Philosophy of Psychopharmacology

Smart Pills, Happy Pills, and Pep Pills

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Preface

At times, new scientific data lead to a revolution in how we think about ourselves. Copernicus's data showed that the Earth and its inhabitants were not situated at the geographic epicentre of the Universe. Darwin's observations indicated that humans did not exist in a natural realm apart from other primates. Freud's cases suggested that the rational conscious mind was not necessarily the primary determinant of human behaviour. This volume begins with the idea that revolutionary data about the brain and the mind, and especially about medications that act on the brain-mind, will fundamentally change our thoughts about humans.

Brain-mind-altering or psychoactive substances, also known as psychotropics, have been used since antiquity for both recreational and therapeutic reasons. Noah celebrated with wine, and Plato philosophized about its appropriate use.[1] Paracelsus knew the value of laudanum, and Pinel not only unshackled the insane but also prescribed opium. Nevertheless, the modern field of empirical psychopharmacology is only a few decades old. Psychopharmacologists have mostly been interested in basic science investigations of the mechanism of new drugs and in clinical studies of their efficacy in treating psychiatric disorders. They have not paid much attention to the more abstract question of whether their data change our understanding of the nature of cognitive science and of psychiatry. This is an important gap, and this volume hopes to begin to close it.

Working with the new psychiatric drugs raises crucial philosophical questions, and so encourages a rethinking of cognitive science and particularly of psychiatry. The value of the new psychiatric drugs as

[1] Plato's "A Touchstone for Courage" (Plato, 1970) is perhaps the first philosophy of psychopharmacology in the West. Aristotle similarly considered issues around alcohol and responsibility (Aristotle, 1980).

things-with-which-to-think (Papert, 1980) lies not only in their efficacy for major psychiatric disorders, but also in their potential use in a range of additional contexts. There is, for example, growing interest in smart drugs to improve intellectual, sporting, or military performance, in mood-brightening and personality-enhancing drugs, and in pep pills to enhance motivation and energy. Scientists and societies are increasingly grappling with questions about using medical treatments, including psychotropics, for purposes that are "Beyond Therapy" (President's Council on Bioethics, 2003), or "Better than Well" (Elliott, 2003).

Such so-called "cosmetic psychopharmacology" (Kramer, 1997) immediately raises a range of conceptual (or metaphysical) questions about the nature of the entities that are used by psychiatrists: How do we best define medical and psychiatric disorders? Are psychiatric disorders a kind of medical disorder, or are they a different kind of category? Can psychotropics change personality, and if so, what are the implications for our concepts of self? How do we distinguish the use of psychotropics for therapy from their use for enhancement, or psychotropic medications from legal substances such as alcohol, illicit substances such as cocaine, and nutrients or nutraceuticals?

Second, psychopharmacological data raise a series of explanatory (or epistemological) questions focused on how to best understand brain-behaviour phenomena. How can we understand the way in which psychotropics work to alter thoughts, feelings, and behaviours, and should our explanations differ from those we develop for understanding how psychotherapy leads to change? How can we best conceptualize placebo and nocebo responses to psychotropics, and the relevant unconscious processes involved? What is the relevance of Darwinian or evolutionary mechanisms when investigating psychopharmacological phenomena?

Third, psychopharmacological data raise a series of moral (or ethical) questions. When is the use of psychotropics for psychiatric disorders appropriate? Depressive realism refers to the phenomenon that people with depression appear to be more realistic in their appraisals of the world, the self, and the future than are people without depression – is depressive realism best left untreated? Should cosmetic psychopharmacology – the treatment of undesirable traits (poor memory, shyness,

impulsivity) that cannot be characterized as psychiatric disorders – be encouraged or deplored, do we believe in a pill for every psychic ill?

To discuss the questions raised by psychopharmacology, we need a framework that can address related questions in philosophy of science, medicine, language, mind, emotion, personal identity, the unconscious, and evolution. I have found it useful to summarize this immense philosophical literature by contrasting two camps – a "*classical*" and a "*critical*" approach to cognitive and clinical science. While this contrast entails a great deal of oversimplification, and may not apply to the work of any particular thinker, it serves as a useful foundation for putting forward an integrative approach to answering the questions of psychopharmacology.

Very briefly, the classical position can be traced back to Plato, runs through the work of the early Wittgenstein, was taken up by the logical positivists, and continues to be a major force in contemporary philosophy. It has viewed cognition in terms of computation, and has defined psychiatric disorders in similarly restrictive ways. In contrast, the critical position also has early roots, was strongly influenced by thinkers like Vico and Herder, played an important role in post-modern movements, and continues to be central for continental philosophy. It has emphasized the importance of human understanding and of social context, and has regarded mental disorders as representing merely another way of living.

Instead, this volume puts forward an approach that highlights the findings of cognitive-affective science; this is a framework that allows for an approach to the brain-mind that emphasizes the embodiment of cognition and affect in neuronal circuitry and in the interaction of people with the physical and social world, and that provides an expansive space for considering psychiatric disorders as complex, significant, and real phenomena. It is an approach that is consistent with a naturalized philosophy, with scientific realism, and also with a range of psychological and philosophical work that views the brain-mind as neither a computational algorithm, nor as a social construct, but rather as fundamentally embodied.

The term "cognitive-affective" is used here rather than merely "cognitive" or "affective", because the affective realm and its integration

with the cognitive one has been too-often ignored in both psychology and philosophy of psychology. The term "brain-mind" is used rather than merely "brain" or "mind", again to emphasize how the two constructs are, in fact, impossible to disentangle. Similarly, I later refer to "psychobiological" mechanisms. These hyphenated constructs, although perhaps clumsy at first, serve to highlight, first, how complex thoughts and feelings are ultimately based in more basic constructs such as body representation, and second, how the brain-mind is not a computational apart-from-the-world passive reflector, but rather a thinking-feeling actor-in-the-world and active constructor.

Psychotropics are remarkably useful things with-which-to-think. This is not only because they are used in a range of different contexts, but also because of the highly complex issues that they raise, touching on questions in philosophy of science, medicine, language, mind, emotion, personal identity, the unconscious, and evolution. Conversely, answers to the questions raised by advances in psychopharmacology may have profound implications for a broad range of philosophical problems, including metaphysical, epistemological, and moral issues. Wittgenstein was fond of the metaphor of philosophy as a useful medical treatment; this volume suggests that psychopharmacology provides a useful subject matter for philosophy.[2]

Insofar as this volume addresses so many well-discussed questions in philosophy, much of it depends on standing on the shoulders of giants. I am particularly indebted to the work of Roy Bhaskar on philosophy of science, George Lakoff on the cognitive science of categories, and Mark Johnson on moral reasoning. Arguments here are informed by a broad range of philosophical work, including writings at the intersection of philosophy and psychiatry – pioneered by Karl Jaspers, and now an increasingly productive area.

At the same time, I would venture that comparatively little philosophical work has been done in the area of psychopharmacology in

[2] The work of a number of important physician-philosophers, such as William James and Karl Jaspers, begins with a careful consideration of psychology and psychopathology. Subsequently, a number of philosophers such as Austin (in the linguistic-analytic tradition) and Merleau-Ponty (in the continental tradition) early on suggested or employed psychiatry as a significant resource for philosophy.

general, and cosmetic psychopharmacology in particular. This volume outlines philosophical questions raised by psychopharmacology, discusses possible answers from the classical and critical perspectives, and draws on the cognitive-affective sciences to provide an integrated set of answers. I hope that by doing so, the volume contributes to providing a conceptual foundation for good clinical psychopharmacology.

Solomon Stein gave me a life-long interest in the question of whether pharmacology was good or bad. Sally and Leslie Swartz were instrumental in helping me to begin on the road to philosophy more than two decades ago. Jeremy Barris, Arnold Abramovitz, Ronald Rieder, and Michael Schwartz gave encouragement at crucial points. Derek Bolton helped give me the courage to pursue the current project. Anton van Niekerk was crucial in providing a supportive intellectual framework within which I could attempt to move forward. Both Derek and Anton gave me a great deal of encouragement, as well as many useful comments on drafts of the manuscript; this work would not have appeared without their generous mentorship. Many other colleagues have helped me think through questions covered here; particular thanks to Ineke Bolt, George Ellis, Jacques Kriel, Wittem Landman, Ronald Pies, and Willem David Walywn for their comments and suggestions on early versions. Finally, I wish to acknowledge with deep gratitude my wife, Heather, and my children, Gabriella, Joshua, and Sarah, who have put up with my irritable mood when attempting to do philosophy, as well as with the inevitable absences from family life that this attempt entailed.

1

Psychopharmacology – a remarkable development

Psychopharmacology, the study of psychotropics, or brain-mind-altering substances, is a fascinating field at the confluence of neurochemistry and behaviour. Basic psychopharmacologists are mostly interested in how psychotropics work, often studying neurochemical properties of different compounds in animal models. Clinical psychopharmacologists are mainly interested in the clinical applications of psychotropics, often working in psychiatric settings. But what exactly are psychotropics? How in fact do they work? How widely are they used, and do they really help people?

In this chapter I begin by outlining the broad scope of psychopharmacology: emphasizing that psychotropics have been long, widely, and intensively used by humankind for a range of purposes; describing the relatively recent birth of modern psychopharmacology as an empirical science; and noting that despite the remarkable progress in the field to date, psychopharmacology is at an early stage in its development. Then, in the next chapter I go on to consider the major philosophical issues raised by the advent of modern psychopharmacology.

The length, breadth, and depth of psychotropic use

And he drank of the wine, and was drunken; and he was uncovered within his tent. (Genesis 9:21, King James Version)

What is better adapted than the festive use of wine, in the first place to test, and in the second place to train the character of a man, if care be taken in the use of it? (Plato, 1970)

Humans use psychotropic agents in a range of different contexts. We imbibe stimulants such as caffeine as part of our regular diet and to enhance our attention and performance, we celebrate social occasions and perform religious rites with alcohol, we experiment with consciousness-altering drugs, and we take psychiatric medications when we suffer from symptoms such as depression and anxiety. There is no reason to suspect that we have not been engaged in these kinds of activities since the dawn of human time (Moreno, 2006a; Playfair, 1987; Rivers, 2001).

This use of psychotropic agents by *Homo sapiens* is remarkable in a number of different ways. For one thing, reliance on psychotropics is a phenomenon that differentiates humankind from most other species. In the laboratory, a range of animals can certainly become addicted to substances. But in the wild, there is only accidental contact with psychotropics. While there have been occasional reports of non-human primate use of plants for medicinal purposes, such reports have rarely if ever extended to psychotropic agents (Rodriguez *et al.*, 1985; Whiten & Boesch, 2001).

Indeed, in comparison to the use of other pharmaceuticals, human use of psychotropics is remarkable for its broad range. Humans throughout the world have long relied on agents that act on organs such as the gut, the skin, or the heart. However, such pharmaceuticals have invariably been restricted to the prevention or treatment of symptoms of disorders. In contrast, psychotropics have a range of other uses, including as an everyday nutrient and social "lubricant" (spirits), a component of religious rituals and spiritual voyages (entheogens), and performance or cognitive enhancers (nootropics).

The use of psychotropics is also notable for its intensiveness. Ginseng, for example, is a psychotropic herb that played a key role in changing the fortune of Chinese dynasties, due to its high demand and the consequent profits earned from its trade (Taylor, 2006). Alcohol, opium, and cocaine are amongst the addictive substances that have been at the centre of underground battles or international wars, again because each has a substantial market. Modern psychotropic medications have been blockbusters for the pharmaceutical industry, earning it billions of dollars in revenue.

This broad and deep range of uses depends in turn on the complexity of our nervous system – which provides multiple targets for psychotropics to act on, and on the importance of this system to our being – so that psychotropics can have wide-ranging and profound effects. It also reflects the vast range of psychotropics available to our species; psychoactive agents are found in abundance in the plant kingdom (e.g. steroidal hormones are found in yams, monoamine oxidase inhibitors are present in St John's wort, alcohol is obtainable from fermented fruits), and are now also readily synthesized in the laboratory.

Pharmacological agents may in general be the same as endogenous compounds (e.g. insulin for diabetes), may act as agonists or antagonists at particular receptors so augmenting or blocking endogenous processes (e.g. diuretics enhance diuresis), or may have complex stabilizing or destabilizing effects (e.g. anticonvulsants lower seizure threshold). In the case of psychotropics, we have agents that employ each of these possibilities (e.g. exogenous testosterone acts in the same way as endogenous testosterone, selective serotonin reuptake inhibitors enhance serotonergic neurotransmission, alcohol has destabilizing effects on neuronal membranes).

The advent of empirical psychopharmacology

He who had drunk of this potion would not shed tears for a whole day even if his mother and his father were to die, and even if his most beloved son were slaughtered before his eyes. (Homer, *Odyssey*)

Psychopharmacology is an interdisciplinary science in which many techniques and branches of knowledge are brought together. In seeking to modify human behaviour by the use of chemical substances, it lies at the crossroads of the biological sciences and the humanities, because every psychopharmacological problem concerns the relationship between the body and the mind. (Delay, 2006)

The history of psychopharmacology is notable for its length and breadth and depth, but the advent of psychopharmacology as an empirical science is a recent development (Healy, 2002). The term

"psychopharmacology" has been in use since the early twentieth century, and gained currency in the 1950s, at a time when the first randomized controlled trials of psychotropic agents were undertaken (Thullier, 1999).[1] The field grew exponentially thereafter, driven by rapid advances in both basic science (e.g. molecular neurobiology, behavioural pharmacology, synthetic chemistry) and in clinical science (e.g. operational diagnosis, symptom measurement, trials methodology).

First-generation psychotropics were often found serendipitously. For example, the first antipsychotic agent, chlorpromazine, was developed as an anaesthetic; when it was later found to decrease psychotic symptoms, further investigation established that it was a dopamine blocker (Thullier, 1999). Similarly, the first monoamine oxidase inhibitor – a powerful class of antidepressants – was developed as an antituberculous drug. Once again, investigation of the mechanisms of action led to a focus on monoamines in depression.

Whereas these early agents often had multiple actions, affecting different receptors, second-generation agents were specifically developed in order to act on one receptor at a time. A well-known example is fluoxetine, originally marketed as Prozac, a selective serotonin reuptake inhibitor (or SSRI). In contrast to the tricyclic antidepressant agents, which act on serotonin and noradrenaline receptors, as well as on the cholinergic system, fluoxetine primarily affects the serotonin system. Interestingly, recent agents have been specifically engineered to act on more than one receptor system. These potentially offer the advantage of altering the multiple neurotransmitter systems that may be involved in complex disorders.

A number of points can be made about modern psychotropics. First, they cannot be likened to neuronal sledgehammers – fluoxetine acts on the product of a single gene (of the 23 000 odd in the human body). Second, their effects are nevertheless complex – serotonin interacts with multiple other systems, so that fluoxetine eventually affects a

[1] One of the first to use the term "psychopharmacology" was Jean Delay, a pioneering French psychiatrist who testified in the Nuremberg trials and who had a doctorate in philosophy. During the student protests of 1968, strongly influenced by the work of psychiatrists or those using examples from psychiatry (Fanon, Foucault, Goffman, Laing, Marcuse, Szasz), his office was ransacked, and he was forced to resign.

range of neuronal circuits and ultimately thoughts and emotions and behaviours. Most psychotropics can be termed neuromodulators – they act on multiple circuits that spread throughout the brain. Third, the adverse effects of psychotropics are sometimes overstated; for example, while some medications are addicting, antipsychotics and antidepressants are not. Fourth, this does not mean they do not have crucially important side effects – they do.

Progress in psychopharmacology has had an enormous influence on the theory and practice of psychiatry. Indeed, psychiatry is now primarily "biological" in its approach – whereas the field (particularly in the USA) was dominated by psychoanalytic theories and practices in the 1950s, by the end of the twentieth century psychiatric research leaned strongly on the neurosciences, and psychiatric practice relied heavily on psychopharmacological interventions (Luhrmann, 2000; Sabshin, 1990; Shorter, 1998). While psychiatrists continue to be trained in psychotherapy, and optimal prescription of psychotropics requires a rigorous appreciation of the psychodynamics of the patient, the shift in the field has been revolutionary in its extent and impact.

These developments need to be understood not only in terms of the scientific advances allowed by the new psychotropics, but also in more socio-political terms. The pharmaceutical industry has played a key role in developing and marketing psychotropic products (Angell, 2004; Degrandpre, 2006; Healy, 2004; McHenry, 2006; Moynihan & Smith, 2002; Smith, 1991; Starcevic, 2002; Szasz, 2001; Valenstein, 1998). Although much research on psychopharmacology is funded by government sources, such as the National Institutes of Health in the USA, most large, randomized, controlled trials on psychotropics are funded by the industry. Indeed, psychotropics have proven to be particularly profitable pharmaceutical agents; the market for these agents amounts to billions of dollars per annum (IMS Health, 2002). Large amounts of money may be devoted even to niche areas, such as work on psychotropics to enhance performance in the military (Moreno, 2006b).

The relationship between academic psychopharmacology and the pharmaceutical industry has been subjected to a number of critiques. There are, for example, important concerns about the objectivity of

academic researchers who are primarily funded by industry (Angell, 2004; Healy, 2004). Clinicians have in turn been criticized for overdiagnosing and overtreating psychiatric disorders (Horwitz & Wakefield, 2007; Moynihan & Smith, 2002). More radically, an antipsychiatry movement, which questions the scientific validity of psychiatric diagnoses, and is concerned that psychiatric interventions are better understood in terms of the control of social deviance, has criticised the use of "chemical straitjackets" and the marketing of psychotropics as panaceas (Breggin, 1993; Ingleby, 1981; Sedgwick, 1982).

Gains and gaps in psychopharmacology

The expectations I have formulated some 25 years ago regarding developments in the pharmacotherapy of depression have not, or only to a small extent, materialized. Neither have they been refuted. (van Praag, 2001)

Critiques of psychopharmacology which emphasize the use of medication to control social deviance, and criticize the use of "chemical straitjackets" and the marketing of psychotropics as panaceas, ignore some empirical data. First, the global burden of psychiatric disorder is enormous, with 5 of the 10 most disabling medical disorders comprising neuropsychiatric conditions (Murray & Lopez, 1996), and second, despite their prevalence and associated impairment, severe psychiatric disorders continue to remain relatively underdiagnosed and undertreated in both developed and developing countries (Demyttenaere *et al.*, 2004). Nevertheless, this volume is primarly concerned with potential problems in the widespread use of psychotropic agents for a range of other psychic ills. While there may have been major gains in psychopharmacology, it is important to also understand the significant gaps in this field.

Modern psychopharmacology has on the one hand arguably achieved remarkable successes. The closure of large, long-term psychiatric hospitals – deinstitutionalization – was largely brought about by the success of antipsychotic agents in treating serious psychotic disorders such as schizophrenia and bipolar disorder. Although depression and anxiety

disorders continue to be underdiagnosed and undertreated, there are now effective medications available for many psychiatric conditions. Although not all data are consistent (Helgason *et al.*, 2004), it is possible that decreases in the prevalence of suicide in some developed countries reflect the better diagnosis and pharmacotherapy of depression (Carlsten *et al.*, 2001).

Modern antipsychotics and antidepressants are relatively safe, well-tolerated, and non-addicting, so that many early concerns about the use of psychotropic agents for psychiatric disorders have diminished over time. New psychotropics are introduced only after carefully conducted randomized controlled trials show both safety and efficacy. The pharmaceutical industry is closely regulated by governmental agencies. Advances in basic mechanisms continue to be made, new agents continue to be introduced, and there is no reason not to suspect that future pharmacological interventions will be even more useful than those currently available.

At the same time, there are notable gaps in our knowledge of the brain-mind in general (Sala, 1999), and of psychopharmacology in particular. First, a full appreciation of the mechanisms of action of psychotropics remains a goal for the future. Although we understand a good deal about the receptors at which most psychotropics act, we understand much less about how changes at these receptors translate into further changes "downstream" at the so-called 2nd and 3rd messenger level, and we do not have a complete understanding of how these changes in turn alter systems that underpin cognition and affect.

Furthermore, currently available psychotropics almost all work by changing monoaminergic neurotransmitter systems; despite the introduction of new and useful drugs in recent decades, these continue to work on similar pathways as did the earliest agents. Thus, although many psychopharmacologists are excited about the progress that has occurred, a number have warned against exaggerating what has been achieved (van Praag, 1998). While modern agents may be better tolerated than older ones, the lack of truly innovative new interventions in psychopharmacology is worrisome to many.

An early idea in psychopharmacology was that of "pharmacotherapeutic dissection"; if disorders A and B responded to medication X but

not Y, while disorders C and D responded to medication Y but not to X – then disorders A and B would have nosological and biological overlap with one another, but not with the overlapping disorders C and D (Klein, 1964). Obsessive–compulsive disorder (OCD), for example, responds more robustly to clomipramine, a predominantly serotoninergic reuptake inhibitor, than to desipramine, an agent that is also a tricyclic antidepressant, but that is predominantly a noradrenergic reuptake inhibitor (Zohar *et al.*, 1988). Furthermore, benzodiazepines are useful in certain anxiety disorders, but not in OCD. Analogously, whereas dopamine blockers typically cause sedation in healthy volunteers, they result in a decrease in psychotic symptoms in those with schizophrenia or bipolar disorder, underscoring the boundaries between psychotic disorders and normality.

Nevertheless, this principle has not been entirely productive in more contemporary research; for example, clomipramine is more effective than desipramine not only for a number of conditions that have much in common with obsessive–compulsive disorder (e.g. body dysmorphic disorder), but also for a number of apparently quite unrelated conditions (e.g. premenstrual dysphoric disorder) (Stein, 2001). Conversely, when a medication is effective, we cannot necessarily deduce a great deal about the mechanisms involved in the relevant disorder. It turns out that there is surprisingly little evidence of serotonergic dysfunction per se in OCD. It is possible that a quite different neurochemical system is at fault in OCD, and that serotonergic medications are effective only via their secondary effects on that other system (Stein, 2002). Furthermore, dopamine-releasing agents are not only effective in improving concentrations in patients diagnosed with attention-deficit/hyperactivity disorder (AD/HD), they may be used by ordinary college students or by military personnel to enhance cognitive performance (Chatterjee, 2006; Kadison, 2005; Vastag, 2004), thus raising questions about the validity of AD/HD as a disorder.

In addition to gaps in our understanding of basic mechanisms in psychopharmacology, there are also important lacunae in clinical psychopharmacology. The majority of randomized controlled trials of psychotropics to date have been undertaken in Western adult populations, over the short term, and in tertiary settings. Regulatory authorities

require only a few positive trials for an agent to be released on the market, typically for a single indication (such as major depression). There are comparatively few data on the use of psychotropics in other kinds of populations (e.g. children), over the long term, and in general psychiatric or primary settings (Klein *et al.*, 2002; Wells, 1999). For many psychiatric disorders, should a first-line medication fail, there is surprisingly little evidence on which to base the choice of a second-line medication (Fawcett *et al.*, 1999; Stein *et al.*, 2005).

Thus, while the advent of modern psychopharmacology has been a remarkable development, this is a young field, and much additional empirical basic and clinical research remains to be done (Klein, 1993; Klein *et al.*, 2002). Of particular relevance to the current volume is the gap in empirical research on "off-label" indications for psychotropic medications. Once a psychotropic medication is made available, additional data on safety may become available on the basis of post-marketing surveillance. However, the prescription of psychotropics for non-registered conditions (for example, the prescription of an antidepressant for depression that does not meet criteria for a major depression) may continue on the basis of clinical judgement rather than empirical trials. The lack of data in this area contributes to the difficulty of the philosophical questions raised by modern psychopharmacology, the focus of the next chapter.

2

Philosophical questions raised by psychopharmacology

In addition to the many empirical questions that remain for psychopharmacology, the field has raised important philosophical issues for the cognitive and clinical sciences. Philosophy of medicine, philosophy of psychology, and philosophy of cognitive science have only recently begun to address conceptual issues in neuroscience (Bechtel *et al.*, 2001; Bennett & Hacker, 2003; Bickle, 2003; Churchland, 2002; Mishara, 2007), and by and large have ignored the area of clinical psychopharmacology. This volume attempts to begin to address this notable gap in the literature.

A host of philosophical questions are raised by modern psychopharmacology. For the purposes of this volume, these can be divided into (1) conceptual or metaphysical questions about categories relevant to psychopharmacology, (2) explanatory or epistemological questions addressing our knowledge of how psychotropics work, and (3) moral or ethical questions about when psychotropics should be used. In the rest of this chapter I will very briefly outline each of these categories of questions; the rest of the volume will then consider each of these categories and questions in turn, exploring them in more detail.

Conceptual questions raised by the effects of psychotropics

Psychopharmacology raises questions about a number of categories employed in psychiatry. Most importantly, it raises the question of how

optimally to define medical and psychiatric disorders.[1] The definition of disorder lies at the heart of philosophy of medicine, and how we think about disorder may well impact on how we think about interventions, including treatment with pharmaceuticals or psychotropics. Some may go so far as to argue that if a particular medical or psychiatric intervention is useful, then this helps define the existence of an underlying medical or psychiatric disorder (Kessler *et al.*, 2003; Reznek, 1988). Is disorder the kind of thing that can be defined in terms of necessary and sufficient conditions (e.g. a *square* has certain essential features), or is it more of a category that mainly reflects particular social practices (e.g. what counts as a *weed* may vary from time to time and place to place)?

A second set of conceptual questions relates to psychotropic medications themselves. The question of how to define a pharmaceutical and a psychotropic are not entirely straightforward. For example, what is the distinction between the use of psychiatric medications for therapy versus enhancement? What are the boundaries between psychiatric medications, legal drugs (alcohol, nicotine), and illicit substances of abuse (cocaine, heroin)? Are nutrients such as the amino acid, tryptophan, which may act to increase serotonergic neurotransmission, best conceptualized as pharmaceuticals (that is, so-called neutraceuticals)? How important is it to draw a distinction between psychotropics that are identical to endogenous compounds and those that act to perturb endogenous mechanisms?

A third set of conceptual questions raised by psychopharmacology is concerned with defining emotions and the self, the person, and his or her character. It seems unproblematic to assert that if an individual imbibes alcohol and acts impulsively or rashly, then a sympathetic audience might characterize this behaviour as out of character. What happens when an individual experiences gradual positive psychological changes in response to a psychotropic, so that they later come to see themselves as having previously suffered from a chronic disorder – have they lived their life "out of character"? These questions in turn raise questions about how best to understand how psychotropics work.

[1] I use the term "disorder" rather than "disease" only by convention. The term "disease" connotes an understanding of precise pathology, which is often absent in psychiatric conditions.

Explanatory questions about how psychotropics work

Psychopharmacology raises the epistemological question of how to understand the mind-body in general and psychotropics in particular. Psychopharmacologists have produced a range of neuroscientific data about how psychotropics act to affect one or other biological system (e.g. benzodiazepines act on the γ-aminobutyric acid or GABA receptor). However, it is unclear whether such work fully addresses the question of how these agents work to change thoughts, feelings, and behaviours (how does a benzodiazepine result in reduced anxiety?). Our accounts of how psychotropics work and of how psychotherapy works seem to operate on entirely different levels of discourse (e.g. we describe a psychotropic as altering a neuronal receptor in the brain, but we describe a psychotherapeutic intervention as leading to a change in the patient's way of thinking or feeling). What is the relationship between such views? An immediate possibility is that psychotherapy affects the software of the mind, but that medication affects the hardware – is such a view valid? The problem of understanding how treatment works also raises the related question of understanding how disorders arise, of conceptualizing how genetic and environmental factors underlie pathology.

A second set of explanatory questions relates to placebo and nocebo effects. Clinical psychopharmacology relies on the use of double-blind placebo-controlled trials in which participants are randomized to receive either active medication or an inert substance, with both physician and patient kept "blind" about the identity of the tablet. In such controlled trials, there is often a sizeable clinical response in patients given the inert substance (the placebo effect). Conversely, a remarkable number of subjects experience adverse events in response to administration of an inert substance (the nocebo effect). How should these phenomena best be conceptualized? How should the unconscious processes at play here be characterized?

A final group of explanatory questions about psychotropics involves the discipline of evolutionary psychology. There is a growing literature which argues that thoughts, feelings and behaviours should not merely be explained in terms of their underlying proximal mechanisms, but that it is also relevant to consider their more distal, evolutionary origins

(Cosmides & Tooby, 2003; Laland & Brown, 2002). Increasingly, evolutionary explanations have been applied to medicine in general (Nesse & Williams, 1994) and to psychiatry in particular (Baron-Cohen, 1997; McGuire & Troisi, 1998; Stevens & Price, 1996). Instead of focusing on the proximal factors that underlie pathology, an evolutionary perspective focuses on the distal or evolutionary mechanisms that create vulnerability to disease. Is such a perspective valuable in understanding the effects of psychotropics?

Moral questions about when to use psychotropics

It seems clear that if a patient has a life-threatening pneumonia then it is a reasonable medical decision to administer an effective antibiotic. By analogy, if a person has a life-threatening depression, it seems logical that it is valuable to arrange for a physician to prescribe an effective antidepressant. However, it is unclear whether this argument would hold for a range of other psychiatric symptoms, such as chronic low-grade depressive symptoms (dysthymia), variations in temperament (such as shyness) or behaviours that seem bad rather than mad (for example, impulsive-aggression).

This problem is made particularly acute by the argument that psychological phenomena, including psychiatric symptoms, can be understood as meaningful within their particular phylogenetic and ontogenetic framework (Bolton & Hill, 1996). Apparently negative or destructive emotions, such as shyness, aggression, or jealousy, have important positive features (Goldie, 2000). Similarly, in the realm of cognition there is the phenomenon of depressive realism – people with depression may be more accurate in judging contingencies between responses and outcomes in the world than people without depression (Haaga & Beck, 1995). Pharmacotherapy of cognitive-affective symptoms, perhaps particularly if unaccompanied by the insight that psychotherapy can bring, therefore arguably runs the risk of being harmful.

What about so-called "cosmetic psychopharmacology"? This term was coined by the psychiatrist Peter Kramer, who addressed this potentially new use of psychotropics in his volume *Listening to Prozac*, perhaps

the first extended meditation on the conceptual implications of modern psychopharmacology for society and for psychiatry (Kramer, 1997). Pharmaceuticals are used increasingly to enhance athletic or sexual performance (Flower, 2004), and plastic surgery is widely used to enhance physical appearance (Bolt *et al.*, 2002). Is there a rationale for using psychotropics to optimize psychological well-being and function, even in the absence of disorder? If novel agents act to improve memory, decrease shyness, or reduce impulsivity, for example, what are the pros and cons of widespread prescription of such agents?

Considerations about when and how it is appropriate to treat disorders and symptoms cross the fact–value divide (Canguilhem, 1966; de Beaufort *et al.*, 2000; Fulford, 1989; Fulford *et al.*, 2005; Hare, 1983; Pellegrino & Thomasma, 1981; Sadler, 1997, 2002; Schaffner, 1999; Wakefield, 1992b). Furthermore, there is a tension in Western society between values of self-improvement, which would encourage people to use novel technologies including psychotropics, and values around tradition and nature, which argue that such changes are not authentic (Elliott, 2003; Parens, 1998b, 2005). Such debate is stirred by technical breakthroughs such as gene therapy (Anderson, 1989; Jonas, 1974; McGee, 1997; Walters & Palmer, 1997), or the development of selective serotonin reuptake inhibitors such as fluoxetine (Prozac). However, the debate has occurred many times in the past; early psychotropics such as barbiturates,[2] cocaine, and benzodiazepines were initially viewed as having significant value as cosmetic psychotropics that were useful even in those who did not suffer from disorders (Elliott, 2003).

Conclusion

There are a number of philosophical questions that relate to psychopharmacology, but that will not be addressed here, as they arguably involve broader issues in philosophy of medicine and psychiatry, or in philosophy of mind, rather than issues more specifically tied to the philosophy of psychopharmacology per se. These include questions such

[2] Barbiturates were perhaps the first synthetic psychotropics marketed as enhancers. In 1863 Adolf van Baeyer synthesized barbituric acid, which he named after his girlfriend Barbara.

as consent with regard to psychotropic medication in research and in the clinic, the use of psychotropic medication to compel truthfulness under interrogation or to end life during euthanasia, and the ethics of animal and stem cell research on psychopharmacology.

On the other hand, the questions raised here will ultimately lead to a whole range of more general philosophical and clinical questions, including questions about how to conceptualize science, language, and mind, about disease and illness, pharmacotherapy and psychotherapy, and placebos and the unconscious. These questions are not the primary focus of the volume, but we need to address them in order to provide a framework for considering the questions raised by psychopharmacology.

While a great deal of work has been done on the philosophy of science, language, mind, and medicine, the intersection between philosophy and psychiatry per se is a more circumscribed one. Relatively little philosophical work has been done in the area of psychopharmacology in general, and cosmetic psychopharmacology in particular.[3] I hope that this volume begins to break some new ground in this area, and by so doing contributes to providing a conceptual foundation for good clinical psychopharmacology.

[3] A number of the questions raised by psychopharmacology are also raised by other branches of science in general (e.g. genetics) and neuroscience in particular (e.g. brain imaging). For example, progress in genetics has raised the question of what it means to be 98% chimpanzee (Marks, 2002), and advances in neuro-imaging raise a number of conceptual questions (Fusar-Poli & Broome, 2006). I will refer at times to this parallel literature.