias

Animals	*Places*	*Social Situations*
spiders	heights	shyness
snakes	closed spaces	strangers
rats	darkness	
cats		

One would hope that phobias, if they are exaggerations of normal tendencies, would be directed at the greatest dangers that we face. Table 9.1 lists some of the most common phobias by category; Table 9.2 shows the greatest real dangers for Americans. A glance at the two tables shows that there is almost no overlap between the list of most-feared things and the list of most-dangerous things (the falls in Table 9.2 are mostly short-distance falls by the elderly at home, not dives from great heights). The lists indicate that phobias probably are not learned, because they fail to engage the greatest dangers of modern life. The statistically most dangerous objects, automobiles and handguns, are seldom the subjects of phobias.

An understanding of phobias begins with the observation that all the common phobias relate to dangers that would have faced our nomadic ancestors. Building fears of these things into the human mind has the advantage that they will be avoided even at the first experiences with them. If a healthy fear of objects and situations that presented danger to our ancestors improved their chances of survival and reproduction, a selective pressure for the evolution of adapted fears would result.

Those who suffer from clinically dysfunctional phobias may simply be at the extreme of apprehensiveness about the objects that all of us treat with some amount of trepidation. The disadvantage of managing fears with adapted genetic mechanisms is that the fears do not change when the environment changes. We live in an industrial society but are stuck with a nomad's fears.

If phobias are exaggerations of normal fears, we might expect to see them in other primates as well. Indeed, many monkey species seem to show unlearned fears of the same sorts that we have. Rhesus monkeys raised in an animal colony, who have never seen a snake, show all the signs of terror when a hose used to wash down their room gets away and swishes across the floor. They scream, jump to the backs of their cages, and display a toothy fear grimace (I have seen this reaction in animals housed at a research facility at the Stanford Medical Center, Stanford, California). The fact that the hose presents no real danger doesn't lessen the panic.

Table 9.2 Risks of death per year

Accident	*Risk*	*Disease*	*Risk*
motor vehicle	1/7,000	heart disease	1/400
gunshot	1/10,000	cancer	1/600
falls	1/20,000	stroke	1/2,000
poison	1/40,000	flu/pneumonia	1/3,000
crossing street	1/60,000		

Source: Cathy Lynn Grossman, *USA Today,* 2001.

Functions of Phobias

For phobias to remain in the human genome, they must confer some benefit. Phobias, or less intense tendencies in the phobic direction, should make people on average more successful. There is indeed some evidence that the objects of common phobias are detected faster and more reliably by people who are fearful of those objects than by others. In a world where these things presented real dangers, the advantage of quick detection is clear.

An experiment on common objects of phobias asked a normal range of subjects to search for fear-relevant pictures (snakes or spiders) hidden in grid-pattern arrays of fear-irrelevant pictures (flowers or mushrooms). In a second condition, they searched for fear-irrelevant pictures. The subjects found the fear-relevant pictures more quickly than fear-irrelevant ones (Öhman, Flykt, & Esteves, 2001). Furthermore, the search for fear-relevant pictures was unaffected by the location of the target in the display or by the number of distracters.

This result suggests that fearful people could search for the fear-relevant targets all at once, in parallel, while they searched for fear-irrelevant targets serially, one at a time. People who were specifically fearful of snakes but not spiders (or vice versa) showed facilitated search for the feared objects but did not differ from controls in search for nonfeared fear-relevant or fear-irrelevant targets. Thus, evolutionarily relevant threatening stimuli were effective in capturing attention, and this effect was further facilitated if the stimulus was emotionally provocative.

Specific phobias are more common in females, but social phobias are about equally frequent in both sexes (American Psychiatric Association, 1994). There is a theory, with an SSSM tinge, that specific phobias seem less common in males because boys in our society are pressured to hide or overcome their fears (Fodor, 1982). It is not clear how this theory accounts for the

choice of phobic objects or for the unlearned, automatic nature of phobias and phobia-like fears.

Phobias are inconvenient, sometimes embarrassing, but seldom debilitating. Other disorders cause more serious problems.

Obsessive-Compulsive Disorder

Roy, an intelligent, articulate boy from a stable family background, has a problem—he feels compelled to wash his hands hundreds of times every day. He is so consumed with it that there is no time for normal activities (Rapoport, 1991). Though his hands become red and raw, still he washes and washes and washes. Why? When asked, he offers vague fears of dirt, contamination, disease. He knows that the behavior is ruining his life, but for him washing is the most important thing he does.

Roy suffers from **obsessive-compulsive disorder** (OCD), a malady whose principal symptom is a compulsion to perform some otherwise rational act to excess. The disorder presents with a wide variety of compulsive acts; usually, a victim is affected by only one or a small number of them. One sufferer may need to keep everything in her environment perfectly neat and orderly, with not a pencil or a hairpin out of place. Another may feel compelled to check that all the doors and windows are locked before leaving home; after they are all checked, though, the victim feels a dread that something may have been forgotten, and the checking starts all over again. In severe cases, constant checking prevents the victim from leaving home at all. Still others must keep their homes so spotless that they spend all their time cleaning.

Like the case of phobias, OCD is an exaggeration of a set of adapted traits that all of us share. In OCD, traits that are advantageous for most people become pathological when pushed too far. High standards become perfectionism, attention to detail becomes obsession with trivia, cleanliness becomes obsessive washing. The adapted traits are inherited with a great degree of variability—some of us are slobs, whereas others are neat and still others have their lives ruined by obsessive behaviors. Everyone has a need for some degree of order, and many people have little rituals that add comfort to their lives. The behaviors descend into OCD if the sufferer experiences them as unwanted and they interfere with leading a normal life. Like Roy, most OCD patients know that they engage in bizarre rituals, but they can't stop themselves.

Treatment

Historically, cases of OCD were treated as weakness of character or dysfunctional parenting, and the treatment was to admonish the helpless victim

to cease and desist, with greater or lesser degrees of pressure. The strategy was uniformly unsuccessful.

Most mental illnesses are related to neurotransmitter systems in the brain that transmit messages between neurons managing motivation, mood, and reward. These neurons are buried deep in the oldest parts of the vertebrate forebrain, in the limbic system and related structures. The two families of neurotransmitters of most concern, the **catecholamines** and the **indoleamines**, are synthesized in the body from amino acids, the components of dietary proteins. Catecholamines begin from the amino acid tyrosine. Through successive biochemical steps it is transformed into dopa, then **dopamine**, then **norepinephrine**, and finally **epinephrine**. Indoleamines begin with the amino acid tryptophan, which is transformed into 5-hydroxytryptophan and then into **serotonin**. Each of the steps in biosynthesis is catalyzed by an enzyme, so that manipulation of either a transmitter or the relevant enzyme can change transmitter levels in the brain.

OCD is related to inherited abnormalities in neurotransmitter function, and the best treatment is a combination of behavior therapy and medication. The most common medications to combat OCD are clomipramine (Anafranil), fluvoxamine (Luvox), sertraline (Zoloft), fluoxetine (Prozac), and paroxetine (Paxil). All are serotonin reuptake inhibitors, increasing the amount of serotonin at CNS (central nervous system) synapses (Kronig et al., 1999). Whether normal ranges of need for order also correlate with CNS serotonin levels is unknown.

Here a cause-and-effect problem arises: Is OCD caused by low or widely fluctuating serotonin levels, or do the low levels result from years of obsessive-compulsive behavior? The test is to administer the drugs that restore normal serotonin levels and see whether the abnormal behavior abates. Relief from the compulsions indicates that the serotonin levels contribute to the disease. If symptoms remain, then the low serotonin may be a consequence of an underlying disorder that causes both OCD and low serotonin levels.

The fact that the major medications both reduce the symptoms and increase available serotonin argues for the first alternative, that neurotransmitter anomalies, presumably with genetic origins, cause the disease. Unfortunately, the medications do not cure the disease: they only suppress the symptoms. Patients must continue taking the medications for life, even after the symptoms have abated.

If such a debilitating disease has genetic roots, evolutionary theory would seem to require that natural selection should eventually reduce the incidence of the disease. There are circumstances, however, under which OCD might persist at low to moderate levels even after evolution has

established an equilibrium. Often it is advantageous to individuals in a population if there is some variation in a trait. Variability in the immune systems of my relatives, for example, is advantageous because at least some of them are likely to survive any disease epidemic.

Applying this idea to OCD, if the amount of need for order is selected to be optimized in the population, and the degree of variability in the trait is also optimized, a group with pathological symptoms might result. They would be at one end of the normal bell curve that describes the distribution of most traits, including personality traits. In the case of personality systems, individuals who are very high or very low on particular traits would appear to be at a disadvantage, but there is a broad range of genetic variation in the middle of the distribution underlying a range of viable strategies. This approach is consistent with attempts to interpret psychopathology in terms of maladaptive extremes on personality dimensions (MacDonald, 1998), and in fact, clinicians recognize wide variations in the severity of the disease. Unfortunately, studies of entire populations including both "normal" subjects and OCD sufferers, measuring the quantitative degree of symptoms in each person, have not been done to test this hypothesis.

The symptoms of this class of diseases can be characterized as exaggerations or extremes of normal personality traits, and like those traits, symptoms of these diseases are more or less continually present

BALANCES OF COSTS AND BENEFITS ●

These diseases are normally classified as major psychoses, serious diseases that incapacitate the patient. The symptoms of these psychoses tend to wax and wane over time, often staying with the patient for life.

Unipolar Depression

Everyone goes through a depression at some time in life, usually in response to a personal loss such as chronic illness, loss of a family member, or the end of a love affair. There is inactivity, social withdrawal, a feeling of sadness and pessimism, eating and sleeping disturbances. This kind of depression serves the useful function of forcing a person to withdraw from normal activities at a time when their effectiveness is reduced.

Depression that arises for no obvious reason, and disables a person for months or longer, is a profound psychopathology called **unipolar depression**. It has been described as "chronic exaggerations of innate behavioral

potentials with which all human beings are equipped by virtue of their humanity" (Stevens & Price, 2000). It has been known at least since Hippocrates' description of melancholia 2,400 years ago. Unipolar depression is almost twice as common in women as in men (Kessler et al., 1994), and often strikes later in life than the other major mental illnesses. The disorder is moderately heritable, with statistical evidence that the genes responsible for promoting it may be the same genes that promote **generalized anxiety disorder**, a chronic anxiety that again has no clear environmental cause (Smoller, Finn, & White, 2000).

Many of those who suffer from depression will also suffer from generalized anxiety disorder at some point in their lives (Mineka, Watson, & Clark, 1998), suggesting that the two diseases are linked. Anxiety, of course, can also be seen as an adaptation to increase alertness and arousal at times of real danger. Its pathological version, though, is associated with almost continuous worry about such issues as money, work, social relationships, or illness itself (Barlow, 1988). The resulting chronic stress can result in immune system malfunctions and gastrointestinal upset due to overactivity of the sympathetic branch of the autonomic nervous system. Normally, this part of the nervous system prepares an animal for fight or flight, in this case inappropriately. So again, normal adapted traits become pathological when exaggerated and triggered without cause.

Despite the general limitation that pathological depression should have no environmental cause, there is evidence that a processing bias in interpreting life events precedes episodes of clinical depression. The bias is tested with a scrambled sentences test, in which sentences can be interpreted in various ways. High scores on the scrambled sentences test, reflecting a negative processing bias, predicted depression symptoms measured 4 to 6 weeks later, even after controlling for concurrent and past depression (Rude, Wenzlaff, Gibbs, Vane, & Whitney, 2002). Those who interpreted events in the worst possible light at the time of the test, then, were more likely than others to show symptoms of clinical depression several weeks later, implying that the victims of depression in the study created in their own minds the negative events that triggered their depression. The study implies that the difference between normal bouts of depression, caused by identifiable life events, and pathological depression, with no obvious cause, might be as simple as a change in the interpretation of everyday events.

Treatment

Unipolar depression is associated with low activities of brain receptors for norepinephrine and serotonin (Schildkraut & Kety, 1967). Drugs that

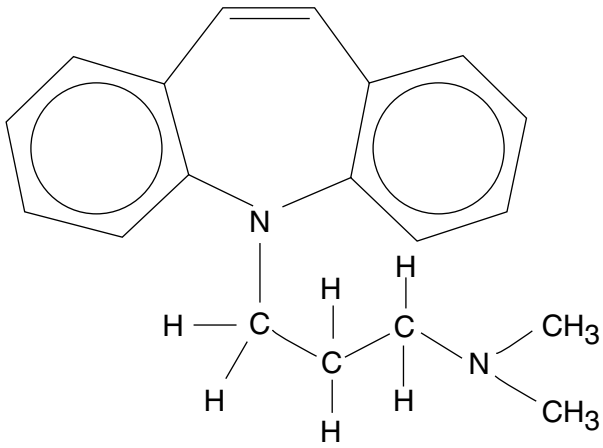


Figure 9.1 Molecular structure of the tricyclic antidepressant imipramine. Other tricyclics have the same three-ring core but different radicals branching out from it.

increase levels of these and chemically related neurotransmitters often alleviate the symptoms, revealing that depression has a basis in brain biochemistry. One class of such drugs is the tricyclic antidepressants, so named because their molecular formula contains three ringlike structures (Figure 9.1). These drugs block the reuptake of norepinephrine and serotonin, and to a lesser extent dopamine, allowing more of the neurotransmitters to remain in the synaptic contacts between neurons (Stahl, 2000). Examples are imipramine (Tofranil) and amitriptyline (Elavil).

A more recently developed class of antidepressants is the selective serotonin reuptake inhibitors such as fluoxetine (Prozac). These drugs have fewer side effects than the tricyclic antidepressants, probably because they are more specific in their targets, but for the same reason, they may not be as effective as tricyclics in combating severe depression (Moeller & Voltz, 2000).

Some of the psychopathology of depression may result from the differences between modern environments and the environments in which humans evolved (Nesse & Williams, 1996). For example, rates of depression may be influenced by contemporary trends toward families removing themselves from close kinship ties as a source of social support. In the Paleolithic world, privacy was not an issue, nor was sustained leisure. Lying in bed all day feeling depressed was not usually an option for people who had no permanent beds. Because nomadic lifestyles demanded some degree of physical activity from everyone, it is perhaps significant that activity can somewhat alleviate the symptoms of unipolar depression.

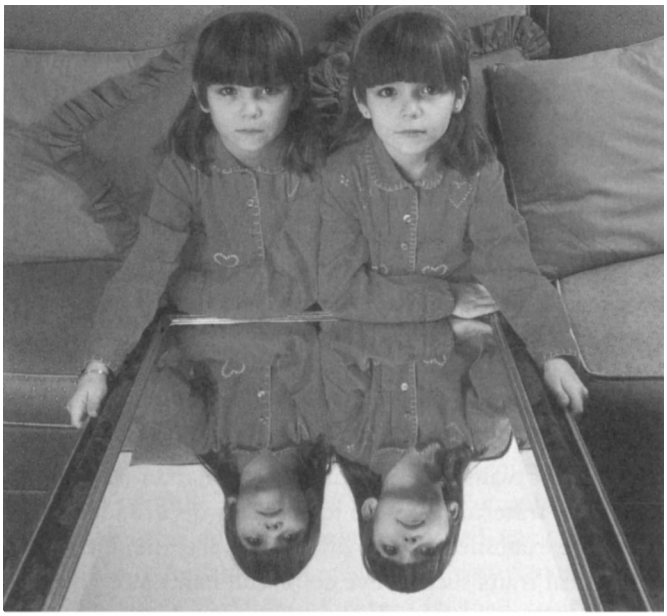
Bipolar Depression

Manic-depressive psychosis—**bipolar depression**—is a very dangerous disease. Left untreated, the mortality rate is about 1 in 5, not from the direct physical effects of the disease but from suicide during the depressive phase. In this disease, periods of severe depression alternate with periods of excessively expansive moods that are similar to the feelings of normal people taking cocaine or amphetamines. There is a feeling of power, of invincibility. The manic sleeps little or not at all for weeks, spends money recklessly, and makes grandiose plans. Like the other psychoses, this disease differs from the mood swings that we all experience in their severity and in the smaller influence of environmental triggers.

There is enormous variability in the balance, timing, and severity of manic and depressive phases between patients, and even over time in a single patient. Some suffer from a milder version of the disease, where the manic phases are called hypomania. Either of the phases might be more lengthy or more severe, and the duration of the cycles (from mania to depression and back again) varies from weeks to years.

Bipolar illness tends to strike men and women equally, at a younger age than unipolar depression. The disorder tends to run in families, a fact that could be due to either environmental or genetic influences, because families have both environment and heredity in common. Both nature and culture, however, provide natural experiments that allow the two factors to be separated. Nature provides a controlled experiment in the contrast between monozygotic and dizygotic twins. Since the monozygotic twins come from the same egg, their genes are identical, and any condition fully determined by heredity will be identical in both of them. Identical twins are always of the same sex, for example. The similarity of traits in a group of pairs of twins is measured in a **concordance rate**, the percentage of twin pairs who share the trait. Bipolar illness is more strongly heritable than unipolar depression, showing a higher concordance in monozygotic twins (Figure 9.2) than in dizygotic twins (Gershon et al., 1976). The concordance is similar whether the twins are reared apart or together, and in cases of adoption is correlated with biological rather than adoptive parents, consistent with a genetic origin of the disease (Kelsoe, 1997).

Unlike victims of the other major psychoses, some of the sufferers from milder forms of this disease have a distinct advantage during the manic phase. They can be or feel as though they are extraordinarily creative, especially in art, literature, and music. Indeed, an astonishing proportion of the great works of literature and music have been produced by people who show



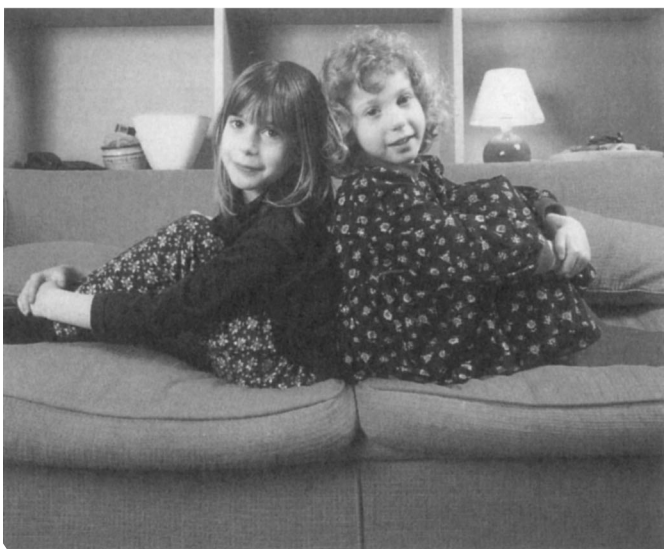


Figure 9.2 Monozygotic (identical) and dizygotic (fraternal) twins. In monozygotic twins, the two halves of the embryo separate after the first division of the egg cell, and each matures into a complete infant. Dizygotic twins come from two eggs released in the same cycle and fertilized separately.

evidence of having suffered from bipolar illness—an unweighted average of five studies of writers and poets cited by Jamison (1995) finds an average of 35% of them to have suffered from a manic-depressive illness, as opposed to about 1% in the general population.

The phenomenon is not a new one: over half of published British poets born between 1705 and 1805 were manic-depressives (Jamison, 1993). Artists with the syndrome include Vincent van Gogh, Paul Gauguin, and Georgia O'Keefe; writers and poets include Mark Twain, Walt Whitman, Hermann Hesse, Edgar Allan Poe, Ernest Hemingway, Tennessee Williams, Ezra Pound, Virginia Woolf, Anne Sexton, and Sylvia Plath; composers include Gustav Mahler, Charles Mingus, Cole Porter, Peter Tchaikovsky, and Robert Schumann. A smaller number of exceptionally creative people have suffered from periodic depression, without any identifiable mania.

Because most of these great artists produced their work long before psychoses were defined in their present way, evidence of their bipolar illnesses was gleaned from their letters, diaries, and the observations of their friends and relatives. Even military leaders such as Alexander the Great and Napoleon may have suffered bipolar swings, conquering the world in one phase and contemplating suicide in the other. Perhaps significantly, violent mood swings do not seem to be common in great scientists.

Not everyone can attain the creative heights of geniuses who are also bipolar, and society could not support a large number of such people. But their extraordinary accomplishments may pave the way for their relatives and descendants, enhancing the inclusive fitness of the manic-depressive geniuses and maintaining the genes that facilitate their illness at a low level in the population. Not all manic episodes are associated with creativity, though—most experience it as a period of extreme irritability, suspiciousness, or destructive rage (Carroll, 1991).

Treatment

The biochemistry of bipolar disorder is quite distinct from that of unipolar depression, despite the similarity of the depressive symptoms. Bipolar psychosis is treated effectively in many cases with lithium, which, in contrast to the complex drugs administered in other conditions, is an element, a light metal. It is one of the smallest and simplest ions in the periodic table. Though lithium is known to affect catecholaminergic and cholinergic neurons and also influences amino acid neurotransmitters (Fieve, 1979), the precise mechanism by which it works remains a mystery (Manji & Lenox, 2000).

Unlike other antipsychotic drugs, lithium is a naturally occurring substance. Lithium probably did not suppress the symptoms in the diet of an

ancestral population, though, allowing the genetic defect to spread unchecked, because the range between a therapeutically effective dose and toxicity is rather narrow. Effective treatment requires constant monitoring by a physician, and sometimes psychological counseling to maintain the lithium regimen despite not having had any symptoms for years. Because humans normally make decisions based on short-term contingencies, long-term compliance is rare without outside support.

Attention Deficit Hyperactivity Disorder

Attention deficit hyperactivity disorder (ADHD) is a disease that seems to appear in societies that require formal education of their children. The syndrome, usually diagnosed in boys, is characterized by hyperactivity (incessant movement without particular goals), impulsivity, and the inability to concentrate on any one thing for more than a few minutes, usually less. Though ADHD-like behavioral functions are apparent from infancy, the family can usually deal with children showing these symptoms until it is time to attend school, where the behaviors are so disruptive that they often prevent the child from functioning in a normal classroom.

ADHD is the most prevalent disorder of early childhood, with estimates ranging from 3% (Ding et al., 2002) to 5% (Shelley-Tremblay & Rosen, 1996) of elementary school children. Approximately half of them continue to show the full disorder in adulthood. Epidemiological studies point to a strong genetic component in the etiology of this disorder (Shelley-Tremblay & Rosen, 1996).

Treatment

ADHD treatment usually involves giving the child amphetamines, disguised by trade names such as Ritalin. The response to chronic low doses of amphetamine-like drugs is said to be "paradoxical," calming the patient and making concentration possible. In turn, the paradoxical response to what would be a strong stimulant in other children is seen as evidence that something was pathological about the child's brain biochemistry in the first place.

A possible explanation of both the disorder and its treatment is that the ADHD child may be chronically sleep-deprived. Normal children, when tired, become more active and irritable, running around the house until exhaustion overtakes them. If this is the case, amphetamine therapy would wake up the affected child to the point where behavioral functioning is more normal. In half of ADHD cases, the symptoms become less severe in adulthood, a phase

of life when sleep requirements decline from their higher childhood levels. There is no direct evidence for this speculative hypothesis, but it seems to be the only one that engages both symptoms and treatment together.

Evolutionary Origins

ADHD was identified as a pathology only in the 20th century and in industrialized countries. But a pattern of high activity and curiosity about everything may have led to a broad-based exposure to the environment that would have been beneficial for Paleolithic nomads. Furthermore, we know that our ancestors inhabited a great variety of environments, so that personality characteristics that today are identified as ADHD pathology may have been adaptive for some environments (Jensen et al., 1997).

Nomads normally are more active than most inhabitants of industrial societies, eating substantially more each day than their settled cousins without becoming obese. Hyperactivity in such an environment might hardly have been noticed. Long periods of concentration on subjects of little intrinsic interest, characteristic of formal education, would not have been an issue. In short, ADHD may not be a pathology at all, but simply an extreme of the normal human behavioral repertoire (MacDonald, 1998) that is incompatible with some contemporary lifestyles. Psychiatrists drug children by the millions to suppress symptoms that may be part of a normal range of adaptive human behaviors.

Even nonpathological behavior patterns can have genetic and biochemical concomitants, though, that help us to understand the behaviors and their origins. As in the case of schizophrenia below, a dopamine receptor may be involved. A dopamine D4 receptor (DRD4) has generated interest because of its association with ADHD, with an increased frequency of a unique gene allele, 7-DRD4, reported in children with ADHD. People with this gene have seven repeats of a 48 base-pair sequence—hence the 7-D designation—whereas most people have fewer repeats (Ding et al., 2002). It is one of the most variable genes in the human genome, with 600 alleles.

If a gene is responsible for the syndrome, it might be detectable even in infants, before socialization has had much of a chance to affect behavior. Indeed, in a structured play situation and on an information-processing task, 1-year-old infants with the 7-DRD4 allele showed less sustained attention and more novelty preference than did infants without the 7-DRD4 allele (Auerbach, Benjamin, Faroy, Geller, & Ebstein, 2001).

Where did the gene come from? There is now evidence that a single mutation, occurring between 30,000 and 50,000 years ago, may have been advantageous to early humans (Ding et al., 2002). Triggering a novelty-seeking

trait, the mutation is found in up to half of diagnosed ADHD cases, implying that it was selected for in early human groups until it spread to its present frequency. The other alleles of this gene are ancient, predating the origin of the human species.

The mutation was discovered by analyzing the DRD4 genes of a worldwide sample, noting the degree of accumulated variation in the gene's DNA, and working backward to find the time when there was no variation at all. The technique is similar to that used to identify the ages of the ancestral Adam and Eve at the beginning of humanity. Consistent with the out-of-Africa hypothesis of human origins, the widest variety in the gene was found in African populations.

The personalities of those possessing the 7-DRD4 gene may have predisposed them to migration. Active, restless, adventure-seeking, and not generally getting along well with their fellows, they would have pioneered the migrations that populated the earth. The hypothesis generates a testable prediction, that the frequency of the gene should be greatest in the groups that moved the farthest from the African cradle of humanity. Indeed, the mutated 7-DRD4 form of the gene is rare or absent among African !Kung Bushmen, the closest group we have to an ancestral population. In contrast, the mutated allele is common in South America, about as far from Africa as you can get via the Asia/Alaska route. A later migration from a center in China into southeast Asia and the Pacific resulted in high frequencies in those regions, and almost none in China (Harpending & Cochran, 2002).

In conclusion, then, a gene that pushed our ancestors into the farthest corners of the earth is now recognized mainly by the disruptive behavior that it fosters in elementary schools.

ILLNESSES THAT CONFER ONLY COSTS ●

Schizophrenia

A homeless man, Rob, wanders down the street, muttering to himself. Afraid to approach a shelter because voices in his head tell him that people there are scheming to stab him in his sleep, and convinced that medications given to him previously are poisons, Rob is unable to hold down a job or plan his life. He suffers from **schizophrenia**, one of the most terrifying and debilitating of the major psychoses. About 1% of the population will have a schizophrenic episode at some time in their lives, making the disease a serious problem for society as well as a disaster for its victims and their relatives.

Diagnosis of schizophrenia has been difficult, with standards that are still shifting. At present, the American Psychiatric Association recognizes three subcategories of the disease; in the early 1990s there were five. All are characterized by combinations of a group of symptoms: positive symptoms, primarily delusions and hallucinations; negative symptoms, including slowing of movements, poverty of speech, flattened affect, and loss of motivation; and disorganized symptoms, such as nonsensical speech and erratic behavior.

Some of the most troubling symptoms of schizophrenia can be characterized as deficits of planning and anticipation functions that are normally handled by frontal brain areas. Schizophrenic patients have great difficulty in performing anticipation tasks, compared with normal controls. Although they can learn sequences almost normally, their anticipatory ability is reduced in comparison to normal controls. These behavioral problems implied to the authors of the study that a working memory deficit is important in schizophrenia (Posada, Franck, Georgieff, & Jeannerod, 2001), but a diagnosis of frontal lobe dysfunction is more likely because some of the symptoms are reminiscent of the deficits due to frontal lobe damage reviewed in Chapter 8.

Indeed, frontal hypoactivity is a part of the pattern of schizophrenic deficits. There is also an interruption in the planning of normal behaviors, as revealed neurologically by a reduced communication between frontal and temporal lobes during talking in schizophrenia (Ford, Mathalon, Whitfield, Faustman, & Roth, 2002). The reduced communication may be the source of bizarre speech in schizophrenics, and underlies the schizophrenic's feeling that his or her actions are being controlled from outside.

The confluence of the loss of a feeling of control with the fact that behavior obviously is still occurring leads many schizophrenics to a conclusion that you or I might also make under the same circumstances—the patient feels controlled from the outside, whether from demons, gods, or implanted microchips.

Genetic Triggers

Many colorful hypotheses have been proposed about the origin of the disorder: mothers who are too warm or too cold, fathers who are too timid or too intimidating, conflicting messages from parents, and so on. None of these ideas has withstood empirical tests, and none has led to an effective therapy.

For a long time it has been known that schizophrenia runs in families; some pedigrees running back four generations show schizophrenics in one generation after another. Using twin studies to separate environmental from

genetic origins of the disease, concordance rates for schizophrenia are found to be substantially higher among monozygotic twins than among dizygotic twins.

Another way to disentangle genetic and environmental effects is to study adopted children. Most of the best studies come from Scandinavia, where social records are so complete that natural and adoptive parents of schizophrenic adoptees can be compared. A primarily environmental trigger would predict that the adoptive parents of schizophrenics would more often show signs of mental illness than would the biological parents. A genetic trigger would predict the opposite—more abnormalities in the biological parents. Pathology was found to be far more common among biological parents than adoptive parents (Kety, Rosenthal, Wender, Schulsinger, & Jacobsen, 1975).

Environmental Triggers

Even for monozygotic twins, however, the concordance rate is less than 100%, suggesting that genes do not play the only role in the development of the disease. In cases where only one twin became schizophrenic, that twin often was the second born, had a lower birth weight, suffered more physiological stress during development, or was seen by the parents as more submissive, fearful, and sensitive than the other twin (Wahl, 1976). Even when only one twin develops the illness, however, the rate of schizophrenia in the children of both twins is the same (Fischer, 1971). Something unknown, but not genetic, apparently prevented the disease from appearing in one of the twins.

Another possible triggering factor for schizophrenia was discovered after a brutal incident during World War II when the Nazis blockaded the Netherlands, causing widespread starvation and malnutrition. Mothers who were pregnant during that period had twice the probability of bearing children who would eventually become schizophrenic (Susser et al., 1996).

There is also a time-of-year effect, with children born in late winter or early spring suffering a 20% greater risk of developing the disease (Mortensen et al., 1999). Although all these factors point to a combination of genetic and environmental influences that trigger schizophrenia, the precise mechanism of the onset of the disease remains obscure.

Biochemistry and Treatment

Until the 1950s there was no effective treatment for schizophrenia. After psychotherapy proved ineffective, the usual procedure was hospitalization until a spontaneous remission occurred. The result was a psychiatric patient population in the United States of about half a million. At this time, Henri

Laborit, a French surgeon, was searching for a drug to relax muscles for surgery. He discovered a drug that also reduced the patient's worrying and preoperative tension. Recognizing the potential of such a drug, Laborit then collaborated with psychiatrists in trying the new drug, chlorpromazine, on psychiatric patients.

Success was so dramatic that the drug and its relatives, the phenothiazines, became widely used. Since then, mental hospitals have been emptied by the use of an array of antipsychotic drugs. As Rob's situation at the start of this section shows, however, drugs alone are not enough to defeat the disease. Like the treatments for other major psychoses, the phenothiazines do not cure the disease—they only suppress its symptoms, and in the case of schizophrenia they are relatively ineffective against the negative symptoms. The drugs are also less effective in some patients than in others.

The antischizophrenic drugs have in common that they reduce brain levels of dopamine, a neurotransmitter associated with neural reward and motivation systems. This fact leads immediately to the dopamine hypothesis, that schizophrenia is caused by an excess of brain dopamine (Creese, Burt, & Snyder, 1976). In fact, the clinical efficacy of phenothiazines is closely related to their effectiveness in reducing brain dopamine concentrations (Figure 9.3). The earliest antischizophrenic drugs had serious motoric side effects, due to interference with other dopamine systems regulating muscle action and posture; newer drugs, taken at much lower doses, have less severe side effects.

There are problems with this hypothesis, though. First, the antipsychotic medications reduce brain dopamine levels in schizophrenic patients within hours, but reduction of symptoms can take weeks. Second, the dopamine system in the brain has turned out to be more complicated than was first thought, with at least five different dopamine receptor systems in the CNS. A modern version of the dopamine hypothesis recognizes that medications may repattern dopamine activity, especially reducing effects in the prefrontal cortex, in addition to an overall decrease in dopamine activity (Goldsmith, Shapiro, & Joyce, 1997; Okubo et al., 1997).

Consistent with this idea is the clinical experience of physicians administering dopamine precursors in patients whose dopamine levels are too low. Parkinson's disease, a malady that strikes mostly the elderly and results in disorders of posture and movement initiation, seems to be related to low dopamine levels in the basal ganglia, forebrain structures that are part of the motor system. Sometimes symptoms of schizophrenia appear in Parkinson's patients who are treated with drugs that increase brain dopamine levels. And people who use enough cocaine or methamphetamine ("speed") for a long enough time develop a syndrome that is indistinguishable from schizophrenia (Angrist, Sathananthan, Wilk, & Gershon, 1974).

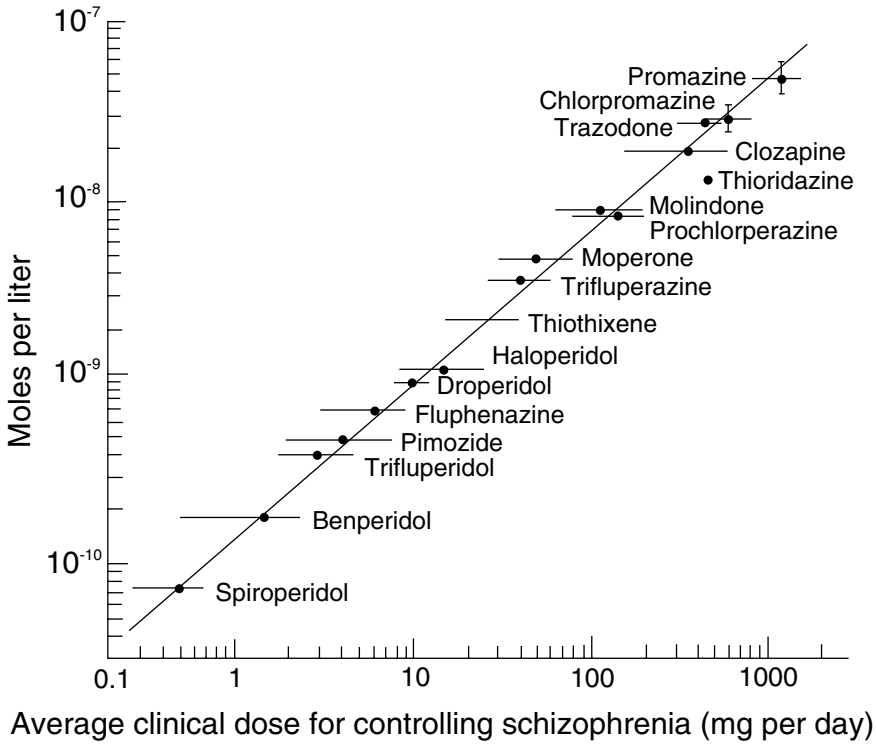


Figure 9.3 Relationship of clinical effectiveness of antipsychotic medications to their ability to neutralize dopamine. The medications that counter dopamine more efficiently are effective in suppressing schizophrenic symptoms at lower doses.

Evolutionary Origins

Although the symptoms of other major psychoses can be interpreted as inappropriately triggered extremes of normal, adaptive reactions, there is no clear adaptive value of schizoid behavior. Surveys of hospitalized patients have shown that all of the major psychoses reduce fertility, with a particularly strong reduction in schizophrenics (Macsorley, 1964). Kin-selection theory would have us look for a benefit in relatives, but the search is in vain—relatives of schizophrenics, and people at risk of developing the disease, have deficits in attention, verbal memory, and gross motor skills (Erlenmeyer-Kimling et al., 2000). There is also a peculiar deficit in relatives of schizophrenics, seeming unrelated to the disorder—their tracking eye movements are deficient, so that they follow objects with a series of jumps called saccades.

In all of these studies, though, there is inconsistency: not all patients or relatives show the deficits, each seeming to have a different pattern. It is possible that several diseases with similar symptoms have been lumped together into the category of schizophrenia, so that any one treatment would be most effective in only one or a few of the disease groups.

There have been speculations that schizophrenia is related to creativity, based partly on the often bizarre but always creative (in the sense of novel) ruminations of schizophrenics, but there is no solid evidence that the creativity in relatives of schizophrenics is significant or directed enough to enhance their biological success. The connection that many cultures have recognized between artistic achievement and mental illness seems to apply more to bipolar disorder than to schizophrenia. One possibility is that schizophrenia is linked to beneficial traits in a way that we do not yet understand. In short, why schizophrenogenic genes persist in the population remains a mystery.

● DRUG ADDICTIONS

One of the dark sides of modern life is a gigantic epidemic of drug addiction, involving hundreds of millions of victims worldwide and causing incalculable damage to individuals, families, and whole societies. The problem is worldwide, affecting wealthy regions and poor ones, from the poles to the tropics, suggesting that addictions are not quirks of particular cultures but universal vulnerabilities. At the same time, in all cultures most people are not addicted to damaging drugs, suggesting that addiction is not inevitable.

Though drugs of abuse are numerous and vary widely from culture to culture, some of them are nearly universal. By far the most damaging of the addictive drugs are alcohol and nicotine. The victims of these drugs outnumber addicts of all other drugs combined by more than an order of magnitude.

One way to measure the damage caused by drugs of abuse is to count the number of deaths they cause. As was the case with studies of family conflict, death is a measure that can be quantified and is difficult to hide. By this measure, alcohol and nicotine each kill hundreds of thousands in the United States each year, cocaine kills about 5,000, and smaller but still significant numbers are lost to other drugs.

The most abused drug in most of the industrialized countries is alcohol. In the United States it is implicated in about 55% of traffic fatalities, 50% of homicides, 30% of suicides, 65% of drownings, 50% of deaths from falls, 52% of deaths in fires, 60% of child abuse cases, and 85% of domestic violence (FitzGerald, 1988).

Not all of this mayhem is caused by alcoholism—sometimes alcohol merely exacerbates existing problems such as depression or family tensions. The addictive properties of alcohol, though, have additional consequences in secondary effects such as lost work productivity and risk of other diseases. Susceptibility to alcoholism is moderately heritable.

Given such appalling numbers, why does addiction continue? The answers are related to the reward and motivational systems built into our brains.

The Pharmacology of Addictive Drugs

Most addictive drugs mimic neurotransmitters related to ancient reward and pain systems deep in the vertebrate brain. Many of the drugs also share botanical origins, either being synthesized in some form by plants or produced by fermentation of plant products.

A particularly well-understood example of drug pharmacology is the case of opiates (heroin, morphine, and their synthetic analogs). These drugs are related chemically to **endorphins,** a group of polypeptides (short proteins) that serve as neurotransmitters in reward centers of the brain stem. Normally, the centers are activated only when a human or animal has done something right—it is physically active, having sex, caring for young. The endorphins act as internal rewards, inducing feelings ranging from well-being to euphoria. But it is sometimes hard work to earn their rewards—the runner's endorphin high requires at least half an hour of strenuous exercise. The major addictive drugs in effect hijack these ancient biological systems, bypassing them to provide the reward without the necessity to do the work. Furthermore, the reward, being concentrated in chemical form far beyond what nature can provide endogenously, can be overwhelming in its intensity.

The Opiates

Humans have used opiate drugs to induce euphoria and deaden pain at least since the beginning of written history, but until recently it was not clear how they worked. And until the advent of modern chemistry, the opiate preparations were impure and could not be easily administered in large doses.

By the early 1970s, several lines of evidence pointed to brain receptors that were sensitive to opiates. First, the drugs could be effective in very small amounts, quantities so small that highly specific receptors had to be involved (Snyder, 1977). The synthetic opiate etorphine, for instance, induces euphoria and deadens pain in doses as small as 0.1 mg, less than the effective dose of lysergic acid diethylamide (LSD). Second, most opiate molecules come in

left-handed and right-handed shapes, called isomers. Only the right-handed isomers are biologically effective. Finally, only a few small regions on the opiate molecules seem to carry the major effects.

An antiopiate drug, naloxone, made this clear. Naloxone was developed by German chemists during World War II, after their supply of opiates from the Turkish poppy had been cut off. As they desperately tried to develop synthetic opiates, they stumbled upon a molecule, very similar to natural opiates, that antagonized their effects. Given to addicts dying of drug overdoses, the drug can almost magically revive the victims.

Using these clues as well as persistence and modern biochemical methods, Pert and Snyder (1973) isolated brain receptors for endogenous opiate-like substances. Once the receptors had been discovered, it was only a matter of time until the natural neurotransmitters that stimulate the receptors were found. A scientific race to find the mystery substances ended in a tie (Hughes et al., 1975; Terenius & Wahlström, 1975) with the discovery of the enkephalins and endorphins. They are surprisingly small polypeptides, only five amino acids long, but they have potent effects.

At the time of their discovery, scientists hoped that endorphins might provide the benefits of opiates but not be addictive, because they are naturally occurring substances. Alas, endorphins turned out to be as addictive as their synthetic cousins. Because they are so dangerous, the body cannot store reserves of these substances; instead, they are synthesized within larger molecules, and the pharmacologically active segments are broken off by specialized enzymes as needed.

If the endogenous opiates are buried so deep in the brain and so well protected pharmacologically, how did plant opiates evolve to mimic some of their functions? The answer comes from an ancient evolutionary invention of the poppy plant. Because plants cannot escape or hide to defend themselves, many of them have evolved into biochemical time bombs, full of toxins to deter their predators.

For the poppy, the solution was a narcotic opiate that induced sleepiness in small doses, and death in large ones, for the animals that tried to feed on the plant. Drugged animals, in turn, are eaten by their predators, rescuing the poppy. Relatively small amounts of morphine are enough to defend the wild poppy—it does not have to manufacture large quantities of the drug. A simple biochemical reaction turned morphine, the poppy's opiate, into the much stronger and more addictive heroin.

When humans discovered the pain-deadening effects of a poppy extract, they began using it for pain relief, and discovered addiction. Synthesis of the endorphins, like most neurotransmitters, is controlled by a negative feedback

that stabilizes their concentrations in the brain. Adding a similar chemical from the outside overstimulates the negative feedback regulatory mechanism, shutting off the biosynthesis of these essential transmitters, making the users become dependent on the outside source. They are addicted. If addicts stop taking the drug, torturing withdrawal symptoms occur until the body gradually restores its own synthesis.

Addictive Drugs and Behavior

Other addictive drugs have similar mechanisms, where synthesis of some neurotransmitter is inhibited by ingestion of a similar substance from outside. Opiates, cocaine, nicotine, all have chemical structures that mimic natural neurotransmitters, and all can shut off synthesis of those essential transmitters to create dependence. The difference in the modern world is that we now have the knowledge and the resources to synthesize or purify these substances, presenting people with temptations that they have never had to face in previous history.

Addiction can occur at reproductive ages, and interferes so severely with normal social interactions that it reduces fitness. Thus a selective pressure against vulnerability to addiction should have removed this vulnerability from the population by natural selection. But the addictions have been technically possible for such a short fraction of the hundred-thousand-year sweep of human history that there has been no opportunity for the human genome to evolve resistance to the major addictive drugs. Furthermore, the major addictive drugs are so closely tied to essential neurotransmitter systems that simple genetic changes are unlikely to offer protection in any case.

Nicotine is a particularly tragic case of addiction, because most of its harmful effects come not from the nicotine itself but from the toxins and carcinogens in the delivery vehicle, tobacco smoke. Nicotine is essential for nicotinic receptors, a class of receptors for the neurotransmitter acetylcholine, and thus makes smoking tobacco addictive. The addiction would be relatively benign if it were not for the toxins, which the smoker willingly accepts to avoid the terrible experience of withdrawal—nicotine is more addictive than heroin.

Delivering drugs through the lungs or directly into the bloodstream sends a more concentrated dose to the brain, by the mechanism of Figure 9.4. If the drug does not have to pass through the diluting effect of general body circulation, the brain's dose is large and rapid. This is why smoking and injection are the most addictive, and the most attractive, means of delivery for many drugs. Unfortunately, they are also the most dangerous.

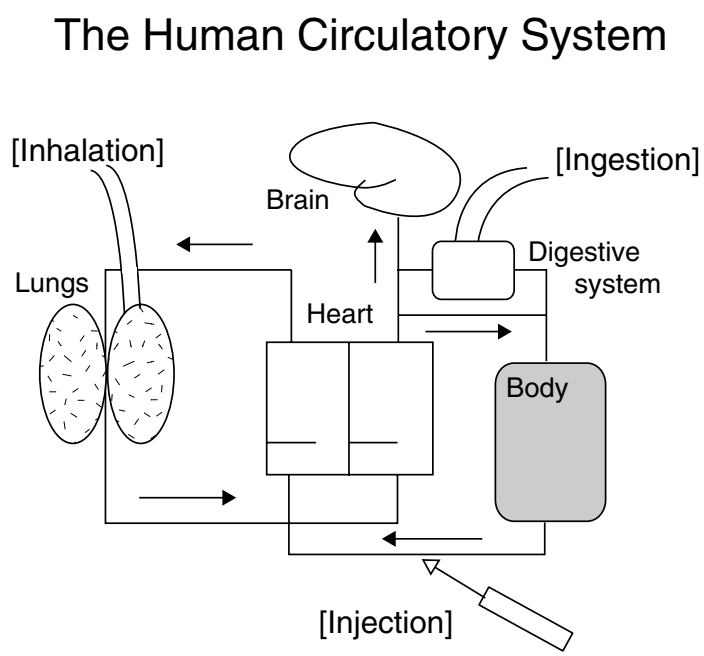


Figure 9.4 Blood circulation in the body, showing routes of drug intake. The blood flows in a figure eight, passing through the heart twice in each cycle. Ingestion by mouth is the slowest way to take a drug because the drug must pass through the digestive system and the body before reaching the brain. Drugs taken by injection and inhalation reach the brain faster and in higher concentration, and thus can be more addictive.

● DRUGS AND MENTAL ILLNESS

Some aspects of mental illness can be regarded not as disturbances of the rational machine but as drug-induced altered states of consciousness. The drugs are not taken voluntarily but are produced internally. Alternatively, the mentally ill person may react abnormally to normal amounts of endogenous psychoactive substances. Therapy includes other drugs to restore the biochemical balance and return the patient to a functioning, if not always normal, state.

The drugs are not cures, though—they only force an alteration in an abnormal biochemical balance without addressing the cause of the

abnormality. Some of them have serious side effects when taken for long periods, and not all patients are helped. Diagnosis is still a difficult problem, and treatment must include insight into the patient's psychological condition as well as drug therapy.

Psychoactive Drugs

Psychoactive drugs reveal a close relationship between motivation and consciousness, for most of them affect both functions. They also demonstrate that consciousness is based on a physical brain process, like any other neurological function, that can be biased by some of the same drugs that influence neurotransmitter systems.

The Biochemistry of Psychoactive Drugs

As was the case for antipsychotic medications, most psychoactive drugs are chemically similar to neurotransmitters in both their structures and their modes of action. The potent hallucinogen mescaline, derived from the peyote cactus, is similar in structure to norepinephrine, and "STP" is also similar to mescaline. Both affect noradrenergic synapses. Cocaine prevents reuptake of norepinephrine into the presynaptic terminals, interfering with further transmission. Figure 9.5 illustrates the similarities in chemical structures of several neurotransmitters and the corresponding psychoactive drugs.

Psilocybin and LSD are molecular expansions of the serotonin molecule. LSD was first synthesized by Swiss biochemist Albert Hoffman with the intent of producing a new psychoactive drug of therapeutic value. He got more than he bargained for, as LSD has potent effects on both perception and state of consciousness, and has at least three distinct pharmacological effects. Each is presumably associated with a different effect on consciousness. LSD blocks serotonin synapses for a few hours (hallucinations), decreases the number of postsynaptic serotonin receptors for a few days (Jacobs & Trulson, 1979) (hallucinatory "flashbacks"), and also interacts with dopamine synapses (psychotic symptoms).

The opiates (morphine and its more powerful derivative, heroin) and their biochemical similarity to the brain's enkephalins have already been discussed. Some of the effects of endogenous opiates may be indirect, through the action of the sometimes addictive drug alcohol (ethanol).

Experiments with tissue cultures show that ethanol inhibits the binding of opiates to their specialized postsynaptic receptors. After long-term exposure, the cells respond by increasing the number of opiate binding sites, an

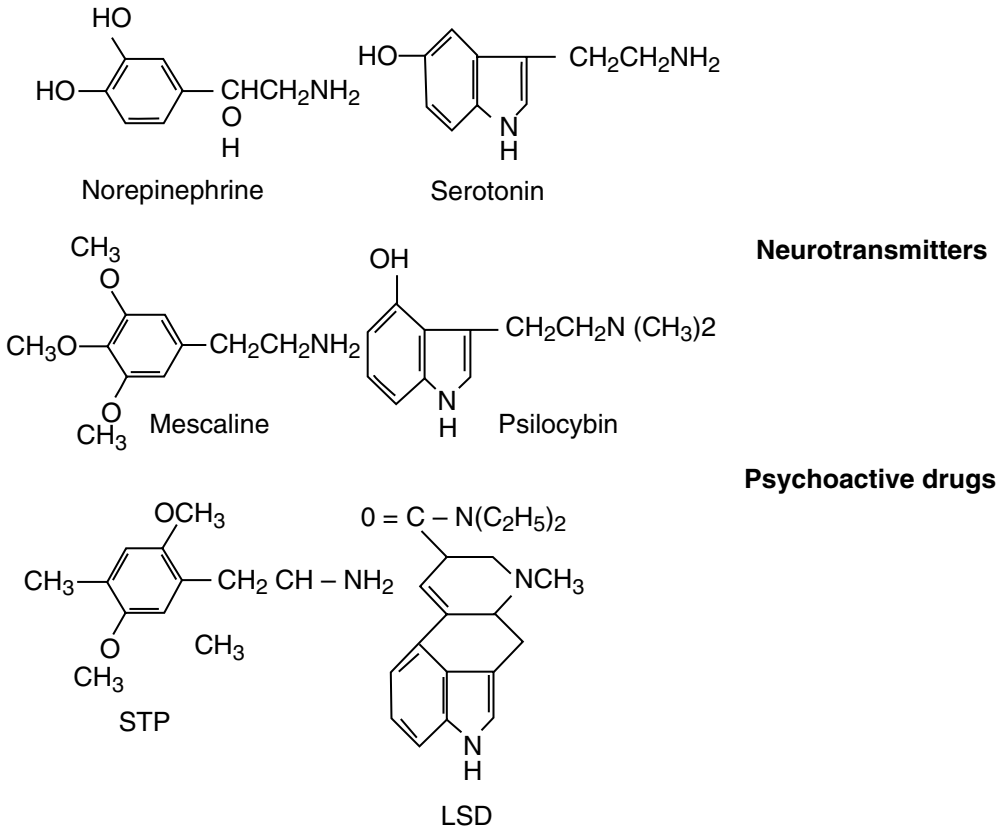


Figure 9.5 Structural similarities of drugs and neurotransmitters. Mescaline and STP are elaborations of the neurotransmitter noradrenalin (norepinephrine). Psilocybin and LSD are related to the neurotransmitter serotonin.

effect that is reversible when the ethanol is withdrawn. The tissue culture effects can be compared with clinical intoxication, tolerance, and withdrawal (Charness, Gordon, & Diamond, 1983), and may explain the addictive effects of this relatively simple molecule. Mercifully, low doses of alcohol have negligible effects on the receptors.

The evolutionary history of addictive drugs suggests that addicts are not freaks of nature, suffering from some bizarre abnormality, nor are they diseased. They are just relatively normal people faced with a temptation that evolution has not prepared them to handle. The immediate rewards of addictive drugs are so overwhelming that the reward systems of the addict's

brain tell him that getting the drugs is more important than anything, and the punishments of withdrawal are so overwhelming that the addict will do anything to avoid them.

The question then becomes not why people become addicted, but why most people do not—after all, we all share the same neurotransmitter biochemistry. Human motivation is based on more than just biochemistry, though, with social and rational components looming particularly large in the regulation of human behavior. Those most prone to addiction may rate high on the personality characteristic of sensation-seeking. Such people actively seek out exciting, stimulating, and even dangerous environments (MacDonald, 1998).

Most people, though, see the overwhelming feelings of drug-induced excitement or well-being or euphoria as false pleasures, forced from the outside and eventually leading only to despair. Long-term planning in the human brain makes it possible for most of us to resist the short-term temptations of addictive drugs.

CONCLUSION: THE DIVERSE ● ORIGINS OF MENTAL ILLNESSES

The genetics of phobias and OCD showed that they are most likely pathological extremes of traits that are normally adaptive. ADHD illustrates a second pattern, a syndrome that causes problems in the modern world but may have been beneficial in some ancestral environments just as it is. Schizophrenia, though related obliquely to a sort of creativity, has no clear benefit in either patients or their relatives. And drug addictions from this perspective are not illnesses at all: rather, they are tragic combinations of the success of plants in combating predation along with the ability of modern humans to purify and/or synthesize their toxins.

There seem to be as many origins of mental illnesses as there are illnesses themselves. None of them are caused by conventional microbes or parasites. All of them, though, can be better understood and treated by examining their evolutionary origins and the forces that maintain susceptibility to them in the human genome.

Understanding mental illnesses leads not to stigmatizing the victims of these serious diseases but to understanding their plight and possibly relieving their symptoms. The previous stigma and fear can be alleviated by the possibility for treatment and by the realization that mental illnesses have physical origins like any other illness. Many victims of mental illnesses can lead relatively normal lives because the pharmacology and the evolutionary origins of their illnesses have been worked out.

It is my hope that the new way of categorizing and understanding mental illnesses introduced in this chapter will serve as an example of the promise of evolutionary psychology to better the human condition by better understanding human origins and the exquisite adaptations that reside in all of us.

● DISCUSSION QUESTIONS

1. Under what conditions might phobias to current dangerous objects and situations find their ways into the human genome?
2. Might there be (or once have been) environmental situations in which schizophrenic behavior offered a selective advantage?
3. Given that addiction is a normal physiological and behavioral response to an abnormal availability of psychoactive drugs, what can be done about social problems of addiction?

● FURTHER READING

Stevens, A., & Price, J. (2000). *Evolutionary psychiatry: A new beginning*. London: Routledge.

Though tinged with obsolete Freudian influence, this book played a large role in establishing evolutionary thought as a tool in understanding mental illnesses.

Nesse, R. M., & Williams, G. C. (1996). *Why we get sick: The new science of Darwinian medicine.* New York: Vintage Books.

This volume includes mental illnesses among a wide variety of physical maladies that are caused or exacerbated by the conditions of modern life.

Rapoport, J. (1991). *The boy who couldn't stop washing*. New York: Penguin Books.

A heartbreaking yet illuminating account of a case of OCD. After describing the case, Rapoport compassionately reviews the etiology, epidemiology, and prognosis of the disease for OCD's victims.