

The Positive Effects of Human Touch on Skin Health

NIVEA SKIN SCIENCE REPORT 2021

CCZ

Contents

6–7	Foreword
8–11	Human Touch: The Secret to Healthy Skin? Discover the Science and Magic behind the Brain-Skin Connection
11	References
14–16	130 Years and Counting: When Skin Comes First An Interview with Dr. May Shana'a
18	Imprint

OREWORD

Foreword by Ralph Zimmerer, Vice President Global NIVEA Brand Identity & Brand Capability

Some time ago at NIVEA, we engaged in a global brand workshop in which we brainstormed about the future of the brand – and challenged ourselves by asking: what has made NIVEA the No. 1 skin care brand in the world?

The answer seemed simple when we looked back at our history. From the beginning, more than 100 years ago, skin always came first at NIVEA. Our focus as a brand has been on studying skin, understanding it deeply, and investing in long-term research to find solutions for keeping skin healthy. Because we have always believed that only when we feel good in our skin – healthy and beautiful – can we reach out to others and bond.

With this in mind, our global skin research team sponsored a dissertation in the early 2010s, which was the cornerstone of an important discovery: our skin cells have a fully functional receptor for oxytocin. This neuropeptide, with its numerous health benefits, is often called the "happiness hormone" because its level in our blood increases if we cuddle and touch people close to our hearts. How encouraging for us at NIVEA! Skin-touch moments and togetherness does more than just make us feel good; it also has the potential to improve our health, well-being, and our skin.

In 2020, our scientists made another important discovery in vitro, confirming the positive effects of oxytocin on sensitive skin. It can make sensitive skin calmer and less prone to stress and inflammation – and it might even have positive effects on the skin aging process. These breakthrough discoveries will influence the way that we prevent and treat a variety of skin issues in the future.

To summarize, the science at hand is clear: there is strong evidence that oxytocin is significantly involved in the beneficial effects of touch for our physical and mental health as well as for healthy, beautiful skin.

That is why we at NIVEA are standing up for more skin-touch opportunities with our new NIVEA #CareForHumanTouch initiative.

Enjoy reading this report and learning more about our research journey. Sending a virtual hug,

RALPH ZIMMERER



7

Oxytocin Formula

Human Touch: The Secret to Healthy Skin?

Discover the Science and Magic behind the Brain-Skin Connection

hen we are feeling sad, lonely, or anxious, few things make us feel better than the embrace of a loved one. Even stroking a beloved pet is enough to create a surge of positive emotions and put us in a better mental state. But these feel-good hormones released by the act of touch do much more than increase our happiness; they have a significant influence on our health and overall well-being in ways that science is only beginning to discover. To understand the mysterious brain-skin connection and the implications of touch on our health, we must look to a powerful hormone with a reputation for playing cupid – oxytocin.

Understanding Oxytocin-The "Love Hormone"

Oxytocin is a neuropeptide – a small protein made of just nine amino acids, the building blocks of proteins. It is mainly produced in certain parts of the brain and then released into the bloodstream, although small amounts are also produced in several other parts of the body, including reproductive organs and even skin cells [1]. Over the years, the scientific community has learned a great deal about the general effects of oxytocin on the body. It is proven to play an essential role in childbirth, and in reproductive and social behaviors. It also contributes to everyday wellbeing [3,4,5], counteracting stress (psychological as well as physiological) [6,7], lowering blood pressure [8], regenerating muscles [9], forging feelings of attachment and creating stronger social bonds [10,11]. Moreover, numerous studies give clear evidence that stroking, cuddling, and physical contact with loved ones correlate with an increased oxytocin level in the blood [3,12,13,14] - suggesting that oxytocin

is released by touch. This correlation between loving touch and increased oxytocin levels has led to oxytocin's popular nickname, "the love hormone."

Numerous studies give clear evidence that stroking, cuddling, and physical contact with loved ones correlate with an increased oxytocin level in the blood - suggesting that oxytocin is released by touch.

While oxytocin's feel-good effects are generally well known, for years scientists have been studying this magical neuropeptide to understand how it works on a deeper level. Scientific studies confirm oxytocin's positive effects on our physical and psychological health, but scientists are still interested in taking a closer look at oxytocin and understanding its regulation at the cellular level. We now know that a hug from a friend, for example, triggers our nervous system to send a signal to the brain, which in turn releases oxytocin. After leaving the brain, oxytocin then travels throughout the body, communicating with all kinds of body cells in our organs, bones, and even our skin. However, only the cells having a specific docking station for oxytocin – a so-called oxytocin receptor – are able to receive the communication signal.

Scientific studies confirm oxytocin's positive effects on our physical and psychological health.

Pro Cys HN Leu Gln 0 Asn NH_2

The oxytocin receptor is located on the surface of the cell. The binding of oxytocin causes structural changes to the receptor. What happens next is fascinating. Like a Rube Goldberg machine or a row of dominoes, a complex chain of reactions is initiated within the cell: enzymes get activated, biological transporting gates are opened, messenger substances are converted, some proteins are produced while some are stopped from being produced, and signaling molecules are released to tell the neighboring cells how to behave. This sounds complicated and precisely regulated, but our cells know exactly how to answer. The response of the cell varies, depending on the type of cell oxytocin binds to. That's one explanation for the wide range of feel-good effects on all kind of body functions, from muscles to blood pressure, just to name a few.

Oxytocin's Role in the **Health of Our Skin**

Now that we know that oxytocin is involved in a multitude of processes in the body, it raises the question: does oxytocin also play a role in our skin? Given that oxytocin has an anti-stress effect, and that the skin is an organ highly vulnerable to stress due to its exposure to all kinds of harmful environmental factors (e.g. UV radiation and air pollution), this question has both urgent and exciting implications for our skin health.

That is why, for years, Beiersdorf R&D has intensively investigated oxytocin biology and its beneficial effects on skin. In the early 2010s, a PhD thesis at Beiersdorf uncovered interesting findings about the oxytocin system in human skin. In the course of this groundbreaking work, it was scientifically proven that the oxytocin receptor is present and fully functional in skin tissue and skin cells [15, 16]. To deeply understand oxytocin's function in human skin, Beiersdorf researchers used a common scientific practice – they artificially removed the oxytocin receptor to observe what happens: without oxytocin, skin cells show signs of increased stress. In addition, skin cells obtained from people suffering from eczema, a common skin disease, show both lower levels of oxytocin and its corresponding receptor – an important finding that clearly connects a lack of oxytocin signaling and diseased skin.

The oxytocin receptor is present and fully functional in skin tissue and skin cells.

This research helped scientists understand what happens when the oxytocin system malfunctions, leading to another logical question: what happens when oxytocin levels in skin are increased?

Thus, in 2020, Beiersdorf researchers performed additional experiments, supplementing skin cells with oxytocin, and the findings clearly indicate a positive effect of oxytocin on skin sensitivity. Oxytocin supplementation lowers the concentrations of cytokines, signaling molecules associated with inflammatory skin diseases like eczema and psoriasis. Even after the addition of inflammatory substances, skin cells kept calm and the secretion of cytokines was reduced, meaning the cells were less vulnerable to inflammation [17]. In other words, oxytocin can help decrease inflammation and skin sensitivity in cell culture systems.

Oxytocin can help decrease inflammation and skin sensitivity in cell culture systems.

But that's not all. The research also suggests that oxytocin can have a positive influence on the skin aging processes. Experimental studies have shown that cytokines are also involved in a phenomenon called senescence – aging of cells. Senescent cells make the skin appear older and less healthy. Supplementation of oxytocin positively influences the biology of senescent skin cells. This finding has been confirmed in the scientific community, indicating that targeting the oxytocin system might be a promising approach to improving age-associated skin changes [18].

Conclusion: Skin Benefits from Human Touch

Oxytocin exerts numerous positive effects on our body and mind, including lowering blood pressure, increasing feelings of attachment, and reducing inflammation. And while there is so much still to learn about this mysterious neuropeptide, one thing is for certain: oxytocin is released by touch, and skin cell metabolism is receptive and responsive to increasing oxytocin levels. Thus, there is strong scientific evidence that oxytocin is significantly involved in the beneficial effects of touch, not only for our physical and mental health, but also for healthy, beautiful skin.

Oxytocin is released by touch, and skin cell metabolism is receptive and responsive to increasing oxytocin levels.

Dr. Tanja Bussmann (born in 1985):
Studied biochemistry at Bielefeld University and the University of Bristol, UK (BA and MSc). In 2015, submission and successful defense of her PhD thesis at the University of Hamburg (in cooperation with the University Medical Center Hamburg-Eppendorf and Beiersdorf AG) in the field of biochemistry. Since 2015, researcher in the Front End Innovation department at Beiersdorf. Work focus: dermatological research on the subject of skin aging and diseased skin, as well as scientific claim support for cosmetic products.



References

- Jurek B., Neumann I.D. "The Oxytocin Receptor: From Intracellular Signaling to Behavior." Physiol Rev. 2018 Jul. 1; 98(3): 1805–1908. doi: 10.1152/physrev. 00031.2017. PMID: 29897293.
- Ding C., Leow M.K., Magkos F. "Oxytocin in metabolic homeostasis: implications for obesity and diabetes management." Obes Rev. 2019 Jan.; 20(1): 22–40. doi: 10.1111/obr.12757. Epub 2018 Sep 25. PMID: 30253045.
- Uvnäs-Moberg K., Handlin L., Petersson M. "Self-soothing behaviors with particular reference to oxytocin release induced by non-noxious sensory stimulation." Front Psychol. 2015 Jan. 12; 5: 1529. doi: 10.3389/ fpsyq.2014.01529. PMID: 25628581; PMCID: PMC4290532.
- Uvänas-Moberg K., Arn I., Magnusson D. "The psychobiology of emotion: the role of the oxytocinergic system."
 Int J Behav Med. 2005; 12(2): 59–65. doi: 10.1207/s15327558ijbm1202 3. PMID: 15901214.
- Ishak W.W., Kahloon M., Fakhry H. "Oxytocin role in enhancing well-being: a literature review." J Affect Disord. 2011 Apr.; 130(1–2): 1–9. doi: 10.1016/j.jad.2010.06.001. Epub 2010 Jul 2. PMID: 20584551.
- Esch T., Stefano G.B. "The neurobiological link between compassion and love." Med Sci Monit. 2011 Feb. 25; 17(3): RA65–75. doi: 10.12659/msm.881441. PMID: 21358615; PMCID: PMC3524717
- Uvnäs-Moberg K. "Antistress Pattern Induced by Oxytocin." News Physiol Sci. 1998 Feb.; 13: 22–25. doi: 10.1152/ physiologyonline.1998.13.1.22. PMID: 11390754.
- Gutkowska J., Jankowski M., Antunes-Rodrigues J. "The role of oxytocin in cardiovascular regulation." Braz J Med Biol Res. 2014 Feb.; 47(3): 206–214. doi: 10.1590/1414-431X20133309. Epub 2014 Mar 18. PMID: 24676493; PMCID: PMC3982941.
- Elabd C., Cousin W., Upadhyayula P., Chen R.Y., Chooljian M.S., Li J., Kung S., Jiang K.P., Conboy I.M. "Oxytocin is an age-specific circulating hormone that is necessary for muscle maintenance and regeneration." Nat Commun. 2014 Jun. 10; 5: 4082. doi: 10.1038/ncomms5082. PMID: 24915299; PMCID: PMC4512838.
- Lee H.J., Macbeth A.H., Pagani J.H., Young W.S. "3rd. Oxytocin: the great facilitator of life." Prog Neurobiol. 2009 Jun.; 88(2): 127–151. doi: 10.1016/j.pneurobio.2009.04.001. Epub 2009 Apr 10. PMID: 19482229; PMCID: PMC2689929.

- Olff M., Frijling J.L., Kubzansky L.D., Bradley B., Ellenbogen M.A., Cardoso C., Bartz J.A., Yee J.R., van Zuiden M. "The role of oxytocin in social bonding, stress regulation and mental health: an update on the moderating effects of context and interindividual differences." Psychoneuroendocrinology. 2013 Sep.; 38(9): 1883–1894. doi:10.1016/j.psyneuen.2013.06.019. Epub 2013 Jul 12. PMID: 23856187.
- Light K.C., Grewen K.M., Amico J.A. "More frequent partner hugs and higher oxytocin levels are linked to lower blood pressure and heart rate in premenopausal women." Biol Psychol. 2005 Apr.; 69(1): 5–21. doi: 10.1016/j. biopsycho.2004.11.002. Epub 2004 Dec 29. PMID: 15740822.
- Odendaal J.S., Meintjes R.A. "Neurophysiological correlates of affiliative behaviour between humans and dogs." Vet J. 2003 May; 165(3): 296–301. doi: 10.1016/s1090-0233(02)00237-x. PMID: 12672376.
- Holt-Lunstad J., Birmingham W.A., Light K.C. "Influence of a 'warm touch' support enhancement intervention among married couples on ambulatory blood pressure, oxytocin, alpha amylase, and cortisol." Psychosom Med. 2008 Nov.; 70(9): 976–985. doi: 10.1097/PSY.0b013e 318187aef7. Epub 2008 Oct 8. PMID: 18842740.
- Deing V., Roggenkamp D., Kühnl J., Gruschka A., Stäb F., Wenck H., Bürkle A., Neufang G. "Oxytocin modulates proliferation and stress responses of human skin cells: implications for atopic dermatitis." Exp Dermatol. 2013 Jun.; 22(6): 399–405. doi: 10.1111/ exd.12155. PMID: 23711064.
- Denda S., Takei K., Kumamoto J., Goto M., Tsutsumi M., Denda M. "Oxytocin is expressed in epidermal keratinocytes and released upon stimulation with adenosine 5'-[y-thio triphosphate in vitro." Exp Dermatol. 2012 Jul.; 21(7): 535–537. doi: 10.1111/j.1600-0625.2012.01507.x. Epub 2012 May 14. PMID: 22583056.
- Duarte I., Silveira J.E.P.S., Hafner M.F.S., Toyota R., Pedroso D.M.M. "Sensitive skin: review of an ascending concept." An Bras Dermatol. 2017 Jul.—Aug.; 92(4): 521–525. doi: 10.1590/abd1806-4841.201756111. PMID: 28954102; PMCID: PMC5595600.
- Cho SY., Kim A.Y., Kim J., Choi D.H., Son E.D., Shin D.W. "Oxytocin alleviates cellular senescence through oxytocin receptormediated extracellular signal-regulated kinase/Nrf2 signalling." Br J Dermatol. 2019 Dec.; 181(6): 1216–1225. doi: 10.1111/bjd.17824. Epub 2019 Jun 23. PMID: 30801661





130 Years and Counting: When Skin Comes First

At the helm of Beiersdorf's global research and development, May Shana'a leads a team of about 900 researchers and developers in four laboratories around the world. Together they continuously search for new biological opportunities in service of healthy and beautiful skin. We talked to Dr. Shana'a about the progress of skin research and the influence of physical touch on skin.

Dr. Shana'a: When you joined Beiersdorf, your task was to turn a big vision into a reality: to be the No. 1 in skin research. What does it take to be the No. 1 today?

To be the No.1 in research today compared to 10 or 20 years ago requires a different approach. The scientific world has changed tremendously and opened new channels for experimentation that we did not have before. When I started my scientific journey, scientists were very private people. They hid their research behind closed doors, kept all the insights for themselves, finished everything – and then wrote the paper. For many reasons, this approach doesn't work any longer. There are so many new scientific advancements and discoveries every day, which is mind-blowing. To even try to be the expert in every field is impossible. Therefore, to be able to compete you must reach out to all the experts outside your company. That is the most important success factor. You must bring together all the information from different disciplines. You must know whom to connect with and how. That applies to universities, institutes, and individual researchers. This is the only way to be ahead of the game. If someone wants to throw another billion euros at me to do research better and faster, I would still say we could not do it alone because we would need to open up and collaborate with the outside world.

This enhanced collaboration leads to great results and speed of delivery. A good and very current example is the discovery of the vaccine against the coronavirus. Under normal circumstances, each company would be secretly

working on it and governments would not be involved. In this case, knowledge is shared across companies. Although the solutions for the COVID-19 vaccine are based on the same mRNA technology, they differ in their stability and maybe efficacy—and that is where the special skills of the scientists come through. What makes it successful is not only the collaboration between scientists but also the collaboration of the whole ecosystem that enabled such discoveries to move as fast as possible. As devastating as this pandemic is, I hope it will inspire us to replicate these processes in the future and to move faster by collaborating. I predict the next generations of Nobel Prize winners will reflect this new reality. More and more prizes will be shared across research entities.

If research today is open, transparent, and collaborative, how does any company even get an edge over the others?

The edge lies in applying the knowledge through innovation. This is where knowledge and experience come to play. You have access to the vast field of research out there – but what do you do with it? That's the secret we don't share. Everybody can do mathematics. But amazing mathematicians can derive insights from the numbers. The same with skin understanding. There is a vast amount of knowledge on aging skin available for everyone, but what you do with that knowledge is what gives you an edge. You will gain an edge if you translate information about aging skin and turn it into a product or recommendation that truly helps the consumer.

How would you describe the progress that skin research has made over the years? What do we know about skin cells today?

You can write books about how the knowledge has changed over the years, even if you just talk about skin in isolation and not how it depends on the rest of the body.

As for the skin cells and what we know about them: what's important for our work is testing the effect of stressors in our labs – not only on the cells, but also on living skin replicas that we cultivate in our laboratory. In addition to investigating the effect of triggers on individual cell cultures, we can research what a series of triggers can do to a cell over time and how the whole skin responds to the same triggers and whether the response eventually produces wrinkles or pimples, causes age spots, or leads to diseases such as atopic dermatitis. Over the years, we have learned more and more about these little triggers and how they are activated. As scientists, we now try to select any of these triggers and see how we can influence them to improve the skin's condition. A good question would be: does physical touch or happiness trigger a reaction of the skin cells?

"Healthy skin is beautiful skin," said Dr. Troplowitz, the cofounder of Beiersdorf. Does healthy and beautiful skin also make you happy?

It's actually the other way round: we know that if you feel good and if you are happy, it affects your health. Scientifically speaking, our brain is an amazingly responsive machine; when it's happy, sad, or tired, it releases materials that affect your body—for example, oxytocin, which is released into your body if you are happy. It travels through your bloodstream and goes everywhere, including your skin. We have evidence that oxytocin is received by the special receptors in the skin. That's good news. So now we know the path and the trigger. We know that oxytocin makes it to the

skin. Now, what does oxytocin do exactly? Imagine it as a visitor – we first need to find out if it is a friendly visitor or a rowdy visitor. And does it accomplish anything? Or does it just come, spend the night, and nothing happens? We must rely on correlations to answer these questions, because we cannot measure directly what it does. The evidence we currently have is that oxytocin can downregulate inflammatory mediators. That simply means you have less inflammation, which is ultimately good for the skin. So that's how happiness affects your skin.

Earlier, you mentioned physical touch as a trigger. Is it really possible that the act of hugging affects your skin?

The human brain can release oxytocin for many reasons—when you enjoy something or you love something or some-body, when you can touch your dog, or have a lovely dinner. All of this makes you happy and releases oxytocin. And when we hug one another, we feel happy—and oxytocin is released then as well. So, yes, it is possible that the act of hugging can improve your skin.

Mediterraneans like me communicate through touch. With COVID-19 in full swing, social distancing means that not only do I have to change the way I communicate, but also that one of my mechanisms for releasing oxytocin is switched off. I don't want to talk only about the effect on beautiful skin here. Oxytocin has many other health benefits. In the end, it is really important for our well-being as humans. If people are isolated for a long period of time, they suffer both mentally and physically. This has been studied by sociologists, psychologists, and other specialists. And when touch happens, it influences all your organs – not only your skin but also your heart, your immune system, etc. It's incredible how all of this is interconnected. And more evidence on the effects of touch on the skin are bound to come over time.

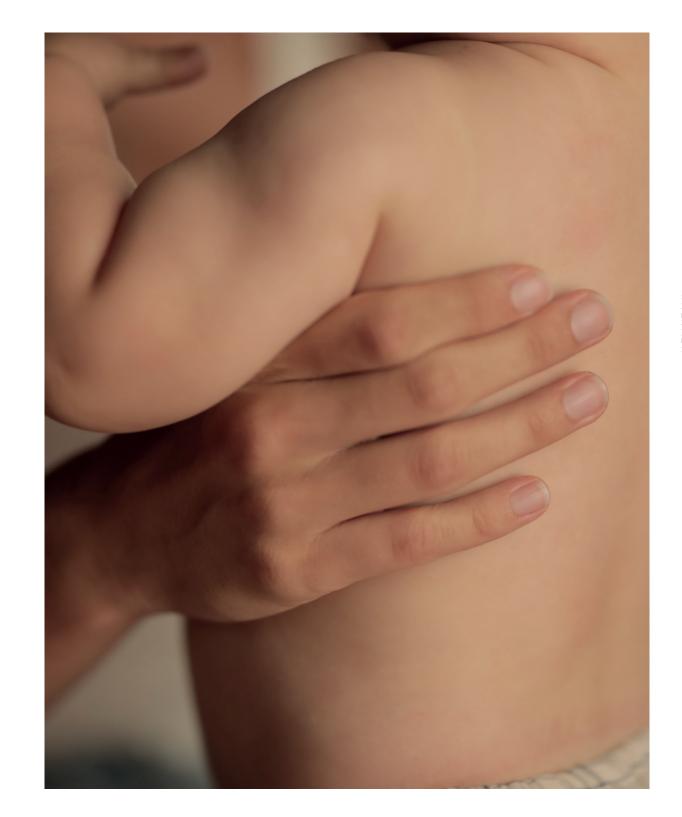
Can you tell us about the role of R&D at Beiersdorf? How important is your environment for the kind of work you do?

It is worth acknowledging that over the 130 years of its existence, Beiersdorf has always invested in Research and Development. R&D is well recognized as a fundamental part of our success. Many companies launch new things all the time, but every now and then you get one or two hits that change the game for that company. It gives the company a boost and propels its growth. The things that provide a serious boost in growth are usually those that involve a fundamental innovation, not just another variety of something that already exists. Growth comes from these special spikes, and these special spikes take time to create. They require unique scientific discoveries. These spikes carry the company over many years. Let's look at one of our oldest spikes, Q10. It was launched over 20 years ago. It is probably one of our biggest franchises and is still a major contributor to Beiersdorf's success. Another spike came with the antistaining technology for deodorants, supplying a boost to the deodorant segment that the latter has been enjoyed for nearly a decade. The latest spike came with Luminous 630, the antipigment ingredient that has made its way to the market and will prove to be one of the biggest spikes in the history of the company.

My simple message is that companies must continuously invest in Research and Development, year after year. Discoveries cannot be planned, and research cannot be switched on and off like an advertising campaign. It's consistent and very hard work, and if you stick to it, it pays off. The evidence is clear in our history.

Dr. May Shana'a, Beiersdorf's Head of Global Research and Development, has more than 30 years of expertise managing global R&D departments at multinational companies. Before joining Beiersdorf, Dr. Shana'a assumed international leadership positions in the research departments of Johnson & Johnson and Unilever in Italy, USA, and the UK. Dr. Shana'a is among the world's leading innovation experts in skin care.





Graphic Design: Nicole R. Schardt

NIVEA Skin Science Report:
The Positive Effects of Human Touch on Skin Health

© 2021, Beiersdorf AG, Global NIVEA Brand Identity and Brand Capability Beiersdorf AG Unnastrasse 48 20245 Hamburg