Medical Xpress

The far-reaching effects of antidepressants

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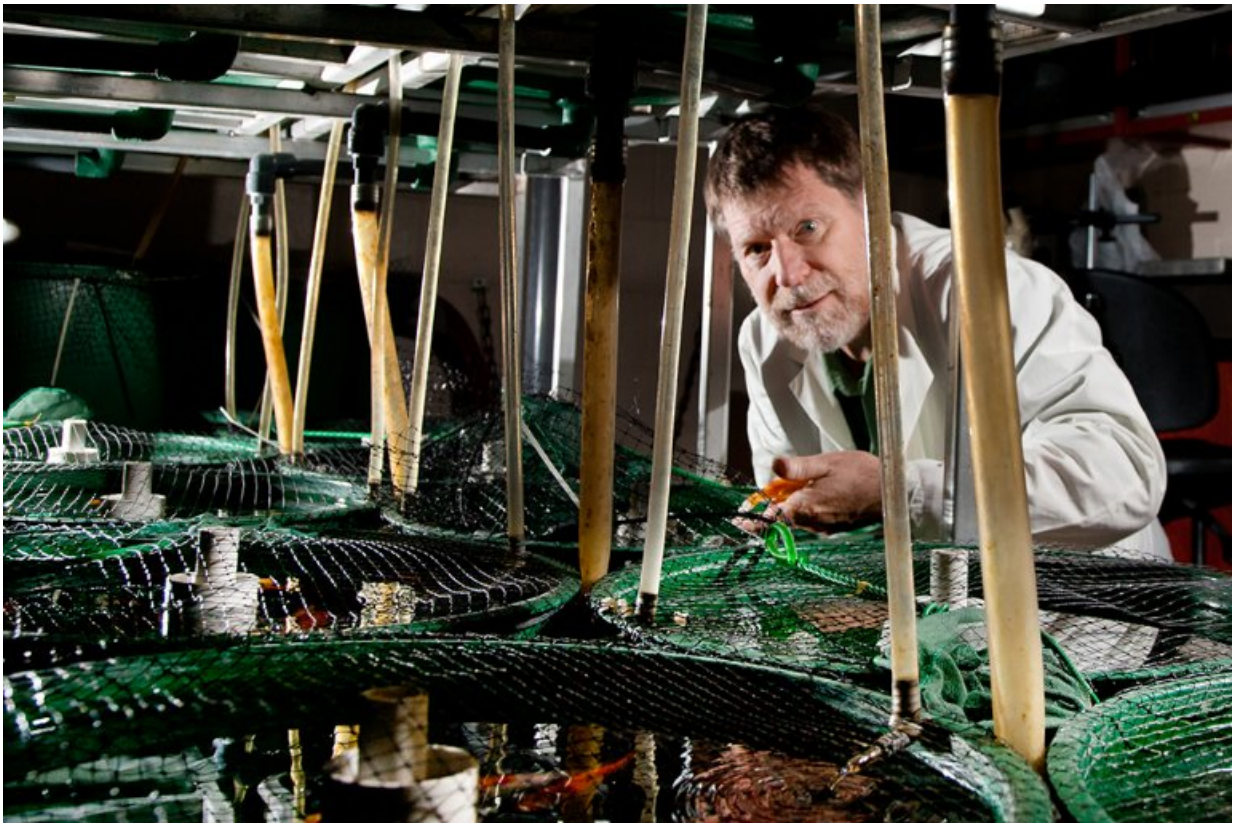

Credit: University of Ottawa

When University of Ottawa biologists Marilyn Vera-Chang and Vance Trudeau began to study the effects of a popular antidepressant on reproduction levels in zebrafish, they stumbled across something that changed the course of their work. We sat down with Professor Trudeau, a University of Ottawa Research Chair in Neuroendocrinology to learn

more.

Please tell us about this research project.

Marilyn Vera-Chang and colleagues under my supervision investigated the effects of fluoxetine—an antidepressant commonly known as Prozac – on reproduction in goldfish and zebrafish, freshwater fish belonging to the carps and minnows family.

What did you discover?

That a cortisol deficiency is induced as a result of the Prozac exposure. Much to our surprise, we discovered that upon exposing fish embryos to fluoxetine for a period of 6 days, cortisol levels dropped in the young fish that persisted till adulthood. An unusual pattern emerged when we measured the residual effects of the medication in the fish's offspring going as far as 3 generations- cortisol and it's response to various stresses remained reduced.

Why is cortisol so important? What role does it play?

Cortisol is best known as the stress hormone. When we experience stress, our cortisol goes up, helps us adapt, then goes back to normal. The same goes for all animals. Cortisol helps the body deal with stress by increasing metabolism and sending a signal to the brain to prompt action.

Animals, including humans, explore their immediate environment to find food, shelter from predators, and to find a mate. The ability to explore one's environment and to react appropriately to stressors is essential to the survival of a species.

In humans, in the short term, cortisol helps us cope with stress. Too

much cortisol can lead to health problems and it is becoming clear that too little cortisol is also equally bad for health. Cortisol deficiency has been associated with conditions such as post-traumatic stress disorder (PTSD), chronic fatigue, burnout, and disruptive behaviors in children.

Why is this important?

This is an important demonstration that in an animal model even a brief ancestral exposure to a common antidepressant modifies the stress response and critical coping behaviors for several generations. In other words, the animals were exposed only once as embryos, but the suppressed stress hormones and reduced exploratory behaviour lasts for generations.

Fluoxetine is a drug often prescribed to pregnant women suffering from depression, anxiety and other mental health issues. Our research highlights the fact that this may be a cause for concern given the high-prescription rates of fluoxetine to pregnant women and the potential long-term negative impacts on humans exposed to these therapeutic drugs.

This effect was also present in the offspring of the fish initially exposed to Prozac, even at low concentrations, comparable to levels found in some rivers and streams. However, the effects were not as prounounced.

What does this mean?

What most people don't realize is that the mechanisms in fish and in humans are actually quite similar, if not identical. This means that there are potential serious implications for humans.

Would you like to add anything else?

Yes. Marilyn and I would like to mention that there are also major

benefits to these types of drugs; in fact, they can be lifesaving in some situations. However, it is important to follow a physician's advice and take the prescribed dose. The future discussion should take into account that such medication have longer-term effects than we ever imagined, as our work clearly shows that what we do today can influence future generations.

The paper "Transgenerational hypocortisolism and behavioral disruption is induced by the antidepressant fluoxetine in male zebrafish Danio rerio" was published today in *PNAS*.

More information: Marilyn N. Vera-Chang et al. Transgenerational hypocortisolism and behavioral disruption are induced by the antidepressant fluoxetine in male zebrafish Danio rerio, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1811695115

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