on sex, drugs and satisfaction

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Pleasure is not a human invention. Experiences that arouse a feeling of contentment are as old as life. They have, in fact, kept life going. It is yet another of Mother Nature's tricks. If an organism perceives something as good, then it will do it again. If you want to keep a species going, the best way to do it is to reproduce. And, if the act of copulation is a pleasant experience, there's a fair chance you'll have another go at it. Eating, sex and social interactions are examples of acts most animals are accustomed to, and for which they are rewarded with a positive feeling. They also happen to be interactions which keep a species alive. But what happens when an animal meets frustration? Following rejection by a potential mate, for example? It finds some other way to quench its desires. Given the chance, *Drosophila melanogaster* will actually turn to alcohol if mating has been denied. Sex and alcohol are part of a highly complex reward system that has had plenty of time to evolve. Recently, scientists discovered the agent which orchestrates both behaviours: Neuropeptide F.

by Thomas Mustaki

Courtesy of the artist

Let there be no misunderstanding: a fly will not spontaneously drown its misery in alcohol when its female counterpart has given it the cold shoulder. But if food soused with alcohol is laid before it, the insect will show a keen preference for it. Because, like sex, alcohol is sensed as a reward. And if a reward is there to take, any animal in its right mind would go for it. Sex is a natural reward; alcohol consumption an artificial one. What the scientists set out to find was whether these two types of pleasure were governed by the same system on the molecular level. It turned out they were. In a nutshell, they discovered that drugs actually hijack the natural reward system. Which explains a lot. It is a discovery that should mark the beginning of important therapies, and which could help people who suffer from afflictions such as stress disorder or drug addiction.

For well over a century now, all sorts of scientists have been trying to understand the fundamentals of animal behaviour. Take Konrad Lorenz and his geese, or Desmond Morris and his naked ape for instance. Why does an animal behave in a certain way? And how? The field is very complex, fascinating and, in some ways, frightening. Is human behaviour, for example, solely determined by the organism's need to survive? Does a child only enjoy an ice-cream because it spells fuel? Or has the pleasure system been diverted somehow? A bit of both no doubt. Tests can now be carried out on the molecular level and behaviourists are able to delve into the parts of animals' central nervous systems that govern given types of behaviour. Thus a neural representation of what is going on is slowly emerging.

Forms of stress – such as sexual rejection or post-traumatic trauma stress syndrome for instance – trigger off certain behaviours that are, more often than not, ruled by a complex reward system. When a male fly plays a love song with its wings, taps its mate gently on the abdomen with its paw, fondly buries its proboscis into the female's private parts and has to suffer rejection, the best way to get over the transient humiliation is to find something that will make it feel better. On the molecular level, Neuropeptide F (NPF) acts as a sort of 'thermometer of pleasure'. When *Drosophila* is denied copulation, the levels of NPF in its brain are low. When it has been able to mate, the levels are high. Low levels of NPF will make the fly seek out an alternative form of pleasure. A fly with high levels of NPF doesn't feel the need to. Therefore, NPF seems to reflect the state of *Drosophila*'s reward system and a fly's subsequent behaviour.

How did scientists discover the link between copulation, ethanol and NPF? Male flies were isolated with three different types of females: virgins, females that had already mated, and virgins whose heads had been removed (...).The male flies were then offered food that had ethanol in it or not. The flies that had copulated ate both types of food. Those that had suffered rejection turned markedly more to the food soused with alcohol. As did those that had spent time with the headless virgins. Why behead them? This was a way of finding out whether flies suffered from rejection, as opposed to non-copulation. As it turned out, that was not the case. The 'headless virgin' males needed alcohol too. Lack of sex was the answer. Furthermore, frustrated flies that were given a chance to mate, subsequently lost interest in alcohol. So besides the direct link between two behaviours, there is also a mechanism which balances the reward system too, by bringing the levels of NPF back to normal.

The explanation sounds straightforward yet, on the molecular level, the mechanisms are far from understood. NPF and its receptor, yes, are at the heart of the system but how does it work? How does NPF link sexual behaviour with alcohol consumption? NPF is expressed in NPF neurons. The peptide has already been linked to alcohol sensitivity in *Drosophila*, and is known to influence behaviours such as larval intake of noxious foods and physical stress for instance. The novelty here, though, is that a given behaviour actually regulates the levels of NPF. As such, this particular regulation constitutes the basis of *Drosophila*'s reward system. This 'reward system' NPF is probably expressed in different neurons and may be linked to the dopaminergic systems, known to play a major role in reward-driven learning.

How about humans? It is very tempting to draw parallels with the mammalian reward system. Mammals have a similar neuropeptide, known as Neuropeptide Y or NPY, which is involved in the regulation of alcohol consumption. As in *Drosophila*, it is likely that drugs expropriate the human reward system, twisting a natural system into something which becomes harmful to the organism though it is felt as something pleasurable. NPY levels in humans have been shown to be low in the event of depression or post-traumatic stress disorders for instance. In rats, NPY levels have been linked to alcohol consumption and drug taking. But no direct connection has yet been made between social experience, NPY and alcohol consumption. *Drosophila* is not a close relative, yet it undoubtedly offers an excellent model for a greater understanding of the processes underlying drug addiction, alcoholism and obesity to name a few. If NPF is injected into a frustrated *Drosophila*, the insect doesn't feel the need to turn to alcohol any more. Could there be something here for people who suffer from various forms of addiction? Perhaps. But let's not stop eating ice-cream.

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Neuropeptide F, *Drosophila melanogaster* (Fruit fly) : Q9VET0

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