New principle for brain-controlled hormone secretion

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Christian Broberger, researcher at Karolinska Institutet in Stockholm, Sweden. Credit: Mika Nitz Pettersson

The concentration of the hormone prolactin in the blood is controlled by dopamine. However, the system can be thrown off balance by certain

drugs, especially antipsychotics, which can result in sexual side effects. A new study from Sweden's Karolinska Institutet in rats, published in the journal *Cell Reports*, shows how dopamine can regulate itself and provides new knowledge about how the side effects arise.

The researchers behind the study examined a group of dopamine producing neurons that control the secretion of prolactin, a hormone that leads to the production of breast milk, suppresses fertility and stimulates appetite in new mothers. Under most circumstances beyond pregnancy, blood levels of prolactin are usually suppressed by the neurotransmitter dopamine, which serves to inhibit the prolactin cells.

But the inhibitory mechanism can be lost, as is commonly seen in patients on antipsychotics that block dopamine receptors, resulting in sexual and reproductive problems such as impotence, low libido, amenorrhoea and infertility.

"Side effects that impair quality of life are fairly common," says Christian Broberger, docent at Karolinska Institutet's Department of Neuroscience. "It's crucial that the prolactin-regulating system is maintained under strict control so that blood levels of the hormone remain stable and adapted to the body's needs, such as during pregnancy."

After measuring the electrical activity of neurons and how they behave when they "talk to each other", the researchers discovered a new feedback regulatory system through which dopamine itself controls the activity of dopamine cells, which continually register the intensity of their own activity.

When they increased the level of dopamine around the cells, the researchers observed that the activity of the dopamine cells slowed down. Their results can lead to a better understanding of how hormone

regulation—and thus the side-effects of neuropsychiatric drugs - arises.

"The autoregulation we describe makes for a faster system, which can be adjusted to avoid such extreme fluctuations," says Dr Broberger.

Was there anything surprising in your results?

"We expected to find some kind of regulation, but that the drugs paradoxically completely inhibit the electrical discharge of dopamine cells came as a surprise. We hope that this information will be of use in the development of drugs with fewer side-effects."

More information: 'Dopamine Autoreceptor Regulation of a Hypothalamic Dopaminergic Network', Stefanos Stagkourakis, Hoseok Kim, David J. Lyons, Christian Broberger, *Cell Reports*, online 14 April 2016.

Provided by Karolinska Institutet

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