The Myth of the Chemical Cure

A Critique of Psychiatric Drug Treatment

Joanna Moncrieff

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To Martin and Ann Moncrieff for being wonderful parents

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Abbreviations

CATIE	Clinical antipsychotic trial of intervention effectiveness
D_1, D_2	Dopamine 1 and 2 receptors
ECT	Electroconvulsive therapy
MAOI	Monoamine oxidase inhibitor
NICE	National Institute of Clinical Excellence
NIMH	National Institute of Mental Health
PET	Positron emission tomography
RCT	Randomised controlled trial
SSRI	Selective serotonin reuptake inhibitor

Note on Nomenclature

I have had to use several terms in this book that I am not comfortable with, but they are in common use and better ones do not exist or are not widely understood. I have not always put them in parentheses because if I did, there would be so many inverted commas that the text would be difficult to read. Thus I refer sometimes to 'mental illness', although I do not consider that psychiatric conditions are usefully or validly regarded as illnesses. I have tried to avoid this term where possible with terms such as psychiatric condition, disorder, disturbance or problem, but none of these terms adequately covers the range of problems that psychiatry deals with. I have frequently used the term 'patient' to describe people who have psychiatric problems because it seems less clumsy than the term 'psychiatric service user' and terms such as 'consumer' have their own particular implications, but this does not mean that I accept all its connotations. I have also referred to psychiatric interventions as 'treatments', which has medical implications that I think would be better avoided, but there is no readily understandable alternative. Although I have used alternatives where possible, I have had to refer to some drugs by names that imply disease specificity, which the whole book is disputing. Thus I have used the term 'antidepressant', for example, because there is no other common designation for these drugs.

1
The Disease-Centred Model of Drug Action in Psychiatry*

Conceptions and misconceptions about psychiatric drugs

Since the 1960s we have lived in an age characterised by the idea that drugs can cure the problems that are now referred to as 'mental illness', but have previously been known as insanity, madness, lunacy and neurosis, among other terms. By 'cure' I mean the idea that drugs can improve symptoms by helping to rectify the underlying pathological mechanism that is presumed to give rise to the symptoms in the first place. Increasingly this way of thinking has spread outside psychiatry and drugs have also come to be seen as having a curative role in all sorts of situations in which people feel they are not performing or functioning as well as they should. Such situations are 'diagnosed' as depression, dysthymia, anxiety, social phobia, substance misuse, compulsive shopping, menstrual dysphoric disorder, etc. and drugs are prescribed for their treatment. The story by which drugs first came to be seen in this way, as specific treatments for specific mental disorders or collections of symptoms, and whether or not this way of thinking about drugs and their actions is justified are the subjects of this book.

I shall argue that there is no real demarcation between previous eras' psychiatric treatments and the theories that justified them and our own; that the need to believe in a cure for psychiatric conditions that drove and sustained people's faith in insulin coma therapy, ECT, radical surgery, sex hormone therapy and many other bizarre interventions is the strongest impetus behind the use of modern-day psychiatric drugs. I shall suggest that the belief that modern drug treatments represent

* Parts of this chapter and the next one are based on two papers I wrote with David Cohen: Moncrieff & Cohen (2005, 2006).

specific cures for specific illnesses is just as mistaken as the belief that insulin coma treatment was an effective and specific treatment for schizophrenia. That is not to say that psychiatric drugs are not sometimes useful and I shall try and outline a way of thinking about them that helps to determine when they might be useful and when they might not be. But viewing the history of modern psychiatric drugs as a continuation of previous psychiatric practice should sound a cautionary note. We have only to look to the relatively recent past to see the proclivity of psychiatrists to subject their patients to invasive, degrading, harmful and not unusually fatal procedures in the name of therapy and to blind themselves to the real nature of their activities (Braslow 1997).

Over the following pages I hope to convince readers that the modern understanding of what drugs do in psychiatry, the basis of psychopharmacology, is fatally flawed; that most knowledge about psychiatric drugs is, at best, only a partial account. This is because it is based on a misconception about the nature of drug action, one that has been inspired and promoted by professional, commercial and political interests. This misconception has led to the misdirection of research, the misinterpretation of available evidence and the obstruction of a fuller and more accurate understanding of what psychiatric drugs do.

The place of drug treatment in psychiatry

It is difficult to overstate the central role that drug treatment plays in modern-day psychiatry. Psychiatric hospitals and community mental health team activities revolve around the various rituals of drug treatment. A United Kingdom survey of psychiatric hospitals found that 98–100% of inpatients were prescribed drugs and that most take several different ones at the same time (Healthcare Commission 2007). Drugs have become the focus of hospital life in a way that ECT and other physical procedures were in the 1940s and 1950s (Braslow 1997). The hospital day is punctuated by the regular 'drug rounds', where patients obediently cue up at a drug trolley to be handed their pills. Then there are the dramatic emergency situations where disturbed people are held down and forcibly injected with drugs. Much discussion and energy among staff is devoted to whether patients are on the right sorts of drugs and to whether or not they are actually taking them. When doctors do hospital 'ward rounds', drug regimens are tweaked, doses increased and new drugs added. Less often some drugs are reduced or discontinued, but drugs are rarely stopped without starting another one. Outside hospitals over 90% of patients in contact with psychiatric services are

prescribed medication (Healthcare Commission 2007). Again, issues about medication are a central feature of meetings between staff and patients. Administering 'depots' (long-acting psychiatric drugs given by intramuscular injection) is one of the main tasks of community psychiatric nurses, and there is much concern among all staff about whether patients are being 'compliant' with their prescribed medication. When patients develop problems of almost any sort, it is invariably suggested that patients have been non-compliant, whether or not there is any evidence of this.

Since the early 1990s, psychiatric drugs have become much more widely prescribed and increasingly familiar to the general public. Drugs such as Prozac and Ritalin have become household names, and books about them have become best-sellers. This is part of a more general increase in consumption of all types of medicines, indicated by the fact that prescriptions issued increased by 56% between 1988 and 2001 in the United Kingdom. However increases in the use of psychotropic drugs have contributed disproportionately to this increase, with prescriptions of antidepressants rising by 243% in the ten years up to 2002 (National Institute for Clinical Excellence 2004). The rise in cost has been even more marked since the majority of the increases in prescribing have been for expensive new classes of psychiatric drugs. Thus costs of antidepressants in the United Kingdom rose by 700% between 1991 and 2002. In the United States, expenditure on psychotherapeutic drugs rose by 2.5 times between 1997 and 2004. The number of purchases rose by 72% and the number of people making a purchase by 55% (Stagnitti 2007). In 2001 antidepressants were the top-selling class of prescription drugs and continue to rank highly along with antipsychotics, anti-anxiety agents and stimulants (National Institute for Health Care Management 2002). Patterns of drug use have also changed. Use of benzodiazepines, such as Valium and Librium, once the best-selling class of psychotropic drugs, has declined relative to other drugs, and the use of antidepressants, antipsychotics and stimulants has risen (Pincus et al. 1998). However the most recent survey of drug use in the United States showed increased use of sedatives, anxiolytics and hypnotics as well as other sorts of drugs (Stagnitti 2007). The most dramatic increases have occurred among young people and children (Cohen et al. 2001).

This increase in use of prescribed drugs has been achieved firstly by extending the boundaries of well-established conditions such as depression and psychosis. Secondly, lesser-known diagnoses such as panic disorder and social phobia have been promoted, and thirdly, drug treatment has started to colonise areas where it was previously thought

to be unhelpful, such as substance misuse and personality disorder. There is also a strong emphasis on the long-term nature of the need for drug treatment in severe mental disorders. For the major psychiatric disorders, such as schizophrenia and manic depression, it is generally suggested that drug treatment is required for life. Even for other less-serious conditions, such as depression treated in General Practice, it is recommended that drug treatment is taken for at least six months after resolution of symptoms (Royal College of Psychiatrists 2007).

Almost all drugs in current use have been introduced into psychiatry since the 1950s. Although drug treatment was common before that time, with extensive use of barbiturates and other sedatives and some use of stimulants, it was rarely given much attention. This was because drugs were generally regarded as having only crude effects, usually acting as chemical forms of restraint (Braslow 1997). However from the 1950s, psychiatric drugs started to arouse considerable interest. Drug treatment changed from something that was given little attention to an exciting activity that was seen as making psychiatry truly scientific (Moncrieff 1999). Part of this transformation consisted of a metamorphosis of the theories about what drugs actually do. Instead of being seen as substances that induced effects that were crude but useful, they came to be seen as specific treatments for specific illnesses. They became 'cures'.

The disease-centred model of drug action

Despite the ubiquity and importance of drugs in psychiatry, very little attention has been paid to the theoretical assumptions that underpin conventional views about what they do and how they work. A certain way of understanding drug action has come to be accepted without any consideration that there might be alternative explanations. Why this should be so is one of the major concerns of this book. But first let us unpick what this mode of understanding consists of.

I have called the current standard view of psychotropic drug action the 'disease-centred model' and its characteristics are outlined in Table 1.1 (Moncrieff & Cohen 2005). This view refers to the idea that drugs are thought to act on the underlying physical disease process. Drugs help to reverse this abnormal process, thus moving the body towards a more normal biological state. As two leading American psychiatrists put it in a rare contemporary discussion of the mechanisms of drug action, 'pharmacotherapeutic agents produce their clinically beneficial effects in an abnormal nervous system' and these effects

Table 1.1 Alternative models of drug action

Disease-centred model	**Drug-centred model**
Drugs help correct an abnormal brain state	Drugs create an abnormal brain state
Therapeutic effects of drugs derive from their effects on presumed disease pathology	Therapeutic effects derive from the impact of the drug-induced state on behavioural and emotional problems
Drug effects may differ between patients and volunteers	Effects do not differ
Outcomes of drug research consist of effects of drugs on measures of the 'disease' and its manifestations or symptoms	Outcomes are the global state produced by drug ingestion and how this interacts with behaviours and experiences
Paradigm: insulin for diabetes	Paradigm: alcohol for social phobia/social anxiety

'counter or compensate for the abnormal pathophysiology' (Hyman & Nestler 1996, 1997) (quotation 1997, p. 440).

The disease-centred model exists in two related forms. One suggests that drugs act on the underlying causes of a disease or condition, such as schizophrenia. The other suggests that drugs act on the pathology responsible for producing certain sets of psychiatric symptoms. Early versions of this model, for example, suggested that neuroleptic drugs were 'anti-schizophrenic in the broad sense' (The National Institute of Mental Health Psychopharmacology Service Center Collaborative Study Group 1964). More recent commentators have suggested that these drugs target the specific basis of psychotic symptoms, but not necessarily the ultimate cause of the condition. For example, antipsychotics are suggested to redress a hypothesised dopamine imbalance responsible for symptoms of acute psychosis without necessarily affecting the underlying cause of this imbalance (Kapur 2003).

Because the disease model is rarely articulated, its existence has to be largely inferred from the way that psychiatric drugs are described and investigated. For example, the way psychiatric drugs are currently named and classified according to the disease they are thought to act upon reflects the disease-centred model of drug action. Thus there are 'antipsychotics' thought to act specifically on the pathology underlying psychosis, 'antidepressants' thought to act on the pathology of depression, 'anxiolytics' thought to act on the pathological basis of anxiety, antimanic drugs thought to act on the pathology of mania, lithium and other 'mood stabilisers' thought to act on the pathological basis of abnormal mood, and 'hypnotics', whose name suggests they are

deemed to work on the mechanisms of abnormal sleep. There is even a drug, clozapine, for the specific condition or situation of 'treatment-resistant schizophrenia'. Coverage of drugs in textbooks of psychiatry and psychopharmacology reflects this system of nomenclature, being organised according to the diseases drugs are meant to treat, not according to the chemical nature or physiological actions of different drugs. In reality, standard drug classification is a little more complex. There are some examples of drugs that are named according to their profile of physiological effects, such as stimulants, although they are now generally discussed under the heading of 'treatments for attention deficit disorder'. Drugs for insomnia are referred to as 'hypnotics', but most of these drugs are benzodiazepines, which are also classified as 'anxiolytics', and it is doubtful that anyone really thinks that they act by reversing the physical disturbance leading to insomnia. Nevertheless, the basic rules consist of classification of drugs by the disease or symptomatology they are thought to treat.

The disease-centred model can also be inferred by the absence of descriptions of characteristic drug-induced effects. In other words, the lack of a drug-centred model or explanation of drug action, described further in Chapter 2, implies a disease-centred understanding of how drugs work. For example, because there is no attempt to describe what sorts of effects are produced by different sorts of antidepressants, there is no acknowledgement that these effects exist and no consideration of how they might impact on someone experiencing emotional distress. Therefore, the 'improvement' or 'response' that antidepressants are thought to produce is suggested by implication to be due to an action on a presumed disease process. Similarly, without an account of the drug-induced state produced by taking the second-generation neuroleptic drugs, there is no rationale for their use apart from the idea that they counteract a disease process.

The disease-centred model also forms the basis on which research on drug efficacy is conducted. In randomised controlled trials (RCT), effects of psychiatric drugs are inferred from patients' scores on symptom measurement scales, which are presumed to measure the manifestations of the underlying disease state. All other effects that drugs produce are designated as 'side effects' and disregarded, unless they are so unpleasant or dangerous that this is impossible. Similarly animal research is conducted by constructing animal 'models' of psychiatric disorders and measuring drug effects on animal behaviours that are thought to be analogous to psychiatric symptoms in humans. Although there are many other questions about the validity of psychiatric research, the point

I want to stress here is that research on psychiatric drugs is predicated on the idea that psychiatric drugs exercise their effects on the manifestations of an abnormal biological state.

The disease-centred model has been imported from general medicine, where, in contrast to what I will suggest about psychiatric drugs, most drug action can be appropriately understood in this way. The purest version of the disease-centred theory of drug action is the idea of the 'magic bullet', a phrase coined by the scientist Paul Ehrlich at the end of the 19th century. Ehrlich first worked on developing antitoxins against infectious diseases such as tetanus and diphtheria, and later developed an arsenic-type drug treatment for syphilis. He used the term 'magic bullet' to describe a drug that acted only against the organism that caused the disease and had no effects on the human body itself. In this ideal sense, even anti-infectious agents are not truly magic bullets. There are no medical drugs whose effects are restricted entirely to correcting the disease process. However the concept illustrates the fact that modern drugs are disease-centred treatments in the sense that they are aimed at the specific pathology of individual diseases. They impact on the body in other ways, but their interaction with a particular disease process is what determines their therapeutic efficacy.

A paradigm case, often referred to by orthodox psychiatrists, is that of insulin treatment for diabetes. Insulin clearly helps to correct the abnormal functioning of glucose regulation that has been identified to be the core of the condition of diabetes. It does not target the ultimate biological cause of diabetes, the failure of the pancreatic glands, but it acts to reverse the consequences of this pathology, the lack of insulin, that produces the symptoms of diabetes. If the disease is understood as a process leading from the original pathology to the symptoms, insulin can be seen as acting directly on a part of this process, albeit not at its original point. The action of many other drugs can be understood in a similar way. Anti-angina drugs act on the pathophysiological pathways that produce angina, bronchodilators act on the physiological basis of reversible airways obstruction. Non-steroidal anti-inflammatory drugs and steroids suppress different parts of the inflammatory process, thus helping to return the body to normal functioning when this process is overreacting. The action of painkilling drugs can also be understood from their action at different points of the processes involved in generating pain. Opiates inhibit nociceptive (pain) stimuli along the fibres that take messages back to the brain, and non-steroidal anti-inflammatory drugs such as aspirin inhibit the production of prostaglandins involved in producing pain and the inflammatory reaction. Thus all these drugs

act on biological processes that are considered to be pathological by virtue of causing symptoms of pain, discomfort, dysfunction and death. Some drugs, such as antihypertensives, act on mechanisms that control blood pressure, which reduces the risk of developing other diseases such as heart disease and strokes. None of these drugs acts on the ultimate underlying cause of the disease process. In this sense they might not be technically be classified as 'cures'. However I am using the term cure in the sense of drugs that have a disease-centred action. In this sense these drugs are all cures, albeit for symptoms rather than diseases. Some medical drugs do act directly on the causative agent of disease. Antibiotics and antivirals target the bacteria or viruses responsible for specific diseases and in this sense they come closer to the notion of a 'magic bullet'. Chemotherapy drugs used in cancer target rapidly proliferating cells, which is what distinguishes cancer cells. Again in the sense that chemotherapy often fails to eliminate the cancer completely, it may not always be considered a 'cure'. However regardless of its ability to remove the pathology completely, it qualifies as a 'cure' in the sense of being a disease-centred treatment that acts on the biological basis of the disease.

The disease-centred model implies that the basic action of a drug can usefully be divided into therapeutic effects and side effects. The therapeutic effects are the drugs' effects on the pathological process and the side effects are manifestations of the same effects on other parts of the body. For example, chemotherapy drugs attack proliferating cancer cells but also attack other cells, especially other rapidly proliferating cells such as in the bone marrow and reproductive system, with harmful consequences. Aspirin and other non-steroidal anti-inflammatory drugs inhibit the synthesis of chemicals called prostaglandins. This process is responsible for their analgesic effect and also, through reducing platelet aggregation, it is probably responsible for aspirin's efficacy in preventing recurrence of heart attacks and ischaemic stroke. However since prostaglandins are involved in protecting the stomach lining, this process can also lead to the well-recognised side effects of increased gastric irritation and bleeding.

The fact that most drugs used in general medicine act in a disease-centred way should come as no surprise since they are usually developed using knowledge about the pathophysiology of particular diseases. Even drugs whose actions were discovered serendipitously can be analysed and understood according to their action on a pathological process. What constitutes pathology or disease in general medicine and where the division between pathology and normality lies are, of course,

not always clear-cut. But for the purposes of this argument what is important is that the action of a drug is understood with reference to the biological process that is involved in generating the state that needs to be rectified and, as such, is considered to be a disease. This is not to suggest that actions of all drugs thought to act in a specific way are completely understood, but enough drugs have been shown empirically to act in a disease-specific way that the disease-centred model can be considered to be a valid guide to drug action in most cases.

Some effects of some medical drugs can be understood as resulting from non-specific effects (that is, effects that are not directed against the disease pathology), consistent with the drug-centred model of drug action outlined in the next chapter. For example, antihistamines may reduce itching in the inflammatory condition of eczema by causing sedation as well as through their specific anti-inflammatory effect. Alcohol may reduce pain primarily because of its sedative and euphoriant effects, although it may also have some direct action on pain pathways. However more powerful specific drugs have largely replaced the use of non-specific agents in physical medicine.

'Chemical imbalances' and psychiatric drug action

The disease-centred model of drug action begs the question of what is the abnormal biological state that drugs correct. The predominant psychiatric theory about this is colloquially referred to as the 'chemical imbalance' theory of psychiatric disorder. This theory suggests that psychiatric disorders or their symptoms are caused by abnormalities in the chemicals in the brain that are involved in transmission of nerve signals, known as neurotransmitters. Examples of neurotransmitters are dopamine, serotonin, adrenalin and noradrenalin (the catecholamines), acetylcholine and many others such as gamma-aminobutyric acid (GABA), glutamate, glycine, opioid peptides and substance P. The list is being added to all the time as scientists reveal the complexity of the process of neurotransmission. The theory goes that abnormalities of different neurotransmitters cause different psychiatric disorders. Dopamine has long been held to be implicated in schizophrenia. In the different versions of this theory that have been propounded over the years, overactivity of the dopamine system has been proposed to cause schizophrenia itself (Meltzer & Stahl 1976; Rossum 1966), positive symptoms of schizophrenia (Davis et al. 1991) or acute psychosis (Kapur 2003). The monoamine theory of depression suggests that depression is caused by a deficiency of the monoamine neurotransmitters, namely serotonin and

noradrenalin (Schildkraut 1965). As I shall discuss in more detail later, these theories are intimately related to the presumption that psychiatric drugs exert their clinical effects according to a disease-based model of drug action. Although biochemical theories are less well established in other disorders, the dopamine theory of schizophrenia and the monoamine hypothesis of depression have a diffuse influence by providing a template for the idea that disorders have a specific biochemical correlate and origin. Discussions about drug treatment for other disorders usually proceed on the assumption that a biochemical basis exists, without feeling the need to state what this is in explicit terms.

Occasionally there are attempts to produce more sophisticated versions of this basic theory. In a rare discussion of mechanisms of drug action in psychiatry, Hyman and Nestler (1996) suggested that therapeutic effects of psychiatric drugs result from brain adaptations to their effects, which 'likely produce therapeutic responses by altering the functional activity of critical neural circuits in the brain'. They do not reject the idea that psychiatric drugs work on specific neurotransmitters, but suggest that this is not simply through effects on neurotransmitter receptors, but through effects on synaptic transmission and complex interacting neural circuits. They still also presuppose that there are underlying abnormalities involving neurotransmitter systems (Hyman & Nestler 1997).

Despite being so rarely acknowledged, the disease-centred model of drug action and its counterpart, the chemical imbalance model of psychiatric disorder, are deeply ingrained in psychiatric culture. I have heard many psychiatrists explain to patients that their symptoms are due to a chemical imbalance, that taking psychiatric medication is like taking insulin for diabetes, that the drugs will help rectify this chemical imbalance and that without the drugs the condition will rapidly recur. The comparison with physical conditions such as diabetes emphasises the presumed physical basis of the problem. It is also employed to reassure depressed patients who are reluctant to take medication for fear of its addictive nature and to frighten patients after psychotic breakdowns into believing that they must take drugs long term.

Official information produced by the psychiatric profession demonstrates the same themes. The British Royal College of Psychiatrists' public information sheet on 'Depression' suggests that 'two ... neurotransmitters (serotonin and noradrenalin) are particularly affected' in depression and claims that 'antidepressants increase the concentrations of these two chemicals at nerve endings, and so seem to boost the function of those parts of the brain that use serotonin and noradrenalin' (Royal College of Psychiatrists 2006). The American Psychiatric Association (APA) says that

'antidepressants may be prescribed to correct imbalances in the levels of chemicals in the brain' (American Psychiatric Association 2005). On psychosis or schizophrenia the Royal College of Psychiatrists (RCP) claims that there are 'abnormalities in the biochemistry of the brain' and 'an imbalance in brain chemistry' (Royal College of Psychiatrists 2004). The APA suggests that antipsychotic medications 'help bring biochemical imbalances closer to normal' (American Psychiatric Association 1996).

Even when they acknowledge that there is no evidence for a 'chemical imbalance' many psychiatrists believe that the term is still justified and appropriate, thereby demonstrating a deep underlying commitment to the idea. Wayne Goodman, a prominent United States psychiatrist commenting on an article highlighting the fact that there was no established link between serotonin abnormality and depression, still maintained that the term chemical imbalance was a 'reasonable shorthand for expressing that this is a chemically or brain based problem and that medications help to normalise function' (quoted in Meek 2006).

The pharmaceutical industry employs similar language in its promotional material. An early advertisement for Prozac suggests that 'Like arthritis or diabetes, depression is a physical illness' (Valenstein 1988, reproduced on p. 181). A leaflet produced in 1996 by a consortium called 'America's Pharmaceutical Research Companies' neatly summarises the idea of the chemical imbalance and its relation to a disease-centred model of drug action:

> Today scientists know that many people suffering from mental illnesses have imbalances in the way their brains metabolise certain chemicals called neurotransmitters. Too much or too little of these chemicals may result in depression, anxiety or other emotional or physical disorders. This knowledge has allowed pharmaceutical company researchers to develop medicines that can alter the way in which the brain produces, stores and releases neurotransmitter chemicals, thereby alleviating the symptoms of some mental illnesses.
>
> (Valenstein 1988, cited on p. 182)

Philosophical considerations

This book concerns the creation of a myth, the myth of the disease-centred model of drug action, and how that myth could be accepted as a real description of the world. It therefore involves questions about the nature of knowledge and the relation between knowledge and power.

Karl Marx was one of the first philosophers to undermine the notion that knowledge is objective and neutral. His analyses of capitalism demonstrated that what was portrayed in one way by the capitalist class was experienced differently from the perspective of the working class. Thus for the owners of capital, the bourgeoisie, capital was an economic necessity and a generator of wealth. For the working class it was a means of exploiting their labour and transforming it into a source of profit for other people. In his early writings Marx used the term *ideology* to describe ideas that were stimulated by class interests and obscured the real nature of social relations: 'ruling ideas are nothing more than the ideal expression of the dominant material relationships' (Marx & Engels 1970, p. 64). By standing aloof from the interests of the ruling class, Marx was able to lay bare the workings of capitalism that had been obscured by a 'bourgeois consciousness' that needed to present the capitalist system as benign and necessary (Marx 1990, p. 175).

Twentieth-century philosophers of science, such as Thomas Kuhn and Paul Feyerabend have also challenged the notion of objective knowledge and revealed the extent to which empirical data is shaped by prior conceptions and interests. This critique was extended by some of its proponents to the terrain of philosophical relativism, a position which maintains that there are no criteria for differentiating one account of the world from another or that there is no uniquely privileged 'truth' (Feyerabend 1975). But, for all its impact elsewhere, relativism has always been rejected by natural science, which simply could not operate on a relativist platform where no theory or fact can be wrong or inferior. It has therefore been able to largely ignore questions about the notion of objective knowledge.

Several philosophers have attempted to arrest the 'slide into relativism' and yet preserve the importance of recognising the influence of extrinsic factors on the production of knowledge (Parker 1992). Critical Realists, influenced by Marx, maintain that the nature of the external world imposes limits on the variety of ways open to us to represent that world. Human interests may skew knowledge away from a true representation of reality. Hence, identifying such interests is important to the process of establishing 'true' and useful forms of knowledge. Unmasking the interests and assumptions enmeshed in certain forms of knowledge is also important because it allows an open and honest debate about what sorts of values and interests scientific knowledge ought to promote (Goldenberg 2006).

The philosophy of Michel Foucault helps us to understand further this relation between interests and knowledge. Foucault was concerned

with the way in which power is a precondition of the development of a body of knowledge and how knowledge could, in turn, function as power. In his lectures on 'Psychiatric Power' Foucault illustrated this thesis with reference to psychiatry. The 'medical authority' of the psychiatric profession, says Foucault, 'functions as power well before it functions as knowledge' (Foucault 2006, p. 3). It is the pre-established power of the profession, the authority it obtained over the process of the management of madness, that enabled the profession to define madness and distress in its own terms, in Foucault's words, enabling 'the great re-transcription of madness as mental illness' (Foucault 2006, p. 346). This form of knowledge reinforced the profession's claim to legitimacy. Foucault describes the 'interplay of a power relationship that gives rise to a knowledge, which in turn founds the rights of this power' (Foucault 2006, p. 346). Although Foucault did not address the role of other players in the formation of psychiatric knowledge, and was in fact wary of locating power in particular groups, preferring to describe power as a system or network, his analysis allows us to understand the symbiosis between the interests of certain groups and the formation of knowledge about psychiatric drugs.

In the spirit of Marx and Foucault I will, in the rest of this book, attempt to uncover the interests that have led to the development and success of the disease-centred model of drug action and its accompanying model of psychic distress. By reflecting on the motives that have generated this model I hope to be able to develop a deeper understanding of how psychiatric drugs work. I will attempt to demonstrate that research evidence, although it has been moulded to fit the disease-centred model, provides little justification for it. I outline an alternative 'drug-centred' approach that is consistent with a wide range of evidence, yields more information about what effects drugs have in different situations and forms a better basis from which to weigh up the pros and cons of drug treatment.

My thesis in this book is that the disease-centred model of drug action has been adopted, and recently widely publicised, not because the evidence for it is compelling, but because it helped promote the interests of certain powerful social groups, namely the psychiatric profession, the pharmaceutical industry and the modern state. Therefore, I offer the following study as an example of the way in which vested interests and the political environment can distort knowledge, in this case successfully deluding most of society for over half a century.

2
An Alternative Drug-Centred Model of Drug Action

The disease-centred model suggests that the important or 'therapeutic' effects of drugs are achieved by their effects on a particular disease process. By acting on the mechanisms of the disease, drugs move the human organism from an abnormal physiological state towards a more normal one. In contrast, the drug-centred model suggests that drugs themselves create abnormal bodily states. In the case of drugs that act on the brain or the nervous system, these states involve an alteration in subjective experience or consciousness. Psychiatric drugs are *psychoactive* drugs which, by their neurophysiological effects alter 'mental and emotional life and behaviour for the duration of the treatment' (Cohen & Jacobs 2007). When we consider drugs that are taken recreationally we have no trouble recognising this fact and we refer to the altered mental state drugs produce as 'intoxication'. But there is no fundamental distinction between drugs used for psychiatric purposes and other psychoactive drugs. They all act on the nervous system to produce a state of altered consciousness, a state that is distinct from the normal undrugged state. The only difference is that the state produced by recreational drugs is pleasurable whereas the effects produced by most psychiatric drugs are experienced as unpleasant. The characteristic features of the drug-induced state vary according to the chemical nature of the particular drug and its interaction with the brain and in subsequent chapters I will describe the features produced by ingesting some commonly prescribed psychiatric drugs.

Drug effects are always subject to individual variation. In other words, people vary in their biological response to drugs and in what they think of different drug-induced effects. The experience of taking a drug is also mediated by the context in which the drug is ingested, including the social circumstances and emotional state of the subject

at the time. For example, someone forcibly injected with a benzodiazepine drug[1] after being brought into hospital against their wishes, possibly by the police, is likely to have a different experience of the effects of this drug compared with a recreational user who chooses to take the same drug. In general, however the characteristic effects of a psychoactive drug are determined by its pharmacological properties, not by the presence of a disease. Therefore, according to the drug-centred model there is no absolute distinction between the response of a patient and that of anyone else.

The drug-centred model suggests that the therapeutic value of a drug is derived from the particular quality of the abnormal state it produces. Some drug-induced effects may be useful or desirable in certain social and interpersonal situations, including the situations that are brought to the attention of psychiatrists and called mental disorders. Deducing what therapeutic effects a drug might have therefore demands a detailed knowledge of the way it changes normal mental functioning which can then be matched up with the effects that the patient or others desire to achieve. But recognising that drugs produce altered states and do not return the body to normal indicates how drugs themselves constitute a source of stress, both physical and psychological. Although it may bring some temporary respite, a state of intoxication is unlikely to be conducive to leading a normal life. Individuals may end up having to struggle to counteract the effects of their drug treatment as well as their original problems. For this reason Peter Breggin, a psychiatrist and famous critic of psychiatric drugs, emphasises that psychiatric drugs impair brain function in the same way as physical intrusions on the brain, such as lobotomy. He calls them 'brain disabling' treatments stating that 'they exert their primary or intended effect by disabling normal brain function' (Breggin 1993b, p. 72). Furthermore, according to Breggin, 'biopsychiatric treatments are deemed effective when the physician and/or patient prefer a state of diminished brain function with its narrowed range of mental capacity or emotional expression' (Breggin 1997, p. 4). The implication that there are no justifiable uses of psychiatric drugs may have limited the appeal of Breggin's ideas to psychiatric professionals and service users, but his work usefully highlights the general character of psychotropic drugs.

The case of alcohol illustrates how a drug-centred model can clarify the potential therapeutic uses of drugs for psychiatric or behavioural problems. Alcohol is a sedative drug that reduces nerve conductivity in the central nervous system. Ingestion of alcohol gives rise to characteristic physiological effects, such as dilation of blood vessels, smooth

muscle relaxation and slowed reaction times. It produces various characteristic subjective experiences and behavioural effects that are dose dependent. At low doses it produces euphoria, some behavioural activation, social disinhibition and mild impairment of intellectual functioning. At higher doses it produces sedation and greater degrees of cognitive impairment. These effects have several consequences. They are responsible for the popularity of alcohol as a social lubricant and recreational substance and they can lead to aggressive and reckless behaviour in some circumstances. They can also help people to overcome behavioural inhibitions. Alcohol might therefore be deduced to have useful effects in social phobia, sometimes referred to as social anxiety disorder, not because the substance corrects an underlying physical abnormality but because some of the effects it produces might in themselves be useful for people experiencing difficulties in social situations. It has in fact long been officially recognised as an effective 'treatment' for social phobia.

Another example of a drug-centred explanation for drug effects is the effects of stimulant drugs on hyperactive children, now officially labelled as having 'attention deficit hyperactivity disorder' (ADHD). Mainstream psychiatry presents stimulants as a disease-specific treatment for this condition, although it cannot account for their mechanism of action. Stimulants are held to have a 'paradoxical' effect in children with attention deficit disorder, that is, their effects are believed to differ from their effects on normal people. However Peter Breggin, along with other critics and some mainstream commentators have long pointed out that the effects on children with attention deficit or hyperactivity are entirely predictable from our knowledge about the overall effects of stimulants on humans and animals (Breggin 2001; Grahame-Smith & Aronson 1992). At high doses stimulants such as amphetamine and methylphenidate (Ritalin) increase motor activity but at lower doses they only increase arousal and focused attention and activity, much like the weaker stimulants nicotine and caffeine. They do this by suppressing reactivity to the environment including social interaction, exploratory behaviour and emotional reactivity. In other words, they cause people to focus narrowly on a single activity and enable them to ignore other stimuli. At higher doses and with prolonged use this effect is magnified and expressed as obsessive and compulsive-type behaviours, and more extremely as stereotypies. These are rhythmic repetitive purposeless movements seen in both animals and humans when given high dose stimulants (they also form the basis of an animal model of psychosis discussed in Chapter 6). Thus, in the short-term low dose stimulants

create a state of reduced responsiveness to environmental stimuli, increased passivity and compliance with set tasks, which may be desirable in hyperactive children, especially in a classroom, where focused attention is required. But this change involves a global reduction in responsiveness and initiative, which may undermine the benefits achieved. Whether the effect persists is another question, since the body rapidly adapts to counter the effects of drugs. Long-term benefits from stimulants have been difficult to demonstrate in controlled trials (Schachter et al. 2001).

Other examples of drug-centred thinking were provided by early proponents of modern psychopharmacology. Pierre Deniker, one of the psychiatrists who first used chlorpromazine, thought that its useful effects were attributable to the induction of an 'an experimental neurological disease' characterised by reduced movement (akinesia) and emotional indifference (Deniker 1960). It was these unique effects that Deniker and other early pioneers thought were responsible for the drug's therapeutic effects in schizophrenia and other cases of psychiatric disturbance (see Chapters 5 and 7 for further discussion of neuroleptic-drug effects). The utility of sedative drugs in anxiety also helps demonstrate the drug-centred model. The lessening of arousal and reduction of nerve conductivity produced by sedative drugs such as benzodiazepines, alcohol and barbiturates reduce anxious thoughts and ruminations, and dampen the heightened physiological arousal associated with these states. Some drug effects in general medicine can also be understood according to a drug-centred model such as the examples of antihistamines and their sedative effects and alcohol's effects on pain, which are described in Chapter 1. However in general, physical medicine prefers to use specific drugs where it can, since these are by definition more powerful.

The drug-centred model of drug action suggests that we can understand effects of drugs that are used therapeutically in essentially the same way as we understand the effects of recreational drugs. In the case of recreational use of drugs, it is effects such as euphoria, stimulation, indifference, disinhibition, psychedelic experiences and some types of sedation that are sought after. These effects are valued as pleasant in themselves, and also as ways of blocking out and anaesthetising people against painful memories and current difficulties. Drugs used in psychiatry have a similar range of effects, and several psychiatric drugs are also drugs of misuse. However these effects can be further discriminated. There are different types of sedation and stimulation, for example. Some drugs, such as benzodiazepines and opiates, produce sedation that is often appealing and others, such as neuroleptics, produce sedation that is generally experienced as unpleasant. Similarly, some drugs produce

stimulant effects that are usually experienced as pleasurable, such as amphetamines and cocaine, whereas others produce stimulant effects that are intensely unpleasant such as the akathisia produced by neuroleptics.

As well as their immediate effects, drugs that are taken long term on a regular and frequent basis induce physical adaptations to the presence of the drug. These can be conceptualised as the body's defence against, or opposition to, the effects of a foreign substance (Breggin 1997; Jackson 2005). For example, long-term use of neuroleptic drugs that block dopamine receptors causes the body to develop increased numbers of these receptors, which also become more sensitive to dopamine (Muller & Seeman 1977, 1978). These adaptations have several consequences. Firstly, they may counteract the immediate effects of the drug so that to achieve these effects larger doses need to be used. This is the phenomenon known as 'tolerance'. Secondly, when the drug is stopped or reduced, especially if this is done suddenly, the bodily adaptations are suddenly unopposed by the presence of the drug. It is these unopposed adaptations that cause withdrawal symptoms and they may cause other problems such as precipitating an episode of psychiatric disorder (Baldessarini & Viguera 1995; Moncrieff 2006). These effects have profound implications for evidence about the efficacy and utility of long-term 'maintenance' treatment in psychiatric disorders as explained in the following section. Another important consequence of the body's adaptations to the presence of a drug is that these adaptations may themselves be harmful and sometimes irreversible, as in the case of tardive dyskinesia, which is thought to be due to overcompensating adaptations to dopamine-blocking drugs (Breggin 1997).

The disease-centred model presumes that drug treatment is a good thing because it helps correct a hypothetical underlying disease state and returns the body towards normal. Any unwanted effects of drugs are classified as 'side effects' and as such receive little attention. In contrast, the drug-centred model presents drug treatment in a much more ambivalent light. According to this model, drug effects cannot be parcelled off into therapeutic and adverse effects as if these were distinct. Instead drugs need to be seen as inducing 'global neurological syndromes' (Cohen 1997). The characteristics of these syndromes might be therapeutic in some ways but will almost certainly have negative implications too. The increased passivity and reduced initiative shown by a child on stimulants may be useful in a classroom but be a hindrance in a summer camp. The sedation produced by benzodiazepines may reduce tension but will also impair vigilance. Drug use is always a fine balancing act between the

benefits that might be gained in some respects and the impairments that drug-induced effects almost always incorporate, especially in the long term. The drug-centred model also helps to alert us to the potential dangers of long-term drug use by stressing that drugs are foreign chemicals that interfere with normal biological functioning. Therefore, the body naturally tries to counteract their effects, sometimes leading to further harmful consequences.

Evaluating models of drug action

It is increasingly recognised that even the most rigorous methodology may not adequately control the influence of groups and individuals that stand to benefit from the results of medical research. The placebo-controlled randomised trial was devised to try and eliminate the effect of extraneous factors. It is designed to distinguish the effects of the general environment plus the natural history of the condition from the specific effects of a particular treatment. However these trials are based on the assumption that drugs act in a disease-centred way on the basis of a specific disease. The placebo or dummy tablet is employed to mimic the process of taking a drug because it is known that the positive expectations people have about the effects of taking treatment may, in themselves, improve the outcome of certain conditions. This is known as the 'placebo effect'. This effect is likely to be particularly influential in psychiatric disorders, especially depression and other 'neurotic' conditions, because of the subjective nature of symptoms and outcomes (Fisher & Greenberg 1993). However the placebo effect is only one aspect of what are called the 'non-specific' effects of treatment, so named to contrast with the specific or disease-centred effects. The drug-centred model suggests that in addition to placebo effects, drugs have non-specific *pharmacological* effects. In other words, they create drug-induced states that may impact on outcome without affecting the disease process. A standard placebo-controlled trial cannot distinguish between whether drugs exert disease-specific effects or whether they create a drug-induced state that suppresses the manifestations of mental disturbance or affects the way it is perceived. For example, various psychoactive drugs may appear to be beneficial in depression because they produce a state of intoxication that masks or supplants people's emotions, rather than having any specific effects on mood.

In addition, these non-specific pharmacological effects may affect people's expectations and thus interact with the placebo effect. The fact that psychiatric drugs are active agents means that they have detectable