The basis of biological explanations and treatments of mental disorders is that behaviour and mood are regulated by brain systems. These allow us to perceive information, integrate that information with past memories and other salient factors, and then respond emotionally and behaviourally. Their disruption results in inappropriate perception, mood and behaviour. This may occur as a result of structural damage, or disruption of chemicals, known as neurotransmitters, responsible for activating different areas of the brain. By the end of the chapter, you should have an understanding of:

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Basic neuro-anatomy as it relates to mental health disorders

The neurotransmitter systems and the key neurotransmitters that influence mood and behaviour

The drug treatments that are used to alter neurotransmitter levels and, hence, mood and behaviour

Three physical interventions used to treat mental health problems: electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), and psychosurgery

Some of the controversies and issues raised by each treatment method.

4.1 The behavioural anatomy of the brain

The brain is an intricately patterned complex of nerve cell bodies. It is divided into four anatomical areas: the hindbrain, midbrain, forebrain and cerebrum.

**Hindbrain, midbrain and forebrain**

The hindbrain contains the parts of the brain necessary for life: the medulla oblongata, which controls respiration, blood pressure and heartbeat; the reticular formation, which controls wakefulness and alertness; and the pons and cerebellum, which correlate muscular and positional information.

Above these lies the midbrain, which also contains part of the reticular system and both sensory and motor correlation centres which integrate reflex and automatic responses involving the visual and auditory systems and are involved in the integration of muscle movements.

Many of the key structures that influence mood and behaviour are situated in the forebrain. These include the following:

- **Thalamus**: links the basic functions of the hindbrain and midbrain with the higher centres of processing, the cerebral cortex. Regulates attention and contributes to memory functions. The portion that enters the limbic system is involved in the experience of emotions.

- **Hypothalamus**: regulates appetite, sexual arousal and thirst. Also appears to have some control over emotions.

- **Limbic system**: a series of structures including a linked group of brain areas known as the Circuit of Papez: hippocampus – fornix – mammillary bodies – thalamus – cingulated cortex–hippocampus. The hippocampus – fornix – mammillary bodies circuit is also involved in memory. The hippocampus is one site of interaction between the perceptual and memory systems. A further part of the system, known as the amygdala, links sensory information to emotionally relevant behaviours, particularly responses to fear and anger. It has been called the ‘emotional computer’ because of its role in coordinating the process that begins with the evaluation of sensory information for significance (such as threat) and then controls the resulting behavioural and autonomic responses.
4.1 THE BEHAVIOURAL ANATOMY OF THE BRAIN

The ventral tegmental area (VTA) is an important nerve tract within the limbic system. Activation of the VTA sends messages to clusters of nerve cells in the nucleus accumbens and the frontal cortex. This linkage, known as the mesolimbic dopamine system, forms the brain's primary reward pathway.

Cerebrum

Above these three sets of structures lies the cerebrum. This is the part of the brain we are most familiar with, and is the most recently evolved part. It contains a number of structures:

- **Basal ganglia**: a dense mass of neurons at its core. It includes the corpus striatum responsible for complex motor coordination.
- **Cortex**: the convoluted outer layer of grey matter comprising nerve cell bodies and their synaptic connections. It is the most highly organized centre of the brain. Most cortical areas are involved to some degree in the mediation of any complex behaviour, although there are centres of functional control within it. It is divided into two functional hemispheres, linked by the corpus callosum, a series of interconnecting neural fibres, at its base. It is divided into four lobes: frontal, temporal, occipital and parietal (see Figures 4.1 and 4.2). As these are involved in the aetiology of a number of mental health and neurological disorders, the function of each will now be considered in more detail.
**Frontal lobes**

The frontal lobes make up about one-third of the mass of the brain. The frontal cortex has an executive function, in that it coordinates a number of complex processes, including speech, motor coordination and behavioural planning. Loss of this executive function, as a consequence of damage, can result in a number of outcomes, including diminished anxiety and concern for the future, impulsiveness, lack of initiative and spontaneity, impairments in recent memory, loss of capacity to think in abstract terms, and an inability to plan and follow through a course of action or to take account of the outcome of actions. Individuals with frontal damage become inflexible and rigid. They have difficulty in shifting from one concept or task to another and changing from one established habit or behaviour to another. This can result in perseveration, where a particular behaviour is continued even in the face of clear instructions to change. The frontal lobes also seem to influence motivation levels. Damage to them can lead to a condition known as adynamia, evident through a complete or relative lack of verbal or overt behaviour. The prefrontal lobes are connected to the limbic system via the thalamus and motor system within the cortex. Links between the prefrontal cortex and the limbic system are activated during rewarding behaviours.
**Temporal lobes**

Although their functions are distributed, there are clear functional centres within the temporal lobes. The location of these centres differs according to handedness. In those who are right-handed, the main language centre is located in the left hemisphere, and visuo-spatial processing is located in the right hemisphere. In left-handed individuals, there is less localization within hemispheres. The temporal lobes are also intimately involved in the sense systems of smell and hearing. They are responsible for the integration of visual experience with those of the other senses to make meaningful wholes. Disruption within the temporal lobes, for example, as a consequence of temporal lobe epilepsy, can result in visual illusions or hallucinations. Olfactory (smell) hallucinations have also been reported, although less commonly. Reflecting the multifaceted functioning of the temporal lobes, these illusions or hallucinations may be accompanied by strong emotions, in particular, fear. The temporal lobes have an important role in memory and contain systems which preserve the record of conscious experience. Damage to one of the temporal lobes results in relatively minor memory difficulties, some of which may be evident on psychometric testing, but may not cause problems to the individual. Damage to both can result in profound memory deficits. Finally, they have an intimate connection with the limbic system and link emotions to events and memories.

**Occipital and parietal lobes**

These lobes are primarily involved in the integration of sensory information. Their functions are distributed and there are no clear functional centres. The occipital lobe is primarily involved in visual perception. Links to the cortex permit interpretation of visual stimuli.

**The synapse**

Each of the millions of interconnecting nerves within the brain is known as a neuron. Activation of systems within the brain is the result of small electrical currents progressing along many different neurons. Critical to the flow of this current are the small gaps between neurons, known as synapses. Here, chemicals known as neurotransmitters are responsible for activation of the system.

Each neuron has a number of fine branches known as axons at its terminal. At the end of these is an area known as the presynaptic terminal which, in turn, is in close proximity to the postsynaptic terminal within the axon of another neuron. Between them is an enclosed area known as the synaptic cleft (see Figure 4.3). Neurotransmitter chemicals are stored within the axon in small pockets known as synaptic vesicles. Electrical stimulation of the nerve results in release of the vesicles’ contents into the synaptic cleft. Once the transmitter has been released into the synaptic cleft, it moves across the gap between the two axons, where it is taken up by specialist cells within the postsynaptic membrane – the receptor cells. Once in the receiving neuron, chemicals known as second messengers are released and trigger the firing of the neuron, continuing the activity of the activated neurological system. If all the transmitter is not taken up by the postsynaptic receptor, further activation may be inhibited either by re-uptake of the unused molecules back into vesicles in the initiating neuron or by degradation by other chemicals, such as monoamine oxidase released into the synaptic cleft.
Neuronal activity itself is mediated by small electrical impulses that travel down the nerve axon towards the nerve ending. When a neuron is at rest, the outside of the cell wall is lined with sodium ions, and the inside wall is lined with potassium ions. When the neuron is stimulated by an incoming message at its receptor site, the sodium ions move from the outer side of the cell membrane to its inside. This starts a wave of electrochemical activity that continues down the length of the axon and results in it 'firing.' Immediately following this, the potassium ions shift from the inside to the outside of the neuron, returning it to its original resting state.

The neurotransmitters

A relatively small number of neurotransmitters have been implicated in the aetiology of the most common mental disorders. The effects of those considered in this chapter are summarized in Table 4.1, and are considered in more detail in the relevant chapters later in the book.

Serotonin

First identified in the 1950s, serotonin is an amino acid, and is synthesized from its precursor L-tryptophan. It is found in the striatum, mesolimbic system, forebrain, cortex, hippocampus, thalamus and hypothalamus. It is thought to be involved in moderating mood, with low levels leading to conditions including depression and obsessive-compulsive disorder.
4.1 The Behavioural Anatomy of the Brain

Norepinephrine

Norepinephrine is a second neurotransmitter involved in depression as well as a number of anxiety disorders. Among other areas, it is found in the hypothalamus, cerebellum and hippocampus. It belongs to a family of chemicals known as catecholamines.

Dopamine

Neurons mediated by dopamine are found in the mesolimbic system, in a brain area known as A10, with links to the thalamus, hippocampus, frontal cortex and the substantia nigra. Dopaminergic dysregulation has been associated with conditions as varied as schizophrenia, autism and attentional deficit/hyperactivity disorders.

GABA

A group of drugs known as benzodiazepines were found to be an effective treatment of anxiety before their mode of action was understood. It is now known that they enhance the action of a neurotransmitter known as gamma-aminobutyric acid (GABA). This carries inhibitory messages: when it is received at the postsynaptic receptor site, it prevents the neuron from firing. Sites of GABA include the brain stem, cerebellum and limbic system.

The autonomic nervous system

Although most explanations of mental health problems focus on neurotransmitters and neurological processes, another system, known as the autonomic nervous system, is also involved in some conditions, particularly those involving stress or anxiety. The autonomic nervous system

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**Table 4.1 The key neurotransmitters, some of the drugs that affect them, and their role in key mental health disorders**

<table>
<thead>
<tr>
<th>Neurotransmitter</th>
<th>Primary disorder</th>
<th>Treatment*</th>
<th>Mode of action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monoamine</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serotonin</td>
<td>↓ in depression</td>
<td>Tricyclics, SSRIs</td>
<td>Prevent re-uptake</td>
</tr>
<tr>
<td>Dopamine</td>
<td>↓ in schizophrenia</td>
<td>Phenothiazines</td>
<td>Block receptor sites</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reserpine</td>
<td>Block vesicular storage</td>
</tr>
<tr>
<td><strong>Catecholamines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>↓ in depression</td>
<td>MAOIs</td>
<td>Prevent degradation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tricyclics</td>
<td>Prevent re-uptake</td>
</tr>
<tr>
<td><strong>Amino acids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GABA</td>
<td>↓ in anxiety</td>
<td>Benzodiazepines</td>
<td>Enhance GABA</td>
</tr>
</tbody>
</table>

* See pp. 87–93.
links the brain to many of the body organs, including the heart, gut and smooth muscles. Its job is to control the activity of these organs in response to the various demands being placed on them, for example, by increasing heart rate, blood pressure and breathing rate during exercise. Overall control of the autonomic nervous system is provided by the hypothalamus. It receives blood-borne and nervous system inputs concerning the state of the body, such as oxygenation and acidity of the blood. In addition, it receives inputs from the cortex and limbic system regarding behavioural and emotional factors. Based on these various inputs, the hypothalamus either increases or decreases activity within the autonomic nervous system and the various organs it controls.

**Autonomic processes**

The autonomic nervous system comprises two subsystems, known as the sympathetic and parasympathetic nervous systems. These arise in the medulla oblongata in the brain stem and travel down the spinal cord. At various points along the spinal cord, they link with other nerves connected to target organs such as the heart, arteries, skeletal muscles and colon. The sympathetic system is involved in arousal, and its activity within the brain and spinal cord is controlled by norepinephrine. High levels of norepinephrine result in increased arousal and activation of the target organs. The parasympathetic system is involved in calming or reducing arousal, and its activity is controlled by levels of the neurotransmitter acetylcholine. The two systems tend to work antagonistically and the level of physical activation of the individual at any one time is a function of the relative dominance of each system.

**Endocrine responses**

Neurotransmitters act quickly, but are unable to maintain activation for long. To enable a sustained response to stress, a second system is activated by the sympathetic nervous system. High levels of sympathetic nervous system activity cause part of the adrenal glands, known as the adrenal medulla, situated above the kidneys, to release hormonal counterparts of the neurotransmitter norepinephrine (and to a lesser extent epinephrine) into the bloodstream. These travel to the target organs, are taken up by receptors, and sustain the action initiated by the neurotransmitters.

When the emotion of stress is experienced, the sympathetic nervous system gains dominance, activates the body and prepares it to deal with physical damage. At its most dramatic, this response is known as the *fight–flight response*. At such times, sympathetic activity is clearly dominant, the heart beats more quickly and more powerfully, blood is shunted to the muscles and away from the gut (hence the experience of 'butterflies'), skeletal muscles tense in preparation for action, and so on. The individual may shake, pace or want to engage in some form of physical activity. This ancient response is clearly advantageous at times when the causes of stress are acute and life-threatening: chronic activation in response to long-term stress or short-term activation at inappropriate times, such as while in a supermarket or bus queue, is more problematic.

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4.2 Drug therapies

Activation of brain systems is dependent on the activity of individual neurons, which, in turn, are mediated by the amount of neurotransmitter available at the postsynaptic receptor site. Too much and the system is overactive; too little, and it is underactive. The goal of drug therapies is to ensure appropriate levels of key neurotransmitters. They do this by one of two actions:

- **Increasing the availability** of the neurotransmitter by preventing re-uptake at the synapse, preventing degradation within the synaptic cleft, or replacing low levels of a particular neurotransmitter with its pharmacological equivalent. Drugs that increase the action of a neurotransmitter are known as agonists.

- **Decreasing availability** of the neurotransmitter by depleting levels of the available transmitter or replacing the active transmitters with an inert chemical. Drugs that inhibit the action of a neurotransmitter are known as antagonists.

Drugs are usually administered by mouth or injection into muscles, and then enter the bloodstream. They enter the brain by permeation from the small blood vessels that pass through it. Designing drugs to influence brain activity has not proven easy. The brain is protected from infection and other blood-borne insults by the blood–brain barrier. In the rest of the body, drugs pass from the blood vessels to target sites through pores in the walls of the blood vessels. The blood vessels in the brain lack these pores, and drugs have to pass directly through the cells of the blood vessel wall. This mechanism means that only drugs using relatively small molecules can pass this barrier, and even then their perfusion will be less than in the rest of the body.

**Treating depression**

**Drugs that increase norepinephrine: MAOIs**

The first potent antidepressants to be developed were known as monoamine oxidase inhibitors (MAOIs). These prevent degradation of norepinephrine (and to a lesser extent, serotonin) by monoamine oxidase within the synaptic cleft and help sustain its action. As was the case of a number of early psychiatric treatments, the discovery of the antidepressant qualities of MAOIs was accidental. Their first use was in the treatment of tuberculosis, where they were found to improve mood in those treated. Since then, MAOIs have become a standard treatment for depression, with a success rate of about 50 per cent.

Despite this, MAOIs have to be used with some caution. As well as working in the brain, they prevent the production of monoamine oxidase in the liver and intestines, where it breaks down tyramine, a chemical that can result in potentially fatal and sudden increases in blood pressure if allowed to accumulate within the body. In order to prevent this, people who take MAOIs have to avoid foods such as cheeses, red wines, Marmite, bananas and some fish that contain tyramine. Eating these foodstuffs may trigger a sudden and potentially fatal rise in blood pressure. Some newer MAOIs, known as reversible selective MAOIs, have been developed that avoid these problems. However, as more recent research has suggested that serotonin is more important in the aetiology of depression than norepinephrine, treatment has mostly changed to drugs that affect...
serotonin levels: the tricyclics, selective serotonin re-uptake inhibitors (SSRIs), and serotonin and norepinephrine re-uptake inhibitors (SNRIs).

**Drugs that increase serotonin: tricyclics, SSRIs and SNRIs**

Three drug groups increase serotonin levels by inhibiting its re-uptake into the presynaptic terminal: the tricyclics (for example, imipramine, amitriptyline), SSRIs (for instance, fluoxetine, sertraline), and SNRIs (venlafaxine, milnacipran and duloxetine). Tricyclics and SNRIs also increase levels of norepinephrine.

The first tricyclic, imipramine, was used initially as a treatment for schizophrenia. It was unsuccessful in this, but did reduce levels of depression in many people. Between 60 and 65 per cent of those who take tricyclics do experience some improvement of symptoms (Hirschfeld 1999). Their effects can take ten or more days to become evident, probably as a result of an initial reduction in the amount of serotonin produced at the presynaptic terminal in response to more being available within the synaptic cleft. Improvements in mood occur as the system adapts to the drug and begins to release normal amounts of serotonin again, with re-uptake prevention finally resulting in an increase in available serotonin. It is important to maintain a therapeutic regime for some months after changes in mood have been achieved: about 50 per cent of users will relapse within a year if tricyclic use is prematurely stopped (Montgomery et al. 1993).

Selective serotonin re-uptake inhibitors are a more recent pharmacological treatment. They increase serotonin levels without affecting norepinephrine levels, which may increase following treatment with tricyclics. Although they may not be more effective than tricyclics, this gives them fewer side-effects such as constipation and dry mouth and they are less dangerous in overdose. Rocca et al. (1997), for example, found that 56 per cent of people who took tricyclics reported an uncomfortably dry mouth, compared with 8 per cent treated with SSRIs. Tricyclics and SSRIs are the most commonly used pharmacological treatments of depression; MAOIs may have therapeutic effects on some individuals who do not respond to these drugs, but the potential risks associated with their use generally make these a second-line treatment. Of concern is evidence of a characteristic SSRI discontinuation syndrome (Tamam and Ozpoyraz 2002). It is usually mild, commences within one week of stopping treatment, resolves spontaneously within three weeks, and consists of a number of physical and psychological symptoms, of which the most frequent are dizziness, nausea, lethargy and headache. Restarting use of an SSRI leads to resolution within 48 hours. To minimize this risk, SSRIs, like other antidepressants, need to be withdrawn gradually. Because SNRIs work on both serotonin and norepinephrine levels, they appear to be more effective in the treatment of depression than are SSRIs. However, like tricyclics, they may have more severe side-effects and discontinuation symptoms (Sir et al. 2005; Stahl et al. 2005).

Side-effects such as a dry mouth may appear somewhat trivial, but they can have a significant impact on those taking these drugs, as one user pointed out:

“The worst thing about the drug was the dry mouth I got with it. And when I say ‘dry mouth’, I really mean it. My mouth and lips were dry all the time. I wanted to drink all the time, so I could refresh my mouth. But that didn’t help much – so I ended up chewing gum all the time – and I hate gum! It may not sound much, but when you are already feeling down, it just adds to the bad feeling.”
Another woman, who benefited from taking SSRIs, commented on a, perhaps, less obvious side-effect.

Taking these drugs was great – I felt so much better on them. But one problem did arise. When I was depressed, the last thing I wanted to do was to have sex with my husband. Now, I can’t wait... but the most frustrating thing is I can’t climax! We have great fun, but it is so frustrating!

Emerging problems
The introduction of SSRIs was not without problems. Perhaps the most widely known controversy involved one of the first of this type of drug to be widely available – Prozac (otherwise known as fluoxetine). This was described by its makers as the first of a new generation of side-effect-free antidepressants. In addition, it rapidly gained a reputation as the only antidepressant that could not only help people who were depressed, but also improve the quality of life of people who were not. It seemed to increase confidence, sociability and to reduce shyness and social anxiety. As a result, it became widely prescribed in the USA, among both those who were depressed and those who needed the emotional lift that it provided.

This initial success was soon mitigated by a series of claims alleging that Prozac had far more side-effects than were initially reported by its makers, the most dramatic of which involved significant behavioural disinhibition that could result in either self-harm or violence towards others. Some of the links with violence were of a secondary nature. Lipinski et al. (1989), for example, reported significant levels of akathisia, a condition involving marked agitation and high levels of impulsiveness, in between 10 and 25 per cent of people who were prescribed Prozac. This may potentially be associated with suicide or aggression. Rothschild and Locke (1991) also reported the case histories of three people who felt suicidal and attempted suicide while being prescribed Prozac. Perhaps the most notorious association between Prozac and violence was the case of Joseph Wesbecker, who shot 20 people in his former workplace, eight of them fatally, before killing himself while he was taking Prozac (Geoffrey 1991). It is important to note that small case studies and sensationalist stories cannot be considered convincing evidence of a link between Prozac and dangerous behaviour, but they have increased the publicity surrounding prescription of the drug.

More empirical studies have indicated a smaller potential risk associated with Prozac than these initial studies may have indicated, and even these are open to alternative explanations. Jick et al. (1995), for example, identified over 170 000 people who had been prescribed one of ten antidepressants over a five-year period. They then compared suicide rates across the various types of antidepressant, reporting them as the ‘rate of suicide per 10 000 person years’. The lowest rate of suicide, 4.7, was found among people taking Lofepramine (a tricyclic); the mean rate was 10.8 suicides per 10 000 years. The highest rate of suicide was found among those taking Prozac: 19.0 suicides per 10 000 years. In an explanation of this finding, the authors noted that many people taking Prozac were at particularly high risk of suicide as a result of factors other than their medication, including a history of feeling suicidal and poor outcome on other antidepressants. After accounting for these factors, the increased risk of suicide in those taking Prozac was less apparent, although suicide rates remained a little higher than the average.
More recently, Gunnell et al. (2005) reported the results of a meta-analysis of drug company data on suicide, suicidal thoughts and self-harm following treatment with a variety of SSRIs or a placebo. Their findings were based on data from over 40 000 individuals in 477 trials of drug effectiveness. Despite this large number of people, their findings were surprisingly equivocal, with evidence of both a protective and a risk-enhancing effect across a number of trials. The relative risk (compared with placebo) for suicide was 0.85, indicating a modestly reduced risk – but the 95 per cent confidence intervals ranged between 0.20 and 3.40, indicating a wide variety of outcomes across trials. A similar picture was found for self-harm and suicidal thoughts. They concluded on this evidence that ‘more research is required’, but that any very small increase in risk should be balanced against the effectiveness of SSRIs in treating depression. Fergusson et al. (2005) found no evidence of any greater risk of suicide associated with SSRIs in comparison with tricyclics in a meta-analysis of the relevant trials. In addition, Yerevanian et al. (2004) found that suicide rates did not differ across SSRIs and tricyclics, and that suicide rates were higher following discontinuation of both SSRIs and tricyclics than during active treatment.

Treating anxiety

**Drugs that enhance the action of GABA: the benzodiazepines**

Although their mode of action is not fully understood, a group of drugs known as benzodiazepines was found in the 1960s to be an effective treatment of anxiety. Benzodiazepines appear to enhance the action of GABA, but do not bind to the same postsynaptic receptor sites. This class of drugs replaced the use of low doses of barbiturates, which made people drowsy, could prove fatal as they led to respiratory failure, and were highly addictive.

The first benzodiazepine was known as chlordiazepoxide (Librium). The best known, Valium, was marketed several years later. By the mid-1980s, benzodiazepines were the most widely prescribed psychotropic medication. However, their prescription has not been without cost. When their use is stopped, levels of anxiety frequently return to pre-morbid levels or above (Power et al. 1990). Sudden withdrawal of these drugs typically results in the rapid recurrence of previous symptoms combined with withdrawal symptoms, including sweating, shaking, nausea and vomiting. As a consequence of this, up to 80 per cent of people who stop taking benzodiazepines after a long period of use relapse and require further treatment. Many people have to be gradually withdrawn from the drugs over extended periods of time – often many months. In general, the shorter the half-life of a drug, the more sudden and severe any withdrawal symptoms (see Table 4.2).

Benzodiazepine use has also been associated with a number of undesirable side-effects, including drowsiness, memory loss, depression and aggressive behaviour including acute rage (Curran 1991). Long-term use may result in irreversible changes. Despite these concerns, benzodiazepines are still regularly prescribed, but now on a more short-term basis than previously. As well as impacting on sites within the brain such as the limbic system, they provide a relaxant effect as a result of their effect on GABA within the spinal cord.

**Drugs that increase norepinephrine and serotonin**

There is increasing evidence that some anxiety conditions, and in particular panic disorder, are mediated, at least in part, by norepinephrine. For these conditions, treatment with antidepressants
has proven more effective than with traditional anxiolytics (Bakker et al. 1999). Treatment is usually with tricyclics rather than MAOIs, for safety reasons: although the primary effect of tricyclics is on serotonin, they also increase norepinephrine levels. Serotonin itself may also be involved in the aetiology of anxiety disorders such as panic and obsessive-compulsive disorder. As a result, these disorders are increasingly treated with both tricyclics and SSRIs (Ballenger 2004).

### Treating schizophrenia

Biological theorists have implicated dopamine in the aetiology of the positive symptoms of schizophrenia (see Chapters 2 and 7). Individuals with these symptoms do not show raised levels of dopamine but appear instead to have an excessive number of dopamine receptor sites on the postsynaptic terminal, making them over-reactive to normal levels of dopamine. The goal of therapy is usually therefore to reduce the number of receptor sites accessible to the dopamine by filling them with inert drugs that mimic dopamine’s chemical composition. A less frequent intervention involves reducing the amount of available dopamine.

### Drugs that reduce dopamine levels

The origin of the present pharmacological treatment of schizophrenia lies in the observations made in the 1940s by a French surgeon, Henri Laborit, that one of the drugs he used as an anti-histamine had a profound calming effect on his patients prior to surgery. The drug was called chlorpromazine. In the early 1950s, this was used experimentally with patients with psychotic symptoms, and rapidly became established as the primary treatment of schizophrenia.

Chlorpromazine belongs to a class of drugs variously known as phenothiazines, neuroleptics or major tranquillizers. They work by blocking the dopamine receptors in the postsynaptic...
receptor sites. Unfortunately, while successful in the short term, their use results in a proliferation of dopamine receptor sites (Strange 1992), adding further to the sensitivity of the postsynaptic receptors and resulting in the need for long-term treatment. They also have a number of significant side-effects. For these reasons, clinicians maintain people with schizophrenia on the lowest effective dose or gradually reduce and stop medication after a period of time in which the individual is functioning normally (see Chapter 7).

The phenothiazines’ main side-effects occur as a result of their impact on the extrapyramidal areas of the brain, including the substantia nigra. These areas are involved in the control of motor activity and coordination. The most common extrapyramidal symptoms are Parkinsonian symptoms. These include stiffness in the arms and legs, facial expressions that are flat and dull, and tremors, particularly in the hands. These symptoms can usually be relieved by drugs that reverse the effects of phenothiazines or a reduction in the amount of drug prescribed. About 20 per cent of those who take phenothiazines for an extended time develop a second condition, known as tardive dyskinesia (APA 2000). Its primary symptoms include involuntary writhing or tic-like movements of the face or whole body. Facial movements include involuntary chewing, sucking and writhing of the tongue in and out of the mouth. Body movements include jerky, purposeless movements of the arms, legs and torso. Its severity varies between a single symptom and a severe whole body problem. These symptoms are difficult to treat and can be irreversible. If detected early, and treatment is stopped immediately, most symptoms will remit. However, many symptoms are similar to those found in schizophrenia and may not be observed – or even result in increased phenothiazine being prescribed. The longer an individual has taken phenothiazines, the less likely their symptoms are to remit, even after the cessation of therapy.

A second approach to the treatment of schizophrenia involves reducing the amount of dopamine available to be released into the synaptic cleft. The action of a drug known as reserpine is to inhibit the synthesis of dopamine. Once existing stores have been utilized, it can take up to two weeks for them to return to normal levels during treatment with reserpine.

**Drugs that reduce NMDA levels**

One additional form of drug has proven effective in the treatment of schizophrenia. Atypical neuroleptics were initially thought to have their action through their impact on NMDA receptors. Drugs such as phencyclidine (PCP, ‘angel-dust’) and ketamine are thought to increase activity in these receptors and cause symptoms similar to those of schizophrenia. Their activity seems to be blocked by the drugs clozapine and risperidone (Morimoto et al. 2002). These drugs may also reduce dopamine activity, possibly indirectly through their influence on serotonin levels, which control dopamine release at times of stress (Pehek et al. 2006).

These atypical neuroleptics are likely to prove a first-line treatment of schizophrenia in the future, as they may not only be more effective than phenothiazines but also cause significantly fewer extrapyramidal symptoms (Tandon and Fleischhacker 2005). Success rates with phenothiazines of about 65 per cent are typical: for the new drugs the success rate is about 85 per cent (Awad and Voruganti 1999). Unfortunately, the medication also carries some costs. Between 1 and 2 per cent of those who take the drug go on to develop agranulocytosis, a potentially fatal reduction in white blood cells, resulting in a need for all those prescribed these drugs to have regular blood tests so they can be withdrawn before this disorder becomes problematic.
Adherence to drug treatments

Any drug can achieve its potential only if it is taken regularly and at therapeutic levels. This is not always the case: up to 50 per cent of people prescribed psychotropic medication either do not take the recommended dose or do not take the drug at all (a figure, incidentally, that reflects a more general failure to adhere to recommended medication of all types within the general population). Bulloch and Patten (2009), for example, reported non-adherence rates in their survey of over 6000 people taking psychotrophic medication of: 34.6 per cent of people taking antipsychotics, 34.7 per cent of those taking sedative-hypnotics, 38.1 per cent for mood stabilizers (in the treatment of bipolar disorder) and 45.9 per cent for antidepressants. The most frequent reason for non-adherence was forgetting. More conscious decisions whether or not to take tablets are often based on a form of cost–benefit analysis, in which the benefits of taking medication, usually in terms of relief from symptoms, are weighed against the costs of taking it, usually the side-effects that accompany use of the drug. The more side-effects a drug has, the less likely those prescribed it are to adhere to its use, particularly where there are no immediate changes in symptoms when doses of a drug are taken or missed, as is the case for many psychiatric drugs. An example of this can be found in the findings of Demyttenaere et al. (1998), who found that 36 per cent of people prescribed the tricyclic amitriptyline failed to take their medication, compared with 6 per cent of those prescribed the SSRI fluoxetine. Level of depression was not predictive of drop-out. However, younger men who experienced severe side-effects were least likely to take the medication.

Not surprisingly, some side-effects are more problematic than others. Lingjaerde et al. (1987) listed a hierarchy of side-effects that people receiving phenothiazines considered most troublesome. In ascending order, these were sleepiness, increased fatiguability, weight gain, tension or ‘inner unrest’, and concentration difficulties. Extrapyramidal effects, which were the main concern of the prescribing psychiatrist, were rated as relatively unimportant. Other factors may also be involved. Day et al. (2005) found that a poor relationship with the prescriber, experience of coercion during admission and low insight predicted a negative attitude towards treatment. This finding is consistent with the findings of Myers and Branthwaite (1992), who found that adherence was greatest when clients and not the doctor chose the times when they took their drugs. Finally, Sirey et al. (2001) found high adherence to medication to be associated with lower perceived stigma of taking drugs, higher self-rated severity of illness, being aged over 60 years, and absence of ‘personality pathology’. Finally, simply considering the medication you are taking to be necessary is a powerful factor in adherence (Jónsdóttir et al. 2008).

The authors note that up to 50 per cent of psychiatric patients do not adhere fully to their prescribed medications. They also note that most studies exploring reasons for this phenomenon are limited by small sample size, focus particularly on people diagnosed with schizophrenia, and are carried out in western cultures. As beliefs about the nature of psychiatric conditions differ in Sub-Saharan Africa from those in the West (beliefs in spiritual causation, for example, are widely prevalent), reasons for adherence or non-adherence to medication are also likely to differ. The aim of this study was therefore to assess the rate of, and reasons for, non-adherence to medication among a variety of psychiatric outpatients in Nigeria.

Method

Participants
Participants were adult outpatients of the psychiatric services in Lagos, Nigeria, selected through random sampling of case files. Inclusion criteria included having a DSM psychiatric diagnosis and taking psychotropic medication for at least one year. Of 362 patients meeting the inclusion criteria, 16 refused to participate, leaving a sample size of 346.

Assessment
Assessment involved completion of questionnaires and clinician assessments. These included:

1. Sociodemographic details
   - Demographic information
   - Level of social support: ‘good’, ‘fair’ and ‘poor’

2. ‘Illness-related’ variables
   - Psychiatric diagnosis, duration, number of episodes, and number of hospitalizations
   - Level of insight: ‘full, partial, or no insight’
   - Brief Psychiatric Rating Scale (BPRS) rated the presence and severity of psychopathology
   - Mini Mental State Examination (MMSE) assessed participants’ level of cognitive functioning
   - Global Assessment of Functioning (GAF) rated health on a 100-point scale from 1 (sickest) to 100 (healthiest)
   - Participants reported the perceived causes of their condition, its expected prognosis and their preferred method of treatment. Causation was rated as predominantly psychosocial, spiritual or biological; perceived prognosis was graded as good, fair, poor, and preferred treatment was summarized as ‘biological’ or ‘spiritual’.
3 Medication variables

- **Extrapyramidal and other side-effects:** assessed as either ‘present’ or ‘absent’ by the clinician
- **Attitude towards medication:** assessed with the 10-item Drug Attitude Inventory (DAI-10)
- **Stigma** associated with psychiatric illness was measured using the Internalized Stigma of Mental Illness (ISMI) scale
- **Adherence** was assessed by using the Morisky Medication Adherence Questionnaire (MMAQ). The questionnaire differentiated between ‘high/good’, ‘medium/fair’ and ‘low/poor’ adherence.

All the questionnaires were translated into Yoruba, the predominant language of the region.

**Findings**

Of those interviewed, 342 provided complete datasets. These were mainly between 20 and 40 years and male (59 per cent). Nearly half (43 per cent) were unemployed. Nearly one-third had a diagnosis of schizophrenia. Forty-two per cent were diagnosed with depression/anxiety disorders. Most (59 per cent) showed no evidence of cognitive deficits on the MMSE, while 59 per cent showed full insight.

<table>
<thead>
<tr>
<th>Variables</th>
<th>% of participants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of medication prescribed</strong></td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>44.5</td>
</tr>
<tr>
<td>Mood stabilizers/antidepressants</td>
<td>18.1</td>
</tr>
<tr>
<td><strong>Presence of extrapyramidal side-effects</strong></td>
<td>19.9</td>
</tr>
<tr>
<td><strong>Presence of other side-effects</strong></td>
<td>28.1</td>
</tr>
<tr>
<td><strong>Medication Adherence categories</strong></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>22.2</td>
</tr>
<tr>
<td>Fair</td>
<td>29.8</td>
</tr>
<tr>
<td>Poor</td>
<td>48.0</td>
</tr>
<tr>
<td><strong>Perceived cause of illness</strong></td>
<td></td>
</tr>
<tr>
<td>Predominantly psychosocial</td>
<td>29.5</td>
</tr>
<tr>
<td>Predominantly spiritual</td>
<td>53.2</td>
</tr>
<tr>
<td>Predominantly biological</td>
<td>17.3</td>
</tr>
<tr>
<td><strong>Perceived best treatment method</strong></td>
<td></td>
</tr>
<tr>
<td>Predominantly spiritual</td>
<td>68.7</td>
</tr>
<tr>
<td>Predominantly biological</td>
<td>31.3</td>
</tr>
</tbody>
</table>
Associates of adherence

Many variables were correlated with levels of adherence, including work status, income, perceived social support, duration of illness and BPRS scores. To identify the independent contribution of each to the level of adherence, they were entered into a logistic regression. Those that remained significantly associated were working status, perceived level of social support, modified ISMI scores, and perceived causation of mental illness. The odds ratio and 95 per cent confidence intervals of the independently associated variables are reported in Table 4.4. This shows, for example, that employed individuals were more than three times more likely to report poor adherence than those who were unemployed, and those with high stigma scores were nearly five times more likely than those with low stigma scores to report poor adherence.

Table 4.4 Odds ratios (OR) and 95 per cent confidence intervals (CI) for the variables independently associated with poor medication adherence

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95 per cent CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Working status</strong></td>
<td></td>
</tr>
<tr>
<td>Presently not employed</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Presently employed</td>
<td>3.42 (2.17 – 5.39)</td>
</tr>
<tr>
<td><strong>Level of social support</strong></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Fair</td>
<td>1.96 (1.15 – 3.35)</td>
</tr>
<tr>
<td>Poor</td>
<td>5.86 (2.87 – 12.17)</td>
</tr>
<tr>
<td><strong>Modified ISMI scores</strong></td>
<td></td>
</tr>
<tr>
<td>0 – 6</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>7 – 12</td>
<td>3.08 (1.83 – 5.22)</td>
</tr>
<tr>
<td>&gt;12</td>
<td>4.70 (2.24 – 9.96)</td>
</tr>
<tr>
<td><strong>Perceived causation</strong></td>
<td></td>
</tr>
<tr>
<td>Biological</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Psychological</td>
<td>2.55 (1.20 – 5.57)</td>
</tr>
<tr>
<td>Spiritual</td>
<td>3.74 (1.87 – 7.74)</td>
</tr>
</tbody>
</table>

Discussion

Forty-eight per cent of the sample reported poor medication adherence: higher than the 33–9 per cent generally reported in Western countries. To the authors’ surprise, those in jobs were much less likely to be adherent than those without jobs – perhaps because side-effects were more problematic for those in work. Low levels of social support were also associated with low
adherence. Whether this is a direct causal link is unclear. High levels of social support may encourage adherence; conversely, high levels of adherence may result in better symptom control and wider access to social support. Of particular interest was the association between poor adherence and self-stigma and a non-biological cause of psychiatric problems. Note that adherence was not associated with the extent to which individuals experienced side-effects of their medication, nor was insight which has been found to be associated with adherence in several Western studies.

While the study had many strengths, not the least of which were the relatively large sample size and coming from a non-Western country, it also had a number of limitations, including grouping all patients together whatever their diagnosis, and being cross-sectional. This makes the direction of association between variables difficult to infer, as noted above.

**Stop and think…**

Taking medication has both benefits and costs. We may experience a relief from symptoms, but at the same time experience a number of side-effects. Most of these are relatively innocuous – although they may have a significant impact on the individual. The dry mouth associated with some antidepressant medication, for example, sounds relatively trivial, but in reality is a significant and uncomfortable consequence. The side-effects of some other medication types may have a longer-term and more significant impact on health. Of note in this context is that these side-effects are frequently experienced immediately an individual starts taking medication – the benefits may take some time, often weeks, before becoming evident.

So, what would influence your adherence to medication? Would you accept significant side-effects in the hope of future gain – and if so, for how long? Many people have an ‘against medication’ bias. If you do, how severe would any mental health problem have to be before you decided to take medication?

**4.3 Electroconvulsive therapy (ECT)**

Electroconvulsive therapy is the brief discharge of an electric current through the brain with the aim of inducing a controlled epileptic convulsion to achieve an improvement in an abnormal mental state. Its origins lie in observations made in the 1930s that stunned pigs appeared particularly sedated and quiet in abattoirs, and justified by anecdotal evidence that people who had epilepsy rarely evidenced any form of psychosis and that their mood following epileptic seizures often improved.

Extrapolating from these observations, physicians attempted to induce epileptic fits in an attempt to treat mood disorders, initially using injections of camphor – a process that proved fatal in a number of cases. An alternative approach was pioneered by two Italian psychiatrist, Ugo Cerletti and Lucio Bini, who found that they could induce seizures by applying electrical
currents to patients’ heads, and began their treatment of schizophrenia. Cerletti later abandoned ECT and sought alternative treatments as a result of his concerns over the physical damage, including jaw dislocation and broken bones, and neurological effects such as memory loss that resulted from the seizures provoked by his treatment.

Until the 1950s, ECT involved placing electrodes on each temple and passing an electric current of between 65 and 140 volts through these ‘paddles’ for half a second or less. This provoked an epileptic fit lasting from half to several minutes. Initially, this was given ‘straight’; that is, with the patient fully conscious. Vigorous convulsive muscle activity frequently led to bone fractures until the introduction of the muscle relaxants given prior to ECT. As awareness of this paralysis led to high levels of anxiety on the part of the recipient, this was soon accompanied by administration of an intravenous barbiturate to render them unconscious during the procedure, a process known as modified ECT. More recently, the electrodes have been placed over the non-dominant hemisphere only, a process known as unilateral ECT. This is thought to result in fewer side-effects. Although schedules of treatment vary, ECT is typically administered two or three times a week in courses ranging from 4 to 12 treatments. Less commonly, it is given fortnightly or monthly for six months or longer to prevent relapse, as continuation or maintenance ECT. Just how ECT achieves any benefits is unclear, although work by Ishihara and Sasa (1999) suggests that it may increase the sensitivity of postsynaptic neurons to serotonin in the hippocampus, increase levels of GABA and reduce levels of dopamine.

The use of ECT peaked and then began to decline substantially in the 1950s following the introduction of a range of psychotropic drug treatments. Nevertheless, its use is still recommended by many psychiatric authorities, including the English National Institute of Clinical Excellence (NICE 2008), who recommended its use in the treatment of depression that is resistant to pharmacological intervention or where there is a strong likelihood of suicide. By contrast, NICE did not find the evidence sufficiently compelling to recommend its use with a second patient group for whom ECT has been frequently prescribed – those with a diagnosis of schizophrenia (NICE 2008).

The ECT controversy

The use of ECT has not been without controversy, and the literature seems to be divided largely into those who enthuse over its use and those who vehemently oppose it. Measured debate is less frequent. Those against its use oppose it on moral grounds as well as question its effectiveness. Thomas Szasz (1971), for example, argued that electricity as a form of treatment ‘requires the sacrifice of the patient as a person, [and] of the psychiatrist as a clinical thinker and moral agent’. This negative view is endorsed by a number of psychological organizations, including the British Psychological Society, which considers that the use of ECT should be prohibited in Britain. Even the psychiatric authorities that endorse its use have acknowledged the controversy. The US National Institutes of Health (NIH) Consensus Statement (1985) observed that ECT had been used inappropriately to treat disorders where there was no evidence of effectiveness and that many of these efforts proved harmful. It also noted that the use of ECT as a means of managing unruly patients, exemplified in the film One Flew over the Cuckoo’s Nest, contributed to its perception as an abusive instrument of behavioural control for patients in mental institutions. The controversy around ECT revolves around the potential harm that may result from its treatment.
The short-term effects are associated with being given an anaesthetic and fitting. Adverse events are rare, but do occur. The NIH Consensus Statement suggested a rate of up to 4.5 deaths per 100 000 treatments, a risk comparable to the use of short-acting barbiturate anaesthetics in other conditions. They also noted that the risk of physical injury was much less than in the past, with a complication rate of 1 per 1300 to 1400 treatments. Problems included tooth damage, vertebral compression fractures, uncontrollable fitting, peripheral nerve palsy and skin burns. Some people also find ECT a terrifying experience, or regard it as an abusive invasion of personal autonomy. Some people experience a sense of shame because of the social stigma they associate with ECT (NIH 1985).

**Effect on memory**

Perhaps the most problematic outcome of ECT is its effect on memory. People who have had ECT typically experience an acute phase of confusion following treatment: it can take them five or ten minutes to remember who they are, where they are or what day it is. It also impairs the ability to learn and retain new information for a period of time following administration and may impact adversely on memories of events that occurred months or even years before treatment. Feliu et al. (2008), for example, found that nearly a month after receiving ECT, patients performed less well than before their treatment on objective measures of recognition memory, and short-term memory of both verbal and visual memory, despite improvements in mood. Similar findings have been found in tests of autobiographical memory. Lisanby et al. (2000) followed 55 people with major depression, randomly allocated to either unilateral or bilateral ECT. Prior to treatment, they obtained detailed autobiographical and impersonal memories and then tested recall of these memories immediately following the course of ECT and at two-month follow-up. A control group who did not have depression or ECT underwent the same testing procedures. All those who received ECT recalled fewer personal and impersonal memories, and in less detail, than controls on both testing occasions. By the second assessment, differences between the two groups who received ECT also emerged: those given bilateral ECT recalled less than those who had unilateral ECT.

**Alternatives to ECT**

Given the problems associated with ECT, a number of researchers have attempted to find alternative methods to achieve the same clinical results – without the unwanted side-effects. Transcranial magnetic stimulation (TMS) is one such approach. It involves passing a series of electrical pulses close to the brain. The coil is held on the scalp – no actual contact is necessary – and the magnetic field passes through the skull and into the brain. Small induced currents can then make brain areas below the coil more or less active, depending on the settings used. Transcranial magnetic stimulation can influence many brain functions, including movement, visual perception, memory, reaction time, speech and mood. The obvious effects of TMS last for very brief periods following stimulation. However, there is some evidence that the procedure may have longer-term effects on mood – and may prove an alternative approach to the use of ECT. In one relevant study, Schulze-Rauschenbach et al. (2005) compared TMS with unilateral ECT in the treatment of major depression. Treatment response was comparable: 46 per cent of people treated with ECT and 44 per cent of those treated with TMS group showed significant clinical improvements.
More encouragingly, while patients treated with ECT showed evidence of memory deficits, those treated with TMS showed no decrement and even improvements in memory. Quite how TMS impacts on mood is not clear. However, animal studies suggest it may result in increases in serotonin and a number of other neurotransmitters including dopamine (Kanno et al. 2003). Although there has been some interest in the use of TMS in other conditions such as anxiety or obsessive-compulsive disorder, it has yet to be shown to be effective (Pigot et al. 2008).

4.4 Psychosurgery

The modern practice of psychosurgery began in the 1930s, when two Portuguese neurologists, Egas Moniz and Almeida Lima, began severing connections to and from the frontal lobes in people with ‘psychoneuroses’. By 1936, the procedure had been developed into what was termed a prefrontal leucotomy (sometimes referred to as a lobotomy). This operation was initially fairly crude, as the surgeon had to estimate where to lesion the brain without any form of neuro-imaging and did so freehand. However, it has gradually become more precise in its anatomical location and procedures. Between 1936 and 1961, over 10 000 people received this type of treatment in the UK. Of these, an estimated 20 per cent of people with schizophrenia and about 50 per cent of those with depression gained some degree of benefit (Malizia 2000). However, 4 per cent died as a result of surgery, 4 per cent developed a severe loss of motivation and up to 60 per cent developed ‘troublesome’ personality changes, while 15 per cent developed epilepsy. Despite these problems, this approach had many advocates, probably because there were no viable alternatives to this treatment for much of this time.

Rates of psychosurgery have fallen dramatically since effective pharmacological alternatives have become available. Now, only about 20 operations are conducted in the UK each year, and only for conditions that have proven unresponsive to a variety of alternative treatments. New, more specific, surgical procedures have also been developed, including the stereotactic subcaudate tractotomy and stereotactic cingulotomy. Stereotactic interventions involve a device called a stereotactic frame which is placed over the brain during operations and, in combination with neuro-imaging, allows highly accurate lesions to be conducted. Neurosurgeons now use a ‘conservative’ approach, creating small initial lesions, which can be added to with later operations should this be required.

Most lesions are created with heated electrodes, with the exception of the subcaudate tractotomy which involves placing radioactive rods in the target area, which destroy parts of the subcaudate brain area through a brief burst of radioactivity before becoming inert. It is usually used for the treatment of severe, intractable depression. Stereotactic cingulotomy is the most commonly used procedure for the anxiety disorders, including obsessive-compulsive disorder (see Chapter 7). The operation is conducted under general anaesthetic and involves placing electrodes into the cingulate bundle in each hemisphere. The tips of the electrodes are then heated to 85 degrees centigrade for about 100 seconds.

Availability of psychosurgery

Psychosurgery is banned by law in some countries, including Germany and some US states. To be given this form of treatment in the UK, an individual has to be resistant to all other attempts
to treat the condition. In treating depression, for example, a candidate for surgery would typically have made more than two serious suicide attempts, have had an initial onset at least 18 years previously, and their present episode would have lasted seven years without a period of remission of at least six months. They would have received over 30 ECT treatments, unusually large doses of antidepressants, and be severely depressed on psychometric testing (Malizia and Bridges 1991). In England and Wales, a panel of three representatives appointed by the Care Quality Commission is required to assess that the person is providing full consent to the operation and that they are likely to benefit from it. In Scotland, this safeguard is evoked only if the person is detained for treatment against their wishes. No patient can be given psychosurgery without their consent.

Post-operative effects

Since the advent of the newer operations, mortality has dropped to one in a thousand cases, and post-operative epilepsy to between 1 and 5 per cent (Jenike 1998). In addition, there is no evidence of reduced intellectual function following surgery. Indeed, many people perform better on psychometric testing following surgery than before, perhaps because their depression is lifted and/or they are no longer taking antidepressant medication. Similarly, there is no evidence of significant ‘personality changes’ following neurosurgery, despite the potential for damage to the frontal lobe, which is considered by many to control functions considered fundamental to an individual’s personality. The tests typically given in these studies do not test for subtle frontal lobe deficits, however, and Jenike (1998) acknowledged that the possibility of such damage cannot be excluded.

A number of people commit suicide following surgery. Whether this is a result of the surgical procedure or would have happened without this intervention is difficult to judge. It is possible that some people who view the operation as the treatment of last resort may commit suicide after disappointing results. Certainly, there is no evidence of this being a direct consequence of surgery. Jenike et al. (1991) found that four of a series of 33 individuals who underwent cingulotomy for the treatment of obsessive-compulsive disorder (OCD) committed suicide in the 13 years following the operation. All four experienced severe depression with prominent suicidal ruminations prior to surgery. The percentage of individuals to make a significant recovery following some form of psychosurgery is reported in Table 4.5.

### Table 4.5 Summary of published outcome data for neurosurgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>‘Good’ outcome (per cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Depression</td>
</tr>
<tr>
<td>Stereotactic subcaudate tractotomy</td>
<td>53</td>
</tr>
<tr>
<td>Cingulotomy</td>
<td>34</td>
</tr>
<tr>
<td>Capsulotomy</td>
<td>60</td>
</tr>
<tr>
<td>Stereotactic limbic leucotomy</td>
<td>55</td>
</tr>
</tbody>
</table>

* OCD obsessive-compulsive disorder.

Source: adapted from Jenike (1998).
How psychosurgery achieves these therapeutic gains is not fully understood. In OCD, it may sever the brain systems driving the behaviours (see Chapter 7). However, preliminary evidence suggests that people with OCD do not improve immediately following surgery. It may take several weeks or months before any benefits are observed. Jenike (1998) speculated that secondary nerve regeneration or metabolic alterations in brain areas other than those actually lesioned may be involved in any changes. What these may be, however, is unclear. This lack of understanding of what surgeons are actually doing provides critics of this approach with strong concerns about the nature and use of psychosurgery (www.antipsychiatry.org).

4.5 Chapter summary

1. The brain is divided into a number of anatomical areas, most of which are in some way related to functions that influence mood or behaviour.

2. Damage to most brain areas will result in deficits that may be evident as emotional or mental health problems.

3. Activity within the brain is mediated by neurotransmitters, which act at the neuronal synapse.

4. Neurotransmitters mediate the activity within brain systems that are responsible for mood and behaviour. The most important to mental health are serotonin, dopamine, GABA and norepinephrine.

5. Drug therapies affect the activity within brain systems by increasing or decreasing levels of neurotransmitters. Antidepressants increase the availability of serotonin (and to a lesser extent norepinephrine); anxiolytics increase levels of GABA; and neuroleptics decrease levels of dopamine.

6. ECT involves passing an electrical current through the temporal lobes of the brain to induce a seizure.

7. Treatment with ECT remains controversial; although it is now much safer than previously, it still evokes strong emotional arguments, among both those who support its use and those who oppose it. A number of medical authorities recommend its use in cases of depression that resist treatment using other methods.

8. ECT is linked to significant measurable memory problems that last a significant period of time. A new alternative, transcranial magnetic stimulation, may prove effective and have fewer such side-effects.

9. Psychosurgery is now used only in extreme cases of OCD or depression.

10. Psychosurgery achieves a moderate degree of clinical benefit in a population where previous, more conservative, treatments have failed, but carries with it a small but significant risk of subtle cognitive deficits.

11. How psychosurgery acts to relieve symptoms is not clear. It may interfere with activity within brain systems that mediate OCD or depression. However, the time frame in which changes occur following surgery indicates the possibility of other, as yet unknown, mechanisms.
4.7 Key terms

Agonist  drug that increases the action of a neurotransmitter.
Antagonist  drug that inhibits the action of a neurotransmitter.
Electroconvulsive therapy (ECT)  treatment involving passing a brief electric current through the temporal lobe(s) as a treatment for depression and schizophrenia.
Executive function  neurological coordination of a number of complex processes, including speech, motor coordination and behavioural planning.
Extrapyramidal symptoms  symptoms that result from low levels of dopamine in the extrapyramidal regions of the brain, often as a result of long-term phenothiazine use. Include Parkinsonism and tardive dyskinesia.
Half-life  the time required for half the quantity of a drug to be metabolized or eliminated by normal biological processes.
Major tranquillizers  see phenothiazines.
MAOI (monoamine oxidase inhibitor)  a form of antidepressant, whose action is on the norepinephrine system.
Perseveration  inability to shift from a cognitive set, resulting in inappropriate repetitive behaviour, including speech.
Phenothiazines  major tranquillizers used to treat schizophrenia, of which the best known is chlorpromazine; their action is usually on the dopaminergic system.
Psychosis  includes a number of mental health conditions, such as schizophrenia, each of which have the common symptom of a loss of contact with reality.
Psychotropic medication  drugs used to treat mental health problems by their action on neurotransmitter levels.
SNRIs (serotonin/norepinephrine re-uptake inhibitors)  antidepressants thought to inhibit neuronal uptake of serotonin, norepinephrine and dopamine in the central nervous system.
SSRIs (selective serotonin re-uptake inhibitors)  a form of antidepressant, whose action is on the serotonergic system.
Tricylic  a form of antidepressant whose action is on the serotonin and norepinephrine systems.
4.8 Further reading