Why serotonin can cause depression and anxiety

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Mood disorders could be caused by a loss of our inherent, reflexive avoidance of aversive events, according to a study published in *PLoS Computational Biology*. Researchers from UCL in London and Columbia University in New York used computational modeling techniques to integrate what appeared to be blatant contradictions between serotonin's roles in different states of health.

Serotonin appears to be one of the major players in mood and a variety of other disorders. But exactly how remains an open question. Imagine walking past a dark alleyway in a dangerous part of some city; although it might be a shortcut, most people wouldn't consider taking it. In healthy subjects, serotonin appears important for this automatic avoidance.

It has long been suggested that over-activity of the serotonin system may relate to mood disorders such as depression and anxiety, as these seem characterized by too much withdrawal and avoidance. However, the new modeling study simply suggests that we think about what happens when these reflexes fail—suddenly you have to think hard to avoid things that used to be avoided reflexively You might for example consider walking down the dangerous alley, be robbed and thus be reminded and taught by additional experience that dark alleys are to be avoided.

In this study Prof. Peter Dayan and Dr. Quentin Huys built a reinforcement learning model of reflexive choices. Agents take actions and as a result of these move through a set of states, some of which are rewarded or punished. As agents progress through this space, they learn

the value of each state—how much punishment or reward is to be expected from this state onwards.

It turns out that adding to the agent's behavioural repertoire a simple reflex, which guides the agent away from an action with potential for poor consequences, does two things: it increases the rewards reaped overall, but, because bad states are now not explored any more, it also prevents them from learning exactly how bad these bad states are. When serotonin drops, say in depression or anxiety, agents have no more recourse to the reflexive avoidance and have to rely on what they learned. Because they have not learned how bad the bad states are, they start exploring states that don't look too bad to them, but in reality are much worse. Serotonin enhancing drugs, such as Prozac, are then suggested to reinstate the reflexive avoidance, and thus to redress the balance.

This study gives insight into some puzzling findings—for example, it argues that the association of depression with aggression may have to do with a lack of reflexive avoidance of it. In addition, stress not only causes depression, but people with depression experience more stressors. Again, this may be related to a dysfunctional reflexive avoidance system. The study, however, vastly oversimplifies a number of issues, such as the flexibility of reflexive actions, and the effect of non-reflexive action choice. These provide interesting avenues for further research, and may in fact give some insight into the co-morbidity of different mood disorders.

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