BIOLOGICAL THERAPIES FOR SCHIZOPHRENIA

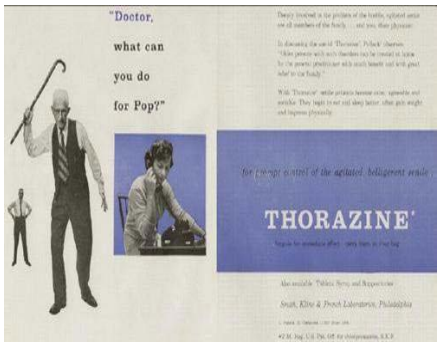
Biological treatments (therapies) arise from the **biological approach** to explaining the causes of mental disorder. Since the biological approach sees mental disorders as being caused by **physical factors**, the therapeutic approaches it favours are also physical. Collectively, they are known as **somatic therapy**.

There are a large number of somatic therapies (e.g. **drugs**, **ECT**, and **psychosurgery**). The two that will be considered here are drugs and psychosurgery. The *descriptive* aspect of an examination question will be knowledge and understanding of what these therapies involve. The *evaluative* aspect will be an evaluation of the therapies in terms of their **effectiveness** (how *well* they work in treating schizophrenia) and **appropriateness** (whether they *should* be used to treat schizophrenia).

Drug therapy (Chemotherapy)

The most common treatment for schizophrenia is by means of **anti-psychotic drugs**. These are also called **neuroleptic drugs** because one of their side effects (see below) is to produce symptoms similar to a neurological disorder (such as Parkinson's disease: see below). There are two types of anti-psychotic drug the **typical** (or **conventional**) and the **atypical** (or **unconventional**).

Typical/Conventional anti-psychotic drugs block **dopamine receptors**, and reduce its effects on thought, emotion, and behaviour. They include the **phenothiazines** (such as **chlorpromazine,** which is marketed under the trade names **Thorazine** and **Largactil**). Other typical anti-psychotics are the **butyrophenones** (**Haloperidol** and **Haldol**) and the **thioxanthenes** (**Navane**). All of these different drugs appear to be as effective as each other in treating schizophrenia.



Atypical/Unconventional anti-psychotic drugs are used with people who do not respond to typical anti-psychotics, and because there are fewer side effects associated with them (see below). They are called atypical because they *seem* to work by blocking **serotonin receptors** rather than dopamine receptors. Examples include the **dibenzazepines** such as **clozapine** (**Clozaril**), **olanzapine** (**Zyprexa**), and **risperidone** (**Risperdal**).

In order to assess the effectiveness of any therapy it is necessary to have some way of *measuring* its effectiveness. Unfortunately, it is not easy to determine what the most effective measurement should be. A lot of clinicians would argue that the most straightforward measurement of effectiveness is an observable change in behaviour. However, other clinicians (especially Freudian psychoanalysts!) would disagree.

Even if clinicians did agree that an observable change was the best measure of effectiveness, there is the further question of *who* decides whether a change has occurred. The therapist him/herself clearly has a stake in believing that their therapy is beneficial, and could not be unbiased no matter how hard they tried. Using the individual who received the therapy and/or their friends and relatives is equally problematical.

In the best kind of studies, *objective assessors* who are *blind* to what treatment a person has received are used to measure effectiveness.

These assessors take a measure of a person's level of functioning before the treatment begins, and then at various times during and after the treatment. As well as the assessors being 'blind', the people receiving the therapy are also not told whether they have received the drug or merely a **placebo**. This is called a **double blind study**.

Note, though, that achieving satisfactory double blind control is not always easy. In studies looking at anti-psychotic drugs, people can sometimes tell if they are receiving a placebo because of the *absence* of side-effects (see below). However, this problem can be overcome by using *active placebos*, which mimic a drug's side-effects but exert no other effect.

In terms of their effectiveness at *reducing* the symptoms of schizophrenia, anti-psychotic drugs are **highly effective** with at least some schizophrenic symptoms. By 1970, more than 85% of all patients in American state mental hospitals were receiving anti-psychotic drugs, and the 'drug revolution' (which began in 1952) had truly arrived. Anti-psychotics rapidly reduce the most disturbing symptoms of schizophrenia (i.e. hallucinations and delusions). They also have a 'marked calming effect', but without impairing consciousness. Hence, they are sometimes called **major tranquillisers**.

The drugs' effects are most marked in the first six months of use, but such was their effectiveness in most people that they eliminated the need for padded cells and straightjackets, and sharply decreased the average amount of time spent in hospital to only a few weeks or months compared with years or a lifetime. In the UK, fewer than 3% of schizophrenics need to be cared for permanently in a hospital. Most are treated as outpatients, and kept on *maintenance doses*, which are just enough to maintain a beneficial effect.

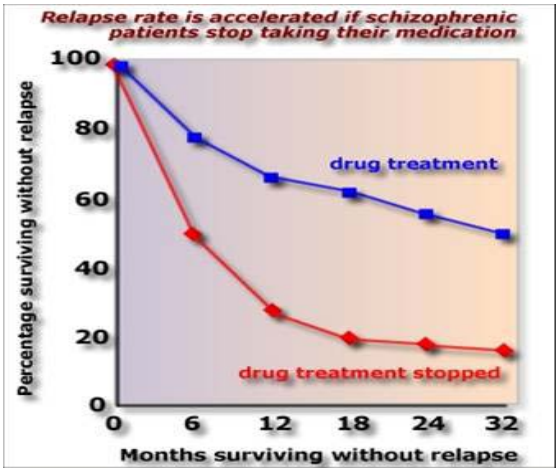
Although conventional anti-psychotics reduce the positive symptoms of schizophrenia (e.g. hallucinations, delusions), which enables many people to live a productive life, they have little if any effect on the negative symptoms (e.g. loss of motivation). However, and as noted previously, the atypical anti-psychotics are used with those who have failed to respond to typical anti-psychotics, which is about 30% of all cases, and research shows that they are more effective in treating both the positive *and* negative symptoms of schizophrenia.

Research has also compared the effectiveness of anti-psychotic drugs with other therapies to treat schizophrenia. These are called studies of the **relative effectiveness** of different kinds of therapy. In one study (**May, 1975**), schizophrenics were given an *anti-psychotic drug*, *psychoanalytic psychotherapy*, *psychoanalytic therapy with an anti-psychotic drug*, or *ECT*. The criteria of success were assessments of improvement as made by nurses and clinicians, measures of relapse rates, and measures of 'release' rates and the duration of hospitalisation.

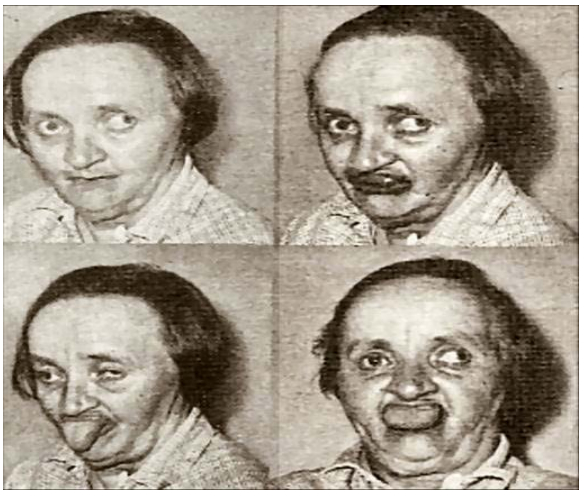
May found that the drug alone, and psychotherapy with an anti-psychotic drug, were the most effective treatments. Since these two treatments *did not differ* from one another in terms of their effects, May concluded that psychotherapy has little or no tangible effects in the treatment of schizophrenia.

If schizophrenia is caused by an excess of dopamine, then it does seem **appropriate** to use drugs which reduce dopamine's effects. However, there would seem to be a weaker case for using atypical anti-psychotics, since the exact way in which they work (blocking serotonin receptors?) isn't known. Perhaps this is not an issue: the fact that the drugs are effective and bring relief when other therapies do not may be all that matters.

What is an issue is whether anti-psychotics *cure* the condition or merely mask its symptoms. Research shows that the symptoms return if the drug being taken is discontinued. Thus, the drugs are not cures for schizophrenia, and a person will need to remain on them for the symptoms to be hidden. This increases the risk of serious and permanent side effects.

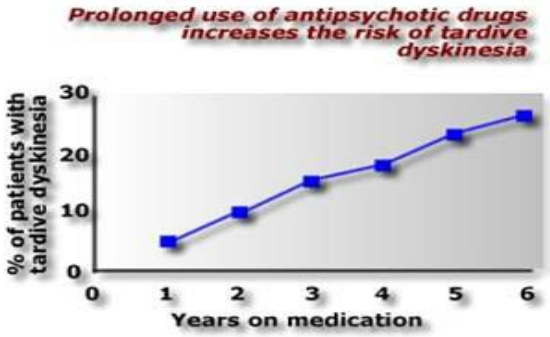


Certainly, the side effects associated with the typical anti-psychotics raise doubts about their appropriateness as a treatment for schizophrenia. **Anticholinergic side-effects** include dry mouth, blurred vision, restlessness, and sexual dysfunction. **Extrapyramidal side-effects** include *acute dystonia* (abnormal body movements, one of which is called the 'Thorazine shuffle'), *akathisia* (restlessness), and *tardive dyskinesia* (loss of control of muscles controlling the mouth, fingers, and legs).



Tardive dyskinesia in a schizophrenic

In *neurolepetic malignant syndrome*, there is severe muscular rigidity accompanied by fever, increased heart rate and blood pressure, coma, and sometimes death. The extrapyramidal side-effects resemble *Parkinson's disease*. This is hardly surprising. Parkinson's disease is associated with a lack of dopamine. Reducing dopamine levels is effectively what anti-psychotic drugs do. Note that the longer an anti-psychotic drug is taken for, the more likely it is that the extrapyramidal side-effects will be *permanent*, even if their use if subsequently discontinued.

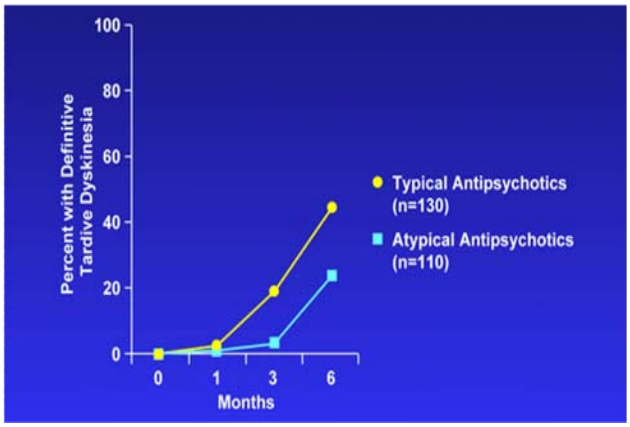


One way of limiting the side-effects is through the use of other drugs. For example, the extrapyramidal side-effects can be controlled by *procycladin (Kemadrine).* However, these drugs have their own side-

effects, which can be controlled by other drugs, and so on. As a result of a person suffering from schizophrenia may being taking several different kinds of drugs.

Another way of limiting the side-effects is through *targeted strategies* or *drug holidays*, in which the drugs are discontinued during periods of remission, and reinstituted when early signs of relapse occur. However, because of the side-effects, some people deliberately stop taking the drugs and their symptoms return. This can be counteracted through the use of a *depot medication*. This is an injection which releases the medication slowly into the body over several weeks. The drug is injected into a large muscle, usually the buttock.

As well as being more effective that typical anti-psychotics, atypical anti-psychotics *could* actually be argued to be more appropriate because they were developed to avoid the side-effects associated with the typical anti-psychotics. Thus, people are less likely to drop out of treatment.



Atypical anti-psychotics are less likely to produce tardive dyskinesia than typical anti-psychotics

However, the atypical drug *clozpine* does produce its own side-effects. The most serious of these is *aganulocytosis* (a decrease in the number of infection-fighting white blood cells) which occurs in about 2% of people who take it, and is potentially fatal. Blood tests must be given on a regular basis. When the cell count drops too low, the drug must be *permanently* discontinued. As with other drugs, the side-effects can be countered, but treatment then becomes very *expensive* with the result that its *availability is limited*.

It has been discovered that one of the atypical anti-psychotics (*risperidone*) actually improves short-term memory (STM). STM is

correlated with improvements in learning *social skills* in psychosocial rehabilitation programmes. This shows how a *biological therapy* can be combined with a *psychological therapy* to produce a treatment method that is better than either of them on their own.

When using anti-psychotic drugs, clinicians face an *ethical dilemma*: if they keep medication to a minimum (in order to minimise side-effects), the chances of relapse are increased. However, if the medication is increased, the greater is the chance that a permanent side-effect will develop.

A further ethical dilemma relates to what the anti-psychotic drugs are *really* being used for. Critics argue that the widespread use of anti-psychotic drugs is inappropriate, because they function as '*chemical straightjackets*' (or '*liquid cosh*'). The argument is that the drugs are *dehumanizing*, take away any sense of *personal responsibility*, and are used as an *agent of social control*. The ethical issue of *informed consent* is also relevant, since schizophrenics are not really in a position to give truly informed consent about their treatment.

A final point worth noting is that drug therapy must take into account the fact that people seeking treatment will come from diverse *cultural* or *ethnic* backgrounds. **Linn, et al (1991)**, for example, have shown that as compared with American schizophrenics, Asian schizophrenics require significantly smaller amounts of anti-psychotic drugs for optimal treatment. The reason for this is unclear, but it is likely that differences in *metabolic rates*, *body fat*, and *cultural practices* (e.g. eating behaviour) are responsible.

Psychosurgery

Psychosurgery refers to surgical procedures that are performed on the brain to treat mental disorders. The term is properly used when the intention is to *purposely* alter psychological functioning. Thus, whilst removing a brain tumour might affect a person's behaviour, it would not constitute a psychosurgical procedure.

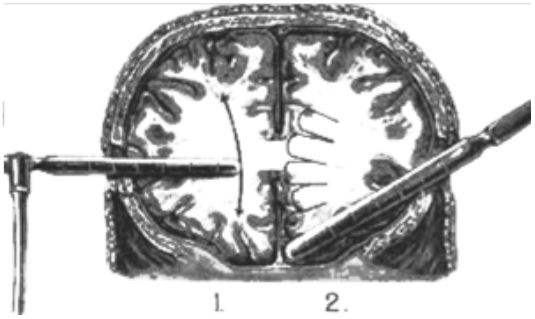
Psychosurgical techniques, albeit primitive ones, have been carried out for a long time. In medieval times, psychosurgery involved 'cutting the stone of folly' from the brains of those considered 'mad'. Modern psychosurgical techniques can be traced to the Second International

Neurological Conference held in London in 1935. There, **Carlyle Jacobsen** reported the effects of removing the pre-frontal areas (the forward-most portion) of the **frontal lobes** in chimpanzees. The procedure apparently abolished the violent outbursts some of the chimpanzees had been prone to.

In the audience was **Egas Moniz**, a Portuguese neuropsychiatrist. Moniz was sufficiently impressed by Jacobsen's findings to persuade a colleague, **Almeida Lima**, to carry out surgical procedures on the frontal lobes of schizophrenics, in an attempt to reduce their aggressive behaviour. The procedure involved severing the neural connections between the pre-frontal areas and the **hypothalamus** and **thalami**. It was believed that this would disconnect *thought* (mediated by the cortex) from *emotion*.

Egas Moniz

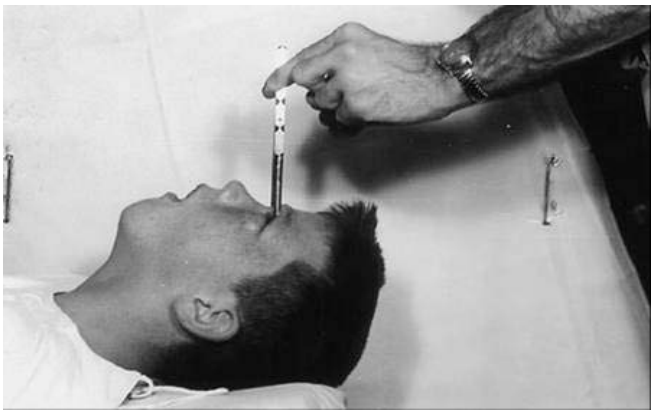
The original 'apple corer' technique involved drilling a hole through the skull covering on each side of the head, and then inserting a blunt instrument (a **leucotome**) which was rotated in a vertical arc. This procedure followed the unsuccessful technique of injecting alcohol to destroy areas of frontal lobe brain tissue.



The 'apple corer' technique

Also at the 1935 conference was **Walter Freeman**, an American neurologist who was not trained as a surgeon. **Freeman & Watts (1942)**

developed and popularised the 'standard' **pre-frontal lobotomy**. The operation became extremely common. Estimates vary as to the number of operations performed in the United States after 1942. One estimate puts it at 40,000, whilst another suggests a more conservative 25,000. Although not surgically trained, Freeman developed his own surgical technique called the **transorbital lobotomy**:



The transorbital lobotomy

After a year of using their own procedure, Moniz and Lima claimed that the operation was highly **effective**, and produced a 70% 'cure' rate. However, Moniz's reports of success were exaggerated. Although he was awarded the Nobel prize for medicine in 1949 'for the discovery of leucotomy in the treatment of some psychoses', it is ironic that Moniz was shot and paralysed by a patient on whom he had performed a lobotomy.

Indeed, there has been a distinct *lack* of careful investigation into the effectiveness of psychosurgery with schizophrenics. For example, one study reported that psychosurgery 'produces little or no changes in intellectual and discriminative ability'. This might be alright, if it was not for the fact that the *ability to knit* after the operation was used as the criterion for change.

Psychosurgery was largely abandoned in the late 1950s, following the introduction of the psychotherapeutic drugs. About 20 operations a year are carried out in Britain, using slightly more refined techniques than those used in the 1940s and 1950s (e.g. **thermal capsulotomies**). However, it is very much a treatment of last resort, which is only used when other treatments have failed to produce a response. Although operations are conducted on people with depression and OCD, psychosurgery is now *never* carried out on schizophrenics (at least in this country).

As far as their **appropriateness** is concerned, psychosurgical techniques to treat schizophrenia lack a scientific basis. The theoretical rationale for the operation devised by Moniz was vague and misguided, with researchers unclear as to why beneficial effects *should* occur, and with no certainty that they *would* occur. Indeed, **David (1994)** has questioned whether or not our knowledge of the frontal lobes (or what he calls *'frontal lobology'*) is anything more than 'psychiatry's new pseudoscience'.

Comparisons of people who underwent psychosurgery to treat their schizophrenia show a marked lack of consistency in their outcome. Behaviour change *is* produced in some individuals, but not in others, and it is difficult to predict who will be affected and how they will be affected. The fact that psychosurgery is *irreversible* also questions its appropriateness as a therapy for anything, let alone schizophrenia.

Like the anti-psychotic drugs, psychosurgery is also associated with some severe and permanent side-effects. In no particular order these include *apathy*, *epileptic-type seizures*, *severe blunting of emotion*, *impaired learning ability*, *intellectual impairments*, *memory loss*, and *death*.

The ethical issue of *informed consent* is also relevant, since schizophrenics are not really in a position to give truly informed consent about their treatment. However, in Britain, Section 58 of the revised *Mental Health Act* contains stringent provisions regarding information to those referred for psychosurgery and their consent to treatment.