

## Scientists explain emotional 'blunting' caused by common antidepressants

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Scientists have worked out why common anti-depressants cause around half of users to feel emotionally "blunted." In a study published today in *Neuropsychopharmacology*, they show that the drugs affect



reinforcement learning, an important behavioral process that allows people to learn from their environment.

According to the NHS, more than 8.3 million patients in England received an <u>antidepressant drug</u> in 2021/22. A widely used class of antidepressants, particularly for persistent or severe cases, is <u>selective</u> <u>serotonin reuptake inhibitors</u> (SSRIs). These drugs target serotonin, a chemical that carries messages between <u>nerve cells</u> in the brain and has been dubbed the "pleasure chemical."

One of the widely reported side effects of SSRIs is "blunting," where patients report feeling emotionally dull and no longer finding things as pleasurable as they used to. Between 40% and 60% of patients taking SSRIs are believed to experience this side effect.

To date, most studies of SSRIs have only examined their short term use, but, for clinical use in depression these drugs are taken chronically, over a longer period of time. A team led by researchers at the University of Cambridge, in collaboration with the University of Copenhagen, sought to address this by recruiting <u>healthy volunteers</u> and administering escitalopram, an SSRI known to be one of the best-tolerated, over several weeks and assessing the impact the <u>drug</u> had on their performance on a suite of cognitive tests.

In total, 66 volunteers took part in the experiment, 32 of whom were given escitalopram while the other 34 were given a placebo. Volunteers took the drug or placebo for at least 21 days and completed a comprehensive set of self-report questionnaires and were given a series of tests to assess cognitive functions including learning, inhibition, executive function, reinforcement behavior, and decision-making.

The team found no significant group differences when it came to "cold" cognition—such as attention and memory. There were no differences in



most tests of "hot" cognition—cognitive functions that involve our emotions.

However, the key novel finding was that there was reduced reinforcement sensitivity on two tasks for the escitalopram group compared to those on placebo. Reinforcement learning is how we learn from feedback from our actions and environment.

In order to assess reinforcement sensitivity, the researchers used a "probabilistic reversal test." In this task, a participant would typically be shown two stimuli, A and B. If they chose A, then four out of five times, they would receive a reward; if they chose B, they would only receive a reward one time out of five. Volunteers would not be told this rule, but would have to learn it themselves, and at some point in the experiment, the probabilities would switch and participants would need to learn the new rule.

The team found that participants taking escitalopram were less likely to use the positive and negative feedback to guide their learning of the task compared with participants on placebo. This suggests that the drug affected their sensitivity to the rewards and their ability to respond accordingly.

The finding may also explain the one difference the team found in the self-reported questionnaires, that volunteers taking escitalopram had more trouble reaching orgasm when having sex, a side effect often reported by patients.

Professor Barbara Sahakian, senior author, from the Department of Psychiatry at the University of Cambridge and a Fellow at Clare Hall, said, "Emotional blunting is a common side effect of SSRI antidepressants. In a way, this may be in part how they work—they take away some of the <u>emotional pain</u> that people who experience depression



feel, but, unfortunately, it seems that they also take away some of the enjoyment. From our study, we can now see that this is because they become less sensitive to rewards, which provide important feedback."

Dr. Christelle Langley, joint first author also from the Department of Psychiatry, added, "Our findings provide important evidence for the role of serotonin in <u>reinforcement learning</u>. We are following this work up with a study examining neuroimaging data to understand how escitalopram affects the brain during reward learning."

**More information:** Chronic escitalopram in healthy volunteers has specific effects on reinforcement sensitivity: A double-blind, placebo-controlled semi-randomised study, *Neuropsychopharmacology* (2023). DOI: 10.1038/s41386-022-01523-x

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