Depression is probably not caused by a chemical imbalance in the brain – new study

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For three decades, people have been deluged with information suggesting that depression is caused by a "chemical imbalance" in the brain – namely an imbalance of a brain chemical called serotonin. However, latest research review shows that the evidence does not support it.

Although first proposed in the 1960s, the serotonin theory of depression started to be widely promoted by the pharmaceutical industry in the 1990s in association with its efforts to market a new range of antidepressants, known as selective serotonin-reuptake inhibitors or SSRIs. The idea was also endorsed by official institutions such as the American Psychiatric Association, which still tells the public that "differences in certain chemicals in the brain may contribute to symptoms of depression". Countless doctors have repeated the message all over the world, in their private surgeries and in the media. People accepted what they were told. And many started taking antidepressants because they believed they had something wrong with their brain that required an antidepressant to put right. In the period of this marketing push, antidepressant use climbed dramatically, and they are now prescribed to one in six of the adult population in England, for example. For a long time, certain academics, including some leading psychiatrists, have suggested that there is no satisfactory evidence to support the idea that depression is a result of abnormally low or inactive serotonin. Others continue to endorse the theory. Until now, however, there has been no comprehensive review of the research on serotonin and depression that could enable firm conclusions either way.

At first sight, the fact that SSRI- type antidepressants act on the serotonin system appears to support the serotonin theory of depression. SSRIs temporarily increase the availability of serotonin in the brain, but this does not necessarily imply that depression is caused by the opposite of this effect. There are other explanations for antidepressants' effects. In fact, drug trials show that antidepressants are barely distinguishable from a placebo (dummy pill) when it comes to treating depression. Also, antidepressants appear to have a generalized emotion- numbing effect, which may influence people's moods, although we do not know how this effect is produced or much about it. Around one in six people in England are prescribed antidepressants. There has been extensive research on the serotonin system since the 1990s, but it has not been collected systematically before. We conducted an "umbrella" review" that involved systematically identifying and collating existing overviews of the evidence from each of the main areas of research into serotonin and depression. Although there have been systematic reviews of individual areas in the past, none have combined the evidence from all the different areas taking this approach.

One area of research we included was research comparing levels of serotonin and its breakdown products in the blood or brain fluid. Overall, this research did not show a difference between people with depression and those without depression.

Another area of research has focused on serotonin receptors, which are proteins on the ends of the nerves that serotonin links up with and which can transmit or inhibit serotonin's effects. Research on the most commonly investigated serotonin receptor suggested either no difference between people with depression and people without depression, or that serotonin activity was actually increased in people with depression – the opposite of the serotonin theory's prediction.

Research on the serotonin "transporter" that is the protein which helps to terminate the effect of serotonin (this is the protein that SSRIs act on), also suggested that, if anything, there was increased serotonin activity in people with depression. However, these findings may be explained by the fact that many participants in these studies had used or were currently using antidepressants.