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Rethinking schizophrenia: Taming demons without drugs

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Antipsychotic drugs may do more harm than good. The tide is turning towards gentler methods, from talking therapies to brain training

"I WAS trembling all the time. I couldn't shave. I couldn't wash. I was filthy," says Peter Bullimore. "I had become the archetypal schizophrenic. People would write on my windows: 'Schizo out' and I had one member of the public slash my face."

Today, that period of Bullimore's life is long behind him. He runs a mental health training consultancy in Sheffield, UK, and travels the world giving lectures on the subject.

You might think that Bullimore's turnaround is thanks to a wonder drug that has brought his schizophrenia under control. On the contrary: it was the side effects of his medication that had brought him so low. Instead, he opted for a seemingly radical course of action – he was slowly weaned off his medications and started a new type of therapy.

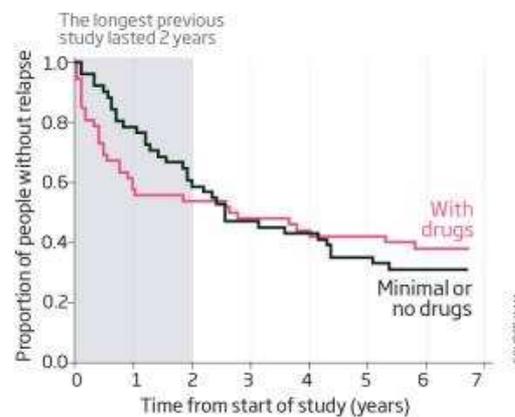
Bullimore's experience may be an extreme case, but we have long known that the drugs used to treat schizophrenia are very far from ideal. The downsides have always been seen as a necessary price to pay for relief from the condition's devastating symptoms, but now that idea is being called into question. Not only are the side effects of these drugs worse than we thought; the benefits are also smaller. Although people need to be taken off their drugs slowly and carefully to avoid a relapse, it looks as though outcomes are better in the long run if medication is kept to a minimum.

Now, there is growing interest in less damaging ways of helping people with the condition, in particular talking therapies, which [research published in *The Lancet* today suggests can be just as effective as medication](#). Other alternatives include using virtual reality and special forms of brain training. "People are starting to think differently about schizophrenia," says Max Birchwood, a psychologist at the University of Warwick in the UK. "Attitudes are definitely changing."

What makes a recovery?

People with schizophrenia are often forced to take antipsychotic drugs for the rest of their lives

Short-term studies had suggested that drugs reduce the risk of relapse – but a recent paper indicates that the longer-term picture is different



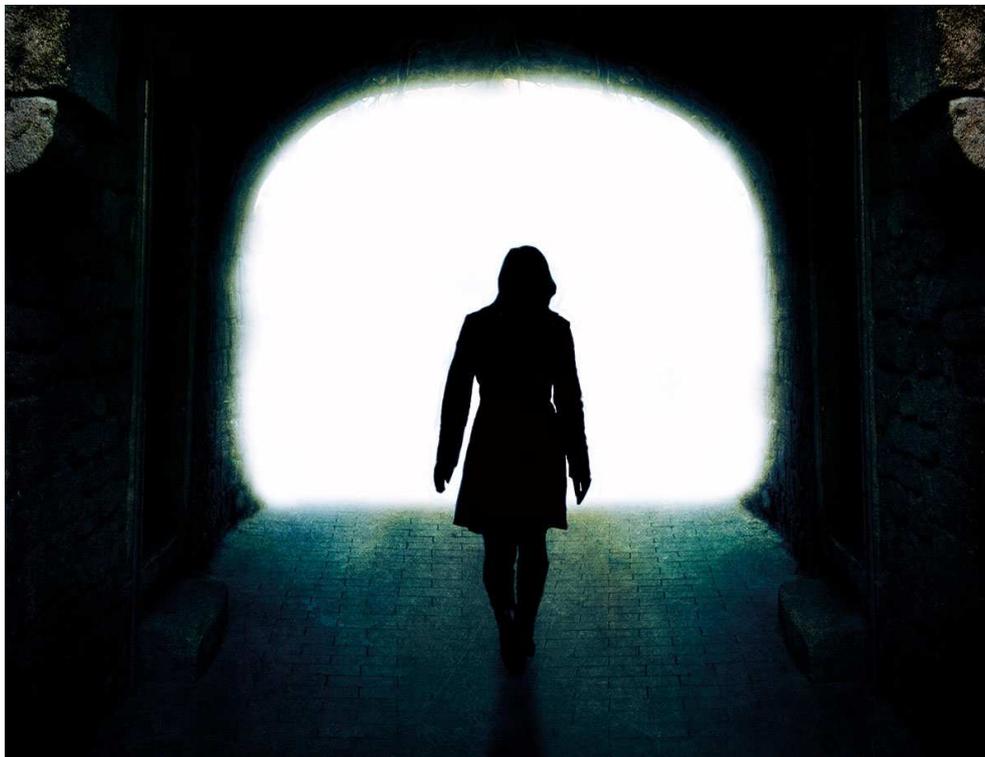
Life without drugs

What's more, people weaned off the drugs have a greater chance of a "functional recovery" – the ability to hold down a job and look after themselves, even if they have occasional symptoms



What makes a recovery?

[Enlarge image](#)



See the light: therapy helps people to escape their demons (*Image: Mohamad Itani/Plainpicture*)

Since it was first described by European psychiatrists in the late 19th century, schizophrenia has often been seen as the most fearsome of all mental illnesses. Those affected usually start behaving oddly in their teens or 20s: hearing voices or seeing things that aren't there, often coupled with paranoid delusions, such as that members of their family want to kill them. These periods of psychosis may come and go unpredictably over the years, and they can be life-wrecking; 1 in 10 people with schizophrenia commits suicide.

Bullimore was 29 when it first hit. Ostensibly his life was on track: he ran a manufacturing business and was married with three children. But during a period of stress and overwork, things started to go badly wrong. He became convinced that cars were following him, and heard voices calling him a pervert. He saw the horror-film character Freddy Krueger looking back at him from mirrors. "It was a very frightening time," he says.

After a particularly terrifying hallucination one night, the next day, Bullimore smashed his business partner over the head with a telephone, then went home and curled up in a chair. "I stopped there for three weeks," he says. "All the voices were really, really bad."

The causes of schizophrenia are frustratingly mysterious. A long-standing theory is that the strange symptoms stem from a person's inability to distinguish between their own [thought processes](#) and inputs from the outside world. The [imagined voices](#) often say things the person could plausibly be thinking themselves, for instance. But that doesn't so neatly explain the hallucinations and delusions, nor the memory and concentration difficulties that often come with schizophrenia.

Many genes that raise the risk of schizophrenia have been discovered, most of which seem to affect brain development or functioning – suggesting that the condition arises when something goes wrong with the brain's wiring as it develops and matures during adolescence. The prevailing theory is that the problems lie in neural networks that use the brain chemical dopamine, in part because drugs such as LSD and amphetamines, which can cause symptoms of psychosis, are known to raise dopamine levels.

Until the 1950s, there was little that doctors could do for someone like Bullimore, other than lock them up in an asylum and sedate them with strong tranquillisers called barbiturates. But then a new class of drugs was developed that proved helpful in treating people in the grip of acute psychosis. These antipsychotics, as they became known, could calm people who were distressed or shouting, without knocking them out like tranquillisers did. The drugs were found to block dopamine signalling, bolstering the theory that overactivity of these pathways caused schizophrenia.

As wider use of antipsychotics allowed people with schizophrenia to live in the community rather than a

psychiatric hospital, they are often credited with bringing an end to the often inhumane asylums. But right from the start these drugs were known to have unpleasant side effects.

Mental fog

The most obvious effects were physical: the slowing down and stiffening of movements. After a few weeks on the drugs, some people start to get strange tics and spasms of their face muscles. But the biggest complaints are about the way the drugs affect a person's thoughts. Antipsychotics seem to slow down people's thinking, worsening the memory and concentration problems caused by the condition itself. "My head was clouded and I couldn't think," remembers Bullimore. A recent study has confirmed suspicions that [long-term use actually shrinks the brain](#).

They can also make people feel both unhappy and highly agitated, a potentially lethal combination, says psychiatrist David Healy, head of the North Wales Department of Psychological Medicine, Bangor, UK. His study of historical records from a Welsh mental hospital showed that [100 years ago people with schizophrenia were no more likely to kill themselves than the general population](#). This suggests it is modern drugs that cause schizophrenia's high suicide rate, he says. "They can produce some of the most uncomfortable experiences a human can have."

Yet the potential side effects were seen as the necessary cost of controlling a dangerous illness. Scores of trials had shown that after a person's initial psychotic breakdown had been brought under control, if they stopped taking their medication they were at higher risk of relapse.

Those studies were short, though, typically lasting from months to a year, with the longest being two years. Now for the first time there has been long-term follow-up of a randomised trial comparing people who stopped taking antipsychotics with those who continued their treatment. The findings have sent shock waves through the world of psychiatry.

In this Dutch study, while the people assigned to the dose-reduction group initially had a higher relapse rate, after two to three years, the people who stayed on their drugs had "caught up", and after seven years differences between the two groups were statistically insignificant ([see graph](#)).

More importantly, those in the dose-reduction group had more than double the chance of achieving what psychiatrists call "functional recovery" – 40 versus 18 per cent ([JAMA Psychiatry, vol 70, p 913](#)). In other words, even though they might have occasional symptoms, they could hold down jobs and look after themselves. "That's what's meaningful to the patient," says Lex Wunderink, a psychiatrist at Friesland Mental Health Services in Leeuwarden, the Netherlands, who led the study. Wunderink speculates that this ability to function independently is being hampered by the dopamine-suppressing effects of antipsychotics.

As the case against the drugs mounts, some are beginning to question whether the dopamine theory itself is right. After all, there has never been strong evidence that people with schizophrenia have overactive dopamine signalling, says Joanna Moncrieff, a psychiatrist who has recently written a polemic against antipsychotics called *The Bitterest Pills*. Along with others, Moncrieff believes antipsychotics may simply be another version of the tranquillisers used back in the 1950s. "If someone's preoccupied by their psychotic symptoms, if you can dampen down their thinking, they lose interest in their delusions," she says.

Today, there are rival theories about the causes of psychosis. Some cases may be caused by an autoimmune reaction to certain proteins on the surface of brain cells. Other research implicates different brain chemicals, including glutamate and serotonin. Several compounds that boost glutamate signalling in the brain have reached early clinical trials, although it is too soon to say if they will pass the larger trials needed to prove their worth.

In the meantime, the problems with antipsychotics are leading to growing interest in a range of alternatives to medication. The most promising are talking therapies like cognitive behavioural therapy (CBT), which aims to train people in new ways of thinking. CBT is often used for depression and anxiety to combat negative thought patterns, but psychiatrists have been sceptical about its usefulness for schizophrenia. "People say CBT can't possibly work – schizophrenia is an intrinsic brain disorder," says Birchwood, who helped pioneer CBT. "How can talking therapy change anything to do with the brain?" Yet many previous studies have shown it to be useful in conjunction with antipsychotics, and the Lancet study shows that it can also work as the sole treatment.

There are at least two possible explanations for how it could work. For starters, people are more likely to descend into psychosis if they are stressed and unhappy – as Bullimore did. "It's a very stress-

sensitive disorder," says Birchwood. Many of the talking therapies help people cope better with everyday problems, such as family arguments, reducing the stress that could trigger a breakdown.

Another benefit of talking therapies is that, while usually unable to eliminate the voices and hallucinations, they do help people feel less disturbed by them. One goal of CBT is to help people realise the voices don't have any power over them. "That enables them to disengage from the voices," says Birchwood.

Rather than CBT, Peter Bullimore received help from informal group therapy that explored the psychological origins of his troubles. Bullimore was sexually abused from the age of 5. "The voices would repeat what the abuser had said," he says. "This was an area of my life I hadn't dealt with."

And it may be possible to enhance the power of talking therapy with a new computer-based technique designed specifically to combat aggressive voices, which looks promising from a small pilot study. Patients were helped to make a computer avatar that "embodies" the voice in their head. Sitting in another room, the therapist then had their speech digitally altered so they could be the voice of the avatar, speaking to the patient through the computer monitor. "We accompany the patient into their own private hell," says Julian Leff, a psychiatrist at the Institute of Psychiatry in London, who designed this approach.

Over several sessions, the patient was encouraged to stand up to the avatar, while the therapist made it become less aggressive in response. The approach helped 15 out of 16 people in the study, who found that it reduced the frequency and intensity of the voices. Three people even reported that they stopped hearing the voices altogether (*British Journal of Psychiatry*, vol 202, p 428). "What they learn to do with the avatar they can then do outside the sessions," says Leff.

A different approach is to target the memory and concentration problems that plague people with schizophrenia. Once done with pen and paper, there are now several "brain training" computer programs in trials that are marketed specifically for this condition. Typically they comprise a range of tasks designed to improve people's mental skills in a variety of ways, particularly memory, attention and logical reasoning.

At the least, this should help people stay in work or education – but the benefits may be even greater. Some think the cognitive problems could lie behind the psychosis, perhaps because they lead people to mix up external sensations with their own thoughts. Carefully [targeted brain training programs](#) could reverse the core symptoms of psychosis if the illness is caught early enough, says Sophia Vinogradov at the San Francisco Medical Center. She says a small, unpublished study done by her group has shown that brain training for people in the early stages of schizophrenia reduced psychotic symptoms.

The turning tide

It is much too soon to say whether brain training can indeed reverse psychosis, but [talking therapies](#) have certainly been shown to reduce relapses. NICE, the agency that produces clinical guidelines for the UK National Health Service, [recommends that talking therapies](#) should be offered to all those with schizophrenia, in addition to antipsychotic drugs. Unfortunately, it is cheaper and easier to just dole out the tablets – only about 1 in 10 people with schizophrenia has access to CBT. "Most [health] trusts have not invested sufficiently in training to deliver these services," says Birchwood.

And many doctors think the evidence favours the continued use of antipsychotics. "Nobody would say that antipsychotics are perfect, but they are effective in preventing relapse," says David Taylor, head of pharmacy at the Maudsley Hospital in London, the UK's largest psychiatric teaching hospital. While the seven-year Dutch study suggests that people do better in the long-term without medication, that needs replicating before it changes practice. "It is something that needs more investigation," he says. In Taylor's experience, people can avoid some of the worst side effects by switching medicines. "They can usually find a drug which is reasonably well tolerated," he says.

And when it comes to people in the throes of a severe psychotic breakdown, Taylor says antipsychotics are the only option. "Acute psychosis is not a pleasant condition. It's extremely frightening and debilitating," he says. "The more rapidly those symptoms can be relieved the better."

Indeed, most of those who favour alternative treatments agree drugs are unavoidable at such times. But subjecting people to a lifetime of compulsory antipsychotics seems to be on the way out. The tide is already turning in some parts of the world, with Finland minimising drug use and New York experimenting with such a policy. The Finnish scheme's success is gaining worldwide attention, and it seems likely that other countries will follow their lead.

There are also efforts to give [people who hear voices](#) practical support to continue with their lives, such as sheltered accommodation or supported employment. "It is possible for people to have ongoing symptoms and yet hold down a job," says Birchwood.

It's a transformation that would be welcomed by Bullimore. These days he still hears voices, although now they are quieter and are usually friendly, or at least neutral. He sometimes hears his dead mother giving guidance, for instance, and another voice helped him write a book. "That was my creative side," he says. "My relationship with my voices has changed. It has woken me up to a new world."

Correction, 15 May 2014: *In a previous version of this article we referred to patients in the Dutch study stopping their medication. However, few patients in this group succeeded in stopping their medication completely. By the last two years of the experiment, 42.3 per cent of this group were living "without substantial antipsychotic medication", compared to 23.5 per cent of the continuation group.*

Leader: "[Antipsychotic drugs are schizophrenia's hidden gulag](#)"

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