

## Hormones, Elvis, and human emotion: Shedding light on what makes people feel and act the way they do

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The velvety voice of Elvis Presley still makes hearts flutter—and in a new study with people who have the rare genetic disorder Williams syndrome, one of the King's classics is among a group of songs that helped to cast light on part of the essence of being human: the mystery of emotion and human interaction.

In a study led by Julie R. Korenberg, Ph.D., M.D., University of Utah/USTAR professor, Circuits of the Brain and pediatrics, people with and without Williams syndrome (WS) listened to music in a trial to gauge emotional response through the release of oxytocin and arginine vasopressin (AVP), two hormones associated with emotion. The study, published June 12, 2012, in *PLoS ONE*, signals a paradigm shift both for understanding human emotional and behavioral systems and expediting the treatments of devastating illnesses such as WS, post-traumatic stress disorder, anxiety, and possibly even autism, according to Korenberg, senior author on the study and one of the world's leading experts in genetics, brain, and behavior of WS.

"Our results could be very important for guiding the treatment of these disorders," Korenberg says. "It could have enormous implications for personal the use of drugs to help people."

The study also is the first to reveal new genes that control emotional responses and to show that AVP is involved in the response to music.



Williams syndrome is a neurodevelopmental disorder caused by the deletion of 25 to 28 genes on one copy of chromosome 7. Those with the disorder look at the world through a unique lens. They may view everyone as their friend, to the point of running up to total strangers and striking up conversations as though they are old acquaintances. They have an affinity for music. But they also experience heightened anxiety, have an average IQ of 60, experience severe spatial-visual problems, and suffer from cardiovascular and other health issues. Despite their desire to befriend people, they have difficulty creating and maintaining social relationships, something that is not at all understood but can afflict many people without WS.

Korenberg and colleagues from the U of U, University of Illinois, Chicago, and the Salk Institute, La Jolla, Calif., conducted a trial with 21 participants, 13 who have WS and a control group of eight people without the disorder. The participants were evaluated at the Cedars-Sinai Medical Center in Los Angeles. Because music is a known strong emotional stimulus, the researchers asked participants to listen to music.

Before the music was played, the participants' blood was drawn to determine a baseline level for oxytocin, and those with WS had three times as much of the hormone as those without the syndrome. Blood also was drawn at regular intervals while the music played and was analyzed afterward to check for real-time, rapid changes in the levels of oxytocin and AVP. Other studies have examined how oxytocin affects emotion when artificially introduced into people, such as through nasal sprays, but this is the one of the first significant studies to measure naturally occurring changes in oxytocin levels in rapid, real time as people undergo an emotional response.

Researchers asked the first participant to listen to the 1950s Elvis classic, "Love Me Tender." The woman showed no outward response to the song, which can be typical not only of people with WS but particularly



of people without the disorder whose faces may be impassive but jump up at the end of an exciting piece, Korenberg points out. But, to elicit a greater response from the remaining test participants, the researchers invited them to bring their favorite music to listen to—and many of them chose heavy metal. Again, there was little outward response to the music.

But when the blood samples were analyzed, the researchers were happily surprised. The analyses showed that the oxytocin levels, and to a lesser degree AVP, had not only increased but begun to bounce among WS participants while among those without WS, both the oxytocin and AVP levels remained largely unchanged as they listened to music. Interestingly, the oxytocin level in the woman who'd listened to "Love Me Tender" skyrocketed compared to the levels of participants who listened to different music.

Korenberg believes the blood analyses strongly indicate that oxytocin and AVP are not regulated correctly in people with WS, and that the behavioral characteristics unique to people with WS are related to this problem.

"This shows that oxytocin quite likely is very involved in emotional response," Korenberg says.

To ensure accuracy of results, those taking the test also were asked to place their hands in 60-degree Fahrenheit water to test for negative stress, and the same results were produced as when they listened to music. Those with WS experienced an increase in oxytocin and AVP, while those without the syndrome did not.

Listening to Elvis was part of a larger study, published in the June 12, 2012 issue of PLoS One, that shows for the first time that oxytocin and another hormone associated with emotion, arginine vasopressin (AVP),



are poorly regulated in people with WS and that atypical levels of oxytocin are linked to both the desire to seek social interaction and decreased ability to process social clues.

WS is ideal for studying how genes influence social behavior and emotion, according to Korenberg. Unlike other social disorders, the cause of Williams syndrome is known, which is critical for pinpointing areas of the brain and genes related to the disorder. It also could be extremely important in finding drug targets for WS.

In addition to listening to music, study participants already had taken three standard social behavior tests that evaluate willingness to approach and speak to strangers, emotional states, and various areas of adaptive and problem behavior. Those test results suggest that increased levels of oxytocin are linked to both increased desire to seek social interaction and decreased ability to process social cues, a double-edged message that may be very useful at times, for example, during courtship, but damaging at others, as in Williams syndrome.

"The association between abnormal levels of oxytocin and AVP and altered social behaviors found in people with Williams Syndrome points to surprising, entirely unsuspected deleted genes involved in regulation of these hormones and human sociability," Korenberg said. "It also suggests that the simple characterization of oxytocin as 'the love hormone' may be an overreach. The data paint a far more complicated picture."

However, the picture is very hopeful, and the study provides a key breakthrough that lights the way to making rapid progress in treating WS, and perhaps Autism and anxiety through regulation of these key players in human brain and emotion, oxytocin and vasopressin. It is important that work in the very near future may allow us to know how to adjust the dial on the OT and AVP system and its effects in different



brain regions in ways that relieve suffering and improve the lives of those with the disorder, according to Korenberg.

In particular, the study results indicate that the missing genes affect the release of oxytocin and AVP through the hypothalmus and the pituitary gland. About the size of a pearl, the hypothalamus is located just above the brain stem and produces hormones that control body temperature, hunger, mood, sex drive, sleep, hunger and thirst, and the release of hormones from many glands, including the pituitary. The pituitary gland, about the size of a pea, controls many other glands responsible for hormone secretion. The results of this study points to new clues as to what makes us and may prevent us from being just a bit more human.

## Provided by University of Utah Health Sciences

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