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Neurobiology

The happiness chemical that sits on top of our DNA

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ABSTRACT

Serotonin is a chemical that can be found in many parts of our body, including the brain. People have described it as a happiness chemical, as it is strongly associated with mood. Farrelly and colleagues show in this elegant study that although we believed we knew most things about serotonin, it can still surprise us

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Sometimes referred to as the happiness chemical, serotonin has a huge role to play in the proper functioning of our bodies. Any imbalance in serotonin levels can lead to all sorts of issues, ranging from intestinal problems to mood changes and depression. In the brain, serotonin is the classical example of a neurotransmitter – a chemical that relays signals from one brain cell to another. When a brain cell is activated, it is said that it 'fires'. At this moment, a neurotransmitter - such as serotonin – is released at a special point where the firing cell and a receptor cell are in contact: the synapse. Here, the neurotransmitter is detected by the target cell, which activates it, and makes it fire as well.

There are many anti-depressant drugs on the market that aim to change the way serotonin affects our brain cells. Most of these drugs lengthen the serotonin signal at the target cell in the synapse. The technical name for these drugs is selective serotonin reuptake inhibitors (SSRIs). These drugs elevate the patient's mood and can also reduce anxiety. It is quite an extraordinary effect, unlikely to be solely explained by increasing the serotonin signal in the brain. A recent study by Farrelly and colleagues published in the journal *Nature* shows us that serotonin has properties that are yet to be fully uncovered. Their study opens up lots of exciting questions on how serotonin might be able to affect us – in much more direct ways than previously thought.

All cells in our body share the same genetic information crucial to their viability, our DNA. If DNA is a cookbook, then you could say that different cells use different recipes (genes) within this book – some pages can be opened and some remain closed. In some cases, sections of the DNA cookbook are completely inaccessible: locked away by so-called histone proteins. Histone proteins form little beads around which the DNA molecule is wrapped to different degrees of tightness. If tight, this part of the DNA is 'closed', and the genetic information within it is inaccessible, but if it is loose, the DNA is 'open' and ready to be read by the cell. The tightness of the wrapping mostly depends on chemical modifications, which affect the histone proteins themselves. Serotonin, it now turns out, can directly sit on one of these histones.

Histones, like all proteins, are basically chains of amino acids. Farrelly and colleagues showed that the histone protein H3 is able to carry a serotonin mark on a very specific amino acid in the chain. This serotonin mark is associated with loosely wrapped DNA, accessible to the cell. So why does serotonin sit on a DNA-packaging protein? The answer to this question came from an experiment in which the amino acid that normally holds the serotonin molecule was changed, thereby preventing serotonin from reaching the histone proteins. This small change led to a disruption in brain cell development and specialization, which argues for a role of serotonin in brain cell development by affecting the tightness of DNA wrapping.

It is the fact that a classical neurotransmitter, serotonin, has now been assigned a new and exciting role in gene expression which created a buzz in the scientific community. The search is on for the ways in which other neurotransmitters, like dopamine (heavily studied in the context of Parkinson's Disease), could affect DNA packaging by modifying histone proteins. It is very likely that this study only explores the tip of the iceberg - but even so, it raises intriguing and important questions touching the everyday lives of many people. Can serotonin's role in gene expression be linked to moods and what effects do our current serotonin-targeting drugs really have? Like always, more questions than answers – but we are surely heading down a new and exciting scientific path.