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Current Opinion in Behavioral Sciences

Carnal pleasures

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Pleasures are tightly intertwined with the body. Enjoyment derived from sex, feeding and social touch originate from somatosensory and gustatory processing, and pleasant emotions also markedly influence bodily states tied to the reproductive, digestive, skeletomuscular, and endocrine systems. Here, we review recent research on bodily pleasures, focussing on consummatory sensory pleasures. We discuss how different pleasures have distinct sensory inputs and behavioural outputs and review the data on the role of the somatosensory and interoceptive systems in social bonding. Finally, we review the role of gustatory pleasures in feeding and obesity, and discuss the underlying pathophysiological mechanisms. We conclude that different pleasures have distinct inputs and specific outputs, and that their regulatory functions should be understood in light of these specific profiles in addition to generic reward mechanisms.

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Current Opinion in Behavioral Sciences 2021, **39**:85–92

This review comes from a themed issue on **Emotion, motivation, personality and social sciences *Positive Affect***

Edited by **Gilles Pourtois, Disa Sauter, Blair Saunders** and **Henk van Steenbergen**

https://doi.org/10.1016/j.cobeha.2021.02.026

Introduction

Pleasure is an inherently carnal experience. Enjoying sex or cuddly comfort with our partner necessitates mutual touching and caressing. Delights of a savoury meal are dependent on the gustatory senses, and the thrills of physical exercise literally require that we put our whole bodies into motion. Once triggered, pleasures also markedly alter our bodily states: sexual arousal rapidly increases blood flow in the genitals, feeding triggers a complex cascade of central and peripheral neurohormonal signalling, and exercise switches our skeletomuscular and cardiovascular systems into top gear. It comes as a no surprise that the way we use our bodies in the long term also causally alters our moods. Regular strenuous physical exercise improves mood while concomitantly lowering stress, depression, and anxiety levels [1]. On the other hand, unhealthy lifestyle choices, for example, habitual overeating leading to obesity, constitutes a risk factor for mood disorders [2], and almost half of patients meeting criteria for medical weight management also meet criteria for mood disorders or other psychiatric conditions [3]. Even pleasures that are less directly tied to allostasis involve the body in many ways. We derive a wide variety of pleasures from simply perceiving others' bodies, ranging from sexual arousal triggered by nudity [4] to aesthetic appreciation of paintings that engages sensorimotor networks in addition to limbic and paralimbic reward circuits [5], to the chills induced by music [6]. Here, we review the role of somatosensation, interoception and gustation across different pleasures in both healthy subjects and patients. We discuss how recent findings point to fine-grained granularity in the bodily basis of different pleasures, focussing on consummatory sensory pleasures derived from sociability and feeding.

Specificity of bodily pleasure responses

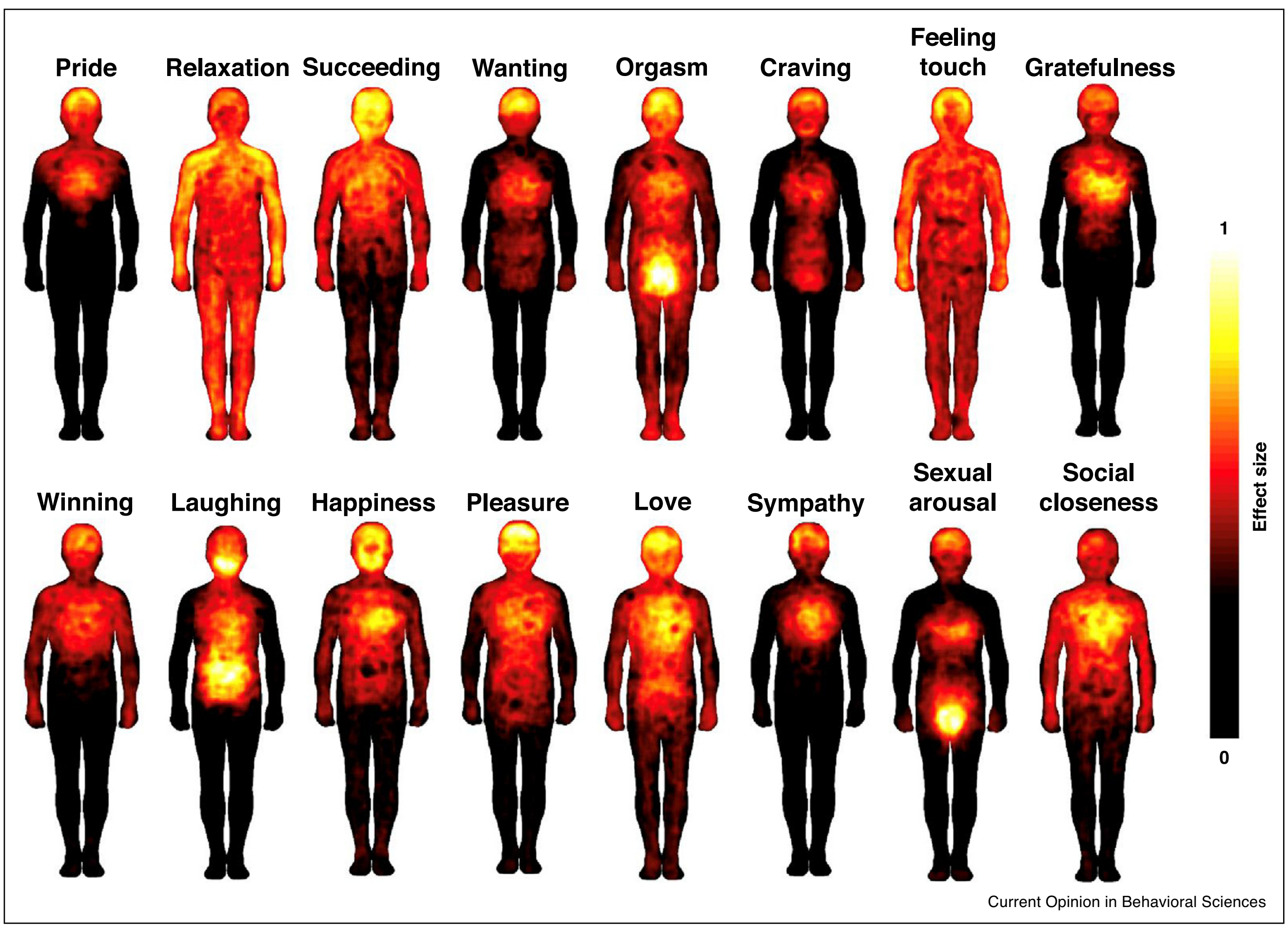
Humans experience powerful hedonic bodily sensations ranging from satiety to sexual arousal, but how specific are the underlying physiological responses? There has been an ongoing debate regarding the specificity of bodily profiles of different emotions, with some meta-analyses supporting [7] and others failing to differentiate between them, not even between pleasure and other emotions [8]. A likely reason for the low nett specificity is the low dimensionality of the measured psychophysiological signals. The most widely used electrodermal measures and electrocardiogram typically index unspecific ANS activity, thus failing to capture more specific autonomic differences between i) emotions and ii) different positive emotions and pleasures. However, existing studies point towards clear physiological differences across different types of pleasure states. For example, simple readouts of ghrelin, leptin, and insulin levels provide an accurate estimate of hedonic eating, that is, for the food's gustatory and rewarding properties [9] yet these endocrine responses are uncoupled from sexual arousal. Subjective sexual arousal — be it triggered by volitional thoughts or automatically by perception of sexual cues — in turn is consistently associated with autonomically governed genital responses [10]. Autonomic indices of sexual arousal (penile/vaginal plethysmography) differentiate this type of pleasure from other pleasures [11], with likely no discernible effects on leptin, ghrelin or insulin levels.

Although physiologically unspecific, analysis of simple self-reports of phenomenological bodily sensations has established that different emotions have discernible and consistent 'feeling signatures' in the body [12••,13]. Importantly, pleasure is one main determinant of the organization of bodily sensation patterns, yet different pleasures feel markedly different in the body (Figure 1) suggesting fine-grained organization of somatosensation and interoception associated with different pleasure systems. Moreover, the more pleasurable a mental or homeostatic feels, the more strongly it is experienced in the body and in the mind [12], indicating a strong tendency for pleasures to override our conscious stream of thought and behaviour. These maps are also consistent across a wide range of Western European (WC) and East Asian (EA) cultures, and independent of subject sex [14], pointing to their biological rather than acquired origin. Together with data from other modalities [15••] these self-report body mapping data clearly suggest that different pleasures are by no means a unified phenomenon in the human body. Thus, although meta-analyses show that all distinct pleasures involve the mesolimbic reward system (ventromedial prefrontal cortex, ventral striatum, amygdala, anterior insula and mediodorsal thalamus) in a comparable fashion [16], different pleasures have distinct inputs (gustatory for feeding, tactile for sexual, interoceptive and procioceptive for physical exercise and so forth) and specific outputs (e.g. the digestive system, the genitals, specific muscle groups, etc.). Accordingly, detailed understanding of the specific bodily inputs and outputs of different pleasures is critical also for understanding pleasure-related pathologies, as we will illustrate further in our discussion of human touch and feeding.

Touch, somatosensation, and pleasure

Touching is one of the most powerful ways of communicating positive affect, and humans and other primates use touching for both triggering sexual arousal and promoting interpersonal bonds. Postnatal skin-to-skin contact

Figure 1



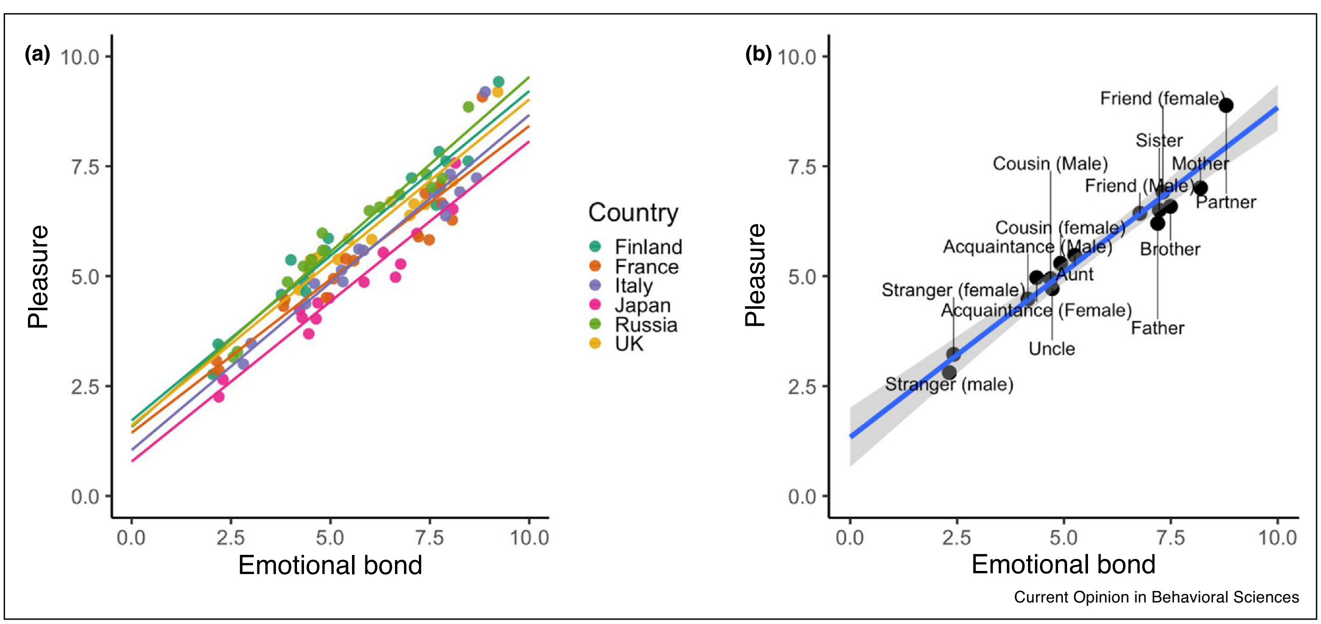
Topography of pleasant feelings in the body. Adapted from Ref. [12••].

promotes bonding between mother and infant, and both the quality and quantity of romantic touch are positively associated with relationship satisfaction in couples [17]. Human skin is broadly tuned for sensing pleasurable touch [18], and pleasure triggered by social touching is an important mediator of social bonding. The closer someone is to us in our social network, the more pleasant their touch feels [19•]. In a series of studies, we have also shown that the human body contains finely tuned relationship-specific touch allowance maps that determine where other members of our social network can touch us. These maps are consistent across Western European and East Asian cultures, and in all cultures the brevity of the touch allowance zones in the body is linearly dependent on the emotional bond between the toucher and the individual being touched [19•,20]. The closer emotional bond two individuals have, the more pleasant touching feels and the larger area is allowed for social touch (Figure 2).

Some aspects regarding the social relationship with the toucher are carried already in the primary somatosensory cortex (S1), and these relationship-specific activation patterns can be resolved from BOLD-fMRI signal with machine learning algorithms [21]. These effects could be argued to reflect differences in touch kinematics across individuals, yet similar effects are also observed when subjects are led to believe that a single toucher is one of two different identities [22]. Pharmacological studies in nonhuman primates [23] suggest that the endogenous mu-opioid receptor (MOR) system mediates the calming effects of affiliative touching, although contradictory evidence also exists for humans [24]. Yet, because interindividual differences in MOR availability are linked with attachment security and prosociality [25], variation of MORs may constitute a risk for psychiatric morbidity. In line with this, socioemotional life history also has a causal role in affective communication with touch. Childhood maltreatment is associated with both altered interpersonal distance preference and neural and experiential processing of social touch, which may both constitute risk factors for interpersonal dysfunctions and psychiatric disorders [26••].

Pleasurable social touching is conveyed by the slow-conducting unmyelinated c-tactile fibers projecting to the insular cortices but not to S1, and c-tactile fibers have long been considered the primary pathway for conveying affiliative touch [27]. Accordingly, patients with fibromyalgia rate both slow (CT-optimal) and fast (CT-suboptimal) brushing as less pleasant than healthy participants, and during fMRI these patients also show deactivation in the right posterior insula while evaluating the pleasantness of touch. This suggests decoupling between early-stage sensory and evaluative processing of affective touch [28]. Although CT-optimal slow stroking or petting has long been considered as the primary mechanism of affiliate touching, hugging and massaging might also convey social proximity between individuals. One recent study found that deep pressure stimulation akin to hugging is experienced as pleasant and calming, and it also yields comparable brain activation as CT-optimized slow

Figure 2



Social bonding with touching is culturally universal. Pleasure caused by social touching is linearly dependent on the strength of the emotional bond with the toucher in a wide range of Western European and East Asian cultures (A). Panel B shows de facto relationships between toucher and the touched persons for data that are averaged across countries. Redrawn from Refs. [19•,20].

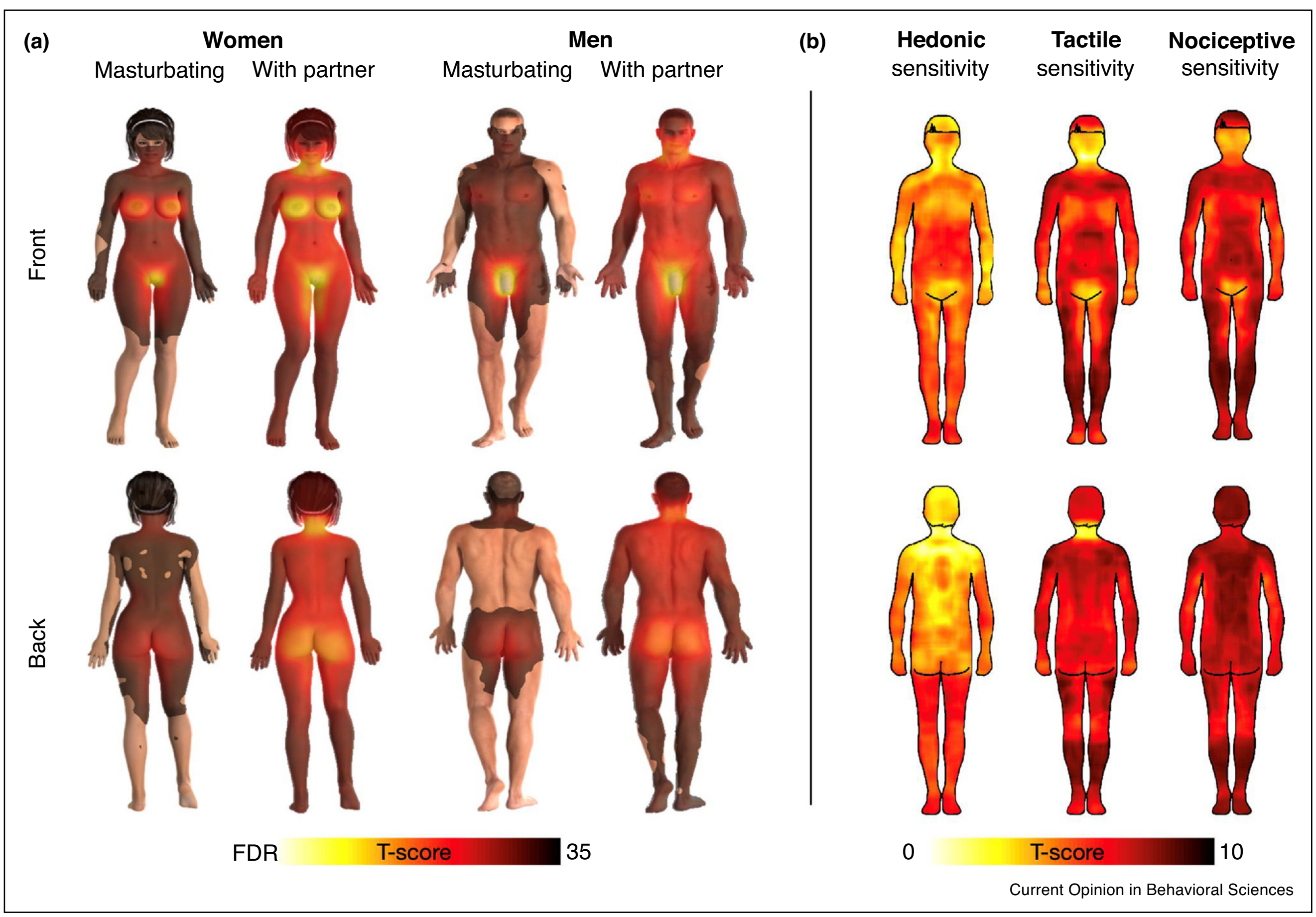
stroking [29•]. Both healthy controls and autistic individuals also find deep touch pressure calming and comforting, even though the latter may dislike CT-optimized stroking [30]. This suggests fine-grained distinctions between different tactile sensory pleasures, although some aspects of the neural coding of the pleasure might be comparable.

Touching is also the most potent way for increasing sexual arousal, and both self-stimulation and partners' caresses can elicit and maintain a sexual arousal state. Yet, there is no evidence of CT innervation in the genitalia, thus, this pathway likely does not play a role in triggering of arousal by touching of the genitals [31], again suggesting elementary physiological differences even in different tactile pleasures such as pleasant sexual and non-sexual touch. This fits with recent work on human erogenous zones [18] that established that sexual self-stimulation is primarily focused on the genital regions (with highest self-reported tactile sensitivity), while sexual touch from partners is also distributed over areas with the c-tactile receptors involved in emotional bonding (Figure 3a). Thus, mutual touching on the non-genital areas during sex with a partner serves not just sexual, but also bonding motives. Indeed, although self-reported tactile and nociceptive sensitivity peak in the genital area, significantly larger areas of the body have high hedonic sensitivity, possibly pertaining to their CT afferents (Figure 3b) and reflecting the role of these inputs in social bonding.

Feeding and gustatory pleasures

When hunger is wrenching our stomach, the first bites of a delicious meal may bring us immense delight. Yet, pleasures and homeostatic balance are not perfectly coupled. Eating a satiating yet unpleasant-tasting meal after an overnight fasting may actually *decrease* pleasure, despite leading to an improvement in the current metabolic state and insulin signalling [32]. Conversely, feeding for just pleasure increases peripheral levels of the 'hunger' hormone ghrelin more than feeding for maintaining energy homeostasis [9,33]. Ghrelin influences signalling in the VTA, which increases food intake and expression of μ-opioid receptors (and subsequent responses to sucrose and chow intake). A bulk of studies have also found that

Figure 3



Pleasure maps in the body. Sex-specific topography of human erogenous zones while masturbating and having sex with partner **(a)**, and hedonic, tactile, and nociceptive sensitivity maps of the human body averaged across sexes **(b)**. Adapted from Refs. [18,20].

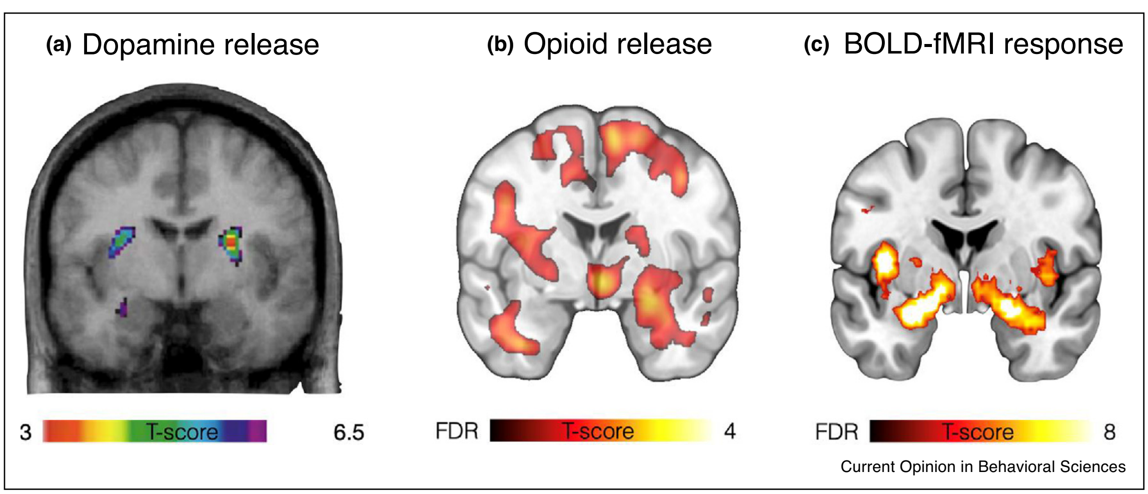
glucose tasting based signalling is an important component in generating the satiety response [34]. This could explain the counterintuitive finding that replacing glucose with artificial sweeteners may lead to weight gain despite lowered energy intake: Weakening the association between sweet taste and post-ingestive outcomes might impair weight regulation [35••] as an individual can no longer anticipate when calories are actually consumed. In line with this, sucralose fails to engage dopaminergic midbrain circuits similarly as sucrose [36], while bariatric surgery decreases preferences for sucrose [37•]. And taxing people's mental capacity suppresses tasting [38], but increases consumption, of particularly high-rewarding sweet and salty products [39], which concurs with less effective coupling between primary insular and secondary orbitofrontal taste processing areas [40].

Numerous neuroimaging studies show that feeding strongly engages the brain's reward circuit [41] and, with positron emission tomography studies implicating involvement of both opioidergic [42] and dopaminergic [43] components of the reward system (Figure 4). In line with this, opiate addicts experience sweetness as more pleasant than drug-naïve controls, while opioid antagonists decrease rewarding properties of sugar in heroin addicts [44]. Also, in healthy humans, opioid agonist morphine increases and antagonist naltrexone decreases the perceived sweetness of sucrose solutions [45]. Accordingly, repeated overstimulation of the reward circuit by overeating in obesity can lead to a vicious circle where high-energy hedonic food intake is constantly increased to compensate for receptor downregulation, leading to weight gain. Illustrating this point, the above-described decreases in liking for mixtures with high-sucrose — or high-fat content following bariatric surgery, concurs with enhanced neural responses to 'sweet' and 'fat' in brain regions implicated in taste and reward [37•]. Finally, weight loss following bariatric surgery rapidly normalizes MOR levels (in 6mo) in morbidly obese patients [46], suggesting a causal role of overweight in MOR downregulation. However, such promising outcomes are partly clouded by the fact that humans have the tendency to compensate lack of pleasure in one domain with pleasure in another. For example, a substantial proportion of patients undergoing bariatric surgery for obesity — thus physically restraining the capacity for feeding — develop a alcohol or substance use disorder [47]. This suggests that tackling pathological hedonic consumption by reining the reward drive and consummatory pleasure could be problematic, as it disregards humans' seemingly unlimited appetite for pleasures, in particular during the refractory post-consummatory period.

Dysregulation of pleasure in the body

Carnal pleasures are strong motivators for adaptive behaviour. They ensure that our bodily needs related to homeostasis, reproduction and safety are fulfilled even when conflicting goals exist. Conversely, many bodily pleasures may be hampered by concomitant bodily displeasure. This is most salient in the link between chronic pain and depression [48], but also in health-related behaviors. For example, initial pain and negative feelings associated with training may discourage individuals from initiating routine physical exercise, although repeated physical exercise will shift the resultant mood from displeasure to pleasure [49]. Many bodily pleasures serve important functions, but seeking them may also trigger compulsive consumption leading to obesity and substance use disorders (SUDs). Dysregulated striatal dopamine and opioid signaling and hypoactive inhibitory circuits in the

Figure 4



Brain responses to bodily consummatory reward. Endogenous dopamine (A) and opioid (B) release triggered by feeding as indexed with neuroreceptor-PET, and (C) meta-analysis map of BOLD-fMRI responses to viewing or eating foods. A adapted from Ref. [43], B adapted from Ref. [32] and C retrieved from the NeuroSynth database on October 7th 2020.

frontal cortex are hallmarks of both SUDs and obesity [50]. Whereas substances of abuse likewise are not needed for anything except the temporary pleasures they generate they do directly tap into allostatic systems that yield reliable pleasure sensations, such that especially in heavy addictions, these can even be 'hacked' at the cost of more natural triggers like food and bonding [51,52].

Self-report data shows that the stronger bodily responses a psychological or somatic state triggers, the more saliently it is experienced in the phenomenological awareness [12••]. Accordingly, it is possible that strong bodily sensations associated with hedonic consumption are critical for the development of addiction-like behaviours. Indeed, most drugs with high abuse potential (ranging from nicotine to alcohol, heroine and amphetamine) trigger strong bodily sensations when consumed. Interestingly, there is a paucity of patient cases with reported addictive or compulsive behaviour towards non-carnal pleasures such as aesthetic experiences derived from music, language, or art. Although the reason for this remains unknow, it is possible that these pleasures rely on highly contextual/learned, complex cognitions [53] that do not consistently yield a bodily response, thus making them unlikely targets of addictions via the somatic feelings linked with reward consumption.

Conclusions: moving beyond a generic pleasure state

We conclude that although different pleasures may have a partially shared neural basis [16], they also have clearly distinct sensory inputs and somatic and behavioral outputs that, so far, remain poorly understood within wider frameworks of candidate pleasure systems. Although different pleasures involve discrete bodily experiences, the specific bodily response patterns across different pleasures remain poorly characterised [8], and we are not aware of studies that have compared the somatic basis of different positive emotions using a systematic and high-dimensional sampling framework. In the future, it is necessary to go beyond simple low-dimensional psychophysiological measurements (ECG, skin conductance) and perform careful delineation using large-scale neurohormonal kits and actual whole-body metabolic imaging during different pleasure states. Recent developments in nuclear medicine imaging allow fast frequency readouts (1 Hz) that actually allow direct *in vivo* molecular imaging of emotion-related bodily phenomena [54•]. Finally, whereas carnal pleasures are less contingent on learning — already neonates show adult-like responses to pleasurable stroking in somatosensory and limbic emotion circuits [55], the bodily basis of 'complex' pleasures more dependent on learning are not equally well understood. Although, as noted already, some such bodily signatures such as pleasurable chills triggered with music have been established [56], this remains an underexplored field. Whereas it is important to keep examining commonalities across different pleasures, studying distinct pleasure profiles may prove just as informative for advancing theory. This calls for a detailed 'carnal taxonomy' of pleasures, through a unified approach that goes beyond neuroimaging and involves detailed endocrinological, psychophysiological and subjective measures of these different pleasures.

Conflict of interest statement

Nothing declared.

Acknowledgements

This study was supported by the Academy of Finland (grants #294897 and #332225), Sigrid Juselius Stiftelse and Signe och august Gyllenberg's stiftelse and the Dutch Research Council (Open Research Area grant #464-18-105).

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Peluso MA, Guerra de Andrade LH: **Physical activity and mental health: the association between exercise and mood**. *Clinics (Sao Paulo)* 2005, **60**:61-70.
2. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BWJH, Zitman FG: **Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies**. *Arch Gen Psychiatry* 2010, **67**:220-229.
3. Switzer NJ, Debru E, Church N, Mitchell P, Gill R: **The impact of bariatric surgery on depression: a review**. *Curr Cardiovasc Risk Rep* 2016, **10**:12.
4. Alho J, Salminen N, Sams M, Hietanen JK, Nummenmaa L: **Facilitated early cortical processing of nude human bodies**. *Biol Psychol* 2015, **109**:103-110.
5. Cinzia D, Vittorio G: **Neuroaesthetics: a review**. *Curr Opin Neurobiol* 2009, **19**:682-687.
6. Mori K, Iwanaga M: **Two types of peak emotional responses to music: the psychophysiology of chills and tears**. *Sci Rep* 2017, **7**:46063.
7. Kreibig SD: **Autonomic nervous system activity in emotion: a review**. *Biol Psychol* 2010, **84**:394-421.
8. Siegel EH, Sands MK, Van den Noortgate W, Condon P, Chang Y, Dy J, Quigley KS, Barrett LF: **Emotion fingerprints or emotion populations? A meta-analytic investigation of autonomic features of emotion categories**. *Psychol Bull* 2018, **144**:343-393.
9. Murray S, Tulloch A, Gold MS, Avena NM: **Hormonal and neural mechanisms of food reward, eating behaviour and obesity**. *Nat Rev Endocrinol* 2014, **10**:540-552.
10. Chivers ML, Seto MC, Lalumiere ML, Laan E, Grimbos T: **Agreement of self-reported and genital measures of sexual arousal in men and women: a meta-analysis**. *Arch Sex Behav* 2010, **39**:5-56.
11. Huberman JS, Chivers ML: **Examining gender specificity of sexual response with concurrent thermography and plethysmography**. *Psychophysiology* 2015, **52**:1382-1395.
12. •• Nummenmaa L, Hari R, Hietanen JK, Glerean E: **Maps of subjective feelings**. *Proc Natl Acad Sci U S A* 2018, **115**:9198-9203

Large-scale behavioural study shows that hedonia is a prime dimension of the interoceptive and phenomenological space of subjective feelings.

13. Nummenmaa L, Glerean E, Hari R, Hietanen JK: **Bodily maps of emotions**. *Proc Natl Acad Sci U S A* 2014, **111**:646-651.

14. Volynets S, Glerean E, Hietanen JK, Hari R, Nummenmaa L: **Bodily maps of emotions are culturally universal**. *Emotion* 2020, **20**:1127-1136.

15. Cowen AS, Keltner D: **Self-report captures 27 distinct categories of emotion bridged by continuous gradients**. *Proc Natl Acad Sci U S A* 2017:E7900-E7909
•• Shows that emotions are discrete entities with fuzzy boundaries between categories.

16. Sescousse G, Caldú X, Segura B, Dreher J-C: **Processing of primary and secondary rewards: a quantitative meta-analysis and review of human functional neuroimaging studies**. *Neurosci Biobehav Rev* 2013, **37**:681-696.

17. 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, **132**:5-94.

18. Nummenmaa L, Suvilehto JT, Glerean E, Santtila P, Hietanen JK: **Topography of human erogenous zones**. *Arch Sex Behav* 2016, **45**:1207-1216.

19. Suvilehto J, Nummenmaa L, Harada T, Dunbar RIM, Hari R, Turner R, Sadato N, Kitada R: **Cross-cultural similarity in relationship-specific social touching**. *Proc R Soc Ser B: Biol Sci* (in press), **286**:1-10.
• Cross-cultural study revealing that social bonding via touching is culturally universal, and that touchability of different individuals is based on their location in an individual's social network.

20. Suvilehto J, Glerean E, Dunbar RIM, Hari R, Nummenmaa L: **Topography of social touching depends on emotional bonds between humans**. *Proc Natl Acad Sci U S A* 2015, **112**:13811-13816.

21. Suvilehto JT, Renvall V, Nummenmaa L: **Relationship-specific encoding of social touch in somatosensory and insular cortices**. *Neuroscience* in press.

22. Gazzola V, Spezio ML, Etzel JA, Castelli F, Adolphs R, Keysers C: **Primary somatosensory cortex discriminates affective significance in social touch**. *Proc Natl Acad Sci U S A* 2012, **109**: E1657-E1666.

23. Fabre-Nys C, Meller RE, Keverne EB: **Opiate antagonists stimulate affiliative behaviour in monkeys**. *Pharmacol Biochem Behav* 1982, **16**:653-659.

24. Loseth GE, Ellingsen DM, Leknes S: **State-dependent mu-opioid modulation of social motivation**. *Front Behav Neurosci* 2014, **8**:15.

25. Turtonen O, Saarinen A, Nummenmaa L, Tuominen L, Tikka M, Armio R-L, Hautamäki A, Laurikainen H, Raitakari O, Keltikangas-Järvinen L, Hietala J: **Adult attachment system links with brain μ-opioid receptor availability in vivo**. *Biol Psychiatry Cogn Neurosci Neuroimaging* 2021, **6**:360-369.

26. Maier A, Gieling C, Heinen-Ludwig L, Stefan V, Schultz J, Güntürkün O, Becker B, Hurlemann R, Scheele D: **Association of childhood maltreatment with interpersonal distance and social touch preferences in adulthood**. *Am J Psychiatry* 2019, **177**:37-46
•• Demonstrates the causal role of childhood maltreatment on neural and phenomenological processing of touch.

27. Olausson H, Lamarre Y, Backlund H, Morin C, Wallin BG, Starck G, Ekholm S, Strigo I, Worsley K, Vallbo AB *et al.*: **Unmyelinated tactile afferents signal touch and project to insular cortex**. *Nat Neurosci* 2002, **5**:900-904.

28. Boehme R, van Ettinger-Veenstra H, Olausson H, Gerdle B, Nagi SS: **Anhedonia to gentle touch in fibromyalgia: normal sensory processing but abnormal evaluation**. *Brain Sci* 2020, **10**:14.

29. Case LK, Liljencrantz J, McCall MV, Bradson M, Necaise A, Tubbs J, Olausson H, Wang B, Bushnell MC: Pleasant deep pressure: expanding the social touch hypothesis. *Neuroscience* in press.
• Functional neuroimaging reveals that in addition to CT optimized touch, also deep pressure touch might convey social affiliation.

30. Grandin T: **Calming effects of deep touch pressure in patients with autistic disorder, college students, and animals**. *J Child Adolesc Psychopharmacol* 1992, **2**:63-72.

31. Liu Q, Vrontou S, Rice FL, Zylka MJ, Dong X, Anderson DJ: **Molecular genetic visualization of a rare subset of unmyelinated sensory neurons that may detect gentle touch**. *Nat Neurosci* 2007, **10**:946-948.

32. Tuulari JJ, Tuominen L, de Boer FE, Hirvonen J, Helin S, Nuutila P, Nummenmaa L: **Feeding releases endogenous opioids in humans**. *J Neurosci* 2017, **37**:8284-8291.

33. Monteleone P, Piscitelli F, Scognamiglio P, Monteleone AM, Canestrelli B, Di Marzo V, Maj M: **Hedonic eating is associated with increased peripheral levels of ghrelin and the endocannabinoid 2-arachidonoyl-glycerol in healthy humans: a pilot study**. *J Clin Endocrinol Metab* 2012, **97**:E917-E924.

34. Swithers SE: **Artificial sweeteners produce the counterintuitive effect of inducing metabolic derangements**. *Trends Endocrinol Metab* 2013, **24**:431-441.

35. Veldhuizen MG, Babbs RK, Patel B, Fobbs W, Kroemer NB, Garcia E, Yeomans MR, Small DM: **Integration of sweet taste and metabolism determines carbohydrate reward**. *Curr Biol* 2017, **27**:2476-2485.e2476
•• Shows that both sweet taste and metabolic processing are required for carbohydrate-triggered reward.

36. Frank GKW, Oberndorfer TA, Simmons AN, Paulus MP, Fudge JL, Yang TT, Kaye WH: **Sucrose activates human taste pathways differently from artificial sweetener**. *Neuroimage* 2008, **39**:1559-1569.

37. Smith KR, Papantoni A, Veldhuizen MG, Kamath V, Harris C, Moran TH, Carnell S, Steele KE: **Taste-related reward is associated with weight loss following bariatric surgery**. *J Clin Investig* 2020, **130**:4370-4381
• Clinical study demonstrating that effectiveness of surgical weight loss is dependent on taste-related reward processing.

38. Liang P, Jiang J, Ding Q, Tang X, Roy S: **Memory load influences taste sensitivities**. *Front Psychol* 2018, **9**:2533.

39. van der Wal RC, van Dillen LF: **Leaving a flat taste in your mouth: task load reduces taste perception**. *Psychol Sci* 2013, **24**:1277-1284.

40. Duif I, Wegman J, Mars MM, de Graaf C, Smeets PAM, Aarts E: **Effects of distraction on taste-related neural processing: a cross-sectional fMRI study**. *Am J Clin Nutr* 2020, **111**:950-961.

41. Stice E, Burger KS, Yokum S: **Reward region responsivity predicts future weight gain and moderating effects of the TaqIA allele**. *J Neurosci* 2015, **35**:10316-10324.

42. Burghardt PR, Rothberg AE, Dykhuis KE, Burant CF, Zubieta JK: **Endogenous opioid mechanisms are implicated in obesity and weight loss in humans**. *J Clin Endocrinol Metab* 2015, **100**:3193-3201.

43. Small DM, Jones-Gotman M, Dagher A: **Feeding-induced dopamine release in dorsal striatum correlates with meal pleasantness ratings in healthy human volunteers**. *Neuroimage* 2003, **19**:1709-1715.

44. Green A, Kaul A, O'Shea J, Sharma E, Bennett L, Mullings EL, Munafò MR, Nutt DJ, Melichar JK, Donaldson LF: **Opiate agonists and antagonists modulate taste perception in opiate-maintained and recently detoxified subjects**. *J Psychopharmacol* 2013, **27**:265-275.

45. Eikemo M, Loseth GE, Johnstone T, Gjerstad J, Willoch F, Leknes S: **Sweet taste pleasantness is modulated by morphine and naltrexone**. *Psychopharmacology* 2016, **233**:3711-3723.

46. Karlsson HK, Tuominen L, Tuulari JJ, Hirvonen J, Honka H, Parkkola R, Helin S, Salminen P, Nuutila P, Nummenmaa L: **Weight loss after bariatric surgery normalizes brain opioid receptors in morbid obesity**. *Mol Psychiatry* 2016, **21**:1057-1062.

47. King WC, Chen J-Y, Courcoulas AP, Dakin GF, Engel SG, Flum DR, Hinojosa MW, Kalarchian MA, Mattar SG, Mitchell JE *et al.*: **Alcohol and other substance use after bariatric surgery: prospective evidence from a U.S. multicenter cohort study**. *Surg Obes Relat Dis* 2017, **13**:1392-1402.

48. Fishbain DA, Cutler R, Rosomoff HL, Rosomoff RS: **Chronic pain-associated depression: Antecedent or consequence of chronic pain? A review**. *Clin J Pain* 1997, **13**:116-137.

49. Saanijoki T, Nummenmaa L, Eskelinen JJ, Savolainen AM, Vahlberg T, Kalliokoski KK, Hannukainen JC: **Affective responses to repeated sessions of high-intensity interval training**. *Med Sci Sports Exerc* 2015, **47**:2604-2611.

50. Volkow ND, Wise RA: **How can drug addiction help us understand obesity?** *Nat Neurosci* 2005, **8**:555-560.

51. Kokavec A: **Is decreased appetite for food a physiological consequence of alcohol consumption?** *Appetite* 2008, **51**:233-243.

52. Kim S, Iyengar U, Mayes LC, Potenza MN, Rutherford HJV, Strathearn L: **Mothers with substance addictions show reduced reward responses when viewing their own infant's face**. *Hum Brain Mapp* 2017, **38**:5421-5439.

53. Rolls ET: **Neurobiological foundations of aesthetics and art**. *New Ideas Psychol* 2017, **47**:121-135.

54. • Badawi RD, Shi H, Hu P, Chen S, Xu T, Price PM, Ding Y, Spencer BA, Nardo L, Liu W *et al.*: **First human imaging studies with the EXPLORER total-body PET scanner**. *J Nucl Med* 2019, **60**:299-303

The first results from a whole-body PET scanner allowing simultaneous dynamic imaging of multiple organs, opening radically new venues for imaging bodily basis of emotions.

55. Tuulari JJ, Scheinin NM, Lehtola S, Merisaari H, Saunavaara J, Parkkola R, Sehlstedt I, Karlsson L, Karlsson H, Björnsdotter M: **Neural correlates of gentle skin stroking in early infancy**. *Dev Cogn Neurosci* 2019, **35**:36-41.

56. Blood AJ, Zatorre RJ: **Intensely pleasurable responses to music correlate with activity in brain regions implicated in reward and emotion**. *Proc Natl Acad Sci U S A* 2001, **98**:11818-11823.