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'Trust hormone' oxytocin helps old muscle work like new, study finds

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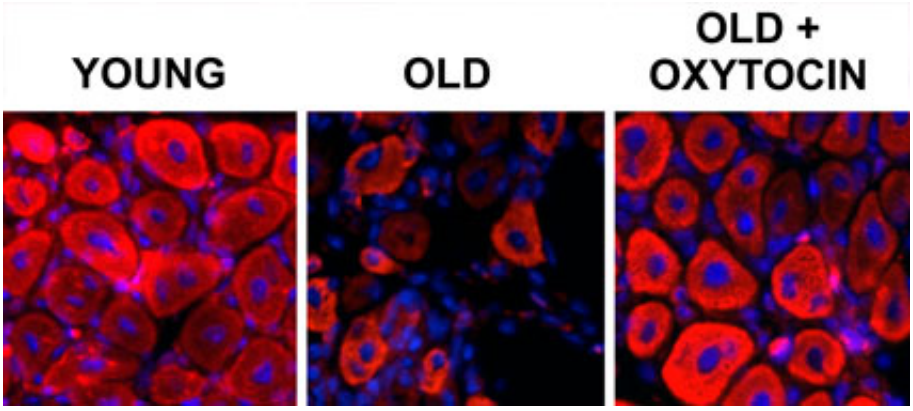

On the left is healthy muscle tissue from a young mouse. The ability of muscle to repair itself decreases with age, as evidenced by the middle image of old muscle tissue, which shows a lower density of muscle fibers, increased scar tissue and inflammation. The addition of oxytocin to the blood of old mice rapidly rejuvenates the old muscle, as shown in the image on the right. Credit: Wendy Cousin and Christian Elabd, UC Berkeley.

Researchers at the University of California, Berkeley, have discovered that oxytocin—a hormone associated with maternal nurturing, social attachments, childbirth and sex—is indispensable for healthy muscle maintenance and repair, and that in mice, it declines with age.

The new study, to be published Tuesday, June 10, in the journal *Nature Communications*, presents oxytocin as the latest treatment target for age-related muscle wasting, or sarcopenia.

A few other biochemical factors in blood have been connected to aging and disease in recent years, but oxytocin is the first anti-aging molecule identified that is approved by the Food and Drug Administration for clinical use in humans, the researchers said. Pitocin, a synthetic form of oxytocin, is already used to help with labor and to control bleeding after childbirth. Clinical trials of an oxytocin nasal spray are also underway to alleviate symptoms associated with mental disorders such as autism, schizophrenia and dementia.

"Unfortunately, most of the molecules discovered so far to boost tissue regeneration are also associated with cancer, limiting their potential as treatments for humans," said study principal investigator Irina Conboy, associate professor of bioengineering. "Our quest is to find a molecule that not only rejuvenates old muscle and other tissue, but that can do so sustainably long-term without increasing the risk of cancer."

Conboy and her research team say that oxytocin, secreted into the blood by the brain's pituitary gland, is a good candidate because it is a broad range hormone that reaches every organ, and it is not known to be associated with tumors or to interfere with the immune system.

A happy hormone

Oxytocin is sometimes referred to as the "trust hormone" because of its association with romance and friendship. It is released with a warm hug, a grasped hand or a loving gaze, and it increases libido. The hormone kicks into high gear during and after childbirth, helping new mothers bond with and breastfeed their new babies.

"This is the hormone that makes your heart melt when you see kittens, puppies and human babies," said Conboy, who is also a member of the Berkeley Stem Cell Center and of the California Institute for Quantitative Biosciences (QB3). "There is an ongoing joke among my

research team that we're all happy, friendly and trusting because oxytocin permeates the lab."

The researchers pointed out that while oxytocin is found in both young boys and girls, it is not yet known when levels of the hormone start to decline in humans, and what levels are necessary for maintaining healthy tissues.

Christian Elabd and Wendy Cousin, both senior scientists in Conboy's lab, were co-lead authors on this study.

Previous research by Elabd found that administering oxytocin helped prevent the development of osteoporosis in mice that had their ovaries removed to mimic menopause.

Extra oxytocin more beneficial for the old

The new study determined that in mice, blood levels of oxytocin declined with age. They also showed that there are fewer receptors for oxytocin in muscle stem cells in old versus young mice.

To tease out oxytocin's role in muscle repair, the researchers injected the hormone under the skin of old mice for four days, and then for five days more after the muscles were injured. After the nine-day treatment, they found that the muscles of the mice that had received oxytocin injections healed far better than those of a control group of mice without oxytocin.

"The action of oxytocin was fast," said Elabd. "The repair of muscle in the old mice was at about 80 percent of what we saw in the young mice."

Interestingly, giving young mice an extra boost of oxytocin did not seem to cause a significant change in muscle regeneration.

"This is good because it demonstrates that extra oxytocin boosts aged tissue stem cells without making muscle stem cells divide uncontrollably," Cousin added.

The researchers also found that blocking the effects of oxytocin in young mice rapidly compromised their ability to repair muscle, which resembled old tissue after an injury.

The researchers also studied mice whose gene for oxytocin was disabled, and compared them with a group of control mice. At a young age, there was no significant difference between the two groups in muscle mass or repair efficiency after an injury. It wasn't until the mice with the disabled oxytocin gene reached adulthood that signs of premature aging began to appear.

"When disabling other types of genes associated with tissue repair, defects appear right away either during embryonic development, or early in life," said Conboy. "To our knowledge, the oxytocin gene is the only one whose impact is seen later in life, suggesting that its role is closely linked to the aging process."

Future treatment options

Cousin noted that oxytocin could become a viable alternative to hormone replacement therapy as a way to combat the symptoms of both female and male aging, and for long-term health. Hormone therapy did not show improvements in agility or muscle regeneration ability, and it is no longer recommended for disease prevention because research has found that the therapy's benefits did not outweigh its health risks.

In addition to healthy muscle, oxytocin is predicted to improve bone health, and it might be important in combating obesity.

Conboy said her lab plans to examine oxytocin's role in extending a healthy life in animals, and in conserving its beneficial anti-aging effects in humans.

She noted that there is a growing circle of scientists who believe that aging is the underlying cause of a number of chronic diseases, including Parkinson's and Type 2 diabetes.

"If you target processes associated with aging, you may be tackling those diseases at the same time," said Conboy. "Aging is a natural process, but I believe that we can meaningfully intervene with age-imposed organ degeneration, thereby slowing down the rate at which we become progressively unhealthy."

Provided by University of California - Berkeley

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