Psychopharmacology

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Psychopharmacology is the generic term for the study and use of drugs to alter brain functioning with the aim of changing mental function. This definition includes the study and use of recreational drugs; of mind- or pleasure enhancers that are supposed to improve on normal functioning; of drugs that are intended to complement other medical or psychological treatments, including drugs designed to enhance the efficacy of psychotherapy; of drugs that are intended to treat physical disorders, but have incidental or occasional effects on the mind; and of drugs that are intended to restore people to normal functioning; and of drugs that counter-act the effects of other drugs. I shall give at least one example from each of these classes, but will give most example from the latter classes since these include the prescribed drugs and therefore the drugs or medication that psychotherapists will most often encounter in their clients.

I shall concentrate on the impact of drugs on the experience of being a client in therapy, but taking medication may also affect the therapist and so questions may sometimes arise about the ethics of taking a particular drug or in a particular dose whilst performing therapy.

There is a considerable amount of information about drugs that is available on the internet, much of it published by reputable bodies for the benefit or practitioners or patients. Careful research may provide reliable information even if no access can be gained to the carefully edited information available to professionals, for example that provided in the online version of the *British National Formulary*. I shall not therefore write in detail about any particular drug, but try to address some of the more general issues that might arise when drug use or abuse are combined with psychotherapy and to consider some of the principles that underly prescribing decisions.

Is psychopharmacology ever justified?

Radical criticisms of the use of drugs in psychiatry have often been made, sometimes extending to complete opposition to the use of drugs at all. These views are often endorsed by the public who, in surveys, regularly prefer talking treatments to drug treatments in psychological disorders (Shulamit?

One kind of argument is a theological one: man is created in God's image, and is therefore already perfect in form. To believe that one can improve upon God's perfection by the use of drugs is a kind of heresy. Many people would endorse this argument when it comes to cognitive or other enhancements, for example the use of stimulants to help people to study or of amyl nitrate to increase sexual pleasure. However although some would argue that illness is also part of God's design for the world, and should not be tampered with, it is difficult to argue that illness is a kind of perfection. In fact most people would probably accept that wounds or diseases render a person imperfect and that treatment of them is in pursuit of God's purposes. My intuition is most people would say that treatment of, say, a child with pneumonia with an antibiotic, is in line with God's purpose or, to put it in humanistic terms, enables the child to have their true destiny or to reach their full potential. But some people might argue that this does not apply to a condition that is 'purely' mental, such as a person who is stricken with grief.

Some psychiatric disorders do approximate to the disease model: the inexorable course of schizophrenia in some people is one example; another is the onset of self-destructive episodes of mania or of profound depression in some people with bipolar disorder. Although psychotherapists may contribute to the amelioration of these conditions, their primary treatment is usually medical. This may be considered inappropriate by a few critics of psychopharmacology, but the strongest criticism is reserved for psychopharmacology in anxiety related disorders or unipolar depression (i.e depression not associated with a past history of being high or 'hypomanic').

Objections to the use of medication in these conditions is made not just on the ethical or religious grounds just mentioned, but on moral and practical grounds, too.

Does taking drugs prevent people from overcoming their own problems?

The moral objections to psychopharmacology often rest on the concept of agency, or responsibility. At the height of the use of benzodiazepines by doctors, during the 1980s in the UK, one of the feminist arguments against their use was that women who were distressed by adverse home circumstances—an

abusive husband for example—were sedated by their doctors and so lost the will to try to rectify the situation. Use of antidepressants or anxiolytics may be seen to be a voluntary abrogation of the responsibility to change one's life or a denial of the power, or agency to do so because taking medication was to frame the problem as a kind of disease in oneself. Not only that, but taking 'tranquillizers' quelled or suppressed the negative emotions that might power a change.

Related to this is the perception by some psychotherapists that taking medication might be a kind of escape from the work of self-reflection and therefore from being honest about oneself and one's situation. This may be linked to the common idea that counselling and psychotherapy are undermined by combining them with psychoactive medication. I consider this later

People who have regularly taken medication for emotional problems do seem more likely to think of medication as their first-line strategy when new problems emerge. So it seems likely that the use of psychoactive drugs does alter a person's preferred choice of coping strategy. But whether this makes them, in the long-run, less resilient in the face of future adversity, as many psychotherapists might argue, cannot be assumed: I shall consider the evidence in a later section.

Are psychoactive drugs a kind of psychotherapy?

Comparisons of the response to drugs and to psychotherapy in people with unipolar depression or anxiety disorders suggest that the outcomes are much more similar than might be expected (Tyrer et al., 1988). The most likely explanation is that both act through a process of what Jerome Frank (Frank, 1961) memorably called 'remoralization'. When medicine was more paternalistic, doctors would sometimes capitalize on this by giving their patients sugar coated pills that were psychopharmacologically inert. To conceal this from their patients, they would term these pills 'placeboes' (from the Latin, placebo or 'I will please') and the pharmacist would have a stock of these inert pills to dispense. The placebo effect remains an important hidden element in psychiatry. A recent re-analysis of the effects of antidepressants that included unpublished as well as published studies demonstrated, for example, that the outcome of antidepressants and the outcome of placebo was no different in people with mild or moderate depression, even though the published studies suggested otherwise (Kirsch et al., 2008).

The passage of time might account for some of the placebo effects: sharp dips in mood or rises in anxiety may just remit given the change of the circumstances that caused the dip in the first place. But in many studies, outcome is compared to being on a waiting list and the outcome of the treated group is normally better than that of the waiting list group, indicating that the placebo effect is a real treatment effect.

Frank argued that the placebo effect accounted for the therapeutic effect of psychotherapy as well as of drugs. There has been continual interest in how it is produced, and what facChivtors increase or decrease it. It is plausibly assumed that believers in drugs benefit more from drug placebos and believers in therapy more from talking treatments: however there is some evidence against this (Chilvers et al., 2001).

Cost-benefit analysis

Drugs cost money, sometimes a lot of money. New drugs cost more than old ones, often because old ones can be made in factories by companies who just make drugs rather than go to the additional expense of developing ones. These generic drugs are the pharmacological equivalent of the eclectic or non-branded therapies, provided by psychotherapists who have not gone to the expense of acquiring the license to provide an acronymic treatment like CBT. Money is not the only cost. Psychotherapy or counselling have time costs. It has been argued that they may cost more than that. Fay Weldon argued in her novel 'Affliction' (written after breaking up with her second husband Ron Weldon who, according to Wikipedia, left her after being told by an 'astrotherapist' that their star signs were incompatible) that they may cost relationships, too.

These costs have to be set against benefits. Benefits, too, may be varied: there may be offset effects in a reduction of the need for other treatment, a decrease in disability leading to increased income, and, of course, a reduction of symptoms. In order to compare symptoms one with another, they are often recast as increments of quality of life.

As placebos are inert, it is sometimes assumed that they have no costs, but this is not so. There may be travel costs, time off work costs, the reduced quality of life for people who get worse with placebos

(the ‘nocebo’ effect), the costs of delaying more active treatment, and most importantly the costs of reducing resilience if, indeed, treatment may do that.

Should psychotherapists know about drugs?

A little knowledge is a dangerous thing, so people say. So is it better for psychotherapists to have no knowledge at all about drugs? The answer to this partly depends on the practice of the psychotherapist or counsellor. Working in private practice will often mean working with a clientele who is rarely taking psychoactive drugs; working in a general practice, the opposite. Working in a school or college setting may mean often working with students who are using street drugs, and working in a substance misuse clinic will almost always mean this.

I would argue that any therapist or counsellor who is likely to work with people taking psychoactive drugs needs to know about them. My primary reason is that I think of counselling or therapy as a kind of primary care, and not as a specilized add-on to other health services. So a counsellor’s role will include recognizing possible side-effects of medication and recommending to a client that they have these investigated. It will also include evaluating if the use of a psychoactive drug is adversely affecting counselling, and more rarely, but no less importantly if a client might benefit from psychotherapy.

The justification that I have just given for knowing about drugs focusses more on knowing the costs of psychoactive drugs and less on the benefits. This is the inverse of psychopharmacology training for doctors, and rather unusually, I will therefore consider drugs according to the categories of their side-effects rather than the customary classification of drugs by the expected benefits—antidepressants, anxiolytics, and so on. Fortunately this side-effect classification is actually simpler than a classification according to main effects. The reason for this is that most of the drugs currently used in psychiatry are presumed to act by either augmenting or competing with naturally occurring chemicals—transmitters—that mediate electrical tranmission in brain, spinal cord, and in smooth muscle.

The transmitter hypothesis of psychopharmacology

Nerve cells conduct signals electrically, but there is always a gap between the membrane at the end of one nerve cell and the membrane at the beginning of another. This tiny gap or synapse normally prevents the electrical current in one nerve from jumping to the next nerve, or to the muscle or end organ. The spark is carried forward by a chemical, released from the nerve carrying the current and acting on the next nerve to create a new spark, leading to a current in that nerve. A surprising range of chemicals are used in the body as 'transmitters' in this way. They include gases such as nitric oxide, simple organic compounds such as amino acids, and more complex chains of amino acids or polypeptides. Nitric oxid leads to the widening or dilation of blood vessels and this is its main therapeutic use, in treating angina and impotence ('Viagra' works this way). Its effects on the brain are only just being understood. This is true of many of the polypeptides too. Often these also act on the gastro-intestinal system as well as on the brain.

Most psychoactive drugs are thought to have their effect by influencing chemical transmission in the synapse (treatments for epilepsy and mania may be exceptions). They may mimic the transmitter and combine with the place or receptor where they attach, or bind, on the nerve to which the spark is being transmitted. If they do, they may stimulate a spark themselves ('agonists') or act as an inert 'blocker' or 'antagonist'. Normally transmitters are quickly destroyed so that their effects are very short-lived but drugs may delay this inactivation either by blocking enzymes that normally break the transmitter down or by blocking the pump that reabsorbs the transmitter ('reuptake inhibitors'). The effect of this is to prolong or potentiate the action of the transmitter.

Tolerance and dependence

One further complication is that the receptors on the nerve to which the spark is being transmitted (the post-synaptic receptor) or in the pump that sucks up the transmitter again (the pre-synaptic receptor) in the nerve down which the spark is travelling may reduce or increase in number. This may be in response to an increase in transmission, and therefore counteract the effect of a drug. Many psychoactive drugs lead to this kind of 'up-' or 'down regulation'. So many psychoactive drugs, if they are stopped, particularly if they are stopped suddenly, may leave transmission in a more parlous state than it was before the drug was started. As a result, some psychiatric disorders may recur or relapse if treatments are stopped suddenly (a 'rebound' effect) and even if this does not happen, more and more drug may be required to produce the same effect ('tolerance'). Tolerance, coupled with

symptoms recurring more and more intensely when the drug's effects have worn off, may lead to dependence.

Dependence seems to be a particular problem for drugs that have an immediate effect on pain, anxiety, or low mood—sometimes collectively called dysphoria. Tolerance and dependence is not generally a problem with drugs that take several weeks to work, as is the case with most treatments for depressive illness or psychosis. One does not need to be an existential psychotherapist to conclude that evolution has worked to ensure that dysphoria persists even if it is artificially abolished and that because dysphoria has an important signal function that is necessary for survival or successful reproduction, or both.

Dependence bedevils psychopharmacology because it contributes to one of the most damaging myths that psychopharmacology should always be avoided because of the risk of dependence.

When are drugs indicated?

There is strong evidence that severe depression, mania, psychosis, and attention deficit disorder improve with drug treatment. The first three are disorders that I have previously mentioned are most 'disease-like' in the minds of many people. Treatability is not in itself an indication that drugs should always be used in these conditions. Depression, for example, spontaneously remits in as many as 85% of people. However, this eventual recovery may take years, and without treatment it is associated with an increased mortality. This is also true of schizophrenia and even ADHD.

Mortality is not the only indication that doctors give for treatment. Increasing quality of life (that is reducing dysphoria and/or reducing disability) is also often given as an indication by doctors but is one that has more opponents. One argument is that dysphoria may be the driver for personal initiatives that might lead to a resolution of the condition and not just an amelioration. One such initiative is psychotherapy or counselling. So some psychotherapists believe that psychotherapy is less likely to be successful if people are taking prescribed psychoactive drugs for this reason. Another contra-indication to medication sometimes given by psychotherapists or counsellors is that psychoactive drugs may affect thinking and feeling and so interfere with the process of therapy.

Psychotherapists do not have to prescribe drugs and are not in a position to either recommend or counsel against their use. What they do need to know, though, are the side effects of medication particularly as these may affect the therapy or counselling itself.

Types of psychopharmacological treatments

Tables ?.1 , ?.2 and ?.3 about here

Conclusions

Psychopharmacology is now an industry as well as a major research area. Given this, it is perhaps surprising that more is not known about the action of commonly used drugs in psychiatry. One reason might be that so much research has focussed on a few transmitters while other possible modes of drug actions have continued to be refractory to investigation. Another is that these few transmitters interact. Another reason is the placebo effect by which expectations rather than the drug itself produce the effect.

Even less is known about subtle side-effects of drugs, such as the reflection or exploration of feeling that are required by psychotherapy or counselling. Since many people who seek psychotherapy and counselling because of a mental disorder are likely to be taking, or at least to have been offered, drug treatment for their condition, psychotherapists do need to know if psychotherapy and pharmacotherapy conflict, as many might assume.

I have considered the possible prejudices that may lead psychotherapists or patients to be suspicious of drug therapy, but I think that there may sometimes be contraindications when the side-effects of drugs might interfere with psychotherapy or counselling. What is known about this is summarized in Table ?.3.

Tables

Table ?.1 Types of psychopharmacological treatment

Enhancers	These drugs aim to increase function above normal. They include stimulants like caffeine and Khat, and disinhibitors like ethanol. They also include nitric oxide sexual stimulants like Viagra and amyl nitrite (both potentiators of nitric oxide), amphetamine and cocaine (for reduced fatigue and greater focussed attention), Ecstasy for better clubbing, and anticholinesterase inhibitors for enhanced memory.
Normalizers	This class of drugs overlaps with the previous one but is justified on the basis that they do not increase function but 'correct' dysfunction. They include anticholinesterases that reduce the early effects of Alzheimer type dementia, dopamine precursors that reduces the early symptoms of Parkinson's disease including those of early dementia, dopamine blockers that reduce some of the symptoms of schizophrenia, drugs that increase frontal lobe function in ADHD by combining an enhancement of both dopamine and serotonin function, and drugs that reduce low mood in depression by enhancing catecholamine and serotonin function in depression. There are also peptide drugs that may prove of value in the future, including opiates that some think may reduce the likelihood of repeated self-injury, through stimulating endorphin transmission and a possible class of future drugs for attachment disorders that will work through oxytocin or vasopressin transmission.
Treatments	Most psychological disorders are 'endogenous'. Those that are not are most often the result of psychosocial adversity for which there is no drug treatment. The number of psychological disorders that are caused by a remediable cause are few, and many of those are the consequences of drug treatments (iatrogenic disorders) or of drug misuse rather than caused by some external, physical agent that can be counteracted by medication. Some inflammations of the brain may present as mental disorders, and so treatment of, for example, cerebral malaria presenting as

	psychosis constitutes a treatment of a mental disorder. Gene therapies or drugs that can directly affect neuronal growth or connectivity may provide treatments in the future.

The psychopharmacology of the common psychiatric disorders, and their 'normalization' is dominated by the pharmacology of a limited number of types of drugs acting on an even more limited number of transmitters (see Box ?.2). Many new drugs turn out to be variants of old ones.

Table ?.2 about here

Table ?.2 'Normalizers' by condition

Condition	Supposed cause	Treatment
Alzheimers disease (the most common causes of dementia)	Destruction of nerve cells, selectively affecting nerves that release acetyl choline (cholinergic neurons)	Drugs that block the enzymes (cholinesterases) that break down acetylcholine, and so increased acetylcholine release
Depression	Reduced catecholamine release (release of norepinephrine particularly) and reduced serotonin release	Drugs that enhance norepinephrine, serotonin, or both
Schizophrenia	Over production of dopamine in the cerebral cortex relative to an underproduction of other transmitters such as glutamate or HDMA	Drugs with complex effects on transmitters but commonly block dopamine and enhance acetylcholine
Anxiety	Complex and probably depend	Drugs that enhance gamma-

	on type of anxiety	aminobutyric acid (GABA) transmission Drugs that enhance serotonin transmission Drugs that block histamine receptors e.g. several of the antipsychotics Drugs that block specific symptoms such as drugs for sleep, or drugs for tremor, by blocking the effects of epinephrine and nor epinephrine

The effect of benzodiazepines is on a fifth transmitter, gamma-aminobutyric acid or GABA, that is released by short inhibitory neurons in many parts of the brain. GABA is derived from another amino-acid transmitter, glutamate. Oddly, glutamate is the main excitatory transmitter in the brain. Inhibitory in this context means that the transmitter makes a neuron less sensitive to the effects of another transmitter, and therefore less likely to carry forward a spark from another neuron. Excitatory transmitters have the opposite effect. Some transmitters may be excitatory in one synapse and inhibitory in another. This happens when there is one receptor in one synapse but a different one in the other synapse. Glutamate has three different receptors, with one sub-type, the NMDA receptor, being the most studied in psychiatry. Norepinephrine and serotonin have many more. Norepinephrine has an alpha and beta sub-type, and each has variants. Serotonin has 7 families of receptor sub-types, each family having several variant sub-types within it. Despite this complexity, many of the side effects of drugs can be inferred from their enhancement or inhibition of these six transmitters: acetylcholine, serotonin, dopamine, norepinephrine, GABA, and glutamate (Box ?.3).

Box ?.3 Transmitters, drugs affecting them, their mode of action on the transmitter and side effects (note this is not a complete list of the side-effects of each medication mentioned. This can be found on guides to drugs such as the British National Formulary, or on the drug packaging)

Transmitter	**Enhance (+) or counteract (-)**	**Common drugs affecting this transmitter**	**Side effects with particular impact on therapy**	**Other selected side effects**
Dopamine (D_2 receptor)	+	Drugs for Parkinson's disease e.g. L-dopa, Drugs for ADHD e.g. amphetamine, methylphenidate		Increased gambling, increased libido, addiction to the drug itself
	-	Antipsychotics, especially high potency antipsychotics,	Lack of reward seeking, reduced task driven behaviour, with a reduction of thoughts and 'blunting' fo feelings, inner restlessness, sedation	Stiffness, tremor ,other symptoms similar to Parkinson's disease. Over-activity of the breast
Serotonin (5-HT $_{2c}$	+	Some antidepressants and anxiolytics	Possible impulsivity, dominant behaviour	'Toxic confusion' may lead to death in rare cases

receptor)		e.g. selective serotonin reuptake inhibitors (SSRIs), some antipsychotics		
	-	Lipid lowering drugs e.g. statins, diet	Panic attacks in predisposed individuals with sensitivity to suffocation, low mood(MILLER, DEAKIN, & ANDERSON, 2000)	Cravings
Catecholamines (epinephrine and norepinephrine)	+	Serotonin and norepineprhine reuptake inhibitors (SNRIs) e.g. venlafaxine, duloxetine , sympathomimetic drugs such as some first generation, tricyclic antidepressants e.g. amitryptiline	Sometimes conflicting effects, depending on whether alpha or beta receptors blocked more but may be agitation, anxiety, rapid heart, irritability	Conflicting effects but blood pressure may be raised along with other physical symptoms associated with stress

	-	Some atypical antipsychotics e.g.quetiapine, clozapine, sertindole, zotepine, some antidepressants e.g. mianserin, mirtazepine	Sedation	Conflicting effects but may include weight gain, rapid heart rate, dizziness on standing
Acetylcholine (muscarinic receptor)	+		Sedation	Constipation, dry mouth blurred vision, difficulty in passing water, eyes more senstitive to light
	-	A very large number of commonly prescribed drugs including the low potency antipsychotics (usually dose over 50 mg per day) e.g. chlorpromazine, clozapine, loxapine, quetiapine, and some tricyclics e.g. amitryptiline		Increase in heart problems, possibly increased in cognitive decline, and possibly increased risk of Alzheimer's disease in elderly, risk of death in overdose

Glutamate (NMDA receptor)	+			Linked to cell death
	-_	Drugs to alter conscious level e.g. methadone (also an opiate), alcohol, phencyclidine, ketamine Drugs for Parkinsonism e.g. amantadine	Disinhibition, reduced ability to store current events in memory, dissociation, psychotic symptoms	
GABA (A receptor)	+	Antiepileptic drugs, benzodiazepine anxiolytics, barbiturates	Impaired memory of current events, sedation(Czubak, Nowakowska, Burda, Kus, & Metelska, 2010)	
	-	Benzodiazepine antagonists, but only used in emergencies		

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