WHAT IF DEPRESSION ISN'T ALL IN THE MIND?

The British doctor, his radical new science and a mental health epidemic
THE DEPRESSION EPIDEMIC:
'We're on the cusp of a revolution'

British psychiatrist Edward Bullmore believes the medical profession is failing thousands of patients. In a groundbreaking book, he claims what doctors are taught about depression is wrong. By William Leith
THE MYSTERY IS, WHY DOES A QUARTER OF THE POPULATION OF THE DEVELOPED WORLD GET DEPRESSED?

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This blind spot was, and still is, part of the medical mind. What Bulmore and his boss couldn’t see was that Mrs P’s symptoms were not uncommon. They were, in fact, symptoms of depression. And it was a common problem. In the developed world, some 25% of the population suffer from depression at some point in their lives. But it was a problem that was not being recognized. It was a problem that was being ignored. It was a problem that was being swept under the carpet.

Ed Bulmore is now 52, a professor of psychiatry at the University of Cambridge. Sitting in his office at Addenbrooke’s Hospital, he will, over the course of an afternoon, tell me some extraordinary things. He will say that Mrs P was probably depressed because she was not depressed. He will say that he could see depression in the mind, and that he could see it in the brain. He will say that he could see depression in the body, and that he could see it in the heart. He will say that he could see depression in the world, and that he could see it in the universe. He will say that he could see depression in the past, and that he could see it in the future. He will say that he could see depression in the present, and that he could see it in the present moment.

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to know what really happens inside the human brain, we’re going to need to wait until we invent a scanner that’s thousands of times more powerful than the ones we have at the moment. “And that won’t happen in my lifetime,” says Bullmore.

We talk about how the brain works. Each brain has about 100 billion neurons, or brain cells. Every thought you have is the effect of tens of thousands of these brain cells making a connection with each other. The more often you have a thought, the stronger the connections become. That’s how we learn. And how do the neurons connect? Electrical currents pass between them, with the aid of proteins called neurotransmitters. We have around 100 different neurotransmitters. Imagine an orchestra with 100 instruments. Some are more important than others.

Serotonin is one neurotransmitter out of this hundred. It’s an important one — it’s the violin. But still, it’s only one instrument. SSRIs prevent the reuptake of serotonin. So they enable neurons to connect — but only in a way that is specific to serotonin. Imagine listening to an orchestra with a very loud violin. It’s better than nothing, and it might suit some people. Others would get sick of it, or their brains might find a way to block it out, which might make them need to turn up the volume even more. I’m speculating here. But that’s all anybody can do, because we don’t have the equipment to get inside that cubic millimetre. We can’t watch neurotransmitters at work while the brain actually thinks.

Around 2010, all the major pharmaceutical companies realised the same thing, more or less at once: that they wouldn’t be able to create a significantly better antidepressant drug by watching people’s brains at work while they were thinking. Not in our lifetime, anyway. “A number of us were invited to join a conference call,” says Bullmore. “And we were told this decision had been made, and was going to be effective immediately. It was a big shock. So then I thought. OK, GSK has made a decision. I understand that. It’s a simple case of people looking at the productivity of an area and seeing it doesn’t match the level of investment.”

The pharmaceutical industry wanted to see how SSRIs worked so they could develop new drugs. But it was a dead end. Bullmore reckons the industry as a whole pulled an annual figure of between £5 and £10 billion from their budgets relating to psychiatry and mood disorders.

“The world wasn’t going to keep giving mental health another chance,” he says. The industry view, he says, was essentially, “It’s got to be different next time.”

So he started thinking about immunology. It was an area rich in discoveries. Until quite recently, people visualised the body’s immune response as a sort of firefight between antigens and antibodies — invaders and defence forces. Inflammation in the form of macrophages, the soldiers of the system, lined up to do battle with the bad guys — the bacteria and viruses. Now people realise it’s a bit more complicated. The bad guys sometimes act like spies, finding ways of disguising themselves as good guys. The good guys send signals to each other all over the body.

Bullmore knew that GlaxoSmithKline had a nearby immunology lab, in Stevenage. He started studying the immune system. He noticed that a few scientists had been making connections between inflammation and depression. “A growing body of knowledge made it seem plausible,” he says. The problem with studying neurotransmitters was that you couldn’t see them at work. But the elements of the immune system — all those tiny soldiers and spies — are much easier to measure. You can find biomarkers. And scientists had recently been looking at the dark side of the immune system. It’s implicated in lots of diseases — multiple sclerosis, heart disease, (proteins that signal inflammation), they display “sickness behaviour” — they become listless and anhedonic. They seem to lose the will to live. They behave exactly like people do when they are depressed. But they are rats. What about humans? Well, a significant percentage of people who have been vaccinated — say, for tuberculosis — say they feel low afterwards. First comes the vaccination, which promotes an inflammatory response. Then comes the low mood. And almost everybody who is treated for hepatitis B with interferon, which floods the body with inflammation, reports feeling depressed afterwards. Around a third of these patients feel depressed for weeks. Very recent work on DNA also shows that many genes common to depressed people “turn out to be genes for immune function”. One of the key genes is olfactomedin 4; the mutation of this gene linked to depression causes a strong inflammatory response to certain types of bacteria when they enter the gut.

Does this bring us closer to solving the mystery of why depression evolved? Might it

**IF YOU TAKE BLOOD FROM PEOPLE WHO SAY THEY ARE DEPRESSED, IT SHOWS A HIGHER LEVEL OF INFLAMMATION**

Alzheimer’s and several types of cancer. Sometimes the good guys turn on us. Might there be a causal connection between the immune system and depression? He would study it if GlaxoSmithKline would fund it. The Medical Research Council got involved, and the Wellcome Trust. The Wellcome Trust Consortium for the Neuroimmunology of Mood Disorders and Alzheimer’s Disease was formed. Bullmore is the lead scientist in the study of mood disorders.

Now Bullmore collects data about the connection between inflammation and depression. He combs the work of other scientists and conducts his own experiments. Here’s what he’s found. If you take blood from people who say they are depressed, it shows a higher level of inflammation than samples from people who are not depressed. In Copenhagen, 73,331 people were tested. There was a “dose-response” relationship between people who reported low moods and inflammation. Blood with a higher inflammatory profile came from people with blacker moods. A study of English children found that inflamed nine-year-olds were more likely to become depressed eighteen-year-olds nine years later.

But this is correlation — it does not prove that inflammation actually causes depression. To try to do that, you can look at experiments with rats. When you inject rats with cytokines be a response to the stresses of the modern world? Thousands of years ago, being flooded with inflammation would have saved our lives. Infected members of a tribe might have had better survival rates, and avoided infecting others, by slinking away quietly and being on their own. Not wanting to eat and being unable to sleep might have promoted survival in lean and dangerous environments. A bout of depression might have helped you by forcing you to reflect, so you could make changes in your life. But pre-modern people lived lives of short, sharp bouts of stress, not the chronic stress we deal with in the 21st century. They were not usually overweight or very old (adipose tissue, or fat, promotes inflammation, as does ageing). They did not catch buses and trains, or pay mortgages, or get divorced. They dealt with storms and harvests. It’s conceivable that depression was useful to them in ways that are no longer useful to us. But maybe if we look right into our medical blind spot — the fact that the mind and the body can’t be easily separated — we will begin to get the help we need.

“We could be on the cusp of a revolution,” writes Bullmore. “I might be wrong. But I think it has already begun.”

*The Inflamed Mind* by Edward Bullmore is published by Short Books on May 3 (£14.99)