Expectations and dopamine can affect outcome of SSRI treatment

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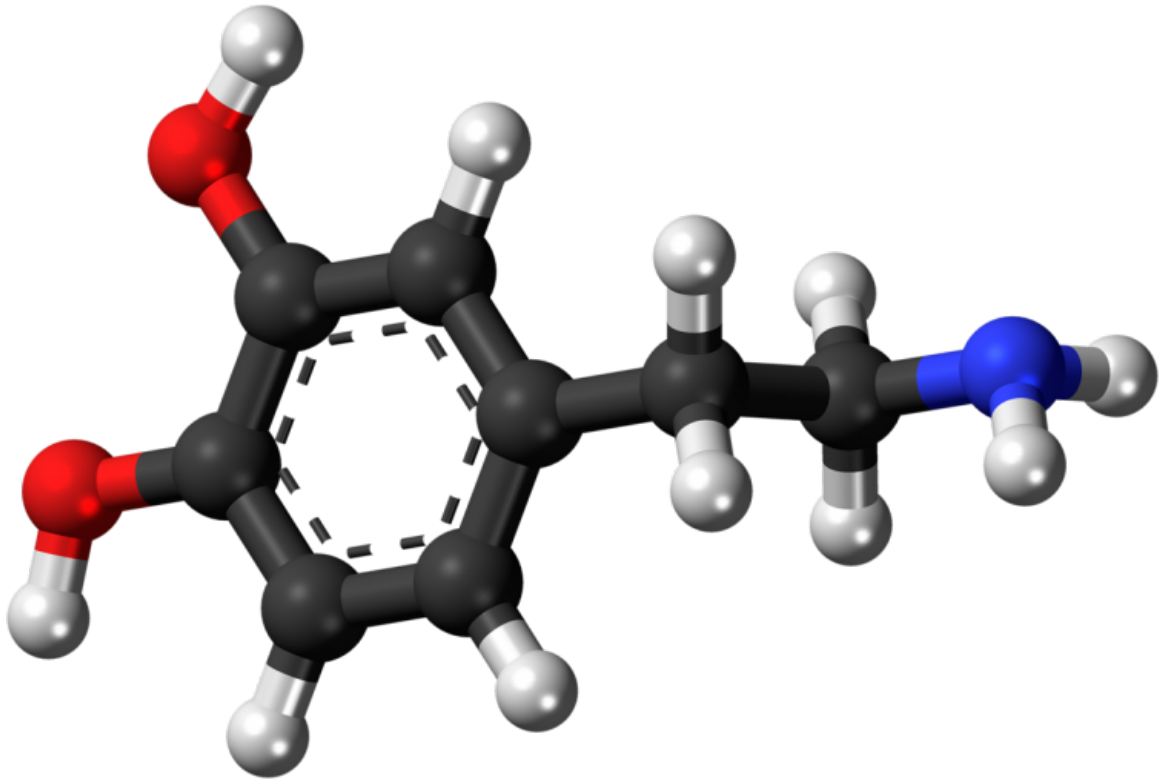

Ball-and-stick model of the dopamine molecule, a neurotransmitter that affects the brain's reward and pleasure centers. Credit: Jynto/Wikipedia

Levels of dopamine and the placebo effect can determine whether patients with social anxieties improve when treated with SSRIs. A new

study shows the effect was four times higher for patients with high expectations of the medication compared with patients with low expectations. This was true even though the groups received the same medical treatment. Although SSRIs influence levels of serotonin in the brain, the effects on dopamine had the greatest impact for improvement.

Selective serotonin reuptake inhibitors (SSRIs) are an established and effective medication for treating depression and anxiety. The placebo effect, where the positive effects of a treatment can increase when a patient expects to be helped, is a well-known phenomenon. The effect can be significant, and it is unclear how much of the improvement results from expectations of the SSRI treatment. It is also unclear whether the expectations use the same mechanism in the brain as SSRI medications (the inhibiting of the transporter protein for serotonin) or whether other neurotransmitters are involved. The new study points to the transporter protein for dopamine being the key.

Researchers at Uppsala University confirmed in a study on social anxiety published in *Translational Psychiatry* that the placebo effect had a major impact on the anti-anxiety effect of the SSRI drug escitalopram. The surprising finding in the study was that the improvement after SSRI treatment can largely be linked to effects on dopamine rather than to the serotonin transporters.

In the study, all the participants were treated with the same clinical dose of escitalopram for nine weeks, but they had different expectations. Half received accurate information about the drug and its effectiveness, while a cover story was used for the other half. Participants in the second group were told that the drug was an 'active placebo' that causes similar side effects as SSRIs but was not expected to alleviate their social anxiety.

"The results showed that almost four times as many patients responded

to the treatment when correct information about the drug was given. This is consistent with previous research showing that expectations affect treatment outcome," says researcher Olof Hjorth.

Positron emission tomography (PET) brain scanning showed that the SSRI drug had the same effect on serotonin and blocked about 80 per cent of serotonin transporters in both groups. This was true even for the group that had low expectations and did not improve.

"This indicates that the pharmacological effect was identical in both groups and that this cannot explain why correct information gave better treatment results. So, inhibiting serotonin transporters is insufficient for achieving good clinical relief from social anxiety using SSRI drugs."

When assessing the transporter protein for dopamine after treatment, however, a clear difference between the groups was observed. Participants who began the treatment knowing that it was an effective drug showed a reduced availability of dopamine transporters in the striatum, a part of the cerebrum, while the opposite was true in the group that was given the cover story. One explanation may be that expectations affected the release of dopamine in the brain's reward pathways. This may have led to differences in the two groups in the proportion of dopamine transporters available after treatment.

"The results indicate that positive expectations arising in the relationship between doctor and patient affect dopamine and enhance the effect of SSRI treatment," says Professor Tomas Furmark, who led the study.

More information: Olof R. Hjorth et al, Expectancy effects on serotonin and dopamine transporters during SSRI treatment of social anxiety disorder: a randomized clinical trial, *Translational Psychiatry* (2021). DOI: 10.1038/s41398-021-01682-3

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