JONATHAN V. WRIGHT, MD'S
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Should Oxytocin Be a Daily Part of Your Bioidentical Hormone Replacement Program?

- Oxytocin is often used when needed to improve intimacy
- Research shows oxytocin can help control obesity, type 2 diabetes, prevent and reverse osteoporosis, rebuild and maintain muscle mass, reduce chronic pain, and regenerate neurons
- Should oxytocin be used daily as part of bioidentical hormone replacement therapy (BHRT)?

Oxytocin is often described as the "hug hormone," the "cuddle chemical," and the "hormone of happiness," but it's commonly known in popular media as the "hormone of love."[1–3] Oxytocin is in fact released by hugging and cuddling, but recent research reveals that oxytocin has far broader effects than those. These effects hold promise for helping to treat some major health issues: diabetes, obesity, osteoporosis, chronic pain, and heart disease.

Oxytocin also appears to favorably affect maintenance of muscle mass (very important for older women), migraines, anxiety, post-traumatic stress disorder, autism, erectile dysfunction, inability to achieve orgasm, vaginal dryness, reproductive function, wound healing, inflammation, mood and mental disorders (including apathy, depression, and schizophrenia), recovery from addiction, and nerve regeneration.

Oxytocin is just nine amino acids bonded together chemically. (For the technically inclined, it's a peptide.) In our brains, it's primarily synthesized in the hypothalamus, toward the base of the brain. Oxytocin is also produced in non-brain areas of the body, including the uterus, ovaries, testicles, retina, and heart.

In humans, oxytocin release in the brain has a daily rhythm, peaking around noon.[4] Oxytocin release can also be triggered by pain.[5] Like nearly all other hormones, oxytocin levels decline with age; oxytocin receptors decline with age in some cell types, too.[6]

The presence of oxytocin receptors tells us that the tissues which have them must be oxytocin-sensitive. Oxytocin receptors are found in heart muscle, the inside lining of blood vessels, kidneys, the pancreas, thymus, pain-sensing nerves, fat cells, and in the prostate, adrenal, and bone-building cells (osteoblasts).[7,8]

Oxytocin and Pain

According to the American Academy of Pain Medicine, 100 million people in the US suffer from chronic pain. This number is greater than the combined number of those who suffer from diabetes (diagnosed and estimated undiagnosed), heart disease, stroke, and all forms of cancer.[9] Individuals suffering chronic pain have significantly lower oxytocin levels and have greater pain sensitivity than healthy individuals. Women with fibromyalgia are very likely to have lower levels of oxytocin. Researchers have reported that oxytocin given to these women improves pain tolerance. Other research has found that oxytocin increased pain tolerance in patients with irritable bowel syndrome and reduced pain in patients with chronic or acute back pain.[10]

Chinese researchers studied three different intranasal oxytocin doses versus placebo in 112 individuals with headache (that is, four groups of twenty-eight individuals). Those receiving 400 ng (nanograms) of oxytocin had the best response, with twenty of the twenty-eight experiencing complete remission, and the remaining eight experiencing partial remission of headache pain. Of those receiving 200 ng of oxytocin, fourteen had complete remission of pain, twelve had partial remission, and two experienced no improvement in their headache pain. This dose-response effect continued to be observed in those receiving 100 ng of oxytocin or placebo.[11]

Seven of nine individuals with chronic pain demonstrated a 30–40% reduction in opioid use and baseline pain when given sublingual oxytocin (10 IU—international units—two to four times daily) in combination with sublingual hCG (human chorionic gonadotropin, 250–500 IU daily). Most requested to continue the treatment after completion of the study.[12] Related research on the use of oxytocin to reduce withdrawal symptoms from alcohol and drugs suggests that oxytocin might be of great benefit in fighting the current epidemic of those addicted to pain medications.[13–15]

CASE REPORT

A physician sent a test to Meridian Valley Lab for an individual with a history of cluster

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OUR PURPOSE

Green Medicine is dedicated to helping you keep yourself and your family healthy by the safest and most effective means possible. Every month, you'll get information about diet, vitamins, minerals, herbs, natural hormones, natural energies, and other substances and techniques to prevent and heal illness, while prolonging your healthy life span.

A graduate of Harvard University and the University of Michigan Medical School (1969), Dr. Jonathan V. Wright has been practicing natural and nutritional medicine since 1973 at the Tahoma Clinic, now in Tukwila, Washington. Based on enormous volumes of library and clinical research, along with tens of thousands of clinical consultations, he is exceptionally well qualified to bring you a unique blending of the most up-to-date information and the best and still most effective natural therapies developed by preceding generations.

In 1992, Dr. Wright was among the original founders of the American Preventive Medical Association—now known as the Alliance for Natural Health USA—which was created to defend integrative doctors from relentless and coordinated attacks from the conventional medical establishment and the government agencies that protect them. Now one of the leading voices in natural health policy, the Alliance for Natural Health USA continues this mission by organizing half a million grassroots activists to protect access to natural, preventive medicine.

Dr. Wright and ANH-USA are proud to be teaming up once again to empower consumers to exercise their inalienable rights to choose their own healthcare, and to warn the public of continual, pervasive attempts from both government and private organizations to restrict them.

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Oxytocin as a Part of a Hormone Replacement Program?

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headaches and migraines four or more days a week for thirty years. Various patent and non-patent medicines had been tried over the years with little relief. The test reported oxytocin below the range of normal. Intranasal oxytocin was started, 20 IU daily. Three weeks after starting treatment, this individual had experienced only one headache. Three months later the physician told us that this individual had only occasional headaches now and they were greatly decreased in both frequency and intensity.

Oxytocin, Obesity and Diabetes

Individuals who are overweight or obese have higher-than-usual amounts of a hormone named leptin. Researchers agree that leptin resistance (caused by too much leptin, just as insulin resistance is caused by too much insulin) plays an important part in obesity.[16] Receptors for leptin are found on the oxytocin-synthesizing neurons of the brain. Oxytocin neurons that are activated by leptin then decrease food intake.

Since it's the oxytocin that decreases food intake, it's been theorized that oxytocin could be used to decrease body fat mass not only in leptin-resistance-related obesity, but also in those with genetic leptin or leptin-receptor deficiencies. Several animal studies and two human studies support this hypothesis.[17] In the animal studies the resulting weight loss appears to be independent of food intake.

Oxytocin receptors have now been found in adipose (fat) tissue at levels similar to oxytocin receptor levels found in the breast, uterus, and other tissues traditionally thought to be the targets for oxytocin stimulation. More oxytocin receptors are found on fat cells in fat mice, and fewer on fat cells in lean mice. Given this, it's not surprising that oxytocin had very little effect on weight and appetite in lean mice. Glucose metabolism and insulin sensitivity in obese mice were also improved with oxytocin administration.

In a human trial involving twenty obese men and women (with a body mass index, or BMI, of 30 or higher), nine participants used 24 IU of intranasal oxytocin twenty minutes before each of three meals and before sleep. Eleven participants used a placebo nasal spray on the same schedule. All were asked not to make any changes to diet and exercise habits.

At the end of four weeks, there was an average weight loss of 10.14 pounds in the oxytocin group, while no significant weight loss occurred in the placebo group. At eight weeks, the average weight loss in the oxytocin group was 19.62 pounds. There were significant reductions in BMI and waist and hip circumference in this group. The therapeutic effect of oxytocin appeared to be greater in participants with a higher initial BMI.[18]

One researcher reports that, as of September 2013, there were "225 completed, ongoing or future investigations in humans [listing] oxytocin in studies of caloric intake, gastric emptying, or obesity." He also reports that oxytocin "may preferentially inhibit the intake of carbohydrates."[19]

In adipose tissue, oxytocin stimulates fatty acid oxidation ("fat burning" in English) and fat breakdown resulting in smaller fat cells. This leads to improved insulin sensitivity and increased glucose uptake in muscle cells. In the pancreas, oxytocin stimulates insulin secretion and may play a role in ß-cell regeneration of B-cells (also called islet cells, which produce insulin and glucagon).[20]

As oxytocin appears to be safe, with no adverse effects being reported at any dose given—remember the huge amounts of oxytocin secreted during childbirth—if you have an obesity problem, with or without diabetes or prediabetes, it might

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be wise to visit a physician skilled and knowledgeable in natural medicine to ask about trying it!

Oxytocin and Osteoporosis

Oxytocin receptors are found on osteoblasts (cells that grow bone) and osteoclasts (cells that "tear down" bone). Osteoblasts share a common precursor cell with adipocyctes (fat cells!). This "common heritage" of osteoblasts and adipocytes is recalled by what happens with early postmenopausal bone loss: the decrease in osteoblasts is balanced by an increase in fat cells right in the bone marrow.[21]

Severe osteoporosis develops in both male and female mice whose bodies either do not produce oxytocin or do not have oxytocin receptors.[22] In animals whose ovaries have been removed (which severely reduces estrogen levels), oxytocin has been found to reverse osteopenia, an earlier phase of osteoporosis.[23]

Twenty postmenopausal women with severe osteoporosis and sixteen healthy women had their oxytocin levels measured. Higher oxytocin correlated with better bone mineral density. Women with severe osteoporosis had the lowest levels of oxytocin. No correlation of oxytocin was found with any other measured parameter, including age.[24]

Young female athletes, and young women with anorexia nervosa who were not having menstrual periods, were found to have lower oxytocin levels and poorer bone structure and strength than healthy young women. In the female athletes, this effect was most pronounced in non-weight-bearing bones.[25, 26]

Oxytocin and Mental Health

A number of small studies report that oxytocin can improve social functioning in autism, including social function and recognition, empathy, repetitive behaviors, and anxiety.[27] In at least one study, ten out of fifteen children had overall improvement at week twelve. Seven of those children maintained their improvement for three months after stopping oxytocin.[28] In another study, eleven men and two women with Asperger syndrome, ranging in age from 17–39, showed improvement in social cooperation and time spent gazing at the eyes after a single 24 IU dose of intranasal oxytocin.[29]

CASE REPORT ONE

A physician called Meridian Valley Lab to consult about a woman with symptoms of extreme mental stress, anxiety, and social isolation. Her oxytocin levels were below the normal range. She had had a positive response to oxytocin, feeling more happiness and joy than she had for several months. However, it was unclear whether the response was entirely due to oxytocin as it also coincided with an extended vacation, although the improvement in feelings of anxiousness and stress began shortly after starting oxytocin and before leaving on vacation. On the way back from vacation the patient lost her oxytocin. She subsequently noticed an increase in anxiety and feeling "disconnected."

CASE REPORT TWO

A physician called Meridian Valley Lab about a woman with symptoms of social isolation and lack of trust and an unfortunate history of sexual abuse, whose oxytocin levels were low-normal. In follow-up, the physician told us that the woman had had a "night and day" response to oxytocin. She was so noticeably better that her neighbor made an appointment to see the physician because she wanted "whatever she got."

Oxytocin and the Heart

Oxytocin receptors are everywhere in the heart as well as in blood vessels. In culture dishes, oxytocin has been shown to stimulate the release of nitric oxide and a hormone which promotes salt excretion (for the technically inclined, ANH, or atrial natriuretic peptide). Oxytocin is abundant in fetal heart tissue, and triggers the development of "regular" heart muscle cells from mouse and rat heart stem cells.[30] The actions of oxytocin on the cardiovascular system include reduction of blood pressure and decreasing heart rate, the force of contraction, and blood vessel dilation.[30, 31]

Multiple animal studies have shown cardiovascular benefits from oxytocin treatment. Diabetic mice were treated with either saline (diluted salt water) or oxytocin for twelve weeks starting at four weeks of age. Saline-treated mice developed cardiac enlargement, fibrosis, death of heart muscle cells, and abnormalities of contraction and relaxation. Oxytocin prevented all these effects, as well as reducing inflammation and oxidative stress on the heart.[32]

Other animal studies have demonstrated that oxytocin can reduce ischemia-reperfusion injury, an injury that occurs when blood flow to the heart is decreased or stopped temporarily and then restarted. In one study, adding oxytocin prior to restricting blood flow (ischemia) resulted in an injury size 66% smaller than in the control group which had received no oxytocin.[33, 34]

Oxytocin levels were measured in twenty-eight women who had recently delivered infants before and during two stressful situations. In the first situation, the women were asked to give a three-minute speech on a recent situation in which they were angry or stressed.

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In the second situation, the women were asked to hold a plastic bag of ice and water on their foreheads for two and a half minutes. (This causes blood vessel constriction and elicits and pain.) The women with higher oxytocin levels had a smaller increase in cardiovascular stress in response to both situations.[35]

Oxytocin and Sexual Function

Oxytocin levels rise with sexual activity, especially with orgasm. The heart-protective effects of oxytocin may be at least one of the underlying reasons for the findings of a 2010 study which reported men who have sex twice or more a week are at lower risk of cardiovascular disease than men who had sex once a month or less.[36]

As mentioned above, oxytocin stimulates nitric oxide release, which causes blood vessel dilation, which in turn can have a positive effect on erectile function. A 2007 study demonstrated that sildenafil—Viagra—which is known to prolong the time before nitric oxide is "broken down," also stimulates the release of oxytocin from brain neurons.[37] However, some may be pleased and some disappointed that no reports have been made about oxytocin causing erections lasting more than four hours.

Two published case reports suggest that oxytocin is certainly worth consideration for male sexual dysfunction.

CASE REPORT ONE

A 33-year-old married father of three with social inhibition and probable Asperger syndrome was treated with 20 IU of intranasal oxytocin twice daily. Although the treatment did not greatly improve his social phobia, he experienced noticeable changes in his sexual relationship with his wife, which she confirmed. "The patient reported that while using oxytocin, he was more spontaneously affectionate with his wife, which led to increased sexual intimacy. Importantly, these effects were present when using the spray, disappeared on discontinuation, and reappeared each of the several times he restarted the medication (after refilling his prescription)."

His sexual function (as measured on the Arizona Sexual Experience Scale) improved by 46%. Libido moved from "very weak" to "somewhat strong"; sexual arousal from "somewhat difficult" to "somewhat easy"; erectile function from "somewhat difficult" to "very easy"; and satisfaction with orgasm from "somewhat satisfying" to "very satisfying." He continued to use the oxytocin spray daily with no problems and continued benefits.[38]

CASE REPORT TWO

An 82-year-old man had been unable to achieve orgasm since age 78 although he was still sexually active with his wife. Several treatments had been tried with only temporary positive success. After determining that there were no pharmaceutical or psychological reasons inhibiting orgasm, he was given oxytocin nasal spray (20–24 IU) and instructed to use it during intercourse at the point when orgasm was desired. This resulted in achievement of orgasm multiple times per week. At the time the report was published, the patient had had continuing success over a period of eight months.[39]

In women and men, oxytocin has been shown to increase the intensity of orgasm and contentment after intercourse, with the effects being more pronounced in men. Women felt more relaxed after intercourse and were more able to share sexual desires and to empathize with their partners.[40]

A small trial of twenty post-menopausal women investigated the use of a topical oxytocin gel versus placebo gel in treating vaginal atrophy. The women were at least two years post-menopause and had significant symptoms of dryness, pain, itching and bleeding during intercourse. Seven of ten days of rubbed-in oxytocin gel normalized vaginal tissue, as confirmed by instrument-aided visual inspection and biopsy, in seven of ten participants in the oxytocin group. There was no improvement seen in the placebo group. Seven participants in the oxytocin group and four in the placebo group also reported a relief of symptoms. There was no difference in circulating levels of oxytocin or estradiol after treatment.[41,42] Topical oxytocin could be of great benefit to those women with vaginal atrophy for whom topical estrogen is not advisable or desired.

Wound Healing

There are many animal studies demonstrating the role of oxytocin in wound healing in a variety of tissue types and injuries: liver, stomach, kidney, skin, colon, and muscle.[43–47] Human and animal trials have shown that wound healing is improved with social support which also helps to improve internal oxytocin levels.[48–52]

A Russian study found that in patients with diabetic foot ulcers, "the introduction of oxytocin in complex treatment activates the processes of vasculogenesis, proliferation of endotheliocytes and histiocytes, that, in turn, results in the effective clearance of the wound and optimal granulation tissue formation."[53] (In English, oxytocin combined with other treatments stimulates new blood vessel formation that helps heal the wound.)

Muscle and Nerve Regeneration

Recent research tells us that oxytocin can help to regrow muscles and nerves! To grow new muscle after damage, muscle stem cells must be activated. Activation declines with aging, but the decline is reversible

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with oxytocin. Oxytocin stimulates muscle cell stem cells, inducing not only repair but also regeneration of new skeletal muscle!

Oxytocin given to old mice has revived muscle stem cell function, resulting in muscle regeneration after injury comparable to that of young, healthy mice. Young mice that were treated with an oxytocin antagonist showed decreased muscle regeneration, similar to that normally seen in old mice. Age-related muscle degeneration is associated with an increase in fibrotic tissue. Fibrotic damage in the muscle tissue of older mice is reversed when oxytocin is given![6]

Since women naturally have much lower testosterone levels than men, and as oxytocin declines with age in women and men—and since women also (by Nature) live longer than men, it's no wonder that there are many more "little old ladies" than "little old men." Women taking bioidentical hormone replacement can help prevent "little old woman syndrome" with testosterone, but as women's replacement testosterone levels are much lower than men's, women should consider keeping very careful track of their oxytocin levels, and supplementing it for sure if levels are low!

Multiple studies suggest that oxytocin plays a role in peripheral nerve regeneration. The mechanism for this seems to be that oxytocin stimulates the release of Nerve Growth Factor (NGF) and Insulin-like Growth Factor 1 (IGF-1). Plasma levels of NGF and IGF-1 measured during labor and lactation (when oxytocin levels are elevated very significantly) are five times as high as circulating levels of these growth factors in pregnant women at term (but before labor) or in healthy, non-pregnant women. IV oxytocin given to female rats resulted in a near tripling of NGF levels.[54]

In another study, oxytocin or serum was given daily to rats whose sciatic nerves had been severed. The oxytocin group had significantly higher numbers of nerve fibers re-grown across the site of the cut at three, nine, and twelve weeks. Electronic testing of muscle function as well as the ability to climb was significantly better in the "oxytocin group" than the "serum group."[55]

Oxytocin, Stress Relief, and Relaxation

ACTH is a hormone released by our pituitary glands. It signals our adrenal glands to make cortisol, which is often called the "hormone of stress." German researchers reported that giving experimental animals an oxytocin blocker increased secretion of ACTH and cortisol. They concluded that in both men and women, oxytocin slows the release of ACTH, so that less of the stress hormone cortisol is released when oxytocin is given.[56]

For this reason, it may be helpful to some of us to take an oxytocin supplement before going to sleep, as well as taking it before other "bedtimes"!

Measuring Your Oxytocin

We can be certain that in just a few years, there will be many, many more health-promoting effects of oxytocin reported. Who would have thought a decade ago that oxytocin might prevent and reverse osteoporosis?

If you're interested in maximum possible healthy longevity, oxytocin is definitely a hormone to consider using if your levels are low. Check with your physician skilled and knowledgeable in natural medicine about measuring your oxytocin levels.

Oxytocin has a very short half-life, only two to three minutes in plasma, although its effects last considerably longer. This short half-life undermines the meaningfulness of serum testing, especially given a normal peak at mid-day. As with many hormones, a 24-hour urine collection is the best way to measure oxytocin levels, as it is able to account for a full day's production, rather than a "snapshot" in time, as is seen with serum or saliva hormone levels.

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LABS OFFERING OXYTOCIN TESTING

Meridian Valley Lab 6839 Fort Dent Way Tukwila, WA 98188 206-209-4200; 855-405-8378 www.MeridianValleyLab.com	24-Hour Urine Oxytocin Oxytocin alone: $129.00 Add-on to other tests: $99.00
Enzo Life Sciences 10 Executive Blvd. Farmingdale, NY 11735 800-942-0430 www.EnzoLifeciences.com	ELISA (serum) $438.00
FFP Labs 576 Upward Road, Suite 8 Flat Rock, NC 28731 828-694-1144	ELISA (serum) $308.00

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In Washington State and nearly thirty other states, individuals can order their own lab tests. Unfortunately, health "insurance" does not cover self-ordered tests, and in Washington State (and some other states) testing labs can send test results, and talk to physicians about them, but are barred by law from telling you what to do about them.

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Endnotes

1. Wilcox, C. *Muscles Love Oxytocin: So-Called "Hug Hormone" Important In Muscle Regeneration*, Discovermagazine.com. Kalmbach Publishing Company, 27 June 2014. Retrieved September 11, 2015, from http://blogs.discovermagazine.com/science-sushi/2014/06/27/new-study-shows-muscles-love-oxytocin/#.VqETxvkrKCp.
2. Dye, L. *A Love Drug? Oxytocin, the "Cuddle Chemical" to Scientists, Makes Mothers More Kind, Say Researchers* - ABC News 2012. Retrieved November 13, 2015, from http://abcnews.go.com/Technology/love-drug-oxytocin-cuddle-chemical-scientists-makes-mothers/story?id=15330910.
3. Gupta, S. *The Hormones Of Happiness And How To Increase Them*. Retrieved November 9, 2015, from http://www.indiatimes.com/health/healthyliving/the-hormones-of-happiness-and-how-to-increase-them-242282.html.
4. Flechas, J. *Alternative Treatment of -Hormonal-Nutrient Protocol to Increase Nitric Oxide*. The Original Internist 2007 (September): 114–144.http://clintpublications.com/clients/19394/documents/SEPT_OI_2007_Pub.pdf (pp.24-43).
5. Yang, H.-P., Wang, L., Han, L., et al. (2013). *Nonsocial Functions of Hypothalamic Oxytocin*. ISRN Neuroscience, 2013:1–13. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4045544/?tool=pmcentrez.
6. Elabd, C et al. (2014). *Oxytocin is an age-specific circulating hormone that is necessary for muscle maintenance and regeneration*. Nature Communications 2014; 5(1762):4082. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4512838/?tool=pmcentrez .
7. Gimpl, G., & Fahrenholz, F. *The oxytocin receptor system: structure, function, and regulation*. Physiological Reviews 2001; 81(2), 629–83. http://physrev.physiology.org/content/81/2/629.long.
8. Moreno-López, Y. et al. *Identification of oxytocin receptor in the dorsal horn and nociceptive dorsal root ganglion neurons*. Neuropeptides 2013; 47: 117–123 http://www.ncbi.nlm.nih.gov/pubmed/23102456.
9. AAPM Facts and Figures on Pain. (2015). Retrieved November 9, 2015, from http://www.painmed.org/patientcenter/facts_on_pain.aspx.
10. Goodin, BR et al. *Oxytocin—a multifunctional analgesic for chronic deep tissue pain*. Current Pharmaceutical Design 2015:21(7);906–13. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4276444/?tool=pmcentrez.
11. Wang, Y-L et al. *The interaction between the oxytocin and pain modulation in headache patients*. Neuropeptides 2013:47(2);93–7. http://www.ncbi.nlm.nih.gov/pubmed/23375440.
12. Tennant, F et al. *Less Intractable Pain and Opioid Consumption Follow Administration of Pregnancy Hormones, Preliminary Study Shows*. In 2014 AAPM Annual Meeting http://www.painmed.org/2014press/files/less-intractable-pain-and-opioid-consumption-follow-administration-of-pregnancy-hormones.pdf.
13. Kovács,GLetal.*Oxytocinandaddiction: a review*. Psychoneuroendocrinology 1998:23(8);945–62. http://www.ncbi.nlm.nih.gov/pubmed/9924746.
14. McGregor, IS et al. *Breaking the loop: oxytocin as a potential treatment for drug addiction*. Hormones and Behavior 2012:61(3);331–9. http://www.ncbi.nlm.nih.gov/pubmed/9924746 .
15. Sarnyai, Z. *Oxytocin as a potential mediator and modulator of drug addiction*. Addiction Biology 2011:16(2);199–201. http://www.ncbi.nlm.nih.gov/pubmed/9924746.
16. Crujeiras, AB., et al. *Leptin resistance in obesity: An epigenetic landscape*. Life Sciences 2015:140;57–63. http://www.ncbi.nlm.nih.gov/pubmed/25998029.
17. Altirriba, J. et al. (2015). *Chronic Oxytocin Administration as a Treatment Against Impaired Leptin Signaling or Leptin Resistance in Obesity*. Frontiers in Endocrinology 2015:6;119. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4525065/?tool=pmcentrez.
18. Zhang, H. et al. *Treatment of obesity and diabetes using oxytocin or analogs in patients and mouse models*. PloS One 2013, 8(5), e61477. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3658979/?tool=pmcentrez.
19. Blevins, JE., & Ho, JM. *Role of oxytocin signaling in the regulation of body weight*. Reviews in Endocrine & Metabolic Disorders 2013:14(4);311–29. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4213929/?tool=pmcentrez.
20. Elabd C. & Sabry I. *Two Birds with One Stone: Possible Dual-Role of Oxytocin in the Treatment of Diabetes and Osteoporosis*. Frontiers in Endocrinology 2015:6; 121. http://www.

Continued from previous page

ncbi.nlm.nih.gov/pmc/articles/PMC4530313/?tool=pmcentrez.

21. Elabd, C et al. *Oxytocin controls differentiation of human mesenchymal stem cells and reverses osteoporosis*. Stem Cells (Dayton, Ohio) 2008: 26(9); 2399–407. http://onlinelibrary.wiley.com/doi/10.1634/stemcells.2008-0127/epdf.
22. Tamma, R. et al. *Oxytocin is an anabolic bone hormone*. PNAS National of the United States of America 2009:106(17);7149–54. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2678458/?tool=pmcentrez.
23. Beranger, GE et al. *Oxytocin reverses ovariectomy-induced osteopenia and body fat gain*. Endocrinology 2014;155(4); 1340–52. http://www.ncbi.nlm.nih.gov/pubmed/24506069.
24. Breuil, V et al. *Oxytocin and bone remodelling: relationships with neuropituitary hormones, bone status and body composition*. Joint, Bone, Spine : Revue Du Rhumatisme, 2011:78(6); 611–5. http://www.ncbi.nlm.nih.gov/pubmed/21441053.
25. Lawson, EA et al. *Nocturnal oxytocin secretion is lower in amenorrheic athletes than nonathletes and associated with bone microarchitecture and finite element analysis parameters*. European Journal of Endocrinology/European Federation of Endocrine Societies 2013: 168(3),457–64 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3679669/?tool=pmcentrez.
26. Lawson, EA et al. *Decreased nocturnal oxytocin levels in anorexia nervosa are associated with low bone mineral density and fat mass*. The Journal of Clinical Psychiatry 2011, 72(11), 1546–51. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3731046/?tool=pmcentrez.
27. Anagnostou, E. et al. *Intranasal oxytocin versus placebo in the treatment of adults with autism spectrum disorders: a randomized controlled trial*. Molecular Autism 2012:3(1);16. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3539865/?tool=pmcentrez.
28. Anagnostou, E et al. *Intranasal oxytocin in the trea tment of autism spectrum disorders: A review of literature and early safety and efficacy data in youth*. Brain Research 2014:1580;188–198. http://www.ncbi.nlm.nih.gov/pubmed/24508578.
29. Andari E et al. *Promoting social behavior with oxytocin in high-functioning autism spectrum disorders*. Proceedings of the National Academy of Sciences 2010:107(9);4389–4394. http://www.pnas.org/content/107/9/4389.full.pdf.
30. Gutkowska J & Jankowski M. *Oxytocin revisited: It is also a cardiovascular hormone*. Journal of the American Society of Hypertension: 2(5);318–25. http://www.ncbi.nlm.nih.gov/pubmed/20409913.
31. Danalache, BA et al. *Oxytocin-Gly-Lys-Arg: a novel cardiomyogenic peptide*. PloS One 2010:5(10);e13643. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2964328/?tool=pmcentrez.
32. Plante, E. et al. *Oxytocin treatment prevents the cardiomyopathy observed in obese diabetic male db/db mice*. Endocrinology 2015:156(4); 1416–28. http://www.ncbi.nlm.nih.gov/pubmed/25562615.
33. Ondrejcakova, M. et al. (2009). *Oxytocin exerts protective effects on in vitro myocardial injury induced by ischemia and reperfusion*. Canadian Journal of Physiology and Pharmacology, 87(2), 137–42. http://www.ncbi.nlm.nih.gov/pubmed/19234577.
34. Moghimian, M. et al. *The effect of acute stress exposure on ischemia and reperfusion injury in rat heart: role of oxytocin*. Stress (Amsterdam, Netherlands) 2012:15(4);385–92. http://www.ncbi.nlm.nih.gov/pubmed/19234577.
35. Grewen, KM & Light, KC. *Plasma oxytocin is related to lower cardiovascular and sympathetic reactivity to stress*. Biological Psychology, 2011:87(3), 340–9. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3225916/?tool=pmcentrez.
36. Hall, SA et al. *Sexual activity, erectile dysfunction, and incident cardiovascular events*. American Journal of Cardiology 2012:105(2),192–7. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2824175/?tool=pmcentrez.
37. Zhang, Z. et al. *Blockade of phosphodiesterase Type 5 enhances rat neurohypophysial excitability and electrically evoked oxytocin release*. The Journal of Physiology 2007:584(Pt 1);137–47. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2277045/?tool=pmcentrez.
38. MacDonald, K & Feifel, D. (2012). *Dramatic Improvement in Sexual Function Induced by Intranasal Oxytocin*. The Journal of Sexual Medicine 2012:9(5);1407–10. http://www.ncbi.nlm.nih.gov/pubmed/22458365.
39. Ishak, WW. et al. (2008). *Male anorgasmia treated with oxytocin*. The Journal of Sexual Medicine 2008;5(4):1022–4. http://www.ncbi.nlm.nih.gov/pubmed/18086171.
40. Behnia, B. et al. (2014). *Differential effects of intranasal oxytocin on sexual experiences and partner interactions in couples*. Hormones and Behavior 2014,65(3):308–318. http://www.ncbi.nlm.nih.gov/pubmed/24503174.
41. Jonasson, AF. *Topical oxytocin reverses vaginal atrophy in postmenopausal women: a double-blind randomized pilot study*. Menopause International 2011:17(4);120–5. http://www.ncbi.nlm.nih.gov/pubmed/22120944.

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42. Al-Saqi, S. *Intravaginally applied oxytocin improves post-menopausal vaginal atrophy*. Post Reproductive Health 2015:21(3);88-97. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4566058/?tool=pmcentrez.
43. Düşünceli, F et al. *Oxytocin alleviates hepatic ischemia-reperfusion injury in rats*. Peptides 2008:29(7);1216–22. http://www.ncbi.nlm.nih.gov/pubmed/18403049.
44. Işeri, SO et al. *Oxytocin ameliorates skin damage and oxidant gastric injury in rats with thermal trauma*. Burns: Journal of the International Society for Burn Injuries 2008:34(3);361–9.http://www.ncbi.nlm.nih.gov/pubmed/17826914.
45. Biyikli, NK et al. *Oxytocin alleviates oxidative renal injury in pyelonephritic rats via a neutrophil-dependent mechanism*. Peptides 2006: 27(9);2249–57. http://www.ncbi.nlm.nih.gov/pubmed/16707192.
46. Işeri, S. O., Sener, G., Sağlam, B., et al. (2005). *Oxytocin ameliorates oxidative colonic inflammation by a neutrophil-dependent mechanism*. Peptides 2005:26(3);483–91.http://www.ncbi.nlm.nih.gov/pubmed/15652655
47. Petersson, M. et al. *Oxytocin increases the survival of musculocutaneous flaps*. Naunyn-Schmiedeberg's Archives of Pharmacology 1998:357(6);701–4. http://www.ncbi.nlm.nih.gov/pubmed/9686948.
48. Broadbent, E., & Koschwanez, H.E. *The psychology of wound healing*. Current Opinion in Psychiatry 2012:25(2);135–40.http://www.ncbi.nlm.nih.gov/pubmed/22156976.
49. Gouin, J.-P et al. *Marital behavior, oxytocin, vasopressin, and wound healing*. Psychoneuroendocrinology 2010:35(7);1082–90. http://www.ncbi.nlm.nih.gov/pubmed/22156976.
50. Vitalo, A. et al. *Nest making and oxytocin comparably promote wound healing in isolation reared rats*. PloS One 2009:4(5);e5523. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2677672/?tool=pmcentrez.
51. DeVries, AC et al. 2006 *Curt P. Richter award winner: Social influences on stress responses and health*. Psychoneuroendocrinology 2007: 32(6);587–603 http://www.ncbi.nlm.nih.gov/pubmed/17590276.
52. Detillion, CE et al. *Social facilitation of wound healing*. Psychoneuroendocrinology 2004:29(8);1004–11. http://www.ncbi.nlm.nih.gov/pubmed/15219651.
53. Gavrilenko, V et al. [*Morphological characteristic of wound healing process in patients with diabetic purulent-necrotic foot lesion treated with oxytocin*]. Morfologiia (Saint Petersburg, Russia) 2003:124(5);24–7. http://www.ncbi.nlm.nih.gov/pubmed/14870468.
54. Luppi, P. et al. *NGF is released into plasma during human pregnancy: an oxytocin-mediated response?* Neuroreport 1993:4(8); 1063–5.http://www.ncbi.nlm.nih.gov/pubmed/8241466.
55. Gümüs, B. et al. (2015). *Effect of oxytocin administration on nerve recovery in the rat sciatic nerve damage model*. Journal of Orthopaedic Surgery and Research 2015:10(1);161.http://www.ncbi.nlm.nih.gov/pubmed/26466786.
56. Neumann ID, Wigger A, Torner L, Holsboer F, Landgraf R. *Brain oxytocin inhibits basal and stress-induced activity of the hypothalamo-pituitary-adrenal axis in male and female rats: partial action within the paraventricular nucleus*. J Neuroendocrinol. 2000 Mar;12(3):235-43.