You need two humans for romantic love. That sounds straightforward enough. But you also need chemistry, as in chemical processes. It is an uncomfortable thought in a society where freewill is all the rage. Yet any of our feelings need a basis on which to work upon. And that is our brain with all its neuronal circuits and neurotransmitters that are being continuously fired from one neuron to another, sending messages of fright, anguish, enthusiasm, sadness, despair, love and surprise to name but a few. So what would be the chemistry at the heart of romantic love? Serotonin. Perhaps... With a notion as ungraspable as love, it is a very tricky business to try and pin it down to the makings of one molecule. Yet that is what a team of scientists tried to do. Their research hypothesis is particularly intriguing: they compared the infatuation we all experience in the early stages of love with a form of obsessive-compulsive behaviour.

There are few feelings more beneficial to a human than those triggered off by love. But love was not given to us for therapeutic purposes. From a purely biological point of view, where poetry has little room, we fall in love for a reason. Indeed, falling in love means falling for a mate. Falling for a mate means – to put it bluntly – sexual intercourse. And sexual intercourse means perpetuation of the species. What is more, falling in love – or so it is believed – is a way of ensuring fidelity, which is far less time- and energy-consuming in the realms of sex than infidelity. Hence, according to such a theory, love would be the doings of evolution. You can agree with it. Or disagree with it. But it has its logic.

Once you start meddling with the notion of love and its chemistry, the curious mind wants to know which chemical entity could be actively involved in such a feeling. In this light, scientists compared a human’s psychological state during the early stages of romantic love with obsessive-compulsive disorder (OCD). The neurotransmitter serotonin, or to be more precise the protein which carries it and is known as serotonin transporter, has a role in OCD in that its concentration is lower in patients suffering from the psychiatric condition than it is in healthy individuals. When individuals madly in love with someone were tested for the level of their serotonin transporters, the scientists found that – like OCD – their concentration was lower. Could that be where the term “lovesick” comes from?

Besides OCD and romantic love, serotonin and its transporter are known for their involvement in mood and behaviour. Neurons filled with serotonin are found in all parts of the brain – which goes to show their importance. The serotonin system seems to be critical in child brain development and the branching out of serotonergic projections. Later on in life, this particular branching or indeed the specific serotonin transporter polymorph that an individual has inherited, can give rise to differences in behaviour and moods depending on the environment. In particular, one individual can be more prone than another to developing a certain
type of psychiatric disorder following stressful situations, depending on the type of serotonin transporter he or she carries. Scientists even suggest here a basis for a difference in masculine or feminine moods or even psychiatric predisposition.

So the serotonin transporter, small as it is, has a far-reaching role in our lives. But how exactly does it work? Serotonin transporter is an integral membrane protein found in the cell membrane of neurons at the level of the presynaptic terminal, one end of which protrudes into the synaptic cleft. This is the part which grabs free serotonin and flings it back into the neuron ready for a new neurotransmitter cycle. But it needs ions to help it. First Na+ binds to the empty transporter in the synaptic cleft. This is the cue for serotonin to bind, followed closely by Cl¯. The threesome then causes a conformational change in serotonin transporter which flips around bringing the part which is usually immersed in the synaptic cleft into the neuron cytoplasm. There it releases the serotonin molecule, thus replenishing the neuron with its neurotransmitter which is now available to spark off a variety of moods. The binding of intracellular K+ then causes the transporter to flip back into its original position with the receiving end in the synaptic cleft; K+ is released and serotonin transporter is ready to bind another ligand.

Consequently, it is not difficult to understand that serotonin transporter is crucial in regulating serotonin activity as well as homeostasis, and thus has a pivotal role in the regulation of moods and behaviours – with normality at one end and mental disorders at the other, notably when the level of serotonin transporters is low. Besides romantic love, the serotonin transporter system is believed to be involved in many other types of behaviours such as appetite, sleep, sex, arousal, addiction, impulsiveness, anxiety, depression, OCD, alcoholism, autism…and even spiritual experiences.

The “romantic love versus OCD” hypothesis has met with scepticism. The individuals chosen for the study were certainly in love but none of them had had sexual intercourse with the ones they had fallen for. This was a prerequisite as the scientists defined romantic love as love where sex had not yet proved to be part of the bargain. This met with controversy. Were all these individuals not just suffering from stress caused by an unsatisfied desire due to repetitive procrastination? A behaviour not so far removed from OCD…

Unsurprisingly, the serotonin system is already a principal site of action of therapeutic antidepressants. Further knowledge of it will provide a greater understanding of the role of serotonin in brain development, the neurocircuits involved in emotional processing and, perhaps more importantly, the basis of a number of neuropsychiatric disorders which could then be the basis for the design of novel psychiatric drugs. So can romantic love really all be brought down to chemistry? And to this chemistry in particular? It will probably always remain a mystery. Is it not daunting, though, to take on board the fact that molecules can have such power over our emotions? And yet, without chemistry, we know that feelings would not exist. Talk about chemistry between people…

**Cross-references to UniProt**

Sodium-dependent serotonin transporter, *Homo sapiens* (Human) : P31645

**References**

1. Marazzati D., Akiskal H.S., Rossi A., Cassano G.B.  
   Alteration of the platelet serotonin transporter in romantic love  
   PMID: 10405096

2. Tek C.  
   Correspondence : To the Editor.  
   PMID: 10722194

3. Nordquist N., Oreland L.  
   Serotonin, genetic variability, behaviour, and psychiatric disorders – a review  
   Upsala Journal of Medical Sciences 115:2-10(2010)  
   PMID: 20187845

**Protein Spotlight** (ISSN 1424-4721), [http://www.proteinspotlight.org](http://www.proteinspotlight.org), is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB). Authorization to photocopy or reproduce this article for internal or personal use is granted by the SIB provided its content is not modified. Please enquire at spotlight@sib-sib.ch for redistribution or commercial usage.