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> ONE MONTH, ONE PROTEIN <

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on the spur of a whim

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There are a number of biological molecules which are involved in a bewildering amount of activities. Serotonin is one. First thought to have the sole potential of contracting blood vessels, over the years serotonin has demonstrated that there is more to it than meets its chemistry. Besides its vasoconstrictor properties, it is also believed to be involved in instances as diverse as embryonic development, mood, appetite, nausea, sleep, body temperature, ageing, premature ejaculation, pain, anxiety, aggression, memory, cognition and migraines. And no doubt, as time goes by – as it inevitably does – yet more activities will be added to serotonin's already impressive panoply. It is hardly surprising, then, that serotonin has been shown to play a part in psychiatric shortcomings such as obsessive compulsive disorder and impulsivity. But serotonin cannot do this by itself; it needs a receptor to which it can bind. A receptor known as the 5-HT receptor.

Zägg, by Isabelle Kurmann

Courtesy of the artist
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Why 5-HT? 5-HT is an abbreviation for 5-hydroxytryptamine which is the chemical structure of serotonin. Although serotonin is still the term which is widely used, it has become inaccurate. And it wasn't even its first designation… Indeed, in the 1930s, Dr. Vittorio Erspamer discovered a substance that was able to contract intestinal muscles. His contemporaries believed that it was adrenaline but Erspamer demonstrated that it was in fact a then unknown amine, which he called enteramine. Almost twenty years later, Drs. Maurice Rapport, Arda Green and Irvin Page came across something in the blood serum that could affect vascular tone, and they called it serotonin. In 1952, however, it became obvious that enteramine and serotonin were one and the same thing. Over the years, though, serotonin has proved to be so versatile that scientists prefer to strip its name down to its essentials, hence 5-HT.

Serotonin's versatility is really just a consequence of the many different receptors it is able to bind to. To date, there are seventeen different types of 5-HT receptors able to trigger off a wide range of activities. Structurally, they are all pretty similar but they have been neatly arranged into seven different families based on their structural or physiological differences. Despite these differences, they are transmembrane G-protein coupled proteins – save one family whose members are cation channels – most of which are intimately involved in blocking or transmitting signals in the central nervous system.

Indeed, most serotonin receptors are made in the brain – though their action is not limited to this part of the body – and are found in the region of the receiving end of the synaptic junction, where they span the membrane. Their role is to await the release of serotonin, bind it, thus relaying whatever signal is to be relayed. Depending on the type of receptor, the message is very different. As mentioned above, the regulation of mood is one such message and 5-HT receptors are one of the major molecules

involved in the effects of the famous – or infamous perhaps – hallucinogenic substances such as LSD. They are also involved in drug addiction and, as recently demonstrated, can participate in behavioural disorders such as impulsivity.

Impulsivity is defined as behaviour which lacks both inhibition of an act and the consideration of consequences following it. The 5-HT2B receptor seems to be the receptor which is able to relay such behaviour. Or indeed a certain variant of 5-HT2B receptor which – so far – has only been found in Finns. In an intriguing piece of research, scientists tested a population of Finnish prisoners who had been convicted for criminal offence in which impulsive behaviour had been diagnosed. They were able to demonstrate that many of the prisoners carried the same variant of the 5-HT2B receptor – a variant which resulted in a non-functional 5-HT2B receptor. Naturally, this does not mean that only Finns suffer from impulsivity. Or indeed that criminality is hereditary. But what it does demonstrate is that, within a given population, impulsivity certainly seems to have a genetic basis.

Does this mean that impulsivity is passed down generations? Impulsivity involves behaviour which can lead to suicide, addiction and violent criminality for instance, but this does not mean that everyone carrying the 5-HT2B receptor variant will necessarily commit suicide, succumb to drugs or kill another human. Like so many other disorders – schizophrenia to name one – our environment is paramount in triggering off certain behaviours. In the case of this particular 5-HT2B variant, factors such as being male, testosterone levels and alcohol played an important part, but there are no doubt many others, not to mention stress.

The 5-HT2B receptor also happens to bind 3,4-methylenedioxymethamphetamine – or ecstasy – a molecule generations of young adults have been popping into their system on Saturday nights for the past few decades. Needless to say, 5-HT receptors are certainly at the heart of modified behaviours of all sorts and it comes as no surprise that they are therapeutic sites of choice for the design of antidepressants, anxiolytics and anti-obsessional drugs for example. The human psyche and its making will always be part of life's mysteries and it is always very reassuring to realise that though genetic factors make up the basis, besides serious psychiatric afflictions, our behaviour, like our personality, are also modelled by what surrounds us, including – one would hope – our own free will.

Cross-references to UniProt

5-hydroxytryptamine receptor 2B, *Homo sapiens* (Human) : P41595

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