Depression and a very unbalanced theory

Most people believe depression is the result of a chemical imbalance in the brain. But a new study has discovered that depressed people have the same levels as everyone else

What is it that psychiatrists claim to have known all along that the public and family doctors have never realized? It's that depression has nothing to do with a chemical imbalance in the brain, the widely held theory that describes depressed people as having low levels of serotonin, a neurotransmitter.

Although this theory has been accepted by the public since the 1990s, a major review has recently established that it's not true: people suffering from chronic depression have similar levels of serotonin as healthy people. The researchers, led by Joanna Moncrieff at University College London (UCL), reviewed 17 studies that had involved more than 160,000 people and concluded that there was no connection between depression and low levels of the chemical in the brain.[1]

Other researchers have been saying similar things for years. In 2005, Jeffrey Lacasse at Florida State University concluded that "there is not a single peer-reviewed article that can be accurately cited to directly support claims of serotonin deficiency in any mental disorder, while there are many articles that present counterevidence."[2]

Yet the idea is embedded in the public consciousness. When Prof. Moncrieff was doing the news-round after the publication of her study, one broadcaster said her discoveries "blew his mind."

He's not alone. A poll found that 80 percent of participants believe the theory to be fact,[3] and, judging by the ongoing growth of SSRI (selective serotonin reuptake inhibitor) prescribing, so does the family doctor. One review estimates the SSRI market is set to grow by 22.5 percent between 2020 and 2027, when it will be worth $18.29 billion—quite an achievement for a family of drugs that is out of patent and inexpensive.[4]

An unbalanced theory

So how did an unproven theory gain so much momentum? It's an idea driven by a drug industry that saw enormous gains to be made from supplying a chemical that could alter another chemical—serotonin—and resolve the intractable problem of depression. It was also enormously attractive to people struggling with chronic depression and to doctors who at last had a solution for their patients.

The idea that a chemical imbalance is the primary cause of depression was put forward as a hypothesis by researchers Seymour Ketty and Joseph Schildkraut in 1965—but what does an imbalance look like and how much serotonin are we supposed to have to maintain a healthy brain? Unable to resolve these thorny questions, psychiatry never took to the theory. The psychiatry "bible," the *DSM* (*Diagnostic and Statistical Manual of Mental Disorders*), doesn't even list low serotonin levels as a possible cause of depression, while the American Psychiatric Press *Textbook of Clinical Psychiatry* isn't exactly enthusiastic either, describing the hypothesis simply as "unconfirmed."[5]

Other researchers have proven the point. One group tried to induce depression in a set of brave participants by reducing serotonin levels in their brains, but nobody felt any different at the end of the experiment.[6]

And long before the drug industry seized on the chemical imbalance theory, researchers had already demonstrated it was false. In an experiment carried out in 1975, researchers boosted levels of serotonin in the brains of a group of depressed patients by giving them L-tryptophan, an amino acid that's a precursor of serotonin—but the participants said there was no improvement in their mental state.[7]

However, perhaps the psychiatric profession protests too much and many psychiatrists were happy to go along with an unproven theory. Moncrieff's fellow researcher, Dr Mark Horovitz, a psychiatrist and clinical research fellow at UCL, said, "I had been taught that depression was caused by low serotonin in my psychiatry training and had even taught this to students in my own lectures. Being involved in this research was eye-opening and feels like everything I thought I knew had been flipped upside down."

SSRI equals profit

Serotonin is a neurotransmitter, a chemical that helps electrical impulses communicate throughout the nervous system, including in the gut and blood platelets. SSRIs are designed to increase levels of the chemical only in the brain, and the first to reach the market—and possibly the most celebrated of them all—was Prozac (fluoxetine), which was launched in 1987. Although it was a

trailblazing drug, it was also the one that came with the most side effects. Later variations, such as Zoloft (sertraline), were considered safer and quickly overtook Prozac in the market, achieving annual sales of $3 billion in the US alone.

According to America's CDC (Centers for Disease Control and Prevention), 13 percent of adult Americans are taking an SSRI, and that rises to 24 percent in women over the age of 60. Most people on an antidepressant are long-term users, and some have been taking them for more than 10 years.[3]

The explosion in SSRI sales was fueled by direct-to-consumer advertising in the US from 1990 to 2010, while family doctors with no specific training in psychiatric problems were invited to conferences in exotic locations where the hypothesis was put forward as fact.

Where's the proof?

But there was a disconnect between the science and the claims about a chemical imbalance made by the drug manufacturers, said Lacasse. In other words, drug company claims weren't supported by science—and any studies that did find a benefit to the drugs were biased and unreliable.

Researchers at the independent Copenhagen Trial Unit analyzed 131 studies and found every one of them was "at high risk of bias and the clinical significance seems questionable." What was clear, however, was the drugs' significant risk of serious adverse reactions. Typical reactions include nausea, dizziness, headache and suicidal thoughts, even driving some to take their own lives.[5]

Other studies found remedies that weren't designed to alter chemical imbalances were just as effective. A Cochrane review found that tricyclics, another family of antidepressants, worked just as well,[10] while the natural remedy, St John's wort, was more effective than a SSRI and had fewer side effects.[11] And in one trial, even a placebo—an inert substance or "sugar pill"—outperformed the drug.[12]

Feeling numb

But depressed people who feel better on an SSRI aren't necessarily kidding themselves. Antidepressants are interfering with brain chemicals—just as alcohol does, come to that—and are causing a numbing effect. Emotional highs and lows are flattened out, but this also lowers libido, one of the most common side effects of SSRIs.

A drug that numbs emotions has a short-term benefit for someone who is unhappy, fearful or confused, Moncrieff says in her blog, but taking a drug that is altering brain chemistry for a long time could have harmful effects—and a quarter of people on a SSRI have been taking the drug for more than a decade.

Beyond that, the drugs are also addictive. "The brain alters to try and counteract the effects of the drug, and then when people miss a dose or stop taking the drug, they experience withdrawal effects," says Moncrieff.

She recommends that anyone taking a SSRI should draw up a list of side effects they experience, such as emotional numbing, as well as any benefits, to decide whether to continue treatment.

But because the brain is changing to compensate for the chemical alterations caused by the drug, she says it's vital that people don't just stop taking them or come off the drugs too quickly.

Withdrawal symptoms can be long and severe, so coming off the drugs should be done gradually and with the help of an experienced practitioner.

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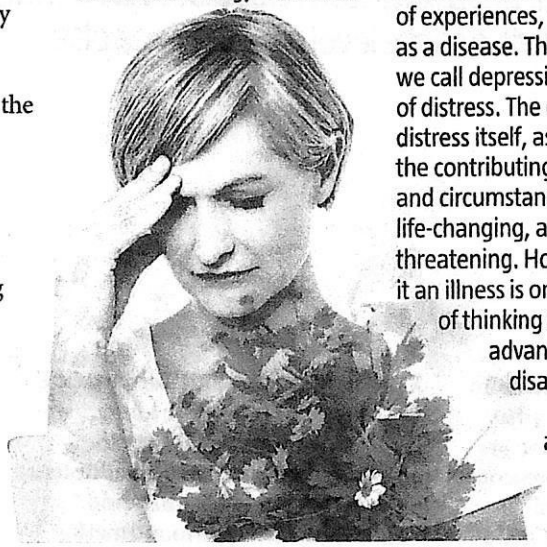
WHAT IS DEPRESSION?

One in seven of us will suffer from depression sometime in our lives. But depression may be an utterly different experience for one person compared to someone else, and psychiatry backs this up.

For a diagnosis of depression, a patient must display five of 10 possible symptoms—such as an inability to cope, insomnia or a lack of energy—but that means the next patient could be suffering from the other five and get the same diagnosis.



Although the serotonin theory has been overthrown, psychiatrists still hold to the belief that depression must somehow have something to do with a brain that isn't functioning properly.

But others say it is more complex than that. The British Psychological Society stated in a report that "depression is best thought of as an experience, or a set of experiences, rather than as a disease. The experience we call depression is a form of distress. The depth of distress itself, as well as the contributing events and circumstances, can be life-changing, and even life-threatening. However, calling it an illness is only one way of thinking about it, with advantages and disadvantages."[1]

Moncrieff agrees. She thinks depression could be a response to adverse childhood events, for instance, or to catastrophic occurrences during adulthood, such as the death of a spouse or job loss.

Biology can play a part. Depression could be a result of an underactive thyroid gland or an infectious disease, such as glandular fever. These require a medical remedy such as a drug or alternative treatment.

If there's no obvious biological cause, non-drug therapies such as CBT (cognitive behavioral therapy) or other "talking cures" could help the depressed patient far more than a SSRI ever could.

And the worst consequence of the chemical imbalance theory is that it's led everyone—patient and doctor—down a false trail for 30 years while the real causes of depression haven't been explored.

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