Researchers find 'missing link' between stress and infertility

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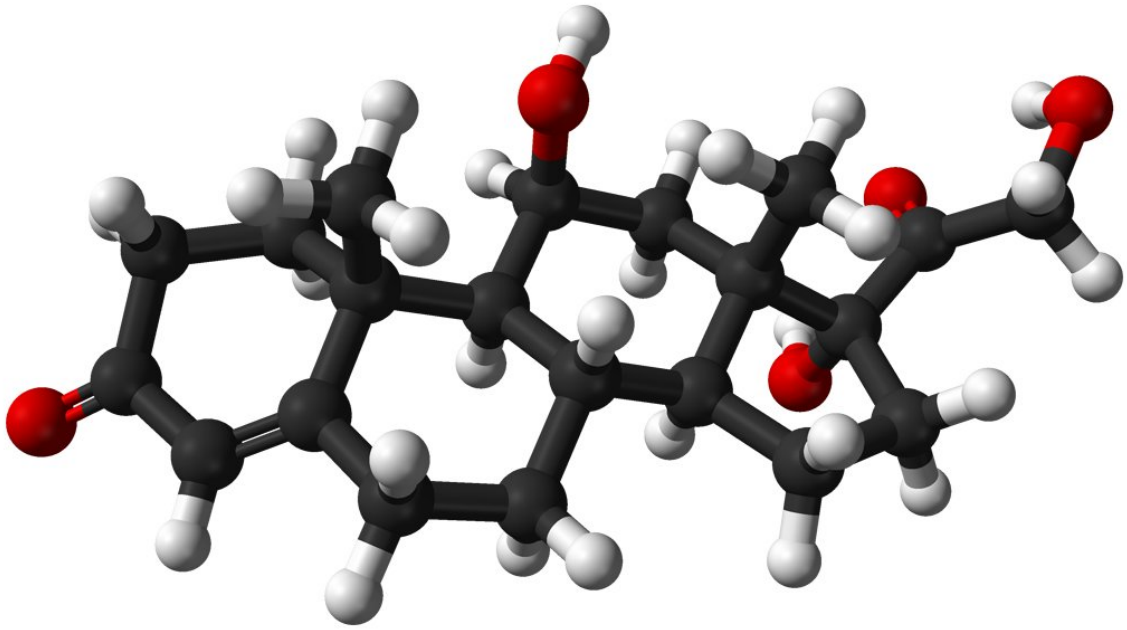

Ball-and-stick model of the cortisol (hydrocortisone) molecule. Credit: Public Domain

Otago researchers have found the "missing link between stress and infertility." Published in *The Journal of Neuroscience*, and led by Professor Greg Anderson of the Centre for Neuroendocrinology, the research has confirmed in laboratory testing that a population of nerve

cells near the base of the brain—the RFRP neurons—become active in stressful situations and then suppress the reproductive system.

"A revolutionary step forward that has become available to neuroscientists in recent years is the ability to control the activity of selected groups of neurons—to either silence or ramp up their activity, and then monitor the outcomes," Professor Anderson says.

"We used cutting edge transgenic techniques to show that when the activity of the RFRP cells is increased, reproductive hormones are suppressed—in a similar manner to what happens during stress, or during exposure to the stress hormone cortisol.

"Amazingly, when we used cortisol to suppress the reproductive hormones but also silenced the RFRP neurons, the reproductive system continued to function as if cortisol wasn't there at all—proving that the RFRP neurons are a critical piece of the puzzle in stress-induced suppression of reproduction."

The reaction was most evident in females.

Professor Anderson started researching the role of RFRP neurons in controlling fertility in mammals about a decade ago.

"I became interested in whether these neurons might be what causes fertility to be suppressed during chronic stress, after reading that these cells become active during stress. This is a question that has remained stubbornly unanswered over the past decades.

"Although it is known that stress steroids—like cortisol—are probably part of the mechanism involved, it is also known that the brain cells that control reproduction are unable to respond to cortisol, so there seemed to be a missing link in the circuit somewhere.

"We have now shown that the RFRP neurons are indeed the missing link between stress and infertility. They become active in stressful situations—perhaps by sensing the increasing levels of cortisol—and they then suppress the reproductive system."

It is possible drugs could be used to block the actions of the RFRP neurons, and that will be the focus of further research for Professor Anderson.

"We'd like to see if we can overcome stress-induced infertility using drugs which block the actions of the RFRP neurons.

"For women struggling with infertility, drugs which block the actions of the RFRP neurons may prove to be a novel therapy. From what we know about these neurons, such a drug wouldn't have any side-effects.

"There are such drugs available, but they're not approved for human use and they would likely need refining," he says.

More information: Asha Mamgain et al. RFamide-related peptide neurons modulate reproductive function and stress responses, *The Journal of Neuroscience* (2020). DOI: 10.1523/JNEUROSCI.1062-20.2020

Provided by University of Otago

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