The best opioids don't come in a bottle …but are found in small enjoyable activities

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Introduction

Chronic pain affects over 1.5 billion people worldwide and its medical management including both non-pharmacological and pharmacological approaches continue to be a challenge. A common pharmacological intervention strategy for persistent pain includes the use of opioids. Opioids are a class of drugs that include the illegal drug heroin, synthetic opioids such as fentanyl, and pain relievers available legally by prescription, such as oxycodone, hydrocodone, codeine, and morphine.

Most people get at least temporary and partial pain relief from opioids hence it is a $13-billion-a-year industry (That's billion, with a B!), however the potential risks versus benefits with their use is continuously being questioned. Studies spanning over a decade have shown that disappointingly, that long-term opioid therapy did not result in long term improvements in pain, function or quality of life (Birke et al 2017).

The prevalent use of opioids to manage chronic pain has led to an opioid epidemic due to the dramatic rise in opioid addiction and over-doses.

Are there alternative options for individuals who need desperate relief from the suffering associated with severe persistent pain?

Are there alternative options for physicians and other health care providers who desperately wish to help them?

The aim of this booklet is to review the current controversies on opioid use for chronic non-cancer pain and provide alternative options for health care professionals and patients to consider.

The use of opioids has been supported for acute post surgery and individuals with cancer pain, however there is now evidence against the use of opioids for patients with fibromyalgia (Littlejohn et al 2016), persistent musculoskeletal conditions such as chronic low back pain (Krebs et al 2018) and chronic pelvic pain (Cichowski et al

2018). For instance a study published in the journal Pain showed that patients with chronic low back pain provided with sham opioids (placebo) had similar improvements in pain and activity levels (Klinger et al 2017).

"Results do not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain" (Krebs et al 2018)

"Chronic opioid therapy is not recommended for chronic pelvic pain" (Cichowski et al 2018)

"There is no evidence that pure opioids are effective in fibromyalgia" (Littlejohn et al 2016)

Even when prescribed for non-cancer pain, the most recent guideline recommends avoiding opioid therapy for longer than 90 days (Rosenberg et al 2018).

Sadly, opioids prescribed by a physician or purchased from a dealer are now killing as many Americans, on an annual basis, as firearms, and shockingly accounts for more deaths than breast cancer. In fact drug overdose deaths related to prescription opioids has now surpassed automobile accidents as the number one cause of accidental death in the United States.

It has been the cause of death for musicians such as Tom Petty and Prince.

Other than the several serious adverse effects and addictions associated with their use, there is another opioid issue that is not getting enough media attention; **Opioid Induced Hyperalgesia (OIH)**. The word *"hyperalgesia"* is used to describe the condition involving an abnormally heightened sensitivity to pain. OIH is the phenomenon of a paradoxical increased pain sensitization secondary to long term opioid exposure.

In simple terms, OIH occurs when exogenous opioids (externally put into the body) actually decrease endogenous opiates production worsening the pain and stress intensity. As this occurs, patients require increasing amounts of exogenous opioids via medications to experience the same level of analgesia and improved mood (Simonnet et al 2003). There are now a number of papers describing the detailed physiology behind the OIH phenomenon (Yang et al 2018, Roeckel et al 2016, Grace et al 2015).

Endogenous opioids

(E.g. endorphin, enkephalins)

Body's own painkiller and mood enhancer

When available, it reduces the need for exogenous opioids

Exogenous opioids

E.g. oxycodone, heroin

Prescribed or illegally purchased

When in excess, reduces the production of endogenous opioids

If a patient has been on opioid medications for several months and continues to worsen, open communication with a physician regarding OIH must be encouraged by asking, *"Could these pain killers be actually making my pain worse? And how can I wean off them?"*

We obviously do not want patients' pain to worsen when they get off the opioids, so what does the research say happens when they are weaned off them?

"Pain intensity following discontinuation of long-term opioid therapy does not, on average, worsen for patients and may slightly improve, particularly for patients with mild-to-moderate pain at the time of discontinuation." (McPherson et al 2018)

The keyword here is on average, there are some who actually get dramatically better when they discontinue all opioids. Sadly opioid tapering off programs are not often successful due to the vast number of dropouts (Kurita et al 2018).

Physicians are truly stuck between a rock and a hard place as on one hand they are obligated to help patients who are suffering from severe and often intolerable pain and on the other hand they must calculate the potential risks for that individual patient. A number of papers are now urging physicians to be more cautious with opioid prescription for non-cancer pain (McCarthy 2016, Moore et al 2017).

What if focus was shifted away from exogenous opioids to endogenous opioids?

Endogenous opioids include the neurotransmitters enkephalin and endorphins which are produced by the central nervous system and the pituitary gland. The word endorphin consists of two parts: endo- and -orphin; these are short forms of the words endogenous and morphine, meaning *"a morphine-like substance originating from within the body"*. In the past two decades several studies have demonstrated the role of endorphins in reducing the intensity and the unpleasantness of experimentally induced painful stimuli (Fields 2004, Kut et al 2011). It is

hypothesized that endorphins play a role in minimizing the negative effects of painful and stressful experiences if they are deemed unnecessary for survival (Guillemin 1977).

However, other than during pain and stress, endorphin production has also been shown to be triggered by various activities such as intense aerobic exercise (Bidari et al 2016), high-intensity interval training (Saanijoki et al 2018), core stabilization exercise (Paungmali et al 2018), listening to music (Vollert et al 2003), singing in a choir (Weinstein et al 2016), creating and maintaining new social relationships (Machin et al 2011), dancing in a social setting (Tarr et al 2015), social touching (Nummenmaa et al 2016), and social laughter (Manninen et al 2017, Dunbar et al 2012).

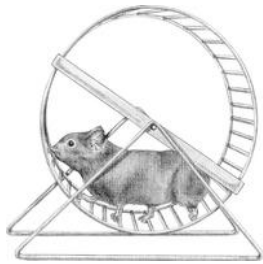
Although there are several options, it must be emphasized that there is no single activity outside of laughter that consistently produces endorphins for everyone. The potential release of endorphin occurs only if the specific activity is valued or pleasurable to the unique individual (Chelnokova et al 2014).

The intention of this paper is to provide health care professionals with several prescription options for potentially releasing endogenous opioids in order to help reduce the need for exogenous opioids. They include participation in (i) **intense physical exercise**, (ii) **self-selected daily life activities**, (iii) **social laughter**, (iv) **social activities**, (v) **social touching**, and (vi) **music therapy**.

Intense Physical Exercise

People who participate in regular physical activity are less likely to develop persistent musculoskeletal pain (Landmark et al 2013). Several animal and human studies have demonstrated that endogenous opioids may play a role in analgesia produced by exercise (Debruille et al 1999, Lima et al 2017, Brito et al 2017). Instead of primarily focusing only on passive interventions for pain elimination, health care providers should ideally be more focused on guiding patients to participate in enjoyable physical activities.

"…long-term voluntary wheel running (in rats) produces analgesia through



activation of endogenous inhibitory mechanisms that include opioids… We propose that exercise resets the nervous system, so that subsequently painful stimuli normally perceived as painful in sedentary individuals, are not perceived as painful in active individuals." (Brito et al 2017)

To stimulate endogenous opioid production, health care providers could prescribe a daily dose of enjoyable moderate intensity physical exercise.

Prescription options:

1) Participate in aerobic, dance or martial arts classes
2) Go for a walk/jog in the park
3) Join a pole walking group

Self-selected daily life activities

For individuals with persistent pain, participation in any form of intensive exercise is often met with much resistance. Although many are aware of the potential benefits of a daily exercise routine, they simply cannot find the motivation or desire to participate in activities that they

deem as potentially dangerous for their body and likely to exacerbate their symptoms.

Perhaps instead of focusing on “exercise” which some find intimidating, health care providers could simply prescribe the gradual return to meaningful and joyful activities of daily living (ADLs).

In one study, as an alternative to exercise, individuals with fibromyalgia were prescribed participation in self-selected lifestyle activities by a physical therapist (Fontaine et al 2010). The aim of each therapy session was to help the patients find practical situations to accumulate short bouts of moderate-intensity physical activity throughout the day. The therapist was also responsible for education on activity scheduling and pacing when doing their ADLs. This is often necessary to prevent people from “over-doing it” and better acknowledge their current limits. They found that accumulating 30 minutes of doing small daily activities (walking the dog, gardening, baking, doing

the laundry, short duration grocery shopping, etc.) throughout the day for 3 months was beneficial in improving pain and functional scores (Fontaine et al 2010).

Another study on patients with persistent low back pain tested a unique yet common sense intervention approach. The intervention was patient-led goal setting facilitated by a physical therapist over a 2-month period (no medication, no manual therapy and no exercise prescription) (Gardner et al 2016).

The patients were given a *"Goal Handbook"* that was used to record their personal goals, their progress, any barriers and strategies to achieve the goals. Over the 2-month period, they had significant improvements in their disability, pain, fear avoidance beliefs, quality of life and self-efficacy which were maintained for another 2 months after the study. What is most fascinating is that the majority of the goals set by the patients were not actually achieved within the 2-month period of the study. It can be hypothesized that the joy felt with the achievements of small goals while in the

pursuit of a grander meaningful goal may be the primary factor that is required to release endorphins.
To stimulate endogenous opioid production, health care providers could focus on patient-led goals to help them return to meaningful and joyful life activities.

Prescription options:

Ask patients “Tell me, what daily life activity is important to you and you really wish to get back into doing?”

1) Yard work and gardening
2) Cooking and baking for the family
3) Cleaning the house (vacuum, dust, tidy up)

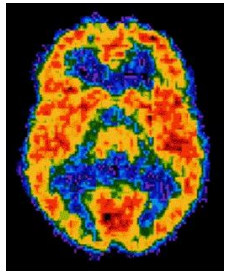
Social Laughter

Charles Darwin's was quite accurate with his original proposal that *“laughter is a kind of tickling of the mind”* (Darwin, 1872).

Laughter is the ultimate expression of positive social emotion, occurring during social interactions for bonding purposes (Scott et al 2014). Considering that laughter is

contagious, the word “social” must be emphasized as research has shown that in humans, laughter (therefore endorphin release) is 30 times more likely to occur in social contexts than when done alone (Provine et al 1989). Social laughter allows simultaneous opioid release among all the members of a group and plays a critical role in allowing humans to live in social networks (Dunbar et al 2012).

Using positron emission tomography (PET) scans, it has been shown that laughter triggers endorphin release in brain regions involved in processing of rewards and nociception leading to both calmness and amusement (Manninen et al 2017).



To stimulate endogenous opioid production, health care providers could prescribe a daily dose of laughter.

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Prescription options:

1) Go to a playground with a child and laugh along

2) Invite friends over to watch a movie 1-2 times week

3) Laugh out loud (LOL) for 1 minute for no reason once at 7am and once at 7pm

Social Activities

The extent of an individual's social relationships has been strongly associated with their health, where those with strong social relationships have been shown to have fewer physical and psychological illnesses and even quicker recovery from surgery (Pearce et al 2017).

There are several papers revealing an association between social isolation and persistent pain where social isolation may increase the risk of developing persistent pain and those who develop persistent pain are more likely to become socially isolated (Inagaki et al 2016, Machin et al 2011).

Studies ranging from primates to humans conclusively show that close social bonds are essential for emotional and physical health; endorphins have been proposed to underlie the interpersonal feelings such as affection that come from both platonic and romantic connections (Keverne et al 1989, Baumeister 1995, Inagaki et al 2016).

So which one comes first? The chicken or the egg? Social isolation or persistent pain? Ironically a study on chicks may help answer that question (Panksepp et al 1980). Healthy social chicks were injected with the opioid blocker naloxone and were then either socially isolated or were put back into the group. The blocking of endorphin increased the chicks' distress vocalization when they were put back into the group indicating they no longer experienced pleasure and comfort from being in a group, but received comfort from being alone.

The same phenomenon has been shown in non-human primates where opioid agonists decreased and antagonists increased social grooming

(Nummenmaa et al 2018). It is concluded that endorphins contribute to the pleasure and comfort we feel when we experience social bonding and connecting with close others.

What can we learn from chicks and primates? If the exogenous opioids (prescribed medications) inhibit our patients' endogenous opioids (endorphins), they will lose pleasure and comfort from social interactions and close relationships. In extreme cases, the disruption of the endogenous opioid system partly explains the antisocial behavior seen in heroin addicts (Nummenmaa et al 2018).


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To partially explain the lack of desire for individuals with persistent pain to socialize one must accept that endorphins are a critical component of social bonding and for day-to-day social connections (Inagaki et al 2016). Ironically individuals with persistent pain would greatly

benefit from maximizing their social support especially in their times of need. To stimulate endogenous opioid production, health care providers could prescribe a daily dose of social connections.

Prescription options:

1) Join a community center program, e.g. cooking, painting, pottery, dance or Yoga classes

2) Plan to meet a family or friend everyday for tea or coffee in a public setting

3) Invite a few friends over for dinner at your home

Social Touching

Skin-to-skin contact has been shown to be vital for healthy mental, emotional and physical development of various animals and new born human infants (Dunbar 2010, Hertenstein et al 2006).

Social touching assists in maintaining the various emotional human bonds ranging from intimate romantic bonds to friendships (Suvilehto et al 2015). Not surprisingly social touch is positively associated with greater positive emotional sensations in closer relationships (Suvilehto et al 2015); therefore the degree of endorphin release associated with social touching is purely based on the individuals' perspective of the experience when being touched. When the social touch is perceived a non-threatening and pleasing (non-sexual), endogenous opioids are released enhancing the social experience (Nummenmaa et al 2016).

In one study male subjects laid in a positron emission tomography (PET) scanner while their partners caressed their bodies in a non-sexual fashion. The study revealed that pleasurable social touch triggered increased μ-opioid receptors availability in the cerebral cortex (Nummenmaa et al 2016).

Primates and humans have evolved to crave the endogenous opioid release associated with social touching in order to maximize social boding and the likelihood of

survival. Perhaps individuals who are deprived of adequate and frequent social touch are at greater risk of dependency on exogenous opioids as they lack the regular production of endogenous opioids. The evolutionary positive emotions associated with opioids are so strong that individuals do not care if the opioid is endogenous or exogenous in its origin; the human body will desperately crave it for its survival. Ironically, long-term opioid therapy has been associated with dissatisfaction with sex life and the suppression of sexual desire (Birke et al 2018).

"Most humans strive for social contacts throughout their lifespan, and lack of social contacts has significant negative consequences for both psychological and somatic health." (Nummenmaa et al 2018)

Although impractical at the moment, perhaps physicians will one day evaluate the risk of opioid addiction of an individual based on the degree of social touching they experienced as a child and the quality of social touching they experience as adults on a daily basis.

To stimulate endogenous opioid production, health care providers could prescribe a daily dose of pleasurable physical contact.

Prescription options:

1) Hug people you meet (if appropriate)
2) Hold the hand of a child or an elderly person
3) Participate in safe consensual physical intimacy

Music Therapy

Music is growingly being used for persistent pain management, as it is inexpensive, with no adverse effects and patients usually report positive experiences with it. Music therapy has been shown to be beneficial to women with fibromyalgia showing improvements in fatigue and sleep quality (Demirbağ et al 2014, Alparslan et al 2016).

"Music therapy should be suggested in pain management for fibromyalgia patients" (Alparslan et al 2016)

A systematic review and meta-analysis based on 14 RCTs found that overall music reduced self-reported persistent pain and depressive symptoms (Garza-Villarreal et al 2017). Interestingly music had greater positive effects when the patient chose the music, compared to when the researcher chose it as the music that is most beneficial for the nervous system appears to be based on the individuals own preference.

Studies have found that music plays a role in reducing both acute and chronic pain as well as the anxiety and depression linked to chronic pain (Guétin et al 2012, Roy et al 2012, Siedliecki et al 2006). The benefits may be due to several factors such as distraction, relaxation and/or pleasure caused by listening to music. Endorphins have also been shown to be critical to experiencing pleasurable emotions evoked with music therapy (Mallik et al 2017). The benefits of music may be seen within two weeks hence

it is recommended that individuals with persistent pain to actively listen to 20-60 minutes of 1-2 daily music sessions for 14 days (Alparslan et al 2016, Guétin et al 2012).

To stimulate endogenous opioid production, health care providers could prescribe a daily dose of pleasurable music.

Prescription options:

1) Listen to 20 minutes of self-chosen music with headphones with full concentration everyday
2) Have pleasant music in the background while cooking, cleaning or before bedtime
3) Put music on and sing in the shower, everyday

Conclusion

With the exponential rise in the prescription of opioids and the growing concern for the rise in over-doses and deaths related to their use, health care providers must offer alternative options for helping individuals coping with severe persistent non-cancer pain. With the possibility of developing OIH, focus must be on maximizing the production of *endogenous* opioids to reduce the need for

prescribed or illegally consumed *exogenous* opioids. Our primary goal as health care providers must be to have patients release their own opioids by minimizing their fears, giving them reassurance and hope that they will improve and by focusing on returning to meaningful functional activities that bring joy into their lives. There is emerging evidence supporting the analgesic benefits of participation in activities which facilitate the opioidergic system. The activities include participation in intense physical exercise, self-selected daily life activities, social laughter, social activities, social touching, and music therapy. It is hypothesized that with the release of the endogenous opioids, even if pain is not eliminated or immediately reduced, the participation in enjoyable life activities may reduce the suffering associated with persistent pain. This is where we can end with an excellent quote.

"I don't mind pain, so long as it doesn't hurt." -Oscar Wilde

References:

1. Alperstein D1, Sharpe L2. The Efficacy of Motivational Interviewing in Adults With Chronic Pain: A Meta-Analysis and Systematic Review. J Pain. 2016 Apr;17(4):393-403.
2. Baumeister RF, Leary MR The need to belong: desire for interpersonal attachments as a fundamental human motivation. Psychol Bull. 1995 May; 117(3):497-529.
3. Bidari A, Ghavidel-Parsa B, Rajabi S, Sanaei O, Toutounchi M. The acute effect of maximal exercise on plasma beta-endorphin levels in fibromyalgia patients. Korean J Pain. 2016 Oct;29(4):249-254.
4. Birke H, Ekholm O, Højsted J, Sjøgren P, Kurita GP1. Chronic Pain, Opioid Therapy, Sexual Desire, and Satisfaction in Sexual Life: A Population-Based Survey. Pain Med. 2018 Jul 2.
5. Birke H, Ekholm O, Sjøgren P, Kurita GP, Højsted J Long-term opioid therapy in Denmark: A disappointing journey. Eur J Pain. 2017 Oct;21(9):1516-1527.
6. Brito RG, Rasmussen LA, Sluka KA. Regular physical activity prevents development of chronic muscle pain through modulation of supraspinal opioid and serotonergic mechanisms. Pain Rep. 2017 Aug 21;2(5):e618.
7. Chelnokova O, Laeng B, Eikemo M, Riegels J, Løseth G, Maurud H, Willoch F, Leknes S Rewards of beauty: the opioid system mediates social motivation in humans. Mol Psychiatry. 2014 Jul; 19(7):746-7.
8. Cichowski SB, Rogers RG, Komesu Y, A 10-yr Analysis of Chronic Pelvic Pain and Chronic Opioid Therapy in the Women Veteran Population. Mil Med. 2018 May 18.
9. Darwin C (1872) Expression of the emotions in man and animals. London: John Murray
10. Debruille C1, Luyckx M, Ballester L, Brunet C, Serum opioid activity after physical exercise in rats. Physiol Res. 1999;48(2):129-33.
11. Demirbağ BC, Erci B (2014) The effects of sleep and touch therapy accompanied by music and aromatherapy on the impact level of fibromyalgia, fatigue and sleep quality in fibromyalgia patients. TAF Prev Med Bull 13(1):5 7–64
12. Dunbar RI The social role of touch in humans and primates: behavioural function and neurobiological mechanisms. Neurosci Biobehav Rev. 2010 Feb; 34(2):260-8.
13. Dunbar RI, Baron R, Frangou A, Pearce E Social laughter is correlated with an elevated pain threshold. Proc Biol Sci. 2012 Mar 22;279(1731):1161-7.
14. Fields HL. Understanding how opioids contribute to reward and analgesia. Reg Anesth Pain Med. 2017 32:242–246
15. Fontaine KR, Conn L, Clauw DJ. Effects of lifestyle physical activity on perceived symptoms and physical function in adults with fibromyalgia: results of a randomized trial. Arthritis Res Ther. 2010;12(2):R55.
16. Gardner T, et al Patient-led Goal Setting: A Pilot Study Investigating a Promising Approach for the Management of Chronic Low Back Pain. Spine (Phila Pa 1976). 2016 Sep 15;41(18):1405-13
17. Garza-Villarreal EA, Pando V, Vuust P, Parsons C. Music-Induced Analgesia in Chronic Pain Conditions: A Systematic Review and Meta-Analysis. Pain Physician. 2017 Nov;20(7):597-610.
18. Grace PM1, Maier SF, Watkins LR. Opioid-induced central immune signaling: implications for opioid analgesia. Headache. 2015 Apr;55(4):475-89.
19. Guétin S, Giniès P, Siou DKA, Picot MC, Pommié C, Guldner E et al. The effects of music intervention in the management of chronic pain: a singleblind, randomized, controlled trial. Clin J Pain. 2012 28(4):329–337
20. Guillemin R, Vargo T, Rossier J. beta-Endorphin and adrenocorticotropin are selected concomitantly by the pituitary gland. Science. 1977 Sep 30; 197(4311):1367-9.
21. Haffajee RL, Mello MM. Drug Companies' Liability for the Opioid Epidemic. N Engl J Med. 2017

Dec 14;377(24):2301-2305.
22. Hertenstein MJ, Verkamp JM, Kerestes AM, Holmes RM The communicative functions of touch in humans, nonhuman primates, and rats: a review and synthesis of the empirical research. Genet Soc Gen Psychol Monogr. 2006 Feb; 132(1):5-94.
23. IMCAPR: Institute of Medicine (US) Committee on Advancing Pain Research C, and Education. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Washington D.C: National Academies Press; 2011
24. Inagaki TK, Ray LA, Irwin MR, Way BM, Eisenberger NI. Opioids and social bonding: naltrexone reduces feelings of social connection. Soc Cogn Affect Neurosci. 2016 May;11(5):728-35.
25. Keverne EB, Martensz ND, Tuite B Beta-endorphin concentrations in cerebrospinal fluid of monkeys are influenced by grooming relationships. Psychoneuroendocrinology. 1989; 14(1-2):155-61.
26. Klinger R, Kothe R, Schmitz J . Placebo effects of a sham opioid solution: a randomized controlled study in patients with chronic low back pain. Pain. 2017 Oct;158(10):1893-1902.
27. Kounang, Nadia Opioids now kill more people than breast cancer. December 21, 2017 CNN https://www.cnn.com/2017/12/21/health/drug-overdoses-2016-final-numbers/index.html
28. Krebs EE, Gravely A, Nugent S, et al Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE Randomized Clinical Trial. JAMA. 2018 Mar 6;319(9):872-882.
29. Kurita GP, Højsted J, Sjøgren P. Tapering off long-term opioid therapy in chronic non-cancer pain patients: A randomized clinical trial. Eur J Pain. 2018 May 13.
30. Kut E, Candia V, von Overbeck J, Pok J, Fink D, Folkers G. Pleasure-related analgesia activates opioid-insensitive circuits. J Neurosci. 2011 Mar 16;31(11):4148-53.
31. Landmark T, Romundstad PR, Borchgrevink PC, Longitudinal associations between exercise and pain in the general population--the HUNT pain study. PLoS One. 2013; 8(6):e65279.
32. Lima LV, DeSantana JM, Rasmussen LA, Sluka KA. Short-duration physical activity prevents the development of activity-induced hyperalgesia through opioid and serotoninergic mechanisms. Pain. 2017 Sep;158(9):1697-1710.
33. Littlejohn GO, Guymer EK, Ngian GS. Is there a role for opioids in the treatment of fibromyalgia? Pain Manag. 2016 May;6(4):347-55.
34. Machin AJ, Dunbar RIM. The brain opioid theory of social attachment: A review of the evidence. Behaviour. 2011;148:985–1025.
35. Mallik A, Chanda ML, Levitin DJ. Anhedonia to music and mu-opioids: Evidence from the administration of naltrexone. Sci Rep. 2017 Feb 8;7:41952.
36. Manninen S, Tuominen L, Dunbar RI Social Laughter Triggers Endogenous Opioid Release in Humans. J Neurosci. 2017 Jun 21;37(25):6125-6131.
37. McCarthy M. Doctors are urged to limit opioid prescribing. BMJ. 2016 Mar 18;352:i1614.
38. McPherson S, Smith CL, Dobscha SK Changes Ii Pain Intensity Following Discontinuation of Long-Term Opioid Therapy for Chronic Non-Cancer Pain. Pain. 2018 Jun 13.
39. Moore K, Lew J, Buttemer S, Kielstra L. First, do no harm: Advocating for opioid prescribing guidelines in Canadian emergency departments. CJEM. 2017 Jul;19(4):324-326.
40. Nummenmaa L, Tuominen L, Dunbar R, et al Social touch modulates endogenous μ-opioid system activity in humans. Neuroimage. 2016 Sep; 138():242-247.
41. Nummenmaa L, Karjalainen T. Opioidergic regulation of pain and pleasure in human social relationships. Neuropsychopharmacology. 2018 Jan;43(1):217-218.
42. Nummenmaa L, Tuominen L. Opioid system and human emotions. Br J Pharmacol. 2018 Jul;175(14):2737-2749.
43. Panksepp J, Bean NJ, Bishop P, Vilberg T, Sahley TL Opioid blockade and social comfort in chicks. Pharmacol Biochem Behav. 1980 Nov; 13(5):673-83.
44. Paungmali A, Joseph LH, Punturee K, Sitilertpisan P, Pirunsan U, Uthaikhup S. Immediate Effects of Core Stabilization Exercise on β-Endorphin and Cortisol Levels Among Patients With

Chronic Nonspecific Low Back Pain: A Randomized Crossover Design. J Manipulative Physiol Ther. 2018 Mar - Apr;41(3):181-188.
45. Pearce E, Wlodarski R, Machin A, Dunbar RIM. Variation in the β-endorphin, oxytocin, and dopamine receptor genes is associated with different dimensions of human sociality. Proc Natl Acad Sci U S A. 2017 May 16;114(20):5300-5305.
46. Provine R. R., Fischer K. R. Laughing, smiling, and talking: relation to sleeping and social context in humans. Ethology 1989. 83, 295–305
47. Roeckel LA, Le Coz GM, Gavériaux-Ruff C, Simonin F. Opioid-induced hyperalgesia: Cellular and molecular mechanisms. Neuroscience. 2016 Dec 3;338:160-182. Jun 23.
48. Rosenberg JM, Bilka BM, Wilson SM, Spevak C. Opioid Therapy for Chronic Pain: Overview of the 2017 US Department of Veterans Affairs and US Department of Defense Clinical Practice Guideline. Pain Med. 2018 May 1;19(5):928-941.
49. Roy M, Lebuis A, Hugueville L, Peretz I, Rainville P (2012) Spinal modulation of nociception by music. Eur J Pain 16(6):870–877
50. Saanijoki T, Tuominen L, Tuulari JJ, Nummenmaa L, Opioid Release after High-Intensity Interval Training in Healthy Human Subjects. Neuropsychopharmacology. 2018 Jan;43(2):246-254.
51. Scott SK, Lavan N, Chen S, McGettigan C (2014) The social life of laughter. Trends Cogn Sci 18:618–620.
52. Siedliecki SL, Good M (2006) Effect of music on power, pain, depression and disability. J Adv Nurs 54(5):553–562
53. Simonnet G, Rivat C. Opioid-induced hyperalgesia: abnormal or normal pain? NeuroReport. 2003;14(1):1–7
54. Suvilehto JT, Glerean E, Dunbar R, Hari R, Nummenmaa L4. Topography of social touching depends on emotional bonds between humans. Proc Natl Acad Sci U S A. 2015 Nov 10;112(45):13811-6.
55. Tarr B, Launay J, Cohen E, Dunbar R Synchrony and exertion during dance independently raise pain threshold and encourage social bonding. Biol Lett. 2015 Oct; 11(10):.
56. Vollert JO1, Störk T, Rose M, [Music as adjuvant therapy for coronary heart disease. Therapeutic music lowers anxiety, stress and beta-endorphin concentrations in patients from a coronary sport group]. [Article in German] Dtsch Med Wochenschr. 2003 Dec 19;128(51-52):2712-6.
57. Weinstein D, Launay J, Pearce E, Dunbar RI, Stewart L. Group music performance causes elevated pain thresholds and social bonding in small and large groups of singers. Evol Hum Behav. 2016;37:152–158.
58. Wilson-Poe AR, Morón JA. The dynamic interaction between pain and opioid misuse. Br J Pharmacol. 2018 Jul;175(14):2770-2777.
59. Yang DZSin B, Beckhusen J, Xia D, Khaimova R, Iliev I. Opioid-Induced Hyperalgesia in the Nonsurgical Setting: A Systematic Review. Am J Ther. 2018 Jan 31

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