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A cautionary note on oxytocin as a treatment for psychiatric disorders

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The hormone oxytocin is known for its widespread effects on social and reproductive processes, and recent data from intranasal administration in humans has produced hope for its use as a therapeutic in autism, schizophrenia, and other disorders.

However, this leap to human use is happening without previous animal studies of long-term oxytocin administration, and without knowledge of the neurobiological mechanisms involved in the behavioral findings.

A new study now published in *Biological Psychiatry* indicates that the promising short-term effects often observed after a single dose of oxytocin may not translate to positive effects after long-term administration.

This research was led by Dr. Karen Bales, Professor and Vice Chair of Psychology at the University of California. She and her colleagues examined the long-term effects of oxytocin treatment using the prairie vole, a small rodent that forms strong life-long pair bonds and is thus often used in studies of social behavior.

Both male and female voles were treated with one of three dosages of intranasal oxytocin, administered daily from weaning through sexual maturity. During this time, the researchers observed and recorded the voles' social interactions. They also conducted tests of social and anxiety-related behaviors in the adult voles, after the oxytocin treatment had finished, allowing them to measure any long-term effects.

As expected, oxytocin treatment increased social behavior in male voles, similar to the effects repeatedly observed in humans. However, the long-term effects were concerning, with male voles showing deficits in their typical behaviors.

"In this study, we showed that long-term exposure to oxytocin in adolescent male prairie voles led to disruption of social bond formation in these males as adults," explained Bales. "Male prairie voles which received a dose similar to that being tested in humans, or even a lower dose, did not form pair-bonds normally with their pair-mate. Instead these males chose to associate with a strange female."

This important finding should suggest caution in the long-term use of intranasal oxytocin in developing humans.

"The fact that long term treatment with oxytocin had the opposite impact of initial doses with the same substance suggests that special strategies will be needed if oxytocin is ever to become a long-term treatment for autism or schizophrenia," said Dr. John Krystal, Editor of Biological Psychiatry.

Bales agrees, and added, "In our continuing research program, we also have preliminary data suggesting that these treatments caused long-term changes in the oxytocin system. Additional animal work, carried out in close consultation with the psychiatrists carrying out clinical trials, will be necessary to use intranasal oxytocin in an informed and responsible way."

More information: The article is "Chronic Intranasal Oxytocin Causes Long-Term Impairments in Partner Preference Formation in Male Prairie Voles" by Karen L. Bales, Allison M. Perkeybile, Olivia G. Conley, Meredith H. Lee, Caleigh D. Guoynes, Griffin M. Downing, Catherine R. Yun, Marjorie Solomon, Suma Jacob, and Sally P.

Mendoza (DOI: 10.1016/j.biopsych.2012.08.025). The article appears in *Biological Psychiatry*, Volume 74, Issue 3, August 1, 2013